The Saudi Arabian Adaptation of the Addenbrooke's Cognitive Examination – Revised (Arabic ACE-R)

Ahmed Saeed Ali Al Salman

Thesis submitted for the degree of Doctor of Philosophy

Mental Health & Wellbeing
Institute of Health & Wellbeing
College of Medicine, Veterinary and Life Sciences

Thesis submitted for the degree of Doctor of Philosophy

Submitted: March, 2013

Abstract

BACKROUND: The population of the Arab World is about 300 million and the Arabic language is one of the six official languages of the United Nations. As with the rest of the world, degenerative neurological conditions represent a major health problem in regions such as the Middle-East where Arab people are in the majority. However, clinical neuropsychology is still in its infancy in this region. Very few tools for the assessment of cognition have been developed for use with Arabic speakers in the Middle-East region. The Addenbrooke's Cognitive Examination – Revised is a brief cognitive assessment tool that has been well validated in its original English version as well as a number of other languages, but never been adapted for use with Arabic speakers. An important issue for the assessment of cognition in this region is the high level of illiteracy, particularly in older adults, making the development of tools that can be used with both literate and illiterate participants a priority.

OBJECTIVES: The studies presented in this thesis involved the translation, adaptation and validation of an Arabic Addenbrookes Cognitive Examination-Revised (ACE-R) and involved data collection from both literate and iliterate participants.

METHODS: The ACE-R was translated into Arabic and the process is described in **Chapter 2**. Critical to the process was the cultural adaption of the test items. Three parallel versions were developed. Data was collected from four participant samples, recruited in Riyadh, Saudi Arabia: (1) Healthy literate (N= 147); (2) Healthy illiterate (N= 283); (3) Literate with a diagnosis of Alzheimer's disease (AD) or Mild Cognitive Impairment (MCI) (N= 54); (4) Illiterate with a diagnosis of AD or MCI (N= 169). **Chapter 3** presents a study of the validity of the Arabic ACE-R in literate participants. Receiver operating curve (ROC) analyses were undertaken to determine the sensitivity and specificity of the Arabic ACE-R to MCI/dementia, as well as positive and negative predictive values. Optimal cut-off scores were determined. **Chapter 4** presents a study of the reliability of the Arabic ACE-R with literate participants. Parallel forms of the Arabic ACE-R were administered on two occasions separated by approximately one week. Test-retest and internal reliability (Cronbach's alpha) were examined. A version of the test was developed for use with non-literate participants and **Chapter 5** presents a study of its validity with this population. **Chapter 6** reports a study of the reliability of the tool with non-literate participants.

Chapter 7 reports normative data for the Arabic ACE-R, identifying fifth percentile cut-off points.

RESULTS: **Literate participants:** Amongst healthy controls Arabic ACE-R data were not normally distributed, hence non-parametric statistics used in analyses. Amongst healthy controls age was correlated with Arabic ACE-R performance (rho = -0.568, $p<0.0001$) and level of education was also correlated with Arabic ACE-R performance (rho = 0.559, $p<0.0001$). As there was a significant difference in age between healthy controls and patient groups, groups were matched for age by removal of young controls and participants also examined in three age bands. Groups were matched for level of education. There were significant differences between each of the three groups examined – Mild Cognitive Impairment, Dementia of the Alzheimer's type and healthy controls. As the MCI group was small, Receiver Operating Curve (ROC) analyses were conducted on the combined MCI/DAT group compared with the healthy control group. Levels of sensitivity/specificity were high. For a cut-off point of 70, sensitivity was 1.000 and specificity was 0.946. The positive and negative predictive values (PPV and NPV) were also high, particular for base rates that are likely to be closer to those found in clinical practice. For literate participants, internal reliability was high (Cronbach's alpha, 0.932) as was total score test-retest reliability (rho=0.944). Individual subscale reliability ranged from rho=0.685 (Fluency) to rho=0.865 (Memory).

Illiterate participants: Amongst healthy controls Arabic ACE-R data was not normally distributed, hence non-parametric statistics were used again. Amongst healthy controls age was correlated with Arabic ACE-R performance (rho = -286, $p<0.001$). As there was a significant difference in age between healthy controls and patient groups, groups were matched for age by removal of young controls and participants were also examined in three age bands. At a group level the data showed that there was a significant difference going from healthy to MCI and from MCI to DAT groups. ROC analyses showed that the Arabic ACE-R distinguished well between the healthy controls and patients with a diagnosis of either MCI or DAT. The optimum cut-off point on the Arabic ACE-R (65) had good sensitivity and specificity. Internal reliability was also high (Cronbach's alpha, 0.987) as was total score test-retest reliability (rho=0.916), with individual sub-scale scores ranging from rho=0.647 (Language) to 0.861 (visuo-spatial).

Analysis of normative data indicated the cut-off scores based on fifth percentile point results in somewhat higher cut-off points that those derived from ROC analyses, particularly for the younger literate participants. Potential reasons for these differences are discussed.

CONCLUSION: The Arabic ACE-R shows good sensitivity and specificity in the detection of patients with a clinical diagnosis of either AD or MCI. This appears to be the case for both literate and illiterate participants. The Arabic ACE-R (Illiterate version) was straightforward to administer with just four tasks being omitted. This study only compared healthy controls and patients with clear evidence of dementia/MCI (and only small numbers of MCI). Because of the strong tradition of caring for older adults within families, and stigma associated with mental health problems, people with dementia are typically not referred to a doctor until the condition appears very clearly. Further research is needed to examine participants in earlier stages of disease and also participants with psychological/mood disorder.

The Arabic ACE-R appears to be a reliable instrument for the assessment of cognitive impairment that may be arising from a degenerative neurological condition for both literate and illiterate participants.

Contents

List of Tables

List of Figures

Acknowledgments

This thesis is dedicated to the soul of my dearest mother. I wish she was still alive to see me obtaining our dream of finishing my PhD degree. Although, there are moments of sadness that my mother cannot share this with me. I am joyful to be nearing the end of this level of higher education.

I would also, like to thank all my family for their support and encouragement.

I would like to thank my supervisor Professor Jonathan Evans for his patience, support, useful comments, and teaching along this stage of education. I will not forget his efforts and encouragement since the first interview until now. I would also like to thank Professor Keith Miller for his cooperation and support in the beginning of this study until his retirement. In addition, I would also like to extend my gratitude to my advisor during the application, Dr. Saeed Wahass.

I would like to share a special thank you to all the staff, colleagues and friends in the department for their care, help, kindness and wishes.

I also have the honour to thank my colleagues who shared with me the application of my study in Saudi Arabia, Prof. Abdul-Rahman Al Tahan, Dr. Hashim Balubaid, and Dr. Fahd Alqeresha. It is an honour to dedicate this effort to the Minister of Higher Education Professor Khalid Alangari and his advisor Mr. Abdullah Alrashed for their support in facilitating the scholarship. The study is also dedicated to His Excellency Dr. Bandar Alqanawy, CEO of King Abdul Aziz Medical City in the National Guard for his support and the endorsement of my application at the King fahad National Guard Hospital. I also thank Dr. Mohamed Aljoma, head of King Abdu Allah International Medical Research center of the city. I also have the honour to thank His Excellency Dr. Sultan Alsederi, the head of the Research Centre in King Faisal Specialist Hospital in Riyadh for his support and his acceptance of my request in my application in the hospital. I am honoured to thank the General Director of Prince Salman Social Center in Riyadh, Mr. Rashad Haron for his support. I also extend a great deal of thanks to Dr. Mohammed Aalkhwaiter, the head of Department of Internal Medicine at King Saud Medical City for his support and encouragement and commitment to overcome all obstacles to make it possible to collect data there.
A great deal of thanks also goes to my colleagues Fatima Alsalman, Fatima Al-Qahtani, Maram Al-Qahtani, Rowan Alhebabi, Sara Alnasser, Alyah Alsalman, Monirah Albahlal, Hanan Altelasi, Randa alkolaib, Amani Alahmari, Rahaf Alabdu-Allah, Dima alsultan, Hana Alsultan, Yosef ben shiblah, Bander Alnasser, Abdul-Malek Aljebarah, Talal Ahereqi and Khalid Almegnaa, who helped me during the application period and I appreciate their hard efforts and patience.

Finally, I thank everyone who tried to do something to make this study run easily.

Declaration

"I hereby declare that I am the sole of author of this thesis, except where the assistance of others has been acknowledged.

This thesis has not been submitted in any form for another degree or personal qualification".

Ahmed Saeed Ali Al Salman March 2013

CHAPTER 1

Introduction, Literature Review And Aims of the Thesis

Chapter 1: Introduction, Literature Review and Aims of the Thesis

1.1 Introduction

This thesis is concerned with the adaptation of a neuropsychological examination tool for the assessment of dementia in Arabic speakers, with a particular focus on application in Saudi Arabia. The thesis begins with an introduction to the relevant literature. A brief history of the historical background to our current understanding of dementia is provided, followed by an account of current definitions of the broad construct of dementia. A description of Alzheimer's disease, the most common form of dementia, is provided along with a brief account of the other main types of dementia. The defining feature of dementia is impairment of cognitive functioning, and in particular memory, though different forms of dementia present with different patterns of impairment in various cognitive domains. The importance of neuropsychological assessment in both diagnosis of dementia and differential diagnosis of different forms of dementia will be highlighted. A number of brief cognitive examination tools have been developed over the years for the purpose of detecting the presence of cognitive deficits and have been employed in the process of diagnosis of dementia. One tool that has emerged recently which has proved to be useful in the assessment of dementia is the Addenbrooke's Cognitive Examination. This tool will be described and a critical appraisal of the evidence for its use in dementia assessment provided. The revised version of the Addenbrooke's Cognitive Examination (ACE-R) has been translated into a number of different languages, but to date there has not been an Arabic version. Arabic is the official language of 26 countries and is the native language of more than 300 million people worldwide (Lewis, 2009). However, there has been little in the way of development

of neuropsychological assessment tools that are linguistically and culturally relevant to Arabic speaking countries. A particular challenge for many countries in the Arabic speaking world is high levels of illiteracy. The current stage of development of neuropsychology in Saudi Arabia will be described. The need for the adaptation and development of neuropsychological assessment tools for application in the Arabic-speaking cultural context of Saudi Arabia will be highlighted and in particular the issue and challenges of developing tests that can be used with people who are illiterate will be discussed.

1.2 Dementia

1.2.1 Historical Background

The word dementia comes from the Latin *demens* meaning 'without a mind'. References to dementia can be found in Roman medical texts and in the philosophical works of Cicero (Cummings and Benson, 1992). The term dementia was first used in clinical practice in the eighteenth century by Pinel and Esquirol (Berchtold & Cotman, 1998).

In the French Revolution dementia became enshrined in law through Article 10 of the Napoleonic Code 1808: *'There is no crime when the accused is in a state of dementia at the time of the alleged act'* (Berrios, 1996). In 1863, Marce described the shrinkage or cortical atrophy, the enlargement of ventricles and "softening" of the brain being associated with dementia (Berrios, 1996).

In 1882, Arnold Pick described cases of cognitive deterioration, notably in language, associated with focal brain atrophy or circumscribed to the temporal and frontal lobes. In 1911, Dr. Alois Alzheimer described the senile plaques and neurofibrillary

tangles, that are common to the brains of people with Alzheimer's type dementia (Rossor, 2001).

1.2.2 Definition and Classification

The Pocket Oxford Dictionary of Current English defines dementia as a chronic or persistent disorder of the mental processes caused by brain disease or injury and marked by memory disorders, personality changes, and impaired reasoning (Oxford Dictionaries, 2008).

There are three commonly used diagnostic classification systems relevant to dementia; the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994); the International Classification of Diseases – 10th Edition (ICD-10; World Health Organisation, 1992); and the National Institute of Neurologic, Communicative Disorders and Stroke - Alzheimer's Disease and related Disorders Association (NINCDS-ADARDA) (McKhann et al., 1984).

Both the DSM-IV (and the updated version, DSM-IV-TR, APA, 2000) and the ICD-10 classification systems provide general definitions of dementia before defining a number of specific forms of dementia. For example DSM-IV-TR (APA, 2000) defines the essential feature of dementia as 'the development of multiple cognitive deficits that include memory impairment and at least one of the following cognitive disturbances: aphasia, apraxia, agnosia, or a disturbance in executive functioning; (p148). The criteria also requires that the deficits be sufficiently severe to cause impairment in occupational or social functioning and must represent a decline from a previously higher level of functioning. The deficits must not occur exclusively during the course of a delirium. DSM IV criteria have been found to have adequate

reliability in relation making the diagnosis of dementia (Knopman et al., 2001; APA, 1994).

In ICD 10, the primary requirement for diagnosis is evidence of a decline in both memory and other cognitive abilities characterized by deterioration in judgement and thinking, such as planning and organizing, and in the general processing of information that is sufficient to impair personal activities of daily living. As with DSM-IV, various forms of dementia are then defined.

The NINCDS-ADARDA definitions are primarily related to the diagnosis of Alzheimer's disease and are discussed later.

1.2.3 Epidemiology and Burden

Dementia imposes a significant burden on caregivers, family, medical and social services, and the community at large. About 24 million persons around the world suffer from dementia and this number is expected to double every 20 years (Ferri, 2006)

The World Health Organisation (WHO) stated in Version 2 Estimates for the Global Burden of Disease 2000 study, published in the World Health Report 2002 (WHO, 2002), that dementia is the 11th leading cause of years lost due to disabilities (YLDs) at a global level, accounting for 2.0% of total global YLDs. Dementia is noted to be difficult to define and detect in the population, but it is clear that dementia causes a substantial burden globally. The burden of dementia affects patients, caregivers, and societies. The report stated that two-thirds of people with dementia live in lower and middle income countries. It appears that across the world there is a problem of under-diagnosis. It was further noted that even in affluent

countries such as Switzerland only 1/3 of the people with dementia receive a diagnosis.

According to the 2003 World Health Report Global Burden of Disease estimated, dementia contributed 11.2% of all years lived with disability among people aged 60 and over; more than stroke (9.5%), musculoskeletal disorders (8.9%), cardiovascular disease (5.0%) and all forms of cancer (2.4%).

In the United Kingdom, a report into the prevalence and cost of dementia prepared by the Personal Social Services Research Unit (PSSRU) at the London School of Economics and the Institute of Psychiatry at King's College London, (Alzheimer's Society, 2007) estimated that there were 683,597 people with dementia in the United Kingdom. This represented one person in every 88 (1.1%) of the entire UK population. This percentage was expected to increase by 38% over the next 15 years and 154% over the next 45 years. Total costs amounted to £17.03 billion, or an average of £25,472 per person with late-onset dementia.

Data on the prevalence of dementia in the Arab world are limited, but a study by Bowirrat et al. (2001) examined prevalence of, and risk factors for, dementia in an elderly Arab population in Israel. Bowirrat et al. found that in a rural community sample of 821 people over the age of 60, the prevalence of dementia of the Alzheimer's type (DAT) was 20.5%, with rates sharply increasing with age. This rate is much higher than estimates of prevalence in Western populations and 3.9 times higher than in a non-Arab population sampled in the same region (Bowirrat 2001, p121; Korczyn et al 1991; 1998). In addition to simple prevalence, Bowirrat et al. also examined the relationship between educational status and the development of dementia given the high rates of illiteracy in this population. Prevalence of DAT was found to be very much higher amongst illiterate participants (27% in illiterate vs 4%

in literate participants). Whilst the specific nature of the relationship between illiteracy and dementia is not clear, this highlights the importance of improving diagnosis of dementia across the world, but particularly in low and middle income countries and in countries with high levels of illiteracy.

In an unpublished study, involving interviews with 11,000 families across Saudi Arabia, it was found that 10.5% of those aged 60 or more were suffering from dementia. Life expenses for a demented person exceeded those of healthy elderly persons. Families who had a demented member suffered greater socioeconomic crises, job loss, divorce, and difficulty in keeping a balance of living expenses for their children and the demented member compared to those families without a member with dementia (Alabeedy & Aldamigh, 2001)

1.2.4 Clinical picture

As noted in relation to diagnostic classification, the core symptom of dementia is cognitive impairment. In the most common forms of dementia this will involve memory impairment, and in addition impairment of other domains of cognition. These cognitive impairments impact upon activities of daily living (ADL) with different aspects of ADL being affected depending upon the nature of the specific cognitive impairment. This can range, in the early stages of dementia, from simple forgetfulness leading to difficulties remembering to do things, through in the later stages to an inability to recognize relatives, difficulty with dressing and self care, and difficulty finding one's way around familiar environments. Eventually, disorientation in time place, and person becomes obvious during the later stages (Gelder et al. 2000).

Behavioural change as described by Goldstein (1975) may be in the form of lack of interests “shrinkage of the milieu”, insisting on routine “organic orderliness”, outbursts of anger, or a “catastrophic reaction” when the patient fails to cope or deal with a given situation because of his or her limited abilities. It has been found that 60% of patients with dementia in the community and 80% of those in nursing homes develop neuropsychiatric symptoms (Jeste, et al., 2008).

These neuropsychiatric symptoms adversely affect quality of life and significant caregiver burden (Jeste, et al., 2008; Salzman, et al., 2008; Rabins, et al., 2007).

The onset of these signs and symptoms may be associated with a change in the surrounding environment of the patient e.g. moving house. Patients are usually brought to treatment by their relatives or caregivers (Brodaty, 1990).

1.2.5 Aetiology

Causes of dementia can be categorised in various groups; degenerative (Alzheimer's, Pick's, Huntington's, Parkinson's, normal pressure hydrocephalus), metabolic (vital organs failure), vascular (occlusion of macro and/or micro cranial arteries) nutritional (B_1, B_{12}, nicotinic acid deficiency), traumatic (head injury & repeated head trauma), drug intoxication and withdrawal (alcohol, anxiolytics-hypnotics), systemic and intracranial infections (septicaemia, HIV, cerebral malaria, encephalitis, meningitis).

This thesis will be primarily concerned with assessment of dementia in the context of degenerative disease and more specifically in relation to diagnosis of the most common form of dementia, Alzheimer’s disease. In the following section the main forms of degenerative diseases leading to cognitive impairment and eventually dementia will be briefly described. There is a range of conditions that may cause

dementia in combination with a range of other symptoms, particularly motor or other physical symptoms. These conditions include Parkinson's disease, Huntington's disease, motor-neurone disease, cortico-basal degeneration, progressive supra-nuclear palsy, Creutzfeldt-Jakob disease and HIV-AIDS. However, this introduction will focus on those conditions where cognitive impairment is typically a primary presenting symptom, and with a particular emphasis on Mild Cognitive Impairment and Alzheimer's disease.

1.3 Degenerative diseases leading to cognitive impairment and dementia

1.3.1. Mild Cognitive Impairment (MCI)

In general clinical practice the term "mild cognitive impairment" is used to describe a mild degree of forgetfulness, not amounting to a dementia state, observed in some elderly people. However, it has been found that 19 – 50% of these individuals progress to dementia, mainly dementia of the Alzheimer's type (DAT), within a period of three years (Chertkow, 2002).

There is a general agreement among researchers and clinicians that individuals with MCI are considered as neither normal nor demented and subjectively and objectively have cognitive deficits (Winblad, et al., 2004; Petersen, 2004).

In a study by Graham et al., (1997), such individuals were described as having "cognitive impairment not dementia" and were subdivided into individuals with age-related memory impairment and those with cognitive impairments which were first manifestations, or prodromal of DAT or other dementias. The latter group is now labelled as having "mild cognitive impairment" (Gauthier, et al., 2006).

It has been observed that some patients with MCI may stabilize, improve or progress to various types of DAT (Panza et al., 2005). A meta analysis (Mitchell & Shiri-Feshki, 2009) examining 41 cohort studies that had investigated rates of conversion from MCI to dementia found that 32.9% converted (with the period of follow up for the included studies) with an annual conversion rate of 9.6%.

Therefore, MCI is thought of as a transitional or a prodromal stage to DAT for a significant proportion of people and there might be a place for therapeutic intervention to slow progression or prevention of this disease, highlighting the importance of early detection.

1.3.1.1 Epidemiology

The prevalence of MCI is found to range from 3% to 53% in different studies (Panza, et al., 2005). This wide range of prevalence is likely to be due to lack of consensus on criteria for MCI in addition to variations in sensitivity and specificity of tests used in screening for such cases. With more strict criteria prevalence is still reported to vary from 1% to 14.9% (Mitchell & Shiri-Feshki, 2009). Identified risk factors for MCI among individuals over 75 years of age were depressive symptoms, increasing age, and less education with incidence rates at 1% - 1.5% annually among this population (Barnes, et al., 2006).

1.3.1.2 Definition and diagnosis

A workgroup of specialists of the American Academy of Neurology (AAN) published in 2001 practice guidelines for the early detection of memory problems and identified the following criteria for an MCI diagnosis (Ganguli, et al., 2001):

- An individual's report of his or her own memory problems, preferably confirmed by another person
- Measurable, greater-than-normal memory impairment detected with standard memory assessment tests
- Normal general thinking and reasoning skills
- Ability to perform normal daily activities

Petersen et al. (1999) recommended further definition of subdivisions of MCI, e.g. when there is a problem of language in the first instance rather than a problem of memory this might be a type of mild cognitive impairment that is an early sign of a dementia other than Alzheimer's disease.

A particular issue in relation to diagnosis/classification may be inconsistency in history taking and the possibility that functional impact on activities of daily living activities to an extent requiring caregiver help (which in this case would point instead to a diagnosis of dementia rather than MCI) is missed (Rosenberg, et al., 2006).

A challenge for the diagnosis of MCI is the accurate measurement of cognitive impairment. Traditional brief cognitive tools may not be sensitive to mild impairment. For example, it has been found that the Mini Mental State Examination (Folstein, et al., 1975) is not a sensitive or specific instrument for diagnosis of mild cognitive impairment (Loewenstein, et al., 2000). It has been found to be insensitive in early AD with amnestic syndrome (Feher, et al. 1992; Greene et al 1996) and fails to detect isolated frontal or linguistic impairments in early FTD (Gregory et al 1997; Hodges et al 1999). The MMSE also lacks measures of executive ability (Naugle

and Kawczak 1989) and is unable to detect language deficits unless they are advanced (Feher, et al. 1992).

Other screening tests for dementia, or more extensive neuropsychological test batteries may require trained personnel and specialised equipment to administer e.g. the cognitive section (CAMCOG) of the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX) (Huppert et al 1995) and the Dementia Rating Scale (DRS) (Mattis 1988). These tests are also not suitable for routine bedside cognitive evaluation (Mathuranath, et al., 2000).

In terms of predicting who will convert from MCI to dementia, it has been found that specific patterns of baseline neuropsychological test performance (Summers & Saunders, 2012), single photon emission computed tomography (SPECT); (Hirao, et al., 2005), and also MRI and cerebro-spinal fluid markers (Vos et al., 2012) may predict conversion from mild cognitive impairment to AD.

1.3.1.3 Treatment

There are no definitive preventive measures or treatments for MCI but it is argued that regular follow-up for cognitive assessment may be supportive (Rosenberg, et al., 2006) and follow up allows for monitoring for decline and conversion to DAT.

Regarding pharmacological interventions, in a randomized clinical trial Donepezil was found to have a transient preventive effect at 1 year (Petersen and Morris, 2005) but it is not recommended for routine use (Rosenberg, et al., 2006). However, any improvement in predicting the outcome of MCI is important for the management and counseling of these patients.

1.3.2. Alzheimer's disease

1.3.2.1 Clinical presentation

The core deficit in Alzheimer's disease, in its typical variant, is an impairment of memory characterized by difficulty in remembering new information. This deficit may be accompanied by one or more other cognitive impairments. The level of impairment is sufficient to impact on independent living and later in the course of the disease patients may become unable to care for themselves and need help in daily activities. Common neuropsychiatric symptoms include apathy, anxiety, agitation, and depression (Cummings, 1996).

1.3.2.2 Epidemiology

Alzheimer's disease (AD) is the most frequent cause of dementia. It affects about 30% of those aged 85 and older and its incidence doubles every 5 years from age 60 (Orange and Ryan, 2000). AD accounts for 70 percent of all cases of dementia in Americans aged 71 and older (Plassman et al., 2007) and it was the fifth-leading cause of death for those aged 65 and older (Heron et al., 2008). When the costs of medical, long-term, and home care, as well as lost productivity for caregivers, are included AD is reported to cost the United States economy an estimated $100 billion annually (Cummings et al., 2002).

Patients with AD usually require continuous supervision and personal care, at least in the middle to later stages of the condition. Accordingly, caregivers may experience high levels of stress, negative socioeconomic effects and it has been found that about one-third of family caregivers of people with AD and other dementias have symptoms of depression (Yaffe, 2002; Taylor, 2008).

1.3.2.3 Pathology

Alzheimer's disease is a progressive disease characterized by depositions of proteins in the brain in the form of plaques and tangles (Linn et al., 1995; Petersen et al., 1999). A protein (Apolipoprotein E) has been identified as a genetic determinant of susceptibility to late-onset AD, although it is not causative in disease onset (Poirier, 1993).

It has been suggested that the pathology in AD is due to accumulation of beta-amyloid - overproduction or failure to break down an amyloid precursor protein leads to amyloid deposition resulting in amyloid plaques, neurofibrillary tangles and cell death (Plassman and Breitner, 2000).

Histopathological investigations show neuronal loss, amyloid deposition, within senile and neuritic plaques, and neurofibrillary tangles (Braak and Braak, 1991; Price et al., 1991). Loss of presynaptic of cholinergic neurons is also evident in late-stage patients (Davis, 1978).

1.3.2.4 Treatment

Approaches to the treatment and management of AD include symptomatic treatment with cholinergic agents, psychotropic medications to control behavioural disturbances, disease modification looking for treatable conditions, family support (Cummings, 1996; Salzman et al., 2008) and more recently cognitive rehabilitation (Clare et al., 2010).

(i) Pharmacological - Some agents are said to possibly provide some protection against AD e.g. moderate daily wine consumption, frequent fish (not shellfish) consumption, and the use of nonsteroidal anti-inflamatory drugs (NSAIDs),

antioxidants (vitamin E), and statins (Chui, 2000) though none are routinely recommended to specifically prevent dementia.

Regarding pharmacological treatment of cognitive symptoms, there is some evidence that acetylcholinesterase inhibitors and vitamin E may delay deterioration in AD (Doody et. al., 2001), though effects are typically modest. The UK's National Institute for Clinical Excellence (NICE) (NICE, 2011) advised use of donepezil, rivastigmine (both approved by FDA as well, Doody, et al., 2000) and galantamine as one component in the management of people with mild and moderate AD. In more severe cases of dementia Memantine – an N-methyl-D-aspartate (NMDA) receptor antagonist – has been shown to be of benefit (Winblad and Poritis, 1999; Reisberg, 2003).

Psychotropic medications are used for behavioural and psychiatric symptoms e.g. agitation, depression, and psychosis but it is argued that only symptoms that cause clinically significant dysfunction should be treated with pharmacological agents (Jeste et al., 2008).

(ii) Cognitive rehabilitation - While initially developed for people brain injury, cognitive rehabilitation can be, with certain modifications, equally applied to people with progressive conditions such as Alzheimer's disease and other dementias, at any stage or degree of severity, including as a palliative care approach towards the end of life (Wilson, 2008).

Neuropsychological rehabilitation in dementia is usually applied on the same lines of the holistic psychotherapeutic approach used in brain injury rehabilitation outlined by Prigatano (1999) and Wilson et al., (2009). Of note is to consider cultural,

religious and linguistic factors that may influence the way in which dementia is understood (Downs et al., 2006).

Strategies commonly used for memory rehabilitation include facilitating remaining episodic memory functioning and support of both encoding and retrieval (Bäckman, 1992), ensuring effortful processing (Bird and Luszcz, 1993), reducing errors during the learning process (Clare et al.,1999; Clare et al., 2000), and encouraging encoding through multiple sensory modalities (Karlsson et al., 1989). Specific methods include spaced retrieval (Camp 1989), cueing (Clare and Wilson 2004), simple mnemonics (Clare et al., 1999), encouraging semantic processing of material (Bird and Luszcz, 1991, 1993) and the use of subject-performed tasks as an aid to encoding (Bird and Kinsella, 1996).

Procedural memory needs to be supported to improve or restore the ability to carry out selected activities of daily living via action-based learning (Hutton et al., 1996). Support of semantic memory can be achieved through repeated rehearsal combined with contextual information (Reilly et al., 2005; Snowden et al., 2002) and demonstration of object use (Bozeat et al., 2004).

Clare et al., (2010) report a randomised controlled trial of cognitive rehabilitation for people with dementia. They demonstrated significant improvement in personal goal achievement in everyday functional goals for participants who received an eight week programme of personalised cognitive rehabilitation compared to participants who received either an attention placebo condition (relaxation training) or a no-treatment condition. Of note in relation to this intervention is the fact that participants were in the early stages of dementia (MMSE≥18), once again highlighting the importance of early identification of dementia.

Whilst Alzheimer's disease is the most common form of dementia a number of other forms of dementia exist and these are briefly discussed in the following section. Whilst many of these forms of dementia share common symptoms with AD, the following sections highlight that there are significant differences in presentation including in terms of patterns of cognitive impairment. Different forms of dementia have different prognoses and different requirements in terms of support for patients and families, pharmacological treatment options. This highlights the need for dementia assessment tools that are able to detect impairments in different domains of cognition, something that is discussed in more detail later.

1.3.3. Vascular Dementia (VaD)

Vascular dementia is the second most common type of dementia and it accounts for about 20% of all dementias in which patients suffer from either large-vessel disease (multi-infarct dementia) or small-vessel disease (lacunar state or Binswanger's disease), or a combination of both (Roman, 2003).

Characteristic clinical features are either due to cortical symptoms; aphasia, amnesia, agnosia, and apraxia or subcortical ones; slowness, depression, forgetfulness, and cognitive deterioration (Cummings and Benson, 1992). VaD usually progresses in a step-wise manner. It often begins with neurological symptoms (e.g. abnormal reflexes, difficulty in walking). Deterioration of memory occurs at a later stage. Compared with AD, the most neuropsychological distinguishing feature of vascular dementia has been the greater deficits in the executive domain than those in AD patients (Looi and Sachdev 1999). Therefore, recognition memory in VaD patient is frequently better preserved than free recall compared with AD patients (Cummings et al, 1994).

1.3.4 Fronto-temporal Dementia (FTD)

Fronto-temporal dementia is a degenerative progressive neurobehavioral syndrome affecting the frontal and anterior temporal lobes of the brain. FTD is characterized by early deterioration in social, interpersonal and personal conduct, early emotional blunting, and early loss of insight or various forms of progressive language disorders (Neary et al. 1998). The clinical presentation and degree of cognitive deficit differ according to the degree of degeneration in the affected area of the brain. Therefore, the syndrome has been subdivided into: 1) a frontal or behavioral variant (FvFTD), 2) a temporal, aphasic (progressive fluent) variant, also called Semantic dementia (SD), and 3) a progressive (nonfluent) aphasia (PA) (Weder, et al. 2007). However, there are other conditions which may present with similar features of FTD e.g. motor neuron disease, progressive supranuclear palsy, and corticobasal degeneration therefore, some authors (Knibb et al. 2006) include these conditions into FTD while others refer to all these conditions as Pick complex or dysexecutive syndrome (Kertesz, 2003).

FTD typically occurs earlier than Alzheimer's disease with onset occurring between 35 to 75 years old. A prevalence of 15 per 100.000 in a population of 45 – 64 years of age has been reported (Ratnavalli et al., 2002) and FTD accounts for 20% of cases of presenile dementias (Snowden et al., 2001).

FTD has a heterogeneous pathology in form of atrophy affecting the prefrontal and anterior temporal neocortex characterized by gliosis, neuronal loss, and superficial spongiform degeneration. Ballooned neurons (Pick cells) have been found to occur with variable frequency in all subtypes (Kertesz and Munoz, 2002). Histologically microvacuolation of the outer cortical laminae due to large neuronal cell loss, or transcortical gliosis is evident (Neary et al., 2005). However, in SD unlike other FTD

sub-types the neuropathological findings are found to be fairly predictable: most patients have ubiquitin-positive, tau-negative neuronal inclusions (Hodges and Patterson, 2007).

1.3.4.1 Frontal (FvFTD) or behavioral variant

The presenting picture correlates with the specific frontal area (orbitobasal, medial, and dorsolateral) being affected. Generally there is insidious onset of personality and behavioural changes and lack of insight. Involvement of the orbitobasal sub-area leads to disinhibition, antisocial behavior, poor impulse control, and stereotypical and ritualistic behaviours (Hodges, 2001). On the other hand, involvement of the medial frontoanterior cingulate sub-area is associated with apathy, hyperorality, and preference for sweet food. Decline in personal and interpersonal conduct and inappropriate sexual gestures are also common (Boxer and Miller, 2005). Echolalia, perseveration, emotional blunting, and mutism may also be present (Hodges, 2001).

Cognitive impairments include; executive function (Boxer and Miller, 2005) attention deficits, poor abstraction, difficulty shifting mental set, and perseveration (Snowden et al. 2001). A deficit in planning and organization is present when there is involvement of the dorsolateral prefrontal cortex (Hodges, 2001).

There is marked heterogeneity in clinical presentations of these *FvFTD* subtypes as a result of differential involvement of brain regions (Snowden et al. 2001). Marked social behavior disruption has been found to be common in patients with predominantly right-hemisphere pathology (Snowden et al., 2002). Hypoactivity and apathy has been observed in patients with frontal FTD, whereas hypomania-like behavior observed in cases of temporal pathology (McMurtray et al., 2006). On the

other hand, right frontal hypoperfusion is associated with lack of insight and left frontal perfusion is associated with decreased hygiene. In left hemisphere FTD there are marked language difficulties and fairly normal behavior whereas in right hemisphere FTD language is preserved but there is more frequent inappropriate behavior (McMurtray et al., 2006).

1.3.4.2 Semantic dementia (SD) or aphasic (progressive fluent) variant

The term 'semantic dementia' was coined by Snowden et al. in 1989 to denote fluent progressive aphasia, defective word comprehension and recognition of people and objects. Later on in 1992 Hodges et al. referred to the consistent finding of anterior asymmetrical bilateral temporal lobe atrophy. The current consensus criteria for diagnosis of SD were formulated by Neary et al. in 1998.

Initially in this form of FTD there is loss of memory for words or a loss of word meaning (Boxer and Miller, 2005) associated with bilateral atrophy of the middle and inferior temporal neocortex (Neary et al., 2005). Speech is fluent with substitute phrases like “things” and “that” but patients are unaware of their comprehension deficits (Boxer and Miller, 2005). Other deficits include; inability to recognise the significance of faces and objects in addition to deficits in on non-verbal tasks using visual, auditory, and other modalities as a result of impairment in conceptual knowledge. Recent memory is intact however, anterograde verbal memory is found to be defective on standard tests e.g. wordlist learning (Knibb and Hodges, 2005).

Other features of patients with SD are impairments in emotional processing and interpersonal coldness. Those with right temporal involvement may show emotional disturbances, bizarre alterations in dress, and limited, fixed ideas (Mc Murtray et al.

2006). Patients with SD are found to be less apathetic and more compulsive than those with Fv FTD (Boxer and Miller, 2005).

1.3.4.3 Progressive (nonfluent) aphasia (PA)

In this type of FTD expressive language is mainly affected in the form of great difficulty in word retrieval while word comprehension is preserved. There is asymmetric associated pathology in the left hemisphere (Neary et al., 2005). There are changes in fluency, pronunciation, or word finding difficulties. Behavioural changes may appear later in the course of the disease (Boxer and Miller, 2005).

Neuropsychiatric symptoms of FTD include; depression, irritability, and euphoria but the most prominent symptoms are apathy and disinhibition (Levy, et al., 1996).

1.3.5 Dementia with Lewy Bodies (DLB)

Dementia with Lewy Bodies (DLB) is associated with the presence in the brain of eosinophilic cytoplasmic inclusions made up of synuclein fibrils seen in ballooned neurons of the brain stem and cortex (Dickson et al., 1996).

Although there is overlap in terms of cognitive impairment with Alzheimer's disease, DLB is often distinguished from AD because of the occurrence of hallucinations, visuospatial perceptual disorder, with somewhat better preserved memory functioning (in the early stages), fluctuating levels of attention/alertness, severe sleep disturbances (Perry, et al, 1990; McKeith et al, 1994) The presence of parkinsonian features and extrapyramidal symptoms are also common (Paulsen et al., 2000; Hardy, 2003).

Prevalence rate of DLB in the community is not precisely known, however, it has been diagnosed at autopsy in 12 – 36% of patients with dementia (Paulsen et al.,

2000; Hardy, 2003), though Knapp and Prince. (2007) suggested that DLB represented about 4% of all dementias in the over 65's.

1.4 Assessment, diagnosis and differential diagnosis in dementia

The preceding sections have highlighted that dementia occurs in a variety of forms as a result of different pathologies affecting different parts of the brain. Snowden et al., (2011) highlight that the change from viewing dementia as a global impairment of intellectual function to a perspective of distinct profiles of cognitive impairment and behavioural changes has important implications for the management of people with these conditions.

To distinguish one form of dementia from another requires a combination of a comprehensive analysis of the clinical history of the patient, a detailed neurological examination, and neuropsychological assessment of cognition and behavior (Snowden et al., 2011).

The patient's history will provide indications of signs and symptoms of any cognitive or intellectual deterioration, behavioural disturbances, and possible co-morbid psychiatric features. A critical feature of the history taking are the observations about impairment in social functioning, given by a reliable informant. There are many validated instruments which can be used in this respect e.g. the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (Jorm, 1994) and The Dementia Questionnaire (DQ) (Kawas et al., 1994)

General physical and neurological examination must be undertaken to detect any cardiovascular, cerebrovascular, endocrinological, or other neurological disorders. In terms of neuroimaging MRI and/or SPECT imaging will contribute to diagnostic confidence, though interestingly Snowden et al. (2011) reported that in their study of

228 patients, neuroimaging was typically carried out after initial clinical diagnosis had been made and hence was seen as having a supportive role, with no patient having their diagnosis changed as a result of imaging findings.

Psychiatric assessment is important to detect treatable conditions such as depression which can mimic dementia (psuedodementia), and to deal with possible co-existing features like agitation, anxiety, and/ or delusions which might complicate the clinical picture of dementia.

1.4.1.Neuropsychological assessment of dementia

As noted, neuropsychological testing is an integral part of the evaluation of suspected cases of dementia. Although cognitive assessment is a non-invasive procedure, given that it will make an important contribution to the diagnostic process, there are considerable risks associated with inaccurate results - false positive results would lead to potential stigma for a person labeled with dementia (Freyne, 2001; Brayne et al., 2007), with the potential for harm as a result of unnecessary treatment given the side effects of dementia medications. False negatives would lead to clinical conditions being missed, a difficulty understanding symptoms for patients and their families, and inappropriate treatment (or no treatment). Cognitive assessment instruments are commonly used for detection of cognitive impairment, differential diagnosis of cause, follow-up of progression, deterioration or assessing severity of cognitive impairment (Woodford and George, 2007).

There are many neuropsychological tests, and batteries of tests, that have been developed to assess different aspects of cognition. Furthermore, quite a large number of instruments have been developed with the specific purpose of assessing

for the presence of dementia. Some of these are relatively lengthy batteries of tests, whilst others are very brief, often described as ‘screening tests’.

In a systematic review of screening tests for cognitive impairment, Cullen et al. (2007) identified thirty-nine screens and examined the evidence for their validity in detecting cognitive impairment. They noted that there are variety of settings in which screening may occur and a variety of reasons that cognitive screening tests may be used. These include brief assessment in the doctor’s office, large scale community screening and domain-specific screening to guide further assessment selection. Cullen et al. concluded that, “no single instrument for cognitive screening is suitable for global use" (Brodaty et al., 1998) though noted that there are a small number of tools for which there is some evidence for their validity in detecting cognitive impairment in a relatively comprehensive set of cognitive domains. Cullen et al. noted that rated highest in terms of validation and coverage of key cognitive domains were those that expand on the Mini-Mental State Examination (MMSE; Folstein, et al., 1975), which is the most commonly used instrument in clinical practice. One of these tests that expands on the MMSE, is relatively brief, but was designed to support the process of differential diagnosis of the various forms of dementia by increasing the range cognitive domains examined as well as examining key domains such as memory in more depth than in the MMSE is the Addenbrooke's Cognitive Examination (Mathuranath, et al., 2000). In the next section the MMSE and ACE, and its revised version ACE-R, (Mioshi et al., 2006) are discussed.

1.4.1.1The Mini Mental Status Examination (MMSE)

The MMSE (Folstein, et al., 1975) is a brief 30-point test that is commonly used to screen, and follow-up, for cognitive impairments as in dementia. The test takes

about 10 minutes to complete and covers arithmetic, language, memory, orientation functions, and motor skills (e.g. copy a drawing of two interlocking pentagons).

A score ≥25 is considered as normal, with impairment defined as mild (21 - 24), moderate (10 - 20), and severe (≤9) (Mungas, 1991). Age and educational level have to be considered in the interpretation of scores (Crum et al., 1993) and physical disorders of hearing (Dean et al., 2009), reading, and writing (or drawing) may affect scoring.

Although the MMSE has a reasonable degree of sensitivity and specificity in identifying dementia (Mohs et al 1983; Rosen et al 1984; Zaudig et al., 1991), it has also been criticised in terms of not sufficiently examining cognitive functions such as frontal-executive skills, visuospatial skills and semantic memory, all of which may be the primary deficits in specific degenerative conditions (e.g. fronto-temporal dementia, Dementia with Lewy bodies; Bak and Mioshi, 2007). Other shortcomings of the MMSE include; variability of accuracy in detection of dementia patients of different ages, education levels and ethnicities (Boustani et al., 2003) and poor sensitivity in detection of cases of MCI (Ganguli et al 2001; Kukull et al 1994). However, some authors (e.g. Kukull et al., 1994) found MMSE to be sensitive when scores are adjusted for age and education.

1.4.1.2 The Addenbrooke's Cognitive Examination (ACE)

The Addenbrooke's cognitive examination (ACE) was developed by Hodges and colleagues (Mathuranath, et al., 2000) at the Memory Clinic at Addenbrooke's Hospital, Cambridge, UK, for the detection and classification of AD and FTD (Stokholm, et al. 2009). The authors stated that there were three reasons for the need for such screening and diagnostic tests: 1) a substantial proportion of patients

previously diagnosed with AD actually have other degenerative conditions such as Dementia with Lewy Bodies or Fronto-temporal dementia (McKeith, et al., 1994) or FTD (Neary, et al., 1998); 2) the availability of disease-modifying agents necessitates early detection of dementia (Gifford and Cummings, 1999); 3) a growing concern about memory impairment in late life among the general population (Verhey, et al., 1993).

Other screening tests for dementia (Folstein, et al 1975; Buschke et al 1999) are either not well established as standard tests (Gifford and Cummings, 1999) or require trained personnel and specialised equipment to administer e.g. the cognitive section (CAMCOG) of the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX) (Huppert et al 1995) and the Dementia Rating Scale (DRS) (Mattis, 1988). Moreover, it is argued that these tests are not suitable for routine bedside cognitive evaluation (Mathuranath, et al., 2000).

As noted, the MMSE (Folstein, et al 1975) is a widely used and validated bedside test (Tombaugh and McIntyre, 1992) but its sensitivity as a stand-alone test is questionable (Kukull et al., 1994). It has been found to be insensitive in early AD with amnestic syndrome (Feher, et al., 1992; Greene et al., 1996) and fails to detect isolated frontal or linguistic impairments in early FTD (Gregory et al 1997; Hodges et al., 1999). The MMSE also lacks measures of executive ability (Naugle and Kawczak, 1989) and is unable to detect language deficits unless they are advanced (Feher, et al., 1992).

Therefore, to overcome those drawbacks of MMSE and other tests of cognitive impairment, based upon their own research (Greene et al., 1996; Gregory et al 1997; Hodges et al., 1999; Hodges et al., 1992) over several years, Mathuranath, et al., (2000) developed the ACE as a brief bedside test battery which does not need a

specialised equipment to administer, and at the same time incorporates the MMSE, and expands the memory, language, and visuospatial components, along with providing tests of verbal fluency.

1.4.1.2.1 Evidence for validity in assessment of dementia

The ACE is a 100-point test consisting of items relating to six domains of cognition including orientation, attention, verbal fluency, memory, language, and visuospatial function. It can be administered in 15 – 20 min and no specialised equipment is needed. Based upon validation data relating to detection of dementia (compared to performance of healthy control participants), the authors provided two cut-off points relating to the detection of cognitive impairment associated with dementia, the lower being 83/100 and the higher being 88/100. Using 88 as the cut-off, the ACE has good sensitivity (93%) and a specificity of 71% (Mathuranath, et al., (2000,) while the lower (83) cut-off has a lower sensitivity (82%), but higher specificity (96%). Moreover, performance on the ACE was found to discriminate well between patients with dementia and those with affective disorders (Dudas, et al., 2005). Given that one of the primary drivers for development of the ACE was to aid differential diagnosis, Mathuranath et al., (2000) examined this and developed what they referred to as the VLOM ratio, which is the ratio of scores on verbal fluency plus language to scores on orientation plus name and address delayed recall memory. In their validation sample the VLOM ratio was relatively good at distinguishing AD patients from FTD patients.

The ACE has been validated in England (Mathuranath, et al., 2000; Bak, et al., 2005), Germany (Alexopoulos, et al., 2007), Denmark (Stokholm, et al., 2009), France (Bier, et al., 2005), and Spain (Garcia-Caballero et al., 2006). However,

transcultural use was limited by difficulty in translation of some questions to languages other than the English language.

1.4.1.3 The Addenbrooke's Cognitive Examination-Revised (ACE-R)

The original Addenbrooke's Cognitive Examination (Mathuranath et al., 2000) had been widely used across the world (Mathuranath et al., 2004; Garcia-caballero et al., 2006) but was replaced by the revised version – the ACE-R (Mioshi et al., 2006). The aim of the revision was to make a number of improvements. The authors stated that the naming component of the ACE suffered ceiling effects, while the visuospatial component was very limited. The authors made design changes to make the test easier to administer, content was modified to facilitate cross-cultural usage and translation, to increase sensitivity and to provide a more balanced contribution of subtests to the final score (Mioshi et al., 2006).

The ACE-R was intended to ensure sensitivity and specificity for detecting cognitive impairment associated with dementia, but the aim was also to make it sensitive to mild cognitive impairment. Three parallel versions were developed (Versions A, B, and C) given the frequent necessity to re-assess patients and thus to avoid patients recalling test items from previous visits on repeated administration. Its 26 components were combined into five specific cognitive domains sub-scores (Mioshi, et al., 2006). These sub-scores include; attention/concentration (18 points), memory (26 points), fluency (14 points), language (26 points), and visuospatial (16 points). The maximum score remained at 100 and the test takes 12 to 20 minutes for administration and scoring.

Mioshi et al., (2006) reported that specific modifications from the ACE included; in the memory domain parallel versions of the name/address recall task and a

recognition trial were added, retrograde memory items were simplified to make them more easily translated; in the fluency tests scaling was modified; in the language domain comprehension of commands was removed, new semantic comprehension questions were added, the pictures for the naming test were changed to reduce ceiling effects and reading of regular words was excluded; in the perceptual domain, there was an expansion of the clock face drawing scoring range, and new tasks (counting of dots arrays, and identifying fragmented letters) were added.

On comparing the ACE-R with ACE there was better performance on the memory ($p< 0.05$) and visuospatial ($p< 0.001$) domains and significant difference in the total score on the ACE-R ($p = 0.04$) in addition to a 100% positive predictive value at the lower cut-off (82) for a range of prevalence rates of dementia (Mioshi, et al., 2006). Mioshi et al. also found that the score designed to differentiate Alzheimer's type dementia from a fronto-temporal presentation (the VLOM ratio) had similar sensitivity, leading to a conclusion that the ratio has clinical utility in differential diagnosis, though they noted that the specificity of the ratio was somewhat better than the specificity. The authors therefore concluded that the ACE-R is a brief, sensitive and specific instrument for the detection of early cognitive impairment and differentiation between AD and FTD.

1.4.1.3.1 Critical appraisal of the ACE and ACE-R

Crawford, Whitnall, Robertson, & Evans, (2012) reported the results of a systematic review of the accuracy and clinical utility of the ACE and ACE-R. They note that 'although dementia screening tools should never be the sole means of diagnostic decision making, the usefulness of dementia screening tools is primarily assessed using measures of diagnostic accuracy' (p661). They identified nine studies, seven

relating to the ACE and two to the ACE-R (they did not include studies using translated/adapted versions) that had examined the diagnostic accuracy of the ACE/ACE-R. Crawford et al. reported that studies reviewed had examined performance in a range of populations and had identified a number of different 'optimal' cut-off points. They concluded that across the range of studies the ACE/ACE-R was statistically robust though noted that this was strongest for application in the memory clinic context where base rates relating to proportion of people with dementia are high compared to community populations. To illustrate this point, Crawford et al. calculated Positive Predictive Values, Negative Predictive values and post-test probabilities for two different base rates (for 54% which is typical for a memory clinic and 1.3% which is more consistent with levels of dementia in the population as a whole). Although the ACE-R was considered by Crawford et al. to be effective at detecting cognitive impairment, it was noted that there is not yet a substantial evidence base relating to its ability to differentiate between mild cognitive impairment and dementia or between different forms of dementia. Nevertheless, Crawford et al. acknowledged that the subscale information available from the ACE-R is a key strength, as it provides clinicians with information that may be useful in guiding further assessment that may in turn differentiate between forms of dementia.

One limitation of the ACE-R is that its scores did not correlate with scores of basic and instrumental activities of daily living among patients with different types of dementias such as AD and FTD (Mioshi et al., 2007).

In relation to psychometric properties, the ACE-R was shown to be reliable on a test of internal consistency (Cronbach alpha; Mioshi et al. 2006) but there are no studies of test-retest (or parallel-form) reliability on this version. There is one small study of

test-retest reliability on a Japanese version (Yoshida et al., 2012) with just 21 participants. Given the importance of repeated assessment in confirming diagnosis or monitoring change (either deterioration or possibly improvement with pharmacological treatment) this is an important area for further research and something that is addressed in this thesis.

Whilst originally developed in English, the ACE-R has subsequently been translated for use in a number of different languages and cultures, though not to date in an Arabic-speaking population.

1.4.1.3.2 Translations and adaptations of the ACE-R

Several issues arise in relation to the use of tests developed in one country in another country (Ardila, 1995). The most obvious is of course language and the need for translation. However, simple word for word translation may not always be possible or appropriate and in order to preserve the main purpose of a particular test (i.e. the specific aspect of cognition being examined) adaptation of test items may be required. Cultural differences may impact on the relevance or familiarity of test items and so once again adaptation may be necessary. Finally it is necessary for validation and reliability studies to be conducted with translated/adapted versions of tests – it is not sufficient to assume that psychometric properties/cut-offs will be the same. Given that important variables such as level of education are known to impact on performance of many cognitive tasks, and given differences in level of education between countries, this highlights the importance of undertaking validation studies with each new version of an assessment tool.

In this respect, Siedlecki et al (2010) point out that neuropsychological tests used in the cognitive assessment of individuals being evaluated for disorders associated

with advanced age, such as dementia, have usually been developed and validated in English-speaking individuals. They report that a frequent outcome of test scores is the overdiagnosis of cognitive disorders in non-English speakers. For example, Bird et al., 1987) found that when a Spanish language version of the Mini-Mental State Exam (MMSE) is administered, Spanish-speaking subjects are more likely to be assessed as impaired, in spite of a normal clinical evaluation.

Similarly, Tuokko et al. (2009) asserted that although neuropsychological batteries are often translated for use across populations differing in preferred language, no assumptions can be made of equivalence in construct measurement across groups. They examined data from the Canadian Study of Health and Aging, a large study of older adults in order to test the hypothesis that the latent variables underlying the neuropsychological battery administered in French or English were the same (invariant). They found that while two of the factors, Long-term Retrieval and Visuospatial speed, showed invariance, that is, reflected the same constructs measured in the same scales, the Verbal Ability factor showed only partial invariance, reflecting differences in the relative difficulty of some tests of language functions. They concluded that this empirical demonstration of partial measurement invariance supported the use of these translated measures in clinical and research contexts and offered a framework for detailed evaluation of the generality of models of cognition and psychopathology, across groups of any sort (Tuokko et al., 2009).

Carvalho and Caramell (2007) translated and adapted the ACE-R for use in the Brazilian population. They carried out two independent translations from English into Portuguese, followed by two independent back-translations in addition to a small number of adaptations relevant to the Brazilian culture and language. Examples of adaptations that were made include modifications to the name and

address and the name of the current president. In the Language-naming item and Language-comprehension item some modifications were made in accordance to Portuguese and Brazilian culture. In the Language-reading section, irregular words were chosen to have similar levels of difficulty in Portuguese and in English. A pilot study was carried out in two stages on 21 healthy individuals 60 years old or more with no history of cognitive decline or neurological deficit with various educational levels. The first step involved 10 individuals following which some further modifications were made. The final ACE-R Portuguese version was tested on the remaining 11 participants.

The mean age was 75.4 ± 7.1 years (range 60 to 89 years). 17 (80.9%) were women and 4 (19.1%) were men. Mean number of years of education was 8.5 ± 4.3 (range 3 - 22 years). The lowest total score was 73, the highest was 98, the mean total score was of 83.3 ± 10.0 points and the test took about 15 minutes on average to be administered. The comprehension of the different items was found to be good.

They concluded that the Brazilian version of the ACE-R was found to be a promising cognitive instrument for testing both in research and clinical settings, but no validation study with dementia patients was reported.

In Germany, Alexopoulos et al., (2007) made two independent translations of ACE-R and provided adaptations of the name and the address recall and recognition tests, the retrograde memory tests and the repetition test. The addresses were chosen to reflect common street names and towns. The questions about “the current Prime Minister” and “the woman who was Prime Minister” from the original English version were replaced by “the name of the current Chancellor” and of “the name of the previous Chancellor”. Regarding the words in the repetition test, these

were chosen to be of low frequency, short in length and easy to articulate, as in the English version. Back translation was undertaken and compared with the original English version and it was found that apart from the adapted items, the new version was very similar to the original one. Alexopoulos et al., (2010) conducted a validation study and reported that optimal cut-off scores for the ACE-R for detecting MCI, AD, and FTD were 86/87, 82/83 and 83/84, respectively. They found that the ACE-R was better than the MMSE only in relation to detection of FTD.

In Greece, Konstaninopoulou et al. (2011) examined internal consistency. They administered a translated version of ACE-R plus a number of alternative items with cultural adaptations to 60 healthy participants, 35 patients diagnosed with dementia. (n=16) of them were diagnosed with Alzheimer's disease and (n=19) of them were diagnosed with frontotemporal dementia. They used Cronbach's alpha to measure the internal consistency. Their results showed high internal consistency, patients with dementia performed worse than controls and effects of gender and education were significant. They concluded that the Greek version of the ACE-R was a brief and reliable instrument for the detection of dementia.

In Romania, to adapt and validate the ACE-R, only relevant linguistic modifications were made and other items were maintained (Popescu et al., 2009). To examine reliability, discriminant and concurrent validity 82 subjects (age range 60 – 80 years, education level $\leq$ 8 years) were subjected to the test. On comparing patients with dementia and patients with cognitive impairment with a control group matched for age and educational level, significant between-group differences were found in: attention, memory, fluency, visuospatial functions. Diagnostic accuracy was 96%, sensitivity was highest at a cut-off point of 86 and specificity improved at the cut-off

score of 83. The authors concluded that their results proved the reliability and validity of the Romanian ACE-R version's usefulness for clinical practice.

Kwak, et al., (2010) reported on the validation of a Korean version of the ACE-R. Again they reported that their primary approach was to translate the test as directly as possible, but with the addition of minor linguistic and cultural adaptations (though the details of these are not provided). In their validation study they found that the optimal cut-off score for distinguishing patients with dementia from healthy controls was somewhat lower (at 78) than for the original version (82/88). They attributed this to differences in age and education, as their sample was a little older and had fewer years of education.

Yoshida et al., (2012) reported on a Japanese version of the ACE-R. They provide a detailed description of the linguistic/cultural adaptations, which included changes to the name and address, retrograde memory, letter fluency, word repetition, naming, comprehension, irregular word reading, and fragmented letters. They undertook back-translation to check consistency with the original English version. They conducted an extensive validation study, finding that the ACE-R J was sensitive and specific for the detection of MCI and dementia, was superior to the MMSE and showed good internal consistency, inter-rater and test-retest reliability (though the latter was only determined with 21 participants). Cut-off scores for MCI (88/89) and dementia (82/83) were similar to the original English version.

In summary, a number of translations/adaptations of the ACE-R have been undertaken. They vary in the extent to which items are simply translated or adapted, highlighting the importance of careful consideration of whether/how items should be adapted to make them culturally relevant, whilst still examining the domain of cognition originally intended and relevant to the assessment of dementia.

To date there has not been an Arabic version of the ACE-R. Given the number of Arabic speakers in the world (estimated at around 300 million) this is a significant omission. The focus of the work reported in this thesis is therefore the translation and adaptation of the ACE-R for use with Arabic speakers, with work being undertaken in the context of Saudi Arabia.

1.5 Dementia in the Arab world

Quoting WHO statistics, Clark and Cummings (2004) stated that in ten selected Middle Eastern nations (including Saudi Arabia) the proportion of the population over the age of 65 will grow at a greater rate than other segments of the populace to 17.1% by the year 2050. Therefore, as with other parts of the world, given that the strongest risk factor for dementia is age, the incidence and prevalence of dementia are likely to rise substantially, constituting a significant social and economic burden as well as a personal tragedy and challenge to families. Furthermore, as noted earlier, the current prevalence of dementia in community samples in Middle Eastern countries appears to be considerably higher than in the Western world. Bowirrat et al.'s (2001) study highlighted that prevalence of dementia amongst people of Arab background was 3.9 times higher than those with non-Arab background in Israel and there was evidence of higher prevalence in illiterate people. Whilst the explanation for the relationship between illiteracy and dementia is not clear (and likely to be mediated by a large number of factors relating to deprivation), these figures highlight the importance of having tools for the assessment of dementia that can be used with people who are not literate. Similar findings were apparent in the recent study of Afgin et al., (2012) who reported that in a community sample of 944 Arab people over 65, prevalence of MCI and AD were high (MCI 30% and AD 9.8%), with age, gender (being female) and years of schooling being predictors of

higher rates. It is not clear what accounts for these findings of very high rates of cognitive impairment. In other parts of the Arab world rates appear to be closer to Western levels. For example in a study of El Tallawy et al. (2012) in Egypt, in a door to door study of 8173 people over 50 years old, prevalence of dementia was 2.2%, rising sharply to 18.48% for those over 80 years.

As diagnosis of dementia is dependent upon interpretation of clinical history, there is potential for differences in prevalence estimates to vary depending on reporting of clinical history by participants or their families and by differences in interpretation by medical staff. Given differences in cultural interpretations of changes in cognition with ageing (Karem and Itani, 2013), it is possible for problems with cognitive functions or everyday functional limitations arising from cognitive dysfunction to be interpreted differently in different cultures, potentially impacting on epidemiological surveys of dementia.

A recent review of literature on dementia in the Arab region (Karam and Itani, 2013) found no epidemiological studies of dementia in Saudi Arabia. Karam and Itani noted that the limited amount of data from a small number of studies in limited parts of the Arab world found prevalence to be associated with age and education with findings in relation to gender mixed. Ferri et al. (2006) conducted a Delphi consensus study (in part because of the lack of available epidemiological evidence) to estimate global dementia prevalence. This consensus approach concluded that for the North Africa and Middle East region, dementia prevalence to be 3.6%, which is lower than for Western Europe, the Americas and the developed Western Pacific region, but higher than South East Asia and the rest of Africa. This study also highlighted that the predicted proportionate increase in dementia prevalence in

North Africa and the Middle East over the subsequent forty years was 385%, substantially greater than the increase of 102% predicted for Western Europe.

Thus whilst precise incidence and prevalence figures for dementia in the Arab world are not clear, and there is very little information available from Saudi Arabia, it seems clear that as with other parts of the world dementia is a major problem for individual sufferers, their families and for states, is likely to increase considerably, is associated with poor or no education and is probably under diagnosed. For the Arab world, including the Kingdom of Saudi Arabia, a particular issue regarding diagnosis is the absence of linguistically and culturally relevant neuropsychological assessment tools. The MMSE with all its drawbacks is the only available instrument which has been validated in Arabic (Al Rajeh et al., 1998).

In the Kingdom of Saudi Arabia (KSA) the number of specialised centres for the assessment and treatment of dementia is very limited. The profession of clinical neuropsychology is in its infancy meaning there is little in the way of translated and culturally adapted tools for neuropsychological assessment. Moreover, the number of illiterate people in KSA is high (Ministry of Economy & Planning, 2004). There is therefore a great need for a brief, easy to administer, culturally adapted and sensitive cognitive test for dementia.

1.6 Aims of thesis

The aims of the thesis are:

- To translate and adapt the ACE-R for use in the Arabic-speaking cultural context of Saudi Arabia, designing parallel versions for repeat testing (Chapter 2).

- Examine the validity of the ACE-R in terms of sensitivity/specificity for detection of dementia and mild cognitive impairment in literate participants (Chapter 3).

- Examine the test-retest reliability of the Arabic ACE-R in literate participants (Chapter 4).

- Examine the validity of the ACE-R in terms of sensitivity/specificity for detection of dementia and mild cognitive impairment in illiterate participants (Chapter 5).

- Examine the test-retest reliability of the Arabic ACE-R in illiterate participants (Chapter 6).

- Collect and report data from a normative sample (Chapter 7).

- Discuss the findings from the studies with regard to use of the Arabic ACE-R in the process of assessing for dementia in literate and illiterate participants (Chapter 8).

CHAPTER 2

Development of the Arabic ACE-R: Translation and Adaptation

Chapter 2: Development of the Arabic ACE-R – Translation and Adaptation

2.1 Introduction

In Chapter 1, it was noted that despite the fact that the Arabic language is one of the six official languages of the United Nations and is spoken as a mother tongue by more than 300 million people (Lewis, 2009), at the present time there are very few neuropsychological assessment tools for which there is an Arabic language version, so limiting the ability of clinicians in Saudi Arabia and other Arabic speaking countries to comprehensively assess cognition. Furthermore, a major issue for populations living in many countries of the Middle East is that there are no cognitive assessment tools validated for use with illiterate people.

Given that the Addenbrooke's Cognitive Examination-Revised (ACE-R) is a brief, sensitive, and easy to administer instrument for the detection of dementia in day to day clinical practice, it would appear to be an ideal instrument to consider for use to the Saudi Arabian context. Although the ACE-R has been translated into a number of different languages there is no Arabic translation of the test. As with other countries and languages, for some items of the ACE-R simply translating them into Arabic is either not possible or appropriate because they are language specific or are not culturally appropriate. As Newman (2007) notes, "to be truly valid and reliable, test items must be adapted to the specific country and region in which they are employed and local norms must be gathered." Given that the ACE-R was constructed in a Western environment, the aims of this first stage of the project were to determine what, if any, cultural adaptations are needed for the Addenbrooke's Cognitive Examination – Revised (ACE–R) to be reliable and valid

in the context of the Kingdom of Saudi Arabia, where the environment and culture are markedly different from those of the UK and then to develop an adapted, Arabic version of the ACE-R.

2.2 The adaptation and translation process

The translation process began with the researcher and three accredited translators based in Riyadh, Saudi Arabia attempting a direct translation of each version (A, B & C) of the original ACE-R into Arabic. Use of accredited translators provided an evaluation of the researcher's basic translation. For most items there was good agreement between the researcher and each of the three translators.

Following some minor modifications to the researcher's version and as a further check on the translation process, the Arabic translations were then given to three new translators also based in Riyadh, who translated them back to English. This process demonstrated that the basic translation was satisfactory for many of the ACE-R test items. This suggests that the intention of the original authors of the ACE-R to provide a test that would be relatively easily translated was at least in part achieved. However, for some of the items this straightforward translation is not appropriate. Some items are language-specific. For example in the repetition task the English word hippopotamus is used as an example of a three syllable word. However the Arabic translation of hippopotomous is in fact a two syllable word. Other tasks could be easily translated directly into Arabic, but would not to be appropriate in the Saudi cultural context. For example, "the name of current Prime Minister" in the English version can be translated, but is unfamiliar because in the Saudi context, the King has the same role as prime minister. Hence, the term prime minister had to be modified.

Once translated and adapted versions of the test had been developed (details of which are provided below), permission was sought from the University of Glasgow Faculty of Medicine Ethics committee for approval to administer the test to healthy controls and also patients with a diagnosis of mild cognitive impairment or dementia in Saudi Arabia (see Chapter 3 for details).

Initially, three healthy Saudi students studying for higher degrees in Glasgow and aged between 35 and 45 volunteered to do the test. They were able to give feedback on a small number of items that needed further modification.

Next the test was given by the researcher in Saudi Arabia to ten control participants who were not suffering from any neuropsychological problems. The healthy controls were inpatients at the Department of Urology and the Department of Cardiology at King Khalid University Hospital and the Prince Salman Social Centre. This step was undertaken to seek impressions of the tool. In addition feedback was obtained from Dr Saeed Wahass, Associate Professor of Clinical Psychology and Professor AbduAllah Aldayel, who provided linguistic advice on the items in the ACE-R dealing with reading (particularly reading of irregular words).

Approval to administer the test to patients with a diagnosis of mild cognitive impairment or dementia was sought from the Faculty of Medicine in King Saud University in Riyadh. This enabled participants to be recruited from both the outpatient and inpatient clinics in King Khalid University Hospital under the direction of Professor Abdul Rahman Altahan, Consultant Neurologist in the Neurology Section. This small number of participants was initially recruited in order to provide an initial check on whether the test was understandable and easy to administer. A final set of three versions of the Arabic ACE-R was then agreed upon.

In the following section, each task in the ACE-R is listed and discussed in terms of whether the item has been directly translated or adapted:

2.3 The Arabic ACE-R

For each subtest in the ACE-R, the original version and the Arabic version are presented, with an account of whether the task has been directly translated or adapted.

2.3.1 Orientation

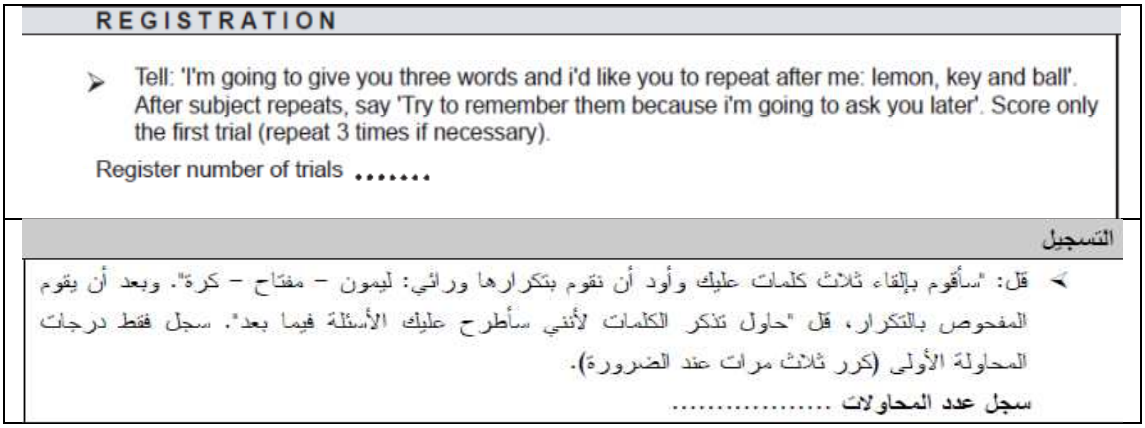
In the original version, this task consists of two sets of five questions relating to orientation in time and place. Each task is scored out of a maximum of five points. For the Arabic version, the orientation questions were directly translated without the necessity to make any modification or change.

ORIENTATION					
➢ Ask: What is the	Day	Date	Month	Year	Season
➢ Ask: Which	Building	Floor	Town	County	Country

التوجه					
➢ اسأل: ما هو	اليوم	التاريخ	الشهر	السنة	الفصل
➢ اسأل: أي	مبنى	طابق	مدينة	المنطقة	الدولة

2.3.2. Registration

This task is the first part of a memory recall task. Three words (Lemon, Key, and Ball) are given for recall later. For the Arabic version, the three words were translated directly.



REGISTRATION

- Tell: 'I'm going to give you three words and i'd like you to repeat after me: lemon, key and ball'. After subject repeats, say 'Try to remember them because i'm going to ask you later'. Score only the first trial (repeat 3 times if necessary).

Register number of trials .....

التسجيل

- قل: "سأقوم بإلقاء ثلاث كلمات عليك وأود أن تقوم بتكرارها ورائي: ليمون – مفتاح – كرة". وبعد أن يقوم المفحوص بالتكرار، قل "حاول تذكر الكلمات لأنني سأطرح عليك الأسئلة فيما بعد". سجل فقط درجات المحاولة الأولى (كرر ثلاث مرات عند الضرورة).

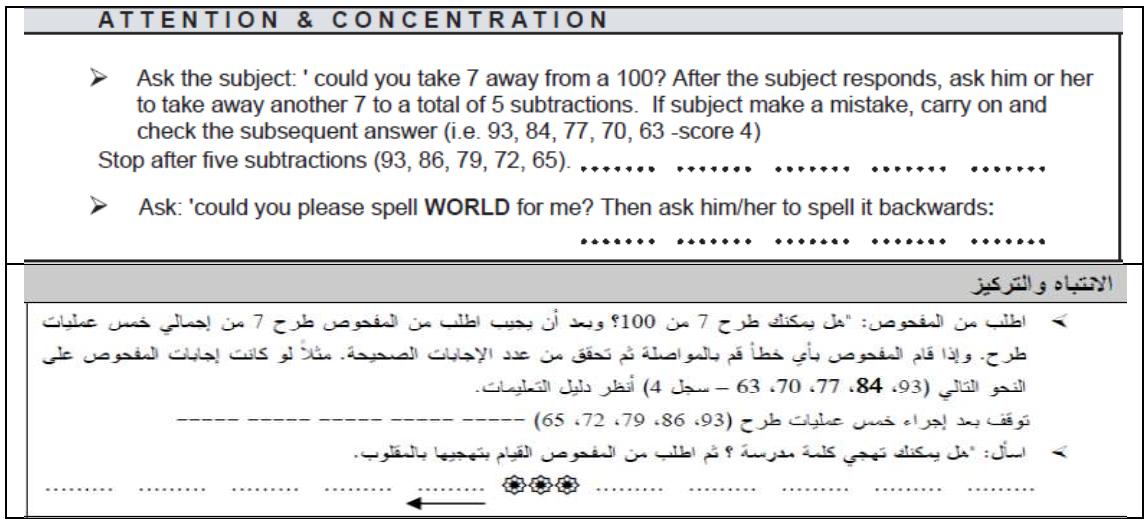
سجل عدد المحاولات .....

2.3.3 Attention & Concentration

In the original, this task involves what is known as 'Serial 7's', in which the participant is asked to subtract 7 from 100 and then continue for five subtractions. If the participant makes a mistake on the arithmetic task, then s/he is asked to spell the word 'World' and then to spell it backwards. Each task is scored out of five and the best performance is recorded.

For the Arabic version the first question was translated directly because it consists of numbers with simple instructions. As to the second question the English word (World) was substituted with the word 'School' in the Arabic language because the English word consists of 5 letters and when translated into Arabic it becomes 4 letters. Therefore the researcher considered this not suitable and replaced it with the word 'School' which consists of 5 letters in the Arabic language. The researcher endeavoured to ensure that the replacement word was a high frequency word like the original word. There is a small arrow under the second part of question two in

this task to indicate that the reverse spelling of the word must be from right to the left. This arrow was put in to take into account the circumstances of the application although it is not used in the English version.



ATTENTION & CONCENTRATION

- Ask the subject: ' could you take 7 away from a 100? After the subject responds, ask him or her to take away another 7 to a total of 5 subtractions. If subject make a mistake, carry on and check the subsequent answer (i.e. 93, 84, 77, 70, 63 -score 4)

Stop after five subtractions (93, 86, 79, 72, 65). ....

- Ask: 'could you please spell **WORLD** for me? Then ask him/her to spell it backwards:

....

الانتباه والتركيز

- اطلب من المفحوص: "هل يمكنك طرح 7 من 100؟ وبعد أن يجيب اطلب من المفحوص طرح 7 من إجمالي خمس عمليات طرح. وإذا قام المفحوص بأي خطأ قم بالمواصلة ثم تحقق من عدد الإجابات الصحيحة. مثلاً لو كانت إجابات المفحوص على النحو التالي (93، **84**، 77، 70، 63 – سجل 4) أنظر دليل التعليمات.

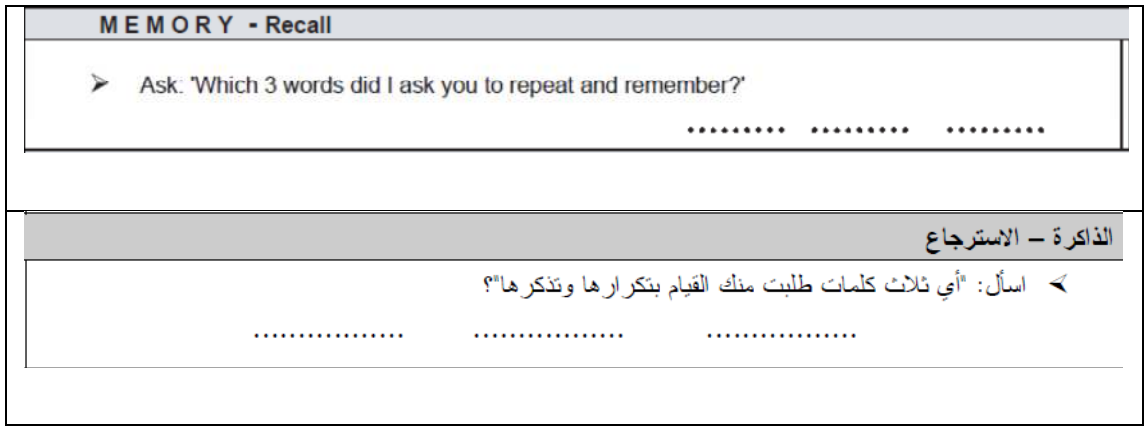
توقف بعد إجراء خمس عمليات طرح (93، 86، 79، 72، 65) ----- ----- ----- ----- ----- ----- -----

- اسأل: "هل يمكنك تهجي كلمة مدرسة ؟ ثم اطلب من المفحوص القيام بتهجيها بالمقلوب.

....

2.3.4 Memory: Recall

This task involves the request to recall the three words presented earlier. The task is scored out of three. The recall question relating to the three items (Lemon, Key, Ball) was translated directly.



MEMORY - Recall

- Ask: 'Which 3 words did I ask you to repeat and remember?'

....

الذاكرة – الاسترجاع

- اسأل: "أي ثلاث كلمات طلبت منك القيام بتكرارها وتذكرها"؟

....

2.3.5 Memory – Anterograde Memory

In the original, this task involved participants being presented with a name and address (in the format of a typical UK address) and then being asked to recall them.

The task is repeated three times and only performance on the third trial is scored. The task is scored out of seven (one point for each element of the name/address recalled correctly).

For the Arabic version, the address was drafted in a way that was consistent with address formats in the Saudi environment, which in fact is relatively common in the wider Arab world. Consistent with the original test, three versions were created for this task. Hypothetical addresses were created so that every version has a different address. Terminology for the house location varied so that in one version the term 'street' (Shareaa شارع) is used, in another version it is 'road' (Tareeq طريق) and in the final version it is 'passageway' (Mamaer ممر). The house number was left without change from the three original English versions. Likewise, there were two individuals with male names and one individual with a female name which is similar to the original English version.

Version A

M E M O R Y - Anterograde Memory

➢ Tell: ' I'm going to give you a name and address and I'd like you to repeat after me. We'll be doing that 3 times, so you have a chance to learn it. I'll be asking you later'

Score only the third trial

	1st Trial	2nd Trial	3rd Trial
Harry Barnes	....	....	....
73 Orchard Close	....	....	....
Kingsbridge	.....	.....	.....
Devon	.....	.....	.....

النسخة أ

الذاكرة – ذاكرة تقدمية

➢ سأقوم بذكر اسم وعنوان عليك، وأود منك تكرارها ورائي – سنقوم بذلك ثلاث مرات لذا فإنه لديك الفرصة لتذكرها. وسأقوم بطرح أسئلة عليك فيما بعد.

سجل فقط درجات المحاولة الثالثة

	المحاولة الأولى	المحاولة الثانية	المحاولة الثالثة
أحمد خالد	.....	.....	.....
منزل 73	.....	.....	.....
حي الأمل	.....	.....	.....
شارع المتنبي	.....	.....	.....
الرياض	.....	.....	.....

Version B

M E M O R Y - Anterograde Memory

➢ Tell: ' I'm going to give you a name and address and I'd like you to repeat after me. We'll be doing that 3 times, so you have a chance to learn it. I'll be asking you later'

Score only the third trial

	1st Trial	2nd Trial	3rd Trial
Linda Clark	....	....	....
59 Meadow Close	....	....	....
Milford	.....	.....	.....
Surrey	.....	.....	.....

النسخة ب

الذاكرة – ذاكرة تقدمية

➢ سأقوم بذكر اسم وعنوان عليك، وأود منك تكرارها ورائي – سنقوم بذلك ثلاث مرات لذا فإنه لديك الفرصة لتذكرها. وسأقوم بطرح أسئلة عليك فيما بعد.

سجل فقط درجات المحاولة الثالثة

المحاولة الثالثة	المحاولة الثانية	المحاولة الأولى	
.....	.....	.....	مها فالح
.....	.....	.....	منزل 59
.....	.....	.....	حي الازدهار
.....	.....	.....	طريق البحر
.....	.....	.....	مكة

Version C

M E M O R Y - Anterograde Memory

➢ Tell: ' I'm going to give you a name and address and I'd like you to repeat after me. We'll be doing that 3 times, so you have a chance to learn it. I'll be asking you later'

Score only the third trial

	1st Trial	2nd Trial	3rd Trial
John Marshall	....	....	....
24 Market Street	....	....	....
Spilsby	.....	.....	.....
Lincolnshire	.....	.....	.....

النسخة جـ

الذاكرة – ذاكرة تقدمية

➢ سأقوم بذكر اسم وعنوان عليك، وأود منك تكرارها ورائي – سنقوم بذلك ثلاث مرات لذا فإنه لديك الفرصة لتذكرها. وسأقوم بطرح أسئلة عليك فيما بعد.

سجل فقط درجات المحاولة الثالثة

المحاولة الثالثة	المحاولة الثانية	المحاولة الأولى	
.....	.....	.....	ناصر سعد
.....	.....	.....	منزل 24
.....	.....	.....	حي السعادة
.....	.....	.....	ممر النور
.....	.....	.....	الدمام

2.3.6 Memory – Retrograde Memory

The original version of the ACE-R asks four questions:

Name of current Prime Minister.

Name of the woman who was Prime Minister.

Name of the USA president.

Name of the USA president who was assassinated in the 1960's.

One point is awarded for each answer.

Some of these are clearly culture-dependent and therefore modifications were required. The aim was to ensure that this tool could be used in a variety of Arabic-speaking countries and not just Saudi Arabia. Different countries have different forms of government and therefore questions were drafted in such a way as to try to ensure that they would apply in a range of countries. In selecting questions the initial aim was to sample semantic knowledge likely to be well-established in most healthy control participants. Various different options were considered, with the final set of question being:

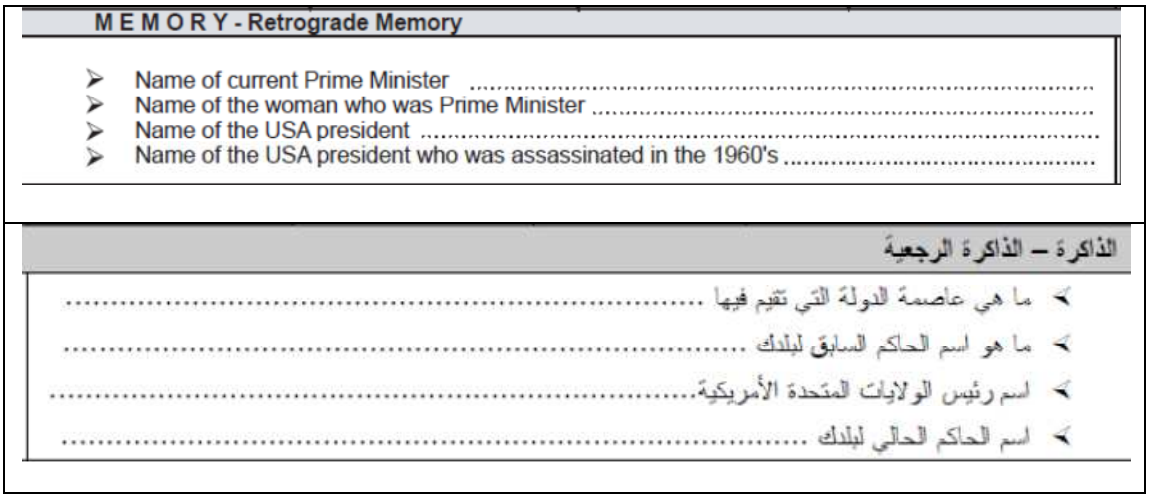
1. "What is the capital city of the country where you live?"

2. "What is the name of the previous governor of your country?"

3. “The name of president of the USA”.

4. "Name of current governor of your country"

These questions should be suitable for any culture or country regardless as to whether they have a king, prime minister, prince, sheikh, or president.



M E M O R Y - Retrograde Memory

- Name of current Prime Minister .....
- Name of the woman who was Prime Minister .....
- Name of the USA president .....
- Name of the USA president who was assassinated in the 1960's .....

الذاكرة – الذاكرة الرجعية

- ما هي عاصمة الدولة التي تقيم فيها .....
- ما هو اسم الحاكم السابق لبلدك .....
- اسم رئيس الولايات المتحدة الأمريكية.....
- اسم الحاكم الحالي لبلدك .....

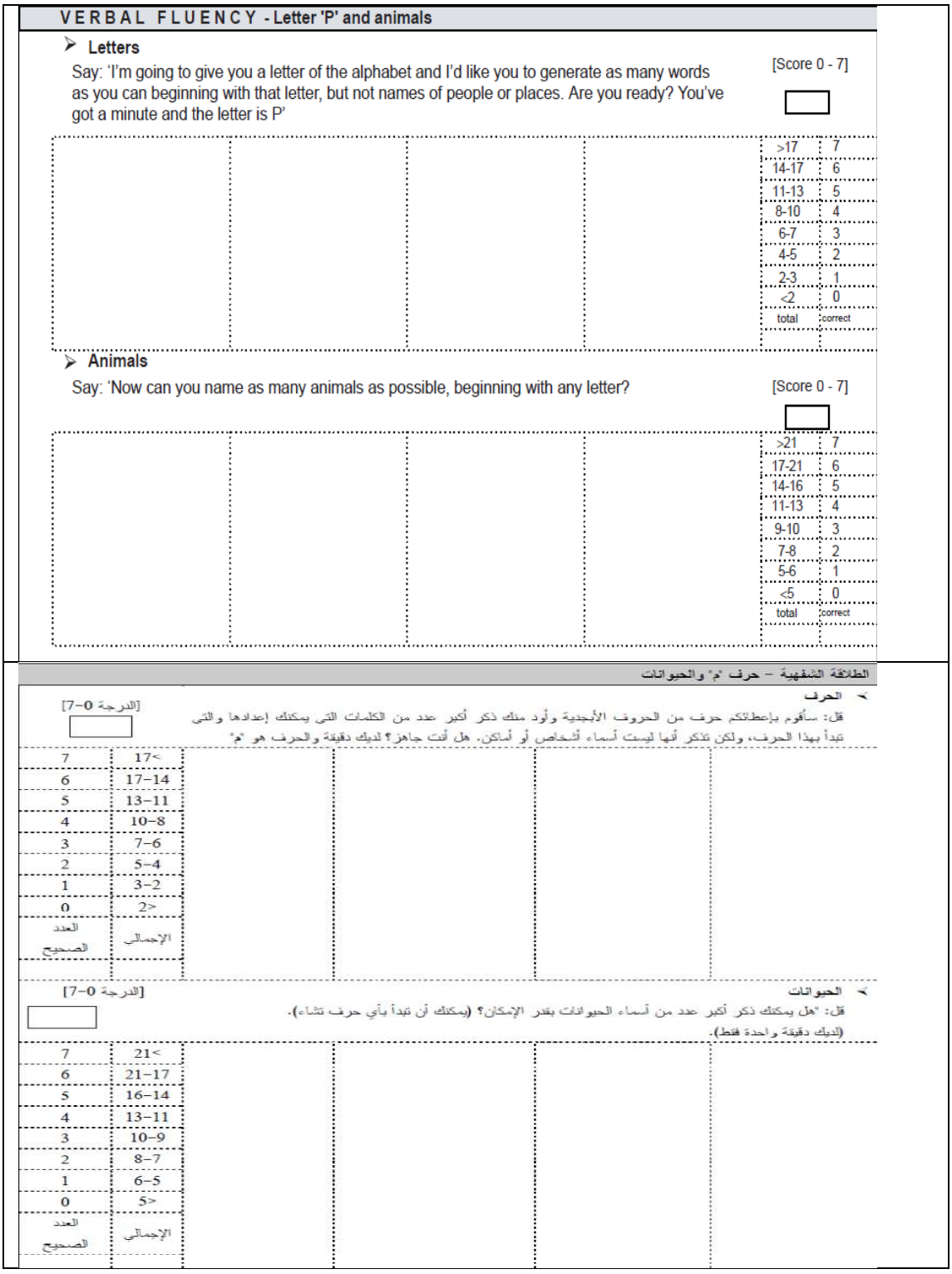
2.3.7 Verbal Fluency

Verbal fluency tests (in which the person has to say in one minute as many words beginning with a specified letter or as many examples of a specified semantic category) are considered to tap a range of cognitive functions, including (particularly in the case of letter fluency) executive functions and (particularly in the case of category fluency) semantic knowledge.

Letter Fluency: The original English version uses the letter P for the verbal fluency task. In normative samples, the letter P tends to produces one of the largest numbers of associations of any letter and is therefore considered an easy letter (Borkowski, et al., 1967). For the Arabic version, the letter ("M" by Arabic language which is written like this م and spoken as meem or **ميم** in Arabic) was selected. It is the thirteenth letter in the Arabic alphabet. It is also considered to have a high frequency of associations, with low level of difficulty (Khalil, 2010).

Animal Fluency: This was translated directly. The phrase (you have one minute to answer this question) has been added to ensure clarity of instructions for participants.

For each task in the original a score out of seven is derived based on the number of words produced in one minute. It was decided to use the same scoring system initially and to examine whether this was effective in contributing to discriminating patients with cognitive impairment from healthy controls once data were collected.



VERBAL FLUENCY - Letter 'P' and animals

➢ **Letters**

Say: 'I'm going to give you a letter of the alphabet and I'd like you to generate as many words as you can beginning with that letter, but not names of people or places. Are you ready? You've got a minute and the letter is P'

[Score 0 - 7]

>17	7
14-17	6
11-13	5
8-10	4
6-7	3
4-5	2
2-3	1
<2	0
total	correct

➢ **Animals**

Say: 'Now can you name as many animals as possible, beginning with any letter?

[Score 0 - 7]

>21	7
17-21	6
14-16	5
11-13	4
9-10	3
7-8	2
5-6	1
<5	0
total	correct

الطلاقة الشفهية – حرف "م" والحيوانات

➢ **الحرف**

[الدرجة 0–7]

قل: سأقوم بإعطائكم حرف من الحروف الأبجدية وأود منك ذكر أكبر عدد من الكلمات التي يمكنك إعدادها والتي تبدأ بهذا الحرف، ولكن تذكر أنها ليست أسماء أشخاص أو أماكن. هل أنت جاهز؟ لديك دقيقة والحرف هو "م"

7	17<				
6	17–14				
5	13–11				
4	10–8				
3	7–6				
2	5–4				
1	3–2				
0	2>				
العدد الصحيح	الإجمالي				

➢ **الحيوانات**

[الدرجة 0–7]

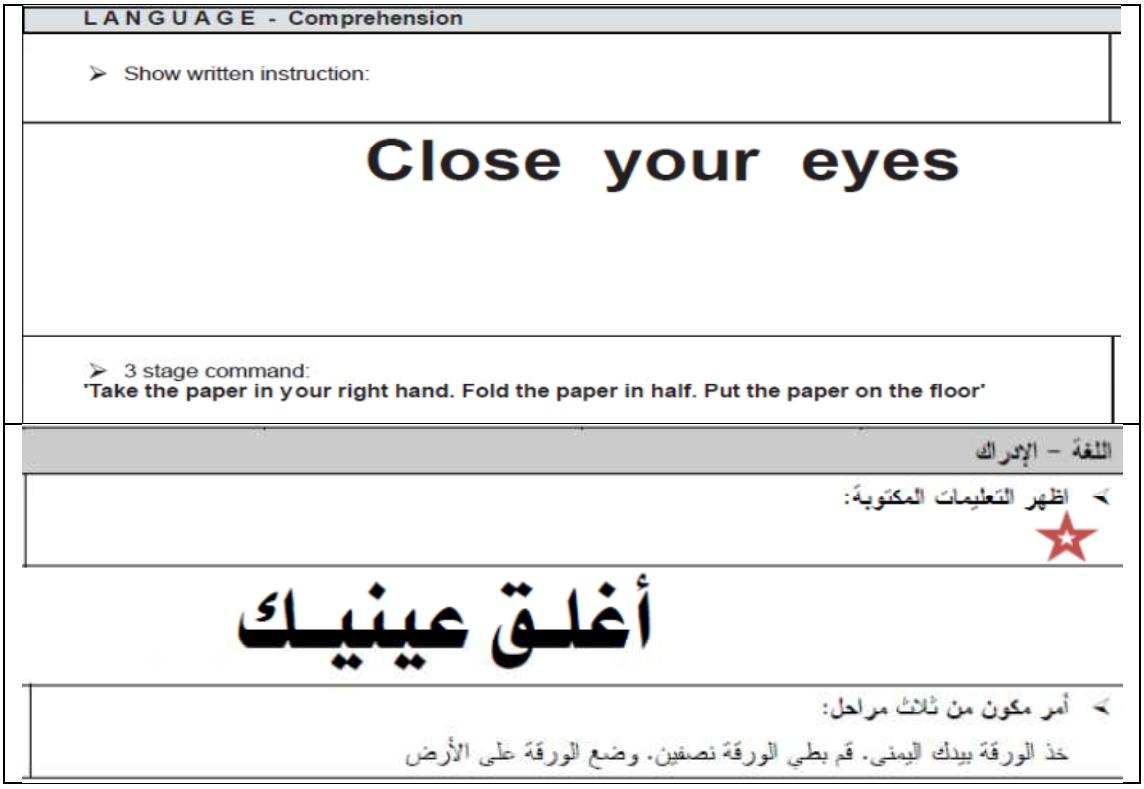
قل: "هل يمكنك ذكر أكبر عدد من أسماء الحيوانات بقدر الإمكان؟ (يمكنك أن تبدأ بأي حرف تشاء). (لديك دقيقة واحدة فقط).

7	21<				
6	21–17				
5	16–14				
4	13–11				
3	10–9				
2	8–7				
1	6–5				
0	5>				
العدد الصحيح	الإجمالي				

2.3.8 Language – Comprehension

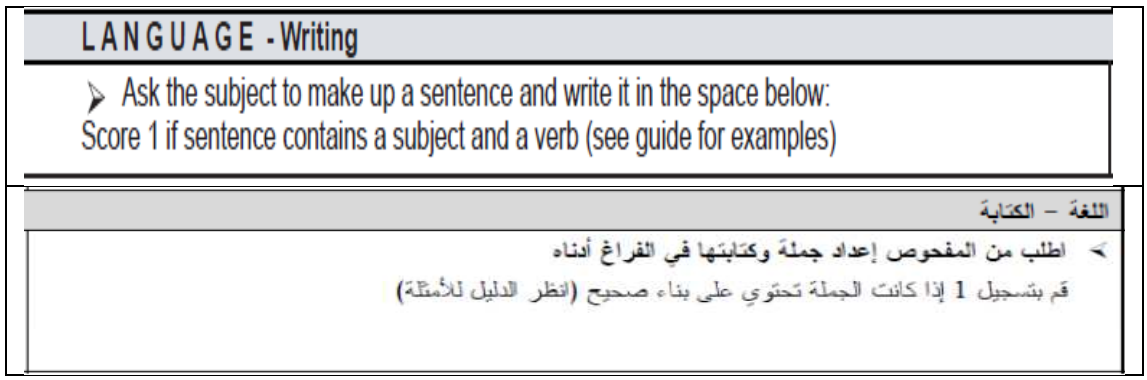
In the original, there are two instructions that participants are asked to follow: (1) Close your eyes; (2) Take the paper in your right hand. Fold the paper in half. Put the paper on the floor. The first task scores one point and the second task is scored out of three. For the Arabic version, these instructions were translated directly as there was no necessity to amend them.

The phrase (**close your eyes**) was written in a large font to be clear for the person examined as it is in the English version of ACE-R. The verb (CLOSE) was translated into Arabic slang language because it is more commonly used in the Arabic culture than the more formal version of the word (and is only used in relation to closing eyes).



2.3.9 Language – Writing

The original version involves a request to write a sentence and achieves one point if the sentence contains a subject and a verb. This task was translated with minor modification of the Arabic grammar which does not need a verb in the sentence to be correct.


LANGUAGE - Writing

➢ Ask the subject to make up a sentence and write it in the space below:
Score 1 if sentence contains a subject and a verb (see guide for examples)

اللغة – الكتابة

➢ اطلب من المفحوص إعداد جملة وكتابتها في الفراغ أدناه
قم بتسجيل 1 إذا كانت الجملة تحتوي على بناء صحيح (انظر الدليل للأمثلة)

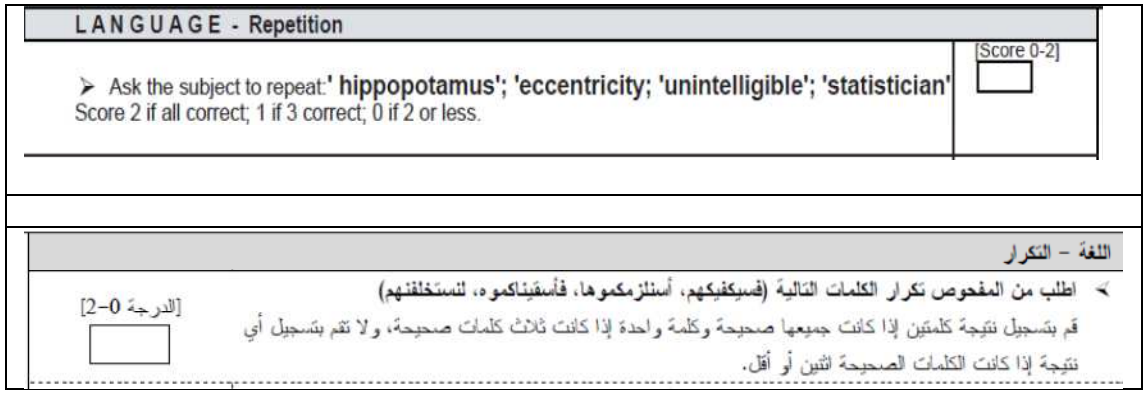
2.3.10 Language – Repetition

This task involves the repetition of four single words and then two short sentences.

Single words: In the original ACE-R there are four words each of which consists of three syllables. The object of the task is to repeat the word correctly. It was not appropriate to translate the words directly from English to Arabic because these words have only one or two syllables in Arabic. A maximum score of two points is awarded if all words are correctly pronounced, with one point for three correct, and zero if two or less words were correct.

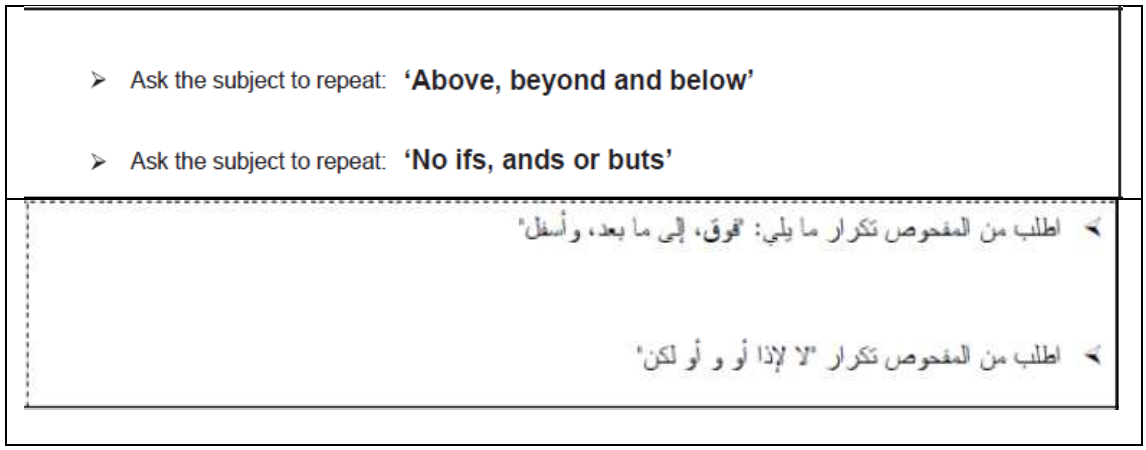
In fact most words in Arabic consist of just one or two syllables. Following consultation with linguistics experts, we found four words in Holy Quran which consist of three syllables. Although rare words, when they were piloted, they did appear to be easy enough for participants to pronounce. The meaning of these

words in English language are (1) 'will deal with them on your behalf' (2) 'forcing them to comply', (3) 'giving water of life', and (4) 'passing on though generations'.



Sentences: The second task in the repetition is divided into two parts, involving repetition of two short sentences that are relatively challenging in terms of working memory and articulation. One point is awarded for each sentence.

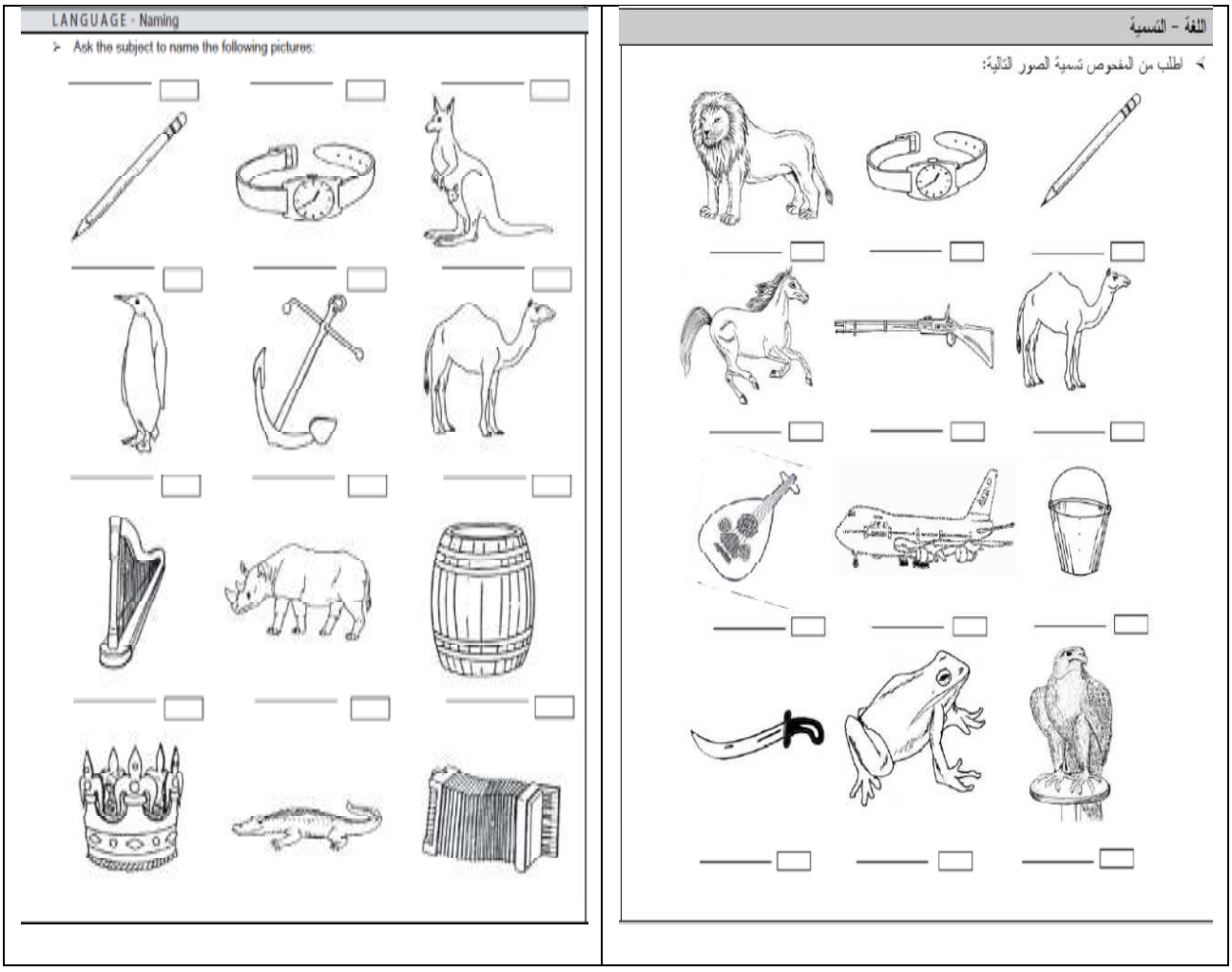
For the first sentence, this was translated directly and nothing was changed. For the second sentence several options were considered to have a sentence that consists of relatively short words that did not form a common phrase, but which could be repeated. After consideration of several options a phrase that in fact maintains a lot of the meaning of the original sentence was identified. Later data collection showed that this task did seem to contribute to differentiating between the healthy controls and patient groups suggesting it was making a useful contribution to the test.



2.3.11 Language - Naming

This task involves naming twelve line drawings of objects, with a total score out of 12. For the Arabic version, three of the original pictures (the watch, pencil and camel) were not changed because they were considered to be familiar to different cultures. However, the other nine pictures were substituted after early testing with the original items suggested that they may be too unfamiliar in Saudi Society.

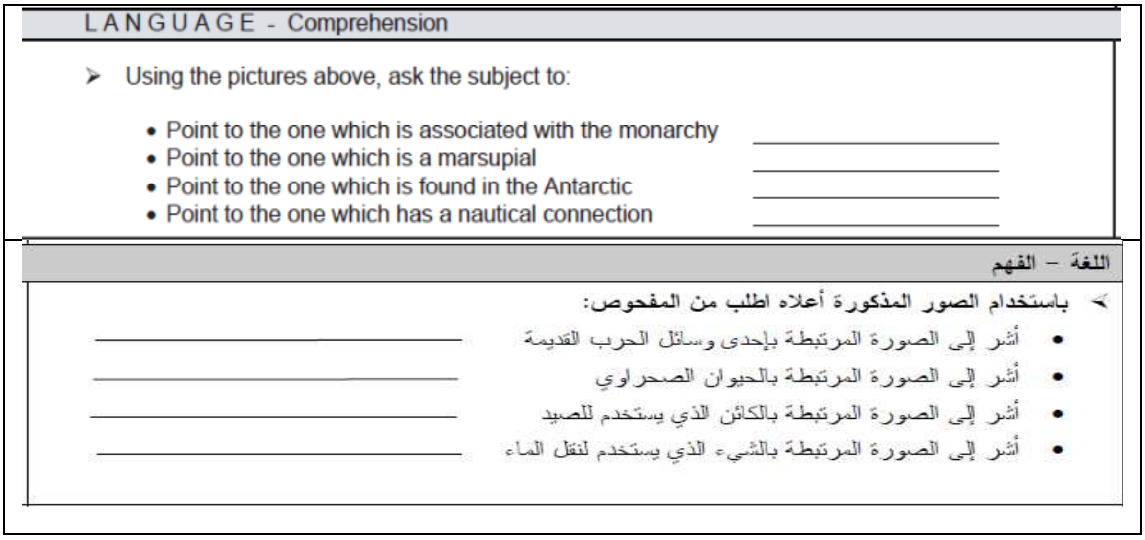
Therefore a set of items that were judged to be neither highly familiar nor very infrequent were identified and a professional draftsman was commissioned to draw them.



2.3.12 Language - Comprehension

In the original, four questions examining semantic knowledge relating to four items in the naming task were asked (with four points). For the Arabic version, four new questions were devised:

1. Point to the picture which is associated with one of the old war tools.
2. Point to the picture which is associated with the desert
3. Point to the picture of the object that is associated with hunting.
4. Point to the picture which is associated with transferring water.



LANGUAGE - Comprehension

- Using the pictures above, ask the subject to:
  - Point to the one which is associated with the monarchy _____
  - Point to the one which is a marsupial _____
  - Point to the one which is found in the Antarctic _____
  - Point to the one which has a nautical connection _____

اللغة – الفهم

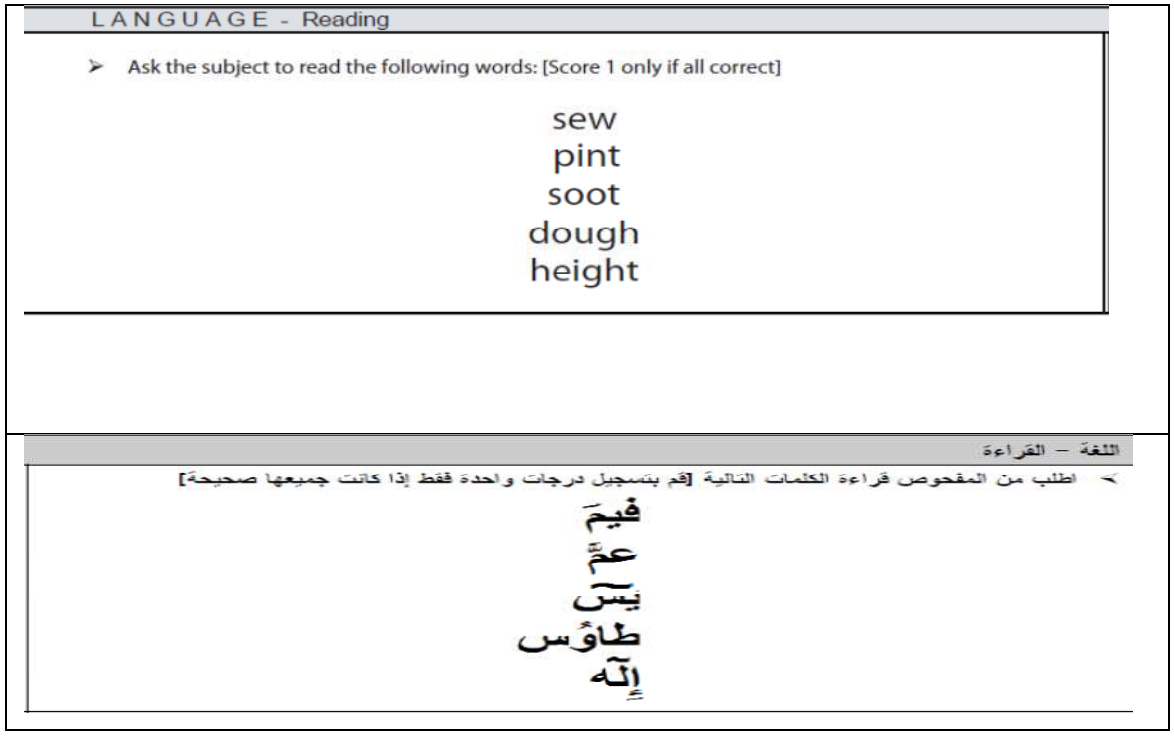
- باستخدام الصور المذكورة أعلاه اطلب من المفحوص:
  - أشر إلى الصورة المرتبطة بإحدى وسائل الحرب القديمة _____
  - أشر إلى الصورة المرتبطة بالحيوان الصحراوي _____
  - أشر إلى الصورة المرتبطة بالكائن الذي يستخدم للصيد _____
  - أشر إلى الصورة المرتبطة بالشيء الذي يستخدم لنقل الماء _____

2.3.13 Language - Reading

In the original version of this task, there are five irregular words which participants are asked to read. Each one is pronounced in a different manner that differs from common pronunciation rules. One point is awarded if all words are pronounced correctly. These words were not directly translated as the same words in Arabic follow conventional pronunciation. In fact, unlike English, Arabic has very few words that do not follow conventional pronunciation rules. However, after consultation with experts in Arabic linguistics, five Arabic words were identified that do not follow

conventional orthography to phonology rules in terms of the letters in the word, with correct pronunciation being indicated by the presence of 'diacritics' (marks or symbols written above the word).

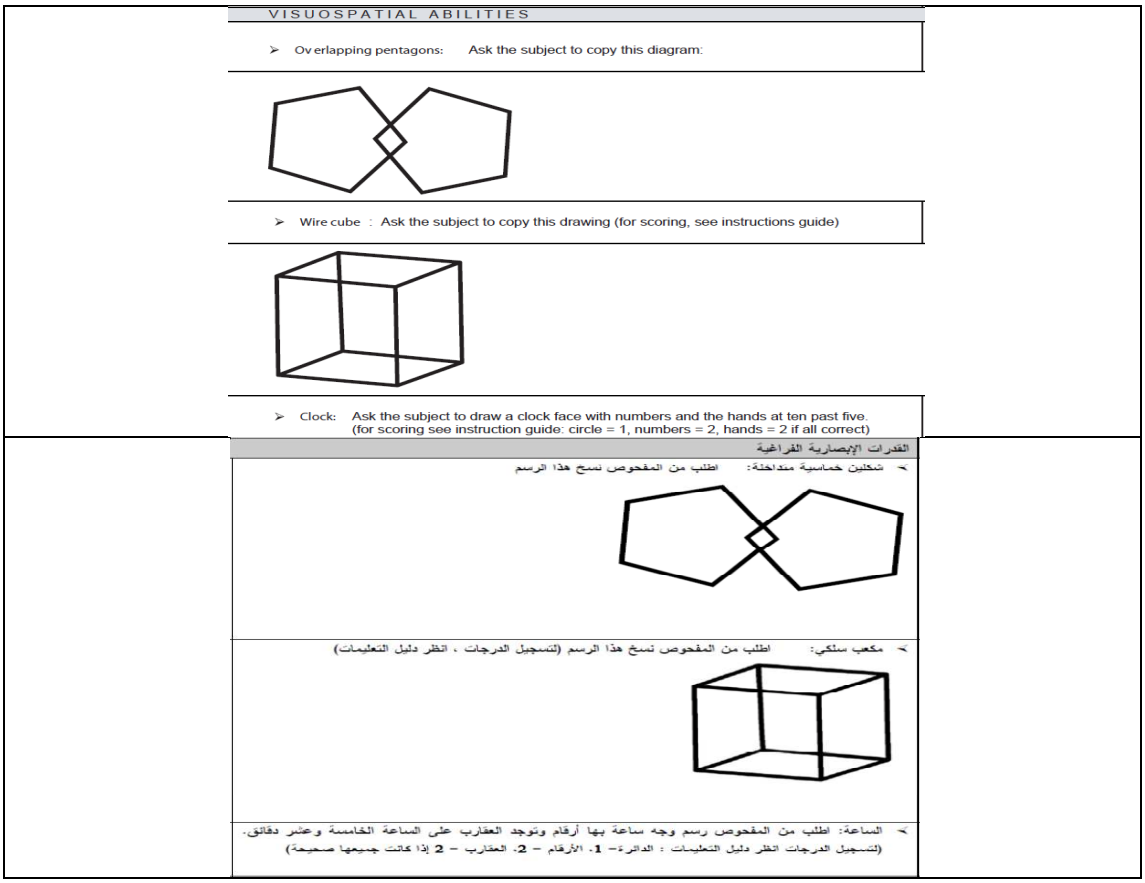
The first word is **"Feema"** which has different meanings depending on the context in which it is being used, but in general it means 'what' or 'while'. The second word is **"Amma"** means "about what?" The third word is **"Yaseen"** is the name of person in the Holy Quran in which it refers to the name of a prophet. The fourth word is **"Tawoos"** which means "the peacock". The last word is **"Elah"** which means "God".



2.3.14 Visuospatial abilities – Overlapping pentagons, Cube and Clock drawing

The original English version involves copying two drawings, the overlapping pentagons and a cube, and then a clock drawing task that involves drawing a clock face, and placing hands at ten past five. One mark is awarded for pentagons, two

for the cube and five for the clock. In the Arabic version, the two figures were use without change apart from location on the page to accommodate the fact that in Arabic is read from right to left (so it is more natural for the figures to be copied to be placed to the right hand side). Instructions relating to the clock drawing were also translated directly.



VISUOSPATIAL ABILITIES

➢ Overlapping pentagons: Ask the subject to copy this diagram:

➢ Wire cube : Ask the subject to copy this drawing (for scoring, see instructions guide)

➢ Clock: Ask the subject to draw a clock face with numbers and the hands at ten past five.
(for scoring see instruction guide: circle = 1, numbers = 2, hands = 2 if all correct)

القدرات الإبصارية الفراغية

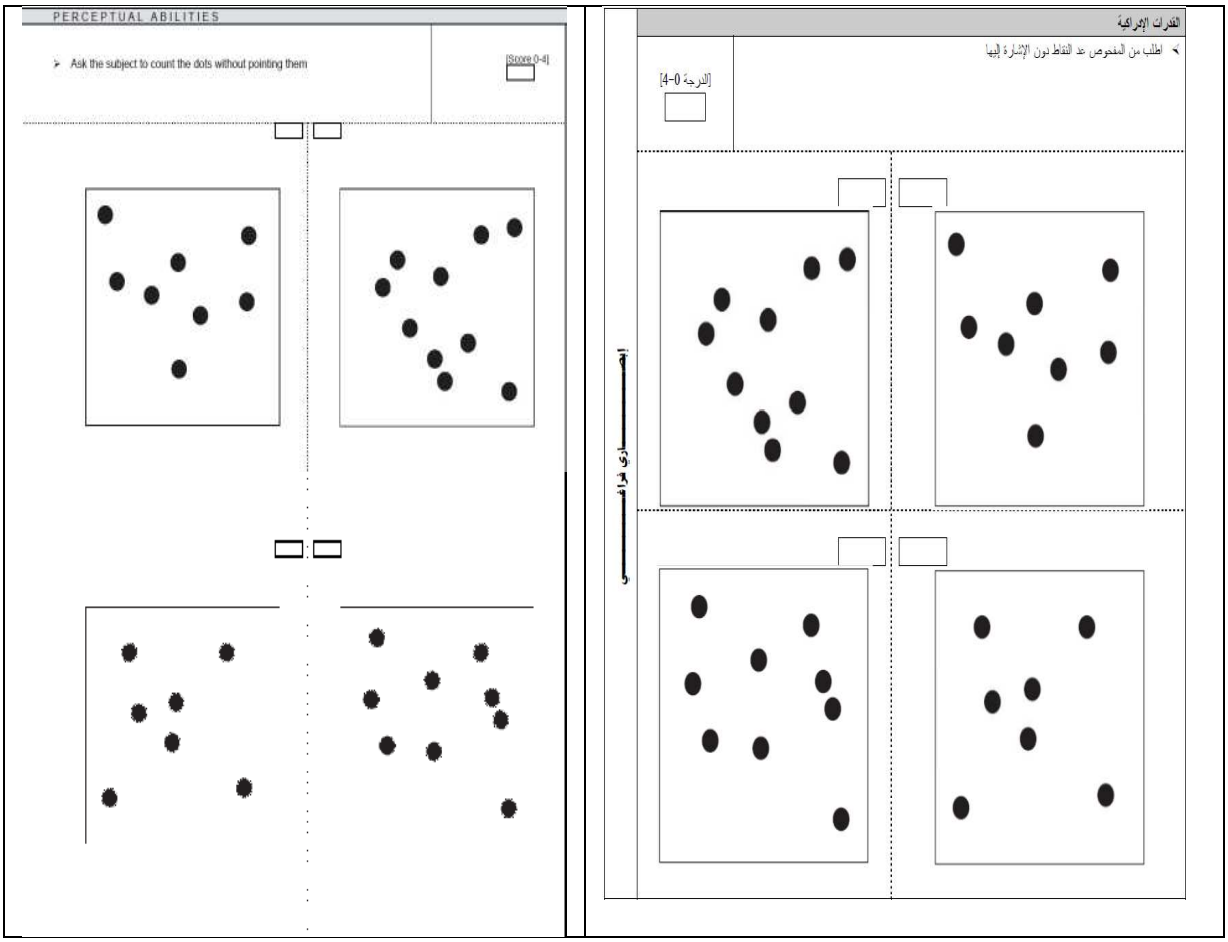
➢ شكلين خماسية متداخلة: اطلب من المفحوص نسخ هذا الرسم

➢ مكعب سلكي: اطلب من المفحوص نسخ هذا الرسم (لتسجيل الدرجات ، انظر دليل التعليمات)

➢ الساعة: اطلب من المفحوص رسم وجه ساعة بها أرقام وتوجد العقارب على الساعة الخامسة وعشر دقائق.
(لتسجيل الدرجات انظر دليل التعليمات : الدائرة– 1، الأرقام – 2، العقارب – 2 إذا كانت جميعها صحيحة)

2.3.15 Visuospatial abilities – Dot Counting

This task involves counting arrays of dots, a task that has been shown to be sensitive to deficits in single point localisation and visual scanning. The four figures from the original version were copied without any change (apart from change in page location so that the order of presentation was preserved for right to left ordering).



2.3.16 Visuospatial abilities – Fragmented letters

The original English version presents the letters K, M, A, T in a fragmented format, a task that has been shown to be sensitive to right posterior hemisphere lesions. Four marks are awarded. For the Arabic version, four Arabic letters were selected with the following conditions:

1) Not to be easily confused between them and other letters.
2) To have no dots (some Arabic letters have dots with the letter).
3) Not to create the impression with the fragmentation that there are dots over or under the letters.

Following many trials with different letters and the fragmentation process, the letters that were included were the Arabic equivalents of the letters M, L, H, and W.

2.3.17 Recall

This test involves recall of the name and address presented earlier, with a maximum of seven points. For the Arabic version, the format of the original task was retained (using of course the Arabic names/addresses)

Version A

RECALL

➢ Ask "Now tell me what you remember of that name and address we were repeating at the beginning"

Harry Barnes 73 Orchard Close Kingsbridge Devon	....	[Score 0-7]

النسخة أ

الاسترجاع

➢ اسأل "والآن أخبرني ما الذي تتذكره عن ذلك الاسم والعنوان اللذين كنا نكررهما في البداية"

أحمد خالد منزل رقم 73 حي الأمل شارع المنتبي الرياض	....	[الدرجة 0-7]

Version B

RECALL

➢ Ask "Now tell me what you remember of that name and address we were repeating at the beginning"

Linda Clark 59 Meadow Close Milford Surrey	....	[Score 0-7]

النسخة ب

الاسترجاع

➢ اسأل "والآن أخبرني ما الذي تتذكره عن ذلك الاسم والعنوان اللذين كنا نكررهما في البداية"

مها فالح منزل 59 حي الازدهار طريق البحر مكة	....	[الدرجة 0-7]

Version C

RECALL

➢ Ask "Now tell me what you remember of that name and address we were repeating at the beginning"

John Marshall 24 Market Street Spilsby Lincolnshire	....	[Score 0-7]

النسخة جـ

الاسترجاع

➢ اسأل "والآن أخبرني ما الذي تتذكره عن ذلك الاسم والعنوان اللذين كنا نكررهما في البداية"

ناصر سعد منزل 24 حي السعادة ممر النور الدمام	....	[الدرجة 0-7]

2.3.18 Recognition

In the original version, a recognition test is carried out if the participant fails one or more items in the recall task. Those items not recalled are then tested in a recognition format in which three alternatives are offered for each item and the participant is asked to select the correct item. For the Arabic version the format was retained, apart from replacement with culturally relevant options as per the recall task.

Version A

RECOGNITION

➢ This test should be done if subject failed to recall one or more items. If all items were recalled, skip the test and score 5. If only part is recalled start by ticking items recalled in the shadowed column on the right hand side. Then test not recalled items by telling "ok, I'll give you some hints: was the name X, Y or Z?" and so on. Each recognised item scores one point which is added to the point gained by recalling.

Jerry Barnes		Harry Barnes		Harry Bradford		recalled	
37		73		76		recalled	
Orchard Place		Oak Close		Orchard Close		recalled	
Oakhampton		Kingsbridge		Dartington		recalled	
Devon		Dorset		Somerset		recalled	

النسخة أ

الإدراك

➢ يجب إجراء هذا الاختبار إذا أخفق المفحوص في تذكر عنصر أو أكثر. وإذا تم تذكر جميع العناصر تخطي الاختبار وقم بتسجيل 5. وإذا تم فقط تذكر جزء ابدأ بوضع العناصر التي تذكرها في الخانة المظللة على الجانب الأيمن. ثم قم بإجراء اختبار حول العناصر التي لم يتم تذكرها بقولك "حسناً" سوف أعطيك بعض التلميحات: هل كان الاسم اكس أو واي أو زد؟ وما إلى ذلك؟ وتكون نتيجة كل عنصر تم تذكره (1) والتي يتم إضافتها للنقطة التي تم الحصول عليها بالتذكر.

حمد عايد	أحمد خالد	أحمد عبد الله	التذكر	
منزل 37	73	76	التذكر	
حي الأماني	حي التهاني	حي الأمل	التذكر	
طريق الأمانة	شارع المتنبي	شارع السعادة	التذكر	
الرياض	الجوف	الخرج	التذكر	

Version B

RECOGNITION

➢ This test should be done if subject failed to recall one or more items. If all items were recalled, skip the test and score 5. If only part is recalled start by ticking items recalled in the shadowed column on the right hand side. Then test not recalled items by telling "ok, I'll give you some hints: was the name X, Y or Z?" and so on. Each recognised item scores one point which is added to the point gained by recalling.

Laura Marshall		Linda Clark		Linda Crawford		recalled	
39		52		59		recalled	
Meadow Close		Gardens Close		Meadow Street		recalled	
Leatherhead		Milford		Redhill		recalled	
Hampshire		Sussex		Surrey		recalled	

النسخة ب

الإدراك

➢ يجب إجراء هذا الاختبار إذا أخفق المفحوص في تذكر عنصر أو أكثر. وإذا تم تذكر جميع العناصر تخطي الاختبار وقم بتسجيل 5. وإذا تم فقط تذكر جزء ابدأ بوضع العناصر التي تذكرها في الخانة المظللة على الجانب الأيمن. ثم قم بإجراء اختبار حول العناصر التي لم يتم تذكرها بقولك "حسناً" سوف أعطيك بعض التلميحات: هل كان الاسم اكس أو واي أو زد؟ وما إلى ذلك؟ وتكون نتيجة كل عنصر تم تذكره (1) والتي يتم إضافتها للنقطة التي تم الحصول عليها بالتذكر.

نوف صالح	مها فالح	نهى صلاح	التذكر	
منزل 39	52	59	التذكر	
حي الازدهار	حي النهار	حي الشاطئ	التذكر	
شارع النهر	طريق البحر	طريق المطار	التذكر	
تبوك	جدة	مكة	التذكر	

Version C

RECOGNITION

➢ This test should be done if subject failed to recall one or more items. If all items were recalled, skip the test and score 5. If only part is recalled start by ticking items recalled in the shadowed column on the right hand side. Then test not recalled items by telling "ok, I'll give you some hints: was the name X, Y or Z?" and so on. Each recognised item scores one point which is added to the point gained by recalling.

John Simons		John Marshall		Joseph Marshall		recalled	
42		28		24		recalled	
Market Street		High Street		Market Square		recalled	
Spilsby		Horncastle		Sleaford		recalled	
Northamptonshire		Lincolnshire		Leicestershire		recalled	

النسخة جـ`

الإدراك

➢ يجب إجراء هذا الاختبار إذا أخفق المفحوص في تذكر عنصر أو أكثر. وإذا تم تذكر جميع العناصر تخطي الاختبار وقم بتسجيل 5. وإذا تم فقط تذكر جزء ابدأ بوضع العناصر التي تذكرها في الخانة المظللة على الجانب الأيمن. ثم قم بإجراء اختبار حول العناصر التي لم يتم تذكرها بقولك "حسناً" سوف أعطيك بعض التلميحات: هل كان الاسم اكس أو واي أو زد؟ وما إلى ذلك؟ وتكون نتيجة كل عنصر تم تذكره (1) والتي يتم إضافتها للنقطة التي تم الحصول عليها بالتذكر.

نادر عبد الله	ناصر سعد	تركي حمد	التذكر	
منزل 42	28	24	التذكر	
حي السعادة	حي الشهادة	حي النفل	التذكر	
ممر النور	شارع النصر	طريق الصخور	التذكر	
حايل	الدمام	أبها	التذكر	

2.3 Subscale scores

In the original English version, from the individual tasks a total score and five subscale scores are calculated. The maximum total score is 100. The subscale scores are (1) Attention and Orientation (18 points); (2) Memory (26 points); (3) Fluency (14 points); (4) Language (26 points) and (5) Visuospatial (16 points). The same scoring system was used for the Arabic version of the test for use with literate participants.

2.4 Arabic ACE-R for literate and illiterate participants.

As discussed in Chapter 1, a major issue in relation to dementia assessment in many countries of the Arab region is low levels of education and literacy, something that is particularly relevant to older adults. Thus the intention was to examine whether the Arabic ACE-R is useful in assessing for dementia in people who are illiterate. A validation study addressing this question is presented in Chapter 5. For that study the Arabic ACE-R was administered excluding tests requiring reading or writing, which included: Fragmented Letters; Reading (Instruction & Irregular words); and Writing tasks. This meant that 7 points were excluded from the original 100 point test format. Thus for each domain of cognition examined the following maximum points were available:: attention/orientation (18 points), memory (26 points), fluency (14 points), language (23 points), visuospatial (12 points) and the maximum total score is 93.

2.5 Recruitment and assessment of participants

In order to recruit and assess a sufficient number of participants for the studies, participants were recruited from several hospitals and a large social centre for retired people in Riyadh, Saudi Arabia. Patient participants were recruited via hospitals including: King Fahad National Guard Hospital under the umbrella of King

Abdul-Aziz Medical City; King Khalid University Hospital under the umbrella of King Saud University; King Saud Medical Complex under the umbrella of the Ministry of Health; Dallah Hospital; and Almubarak Hospital. Patient participants who met the inclusion criteria were identified by Consultant Neurologists in each hospital. Healthy controls were recruited from amongst family and friends of patients at the hospitals and from Prince Salman Social Centre, Riyadh. Given the size of Riyadh, the number of hospitals from which recruitment was to take place and the number of participants that it was intended to recruit, it was impractical for the researcher alone to assess a sufficient number of participants required. Hence a number of research assistants were enlisted to assist with data collection. In order to do this, the researcher contacted the Neurological Departments of five hospitals and the biggest social centre for retired people to ask if staff members willing to act as research assistants could be identified. In this way, eighteen research assistants were identified, all of whom had experience of working in health or social care settings. The assistants were willing to become involved in the research as a modest remuneration was offered and the experience they would gain could also be beneficial to them in their future studies or careers. The researcher organized two one-day workshops for all the research assistants in order to ensure that they were aware of the purpose and of the research, to train them in the administration of the Arabic ACE-R and familiarise them with the ethics procedures associated with the study. The researcher held weekly supervision meetings with the assistants to ensure fidelity of the assessment process. This approach to data collection enabled a sufficient sample of participants to be assessed in both clinical and normative groups.

2.6 Conclusion

Much of the Arabic ACE-R was constructed by relatively straightforward direct translation of items from the original English version. As discussed earlier, it was noted by Mioshi et al (2006) that one of the aims of the modifications to the original ACE was to make a test that could be relatively easily translated/adapted to different languages and cultures. It would appear this aim was at least partially achieved. However, a number of tasks required adaptation to make them linguistically or culturally relevant for use with Arabic speakers, and in particular for application in Saudi Arabia. For some items, particularly those in the language domain, there were not straightforward equivalents and so attempts were made to develop tasks that would be consistent with the main purpose of the original task. The extent to which these tasks are useful in contributing to assessment of cognitive impairment (and hence assisting in the diagnosis of dementia) was examined in the validation studies.

In Chapter 3, the first validation study is reported. This examined the use of the Arabic ACE-R with literate participants, addressing the question of whether the test can distinguish between patients with a diagnosis of Mild Cognitive Impairment, dementia of the Alzheimer's type and healthy controls.

CHAPTER 3

Validity of the Arabic ACE-R with Literate Participants

Chapter 3: Validity of the Arabic ACE-R with Literate Participants

3.1 Introduction

Arabic is the official language of 26 countries and is the native language of more than 250 million people worldwide. However, there has been very little in the way of translation, adaptation and validation of Arabic forms of neuropsychological instruments. The Addenbrookes Cognitive Examination- Revised (ACE-R) is a brief cognitive screening tool that has been well validated in relation to the assessment of cognitive impairments associated with dementia. The present study involved the translation, adaptation and validation of an Arabic ACE-R. The study involved data collection from both literate and non-literate participants. In this chapter, data from the literate participants will be presented and the validity of the Arabic ACE-R was examined. Data on non-literate participants will be reported in Chapter 5. The ACE-R has been demonstrated to be sensitive to the early stages of dementia. In the present study a three groups of participants were included – participants with a diagnosis of dementia, participants with a diagnosis of Mild Cognitive Impairment (MCI) and a group of healthy control participants. The study investigated whether the Arabic ACE-R is able to distinguish between healthy controls, patients with dementia and patients with MCI. The study also examined the sensitivity, specificity, positive predictive value and negative predictive values for optimal cut off points identified through Receiver Operating Curve (ROC) analysis. It was hypothesised that Arabic ACE-R total scores would be significantly different between healthy controls, people with a diagnosis of dementia and people with a diagnosis of Mild Cognitive Impairment. Furthermore it was hypothesised that the area under the curve data would reflect at least good separation of healthy controls from patients with a diagnosis of dementia or mild cognitive impairment.

3.2 Method

3.2.1 Participants

Data was collected from three samples: (1) Healthy literate participants (N=147); (2) Literate participants with a clinical diagnosis of dementia of the Alzheimer's type (DAT) (N=44). (3) Literate participants with a clinical diagnosis of Mild Cognitive Impairment (MCI) (N=10). Independent neurologists who were blind to Arabic ACE-R scores made the clinical diagnoses. Diagnosis of dementia was made on the basis of ICD 10 criteria. Diagnosis of MCI was based on criteria of patients' subjective complaints of memory impairment, where possible corroborated by a relative, essentially preserved activities of daily living and not meeting criteria for dementia (Petersen and Morris, 2005).

Participants were 50 years of age or older, had Arabic as their first language, had adequate vision and hearing to complete the assessment, and no history of substance abuse (alcohol or drugs) or previous psychiatric disorder.

Patient participants were recruited via hospitals in Riyad, Saudi Arabia including: King Fahad National Guard Hospital under the umbrella of King Abdul-Aziz Medical City; King Khalid University Hospital under the umbrella of King Saud University; King Saud Medical Complex under the umbrella of the Ministry of Health; Dallah Hospital; and Almubarak Hospital. Healthy controls were recruited from amongst family and friends of patients at the hospitals and from Prince Salman Social Centre, Riyadh.

Demographic information including age, gender, handedness, and level of education were collected from each participant.

Ethical approval for the study was granted by the University of Glasgow Faculty of Medicine Ethics committee and approval was also gained from each of the participating hospitals. Participants were provided with an information sheet detailing the study. Following the opportunity to read the sheet and ask questions about the study, participants gave written consent to participate. The Arabic ACE-R was then administered.

3.2.2 The Arabic ACE-R

The ACE-R consists of 5 sub-scales. Each sub-scale concentrates on one cognitive dementia as follows: attention/orientation (18 points), memory (26 points), fluency (14 points), language (26 points), visuopatial (16 points) and the highest score is 100.

The ACE-R was translated into Arabic (and back-translated by independent translators to check for accuracy). Some items were adapted for use in an Arabic cultural context. Consistent with the original version in English, three different versions were developed (Version A; Version B and Version C), which differ just in terms of the name and address used for the memory recall task. A detailed description of the translation and adaptation process is provided in Chapter 2.

The Arabic ACE-R, like the original, usually takes about 15 to 20 minutes to administer. The version of the tool to use with each person was randomised. Detailed comparisons of performance on the different versions are presented in Chapter 7.

3.3 Results

Initially, 147 healthy controls, 44 DAT and 10 MCI patients were recruited. Demographic data collected included age, gender, handedness and level of education achieved. In relation to level of education, an ordinal scale of different levels of education was developed in order to compare highest level of education achieved between groups of participants. This went from 0 (no education) through to 11 (PhD), and is shown in Table 3.1. Demographic data on the participants are presented in Table 3.2.

Table 3.1: Ordinal scale reflecting different levels of education achieved

Level	Level of education
0	No education
1	Attended some elementary school
2	Completed elementary school
3	Attended some intermediate school
4	Completed intermediate school
5	Attended some of high school
6	Completed high school
7	Diploma
8	Batchelors
9	Higher Diploma
10	Masters
11	PhD

Table 3.2: Demographic data on initial samples of literate participants

	Healthy	MCI	DAT
Number	147	10	44
Gender m/f	115/32	8/2	31/13
Mean (S.D) age	61.41 (7.55)	64.00 (7.42)	64.45 (6.82)
Education (median)	6	5	4
Handedness R/L	121/26	7/3	33/11

Figure 3.1 presents a histogram of the distribution of Arabic ACE-R total scores across the whole sample.

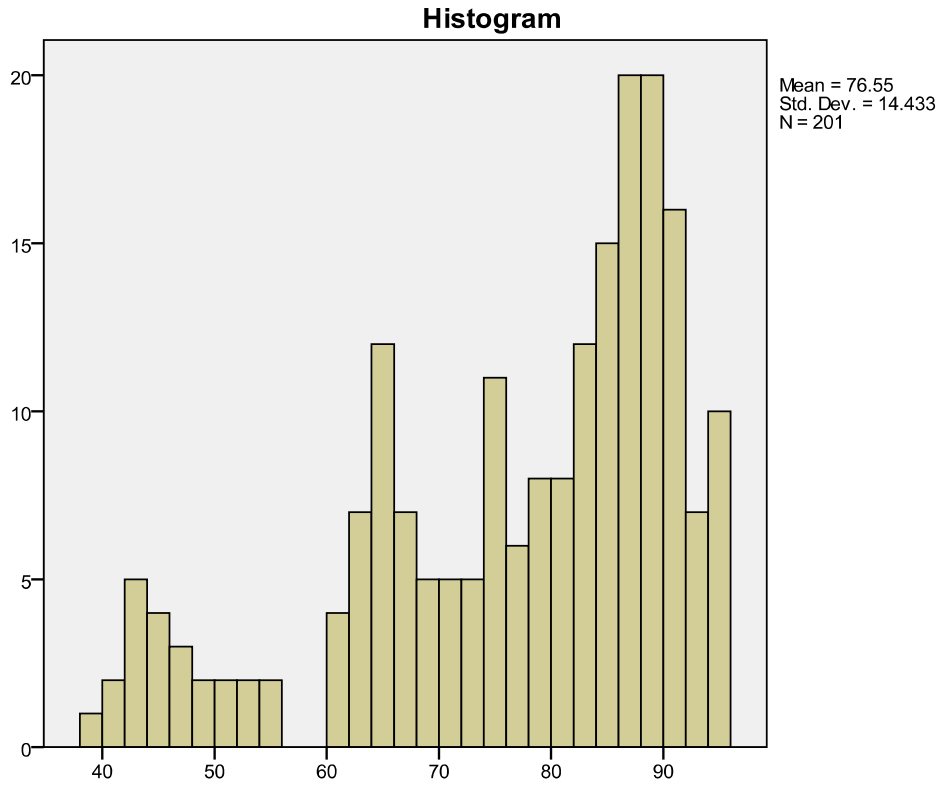


Figure 3.1 Histogram of the distribution of ACE-R total scores across the whole sample

An examination of the distribution of the Arabic ACE-R total score data for the healthy controls showed that the distribution was not normally distributed (Shapiro Wilk =0.951, p<0.001). Given that the data did not meet assumptions for parametric data analyses, and given that one of the groups was very small, non-parametric analyses were undertaken in subsequent analyses.

Krushkal Wallis analysis showed that there was a significant difference in the ages of the different the groups (Chi-square = 7.83; df=2, p=0.020). Therefore the question of whether there was a relationship between age and performance on the primary outcome measure (Arabic ACE-R total score) was examined. Correlation analysis for the healthy control data showed that there was a significant correlation

between age and Arabic ACE-R total (rho= -0.568, p<0.001). However, given that non-parametric analysis was to be performed, it was not possible to simply include age as a covariate in analyses.

In order therefore to compare groups without the confounding effect of age, it was necessary to match the groups more closely in terms of age. A much larger number of healthy control participants had been recruited in order to collect normative data for the test and this included a number of people between the ages of 50 and 55, of whom there were almost none in the patient sample. Therefore participants in the healthy control sample under the age of 55 were removed. The age of 55 was selected as the cut off point as all of the patient participants apart from one were above this age. One participant with a diagnosis of dementia who was considerably older than any controls was also removed. Table 3.3 presents data on the revised samples.

Table 3.3: Demographic data on revised samples of literate participants

	Healthy	**MCI**	**DAT**
Number	129	10	43
Gender m/f	102/27	8/2	30/13
Mean (S.D) age	62.77 (7.05)	64.00 (7.42)	64.09 (6.46)
Education (median)	6	5	4
Handedness R/L	104/25	7/3	32/11

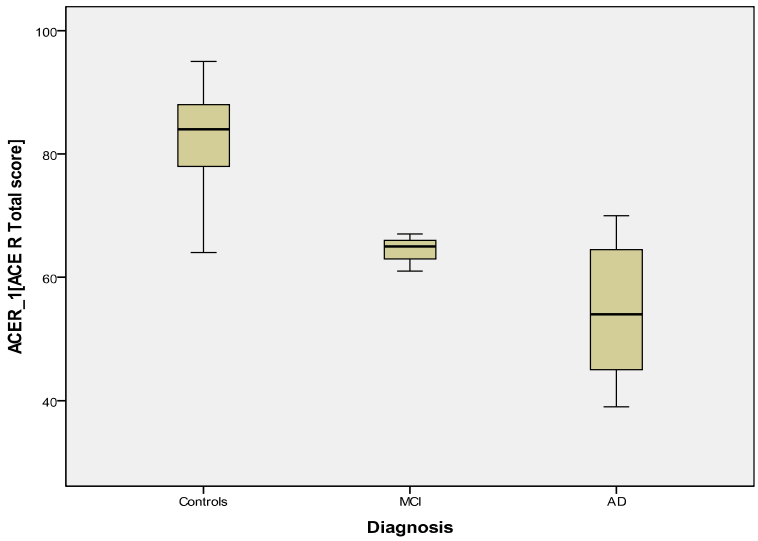
In the revised sample there was no difference in age between the groups (Chi-square=2.229, df=2, p=0.328). There was also no significant difference in level of education (Chi-square =5.416, df=2, p=0.067) or gender ratio (Chi Squared= 1.629, df=2, p=0.443) or handedness (Chi Squared= 1.200, df=2, p=0.549).

Table 3.4 presents the median scores for performance of each of the groups on the Arabic ACE-R and the Arabic ACE-R subscales. Figures 3.2 – 3.7 provide boxplots for the data on Arabic ACE-R Total and subscale scores.

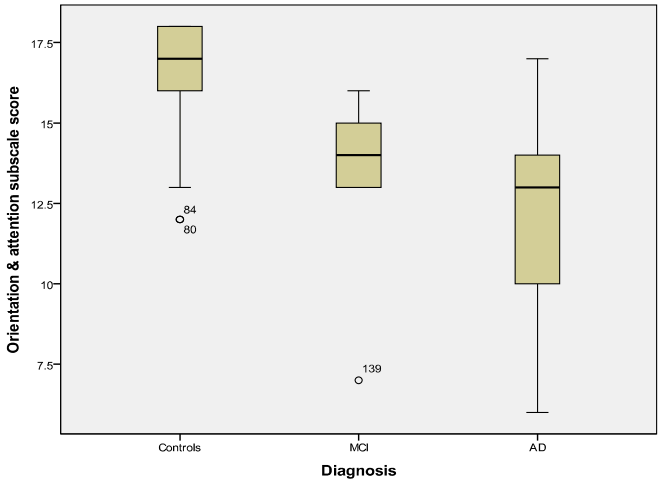
Table 3.4: Median scores for performance of each group on the Arabic ACE-R Total and the Arabic ACE-R sub-scales.

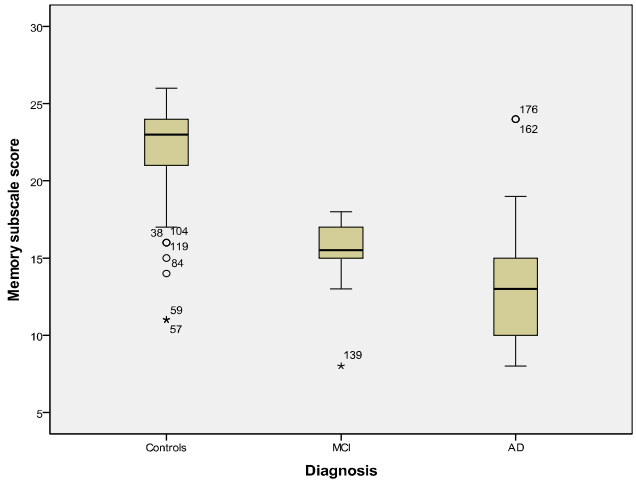
Test	Healthy	MCI	DAT
Arabic ACE-R Total (Max=100)	84	65	54
Arabic ACE-R Attention & Orientation (Max = 18)	18	13	12
Arabic ACE-R Memory (Max=26)	23	16	12
Arabic ACE-R Fluency (Max=14)	7	6	6
Arabic ACE-R Language (Max=26)	24	19.50	19
Arabic ACE-R Visuospatial (Max=16)	13	8	6

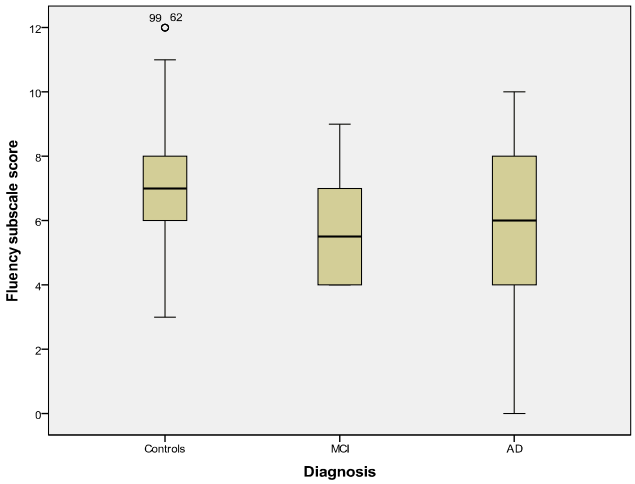
Figure 3.2 Boxplot for Arabic ACE-R data showing median, lower and upper quartiles, and largest values that are not outliers.

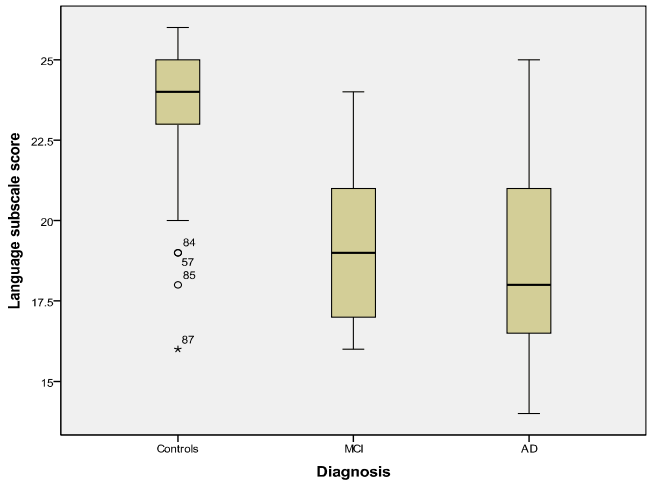


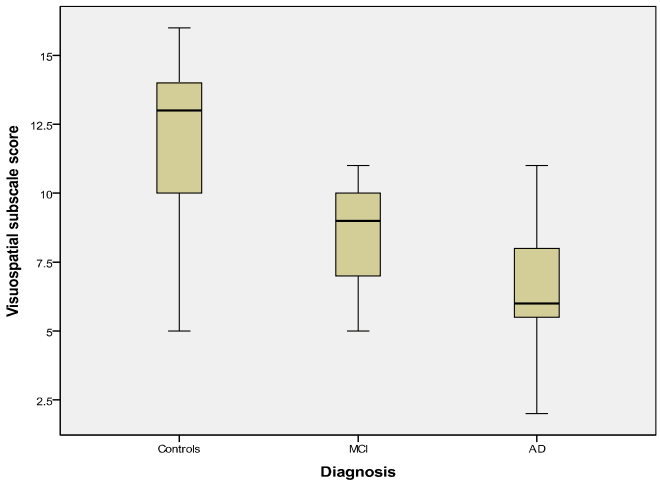
Figures 3.3 – 3.7 Boxplots for Arabic ACE-R sub-scale data showing median, lower and upper quartiles, largest values that are not outliers, outliers (defined as more than 1.5 box lengths above or below the box and marked with a o) and extreme cases (defined as more than 3 box-lengths above or below the box and marked with a *).











Consistent with negative skew of the total score, it is clear from the boxplots that several subscale scores were negatively skewed towards a ceiling for the healthy controls. This was particularly evident for the Orientation, Language and Visuospatial subscales. Within the language scale, the naming test was relatively easy for healthy controls, with most scoring near full marks. However, there was a much wider range of performance amongst patient participants, as one would expect. The range of scores for the MCI patients was much smaller than for the other two groups, though this sample only consisted of 10 participants and therefore chance sampling may account for this finding.

Krushkal-Wallis analysis comparing the three groups showed significant differences on all of the test measures ($p<0.001$). Results from the post-hoc analysis using Mann-Whitney tests to examine differences between each of the pairs of groups are shown in Table 3.5. The table also shows effect sizes (r) for each of the differences.

Table 3.5: Results from the post-hoc analysis using Mann-Whitney tests to examine differences between each of the pairs of groups

Test	Healthy vs MCI	Healthy vs DAT	MCI vs DAT
Arabic ACE-R Total	Z= -4.990** r=.423	Z= -9.476** r=.722	Z= -2.449* r=.336
Arabic ACE-R Attention & Orientation	Z= -4.158** r=.352	Z= -8.082** r=.616	Z= -1.583 ns r=.217
Arabic ACE-R Memory	Z= -4.569** r=.387	Z= -8.163** r=.622	Z= -2.057* r=.282
Arabic ACE-R Fluency	Z= -2.714** r=.230	Z= -3.038** r=.231	Z= -0.471 ns r=.064
Arabic ACE-R Language	Z= -4.342** r=.368	Z= -7.811** r=.595	Z= -0.343 ns r=.047
Arabic ACE-R Visuospatial	Z= -2.970** r=.251	Z= -7.428** r=.566	Z= -2.247* r=.308

**p<0.05 ** p<0.01 ns = not significant*

To explore the sensitivity and specificity of specific cut-off points on the Arabic ACE-R to detection of cognitive impairment associated with dementia and mild cognitive impairment, a series of Receiver Operating Curve (ROC) Analyses were

undertaken. Two different ROC analyses were undertaken. The first examined the separation of healthy controls from all the patients combined (i.e. separating controls from DAT/MCI combined). The second examined the separation of DAT patients and MCI patients. For these analyses, Arabic ACE-R totals were used.

3.3.1 Healthy Controls vs Patients (MCI/DAT)

Figure 3.8 shows the ROC curves (Sensitivity plotted against 1-specificity) for the Arabic ACE-R Total score. The Area Under the Curve analysis statistic for the Arabic ACE-R was 0.991 which reflects the strong separation of the positive cases (DAT/MCI) from the healthy controls.

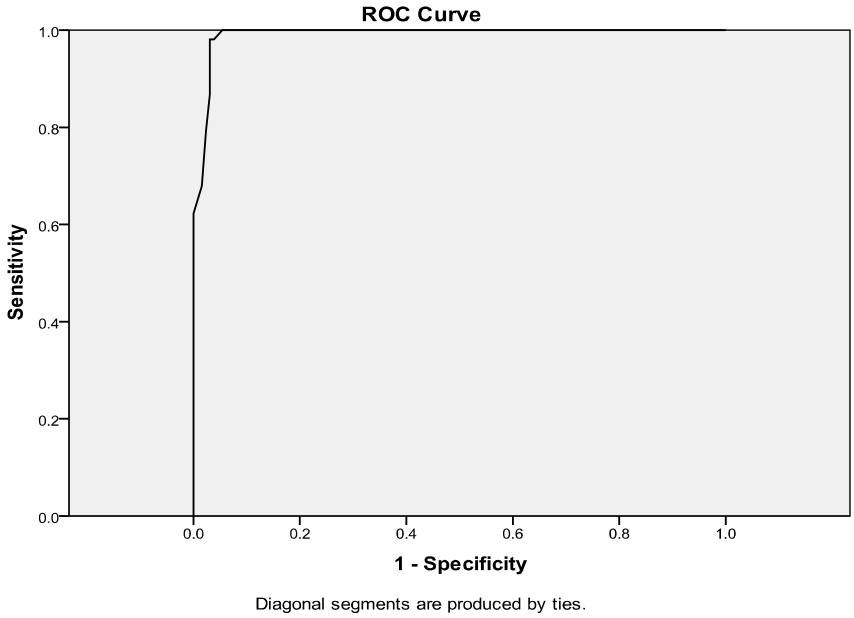


Figure 3.8 ROC curve for the ACE-R Total score comparing healthy controls with patients (MCI/DAT)

The ROC analysis demonstrated that a cut-off point of 70 on the ACE-R had a sensitivity of 1.000 and specificity of 0.946, reflecting the excellent separation of patients and controls. However, it also reflects some overlap for a small number of participants.

3.3.2 MCI vs DAT

Figure 3.9 shows the ROC curves for the ACE-R Total score. The Area Under the Curve analysis statistic was 0.750 reflecting fair separation of the positive cases (dementia) from the MCI patients (albeit much weaker than the separation between controls and DA/MCI combined).

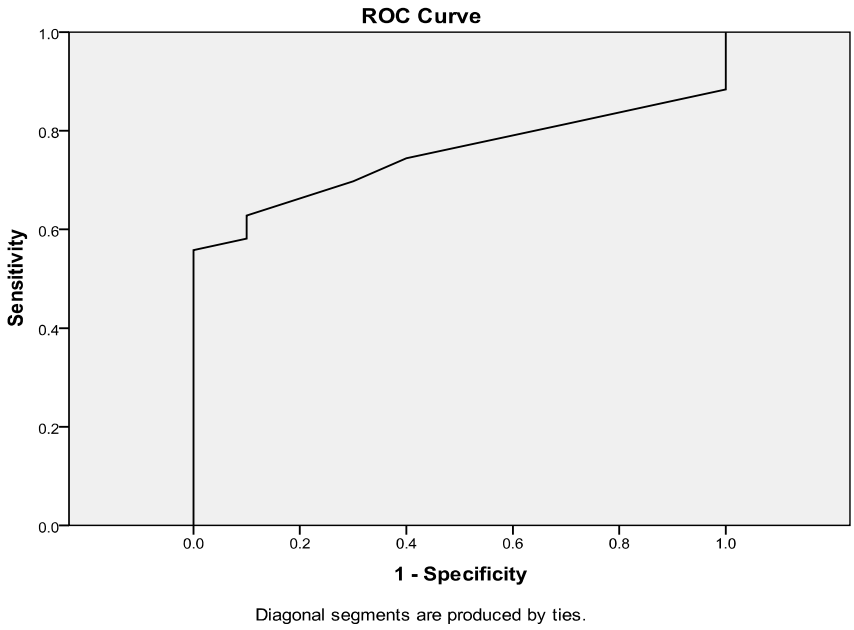


Figure 3.9 ROC curves for the ACE-R Total score comparing MCI and DAT patients

The ROC analysis demonstrated that a cut-off point of 63 on the ACE-R had a sensitivity of 0.698 and specificity of 0.700, reflecting a relatively poor separation of DAT patients from the MCI with much overlap of scores for participants.

Given that it had been demonstrated that there was a relationship between Arabic ACE-R performance and age, further analyses were undertaken on separate age bands. Table 3.6 therefore presents the results of ROC analyses including Area Under the Curve statistics, cut-off points and their associated sensitivities and specificities for each of two age bands (<60 years and ≥60 years). For the ≥60

years group data relating to two cut-off points are presented to illustrate the impact on sensitivity and specificity of varying cut points.

Table 3.6: ROC analyses including Area Under the Curve statistics, cut-off points and their associated sensitivities for each of two age bands (<60 years and ≥60 years).

	Area under curve	Cut off	Sensitivity	Specificity
<60 years	0.999	68	0.929	1.000
≥60 years	0.986	69	1.000	0.947
		65	0.821	0.960

In addition to calculation of sensitivity and specificity, positive and negative predictive values were also calculated. The positive predictive value (PPV), sometimes called the post-test probability, refers to the probability that an individual who is predicted by a test to have the condition of interest actually has the condition. The negative predictive value (NPV) refers to the probability that a test is correct when it predicts that the condition is absent (Smith, Ivnik and Lucas, 2008). Unlike sensitivity and specificity, positive and negative predictive values are influenced by the base rate (BR) of the condition of interest. The base rate is the proportion of people in the population, or a relevant reference sample, who have the condition of interest (i.e. the prevalence of the condition). The relevant reference sample depends on the nature of the context in which testing is taking place. For example, if assessment is taking place in the context of a memory clinic where quite a large proportion of people being tested will have the condition of interest (e.g. dementia) the base rate will be quite high. However if testing is taking place as part of some form of population level sampling (e.g. a large survey of an entire

community), then the base rate will be much lower, and closer the actual prevalence in the population as a whole.

Positive predictive value and negative predictive value are related to sensitivity (Sn), specificity (Sp) and base rate (BR) as follows:

$$PPV = BR*Sn / \{(BR*Sn) + [(1-BR)*(1-Sp)]\}$$

$$NPV = (1-BR)*Sp / \{[(1-BR)*Sp] + [BR*(1-Sn)]\}$$

The question therefore arises as to what is the most appropriate base rate figure to use. Mioshi et al. (2006) presented data for a range of base-rates that would reflect possible base rates in different contexts, ranging from 5% to 40%. As noted in Chapter 1, data on prevalence of dementia in Saudi Arabia is scarce. In Bowirrat et al.'s (2001) study of the prevalence of dementia in an elderly Arab Israeli population, prevalence ranged from 8% in those under 70 to 51% in those over 80. Here we therefore present PPV and NPV figures for base rates ranging from 5% to 50%. The upper figure is likely to be closer to the base rate for presentation within a memory clinic context. Table 3.7 provides PPV data for the sample as a whole and for each age band, based on sensitivity and specificity data obtained from the samples and Table 3.8 provides NPV data for the sample as a whole and for each age band.

Table 3.7 PPV data for the sample as a whole and for each age band, based on sensitivity and specificity data obtained from the samples.

Age Bands	ACE-R Cut offs	Sensitivity/ Specificity	Positive Predictive Value at different rates				
			5%	10%	20%	40%	50%
Whole sample	70	1.000/0.946	0.494	0.673	0.822	0.925	0.949
<60yrs	68	0.929/1.000	1.000	1.000	1.000	1.000	1.000
≥60yrs	69	1.000/0.947	0.498	0.677	0.825	0.926	0.950
	65	0.821/0.960	0.519	0.695	0.836	0.931	0.953

Table 3.8 NPV data for the sample as a whole and for each age band, based on sensitivity and specificity data obtained from the samples.

Age Bands	ACE-R Cut offs	Sensitivity/ Specificity	Negative Predictive Value at different rates				
			5%	10%	20%	40%	50%
Whole sample	70	1.000/0.946	1.000	1.000	1.000	1.000	1.000
<60yrs	68	0.929/1.000	0.996	0.992	0.982	0.954	0.933
≥60yrs	69	1.000/0.947	1.000	1.000	1.000	1.000	1.000
	65	0.821/0.960	0.990	0.979	0.955	0.889	0.842

3.4 Discussion

This study investigated the validity of an Arabic version of the ACE-R. The results of the study suggest that the Arabic ACE-R is a valid tool for the assessment of dementia in Arabic-speaking people. There were significant differences between each of the three groups examined – Mild Cognitive Impairment, Dementia of the Alzheimer's type and healthy controls. As the MCI group was small, Receiver Operating Curve (ROC) analyses were conducted on the combined MCI/DAT group

compared with the healthy control group. Levels of sensitivity/specificity were high. For a cut-off point of 70 (70 or below indicating presence of disease), sensitivity was 1.000 and specificity was 0.946. The positive and negative predictive values (PPV and NPV) were also high, particularly for base rates that are likely to be closer to those found in clinical practice (e.g. in a memory clinic) where a relatively large proportion of people referred are likely to have dementia, at least compared to wider population levels. At lower levels of the base rate such as the 5% rate, PPV levels drop considerably (to 0.494 for the whole sample) though NPV levels remained robust (1.000 for the whole sample, dropping to 0.990 for the 65 cut off point in the ≥60 year old group). These data highlight that as base rates drop, the proportion of people predicted by a test such as the Arabic ACE-R to have dementia who actually have the condition will drop considerably. However, as noted, the most common situations in which a test such as the Arabic ACE-R will be used are clinical situations where the actual base rates are considerably higher.

It is notable that the cut-offs are lower than those of the original validation study for the ACE-R (Mioshi et al., 2006) or for some of the translated/adapted versions. For example, in Mioshi et al.'s (2006) study, which was in Cambridge, UK, data for two cut-off points (88 and 82) were provided as sensitivity/specificities differed between them - the sensitivity of the cut-off 88 was 0.94 and the specificity was 0.89, while the sensitivity of 82 was 0.84 and the specificity 1.00. In Yoshida et al. (2011) which was examining a Japanese version, the cut-offs point suggested were 88/89 for MCI and 82/83 for Dementia. The sensitivity of 88/89 was 0.87 and the specificity was 0.92 while the sensitivity of 82/83 was reported to be 0.99 and the specificity was 0.99. For the Korean version (Kwak et al., 2010), the optimal cut-off was slightly lower at 78 (sensitivity 0.93; specificity 0.95). The mean/median score on the Arabic ACE-R for healthy controls (mean 83.8, median 85) is lower than for

the UK sample (mean 93.7) and Japanese sample (mean 93.3) but similar to the Korean sample (mean 80.7). There would appear to be several possible reasons for the lower scores on the Arabic ACE-R (at least as compared with the UK and Japanese samples). One possibility is that the adapted items are more difficult than the originals. The original ACE-R is relatively easy for most healthy controls (hence a mean score that is not far off the maximum possible) and so this potentially masks a wider range of ability amongst healthy controls within the cognitive domains being examined. If the Arabic ACE-R items are more challenging, then one might expect a wider range of performance (which was evident) and hence an overall lower level. Another potential explanation is that the sample of Saudi healthy controls has a wider range of general intellectual ability/education that limits performance on the test. Given that levels of education, particularly amongst older Saudis are lower than those of people in the UK and Japan, it may be that education and a familiarity with tests of this sort played a part in the lower performance on the task. In terms of 'difficulty', some tasks (e.g. Orientation, Naming) were in fact apparently easy, at least for healthy controls who showed strongly skewed data, with close to ceiling performance for many people. For the Memory and Fluency subscales the scores amongst healthy controls were not at ceiling. The Memory subscale data was negatively skewed in controls, but showed a relatively long tail. For Fluency the data were normally distributed and off the ceiling (and floor) for all groups. Although the overall performance of healthy controls was lower in terms of total scores, the sensitivity/specificity of the Arabic ACE-R remained high. Again here this was in part because the scores from the patient groups were substantially lower than the controls, so separating them with very little overlap. One issue relevant to this finding is that only a small number of people with a diagnosis of MCI were recruited, and most people who took part already had a diagnosis of dementia. Within Saudi

culture, there is a strong tradition within families of caring for elderly relatives and it may therefore be that people tend to present to services somewhat later than people might in countries such as the UK and Japan. Development of services and awareness of dementia may also be less in Saudi Arabia. Furthermore, a wider lack of awareness of the symptoms of dementia may again mean that changes are not recognized as potentially abnormal. Bener and Ghuloum (2011) noted that stigma associated with mental illness is particularly high in the Middle East. In a study of 3,300 Qatari and other Arab expatriates they concluded that knowledge of common mental illnesses was generally poor and this was particularly the case amongst women in their sample. Thus there would appear to be multiple reasons why people who are beginning to experience symptoms of dementia may not present to services until there is clear impairment or functional difficulties. It may therefore be that for this reason the patients who took part in this study were not at the very earliest stages of dementia (albeit some of the MCI patients were) and this contributed to clear separation of the patient group from the healthy control group. Other measures of severity of dementia were not available during this study, though it would have been useful to have some other measure of severity of impairment and functional disability such as the Clinical Dementia Rating Scale (Hughes et al., 1982) to provide some comparison with studies from other countries. In time as services, and awareness of those services develop, it would be useful to re-examine the sensitivity/specificity of the Arabic ACE-R. Another approach to defining impairment on cognitive tests is by defining a percentile value of healthy controls' performance (most commonly the 5th percentile) as a cut-off for impairment. This approach is examined in Chapter 7.

Although overall scores for the Arabic ACE-R were lower than the original English version, the Arabic ACE-R also showed a skewed distribution amongst the healthy

participants, with the majority of scoring towards the top end of the scale. Whilst not quite showing a ceiling effect, it does suggest that the majority of participants can do most of the scale with relatively little difficulty. Most cognitive abilities (e.g. memory) show a range of performance in the healthy population when the challenge is greater (e.g. in memory tasks using more items such as in story recall or word list tasks). What this may mean is that the scale may not be sensitive to mild impairments in a cognitive ability. This may not be a problem if the task is to identify the presence of dementia (i.e. sufficient impairment of cognition to impact on the ability to carry out everyday activities) but may mean that the test is insensitive to mild impairment. In the present study all patient participants had a diagnosis of either MCI or DAT, but there were only 10 MCI cases. Hence, it is difficult to draw firm conclusions regarding the diagnostic sensitivity/specificity of the Arabic ACE-R to MCI. However the overall pattern of performance of the different participant groups was broadly similar to previous studies. Consistent with what one would expect (Mioshi et al., 2006; De jager et al., 2003; Grundman et al., 2004) it was the memory subscale that showed the largest difference of all the subscales when the MCI group were compared with the healthy controls, though there were significant group differences between the MCI group and the healthy controls on all of the subscales, which suggests that although this group of 10 participants had a diagnosis of MCI, it is possible that they were not at the very earliest stages of a progressive process. This again suggests that further research is needed to examine the sensitivity of the test to the very early stages of MCI/dementia.

It was noteworthy that the Fluency subscale, which combines letter fluency and category fluency showed the lowest difference between the groups. This was a little surprising as verbal fluency is considered to reflect, to some extent, executive functions, and category fluency reflects semantic memory integrity, both of which

may be affected in dementia (Hall et al., 2012), though to the best of our knowledge this has not been formally demonstrated in Arabic speakers. Amongst the groups there was a wide range of performance on these tasks with no ceiling or floor effects apparent. As noted in Chapter 2, the Arabic letter *meem* was selected as it is a relatively high frequency first letter in Arabic words (Khalil, 2010). One possibility therefore was that the letter choice made the task too easy and hence non-discriminating. However, as noted there was no ceiling effect with a wide range of performance amongst healthy controls. In relation to category fluency, the performance of healthy controls was broadly similar to normative data from healthy English speakers with up to 8 years of education, and a little lower than more educated English speakers (see Strauss, Sherman and Spreen, 2006, p 510). It is therefore not clear why this subscale did not show greater sensitivity to dementia and this is an area that would benefit from further investigation.

Some observations on the test items also emerged from testing participants, highlighting some of the challenges of adapting existing tools to a new cultural context. For example, on the orientation task, a question about the season was retained from the original English, but within the context of Saudi Arabia it is the case that seasons are perhaps a less distinct concept than in Western Europe because of the nature of the environment and desert climate. In fact, there are only two very clear seasons, winter and summer. Whilst autumn and spring can be defined in the region, they are less distinct and shorter periods than elsewhere. Furthermore, given that the Islamic calendar is tied to movement of the moon rather than movement around the sun, this means that particular seasons are not as clearly linked to a particular time in the calendar in the way they are with a Gregorian calendar. This again means that the concept of a season may be considered less strong than in other countries. Thus scoring was essentially

adjusted so that a response of winter or summer was accepted as long as the answer was consistent with the weather in the transition period between summer and winter (and vice-versa).

A major advantage of the ACE-R over other briefer cognitive screening tools is that it examines more domains of cognition than many others whilst still remaining relatively brief to administer (Cullen et al., 2007). However it should be acknowledged that it is nevertheless still longer than some other tests, taking about 15-20 minutes to administer compared to the five minutes or less for some tests such as the Mini Mental State Examination. As noted already, the present study included participants with memory impairments (by virtue of having a diagnosis of MCI or DAT), and so were not presenting with other forms of more focal dementia such as fronto-temporal dementia (behavioural variant or semantic dementia) or some of the more posterior dementias that tend to present with deficits in visuospatial functioning. It is likely that a tool such as the ACE-R (and the Arabic ACE-R) would be more sensitive to subtle language, perceptual or executive functions than briefer tools, but this remains to be demonstrated in the Arabic ACE-R.

The present study was limited to literate participants, but as noted in Chapter 1, a large proportion of the population of Saudi Arabia (and the wider Arab world) are not literate. There is also evidence of increased rates of dementia in non-literate populations. Therefore there is a need for assessment tools that can be used with people who are illiterate and this was the focus of the study presented in Chapter 5.

This chapter has provided evidence for the validity of the Arabic ACE-R. For a test to be useful it is also necessary to demonstrate that it is reliable. The following chapter examines the reliability of the Arabic ACE-R in a literate sample.

CHAPTER 4

Reliability of the Arabic ACE-R with Literate Participants

Chapter 4: Reliability of the Arabic ACE-R in Literate Participants

4.1 Introduction

This Chapter examines the reliability of the Arabic ACE-R. Two samples of participants were studied, a group of healthy adults and a group of participants with a diagnosis of either Mild Cognitive Impairment or Dementia.

Reliability refers to the consistency of a test, or 'the regularity with which it [the test] generates the same score under similar retest conditions or the regularity with which different parts of a test produce similar findings' (Lezak, et al., 2004, p.109). It is critical that a test is shown to be both valid *and* reliable if it is to be useful in clinical practice. The greater the reliability of a test, the more confident one can be in a person's score on any one occasion. Given the importance of an assessment for evidence of cognitive impairment that may be associated with a progressive disease such as Alzheimer's disease, it is vital that an individual test score is as close as possible to the true score for that person at that time. Furthermore, tests such as the Addenbrookes Cognitive Examination may be used to measure decline over time to support a diagnosis of a progressive condition, or as means of measuring stability (or even possibly improvement) in the context of therapeutic interventions such as treatment with cholinesterase inhibitors. To measure change, or possibly lack of change, over time, a reliable measure is required, otherwise fluctuations in test scores may be interpreted as real changes, but in fact just reflect measurement error.

There are various forms of reliability that can be examined. These include inter-rater, test-retest, parallel form and internal reliability. Parallel form reliability refers to the correlation between scores on two different forms of a test. Internal reliability

refers to the consistency with which items within a test or test battery produce similar findings and is commonly measured using Cronbach's alpha. To date in the literature, to the best of our knowledge only internal consistency has been examined in relation to the original English version, with Mioshi et al. (2006) reporting a Cronbach alpha of 0.8. For the Korean version (Kwak et al., 2010) the Cronbach alpha was reported to be 0.84. For the Japanese version, Yoshida et al. (2012) found Cronbach alpha to be 0.903. Yoshida et al. also examined inter-rater reliability which was reported to be good (intraclass correlation coefficient 0.999). Test-retest reliability was also examined by testing 21 participants (two controls, four MCI and 15 AD patients) four weeks after first testing. It is not stated whether the same version of the test was used or whether a parallel version was administered on the second occasion. Results showed good test-retest reliability (ICC = 0.833).

The present study examined the parallel form reliability and internal reliability of the Arabic ACE-R.

4.2 Method

4.2.1 Participants

The participants for this study were the same as those described in Chapter 3. Data was collected from three samples: (1) Healthy literate participants (N=147); (2) Literate participants with a clinical diagnosis of dementia of the Alzheimer's type (DAT) (N=44). (3) Literate participants with a clinical diagnosis of Mild Cognitive Impairment (MCI) (N=10). For the purpose of the present study, given that the MCI group was small, data from this group was combined with the data from the AD group. Diagnosis was made on the basis of ICD 10 criteria by independent neurologists who were blind to Arabic ACE-R scores.

Participants were 50 years of age or older, had Arabic as their first language, had adequate vision and hearing to complete the assessment, and no history of substance abuse (alcohol or drugs) or previous psychiatric disorder.

Patient participants were recruited via hospitals in Riyadh, Saudi Arabia including: King Fahad National Guard Hospital under the umbrella of King Abdul-Aziz Medical City; King Khalid University Hospital under the umbrella of King Saud University; King Saud Medical Complex under the umbrella of the Ministry of Health, Dallah Hospital, and Almubarak Hospital. Healthy controls were recruited from amongst family and friends of patients at the hospitals and from Prince Salman Social Centre.

Ethical approval for the study was granted by the University of Glasgow Faculty of Medicine Ethics committee and approval was also gained from each of the participating hospitals.

4.2.2 The Arabic ACE-R

Development of the Arabic ACE-R was described in Chapter 2. As previously noted, three versions (A, B & C) were developed. Each version has same format and much of the content is similar. However, consistent with the original version (Mioshi et al., 2006) each version has different information for the anterograde memory task which involves remembering a name and address. All other items are the same in each version.

4.2.3 Procedure

Following completion of informed consent procedures and recoding of basic demographic information, the Arabic ACE-R was administered. The version

administered first was selected at random from the three versions. Administration takes about 15-20 minutes on average. Participants were then invited to return approximately one week later. A different version of the Arabic ACE-R was then administered, with the version being randomly selected from the two versions that had not been administered previously.

4.2.4 Analysis

Data analyses were undertaken for all participants combined and separately for the healthy control and patient participant samples. The Arabic ACE-R total score and sub-scale scores were examined. To investigate the reliability of the Arabic ACE-R the following analyses were undertaken:

1. The correlation between performance on the ACE-R at the first and second assessment occasions.

2. Data were analysed to determine whether there was any significant difference in scores between the first and second assessment occasions.

3. Data were analysed to determine whether there was any difference between versions undertaken in the first assessment. As the version to be used was selected at random it was expected that the tests would not differ on average. If a significant difference was found this would suggest that one or more test may be easier (or more difficult) than the others.

4. Internal reliability was examined using Cronbach's alpha to examine consistency of scores on the individual items that make up the Arabic ACE-R total scores and sub-scale scores. For a test to be considered to have at least acceptable internal consistency, it has been suggested that Cronbach's alpha should be at least 0.7 (Cronbach and Shavelson, 2004)

Relating to these analyses, the following hypotheses were tested:

1. There will be significant positive correlation between ACE-R total and sub-scales scores on each of the test occasions.
2. There will be no significant difference in Arabic ACE-R total and sub-scale scores on each of the test occasions
3. There will be no significant difference between scores on each of the three versions administered on the first test occasion.
4. There will be a significant Cronbach's alpha coefficient, of at least 0.7 or greater.

4.3 Results

Data from 201 participants was collected in total. Of those, 147 were healthy controls and 54 were participants with a diagnosis of either MCI or dementia. Basic demographic data are presented in Table 4.1.

Table 4.1: Demographic data on literate participants

	Healthy Controls	Patients
Number	147	54
Gender m/f	115/32	39/15
Mean (S.D) age	61.41 (7.55)	64.37 (6.87)
Education (median)*	6	4
Handedness R/L	121/26	40/14

* Relates to level of education scale described in Chapter 3, Table 3.1.

Table 4.2 presents results for parallel form correlation analysis on the Arabic ACE-R scores for the whole sample (healthy controls and patients combined) and for healthy controls and patients separately. Correlations between scores on the two

test occasions are presented. As the data were not normally distributed (see Chapter 3), spearman correlations were used.

Table 4.2: Results for parallel form correlations on the Arabic ACE-R Total and sub-scale scores.

Arabic ACE-R Score	Whole sample (n=201)	Healthy controls (n-147)	Patients (n=54)
ACE-R Total Score	.946**	.885**	.825**
Attention & Orientation	.762**	.475**	.659**
Memory	.849**	.666**	.725**
Fluency	.677**	.654**	.647**
Language	.716**	.632**	.431**
Visuospatial	.873**	.785**	.757**

Table 4.3 presents data from the analyses examining the differences between the median scores on each of the parallel forms for the whole sample (healthy controls and patients combined) and for healthy controls and patients separately.

Table 4.3: Results of Wilcoxon tests on parallel forms for the Arabic ACE-R Total and sub-scale scores.

Arabic ACE-R Score	Whole sample (n=201)	Healthy controls (n-147)	Patients (n=54)
ACE-R Total Score	Z=-2.224 p=.026*	Z=-1.013 P=.311	Z=-2.523 P=.012*
Attention & Orientation	Z-=-1.615 P=.106	Z=-1.955 P=.051	Z=-.210 P=.833
Memory	Z=-.390 P=.696	Z=-.488 P=.626	Z=-.037 P=.970
Fluency	Z=-.850 P=.395	Z=-.171 P=864	Z=-1.629 P=.103
Language	Z=-.548 P=.584	Z=-.399 P=.690	Z=-1.320 P=.187
Visuospatial	Z=-.291 P=.771	Z=-.274 P=.784	Z=-1.033 P=.302

Table 4.4 presents results of the analyses to determine whether there was any difference between versions of the Arabic ACE-R undertaken in the first

assessment. Results are presented for the whole sample. Using Kruskal Wallis analysis there was no significant difference in the scores of the difference versions used at time 1 (Chi Squared = 0.012 p=0.994) or at time 2 (Chi Squared = 0.62, p= 0.970). As memory is the one item that is different between the versions of the test, this item was examined separately. Again using Kruskal Wallis analysis, there was no significant difference in the scores of the different versions used at time 1 (Chi Squared = 0.263 p=0.877) or at time 2 (Chi Squared = 1.154, p= 0.562).

Table 4.4: Median (interquartile range) score of each version of Arabic ACE-R administered at time 1 and time 2

Arabic ACE-R score	Whole sample (Time 1)	Whole sample (Time 2)
ACE-R Total score Version A (Max=100)	81 (65 – 88.5)	82 (68- 88.5)
ACE-R Total score Version B (Max=100)	81 (68 – 87)	83 (68 – 89)
ACE-R Total score Version C (Max=100)	82 (69.5 – 89)	82 (68 – 88.5)
Memory score in Version A (Max=26)	22 (15 – 24)	23 (16-24)
Memory score in Version B (Max=26)	22 (18 – 24)	22 (18-24)
Memory score in Version C (Max=26)	23 (17 – 24)	22 (16.5 – 24)

Table 4.5 presents the results of the internal reliability analyses using the Cronbach's alpha procedure in relation to the 23 items that make up the total ACE-R score. Results are presented for the whole sample (healthy controls and patients combined) and for healthy controls and patients separately.

Table 4.5: Cronbach's alpha scores for Arabic ACE-R total and sub-scale scores at time 1 & time 2

Arabic ACE-R Score	Whole sample (n=201)	Healthy controls (n-147)	Patients (n=54)
ACE-R Total Score T1	.908	.769	.819
ACE-R Total Score T2	.909	.810	.812
Attention & Orientation T1	.443	.136	.379
Attention & Orientation T2	.535	.273	.320
Memory T1	.870	.698	.665
Memory T2	.859	.623	.646
Fluency T1	.731	.706	.771
Fluency T2	.725	.623	.854
Language T1	.645	.411	.523
Language T2	.690	.533	.671
Visuospatial T1	.696	.613	.085
Visuospatial T2	.713	.595	.399

4.4 Discussion

The results of the analyses in this study suggest that the Arabic ACE-R is a reliable instrument. Consistent with the original version (Mioshi et al., 2006) three versions of the tool were created. These differed only in relation to the name and address items used to test memory. In this study reliability was examined in two different ways as parallel form reliability and internal consistency were tested. Given that cognitive screening tools are used to measure change over time it is vital that they are shown to have temporal stability, producing the same results on separate occasions (when no change is expected). In the present study the Arabic ACE-R total score was shown to have good parallel form reliability, with correlations of rho= 0.946 for the whole sample, rho =0.885 for the healthy controls and 0.825 for the patient group. For the subscale scores, correlations varied and while most were also reasonable, they were lower than for the total score and for a small number (e.g. Language subscale in the patient group) figures were quite low. It is to be expected that sub-scale scores would be lower than total scores (reliability will increase as number of items increases). For the Language subscale score, there

seemed to be a small number of people who improved scores from time 1 to time 2, though this was not enough to produce a significant difference between the two times, and none of the individual sub-tests that make up the language sub-scale score showed a systematic change over time. It does suggest that this scale may be less reliable than the other subscales.

As well as correlation between Time 1 and Time 2, it is necessary to examine for systematic change between the two time points, as a systematic increase can lead to high correlations despite significant change in level of scores. There was no evidence of systematic change in scores in the healthy controls. However for the patients the analysis suggested there was a significant change from Time 1 to Time 2 in ACE-R total scores. There was evidence of a small increase in scores, but the actual difference was very small such that median scores were actually identical (19/26 on each occasion). If one examines mean scores, the mean for the ACE-R total at Time 1 was 56.78 and at Time 2 it was 58.33, so that the actual increase was 1.55 points on a 100 point scale. This suggests that although there possibility of a very small practice effect exists, in practice this is not large enough to have implications for interpreting changes in scores over time.

The other approach to examining reliability that was examined was internal consistency using Cronbach's alpha (Cronbach and Meehl, 1955). For the Arabic ACE-R alpha was 0.908 in time 1 and .909 in time 2 which are considered excellent and consistent with the previous findings from Mioshi et al. (2006) in which alpha was 0.80, Kwak et al. (2010) who reported alpha to be 0.84 and Yoshida et al. (2011) who found Cronbach alpha to be 0.903. For the subscales the Cronbach alpha scores were more varied and some were relatively low. In part this reflects the smaller number of items included in each subscale. Furthermore, for some items

score ranges are very small, reducing correlations and hence impacting on overall Cronbach alpha score. Nevertheless, there were clearly some changes in scores which were not systematic (as there were no significant differences from Time 1 to Time 2) but highlight that clinicians must be cautious in interpreting small changes on sub-scale scores from one occasion to another.

In summary, this study provides evidence the Arabic ACE-R shows good reliability. This should give clinicians the confidence to interpret scores at both one-off testing sessions and in relation to monitoring of change over time. However the study also highlights that the total score is the most reliable measure and it is therefore this score that is most useful in forming judgments regarding presence or absence of cognitive impairment.

Chapters 2 and 4 have examined the performance of the Arabic ACE-R in relation to use with literate participants. However, as highlighted in the introduction, the very large proportion of the population in the Arabic-speaking world is not literate and this is the case in Saudi Arabia. The next two chapters therefore present studies of the validity and reliability of the Arabic ACE-R with illiterate participants.

CHAPTER 5

Validity of Arabic ACE-R With Illiterate Participants

Chapter 5: Validity of Arabic ACE-R with Illiterate Participants

5.1 Introduction

As noted in Chapter 1, illiteracy is a major problem in the Arab world, including Saudi Arabia. The Saudi 2004 census results show that the percentage of the population over 50 who were illiterate was 61%. More specifically, 43% of men and 80% of women were illiterate. In several studies, low schooling has been found to be a risk factor for dementia (Bowirrat, et.al., 2001; Ott et al., 1995; Korczyn, Kahana, Galper, 1991).

Data on the prevalence of dementia in the Arab world are limited, but a study by Bowirrat et al. (2001) examined prevalence of, and risk factors for, dementia in an elderly Arab population in Israel. They focused particularly on the relationship between educational status and the development of dementia given the high rates of illiteracy in this population. Bowirrat et al. found that in a rural community sample of 821 people over the age of 60, the prevalence of dementia of the Alzheimer's type (DAT) was 20.5%, with rates sharply increasing with age. This rate is much higher than estimates of prevalence in Western populations and 3.9 times higher than in a non-Arab population sampled in the same region (Bowirrat et al., 2001, p121; Korczyn et al 1991; 1998). Furthermore, prevalence of DAT was very much higher amongst illiterate participants (27% in illiterate vs 4% in literate participants). Although there are a number of potential confounding factors that might explain this relationship, studies such as this highlight the importance of assessing cognition in illiterate as well as literate participants. Many tests of cognition, including the commonly used screening tools such as the Mini Mental State Examination involve tasks that require the ability to read and write. What are needed therefore are tests

that can adequately examine the cognitive skills likely to be impaired in dementia without making demands on reading or writing skills. The Addenbrookes Cognitive Examination – Revised (Mioshi et al. 2006) has been demonstrated to show good sensitivity and specificity to dementia in Western populations used in its original English form, as well as in a range of other cultures/languages with translated versions (e.g. Mathuranah et al., 2004; Carvallho and Caramelli 2007; Kwak et al., 2010; Yoshida et al. 2012; Heo et al., 2012). One of the tests have been developed for use with illiterate Telugu speakers (Mioshi, personal communication) but to the best of our knowledge no data have been published on use of the Addenbrookes Cognitive Examination with illiterate participants. Chapter 3 presented evidence that a translated and culturally adapted Arabic version of the ACE-R also showed good sensitivity and specificity to dementia in literate Arabic speakers in Saudi Arabia. The present study examined whether a modified version of the Arabic ACE-R was useful in the assessment for dementia in an illiterate sample of Arabic speakers in Saudi Arabia.

5.2 Method

5.2.1 Participants

Data was collected from two samples: (1) Healthy illiterate participants (N=283; including 160 males and 123 females) (2) Illiterate patients with a clinical diagnosis of dementia of the Alzheimer's type (DAT; N= 123, including 74 males and 49 females) or MCI: (N=46 including 22 males and 24 females). Diagnosis was made on the basis of ICD 10 criteria by independent neurologists who were blind to Arabic ACE-R scores. Diagnosis of MCI was based on criteria of presence of subjective complaints of memory impairment where possible corroborated by a relative,

essentially preserved activities of daily living and not meeting criteria for dementia. (Petersen and Morris, 2005).

Participants were 50 years of age or older, had Arabic as their first language, had adequate vision and hearing to complete the assessment, and no history of substance abuse (alcohol or drugs) or previous psychiatric disorder.

Patient participants were recruited via hospitals in Riyadh, Saudi Arabia including: King Fahad National Guard Hospital under the umbrella of King Abdul-Aziz Medical City; King Khalid University Hospital under the umbrella of King Saud University; King Saud Medical Complex under the umbrella of the Ministry of Health, Dallah Hospital, and Almubarak Hospital. Healthy controls were recruited from amongst family and friends of patients at the hospitals and from Prince Salman Social Centre. All participants reported being never able to read or write and none had any formal schooling.

Demographic information including age, gender, and handedness were collected from each participant.

Ethical approval for the study was granted by the University of Glasgow Faculty of Medicine Ethics committee and approval was also gained from each of the participating hospitals. Participants were provided with information about the study which was read to them by the researcher. A consent form was also read to the participant and following the opportunity to ask questions about the study, participants gave consent to participate via a signature or usual mark. In addition a relative was asked to countersign the consent form.

5.2.2 The Arabic ACE-R

The ACE-R consists of 5 sub-scales. Each sub-scale concentrates on one cognitive dementia as follows: attention/orientation, memory, fluency, language, and visuopatial.

The original English version of the ACE-R was translated into Arabic (and back-translated by independent translators to check for accuracy). Some items were adapted for use in an Arabic cultural context. Consistent with the original version in English, three different versions were developed (Version A; Version B and Version C), which differ just in terms of the name and address used for the memory recall task. A detailed description of the translation and adaptation process is provided in Chapter 2.

For the illiterate participants, the Arabic ACE-R was administered excluding tests requiring reading or writing, which included: Fragmented Letters; Reading (Instruction & Irregular words); and Writing tasks. This meant that 7 points were excluded from the original 100 point test format. Thus for each domain of cognition examined the following maximum points were available: attention/orientation (18 points), memory (26 points), fluency (14 points), language (23 points), visuospatial (12 points) and the maximum total score is 93.

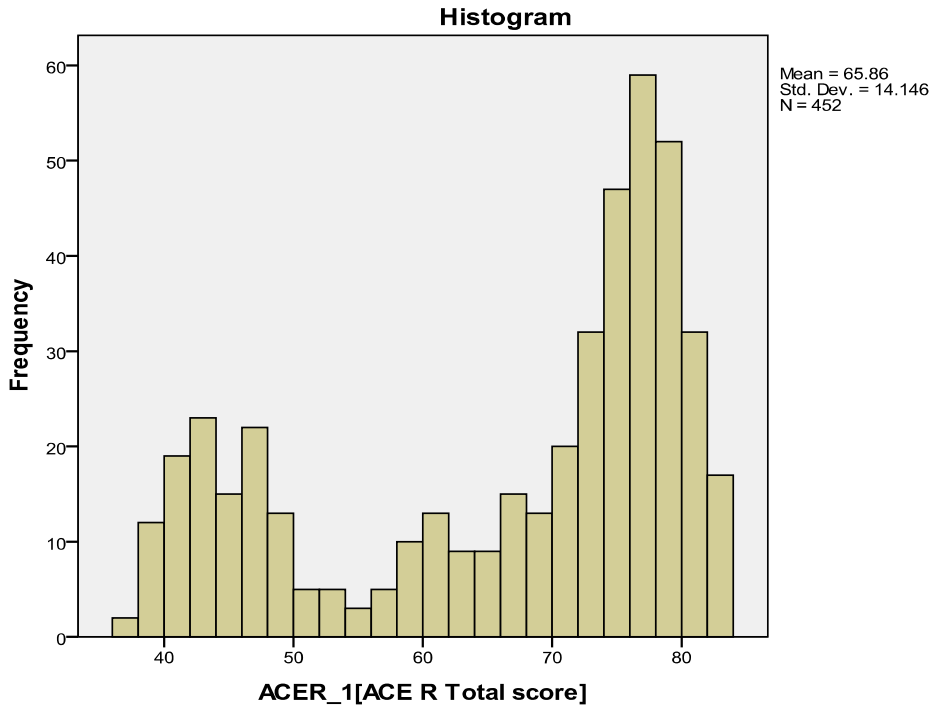
5.3 Results

283 healthy controls, 123 DAT and 46 MCI patients were recruited. Demographic data collected included age, gender, and handedness and are presented in Table 5.1.

Table 5.1 Demographic data on initial samples of illiterate participants

	Healthy	MCI	DAT
Number	283	46	123
Gender m/f	160/ 123	22/ 24	74/ 49
Mean (S.D) age	60.84 (6.57)	62.61 (8.65)	65.46 (5.76)
Handedness L/R	62/221	9/37	18/105

Figure 5.1: Histogram of the Arabic ACE-R total scores for the whole sample (healthy controls, MCI and DAT).



Arabic ACE-R data were examined with regard to normality. A Shapiro-Wilk test indicated that data for the whole sample were not normally distributed (W=0.81, df 452, p<0.001), and this also applied to healthy controls (W=0.958, df 283, p<0.001) and to patients (W=0.903, df 169, p<0.001). As a result, non-parametric statistical analysis was undertaken. It was noted that the groups were different in age. Data on age were examined using a Kruskall Wallis test. This showed a significant difference between the groups (Chi Squared 49.08, df 2, p<0.0001). Further analysis using Mann Whitney tests revealed no significant difference in the ages between Controls and MCI (U=6087, p=0.480), but a significant difference between

Controls and DAT (U=9689.50, P<0.001) and between MCI and DAT (U= 1974.00, p=0.002).

Therefore the question of whether there was a relationship between age and performance on the primary outcome measure (Arabic ACE-R total score) was examined. Correlational analysis for the healthy control data showed that there was a modest, but significant correlation between age and Arabic ACE-R total (rho= -0.291, p<0.001). However, given that non-parametric analysis was to be performed, it was not possible to simply include age as a covariate in analyses.

In order therefore to compare groups without the confounding effect of age, it was necessary to match the groups more closely in terms of age. A much larger number of healthy control participants had been recruited in order to collect normative data for the test and this included a number of people between the ages of 50 and 60, of whom there were very few in the patient sample (apart from a few in the MCI group). The DAT patients group also contained a number of participants over the age of 75, of whom there were very few in either of the other samples. Therefore to remove the confound of age from a comparison of the groups, it was necessary to exclude some of the younger controls (all those aged under 59) and younger MCI cases (aged under 55) and also to exclude some of the older DAT cases (aged over 75). Table 6.2 presents data on the revised samples.

Table 5.2 Demographic data on revised samples of illiterate participants

	Healthy	**MCI**	**DAT**
Number	171	39	115
Gender m/f	95/76	18/21	66/49
Mean (S.D) age	64.67 (5.50)	64.38 (8.19)	64.54 (4.73)
Handedness L/R	37/134	8/31	18/97

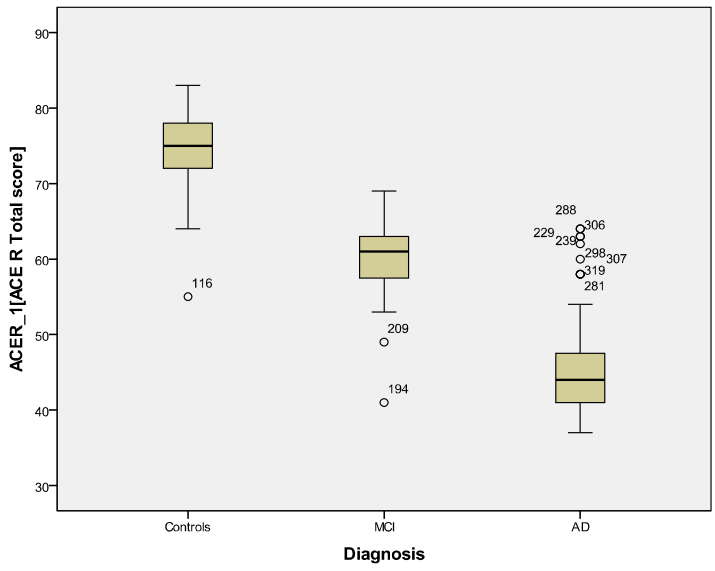
In the revised sample there was no difference in age between the groups (Chi-square=2.519, df=2, p=0.284). There was also no difference in gender ratio (Chi Squared= 1.520, df=2, p=0.468) or handedness (Chi Squared= 1.612, df=2, p=0.447).

Table 5.3 presents the median (and interquartile range) scores for performance of each group on the Arabic ACE-R Total and the Arabic ACE-R sub-scales. Figures 5.2 – 5.7 provide boxplots for the data on MMSE, Arabic ACE-R Total and subscale scores.

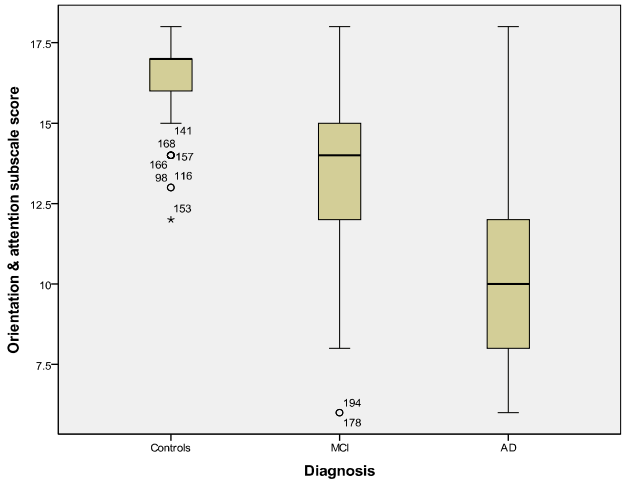
Table 5.3: Median (and interquartile range) scores for performance of each group on the Arabic ACE-R Total Score and the Arabic ACE-R sub-scales.

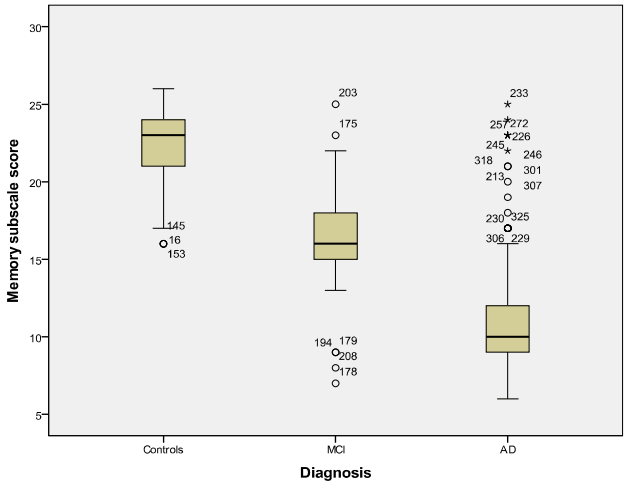
Test	Healthy	MCI	DAT
Arabic ACE-R Total (Max=93)	75 (72-78)	61 (57-63)	44 (41-48)
Arabic ACE-R Attention & Orientation (Max=18)	17 (16-17)	14 (12-15)	10 (8-11)
Arabic ACE-R Memory (Max=26)	23 (21-24)	16 (15-18)	10 (9-11)
Arabic ACE-R Fluency (Max=14)	6 (5-6)	4 (3-5)	4 (3-4)
Arabic ACE-R Language (Max=23)	21 (20-22)	19 (17-20)	17 (16-18)
Arabic ACE-R Visuospatial (Max=12)	9 (7-10)	8 (6-9)	5 (5-5)

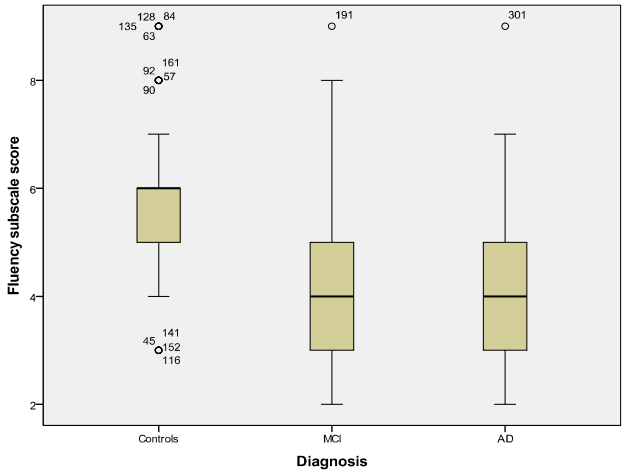
Figure 5.2 Boxplot for Arabic ACE-R data showing median, lower and upper quartiles, largest values that are not outliers and outliers (defined as more than 1.5 box lengths above or below the box)

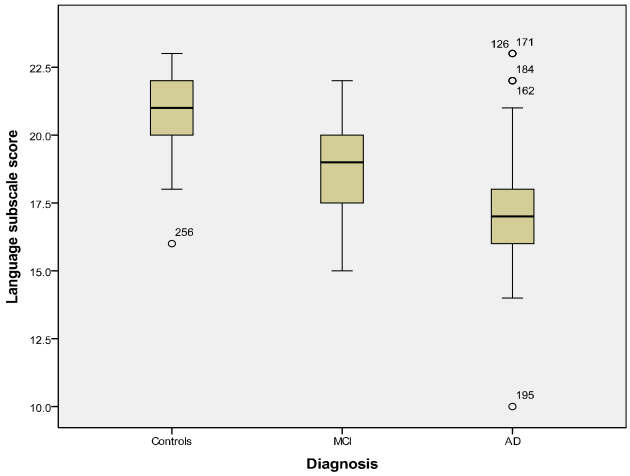


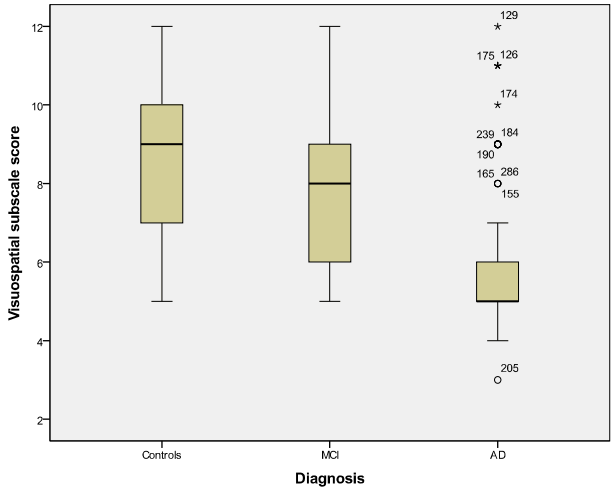
Figures 5.3 – 5.7 Boxplots for Arabic ACE-R sub-scale data showing median, lower and upper quartiles, largest values that are not outliers, outliers (defined as more than 1.5 box lengths above or below the box) and extreme cases (defined as more than 3 box-lengths above or below the box











As would be expected given that the distribution of total scores was negatively skewed, some, but not all, of the subscale distributions were also skewed. For example, the orientation subscale was near the ceiling for the healthy controls. For the language subscale score, this was off the ceiling, though the distribution of scores on the naming test was near the ceiling for many of the healthy participants. The visuospatial subscale did not show a marked skew, though it was noteworthy that the cube drawing task was clearly challenging for many of the healthy illiterate controls, with around 50% scoring zero on this task.

Krushkal-Wallis analysis comparing the three groups showed significant differences on all of the test measures (all p<0.001). Results from the post-hoc analysis using Mann-Whitney tests to examine differences between each of the pairs of groups are shown in Table 6.4. Correlation effect sizes (r) are also shown.

Table 5.4: Results from the post-hoc analysis using Mann-Whitney test to examine differences between each of the pairs of groups

Test	Healthy vs MCI	Healthy vs DAT	MCI vs DAT
Arabic ACE-R Total	Z= -9.540** r=.658	Z= -14.334** r=.847	Z= -8.134** r=.655
Arabic ACE-R Attention & Orientation	Z= -7.947** r=.548	Z= -12.789** r=.756	Z= -4.685** r=.377
Arabic ACE-R Memory	Z= -8.616** r=.594	Z= -13.206** r=.780	Z= -5.429** r=.437
Arabic ACE-R Fluency	Z= -7.064** r=.487	Z= -10.536** r=.623	Z= -.239ns r=0.019
Arabic ACE-R Language	Z= -7.145** r=.493	Z= -12.594** r=.744	Z= -3.859** r=0.310
Arabic ACE-R Visuospatial	Z= -3.184** r=.219	Z= -10.620** r=.627	Z= -5.277** r=.425

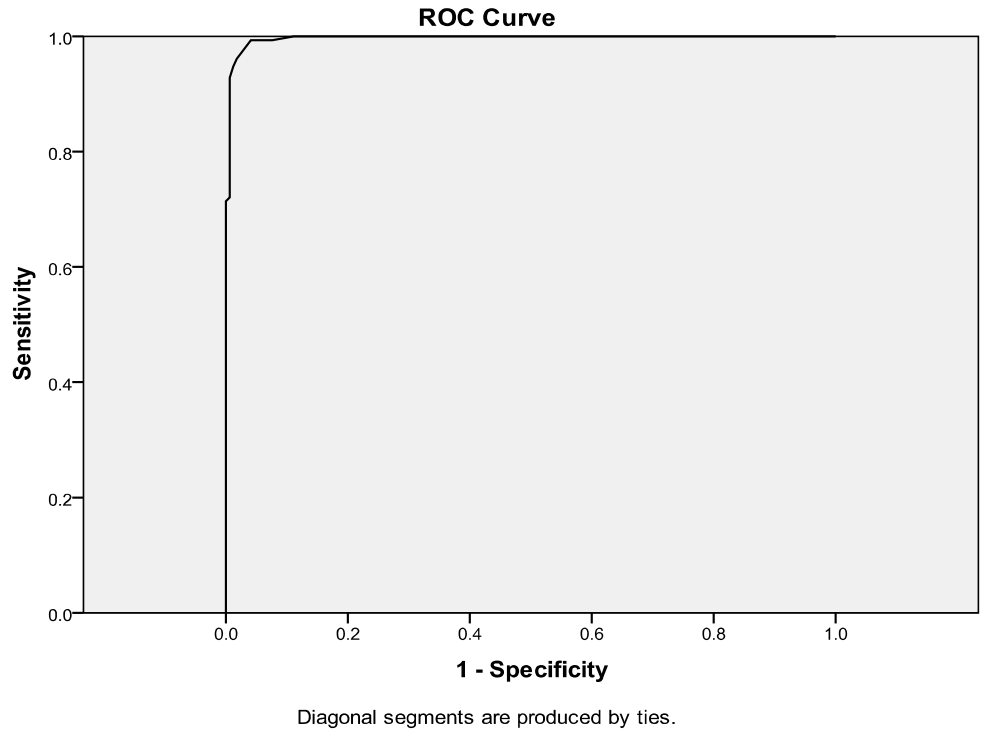
**p<0.05*
*** p<0.01*
ns = not significant

To explore the sensitivity and specificity of specific cut-off points on the Arabic ACE-R to detection of cognitive impairment associated with dementia and mild cognitive impairment, a series of Receiver Operating Curve (ROC) Analyses were undertaken. Two different ROC analyses were undertaken. The first examined the separation of healthy controls from all the patients combined (i.e. examining separation of the MCI and DAT patients combined from the healthy controls). The second examined the separation of DAT and MCI patients

5.3.1 Healthy Controls vs MCI & DAT

Figure 5.8 shows the ROC curves (Sensitivity plotted against 1-specificity) for the ACE-R Total score comparing healthy controls with patients (MCI/DAT). The Area Under the Curve analysis statistic for the ACE-R was 0.997 which reflects the strong separation of the positive cases (DAT/MCI) from the healthy controls.

Figure 5.8 ROC curve (Sensitivity plotted against 1-specificity) for the ACE-R Total score comparing healthy controls with patients (MCI/DAT)

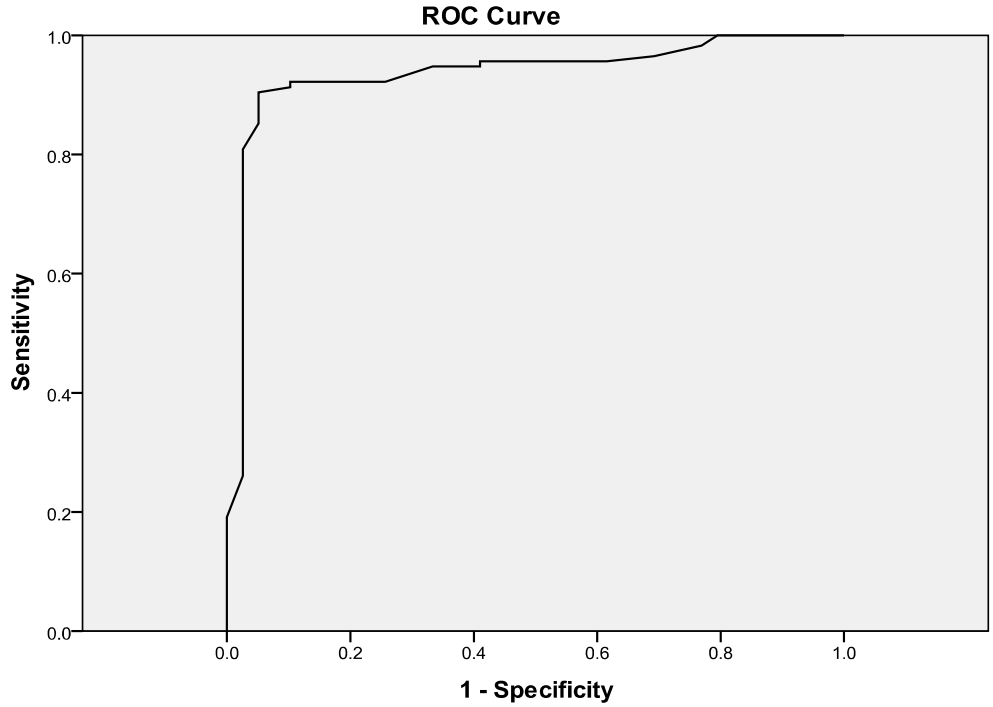


The ROC analysis demonstrated that a cut-off point of 65 on the ACE-R had a sensitivity of 0.961 and specificity of 0.982, reflecting the strong separation of patients and controls. However, it also reflects some overlap for some participants.

5.3.2 MCI vs AD

Figure 5.9 shows the ROC curves for the ACE-R Total score comparing between patients (MCI vs DAT). The Area Under the Curve analysis statistic for the ACE-R was 0.936.

Figure 5.9 ROC curve (Sensitivity plotted against 1-specificity) for the ACE-R Total score comparing healthy controls with patients (MCI/DAT)



The ROC analysis demonstrated that a cut-off point of 52 on the ACE-R had a sensitivity of 0.904 and specificity of 0.949, reflecting a good separation of AD patients from the MCI with modest overlap of scores for participants.

Given that it had been demonstrated that there was a relationship between Arabic ACE-R performance and age, further analyses were undertaken on separate age

bands. Table 5.5 therefore presents the results of ROC analyses including Area Under the Curve statistics, optimum cut-off points and their associated sensitivities and specificities for each of three age bands (<60 years, 60-69 years and ≥70 years). For the <60 years group, data relating to two cut-off points are presented to illustrate the impact on sensitivity and specificity of varying cut points.

Table 5.5: ROC analyses including Area Under the Curve statistics, cut-off points and their associated sensitivities and specificities for each of three age bands (<60 years, 60-69 years and ≥70 years).

	Area under curve	Cut off	Sensitivity	Specificity
<60 years	0.997	67 64	1.000 0.930	0.968 0.992
60 – 69 years	0.998	65	0.989	0.984
≥70years	0.989	64	0.857	1.000

In addition to calculation of sensitivity and specificity, positive and negative predictive values were also calculated using the formula presented in Chapter 3. As noted in Chapter 3, the positive predictive value (PPV) refers to the probability that an individual who is predicted by a test to have the condition of interest actually has the condition. The negative predictive value (NPV) refers to the probability that a test is correct when it predicts that the condition is absent (Smith, Ivnik and Lucas, 2008). It was also noted in Chapter 3 that positive and negative predictive values are influenced by the base rate (BR) of the condition of interest. Given that prevalence of dementia in older illiterate adults is at least as high, and almost certainly higher, than amongst literate adults, it seemed appropriate to use the same range of base rates in order to calculate PPV and NPV for the present sample. Tables 5.6 and 5.7 provide PPV and NPV data respectively for the sample

as a whole and for each age band, based on sensitivity and specificity data obtained from the samples.

Table 5.6 PPV data for the sample as a whole and for each age band, based on sensitivity and specificity data obtained from the samples.

Age Bands	ACE-R Cut offs	Sensitivity/ Specificity	Positive Predictive Value at different rates				
			5%	10%	20%	40%	50%
Whole sample	65	0.961/0.982	0.738	0.856	0.930	0.973	0.982
<60 years	67 64	1.000/0.968 0.930/0.992	0.621 0.859	0.776 0.928	0.886 0.966	0.954 0.987	0.968 0.991
60 – 69 years	65	0.989/0.984	0.764	0.872	0.939	0.976	0.984
≥70years	64	0.857/1.000	1.000	1.000	1.000	1.000	1.000

Table 5.7 NPV data for the sample as a whole and for each age band, based on sensitivity and specificity data obtained from the samples.

Age Bands	ACE-R Cut offs	Sensitivity/ Specificity	Negative Predictive Value at different rates				
			5%	10%	20%	40%	50%
Whole sample	65	0.961/0.982	0.997	0.996	0.990	0.974	0.962
<60 years	67 64	1.000/0.968 0.930/0.992	1.000 0.996	1.000 0.992	0.886 0.982	1.000 0.955	1.000 0.934
60 – 69 years	65	0.989/0.984	0.999	0.998	0.997	0.992	0.988
≥70years	64	0.857/1.000	0.992	0.984	0.965	0.912	0.874

5.4 Discussion

To the best of our knowledge, this is the first study that has reported the performance of illiterate participants on the Addenbrooke's Cognitive Examination – Revised (ACE-R). The study demonstrated that it was feasible to adapt the ACE-R for use with people who cannot read and write, by the exclusion of a small number of tasks. The illiterate participants were able to engage with the assessment and give responses for all tasks that were appropriate for them. The results suggest that the Arabic ACE-R may provide a useful tool for cognitive screening in illiterate Arabic speakers.

Bowirrat et al. (2001) highlighted that rates of dementia of the Alzheimer Type (DAT) may be considerably higher amongst the illiterate population compared to the literate population. The present study was not epidemiological in nature, but it is noteworthy that recruitment rates were considerably greater for illiterate participants compared to a parallel study of literate participants (presented in Chapter 3), with approximately three times as many illiterate compared to literate participants recruited. It is also clear from the most recent census data that in Saudi Arabia rates of literacy remain low in older adults, particularly amongst women. These data clearly highlight the importance of having assessment tools for screening cognitive impairment in people who are illiterate.

At a group level the data showed that there was a significant difference going from healthy to MCI and from MCI to DAT groups (and of course a very large difference between healthy and DAT), consistent with previous studies of Mioshi et al. (2006), Grundman et al. (2004) and Bozoki et al. (2001).

As with the literate participants, the total score and some of the tests (e.g. orientation and naming) showed skewed distributions in healthy control participants with near ceiling performance on some tasks suggesting some tasks were relatively easy for healthy people. By contrast some tasks might be considered to be difficult for even healthy controls, as for example around 50% of healthy illiterate participants scored zero on the cube drawing task. For the fluency task, the size of the difference between the controls and the patients groups was also less than for some of the other subscales. There were still large differences between the controls and patient groups, though this task did not distinguish the MCI and AD patient groups. It was noted in Chapter 2 that the scoring system from the original English version of the ACE-R was used. In the current sample overall task performance (number of words and animals produced) was lower than for the original sample for all groups (Mioshi et al., 2006) raising the question as to whether the scoring system could have been modified. The original scoring system was adopted because it is relatively fine grained at the lower end of scores (the first four points relate to increments of just two additional words for each one point increase on the scoring system) and therefore it seemed appropriate to use the same system. However, in future research with larger numbers of MCI patients, it would be appropriate to examine whether an even finer grain classification of scores at the lower end would increase sensitivity to differences between groups. Nevertheless, ROC analyses showed that the Arabic ACE-R (using the total score) distinguished well between the healthy controls and patients with a diagnosis of either MCI or DAT. Thus the optimum cut-off point on the Arabic ACE-R (65) had good sensitivity and specificity. The Area Under the Curve data for the Arabic ACE-R (0.997) could be classified as excellent.

Compared to the literate sample reported in Chapter 3, cut-off scores based on the Arabic ACE-R Total score were, as expected, lower - there are seven less points available on the version for illiterate participants compared to literate participants. It is noteworthy that the cut-off point was, though, only five points below that for the literate sample. It is not clear what might account for the difference, though these data suggest that the literate participants recruited may have been a little more impaired than the illiterate participants (at a group level).

The finding that the sensitivity and specificity for Arabic ACE-R was very high is promising. As discussed in Chapter 3 in relation to literate participants, one caveat to this is the possibility that those recruited to the study may not have been at the very mildest stage of dementia. As noted, the number of MCI patients was again modest, reflecting perhaps that this diagnosis is used less in the Saudi context. It was discussed in Chapter 3 that one possibility is that patients do not present to services in the very earliest stages of dementia, and perhaps not as early may be the case in Western countries. This seems to be the case for both literate and illiterate participants. As noted, there is a strong tradition in the Arabic region and especially in Saudi Arabia of caring for older people within families. Islamic teaching encourages people to respect elderly people and provide care for them. This may mean that changes in cognition such as memory changes are normalized and accommodated within the family, rather than being attributed to a disease process. Furthermore, a wider lack of awareness of the symptoms of dementia may again mean that changes are not recognized as potentially abnormal (Bener and Ghuloum 2011). Thus there would appear to be multiple reasons why people who are beginning to experience symptoms of dementia may not present to services until there is clear impairment or functional difficulties. Other measures of severity of dementia were not available during this study, though it would have been useful to

have some other measure of severity of impairment and functional disability to provide some comparison with studies from other countries.

One issue that arises from the possibility that patients were not at the earliest stages is that the cut-off points may be lower than might be expected if more patients at a very early stage had been included. The other approach to considering cut-off points is to base these entirely on data from the healthy controls. Thus in Chapter 7, normative data from the healthy illiterate population is presented and potential cut-off points derived from this sample are presented.

In the present study control participants were healthy and not presenting to health services with any complaints regarding cognitive functioning. However, in the clinical context tests such as the ACE-R are most often used in the context of a specialist memory clinic or more general neurology/psychiatry outpatient clinic. When people experiencing memory or other cognitive problems are referred to such clinics the diagnostic challenge is to determine whether cognitive problems being experienced in day to day life are the result of a dementia or some other psychological process (e.g. depression, anxiety). The present study does not therefore address the question of how effective the Arabic ACE-R is in distinguishing between those with mood disorder, but not dementia and those with dementia. Future research should investigate this issue.

Inspection of the Arabic ACE-R subscale scores showed that the effect sizes for the differences between the groups varied across the cognitive domains assessed. None were as large as the total score. For the comparison between healthy controls and both patient groups there were significant differences on all subscales, but considerable variations in effect sizes, with the smallest being for the visuospatial sub-scale for the healthy vs MCI comparision. This is not unexpected given that a

diagnosis of MCI is primarily focused on impairments of memory and one might therefore not expect relatively simple perceptual tasks to be markedly impaired in this group. The boxplot for this subscale clearly reflects the large overlap in performance between the groups. By comparison, in the DAT group, where one would expect more widespread impairment, there was a considerably greater difference between the groups, including between the DAT and MCI groups.

This chapter has provided evidence for the validity of the Arabic ACE-R with illiterate participants. The following chapter examines the reliability of the Arabic ACE-R in an illiterate sample.

CHAPTER 6

Reliability of Arabic ACE-R With Illiterate Participants

Chapter 6: Reliability of the Arabic ACE-R in illiterate participants

6.1 Introduction

As noted in Chapter 5, although one version of the ACE-R (in Telugu) has been developed for use with illiterate participants, to the best of our knowledge no data have been reported previously on the use of the ACE-R with illiterate participants.

This Chapter examines the parallel form reliability and internal consistency of the Arabic ACE-R with illiterate participants. Two samples of illiterate participants were studied, a group of healthy adults and a group of participants with a diagnosis of either Mild Cognitive Impairment or Dementia.

6.2 Method

6.2.1 Participants

The participants for this study were the same as those described in Chapter 5. Data was gathered from three samples. The first comprised 283 healthy, illiterate participants, of whom 160 were male and 123 female, while the second consisted of 123 illiterate patients (74 male and 49 female) who had been clinically diagnosed with DAT and 46 illiterate patients (22 males and 24 females) who had been clinically diagnosed with MCI. The diagnoses were made by independent neurologists blind to the Arabic ACE-R scores and based on ICD 10 criteria.

Patient participants were recruited through hospitals in Riyadh, Saudi Arabia. These were King Fahad National Guard Hospital, part of King Abdul-Aziz Medical City; King Khalid University Hospital of King Saud University; King Saud Medical Complex, run by the Ministry of Health, Dallah Hospital, and Almubarak Hospital.

The healthy participants in the control group were recruited from the relatives and friends of patients at the aforementioned hospitals and from Prince Salman Social Center. All of the participants stated that they could not read or write and none had had any formal education.

Ethical approval for the study was given by the University of Glasgow Faculty of Medicine Ethics committee and was also obtained from each participating hospitals.

6.2.2 The Arabic ACE-R

Development of the Arabic ACE-R was described in Chapter 2. As previously noted, three versions (A, B & C) were developed. Each version has same format and much of the content is similar. However, consistent with the original version (Mioshi et al. 2006) each version has different information for the anterograde memory task which involves remembering a name and address. All other items are the same in each version.

As described in Chapter 5, the Arabic ACE-R was administered to the illiterate patients with the omission of tests that required reading or writing. These were Fragmented Letters, Reading (Instruction & Irregular words), and Writing tasks. This meant that 7 points were missing from the original 100-point test format. Hence, for each aspect of cognition tested the maximum points obtainable were: attention/orientation (18 points); memory (26 points); fluency (14 points); language (26 points); and visuospatial (16 points); with a maximum total score of 93.

6.2.3 Procedure

Following completion of informed consent procedures and recording of basic demographic information, the Arabic ACE-R was administered. The version

administered first was selected at random from the three versions. Administration takes about 15-20 minutes on average. Participants were then invited to return approximately one week later. A different version of the Arabic ACE-R was then administered, with the version being randomly selected from the two versions that had not been administered previously.

6.2.4 Analysis

Data analyses were undertaken for all participants combined and separately for the healthy control and patient participant samples. The Arabic ACE-R total score and sub-scale scores were examined. To investigate the reliability of the Arabic ACE-R the following analyses were undertaken:

1. The correlation between performance on the ACE-R at the first and second assessment occasions.

2. Data were analysed to determine whether there was any significant difference in scores between the first and second assessment occasions.

3. Data were analysed to determine whether there was any difference between versions undertaken in the first assessment. As the version to be used was selected at random it was expected that the tests would not differ on average. If a significant difference was found this would suggest that one or more test may be easier (or more difficult) than the others.

4. Internal reliability was examined using Cronbach's alpha to examine consistence of scores on the individual items that make up the Arabic ACE-R total scores and sub-scale scores. For a test to be considered to have at least acceptable internal consistency, it has been suggested that Cronbach's alpha should be at least 0.7 (Cronbach and Shavelson, 2004)

Relating to these analyses, the following hypotheses were tested:

1. There will be significant positive correlation between ACE-R total and sub-scales scores on each of the test occasions.
2. There will be no significant difference in Arabic ACE-R total and sub-scale scores on each of the test occasions
3. There will be no significant difference between scores on each of the three versions administered on the first test occasion.
4. There will be a significant Cronbach's alpha coefficient, of at least 0.7 or greater.

6.3 Results

Data from 452 participants was collected in total. Of those, 283 were healthy controls, 46 were participants with a diagnosis of MCI and 123 had a diagnosis of DAT. Basic demographic data are presented in Table 6.1.

Table 6.1: Demographic data on illiterate participants

	Healthy	MCI	DAT
Number	283	46	123
Gender m/f	160/ 123	22/ 24	74/ 49
Mean (S.D) age	60.84 (6.57)	62.61 (8.65)	65.46 (5.76)
Handedness L/R	62/221	9/37	18/105

Table 6.1 presents results for parallel form correlational analysis on the Arabic ACE-R scores for the whole sample (healthy controls and patients combined) and for healthy controls and patients separately. Correlations between scores on the two test occasions are presented. As the data were not normally distributed (see Chapter 5), spearman correlations were used.

Table 6.2: Results for parallel form correlations on the Arabic ACE-R Total and sub-scale scores.

Arabic ACE-R Score	Whole sample (n=452)	Healthy controls (n-283)	Patients (n=169)
ACE-R Total Score	.916**	.692**	.850**
Attention & Orientation	.733**	.093	.839**
Memory	.812**	.327**	.835**
Fluency	.670**	.345**	.422**
Language	.638**	.148*	.393**
Visuospatial	.686**	.748**	.822**

Table 6.2 presents data on median an interquartile ranges for the Arabic ACE-R total and subscales scores on each of the testing occasions. Table 6.3 then presents results from the analyses examining the differences between scores on the two testing occasions for the whole sample (healthy controls and patients combined) and for healthy controls and patients separately.

Table 6.3 Median (and interquartile ranges) for the whole sample, healthy controls and patients on each of the testing occasions.

Arabic ACE-R Score	Whole sample (n=452)	Healthy controls (n-283)	Patients (n=169)
ACE-R Total Score T1 (Max=93)	72 (52.3-77)	76 (73-79)	46 (42.5-58)
ACE-R Total Score T2 (Max=93)	72 (52-77)	76 (73-78)	47 (42-59)
Attention & Orientation T1 (Max=18)	12 (16-17)	17 (16-17)	10 (8-13)
Attention & Orientation T2 (Max=18)	12 (16-17)	17 (16-17)	10 (8-13)
Memory T1 (Max=26)	22 (13.3-24)	23 (22-24)	10 (9-16)
Memory T2 (Max=26)	13 (21-23)	23 (22-24)	11 (9-16)
Fluency T1 (Max=14)	5 (4-6)	6 (5-7)	4 (3-5)
Fluency T2 (Max=14)	5 (4-6)	6 (5-7)	4 (3-4)
Language T1 (Max=23)	20 (18-21)	21 (20-22)	17 (16-19)
Language T2 (Max=23)	20 (18-21)	21 (20-21)	18 (17-19)
Visuospatial T1 (Max=12)	8 (5-10)	9 (8-10)	5 (5-7)
Visuospatial T1 (Max=12)	8 (5-10)	9 (8-10)	5 (5-7)

Table 6.4 Results of Wilcoxon tests on parallel forms for the Arabic ACE-R Total and sub-scale scores.

Arabic ACE-R Score	Whole sample (n=452)	Healthy controls (n-283)	Patients (n=169)
ACE-R Total Score	Z=-1.100 p=0.271	Z=-1.143 p=0.253	Z=-0.322 p=0.747
Attention & Orientation	Z-=-0.768 p=0.442	Z=-0.487 p=0.626	Z=-.0.691 p=0.489
Memory	Z=-1.577 p=0.115	Z=-1.578 p=0.115	Z=-.468 p=0.640
Fluency	Z=-1.282 p=0.200	Z=-1.745 p=0.081	Z=-0.269 p=0.788
Language	Z=-1.099 p=0.272	Z=-2.627 p=0.009*	Z=-1.129 p=0.259
Visuospatial	Z=-2.132 P=0.032	Z=-2.396 p=0.017*	Z=-0.235 p=0.814

Table 6.5 presents data (median and interquartile range) for the three different versions of the Arabic ACE-R for the first and second administrations. Data are presented for Arabic ACE-R total scores and for the Memory subscale (as this is the one item that differs between versions). Results are presented for the whole sample. Using Kruskal Wallis analysis there was no significant difference in the scores of the different versions used at Time 1 (Chi Squared = 0.035, df=2, p=0.983). At Time 2 there was a significant difference between the version (Chi Squared = 10.01, df=2, p=0.007). As memory is the one item that is different between the versions of the test, this item was examined separately. Again using Kruskal Wallis analysis, there was no significant difference in the scores of the different versions used at time 1 (Chi Squared =0.002, df=2, p=0.999) but again there was a statistically significant difference at Time 2 (Chi Squared = 7.383, df=2, p=0.025).

Examination of Table 6.4 shows that medians for the sample were very similar for each version for Arabic ACE-R total and Memory subscale scores. The interquartile range data show that for Version C at Time 2, there was a slightly higher level of the

25th percentile point for both the Total and Memory scores. To examine the extent to which this might have impacted on reliability, parallel-form correlations were re-run on Arabic ACE-R Total scores with participants split into the three groups based on which version they had second. This showed that the parallel form correlations were: Version A second (rho=0.916, p<0.001), Version B second (rho=0.938, p<0.001), Version C second (rho=0.865, p<0.001). This suggest that there was a slightly lower reliability for those who had Version C second, but reliability levels nevertheless remained high. Interestingly when the participants were split by which version they had first there the parallel-form correlations were all very similar and all above 0.9: Version A first, rho=0.923, p<0.001; Version B first, rho=0.910, p<0.001; Version C first, rho=0.913, p<0.001.

Table 6.5 Median (interquartile range) score of each version of Arabic ACE-R administered at time 1 and time 2

Arabic ACE-R score	Whole sample (Time 1)	Whole sample (Time 2)
ACE-R Total score Version A (Max=93)	72 (49.75 - 77.25)	72 (50 - 77)
ACE-R Total score Version B (Max=93)	72 (51.5 – 77)	73 (52 – 77)
ACE-R Total score Version C (Max=93)	73 (55.5 – 77)	72 (58 – 76)
Memory score in Version A (Max=26)	22 (11 - 24)	21 (11.75 – 23)
Memory score in Version B (Max=26)	21 (13 - 24)	22 (13.5 – 24)
Memory score in Version C (Max=26)	22 (15 – 23.5)	21 (16-23)

Table 6.6 presents the results of the internal reliability analyses using the Cronbach's alpha procedure in relation the 19 items that make up the total ACE-R score. Results are presented for the whole sample (healthy controls and patients

combined) and for healthy controls and patients separately. Results are presented for the test done at Time 1 and at Time 2

Table 6.6 Cronbach's alpha scores for Arabic ACE-R total and sub-scale scores

Arabic ACE-R Score	Whole sample (n=452)	Healthy controls (n-283)	Patients (n=169)
ACE-R Total Score T1	.910	.591	.855
ACE-R Total Score T2	.917	.576	.862
Attention & Orientation T1	.588	.201	.540
Attention & Orientation T2	.576	.163	.481
Memory T1	.897	.396	.846
Memory T2	.901	.446	..855
Fluency T1	.816	.724	.685
Fluency T2	.793	.668	.539
Language T1	.607	-.079	.341
Language T2	.566	.136	.322
Visuospatial T1	.516	.398	.233
Visuospatial T2	.565	.434	.416

6.4 Discussion

The results of the analyses in this study suggest that the Arabic ACE-R for illiterate participants is a reliable instrument. As for the literate participants, three versions of the Arabic ACE-R were created for use with illiterate participants. These differed only in terms of the memory subscale items (name and address). As the memory subscale was administered in its entirety with the illiterate participants, this means that three parallel versions can be used for repeat assessments with illiterate participants.

In this study reliability was examined in two different ways as parallel form reliability and internal consistency were tested. The Arabic ACE-R (Illiterate Version) total score was shown to have good parallel form reliability, with a correlation of rho=0.916 for the whole sample. For the separate sub-groups the correlations were

a little lower being rho=0.692 for the healthy controls and rho=0.850 for the patient group. The smaller correlation for the healthy controls would appear to be the result of a more restricted range of scores than those that were found for the patient group or the sample as a whole. This can be seen from the data presented in Table 6.3, which showed that the ACE-R interquartile range was limited, reflecting a ceiling effect in the healthy control group. This inevitably has an impact on correlations. However in the whole sample (and in the patient group alone) the range of scores was much wider and therefore the correlation coefficient gives a more accurate indication of the reliability of the test.

For the subscale scores, correlations varied considerably with some being reasonable whilst others were very low. Of the 15 correlations examined (five subscales for the whole sample, healthy controls and patient groups) only four were greater that 0.8 (which is considered to be the minimum value required for a reliable measure (Field and Hole, 2003). However, once again it would appear that this was largely the result of a limited range of scores, particularly in the healthy controls. It is noteworthy that for the patient group, three subscales (Orientation & Attention, Memory and Visuospatial) had correlation coefficients that were greater than 0.8.

As well as the correlation between Time 1 and Time 2 scores, the differences between the scores for the two times were tested to determine whether there was any systematic increase or decrease in scores over time. For the Total scores there were no systematic changes evident, something which applied to the whole sample as well as for the healthy controls and patient groups individually. Thus there did not appear to be any practice effect evident. In relation to the subscale scores, most did not show significant differences over time. However two subscale scores, Language and Visuospatial did show a significant change. For the Language there was in fact

a very slight decrease in scores between the two testing occasions, but this was not sufficient to change the median score (means changed by 0.2 points) and hence this would not be of any clinical significance. For the Visuospatial subscale, there was a very slight increase in scores, but again this was not sufficient to impact on median and interquartile ranges (means increased by 0.2 points) and hence once again it appears that this does not represent a significant threat to the reliability of the scale.

The other approach to examining reliability that was examined was internal consistency using Cronbach's alpha (Cronbach and Meehl, 1955). For the Arabic ACE-R alpha was 0.910 in time 1 and 0.917 in time 2 which are considered excellent and consistent with the previous findings from previous ACE-R studies as noted in Chapter 4.

For the subscales the alpha scores were more varied and some were relatively low though results were above 0.8 for both Memory and Fluency subscales. As noted in Chapter 4, in part, the wide range of alpha scores reflects the smaller number of items included in the subscales, with some tasks having small score ranges, reducing correlations and hence impacting on overall Cronbach alpha score.

As was found for the Arabic ACE-R for literate participants, the version designed for use with illiterate participants appears to be sufficiently reliable for use for both one-off assessments and repeat testing. However once again it was the Total score that proved to be most reliable. This is to be expected as the more items that contribute a score the more likely it is to be reliable. This has been found with other test batteries such as the Wechsler Adult Intelligence Scale (WAIS IV) where it is found

that Index Scores have higher levels of reliability that the individual subscale or subtest scores which contribute to the Index scores.

CHAPTER 7

Normative Data

Chapter 7: Normative data for the Arabic Cognitive Examination – Revised

7.1 Introduction

The previous four chapters of this thesis have provided evidence that the Arabic ACE-R is a valid and reliable tool for the assessment of cognition as one component of a broader diagnostic assessment for dementia process. It was shown that the tool could be used with both literate and illiterate participants. In both groups there were significant differences in the scores of those with a diagnosis of Mild Cognitive Impairment (MCI) or dementia of the Alzheimer's type and healthy controls. Levels of both sensitivity and specificity were high and as a result cut-off scores could be identified for both literate and illiterate participants. It was noted however that one issue in relation to use of these cut-off scores is that the comparison groups were people with a clear diagnosis of MCI/dementia and healthy controls. It was emphasised too that numbers of people with MCI were relatively low and given the possibility that may people with dementia do not present to services until there is considerable impairment, this may account for the very clear separation of the groups in terms of the scores on the Arabic ACE-R. One possibility this raises is that the cut-off scores might be relatively low and as a result may not identify people with more mild impairment in the early stages of dementia.

Another approach to identifying impairment on cognitive tests is to define impairment in terms of abnormality of scores. In fact this is the most common approach to defining impairment on cognitive tests as it is relatively rare for there to be very high levels of complete separation of clinical groups and healthy controls on tests of cognition. Level of abnormality can be represented in terms of standard scores (reflecting number of deviations away from the mean that a scores lies) or in

terms of percentiles (Crawford, 2012). Crawford (2012) makes a strong case that percentiles should play a central role in the interpretation of neuropsychological test scores (p132). In terms of level of abnormality it is most common to define impairment as scores below the 5th percentile of a normative sample. It is of course always important to remember that the 5th percentile means that five percent of healthy people scored at or below this level. But this level provides a reasonable compromise between the probability of false positives and false negatives in the interpretation of performance (Willmes, 2010).

This chapter therefore presents normative data for the Arabic ACE-R, for both illiterate and illiterate populations. Cut-off points based on the fifth percentile are derived and reported for ACE-R total score and for each of the five sub-scale scores.

7.2 Method

7.2.1 Participants

Data from two groups of healthy participants are reported. The first group, comprised 147 healthy literate participants (115 male; 32 female) and the second group consisted of 283 healthy illiterate participants (160 male; 123 female). These are the larger samples of participants from whom matched groups were selected for analysis in Chapters 3 and 5 and the same participants as were used for the reliability analyses in Chapters 4 and 6. Recapping briefly, participants were 50 years old or over, were native speakers of Arabic, had adequate vision and hearing to complete the assessment, and no history of substance abuse (alcohol or drugs) or previous psychiatric disorders. Healthy Participants were recruited from the

Prince Salman Social Centre, Riyadh and from amongst family and friends of patients recruited for previously reported studies.

As noted previously, ethical approval for the study was given by the University of Glasgow, Faculty of Medicine, Ethics Committee and approval was also obtained from each of the participating hospitals and the Prince Salman Social Centre. Participants were given a leaflet with information about the study. After reading the leaflet (or it being read to them) and being given the opportunity to ask any questions they may have had about the study, participants gave their consent to participation.

The Arabic ACE-R was then administered for the literate sample as was detailed in Chapter 3 and as detailed in Chapter for the illiterate sample.

7.2.2 Analysis

The two complete samples consisted of 147 literate and 283 illiterate participants. Inspection of the data from these samples revealed that for some sub-scale scores there were outliers (defined as values that are more than 1.5 times the interquartile range away from the bottom or top of the interquartile range) and extreme cases (defined as values that are more than 3 times the interquartile range away from the bottom or top of the interquartile range). These were illustrated in Figures 3.2 - 3.7 for the literate sample and in Figures 5.2 - 5.7 for the illiterate sample. Although the sample sizes were reasonably large, particularly for the illiterate sample, if one is identifying fifth percentile points, outliers and extreme cases may have a considerable influence on cut off points. For example in relation to the literate participants, 5% of the whole sample is just 7 people and so a small number of outliers might significantly affect the identification of a cut-off point. Whilst none of

the healthy participants had a neurological or psychiatric condition diagnosed it was possible that some did have some level of impairment but had not presented to services. Alternatively some participants may have misunderstood instructions or not fully engaged with particular components of the test. To address the possibility that outliers and extreme scores would skew cut-off scores, it was decided to exclude cases statistically identified as outliers or extreme cases. Whilst this raises the possibility that the full range of normal scores is not represented in the data, on balance it was considered safer to exclude these outliers.

The procedure for removal of outliers was first to separate the groups into age bands. For the literate sample, two age bands (50-59 and 60+) are presented as the number of healthy controls over 70 years old was relatively small. For the illiterate sample, three age bands (50-59. 60-69 and 70+) are reported. For each subscale score boxplots were used to identify outliers and extreme scores using the age banded data. These scores were then removed from the relevant subscale score and given that they would also have an impact on total scores, the total score for each outlier/extreme score was also excluded.

Data are therefore presented for ACE-R total scores and each of the sub-scale scores. Given that distributions of scores significantly deviated from a normal distribution, medians, interquartile ranges and 5% cut-off points are reported. Furthermore, given that it was established that age has an effect on Arabic ACE-R scores, data are presented for separate age bands. For the literate sample, two age bands (50-59 and 60+) are presented as the number of healthy controls over 70 years old was relatively small. For the illiterate sample, three age bands (50-59. 60-69 and 70+) are reported.

7.3 Results

7.3.1 Literate sample - For the literate sample the process of removing outliers meant that a total of 127 participants were included. There were 21 women and 106 men. There was no difference in the ACE-R Total scores for the women compared to the men (U=1060, p=0.730) so all participants are considered together. Table 7.1 presents data for median, interquartile range and fifth percentile for the whole literate sample and for the two age groups separately for the Arabic ACE-R Total score and each of the sub-scale scores.

It can be seen from Table 7.1 that there was a considerable difference in the Arabic ACE-R Total scores between the younger and older age bands, reflected in the medians, interquartile ranges and the fifth percentile cut off scores. To investigate this issue further the level of education of the participants in the two age bands was investigated because it was recognised that one of the major changes in Saudi society in recent decades has been the increase in levels of education. The importance of addressing level of education was highlighted in the study of Mathuranath et al. (2007), who found that level of education had a marked effect on the Malayalam version of the original ACE (M-ACE), with mean total M-ACE scores ranging from 42.8 for those with no education to 83.4 for those with more than 12 years of education. Therefore, in the present sample the level of education achieved (which was coded on an 11 point scale ranging from no education to PhD level) was compared for the two age bands. A Mann Whitney test revealed a significant difference in level of education between the two groups (U=1480.5, Z= -4.843, $p<0.001$, r=0.399). Examining the impact of education further, if age and level of education are entered into a regression model with ACE-R total as the dependent variable, a significant model is obtained (adjusted $r^2 = 0.509$) that includes both age

(β = -0.487; t= -7.175, p<0.001) and education (β = 0.370; t= 5.451, p<0.001). Consideration was therefore given to producing norms for the literate sample split by both age group and education level. However, even if education was just split into two levels, for some cells the numbers would be very low. Furthermore, examination of the data revealed that within each age band the difference between those with high and low education in terms of total ACE-R scores 5th percentile cut-offs was small (1-2 points) and therefore it was not considered appropriate to divide the normative tables further by education.

Table 7.1 Median, interquartile range and fifth percentile cut-offs for the literate sample

		ACE Total (Max=100)	Orient-ation	Memory	Fluency	Language	Visuo-spatial
Whole Sample	Median IQR 5%	86 82-90 73	18 17-18 14	23 22-2 19	7 6-9 4	25 24-25 21	13 10-15 6
50's	Median IQR 5%	89 87-92 83	18 17-18 16	24 23-25 21	7 7-9 4	25 24-25 22	14 13-15 9
60+	Median IQR 5%	82 77-86 71	17 16-18 13	23 21-24 18	7 6-9 4	24 23-25 20	11 9-13 6

7.3.2 Illiterate sample - For the illiterate sample the process of removing outliers meant that a total of 265 participants were included. There were 115 women and 150 men. A comparison of Arabic ACE-R total scores between men (Median = 78, Mean 76.96) and women (Median = 75, Mean 74.88) showed a modest, but significant difference (U=5617.5, p>0.001, r=0.30). Consideration was given to therefore presenting data broken down by gender in addition to age band. However, a potential problem with this approach is that it would mean that some of the subsets of data (e.g. men/women over 70 years) would be very small. Furthermore, an exploratory analysis of the fifth percentile cut off points for each age band for men and women separately revealed that there was no difference at all for the 60's and 70's age bands (albeit the result for the latter group must be tentative as

numbers were small), and for the 50's there was a two point difference (71 versus 73), with the figures being one point either side of the whole group fifth percentile point of 72 (see table 7.2). it was decided therefore not to break the data down further than by age band. Table 7.2 therefore presents data for median and interquartile range and fifth percentile points for the whole illiterate sample, and then broken down by age band, for the Arabic ACE-R Total score and each of the sub-scale scores.

Table 7.2 Median, interquartile range and fifth percentile cut-offs for the illiterate sample

		ACE Total (Max=93)	Orientation	Memory	Fluency	Language	Visuospatial
Whole Sample	Median IQR 5%	76 74-79 69	17 17-18 14	23 22-24 19	6 5-7 4	21 21-22 19	9 8-10 5
50's	Median IQR 5%	77 75-80 72	17 17-18 15	24 22-24 20	6 5-7 4	21 20-22 19	10 8-11 6
60's	Median IQR 5%	76 73-78 69	16 16-17 14	23 22-24 19	6 5-7 4	21 20-22 19	9 8-10 5
70+	Median IQR 5%	73 70-76 66	17 16-17 13	21 19-23 16	5 5-6 4	21 20-21 18	8 6-9 4

7.4 Discussion

This chapter has presented normative data for literate and illiterate participants, including for the whole of each sample as well as for differing age bands for each sample. It was noted in the introduction to this chapter that one concern with deriving cut-off points on the basis of sensitivity/specificity data when healthy controls are compared with patient groups is that cut-off points may have been lower than might be appropriate. It appears that this concern was justified in that cut-off points based on fifth percentile scores are somewhat higher than those based on sensitivity/specificity to diagnostic group. This is illustrated most clearly in

relation to the younger literate participants. As noted in Chapter 3, the cut off point based on sensitivity/specificity data for the under 60 group was 68. However, if a cut off is based on a fifth percentile score then it is 83, some 15 points higher. For the older group (60+ years) the difference in approaches was less dramatic, with the cut-off from sensitivity/specificity data being either 65 or 69 depending on which sensitivity/specificity measure is preferred, and 71 based on the fifth percentile. There was a considerable difference in cut-off point for the younger (50's) and older (60+) groups. This highlights the importance of separating out the data by age band. This may of course simply be a reflection of the ageing process. However, the degree of impact of age in the literate group appears to be greater than was evident in the original English version (Mioshi et al., 2006). The result is not being accounted for by the wider age range of the 60+ group (which has an age range from 60 – 85) as if one runs the analysis just including participants in the 60-69 age range the fifth percentile cut off point is the same as for the whole 60-85 group. One possible explanation for the discrepancy between younger and older groups lies in the differences in level of education between the groups. Data analysis showed that the younger group had a considerably higher median level of education (their median being High School level) compared to the older group (whose median level of education was Intermediate, which is between Elementary and High School level). The most likely explanation for this discrepancy is a change in provision of education over recent decades in Saudi Arabia. As noted access to education has until recent years been relatively limited, particularly for women, but in the last few decades there has been a considerable cultural change in terms of expectations regarding level of education. Thus this difference may be representative of differences in education level amongst the wider Saudi population. However, another possibility is that the difference is down to differences in sampling. In

relation to where the groups differed in terms of cognitive domains, there was some difference across most of the domains, with the exception of verbal fluency. It is possible that higher levels of education provide greater familiarity with being examined on mental tests and perhaps more confidence in undertaking assessments of mental functioning which may result in higher scores. Alternatively differences in education may reflect differences in underlying cognitive ability in participants, which has inadvertently resulted from the sampling. One obvious issue this raises though is that the difference in cut-off between someone who is 59 and someone who is 60 is very large. This too has implications for participants who are being followed up and who might change age band during the course of a follow up period. This highlights the importance of being very cautious about the use of cut-off scores.

In the present sample whilst there was an impact of education with the age bands, in terms of total points difference between those with higher and lower levels of education was relatively modest. This contrasts with the findings of Mathuranath et al., (2007) who found a very marked difference between those with the highest and lowest levels of education. However, the studies are not directly comparable as the Mathuranath et al. study was on a translated version of the ACE rather than the ACE-R, and Mathuranath et al. also included participants with no education (who were separated out in the present studies).

For the illiterate sample, the cut-offs for the three age bands (50's, 60's 70+) based on sensitivity/specificity were 67/65/64. Based on fifth percentile scores they were 72/69/66. So once again there was some discrepancy and this was most marked in the youngest groups, although not as great as for the literate sample. As for the literate sample, there were small differences across most of the domains apart from

fluency. If one compares scores for the literate and illiterate samples, then the difference is broadly consistent with the number of points that were unavailable for the illiterate group as a result of tests being excluded, though the illiterate group were a little further below this simple arithmetic difference - there were seven points not available to the illiterate group and in terms of the two samples as a whole there was a 10 point difference between medians. For the 50 year olds in each group there was a 12 point difference. In relation to the literate 60+ group, they were six points above the illiterate 60 year olds and nine points above the illiterate 70+ group. Broadly therefore the two groups appeared to be approximately similar in performance on tests that were included for both groups.

In summary, this Chapter has presented normative data that may be used to supplement test interpretation. Previous validation chapters have derived cut-off scores based on sensitivity/specificity analysis, but this chapter highlights that those cut-off points may in fact lack sensitivity to earlier stages of dementia, something that is discussed in more detail in the next chapter.

CHAPTER 8

General Discussion

Chapter 8: General Discussion

This thesis has described the development of an Arabic version of the ACE-R, presented four studies examining the validity and reliability of this tool with literate and illiterate participants and provided a set of normative data against which performance of people undergoing clinical assessment can be compared.

In Chapter 2, the process of translation and adaption of the test was outlined. Much of the original test could be simply translated, but a number of tests required adaptation. This appears to be similar to the experience of a number of other researchers who have adapted the tool for use in different languages (e.g. Kwak et al., 2010; Yoshida et al., 2012). In that process it was noted that some tests were more challenging to adapt and the success of the adaptation would in part be determined by the extent to which the tool was successful in distinguishing participants with clinical conditions such as MCI or DAT from healthy controls. The evidence from the validation studies would suggest that this process was largely successful. However, some interesting issues arose during administration of the test. For example an issue arose with the retention of an orientation question regarding the season which is not as straightforward as in the UK where the test was originally developed. In any subsequent revision of the Arabic ACE-R it might be appropriate to modify this item, either in terms of clarifying the scoring, or perhaps replacing it with an alternative (e.g. ‘what is the name of the next festival?’). With regard to the Language items which were amongst the most challenging to adapt, for the literate participants examined in Chapter 3 it was found that this subscale did show a difference between healthy controls and both participants with MCI and those with DAT, but did not distinguish between MCI and DAT. This is perhaps a little surprising in that MCI is primarily seen as a disorder of memory

whereas one might expect participants with dementia to have broader deficits including language problems. For the illiterate participants in Chapter 5, this was indeed the case as there was a significant difference between MCI and DAT patients on this subscale score (though their scores on the Language subscale obviously excluded the reading tasks). In this subscale there may have been some tasks that were too easy (e.g. Naming, on which most controls scored near ceiling) and others (e.g. Reading, for the literate participants) were too difficult - only about a third of MCI patients and a third of AD patients and two thirds of controls could successfully read all five words. This perhaps implies that the task was quite demanding compared to the original English version. However, given the small number of MCI patients in this sample, it may be premature to change the reading task at this early stage of investigation. Furthermore, the focus of this research has been on MCI/DAT and not on conditions such as progressive aphasias or stroke, for which specific language disorders are more likely to be evident. Thus it may be appropriate to use the test with participants known to have specific language disorders to determine how useful it is before major modification.

For the verbal fluency tasks (letter fluency and animal fluency) the same scoring system was used as for the original version of the ACE-R. The Arabic letter *meem* was selected as it is high frequency. Performance on the verbal fluency sub-scale was one of the least discriminating (between patients and controls) for both literate and illiterate samples. This contrasts with what Mioshi et al. (2006) and Yoshida et al., (2012) found, which was that fluency was more discriminating than attention/orientation, language and visiospatial subscales (comparing MCI with healthy controls). One possibility that was considered was that the task was too easy and hence many patients could perform as well as controls. There was some evidence that this was *not* the case as in both literate and illiterate samples there

was a wide range of performance (i.e. no apparent ceiling effect). Performance of the participants in this Arabic sample was below that for the original English version (Mean for Fluency sub-scale in Mioshi et al. 2006 was 11.9/14, in Yoshida et al. 11/14 and in this sample for literate participants mean was 7.49/14 and for illiterate participants it was 5.89/14). However it is known that level of education affects performance on verbal fluency tasks in both English speakers (Crawford et al., 1992) and Arabic speakers (Khalil, 2010) and given the wide range of education amongst the present samples, the lower overall performance is not surprising. However, this still does not explain why this task was not more discriminating between groups. It remains possible that because the high frequency letter *meem* was used, that patients were able to generate sufficient items to mean that they remained closer to the performance of controls than was the case for the groups in Mioshi et al. or Yoshida et al., than perhaps might have been the case if a more demanding letter had been used. This could be examined in future studies.

Returning to the primary validation studies, Chapters 3 and 5 presented data that suggest that the Arabic ACE-R is a sensitive and specific tool for the detection of cognitive impairment associated with MCI and DAT in both literate and illiterate participants. The development of a test that can be used with both literate and illiterate participants is particularly important for people in the Arabic-speaking world, where illiteracy rates remain high. The performance of both groups of participants was similar to each other and to performance of people on other language versions of the test, including the original version (Mioshi et al., 2006). For example, the data were skewed towards the top end of the score range, suggesting that for most people, at least most healthy controls, the test was relatively easy. This suggests that the test is not likely to be experienced as difficult which may make compliance with assessment better. In both literate and illiterate samples, cut-

off scores with good sensitivity and specificity could be derived as there was good separation of the patient and control groups. However, some caution is necessary in relation to these cut-off scores. It was noted that for both literate and illiterate groups the numbers of patients recruited with a diagnosis of Mild Cognitive Impairment were relatively small. What this means is that the majority of influence on cut-off scores comes from the Alzheimer's group. This in turn means that in these studies the main comparison was between clearly healthy people and clearly impaired people. Whilst this was an important first step in the validation of this test, further work is need to examine the performance of test with more patients with MCI, but in addition with patients who present to their doctor with complaints of memory or other cognitive problems. Many people who are concerned about their memory may in fact have psychological conditions such as depression or anxiety, and experience difficulties with memory and concentration in everyday life, but do not have dementia. The main task for memory clinics is perhaps to differentiate those with dementia from those with other, non-progressive conditions. Larner (2007) reported on use of the ACE-R in clinical practice in which he compared scores for patients diagnosed with dementia compared to those without (the latter group including people with a diagnosis of MCI, affective disorder and 'purely subjective memory impairment') and noted that whilst sensitivity of the original cut-off scores was good, specificity was less good. This is not surprising in that people presenting at a memory clinic may have some memory impairment, but just not due to progressive conditions such as Alzheimer's disease. When Larner adjusted the cut-off down, sensitivity remained high, and specificity improved considerably. Thus in relation to the Arabic ACE-R, it would be useful to examine sensitivity and specificity of the derived cut-offs in a typical sample attending clinics. Related to this issue, the normative data presented in Chapter 7 raise the opposite issue in that if

one derives cut-offs based on 5th percentile performance of healthy controls (an approach used in many cognitive assessment tools) the cut-off points are higher than those based on ROC analysis when patients are compared with controls. Once again, this finding suggests that further validation work is needed to examine performance of the Arabic ACE-R in relation to clinic samples that include people who present with complaints of memory difficulties but who do not have dementia. Furthermore, one of the original purposes of developing the ACE/ACE-R was to aid differential diagnosis of different forms of dementia. For the present studies with the Arabic ACE-R the original aim was to include patients with diagnoses other than Alzheimer's, and examine the extent to which profiles of performance (e.g. similar to the VLOM ratio reported in the original studies (Mathuranath et al., 2000; Mioshi et al. 2006). However, it became clear very early in the recruitment process that the numbers of patients receiving diagnoses other than Alzheimer's disease was very low and therefore it was decided to concentrate on just the MCI and Alzheimer's disease groups. There are a number of potential reasons for this issue. One is that conditions such as fronto-temporal dementias, dementia with Lewy bodies etc. have lower incidence in Saudi Arabia. In the absence of epidemiological data this cannot be determined for sure, but seems unlikely given that levels of dementia in other parts of the Arab world would appear to be similar to, or higher than, other parts of the world. Other possibilities therefore are that patients present later to services such that they are less likely to present with relatively focal disorders that might be more likely to lead to diagnoses other than Alzheimer's disease. Furthermore, in the absence of detailed, standardised neuropsychological evaluation tools it is likely to be more difficult to differentiate different forms of dementia (Snowden et al., 2011), and hence Alzheimer's disease becomes the default diagnosis. One implication of this is that within the samples who participated in the present studies, it may have

been the case that some patients had forms of dementia other than Alzheimer's disease, but this could not be determined. The use of a tool such as the Arabic ACE-R may contribute to more accurate diagnosis in the future.

Apart from one small study of 21 participants with the Japanese ACE-R (Yoshida et al., 2012), to the best of our knowledge, test-retest reliability has not been examined in the ACE-R. Given that the ACE-R is very likely to be repeated with participants either for confirming diagnosis or monitoring change, it is vital that test-retest reliability is established. In Chapters 4 and 6, the test-retest (or more specifically parallel-form reliability) as well as internal reliability of the Arabic ACE-R for use with literate and illiterate participants was examined. The results suggested that the tool, in both its forms, had good reliability. It was noted that reliability is highest for the Total score, whereas for some of the subscale scores, reliability was lower. This finding suggests that one should be more cautious in interpreting sub-scale scores and particularly interpreting small changes from one test occasion to another. The finding of high reliability for the Arabic ACE-R Total score suggests that this score will be most useful for diagnostic purposes and particularly for monitoring change over time.

As noted, Chapter 7 presented normative data for the Arabic ACE-R, with alternative cut-off points derived from 5^{th} percentile points. Examination of the normative data highlighted that age and education both impacted on performance for the literate sample and age impacted on performance for the illiterate sample. For this reason age banded normative data were calculated. Education banded groups were not defined for the literate sample because sample sizes in each cell would drop to low numbers and because preliminary examination of the data suggested that within each age band education made only a small difference (a

couple of points). However, these findings once again highlight the importance of using cut-offs points with some caution.

There are many challenges associated with the development of tools for the assessment of cognition in a cultural and linguistic context in which use of such tools is not well established. The approach adopted here was to adapt a tool developed in a Western, English-speaking, context for use in a Middle Eastern, Arabic-speaking, context. As has been highlighted throughout the thesis this brings many challenges given the differences between these contexts. The most obvious is the linguistic difference which means that not all items can be simply translated, but must take account of the form of the language (e.g. Arabic having few irregular words). However there are many more differences that are relevant. The educational and socioeconomic context is clearly relevant, leading of course to the need for versions of the test that can be used with illiterate participants. In relation to education, gender is also relevant given the large discrepancies in level of education between men and women. In addition to not being able to read, a more general unfamiliarity with being tested may impact on the performance of people with little exposure to formal education and this may affect performance in ways that have not been formally measured here. Cultural traditions relating to care of the elderly and infirm within the family context have also been highlighted as potentially relevant in meaning that patients may present to services relatively later than those in a Western context or there may be marked variations within the culture relating to socio-economic status or educational background in terms of when people present to services. When there are cultural, socioeconomic, ethnicity and gender factors that may impact on test performance, this means that such factors ideally need to be taken into account in relation to normative data, but this then places a great challenge on the numbers of people who must be tested so each relevant cell in a

table of norms must contain sufficient numbers of participants with which to compare. This places a significant burden on the process of collecting normative data. It is clear that these issues need to be addressed in future work, but are significant challenges for those developing tools for assessing cognition in new contexts.

An alternative to the approach of adapting tests developed in another cultural and linguistic context would be to work from first principles within the target country/culture. This would be ideal perhaps, but is limited by the fact that there is also a lack of more basic research upon which to drive development of relevant assessment tools. For example, as discussed earlier, there is a lack of good epidemiological data on prevalence of dementia in the Middle East (Karam and Itani, 2013; Ferri, 2006) and there is little work on detailed examination of how dementia presents in the Arab world (in part of course because of a lack of available tools). But further investigation of how cognitive and functional changes associated with dementia pathology manifest themselves would potentially lead to better, more culturally specific and therefore more sensitive assessment tools.

The comparison groups in the studies examined here were people with a diagnosis of dementia or MCI, or healthy controls. Thus when comparing performance on a cognitive test, an assumption is made that differences in test performance are related to the presence/absence of dementia/MCI pathology. Now, it has been noted and discussed that factors such as education and age also have and known impact on test performance and hence were taken into account by matching groups when comparisons were being made or providing separate norms. However there is a range of other potential confounding factors that could potentially impact on cognition and which might have systematically differed between the groups

(potentially explaining some of the difference between groups). These include factors such as current medical illness such as cerebrovascular disease, current medication load, smoking status, carer depression, patient depression etc. Ideally, future research should attempt to measure important confounders to ensure group matching or use statistical analysis methods to control for them.

The studies presented in this thesis therefore extend the evidence base that suggests that cognitive screening tools such as the ACE-R have a useful role to play in the assessment of people who may be experiencing dementia. Given that there has been only one very small previous study of the test-retest reliability of the ACE-R, also for a translated version (Yoshida et al. 2012), the reliability studies in this thesis add to the evidence relating to the psychometric properties of the ACE-R. Consistent with a number of other studies, the work presented in this thesis has demonstrated that the ACE-R can be adapted for use in a different linguistic and cultural context, but it has been clearly shown that adaption (and not just translation) was required, and culture-specific norms are particularly important given the overall differences in level of scoring between the Arabic ACE-R and the original. A particularly important contribution of the studies reported here is the evidence that the Arabic ACE-R can be used with people who are illiterate. Around the world, there are many countries with large numbers of people who are illiterate not as a result of intellectual disability but through lack of access to education. This group is very rarely considered in the neuropsychological literature which is dominated by studies in Western contexts. A small number of recent studies have begun to address this issue (e.g. Gómez et al., 2013; Yildiz et al., 2013) which is a positive development, though there are clearly many regions of the world where this remains a major issue, including in the Arab region.

8.1 Future research

Throughout the thesis areas for future research have been identified. One of the most important of these areas is to examine the performance of the Arabic ACE-R in relation to diagnostic sensitivity and specificity (and positive and negative predictive values) when used with more typical clinic samples comprising of patients with memory complaints arising from conditions other than dementia (particularly when there is no pathology evident). It should be remembered that a test such as the ACE-R tests cognition and not a specific pathology. Therefore if someone has impaired cognition arising from other neurological conditions such as head injury or stroke or from psychological conditions such as depression, it is quite likely that they will perform less well than healthy controls. A neuropsychological test alone cannot diagnose Alzheimer's disease – diagnosis is dependent on a careful consideration of the patient's history and other biological measures. However, the test does need to be able to contribute to distinguishing people with subjective complaints of memory difficulties (with no pathology) from those with memory (or other cognitive) impairment arising from organic pathology. The extent to which the test is useful in contributing to differential diagnosis (particularly distinguishing Alzheimer's disease from fronto-temporal dementia and Lewy body dementia) based on profiles of sub-test scores also needs to be examined.

Some minor modifications may be beneficial in improving the performance of the test. Modifications to the Orientation test (in relation to the question regarding the season) may be helpful. Some further examination of use of letters other than *meem* would be interesting. Further consideration could be given to words used in the reading test and this should be informed by literature, as it emerges, on the nature of language impairment in Arabic speakers with dementia.

Consistent with the original, the Arabic ACE-R has three parallel versions, though the only difference between the versions is the name and address test that contributes to the memory sub-scale The possibility of including alternative versions of some of the other tasks would also be useful in order to minimise possibilities practice effects or rehearsing of questions by patients between assessments. Finally, an updated version of the original English ACE-R has recently become available and referred to as the ACE-III, although validation/reliability data for this version are not yet published. A small number of items in the ACE-R have been modified and consideration will therefore be given to the extent to which these modifications may also be relevant to the Arabic ACE-R.

8.2 Conclusion

The five studies in this thesis provide evidence that a version of the Addenbrookes Cognitive Examination – Revised, culturally adapted for application in Saudi Arabia appears to be valid and reliable instrument for the assessment of cognition in older adults who may be developing dementia. Further work is required to examine its use in the everyday clinical environment, but evidence suggests the tool may make a useful contribution to the early diagnosis of mild cognitive impairment and dementia.

REFERENCES:

Afgin AE; Massarwa M; Schechtman E; Israeli-Korn SD; Strugatsky R; Abuful A; Farrer LA; Friedland RP; Inzelberg R. (2012) High prevalence of mild cognitive impairment and Alzheimer's disease in arabic villages in northern Israel: impact of gender and education. Journal of Alzheimer's Disease, 29 (2), pp. 431-9

Alabeedy, I.M. & Aldamigh, S.A. (2001). Dementia Disease in Saudi Arabia: epidemiology and related features (unpublished) *Sultan Bin Abdulaziz Al-Saud charity Foundation.*

Alexopoulos P, Ebert A, Richter-Schmidinger T, Schöll E, Natale B, Aguilar CA, Gourzis P, Weih M, Perneczky R, Diehl-Schmid J, Kneib T, Förstl H, Kurz A, Danek A, Kornhuber J. (2010) Validation of the German revised Addenbrooke's cognitive examination for detecting mild cognitive impairment, mild dementia in alzheimer's disease and frontotemporal lobar degeneration. Dementia and Geriatric Cognitive Disorders, 29(5), 448-56.

Alexopoulos, P. Mioshi, E. Greim, B. and Kurz, A. (2007). Brief Assessment of cognitive mental status in German: The Addenbrooke's Cognitive Examination (ACE) and the Addenbrooke's Cognitive Examination Revised (ACE-R). *European Journal of Geriatrics,* 9(4), 175 – 180.

Al Rajeh, S. Ogunniyi, A. Awada, A. Daif, A.K. & Zaidan, R. (1998). Validation of the Arabic version of the mini-mental state examination. *Annals of Saudi Medicine* 19(2), 150-152.

Alzheimer's Society (2007). Dementia UK: A report into the prevalence and cost of dementia prepared by the Personal Social Services Research Unit (PSSRU) at the London School of Economics and the Institute of Psychiatry at King's College London, for the Alzheimer's Society. *Alzheimer's Society*. pp. 1 – 12.

American Psychiatric Association (1994). Diagnostic and Statistical Manual of Mental Disorders, 4th edition (*DSM-IV). American Psychiatric Association, Washington, DC.*

American Psychiatric Association (2000). A Text Revision of Diagnostic and Statistical Manual of Mental Disorders, 4th edition (*DSM-IV-TR). American Psychiatric Association, Washington, DC.*

Ardila, A. (1995) Towards a cross-cultural neuropsychology. Journal of Social and Evolutionary Systems, 19, 3, 23728.

Bäckman, L. (1992). Memory training and memory improvement in Alzheimer's disease: rules and exceptions. *Acta Neurologica Scandinavica. Supplementum* 139, 84 – 89.

Bak, T.H. & Mioshi, E. (2007). A cognitive bedside assessment beyond the MMSE: the Addenbrooke's Cognitive Examination. *Practical Neurology* 7(4), 245-9.

Bak, T.H. Rogers, T.T. Crawford, L.M. Hearn, V.C. Mathuranath, P.S. Hodges, J.R. (2005). Cognitive bedside assessment in atypical parkinsonian syndromes. *Journal Neurol Neurosurg Psychiatry* 76,420 – 422.

Barnes DE, Alexopoulos GS, Lopez OL, Williamson JD, Yaffe K (2006). Depressive symptoms, vascular disease, and mild cognitive impairment. *Archives of general psychiatry* 63, 273–280.

Bener**,** A**.** & Ghuloum**,** S. (2011) Gender differences in the knowledge, attitude and practice towards mental health illness in a rapidly developing Arab society. *International Journal of Social Psychiatry*. 57(5) 480–486.

Berchtold, N. C. and Cotman, C. W. (1998). Evolution in the Conceptualisation and Alzheimer's disease: Greco-Romanperiod to the 1960s. *Neurobiology of aging* 19, 173 – 189.

Berrios, G. E. (1996) *The History of Mental Symptoms*. Cambridge: Cambridge University Press.

Bier, J.C. Donckels, V. Van, E.E. Claes, T. Slama, H. Fery, P. Vokaer, M. (2005). The French Addenbrooke's Examination is effective in detecting dementia in a French-speaking population. *Dementia and geriatric cognitive disorders*, 19, 15 – 17.

Bird, H. R., Canino, G., Stipec, M. R., & Shrout, P. (1987). Use of the Mini-mental state examination in a probability sample of a Hispanic population. *The Journal of Nervous and Mental Disease,* 175, 731–737.

Bird, M. & Kinsella, G. (1996). Long-term cued recall of tasks in senile dementia. *Psychology and Aging,* 11, 45-56.

Bird, M. & Luszcz, M. (1993). Enhancing memory performance in Alzheimer's disease: acquisition assistance and cue effectiveness. *Journal of Clinical and Experimental Neuropsychology,* 15, 921-932.

Bird, M. & Luszcz, M. (1991). Encoding specificity, depth of processing, and cued recall in Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology*, 13, 508 – 520.

Borkowski, J. G., Benton, A. L., & Spreen, O. (1967). Word fluency and brain damage. *Neuropsychologia*, *5*(2), 135–140. doi:10.1016/0028-3932(67)90015-2.

Boustani M, Petersen B, Hanson L, Harris R, Lohr K. (2003). Screening for dementia in primary care: A summary of the evidence for the US preventive services task force. *Annals of Internal Medicine,* 138, 927 - 942.

Boxer, A.L. & Miller, B.L. (2005). Clinical features of frontotemporal dementia. *Alzheimer Disease & Associated Disorders,* 19(Suppl 1), S3-6.

Bozeat, S. Patterson, K. & Hodges, J.R. (2004). Relearning object use in semantic dementia. *Neuropsychological Rehabilitation,* 14, 351-363.

Bozoki, A., Giordani, B., Heidebrink, J. L., Berent, S., & Foster, N. L. (2001). Mild cognitive impairments predict dementia in nondemented elderly patients with memory loss. *Archives of Neurology*, 58(3): 411.

Bowirrat, A. Treves, T.A. Friedland, R.P. & Korczyn, A.D. (2001). Prevalence of Alzheimer's type dementia in an elderly Arab population*. European Journal of Neurology,* 8, 2, 119 – 123

Braak, H. and Braak, E. (1991). Neuropathological staging of Alzheimer-related changes. *Acta Neuropathologica*, 82, 239 – 259.

Brayne, C. Fox, C. & Boustani, M. (2007). Dementia screening in primary care: is it time? *The Journal of American Medical Association,* 298(20), 2409–2411

Brodaty, H. Clarke, J. Ganguli, M. Grek, A. Jorm, A.F. Khachaturian, Z. & Scherr, P. (1998). Screening for Cognitive Impairment in General Practice: toward a consensus. *Alzheimer Disease and Associated Disorders*, 12, 1 – 13.

Brodaty H. (1990). Low diagnostic yield in a memory disorders clinic. *International Psychogeriatrics,* 2, 149–159.

Buschke, H. Kuslansky, G. Katz, M. Stewart, W.F. Sliwinski, M.J. Eckholdt, H.M. & Lipton, R.B (1999). Screening for dementia with the memory impairment screen [see comments]. *Neurology,* 52, 231 – 238.

Camp, C.J. (1989). Facilitation of new learning in Alzheimer's disease. In: Gilmore G, Whitehouse P, Wykle M, editors. Memory and aging: theory, research and practice. *New York: Springer*, p. 212 – 225.

Carvalho, V. A. & Caramelli, P. C. (2007). Brazilian adaptation of the Addenbrooke's Cognitive Examination-Revised (ACE-R). *Dementia & Neuropsychologia* 2, 212-216.

Chertkow, H. (2002). Mild Cognitive Impairment *Current Opinion in Neurology,* 15: 401–407

Chui, H. (2000). Vascular dementia, a new beginning: shifting focus from clinical syndrome phenotype to ischemic brain injury*. Neurologic Clinics*, 18, 951 – 977.

Clark, D.G. & Cummings, J.L. (2004). The Diagnosis and Management of Dementia. *Middle East Journal of Family Medicine*, Vol. 2 (5).

Clare, L., Linden, D. E. J., Woods, R. T., Whitaker, R., Evans, S. J., Parkinson, C. H., Van Paasschen, J., et al. (2010). Goal-oriented cognitive rehabilitation for people with early-stage Alzheimer disease: a single-blind randomized controlled trial of clinical efficacy. *The American journal of geriatric psychiatry□: official journal of the American Association for Geriatric Psychiatry*, *18*(10), 928–39. doi:10.1097/JGP.0b013e3181d5792a

Clare, L. Wilson, B.A. Carter, G. Gosses, A. Breen, K. & Hodges, J.R. (2000). Intervening with everyday memory problems in early Alzheimer's disease: an errorless learning approach. *Journal of Clinical and Experimental Neuropsychology,* 22, 132 – 146.

Clare, L. Wilson, B.A. Breen, K. & Hodges, J.R. (1999). Errorless learning of face-name associations in early Alzheimer's disease. *Neurocase*: *The Neural Basis of Cognition*, 5, 37 – 46.

Clare, L. & Wilson, B.A. (2004). Memory rehabilitation for people with early-stage dementia: a single case comparison of four errorless learning methods. *Zeitschrift für Gerontopsychologie und – Psychiatrie,* 17, 109 –117.

Crawford, J.R., Moore, J.W. & Cameron, I.M. (1992) Verbal fluency: A NART based equation for the estimation of premorbid performance. British Journal of Clinical Psychology, 31, 327-329.

Crawford, S., Whitnall, L., Robertson, J., & Evans, J. J. (2012). A systematic review of the accuracy and clinical utility of the Addenbrooke's Cognitive Examination and the Addenbrooke's Cognitive Examination-Revised in the diagnosis of dementia. *International journal of geriatric psychiatry*, *27*(7), 659–69. doi:10.1002/gps.277.

Cronbach, L. J. (1951). Coefficient alpha and the internal structure of tests. *Psychometrika*. 16, 297-334.

Cronbach, L. J. & Meehl, P. E. (1955). Construct Validity in Psychological Tests *Psychological Bulletin*, 52: 281-302

Cronbach, L. J. & Shavelson, R.J. (2004). My Current Thoughts on Coefficient Alpha and Successor Procedures. *Educational and Psychological Measurement*, 64, no. 3 (June 1), 391- 418. doi:10.1177/0013164404266386.

Crum, R.M., Anthony, J.C., Bassett, S.S., Folstein, M.F. (1993) Population-based norms for the Mini-Mental State Examination by age and educational level. Journal of the American Medical Association, 12, 269, 2386-2391.

Cullen, B. O'Neil, B. Evans, J.J. Coen, R.F. & Lawlor, B. (2007). A review of Screening Tests for Cognitive Impairment. *Journal Neurology Neurosurgery & Psychiatry*, 78, 790 – 799.

Cummings, J. (1996). Neuropsychiatric assessment and intervention in Alzheimer's disease. *International Psychogeriatrics,* 8, 25 – 30.

Cummings, J.L. & Benson, D.F. (1992). *Dementia: A Clinical Approach*. Boston: Butterworth-Heinemann.

Cummings, J.L. Frank, J.C. Cherry, D. Kohatsu, N. Kemp, B. Hewett, L. & Mittman, B. (*2002).* Guidelines for managing Alzheimer's disease: assessment (pt 1)*. American family Physician,* 65, 2263 – 2272.

Cummings, J.L. Mega, M. Gray, K. Rosenberg-Thompson, S. Carusi, D.A. & Gorebein, J. (1994). The Neuropsychiatric Inventory:comperhensive assessment of psychopathology in dementia. *Neurology,* 44, 2308 – 2314.

Davis, P. (1978). Studies on the neurochemistry of central cholinergic systems in Alzheimer's disease. Senile Dementia Disorders. *New York: Raven Press,* 453 – 468.

Dean, P.M. Feldman, D.M. Morere, D. & Morton, D. (2009). Clinical evaluation of the mini-mental state exam with culturally deaf senior citizens. *Archives of Clinical Neuropsychology,* 24 (8), 753–60.

De Jager, C. A., Hogervorst, E., Combrinck, N. & Budge, M. M. (2003). Sensitivity and specificity of neuropsychological tests for mild cognitive impairment, vascular cognitive impairment and Alzheimer's disease. *Psychological Medicine*, 33:1039–105.

Downs, M. Clare, L. & Mackenzie, J. (2006). Understandings of dementia: Explanatory models and their implications for the person with dementia and therapeutic effort. In J. C. Hughes, S. J. Louw, & S. R. Sabat (Eds.), Dementia: Mind, meaning and the person. *Oxford: Oxford University Press*.

Dickson, D.W. Feany, M.B. Yen, S.H. Mattiace, L.A. & Davies, P. (1996). Cytoskeletal pathology in non-Alzheimer degenerative dementia: new lesions in diffuse Lewy body disease, Pick's disease, and corticobasal degeneration. *Journal of Neural Transmission. Supplementum*, 47, 31-46.

Doody, R.S. Stephens, J.C. Beck, C. Dubinsky, R.M. Kaye, J.A. Gwyther, L. Mohs, R.C. Thal, L.J. Whitehouse, P.J. DeKosky, S.T. & Cummings, J.L. (2001). Practice parameters: management of dementia. *Neurology,* 56, 1154 – 1166.

Doody, R.S. Stevens J.C. Beck C. Dubinsky, R.M. Kaye, J.A. Gwyther, L. Mohs, R.C. Thal, L.J. Whitehouse, P.J. DeKosky, S.T. & Cummings, J.L. (2000). Practice parameter: management of dementia (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology,* 54, 1446 – 1447.

Dudas, R.B. Berrios, G.E. & Hodges, J.R. (2005). The Addenbrooke's Cognitive Examination in the differential diagnosis of early dementia versus affective disorder. *The American Journal of Geriatric Psychiatry*, 13, 218 – 226.

El Tallawy, H. N., Farghly, W. M., Shehata, G. A., Rageh, T. A., Hakeem, N. A., Abo-Elfetoh, N., & El-Moselhy, E. A. (2012). Prevalence of Dementia in Al Kharga District, New Valley Governorate, Egypt. *Neuroepidemiology*, 38(3): 130-137.

Feher, E.P. Mahurin, R.K. Doody R.S. Cooke, N. Sims, J. & Pirozzolo, F.J. (1992). Establishing the limits of the minimental state. examination of ‘‘subtests’’*. Archives of Neurology,* 49, 87– 92.

Ferri, F. F. (2006) *A Practical Guide to the Differential Diagnosis of Symptoms, Signs, and Slinical Disorders*. *Second Edition*. Mosby Elsevier.

Ferri, C.P., Prince, M., Brayne, C., Brodarty, H., Fratigilioni, L. et al. (2005). Global prevalence of dementia: a Delphi consensus study. *Lancet*, 366, 9503, 2112-2117.

Field, A. & Hole, G. (2003) *How to Design and Report Experiments.* London: Sage

Folstein, M.F. Folstein, S.E. McHugh, P.R. (1975). ""Mini-mental state". A practical method for grading the cognitive state of patients for the clinician". *Journal of psychiatric research,* 12 (3), 189 – 98.

Freyne, A. (2001). Screening for dementia in primary care – available proposition? *Irish Journal of Psychological Medicine*, 18(2), 75 – 77.

Ganguli, M.. Tangalos, E. G. Cummings, J. L. &. DeKosky, S. T. (2001). Practice parameter: Early Detection of dementia: Mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*, 56, 1133 – 1142.

Garcia-Caballero, A. Garcia-Lado, I. Gonzalez-Hermida, J. Recimil, M.J. Area, R. Manes, F. Lamas, S. & Berrios, G.E. (2006). Validation of the Spanish version of the Addenbrooke's Cognitive Examination in a rural community in Spain. *International Journal of Geriatric Psychiatry,* 21(3), 239 – 245.

Gauthier, S. Reisberg, B. Zaudig, M Petersen, R.C. Ritchie, K. Broich, K. Belleville, S. Brodaty, H. Bennett, D. Chertkow, H. Cummings, J.L. de Leon, M. Feldman, H. Ganguli, M. Hampel, H. Scheltens, P. Tierney, M.C. Whitehouse, P. & Winblad, B. (2006). International Psychogeriatric Association Expert Conference on Mild Cognitive Impairment: mild cognitive impairment. *Lancet,* 367, 1262 – 1270**.**

Gelder, M. Gath, D. Mayou, R. & Cowen, P. (2000). *Oxford Textbook of Psychiatry*. Oxford: Oxford University Press, p. 313.

Gifford, D.R. & Cummings, J.L. (1999). Evaluating dementia screening tests: methodologic standards to rate their performance [editorial comment]. *Neurology*, 52: 224 – 227.

Goldstein, K. (1975) Functional disturbances in brain damage. In M.F.Reiser (Ed.) *American Handbook of Psychiatry* (pp.182-207). New York: Basic Books.

Gómez, F., Zunzunegui, M.V., Lord, C., Alvardo, B., & Garcia, A. (2013). Applicability of the MoCA-S in populations with little education in Colombia. *International Journal of Geriatric Psychiatry,* 28, 8, 813-820

Graham, J.E. Rockwood, K.. Beattie, B.L. Eastwood, R. Gauthier, S. Tuokko, H. & McDowell, I. (1997). Prevalence and severity of cognitive impairment with and without dementia in an elderly population. *Lancet*, 349, 1793 – 1796.

Greene, J.D. Baddeley, A.D. & Hodges, J.R. (1996). Analysis of the episodic memory deficit in early Alzheimer's disease: evidence from the doors and people tests. *Neuropsychologia,* 34, 537 – 551.

Gregory, CA. Orrel, M.Sahakian, B. & Hodges, J.R. (1997). Can fronto-temporal dementia and Alzeheimer's disease be differentiated using a brief battery of tests? *International Journal of Geriatric Psychiatry*, 12, 375 – 83.

Grundman, M., Petersen, R. C., Ferris, S. H., Thomas, R. G., Aisen, P. S., Bennett, D. A., & Thal, L. J. (2004). Mild cognitive impairment can be distinguished from Alzheimer disease and normal aging for clinical trials. *Archives of Neurology*, 61(1): 59.

Hall, J R. Harvey, M. Vo, H.T. & O'Bryant, S.E. (2012) Performance on a measure of category fluency in cognitively impaired elderly. *Aging, Neuropsychology, and Cognition,* 18, 3, 353 – 361

Hardy, J. (2003). The relationship between Lewy body disease, Parkinson's disease, and Alzheimer's disease. *Annals of the New York Academy Sciences*, 1991, 167 – 70.

Heo, J. H., Lee, K. M., Park, T. H., Ahn, J. Y., & Kim, M. K. (2012). Validation of the Korean Addenbrooke's Cognitive Examination for Diagnosing Alzheimer's Dementia and Mild Cognitive Impairment in the Korean Elderly. *Applied Neuropsychology*, 19(2): 127-131.

Heron, M.P. Hoyer, D.L., Xu, J., Scott, C. Tejada-Vera, B. & Division of Vital Statistics (2008). Deaths: Preliminary Data for 2006. National Vital Statistics Reports. Vol. 56, no. 16. Hyattsville, Md.: *The National Center for Health Statistics.*

Hirao, K. Ohnishi, T. Hirata, Y. Yamashita, F. Mori, T. Moriguchi, Y. Matsuda, H. Nemoto, K. Imabayashi, E. Yamada, M. Iwamoto, T. Arima, K. & Asada, T. (2005). The prediction of rapid conversion to Alzheimer's disease in mild cognitive impairment using regional cerebral blood flow SPECT. *NeuroImage* 28, 1014 – 1021.

Hodges, J.R.. (2001). Frontotemporal dementia (Pick's disease): clinical features and assessment. *Neurology*, 56**,** S6 –10.

Hodges, J.R. & Patterson, K. (2007). Semantic dementia: a unique clinicopathological syndrome. *The Lancet Neurology,* 6, 1004 –14.

Hodges, J.R. Patterson, K. Oxbury, S. & Funnell, E. (1992). Semantic dementia. progressive fluent aphasia with temporal lobe atrophy. *Brain,* 115, 1783 – 1806.

Hodges, J.R. Patterson, K. Ward R. Garrard, P. Bak, T. Perry, R. & Gregory, C. (1999). The differentiation of semantic dementia and frontal lobe dementia (temporal and frontal variant of frontotemporal dementia) from early Alzheimer's disease: a comparative neuropsychological study. *Neuropsychology*, 13, 31 – 40.

Hughes, C.P., Berg, L., Danziger, W.L., Coben, L.A., Martin, R.L. (1982). A new clinical scale for the staging of dementia. *British Journal of Psychiatry*, 140, 566–572

Huppert, F..A. Brayne, C. Gill, C. Paykel, E.S. & Beardsall, L. (1995). CAMCOG – a concise neuropsychological test to assist dementia diagnosis: socio-demographic determinants in an elderly population sample. *British Journal of Clinical Psychology*, 34, 529 – 541.

Hutton, S. Sheppard, L. Rusted, J. M. & Ratner, H.H. (1996). Structuring the acquisition and retrieval environment to facilitate learning in individuals with dementia of the Alzheimer type. *Memory*, 4, 113-130.

Jeste, D.V. Blazer, D. Casey, D. Meeks, T. Salzman, C. Schneider, L. Tariot, P. & Yaffe, K. (2008). ACNP White Paper: update on use of antipsychotic drugs in elderly persons with dementia. *Neuropsychopharmacology*, 33, 957 – 970.

Jorm, A. F. (1994). A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. *Psychological Medicine,* 24, 145 – 153.

Karam, G. & Itani, L. (2013) Dementia: a review from the Arab region. *The Arab Journal of Psychiatry*, 24, 1, 77-84.

Karlsson, T. Bäckman, L. Herlitz, A. Nilsson, L-G. Winblad, B. & Osterlind, P-O. (1989). Memory improvement at different stages of Alzheimer's disease. *Neuropsychologia*, 27, 737 – 742.

Kawas, C. Segal, J. Stewart, W. F. Corrada, M. & Thal, L. J. (1994). A Validation Study of Dementia Questionnaire. *Archievs of Neurology*, 51, 901 – 906.

Kertesz A. (2003). Pick Complex: an integrative approach to frontotemporal dementia: primary progressive aphasia, corticobasal degeneration, and progressive supranuclear palsy. *Neurologist*, 9, 311 – 7.

Kertesz, A. Davidson, W. & Fox, H. (1997). Frontal behavioral inventory: diagnostic criteria for frontal lobe dementia. *Journal of the Neurological Sciences*, 24(1), 29 – 36.

Kertesz, A. & Munoz, D.G. (2002). Frontotemporal dementia. *Medical Clinics of North America.* 86(3), 501 – 18.

Khalil, M. (2010). Preliminary Arabic normative data of neuropsychological tests: The verbal and design fluency. *Journal of Clinical and Experimental Neuropsychology,* 32, 9, 1028 – 1035.

Knapp, M., & Prince, M (2007) Dementia UK: Full Report, *Alzheimer's Society*

Knibb, J.A. & Hodges, J.R. (2005). Semantic dementia and primary progressive aphasia. A problem of categorization? *Alzheimer disease and associated disorders*, 19(Suppl 1), S7 – S14.

Knibb, J.A. Kipps, C.M. & Hodges, J.R. (2006). Frontotemporal dementia. Current Opinion in *Neurology*, 19(6), 565 – 71.

Konstantinopulou, E., Kosmidis, M.H., Ioannidis, G., Kiosseoglou, D., & Karacostas, D. (2011). Adaptation of Addenbrooke's Cognitive Examination – Revised for the Greek population. *European Journal Neurology* 18, 442 – 447.

Korczyn, A. D., Kahana, E., & Galper,Y. (1991). Epidemiology of dementia in Ashkelon, Israel. *Neuroepidemiology*, 10:100–100

Korczyn, A. D., Kahana, E., & Friedland, R. P. (1998). Education and dementia. In: *Lomranz J, ed. Handbook of Aging and Mental Health: An Integrative Approach*. Plenum Press, New York.

Knopman, D.S. DeKosky S.T. Cummings, J.L. Chui, H. Corey-Bloom, J. Relkin, N. Small, G.W. Miller, B. & Stevens, J.C. (2001). Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology,* 56, 1143 –1153.

Kukull, W.A. Larson, E.B. Teri, L. Bowen, J. McCormick, W. & Pfanschmidt, M.L. (1994). The Mini-Mental State Examination score and the clinical diagnosis of dementia. *Journal of Clinical Epidemiology*, 47, 1061 – 1067.

Kwak, Y.T. Yang, Y. & Kim, G.W. (2010) Korean Addenbrooke's Cognitive Examination Revised (K-ACER) for differential diagnosis of Alzheimer's disease and subcortical ischmic vascular dementia. *Geriatrics and Gerontology International,* 2010 10, 295 – 301

Larner, A.J. (2007). Addenbrooke's Cognitive Examination-Revised (ACE-R) in day-to-day clinical practice. *Age Ageing*, 36, 685 – 6.

Levy, M.L. Miller, B.L. Cummings, J.L. Fairbanks, L.A. & Craig, A (1996). Alzheimer's disease and frontotemporal dementias: behavioural distinctions. *Achieves of Neurology*, 53, 687 – 690.

Lewis, M.P. (ed.), 2009. Ethnologue: Languages of the World, Sixteenth edition. Dallas, Tex.: SIL International. Online version: http://www.ethnologue.com/.

Lezak, M.D. Howieson, D.B. & Loring, D.W. (2004) Neuropsychological Assessment: Fourth Edition. *Oxford: Oxford University Press.*

Linn R.T. Wolf, P.A. Bachman, D.L. Knoefel, J.E. Cobb, J.L. Belanger, A.J. Kaplan, E.F. & D'Agostiono, R.B. (1995). The preclinical phase of probable Alzheimer's disease**.** *Achieves of Neurology,* 52**,** 485 – 490**.**

Loewenstein, D.A. Barker, W.W. Harwood, D.G. Luis, C. Acevedo, A. Rodriguez, I. & Duara, R. (2000). Utility of a modified Mini-Mental State Examination with extended delayed recall in screening for mild cognitive impairment and dementia among community dwelling elders. *International Journal of Geriatric Psychiatry,* 15, 434 –440.

Looi, J.C. & Sachdev, P.S. (1999). Differentiation of vascular dementia from AD on neuropsychological tests. *Neurology,* 53, 670 – 678.

Mathuranath, P.S., Cherian, J.P., Mathew, R., George, A., Alexander A., Sarma, S.P. (2007). Mini Mental State Examination and the Addenbrooke's Cognitive Examination: Effect of education and norms for a multicultural population. *Neurology India*, 55, 2, 106-110.

Mathuranath, P.S. Hodges, J.R. Mathew, R. Cherian, P.J. George, A. & Bak, T.H. (2004). Adaptation of the ACE for a Malayalam speaking population in southern India. *International Journal of Geriatric Psychiatry,* 19(12), 1188 – 1194.

Mathuranath, P.S. Nestor, P.J. Berrios, G.E. Rakowicz, W. & Hodges, J.R. (2000). A Brief Cognitive Test Battery to Differentiate Alzheimer's Disease and Frontotemporal Dementia. *Neurology*, 55(11), 1613 – 1620.

Mattis, S. (1988). Dementia Rating Scale. Odessa, FL: Psychological Assessment Resources, Inc.

McKeith, I.G. Fairbairn, A.F. Bothwell, R.A. Moore, P.B. Ferrier, I.N. Thompson, P. & Perry, R.H. (1994). An evaluation of the predictive validity and inter-rater reliability of clinical diagnostic criteria for senile dementia of Lewy body type. *Neurology,* 44, 872 – 877.

McKhann, G. Drachman, D. Folstein, M. Katzman, R. Price, D. & Stadlan, E. (1984). Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology*, 34, 939 – 974.

McMurtray, A.M. Chen, A.K. Shapira, J.S. Chow, T.W. Mishkin, F. Miller, B.L. & Mendez, M.F. (2006). Variations in regional SPECT hypoperfusion and clinical features in frontotemporal dementia. *Neurology*, 66**,** 517 – 522.

Ministry of Economy & Planning (2004). Detailed Results Population & Housing Census. pp. 70 – 75.

Mioshi, E. Dawson, K. Mitchell, J. Arnold, R. and Hodges, J. R. (2006). The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *International Journal Geriatric Psychiatry*, 21, 1078 – 1085.

Mioshi, E. Kipps, C.M. Dawson, K. Mitchell, J. Graham, A. & Hodges, J.R. (2007). Activities of daily living in frontotemporal dementia and Alzheimer disease. *Neurology,* 68(24), 2077– 2084.

Mitchell, A.J., & Shiri-Feshki, M. (2009). Rate of progression of mild cognitive impairment to dementia--meta-analysis of 41 robust inception cohort studies. *Acta psychiatrica Scandinavica*, *119*(4), 252–65. doi:10.1111/j.1600-0447.2008.01326.x

Mohs, R.C. Rosen, W.G. & Davis, K.L. (1983). The Alzheimer's disease assessment scale: an instrument for assessing treatment efficacy. *Psychopharmacology Bulletin*, 19, 448 – 450.

Mungas, D. (1991) In office mental status testing: A practical guide. Geriatrics, 6, 7, 54- 58.

National Institute for Clinical Excellence (2011). Technology Appraisal Guidance No. 217.

Naugle, R.I. & Kawczak, K. (1989). Limitations of the Mini-Mental State Examination. *Cleveland Clinic Journal of Medicine,* 65, 277 – 281.

Neary, D. Snowden, J.S. Gustafson, L. Passant, U. Stuss, D. Black, S. Freedman, M. Kertesz, A. Robert, P.H. Albert, M. Boone, K. Miller, B.L., Cummings, J., Benson, D.F. (1998). Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology*, 6, 1546 – 54.

Neary, D. Snowden, J. & Mann, D. (2005). Frontotemporal dementia. *The Lancet Neurology*, 4(11), 771 – 80.

Newman, J. P. (2007). Mini Mental Status Examination and the Addenbrooke's Cognitive Examination: Effect of education and norms for a multicultural population. *Neurology India* 2007;55:99.

Orange, J.B. & Ryan, E.B. (2000). Alzheimer's disease and other dementias: implications for physician communication. *Clinics in Geriatric Medicine, [review].*16, 153-173, xi.

Ott, A., Breteler, M.M., Van-Harskam, F., Claus, J.J., van der Cammen, T.J., Grobbee, D.E., & Hofman, A. (1995). Prevalence of Alzheimer's disease and vascular dementia: association with education. The Rotterdam study. *British Medical Journal* 310**:** 970–973.

Oxford Dictionaries (2008) Pocket Oxford Dictionary and Thesaurus. Oxford: Oxford University Press.

Panza F. D'Introno, A. Colacicco, A.M. Capurso, C. Del Parigi, A. Caselli, R.J. Pilotto, A. Argentieri, G. Scapicchio, P.L. Scafato, E. Capurso, A. & Solfrizzi, V. (2005). Current epidemiology of mild cognitive impairment and other predementia syndromes. *American Journal of Geriatric Psychiatry*, 13, 633 – 644.

Paulsen, J.S. Ready, R.E. Stout, J.C. Salmon, D.P. Thal, L.J. Grant, I. & Jeste, D.V. (2000). Neurobehaviors and psychotic symptoms in Alzheimer's disease*. Journal of the International Neuropsychological Society*, 6(7), 815 – 20.

Perry, R.H. Irving, D. Blessed, G. Fairbairn, A. & Perry, E. (1990). Senile dementia of Lewy body type – a clinically and neuropathologically distinct form of Lewy body dementia in the elderly. *Journal of the Neurological Sciences,* 95, 119 –139.

Petersen, R.C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of internal medicine,* 256, 183 –194.

Petersen, R.C. & Morris, J.C. (2005) Mild cognitive impairment as a clinical entity and treatment target. *Archives of Neurology,* 62, 1160 –1167.

Petersen, R.C. Smith, G.E. Waring, S.C. Ivnik, R.J Tangalos, E.G. & Kokmen, E (1999). Mild cognitive impairment: clinical characterisation and outcome. *Archives of Neurology*, 56, 303 – 308.

Plassman, B. & Breitner, J. (2000). The genetics of Alzheimer's disease. In: *Dementia 2nd Edition*. Edited by J O'Brien, D Ames and A Burns. Arnold.

Plassman, B.L. Langa, K.M. Fisher, G.G. Heeringa, S.G. Weir, D.R. Ofstedal, M.B. Burke, J.R. Hurd, M.D, Potter, G.G. Rodgers, W.L. Steffens, D.C. Willis, R.J. & Wallace, R.B. (2007). Prevalence of Dementia in the United States: The Aging, Demographics, and Memory Study. *Neuroepidemiology*, 29, 125–132.

Poirier J. Bertrand, P. Poirier, J. Kogan, S. Gauthier, S. Poirier, J. Davignon, J., Bouthillier, D. & Davignon, J. (1993). Apolipoprotein E polymorphism and Alzheimer's disease. *The Lancet*, 342, 697– 699.

Popescu, C., Tudose, C., Niculescu, R., Popa, N., Popa, D., Scripcă, R., Petrescu, A-M., Sandu, C., Leremie, R., Rus, O. & Dobrică, E. (2009) A Romanian adaptation of the Addenbrookes Cognitive Examination Scale. Revista Romana de Psihiatrie, 2-3.

Price, J.L. Davis, P.B. & Morris, J.C. & White, D.L. (1991). The distribution of tangles, plaques, and related immunohistochemical markers in healthy aging and Alzheimer's disease. *Neurobiology of Aging*, 12, 295 – 312.

Prigatano, G. P. (1999). Principles of neuropsychological rehabilitation. *New York: Oxford University Press*.

Rabins, P.V., Blacker, D., Rovner, B.W., Rummans, T., Schneider, L.S., Tariot, P.N., Blass, D.M., McIntyre, J.S., Charles, S.C., Anzia, D.J., Cook, I.A., Finnerty, M.T., Johnson, B.R., Nininger, J.E., Schneidman, B., Summergrad, P., Woods, S.M., Berger, J., Cross, C.D., Brandt, H.A., Margolis, P.M., Shemo, J.P., Blinder, B.J., Duncan, D.L., Barnovitz, M.A., Carino, A.J., Freyberg, Z.Z., Gray, S.H., Tonnu, T., Kunkle, R., Albert, A.B., Craig, .T.J., Regier, D.A., & Fochtmann, L.J. (2007). Practice guidelines for the treatment of patients with Alzheimer's disease and other dementias. *American Journal of Psychiatry*.164 Suppl. 12:5–56.

Ratnavalli, E. Brayne, C. Dawson, K. & Hodges, J.R. (2002). The prevalence of frontotemporal dementia. *Neurology*, 58(11), 1615 – 21.

Reilly, J. Martin, N. & Grossman, M. (2005). Verbal learning in semantic dementia: is repetition priming a useful strategy? *Aphasiology,* 19, 329 – 339.

Reisberg, B. Doody, R. Stöffler, A. Schmitt, F. Ferris, S. Möbius, H.J. Memantine Study Group (2003). Memantine in moderate-to-severe Alzheimer's disease. *The New England Journal of Medicine*, 348, 1333 –1341.

Roman, G.C. (2003). Vascular dementia: Distinguishing characteristics, treatment, and prevention. *Journal of American Geriatric Society,* 51(5 Suppl Dementia), S296 – 304.

Rosen, W.G. Mohs, R.C. & Davis, K.L. (1984). A new rating for Alzheimer's disease. *The American Journal of Psychiatry* 141, 1356 – 1364.

Rosenberg, P. B. Johnston, D. & Lyketsos, C. G. (2006). A Clinical Approach to Mild Cognitive Impairment. *The American Journal of Psychiatry*, 163, 1884 – 1890.

Rossor, M. (2001). Pick's disease: a clinical overview. *Neurology,* 56 (Suppl. 4), S3 –5.

Salzman, C. Jeste, D.V. Meyer, R.E. Cohen-Mansfield, J. Cummings, J. Grossberg, G. Jarvik, L. Kraemer, H. Lebowitz, B. Maslow, K. Pollock, B. Raskind, M. Schultz, S. Wang, P. Zito, J.M. & Zubenko, G.S. (2008). Elderly patients with dementia-related symptoms of severe agitation and aggression: consensus statement on treatment options, clinical trials methodology, and policy. *Journal of Clinical Psychiatry*, 69(6), 889 – 898.

Siedlecki, K. L., Manly, J. J., Brickman, A. M., Schupf, N., Tang, M. X., & Stern, Y. (2010). Do neuropsychological tests have the same meaning in Spanish speakers as they do in English speakers? *Neuropsychology*, 24(3), 402-411.

Smith, G. E., Ivnik, R. J., Lucas, J. A. (2008). Assessment techniques: Tests, test batteries, norms, and methodological approaches. In Morgan J, Ricker J, editors. *Textbook of Clinical Neuropsychology*. New York: Taylor & Francis, pp. 38–57.

Snowden, J.S. Bathgate, D. Varma, B. Blackshaw, A. Gibbons, Z.C. & Neary, D. (2001). Distinct behavioral profiles in frontotemporal dementia and semantic dementia. *Journal of Neurology Neurosurgery Psychiatry*, 70, 323 – 332.

Snowden J.S., Goulding P.J., & Neary D. (1989) Semantic dementia: a form of circumscribed cerebral atrophy. *Behavioural Neurology*, *2*, 167-182

Snowden, J.S. Neary, D. & Mann, D.M. (2002). Frontotemporal dementia. *British Journal of Psychiatry*, 180**,** 140 – 3.

Snowden, J.S., Thompson, J.C., Stopford, C.L., Richardson, A.M. T., Gerhard, A., Neary, D., Mann, D.M.A. (2011) The clinical diagnosis of early-onset dementias: diagnostic accuracy and clinicopathological relationships. *Brain, 134*, 9, 2478- 2492.

Stockholm, J. Vogel, A. Johannsen, P. & Waldemar, G. (2009). Validation of the Danish Addenbrooke's Cognitive Examination as a Screening Test in a Memory Clinic*. Dementia and Geriatric Cognitive Disorders*, *27*, 361 – 365.

Strauss, E. Sherman, E.M.S. & Spreen, O. (2006) A Compendium of Neuropsychological Tests. *Oxford: Oxford University Press.*

Summers, M. J., & Saunders, N. L. J. (2012). Neuropsychological measures predict decline to Alzheimer's dementia from mild cognitive impairment. *Neuropsychology*, *26*(4), 498–508. doi:10.1037/a0028576

Taylor, DH Ezell, M Kuchibhatla, M Ostbye, T & Clipp, EC. (2008). Identifying the trajectories of depressive symptoms for women caring for their husbands with dementia. *Journal of the American Geriatrics Society,* 56(2), 322 – 327.

Tombaugh, T.N. & McIntyre, N.J. (1992). The Mini-Mental State Examination: a comprehensive review [see comments] *Journal of the American Geriatrics Society*, 40, 922 – 935.

Tuokko, H. A., Chou, P. H. B., Bowden, S. C., Simard, M., Ska, B., & Crossley, M. (2009). Partial measurement equivalence of French and English versions of the Canadian Study of Health and Aging neuropsychological battery. *Journal of the International Neuropsychological Society,* 15, 416 – 425.

Verhey, F.R. Jolles, J. Ponds, R.W. Rozendaal, N. Plugge, L.A. de Vet, R.C. Vreeling, F.W. & van der lugh, P.J. (1993). Diagnosing dementia: a comparison between a monodisciplinary a multidisciplinary approach. *The Journal of Neuropsychiatry and Clinical Neurosciences*, 5, 78 – 85.

Vos, S., van Rossum, I., Burns, L., Knol, D., Scheltens, P. Soininen, H., Wahlund, L.O., Hampel, H., Tsolaki, M., Minthon, L., Handels, R., L'Italien, G., van der Flier, W., Aalten, P., Teunissen, C., Barkhof, F., Blennow, K., Wolz, R., Rueckert, D., Verhey, F., Visser, PJ. (2012) Test sequence of CSF and MRI biomarkers for prediction of AD in subjects with MCI. *Neurobiology of Aging, 33, 10*, 2272-2281.

Wilson, B.A. (2008). Neuropsychological rehabilitation. *Annual Review of Clinical Psychology*, 4, 6.1 – 6.22.

Wilson, B.A. Gracey, F. Malley, D. Bateman, A. & Evans, J.J (2009). The Oliver Zangwill Centre approach to neuropsychological rehabilitation. In: Wilson, B.A. Gracey, F. Evans, J.J. and Bateman, A. Neuropsychological Rehabilitation: theory, models, therapy and outcome. *Cambridge University Press*, pp. 47 - 67.

Weder, N.D., Aziz, R., Wilins, J., & Tampi, R. R. (2007). Frontotemporal Dementias: A Review. *Annals of General Psychiatry,* 6:15.

Willmes, K. (2010) The methodological and statistical foundations of neuropsychological assessment. In J.M. Gurd, U. Kischka, and Marshall, J.C. (eds) The Handbook of Clinical Neuropsychology, 2nd Edition. OUP: *Oxford.*

Winblad, B., Palmer, K. Kivipelto, M. Jelic, V. Fratiglioni, L. Wahlund, L.O. Nordberg, A. Backman, L. Albert, M. Almkvist, O. Arai, H. Basun, H. Blennow, K. de Leon, M. DeCarli, C. Erkinjuntti, T. Giacobini, E. Graff, C. Hardy, J. Jack, C. Jorm, A. Ritchie, K. van Duijn, C. Visser, P. & Petersen, R.C. (2004). Mild cognitive impairment: beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *Journal of Internal Medicine,* 256, 240 – 246.

Winblad, B. & Poritis, N. (1999). Memantine in severe dementia: results of the M-BEST study. (Benefit and efficacy in Severely Demented Patients during Treatment with Memantine*). International Journal of Geriatric Psychiatry,* 14, 135 – 146.

Woodford, H.J. & George, J. (2007). Cognitive assessment in the elderly: a review of clinical methods. *Quarterly journal of medicine,* 100, 469 – 84.

World Health Organization (1992). Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10). Geneva: WHO.

World Health Organization (2002). World Health Report. Reducing Risks, Promoting Healthy Life. Geneva.

Yaffe, K. Fox, P. Newcomer, R. Sands, L. Lindquist, K. Dane, K. Kenneth, E.. & Covinsky, K.E. (2002). Patient and caregiver characteristics and nursing home placement in patients with dementia. *Journal of the American Medical Association*, 287, 2090 – 2097.

Yildiz, G.B., Isik, A.T., Ur, E., Aydemir, E., Ertas, C., Cebi, M. et al. (2013) COST: Cognitive state test, a brief screening battery for Alzheimer's disease in illiterate and literate patients. *International Psychogeriatrics,* 25, 3, 403-412.

Yoshida, H., Terada, S., Honda, H., Kishimoto, Y., Takeda, N., Oshima, E., Hirayama, K., et al. (2012). Validation of the revised Addenbrooke's Cognitive Examination (ACE-R) for detecting mild cognitive impairment and dementia in a Japanese population. *International psychogeriatrics / IPA*, *24*(1), 28–37. doi:10.1017/S1041610211001190.

Zaudig, M. Mittelhammer, J. Hiller, W. Pauls, A. Thora, C. Morinigo, A. & Mombour, W. (1991). SIDAM A structured interview for the diagnosis of dementia of the Alzheimer type, Multi- Infarct Dementia and Dementias of other Aetiology according to ICD-10 and DSM-IIIR. *Psychological Medicine*, 21, 225 – 236.

APPENDICES:

Kingdom of Saudi Arabia
Ministry of Higher Education
College of Medicine
& King Khalid Univ. Hospital

بسم الله الرحمن الرحيم

المملكة العربية السعودية
وزارة التعليم العالي
جامعة الملك سعود
كلية الطب
ومستشفى الملك خالد الجامعي

Date: 19 Rajab 1430-H / 12 July 2009-G التاريخ No.: 09/2339/R الرقم:

Ahmed Al Salman, Ph.D. Student
University of Glasgow
U. K.

Subject: Research Project title: ***"Saudi Arabian Adaption of the Addenbrooke's Cognitive Examination – Revised (ACE-R)"***

Dear Dr. Al Salman,

Your above-mentioned research project was reviewed by members of the College of Medicine Research Ethics Committee and discussed in meeting no. 10 (1429-1430) held on 15 Rajab 1430-H (i.e., 8th July 2009-G). The project is approved from the ethical point of view.

We wish you success in your research.

Sincerely yours,

Professor Ahmed S. BaHammam
Chairman, Research Ethics Committee
College of Medicine
King Saud University
Riyadh, Saudi Arabia

Kingdom of Saudi Arabia
National Guard-Health Affairs
King Abdulaziz Medical City

المملكة العربية السعودية
الحرس الوطني – الشؤون الصحية
مدينة الملك عبدالعزيز الطبية

Institutional Review Board 16586/16669 1515 14567 IRBCUN Research@ngrc.med.sa

MEMORANDUM

Ref. #: IRBC/103/09

Date: (G) 19 December 2009
(H) 21 Dhu- Al Hijjah 1430

To: Dr. Ahmed Saeed Alf Al Salman
PHD Student
Glasgow, Scotland, UK. Faculty of medicine)

Subject: Protocol RC09-054: "'Saudi Arabian Adaptation of the Addenbrooke's Cognitive Examination-Revised'(ACE-R)"

This is in reference to your subject proposal, which has been expedited reviewed by the IRB on 19th of December 2009 providing that you clarify control measures to the confidentiality risk.

Your research proposal is **approved for one year** commencing from the above date with the following conditions:

TERMS OF APPROVAL:

1. **Annual Reports:** Continued approval of this project is depencent on the submission of an Annual Report. Please provide KAIMRC with an Annual Report determined by the date of your letter of approval.
2. **Amendments to the approved project:** Changes to any aspect of the project require the submission of a Request for Amendment to KAIMRC and must not begin without an approval from KAIMRC. Substantial variations may require a new application.
3. **Future correspondence:** Please quote the project number and project title above in any further correspondence.
4. **Monitoring:** Projects may be subject to an audit or any other form of monitoring by KAIMRC at any time.
5. **Retention and storage of data:** The PI is responsible for the storage and retention of original data pertaining to a project for a minimum period of five years.

R. Kashmeery

Prof. Amin Kashmeery
Head, Biomedical Ethics Section
National Guard Health Affairs

AK/AA/msm

P. O. Box 22490, Riyadh 11426
Tel. 2520088
Telex : 403450 NGRMED SJ

ص.ب ٢٢٤٩٠ الرياض ١١٤٢٦
تلفون : ٢٥٢٠٠٨٨
تلكس : NGRMED ٤٠٣٤٥٠

KFH-MATERIALS 14574 (05/96) (ORACLE 29753)

بسم الله الرحمن الرحيم

DALLAH HOSPITAL

DALLAH HEALTHCARE CO

مستشفى دلة

شركة دلة للخدمات الصحية

الموافق : ٢٠١٢/٠٧/٢٤م

الرقم : ٢٣ / ع د / ٩ .

الأخ / أحمد سعيد آل سلمان المحترم

السلام عليكم ورحمة الله وبركاته ،،،

اشكركم على اهتمامكم بالبحث ، ونرجو من الله لكم التوفيق ، أما فيما يتعلق بسرعة باجراء البحث في مستشفى دلة ، وحيث ذكرتم أنه ذلك كان بتوجيه الأستاذ الدكتور / عبدالرحمن الطحان (استشاري أمراض الأعصاب) ، لا مانع مع ضرورة إتباع التالي :-

١. خطاب من الدكتور / عبدالرحمن الطحان بالموافقة على إجراء البحث على مرضاه وعلى مسؤوليته مع ضمان المحافظة على سرية المعلومات الشخصية للمرضى .
٢. بناء على ما ذكر أعلاه ، فإن المستشفى يخلي مسؤوليته القانونية تجاه المرضى .

شاكرين لكم وتقبلوا تحياتنا ،،،

د. محمد بن راشد الفقيه

رئيس مجلس الإدارة بالانابة

- نسخة مع التحية لـ :
✓ د. عبدالرحمن الطحان
✓ الملف

MEMBER OF DALLAH ALBARAKA GROUP

عضو مجموعة دلة البركة

ص . ب ٨٧٨٣٣ - الرياض ١١٦٥٢ - المملكة العربية السعودية - هاتف : ٤٧٠٢٧٧٧ - فاكس : ٤٧٠٢٧٢٥

P. O. Box 87833 - Riyadh 11652 - Kigdom of Saudi Arabia - Tel. 4702777 - Fax 4702725

WWW.dallah-hospital.com

Kingdom of Saudi Arabia
Ministry of Health

المملكة العربية السعودية
وزارة الصحة

KING SAUD MEDICAL CITY

To whom it may concern

Riyadh 2nd January 2011

Dear Mr. Ahmed Saeed Al Salman

Thank you for choosing King Saud Medical City for conducting your research entitled"Saudi Arabian Adaptation of the Addenbrook's Cognitive Examination Revised" from April 11th to September 20th 2010.

We herewith issue this letter of termination of your study.

Dr. Tarig S.A. Al Khuwaitir MB BS, Arab BIM, MRCP (UK), FRCP (Ed)

Consultant Physician
Chairman Department of Medicine
Chairman Research and Clinical Trials Committee
Deputy CEO for Medical Affairs
King Saud Medical Complex
Ministry of Health
Riyadh
Kingdom of Saudi Arabia

المرفقات ..... التاريخ ..... الرقم .....

AL-MOBARAK HOSPITAL

مستشفى المبارك

2010/3/15م

الموضوع: خطاب موافقة

المحترم

الدكتور / أحمد سعيد آل سلمان

كلية الطب بجامعة جلاسكو - بريطانيا

السلام عليكم ورحمة الله وبركاته ،،،،،

لا مانع لدينا من قبول تطبيق الدراسة المسماه:

(Saudi Arabian Adaptation of Addenbroks Cognitive Examination-revised).

وتقبلوا تحياتنا ،،،،،

المدير العام

خالد دخيل الله الخثعمي

AL-MOBARAK HOSPITAL

طريق الملك فيصل - الرياض ١١٤٥٤ - ص.ب ١٥٥٦٣ - المملكة العربية السعودية - ترخيص رقم ١١٦٨/١٢ - هاتف: ٤٠١٥٢٨٢ - فاكس: ٤٠١٥٠١٨

King Faisal Road - Riyadh 11454 - P.O.Box: 15563 - Kingdom of Saudi Arabia - Licence : 1168/12 - Tel. 4015282 - Fax: 4015018

مـركز الأميـر سلـمـان الإجتمـاعي
Prince Salman Social Center

الرقم : /د/ ٣٠
التاريخ : ١٤٣٠/١٢/١٥ هـ الموافق ٢٠٠٩/١٢/٢ م
الموضوع : خطاب موافقة .

المحترم
الدكتور / أحمد سعيد آل سلمان
كلية الطب بجامعة جلاسكو - بريطانيا

السلام عليكم ورحمة الله وبركاته .. وبعد:
لا مانع لدينا من قبول تطبيق الدراسة المسماه

(Saudi Arabian Adaptation of Addenbroks Cognitive Examination-Revised).

وتقبلوا تحياتنا ،،،

مركز الأمير سلمان الإجتماعي
Prince Salman Social Center

رشاد سعيد هارون
المدير العام

Tel. 450 0808 Fax 450 0909 هاتف: ٤٥٠٠٨٠٨ ـ فاكس: ٤٥٠٠٩٠٩
P.O.Box 27400 Riyadh 11417 Saudi Arabia ص ب ٢٧٤٠٠ الرياض ١١٤١٧ المملكة العربية السعودية

University of Glasgow

ورقة معلومات للمشاركين

أختبار أدنبروكس المعرفي المنقح على البيئة السعودية

(ACE- R)

دعوة للمشاركة في دراسة بحثية:
أنت مدعو للمشاركة في هذه الدراسة البحثية التي نرغب أن تسهم في إيجاد أداة تشخيصية قيمة تشخص مرض خرف الشيخوخة في بداية الإصابة بالمرض مما يسهل عملية التدخل العلاجي في بداية وجود المشكلة. قبل أن تقرر المشاركة، إعلم أنه من المهم بالنسبة لك أن تفهم لماذا يجري البحث؟ وعلى ماذا يشتمل؟ يرجى التكرم بقراءة المعلومات التالية بعناية ومناقشتها مع الباحث إذا كنت ترغب في ذلك. الرجاء أن تسأل ما إذا كان هناك أي شيء غير واضح أو إذا كنت ترغب في مزيد من المعلومات.

نشكركم على حرصكم على المشاركة وقراءة التعليمات.

الغرض من هذه الدراسة:
تهدف هذه الدراسة إلى تقنين أداة عصبية نفسية جديد في المجال الإكلينيكي تسمى "أختبار أدنبروكس المعرفي المنقح" على المجتمع السعودي. هذه الإداة سوف تسهم هذا تحسين خدمات الرعاية الصحية التي تعطى لكبار السن وخاصة في المملكة العربية السعودية وغيرها من الدول العربية الأخرى بشكل عام. هذه الدراسة سوف تفتح أفقا جديدا لتقييم الأمراض التي تصيب كبار السن فيما يتعلق بالدماغ. وهكذا، فإن نتائج هذه الدراسة في توظف للتنبوء حول طبيعة أمراض الدماغ وتحولاتها والتغيرات التي تحدث في مراحل المرض. هذا ربما قد يساعد على منع أو الحد من بعض الأعراض التي تصيب أمراض الدماغ حين يصاب المريض بمرض الخرف.

لماذا تم اختياري؟

العينة المستهدف هي من كبار السن من سن 50 فأكثر، من المرضى المصابين بخرف الشيخوخة أو من الأصحاء.

هل لا بد لي من المشاركة؟
أنت حر في أن تقرر ما إذا كانت تريد المشاركة أو لا. إذا قررت المشاركة، يتم منحك هذه الورقة التي تتضمن معلومات عن الدراسة ويمكنك الاحتفاظ بها وسوف نطلب منك التوقيع على نموذج الموافقة. أيضا إذا قررت المشاركة فأنت لديك كامل الحرية في الانسحاب في أي وقت وبدون إبداء أي سبب ولكن تذكر أن مشاركتك ذات أهمية بالغة بالنسبة لنا، وسوف تعد مشاركة في وطنية تهدف للصالح العام. المشاركة سوف تكون في جولتين بينهما أسبوعين كحد أقصى.

ماذا سيحدث لي إذا كنت تشارك؟
أولا، سوف يطلب منك استكمال الفحص مع الباحث. قد يستغرق الاختبار 20 دقيقة كحد أقصى للانتهاء منه. لأيس مهما أن تكتب أو تدلي بمعلوماتك الشخصية مثل اسمك على أوراق الاختبار. نحن نركز على نتائج الدراسة ومدى قدرتها عل تحسين عمليات المعالجة في المستقبل.

السلبيات والمخاطر المحتملة من المشاركة:
لا توجد مخاطر كبيرة أو سلبيات عند قيامك بالمشاركة. إذا كنت تشعر بالتعب يمكنك أخذ قسط من الراحة لفترة من الوقت ثم المتابعة.

v.1., 15 June 2009

فوائد المشاركة:

مشاركتكم في هذه الدراسة هو طوعي و سوف تحصل على 10 £ (50 SR) لتغطية نفقات التنقل للمشاركة في هذه الدراسة. كل المعلومات التي تم جمعها خلال هذه الدراسة تعطينا فهم أفضل لطبيعة أمراض الدماغ خصوصا ماوهو شائع عند المسنين. قد تكون النتائج مفيدة جدا في تحسين العلاج وإعادة التأهيل للمرضى.

هل سيتم الاحتفاظ بسرية مشاركتي في هذه الدراسة؟

سيتم الاحتفاظ بأية معلومات تم جمعها عنك خلال هذه الدراسة بسرية تامة. ولن يتم التعرف عليك نهائيا، وسوف تعطى رقم تعريفي بدل إستخدام اسمك أو أي معلومات شخصية عنك. كل ما يخصك من معلومات شخصية سوف يتم إزالتها حتى لا يتم التعرف عليك.

ما هي الجهة المنظمة واني سوف تدفع نفقات البحث؟

سيقوم طالب الدكتوراه في جامعة جلاسكو أحمد آل سلمان بتنظيم وإدارة هذا البحث وستتولى كلية الطب/ قسم الطب النفسي بتمويل البحث. وسوف يشرف على البحث البروفسور جوناثان إيفانز، من جامعة غلاسكو، والدكتور سعيد وهاس رئيس قسم علم النفس الاكلينيكي في قسم العلوم العصبية في مدينة الملك فهد الطبية.

ماذا سيحدث لنتائج الدراسة البحثية؟

المعلومات التي تم جمعها تشكل جزءا من أطروحة (دكتوراه) الدكتوراه في جامعة غلاسكو. وهذه النتائج قد يتم نشرها في واحد أو أكثر المجلات العلمية المتخصصة، وربما سوف يتم تقديمها في مؤتمرات علمية. ولكن يجب أن تعلم أنه لن يمكن التعرف عليك من البيانات من أي تقرير أو منشور.

الاتصال للحصول على مزيد من المعلومات

إذا كان لديك أي أسئلة أو ترغب في الحصول على ملخص الدراسة بمجرد الانتهاء منه، يرجى الاتصال ب:

Ahmed Al Salman
University of Glasgow, College of Medicne
Section of Psychological Medicine
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
Tel.: +44 141 211 0694
E-mail: alsalman_ahmed@hotmail.com

نشكركم على المشاركة في هذه الدراسة

هذا المشروع تمت الموافقة عليه من لجنة الأخلاقيات بكلية الطب بجامعة جلاسكو بالمملكة المتحدة

University of Glasgow

اسم المستشفى:
رقم المستشفى:
رقم الدراسة:
رقم تعريف الموضوع لهذه التجربة:

نموذج الموافقة

عنوان الدراسة : **تقنين النسخة المنقحة من إختبار أدنبروكس المعرفي على البيئة السعودية**

اسم الباحث : أحمد بن سعيد بن علي آل سلمان

الرجاء التأشير في الخانات التالية :

1) أقر أنني قرأت وفهمت المعلومات الخاصة بالدراسة عاليه، و المؤرخة في .....وكانت لدي الفرصة الكاملة لسؤال عما أريد سؤاله حول مشاركتي بالدراسة.

☐

2) أقر أنني فهمت طبيعة مشاركتي كمتطوع، وأنه لدي الحرية الكاملة في الإنسحاب بأي وقت أريد بدون إبداء اسباب، بدون أي تأثير على حقوقي القانونية.

☐

3) أوافق على أن أكون طرفاً في الدراسة أعلاه.

☐

اسم المشارك ..... التاريخ ..... التوقيع .....

اسم الشخص الذي سيقوم بإعطاء نموذج الموافقة (في حالة لم يكن الباحث بنفسه).....

التاريخ ..... التوقيع .....

اسم الباحث ..... التاريخ ..... التوقيع .....

1 نسخة للباحث
1 نسخة للمشارك

Faculty of Medicine
Ethics Committee

P.I.S. (June 2003)

University of Glasgow

Participant information sheet

Saudi Arabian Adaptation of Addenbrooke's Cognitive Examination- Revised (ACE- R)

Invitation to take part in a research study

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with the researcher if you wish. Please ask if there is anything that is not clear or if you would like more information.

Thank you for reading this.

Purpose of the study

This study aims to adapt a new clinical neuropsychological assessment called Addenbrooke;s Cognitive Examination – Revised on Saudi society. This assessment will contribute to improve the health care services which are given to the elderly people especially in Saudi Arabia and the other Arabic countries in general. This study will open a new horizon of evaluation of elderly diseases especially which belong to the brain. Thus, the outcomes of this study will employ in prediction about nature of brain diseases and their transformations and changes which happen in the stages of disease. This maybe helps us to prevent some symptoms of some types of brain diseases.

Why have I been chosen?

Elderly people over 50, whether patients or healthy, have been invited to take part in the study.

Do I have to take part?

You are free to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason but remember that your participation is very important for us and will gain the general welfare. The participation will be in two rounds and between of them two weeks maximum.

What will happen to me if I take part?

First, you will be asked to complete the examination with the researcher. The examination will take maximum 20 minutes to finish it. It is not necessarily to write your personal information like your name on the examination papers. We are focus on the results of study to improve the treatment processes in the future.

v.1., 15 June 2009

Possible disadvantages and risks of taking part
There are no significant risks or disadvantages to taking part. If you feel tired you can take a break for a while and then continue.

Benefits of taking part
Your participation in this study is voluntary and will receive £10 (SR 50) to cover travel expenses for taking part in this study. The information collected during this study will give us a better understanding of the nature of brain diseases especially which are common in the elderly people. The results may be very useful in improving treatment and rehabilitation of patients.

Will my taking part in this study be kept confidential?
Any information collected, about you during this study will be kept strictly confidential. You will only be identified by an identification number and any information about you will have your name any other personal information removed so that you cannot be recognised from it.

Who is organizing and paying for the research?
This research study is organised by Ahmed Al Salman, Doctoral Research Student at the University of Glasgow, and funded by College of Medicine, Section of Psychological Medicine. This research is supervised by Professor Jonathan Evans, University of Glasgow and Dr. Saeed Wahas, Head of Clinical Psychology Section in Department of Neurology Science in King Fahad Medical City.

What will happen to the results of the research study?
The information collected will form part of a doctoral (PhD) thesis at the University of Glasgow, may contribute to one or more publications and may be presented at conferences. It will not be possible to identify you from the data from any report or publication.

Contact for Further Information
If you have any questions or would like to receive a summary of the study once it has been completed, please contact:

Ahmed Al Salman
University of Glasgow, College of Medicine
Section of Psychological Medicine
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
G12 0XH.
Telephone: 0141 211 0694
E-mail: alsalman_ahmed@hotmail.com

Thank you for taking part in this study!

The project has been approved by the Faculty of Medicine Ethics Committee.

University of Glasgow

Subject Identification Number for this trial:

CONSENT FORM

Title of Project: ***Saudi Arabian Adaptation of the Addenbrooke's Cognitive Examination-Revised (ACE-R)***

Name of Researcher: Ahmed Saeed Ali Al Salaman

Please initial box

1. I confirm that I have read and understand the information sheet dated..... for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐

3. I agree to take part in the above study. ☐

Name of subject	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

1 for subject; 1 for researcher

اختبار أدنبروكس المعرفي (ACE-R)
النسخة المنقحة أ (2012)

الاسم:
تاريخ الميلاد:
رقم الملف الطبي:
هل الشخص يعتمد على اليد اليمنى أو اليسرى في العمل؟
.....

تاريخ الاختبار: ...../...../.....
اسم الفاحص: .....
سن ترك التعليم: .....
الوظيفة: .....

التوجه

➢ اسأل: ما هو	اليوم	التاريخ	الشهر	السنة	الفصل	[الدرجة 0-5]
	.....	.....	.....	.....	.....	
➢ اسأل: أي	مبنى	طابق	مدينة	المنطقة	الدولة	[الدرجة 0-5]
	.....	.....	.....	.....	.....	

التسجيل

➢ قل: "سأقوم بإلقاء ثلاث كلمات عليك وأود أن تقوم بتكرارها ورائي: ليمون – مفتاح – كرة". وبعد أن يقوم المفحوص بالتكرار، قل "حاول تذكر الكلمات لأنني سأطرح عليك الأسئلة فيما بعد". سجل فقط درجات المحاولة الأولى (كرر ثلاث مرات عند الضرورة). [الدرجة 0-3]

سجل عدد المحاولات .....

الانتباه والتركيز

➢ اطلب من المفحوص: "هل يمكنك طرح 7 من 100؟ وبعد أن يجيب اطلب من المفحوص طرح 7 من إجمالي خمس عمليات طرح. وإذا قام المفحوص بأي خطأ قم بالمواصلة ثم تحقق من عدد الإجابات الصحيحة. مثلاً لو كانت إجابات المفحوص على النحو التالي (93، **84**، 77، 70، 63 – سجل 4) أنظر دليل التعليمات. [الدرجة 0-5]

توقف بعد إجراء خمس عمليات طرح (93، 86، 79، 72، 65) ----- ----- ----- ----- -----

➢ اسأل: "هل يمكنك تهجي كلمة **مدرسة** ؟ ثم اطلب من المفحوص القيام بتهجيها بالمقلوب.

.... ❀❀❀ ....

بالنسبة لأفضل أداء للعمل

الانتباه والتوجه

الذاكرة – الاسترجاع

➢ اسأل: "أي ثلاث كلمات طلبت منك القيام بتكرارها وتذكرها"؟ [الدرجة 0-3]

....

الذاكرة – ذاكرة تقدمية

➢ سأقوم بذكر اسم وعنوان عليك، وأود منك تكرارها ورائي – سنقوم بذلك ثلاث مرات لذا فإنه لديك الفرصة لتذكرها. وسأقوم بطرح أسئلة عليك فيما بعد. [الدرجة 0-7]

سجل فقط درجات المحاولة الثالثة

	المحاولة الأولى	المحاولة الثانية	المحاولة الثالثة
أحمد خالد	.....	.....	.....
منزل 73	.....	.....	.....
حي الأمل	.....	.....	.....
شارع المتنبي	.....	.....	.....
الرياض	.....	.....	.....

الذاكرة – الذاكرة الرجعية

➢ ما هي عاصمة الدولة التي تقيم فيها .....
➢ ما هو اسم الحاكم السابق لبلدك ..... [الدرجة 0-4]
➢ اسم رئيس الولايات المتحدة الأمريكية.....
➢ اسم الحاكم الحالي لبلدك .....

الذاكرة

7/1

الطلاقة الشفهية – حرف "م" والحيوانات

الطلاقة اللفظية

الحرف [الدرجة 0-7]

قل: سأقوم بإعطائكم حرف من الحروف الأبجدية وأود منك ذكر أكبر عدد من الكلمات التي يمكنك إعدادها والتي تبدأ بهذا الحرف، ولكن تذكر أنها ليست أسماء أشخاص أو أماكن. هل أنت جاهز؟ لديك دقيقة والحرف هو "م"

7	17<				
6	17-14				
5	13-11				
4	10-8				
3	7-6				
2	5-4				
1	3-2				
0	2>				
العدد الصحيح	الإجمالي				

الحيوانات [الدرجة 0-7]

قل: "هل يمكنك ذكر أكبر عدد من أسماء الحيوانات بقدر الإمكان؟ (يمكنك أن تبدأ بأي حرف تشاء). (لديك دقيقة واحدة فقط).

7	21<				
6	21-17				
5	16-14				
4	13-11				
3	10-9				
2	8-7				
1	6-5				
0	5>				
العدد الصحيح	الإجمالي				

اللغة – الإدراك

اللغة

اظهر التعليمات المكتوبة: [الدرجة 0-1]

أغلق عينيك

أمر مكون من ثلاث مراحل: [الدرجة 0-3]

خذ الورقة بيدك اليمنى. قم بطي الورقة نصفين. وضع الورقة على الأرض

اللغة – الكتابة

اطلب من المفحوص إعداد جملة وكتابتها في الفراغ أدناه: [الدرجة 0-1]

قم بتسجيل 1 إذا كانت الجملة تحتوي على بناء صحيح (انظر الدليل للأمثلة)

اللغة – التكرار

➢ **اطلب من المفحوص تكرار الكلمات التالية (فسيكفيكهم، أسنلزمكموها، فأسقيناكموه، لنستخلفنهم)**

قم بتسجيل نتيجة كلمتين إذا كانت جميعها صحيحة وكلمة واحدة إذا كانت ثلاث كلمات صحيحة، ولا تقم بتسجيل أي نتيجة إذا كانت الكلمات الصحيحة اثنين أو أقل.

[الدرجة 0–2]

➢ * **اطلب من المفحوص تكرار ما يلي:** "فوق، إلى ما بعد، وأسفل"

[الدرجة 0–1]

* **اطلب من المفحوص تكرار:** "لا إذا أو و أو لكن"

[الدرجة 0–1]

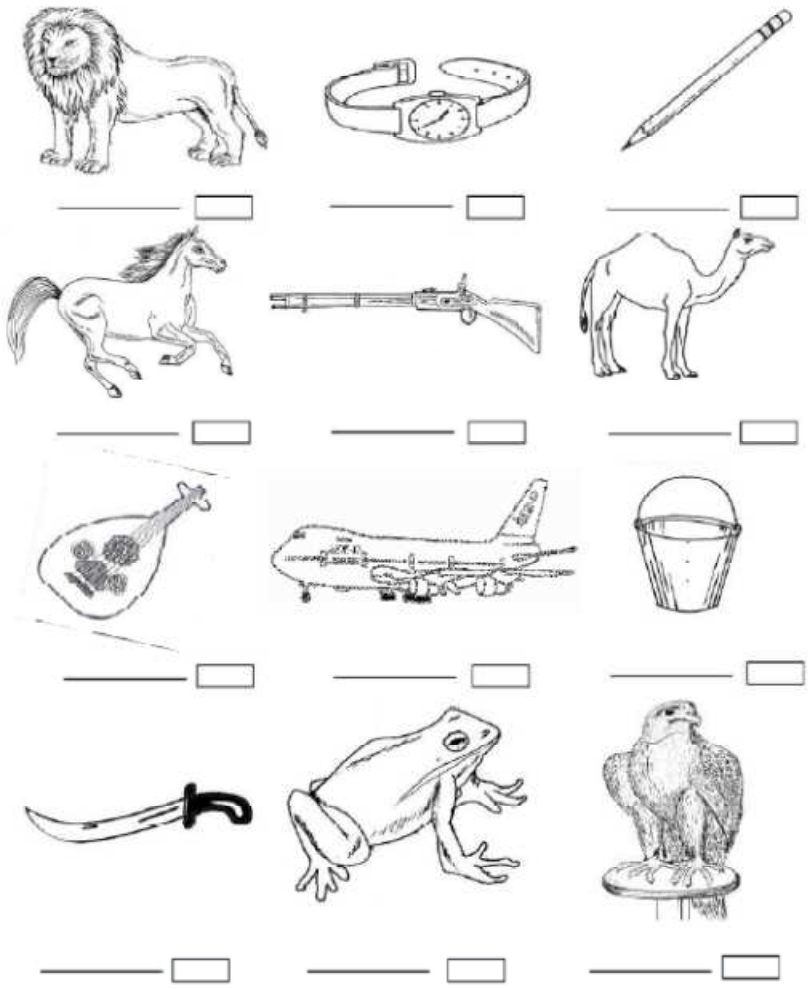
اللغة – التسمية

➢ **اطلب من المفحوص تسمية الصور التالية:**

[الدرجة 0–2]

(قلم مرسم + ساعة)

[الدرجة 0–10]



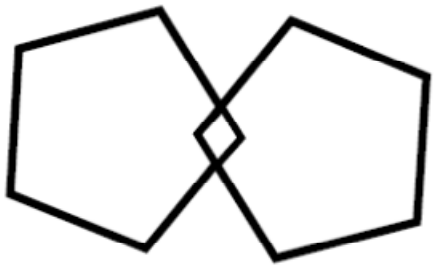
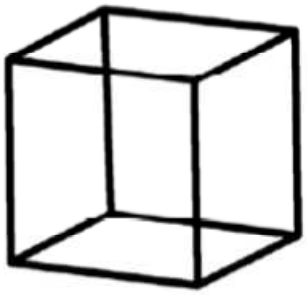
اللغة – الفهم

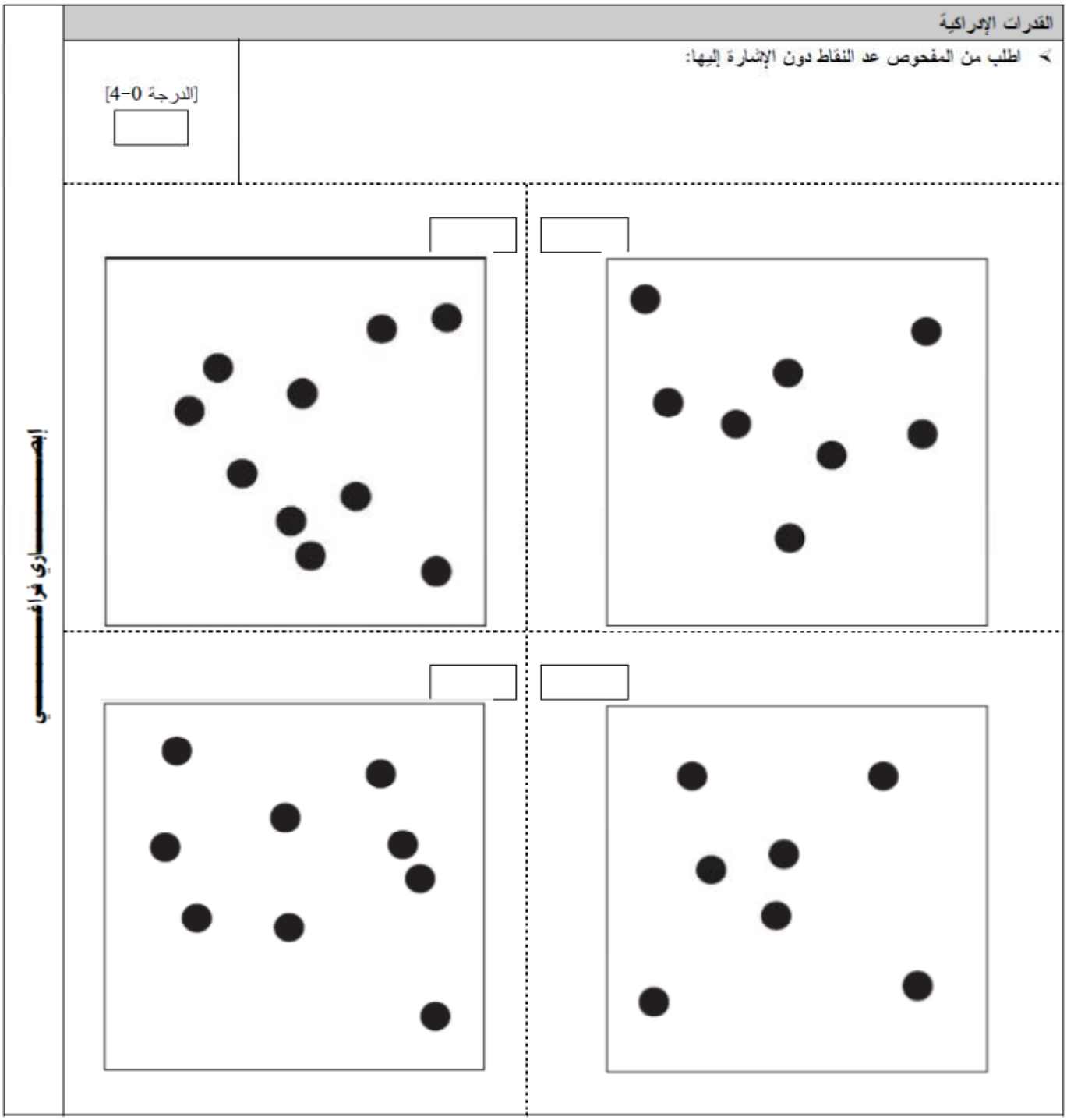
➢ **باستخدام الصور المذكورة أعلاه اطلب من المفحوص:**

[الدرجة 0–4]

- أشر إلى الصورة المرتبطة بإحدى وسائل الحرب القديمة _____
- أشر إلى الصورة المرتبطة بالحيوان الصحراوي _____
- أشر إلى الصورة المرتبطة بالكائن الذي يستخدم للصيد _____
- أشر إلى الصورة المرتبطة بالشيء الذي يستخدم لنقل الماء _____

7/3

اللغة	اللغة – القراءة	
	➢ اطلب من المفحوص قراءة الكلمات التالية [قم بتسجيل درجات واحدة فقط إذا كانت جميعها صحيحة]  فيمَ عمَّ ليسَ طاوُس إلٰه	[الدرجة 0-1]
إبصاري فراغي	القدرات الإبصارية الفراغية	
	➢ شكلين خماسية متداخلة: اطلب من المفحوص نسخ هذا الرسم 	[الدرجة 0-1]
	➢ مكعب سلكي: اطلب من المفحوص نسخ هذا الرسم (لتسجيل الدرجات ، انظر دليل التعليمات) 	[الدرجة 0-2]
	➢ الساعة: اطلب من المفحوص رسم وجه ساعة بها أرقام وتوجد العقارب على الساعة الخامسة وعشر دقائق. (لتسجيل الدرجات انظر دليل التعليمات : الدائرة= 1، الأرقام = 2، العقارب = 2 إذا كانت جميعها صحيحة)	[الدرجة 0-5]


القدرات الإدراكية
اطلب من المفحوص عد النقاط دون الإشارة إليها:
[الدرجة 0–4]
إدراك بصري فراغي

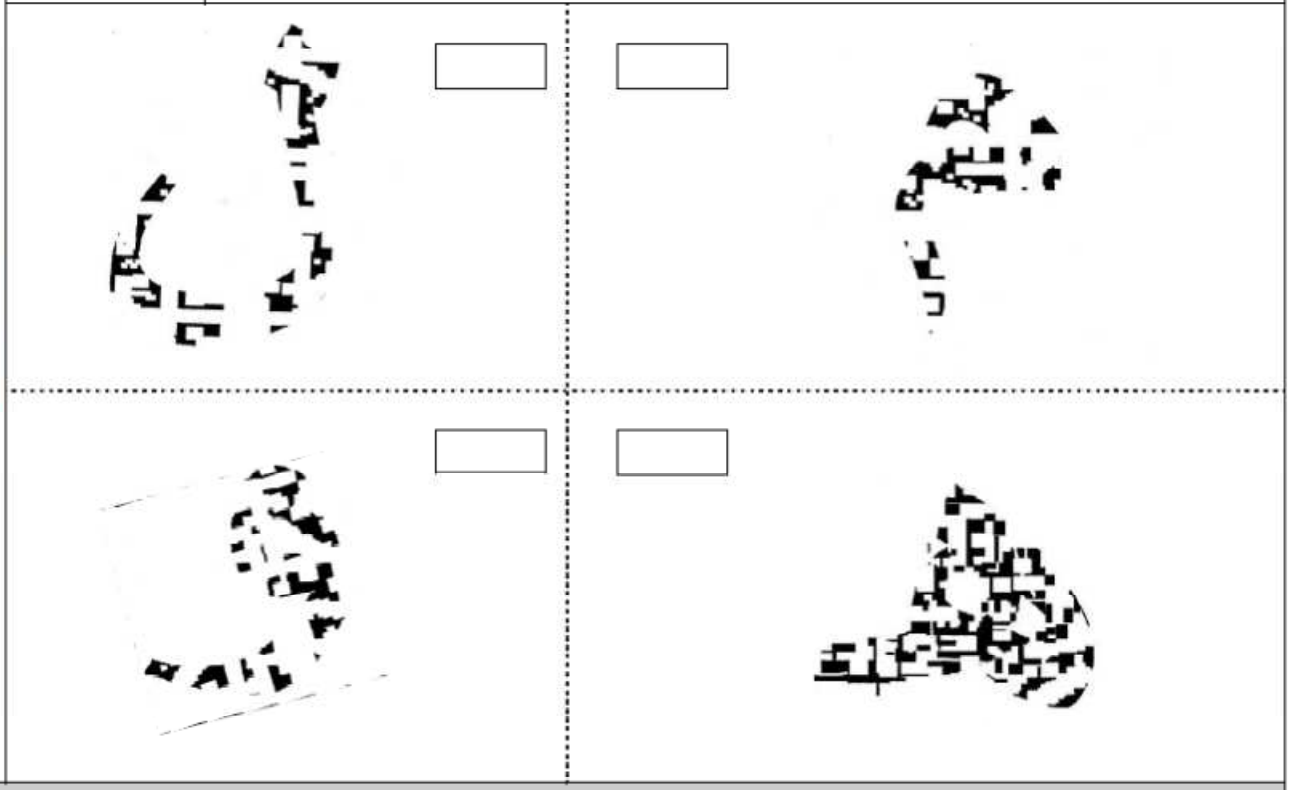
7/5

القدرات الإدراكية

إبصاري فراغي

- اطلب من المفحوص التعرف على الحروف:

[الدرجة 0-4]



الاسترجاع

الذاكرة

- اسأل "والآن أخبرني ما الذي تتذكره عن ذلك الاسم والعنوان اللذين كنا نكررهما في البداية"

أحمد خالد	.....
منزل رقم 73	.....
حي الأمل	.....
شارع المنتبي	.....
الرياض	.....

[الدرجة 0-7]

الإدراك

- يجب إجراء هذا الاختبار إذا أخفق المفحوص في تذكر عنصر أو أكثر. وإذا تم تذكر جميع العناصر تخطي الاختبار وقم بتسجيل **5**. وإذا تم فقط تذكر جزء ابدأ بوضع العناصر التي تذكرها في الخانة المظللة على الجانب الأيمن. ثم قم بإجراء اختبار حول العناصر التي لم يتم تذكرها بقولك "حسناً" سوف أعطيك بعض التلميحات: هل كان الاسم اكس أو واي أو زد؟ وما إلى ذلك؟ وتكون نتيجة كل عنصر تم تذكره **(1)** والتي يتم إضافتها للنقطة التي تم الحصول عليها بالتذكر.

[الدرجة 0-5]

حمد عايد	أحمد خالد	أحمد عبد الله	التذكر	
منزل 37	73	76	التذكر	
حي الأماني	حي التهاني	حي الأمل	التذكر	
شارع المنتبي	طريق الأمانة	شارع السعادة	التذكر	
الرياض	الجوف	الخرج	التذكر	

7/6

الدرجات العامة لمجموعة المتعلمين:

الدرجات العامة		
اختبار أدنبروكس المعرفي (المنقح)	/100	
الدرجات الفرعية		
الانتباه والتوجيه	/18	
الذاكرة	/26	
الطلاقة	/14	
اللغة	/26	
القدرات الإبصارية الفراغية	/16	

الدرجات العامة لمجموعة الأميين:

الدرجات العامة		
اختبار أدنبروكس المعرفي (المنقح)	/93	
الدرجات الفرعية		
الانتباه والتوجيه	/18	
الذاكرة	/26	
الطلاقة	/14	
اللغة	/23	
القدرات الإبصارية الفراغية	/12	

اختبـــار أدنبروكـــــس المعرفـــــي (ACE-R)
النسخـــة المنقحـــــة ب (2012)

الاسم:	تاريخ الاختبار: ...../...../.....
تاريخ الميلاد:	اسم الفاحص:.....
رقم الملف الطبي:	سن ترك التعليم: .....
هل الشخص يعتمد على اليد اليمنى أو اليسرى في العمل؟	الوظيفة: .....

الانتباه والتوجه

التوجه

➢ اسأل: ما هو	اليوم	التاريخ	الشهر	السنة	الفصل	[الدرجة 0–5] ☐
➢ اسأل: أي	مبنى	طابق	مدينة	المنطقة	الدولة	[الدرجة 0–5] ☐

التسجيل

➢ قل: "سأقوم بإلقاء ثلاث كلمات عليك وأود أن تقوم بتكرارها ورائي: ليمون – مفتاح – كرة". وبعد أن يقوم المفحوص بالتكرار، قل "حاول تذكر الكلمات لأنني سأطرح عليك الأسئلة فيما بعد". سجل فقط درجات المحاولة الأولى (كرر ثلاث مرات عند الضرورة). [الدرجة 0–3] ☐

سجل عدد المحاولات .....

الانتباه والتركيز

➢ اطلب من المفحوص: "هل يمكنك طرح 7 من 100؟ وبعد أن يجيب اطلب من المفحوص طرح 7 من إجمالي خمس عمليات طرح. وإذا قام المفحوص بأي خطأ قم بالمواصلة ثم تحقق من عدد الإجابات الصحيحة. مثلاً لو كانت إجابات المفحوص على النحو التالي (93، **84**، 77، 70، 63 – سجل 4) أنظر دليل التعليمات. [الدرجة 0–5] ☐ بالنسبة لأفضل أداء للعمل

توقف بعد إجراء خمس عمليات طرح (93، 86، 79، 72، 65) ----- ----- ----- ----- -----

➢ اسأل: "هل يمكنك تهجي كلمة **مدرسة** ؟ ثم اطلب من المفحوص القيام بتهجيها بالمقلوب.

.... ❀❀❀ ....

الذاكرة

الذاكرة – الاسترجاع

➢ اسأل: "أي ثلاث كلمات طلبت منك القيام بتكرارها وتذكرها"؟ [الدرجة 0–3] ☐

....

الذاكرة – ذاكرة تقدمية

➢ سأقوم بذكر اسم وعنوان عليك، وأود منك تكرارها ورائي – سنقوم بذلك ثلاث مرات لذا فإنه لديك الفرصة لتذكرها. وسأقوم بطرح أسئلة عليك فيما بعد. [الدرجة 0–7] ☐

سجل فقط درجات المحاولة الثالثة

	المحاولة الأولى	المحاولة الثانية	المحاولة الثالثة
مها فالح	.....	.....	.....
منزل 59	.....	.....	.....
حي الازدهار	.....	.....	.....
طريق البحر	.....	.....	.....
مكة	.....	.....	.....

الذاكرة – الذاكرة الرجعية

➢ ما هي عاصمة الدولة التي تقيم فيها .....
➢ ما هو اسم الحاكم السابق لبلدك .....
➢ اسم رئيس الولايات المتحدة الأمريكية.....
➢ اسم الحاكم الحالي لبلدك ..... [الدرجة 0–4] ☐

الطلاقة الشفهية – حرف "م" والحيوانات

الطلاقة اللفظية

➢ **الحرف** [الدرجة 0-7]

قل: سأقوم بإعطائكم حرف من الحروف الأبجدية وأود منك ذكر أكبر عدد من الكلمات التي يمكنك إعدادها والتي تبدأ بهذا الحرف، ولكن تذكر أنها ليست أسماء أشخاص أو أماكن. هل أنت جاهز؟ لديك دقيقة والحرف هو "م"

7	17<				
6	17-14				
5	13-11				
4	10-8				
3	7-6				
2	5-4				
1	3-2				
0	2>				
العدد الصحيح	الإجمالي				

➢ **الحيوانات** [الدرجة 0-7]

قل: "هل يمكنك ذكر أكبر عدد من أسماء الحيوانات بقدر الإمكان؟ (يمكنك أن تبدأ بأي حرف تشاء). (لديك دقيقة واحدة فقط).

7	21<				
6	21-17				
5	16-14				
4	13-11				
3	10-9				
2	8-7				
1	6-5				
0	5>				
العدد الصحيح	الإجمالي				

اللغة – الإدراك

اللغة

➢ **اظهر التعليمات المكتوبة:** [الدرجة 0-1]

أغلق عينيك

➢ **أمر مكون من ثلاث مراحل:** [الدرجة 0-3]

خذ الورقة بيدك اليمنى. قم بطي الورقة نصفين. وضع الورقة على الأرض

اللغة – الكتابة

➢ **اطلب من المفحوص إعداد جملة وكتابتها في الفراغ أدناه:** [الدرجة 0-1]

قم بتسجيل 1 إذا كانت الجملة تحتوي على بناء صحيح (انظر الدليل للأمثلة)

اللغة – التكرار

➢ **اطلب من المفحوص تكرار الكلمات التالية (فسيكفيكهم، أستلزمكموها، فأسقيناكموه، لتستخلفنهم)**

قم بتسجيل نتيجة كلمتين إذا كانت جميعها صحيحة وكلمة واحدة إذا كانت ثلاث كلمات صحيحة، ولا تقم بتسجيل أي نتيجة إذا كانت الكلمات الصحيحة اثنين أو أقل.

[الدرجة 0-2]

➢ * **اطلب من المفحوص تكرار ما يلي:** "فوق، إلى ما بعد، وأسفل"

[الدرجة 0-1]

* **اطلب من المفحوص تكرار:** "لا إذا أو و أو لكن"

[الدرجة 0-1]

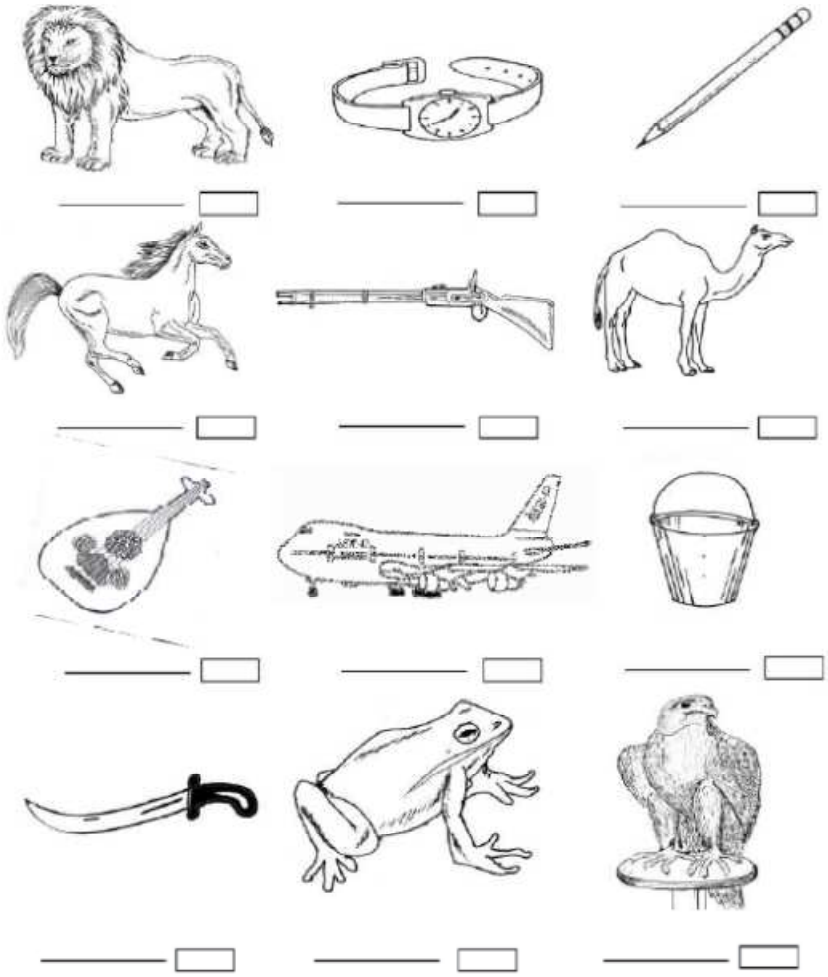
اللغة – التسمية

➢ **اطلب من المفحوص تسمية الصور التالية:**

[الدرجة 0-2]

(قلم مرسم + ساعة)

[الدرجة 0-10]



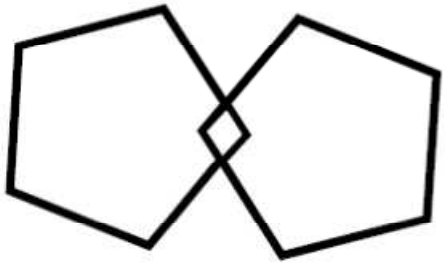
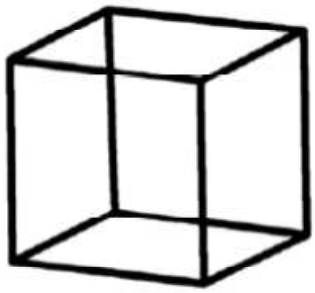
اللغة – الفهم

➢ **باستخدام الصور المذكورة أعلاه اطلب من المفحوص:**

[الدرجة 0-4]

- أشر إلى الصورة المرتبطة بإحدى وسائل الحرب القديمة _____
- أشر إلى الصورة المرتبطة بالحيوان الصحراوي _____
- أشر إلى الصورة المرتبطة بالكائن الذي يستخدم للصيد _____
- أشر إلى الصورة المرتبطة بالشيء الذي يستخدم لنقل الماء _____

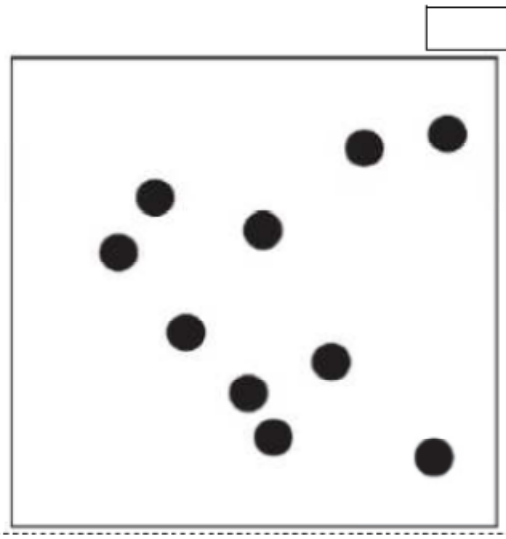
7/3

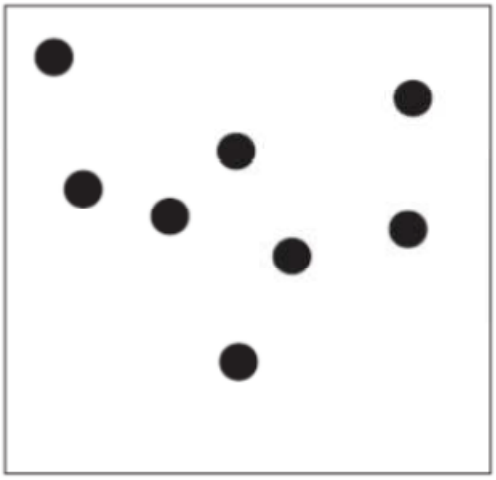
اللغة	اللغة – القراءة	
	➢ اطلب من المفحوص قراءة الكلمات التالية [قم بتسجيل درجات واحدة فقط إذا كانت جميعها صحيحة]	[الدرجة 0-1]
	فيمَ عمَّ يسٓ طاوٗس إلٰه	
إبصاري فراغي	القدرات الإبصارية الفراغية	
	➢ شكلين خماسية متداخلة: اطلب من المفحوص نسخ هذا الرسم 	[الدرجة 0-1]
	➢ مكعب سلكي: اطلب من المفحوص نسخ هذا الرسم (لتسجيل الدرجات ، انظر دليل التعليمات) 	[الدرجة 0-2]
	➢ الساعة: اطلب من المفحوص رسم وجه ساعة بها أرقام وتوجد العقارب على الساعة الخامسة وعشر دقائق. (لتسجيل الدرجات انظر دليل التعليمات : الدائرة= 1، الأرقام = 2، العقارب = 2 إذا كانت جميعها صحيحة)	[الدرجة 0-5]

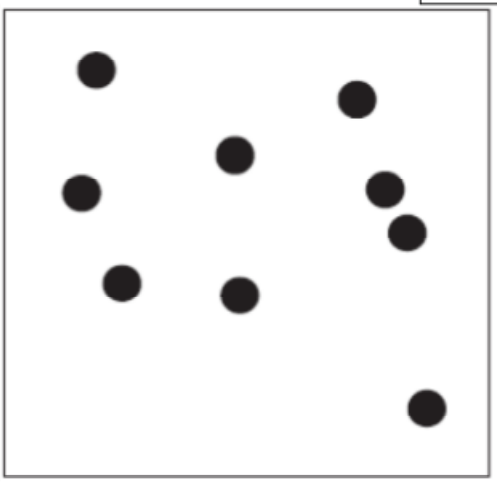
القدرات الإدراكية

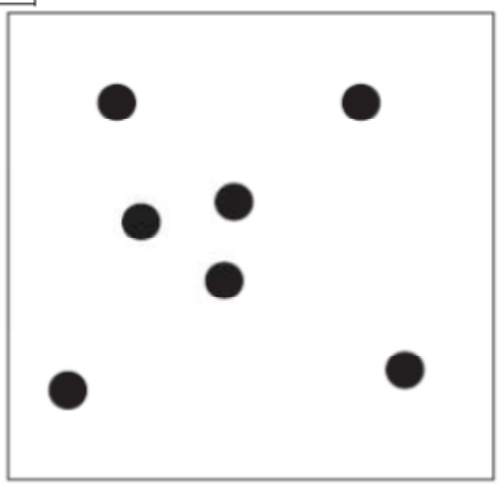
➢ اطلب من المفحوص عد النقاط دون الإشارة إليها:

[الدرجة 0–4]









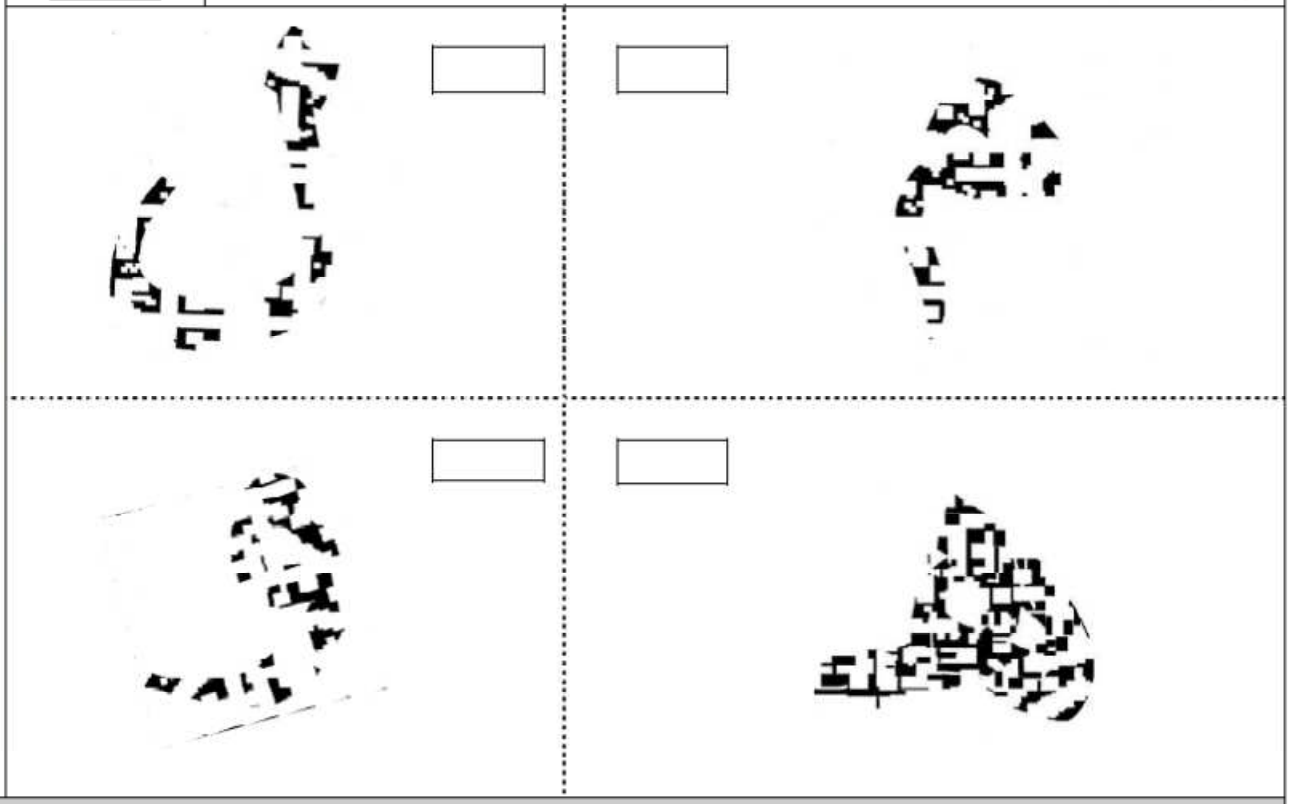
إبصاري فراغي

القدرات الإدراكية

إبصاري فراغي

- اطلب من المفحوص التعرف على الحروف:

[الدرجة 0-4]



الاسترجاع

الذاكرة

- اسأل "والآن أخبرني ما الذي تتذكره عن ذلك الاسم والعنوان اللذين كنا نكررهما في البداية"

مها فالح	....
منزل 59	.....
حي الازدهار	.....
طريق البحر	....
مكة	.....

[الدرجة 0-7]

الإدراك

- يجب إجراء هذا الاختبار إذا أخفق المفحوص في تذكر عنصر أو أكثر. وإذا تم تذكر جميع العناصر تخطى الاختبار وقم بتسجيل 5. وإذا تم فقط تذكر جزء ابدأ بوضع العناصر التي تذكرها في الخانة المظللة على الجانب الأيمن. ثم قم بإجراء اختبار حول العناصر التي لم يتم تذكرها بقولك "حسناً" سوف أعطيك بعض التلميحات: هل كان الاسم اكس أو واي أو زد؟ وما إلى ذلك؟ وتكون نتيجة كل عنصر تم تذكره (1) والتي يتم إضافتها للنقطة التي تم الحصول عليها بالتذكر.

[الدرجة 0-5]

نوف صلاح	مها فالح	نهى صلاح	التذكر	
منزل 39	52	59	التذكر	
حي الازدهار	حي النهار	حي الشاطئ	التذكر	
شارع النهر	طريق البحر	طريق المطار	التذكر	
تبوك	جدة	مكة	التذكر	

الدرجات العامة لمجموعة المتعلمين:

الدرجات العامة		
اختبار أدنبروكس المعرفي (المنقح)	/100	
الدرجات الفرعية		
الانتباه والتوجيه	/18	
الذاكرة	/26	
الطلاقة	/14	
اللغة	/26	
القدرات الإبصارية الفراغية	/16	

الدرجات العامة لمجموعة الأميين:

الدرجات العامة		
اختبار أدنبروكس المعرفي (المنقح)	/93	
الدرجات الفرعية		
الانتباه والتوجيه	/18	
الذاكرة	/26	
الطلاقة	/14	
اللغة	/23	
القدرات الإبصارية الفراغية	/12	

اختبـــار أدنبروكـــس المعرفـــي (ACE-R)
النســخــة المنقحـــة ح (2012)

الاسم:	تاريخ الاختبار: ...../...../.....
تاريخ الميلاد:	اسم الفاحص:.....
رقم الملف الطبي:	سن ترك التعليم: .....
هل الشخص يعتمد على اليد اليمنى أو اليسرى في العمل؟	الوظيفة: .....

التوجه

➢ اسأل: ما هو	اليوم	التاريخ	الشهر	السنة	الفصل	[الدرجة 0–5]
➢ اسأل: أي	مبنى	طابق	مدينة	المنطقة	الدولة	[الدرجة 0–5]

التسجيل

➢ قل: "سأقوم بإلقاء ثلاث كلمات عليك وأود أن تقوم بتكرارها ورائي: ليمون – مفتاح – كرة". وبعد أن يقوم المفحوص بالتكرار، قل "حاول تذكر الكلمات لأنني سأطرح عليك الأسئلة فيما بعد". سجل فقط درجات المحاولة الأولى (كرر ثلاث مرات عند الضرورة). [الدرجة 0–3]

سجل عدد المحاولات .....

الانتباه والتركيز

➢ اطلب من المفحوص: "هل يمكنك طرح 7 من 100؟ وبعد أن يجيب اطلب من المفحوص طرح 7 من إجمالي خمس عمليات طرح. وإذا قام المفحوص بأي خطأ قم بالمواصلة ثم تحقق من عدد الإجابات الصحيحة. مثلاً لو كانت إجابات المفحوص على النحو التالي (93، **84**، 77، 70، 63 – سجل 4) أنظر دليل التعليمات. [الدرجة 0–5]

➢ اسأل: "هل يمكنك تهجي كلمة **مدرسة** ؟ ثم اطلب من المفحوص القيام بتهجيها بالمقلوب.

....

بالنسبة لأفضل أداء للعمل

الانتباه والتوجه

الذاكـــــرة

الذاكرة – الاسترجاع

➢ اسأل: "أي ثلاث كلمات طلبت منك القيام بتكرارها وتذكرها"؟ [الدرجة 0–3]

....

الذاكرة – ذاكرة تقدمية

➢ سأقوم بذكر اسم وعنوان عليك، وأود منك تكرارها ورائي – سنقوم بذلك ثلاث مرات لذا فإنه لديك الفرصة لتذكرها. وسأقوم بطرح أسئلة عليك فيما بعد. [الدرجة 0–7]

سجل فقط درجات المحاولة الثالثة

	المحاولة الأولى	المحاولة الثانية	المحاولة الثالثة
ناصر سعد	.....	.....	.....
منزل 24	.....	.....	.....
حي السعادة	.....	.....	.....
ممر النور	.....	.....	.....
الدمام	.....	.....	.....

الذاكرة – الذاكرة الرجعية

➢ ما هي عاصمة الدولة التي تقيم فيها ..... [الدرجة 0–4]

➢ ما هو اسم الحاكم السابق لبلدك .....

➢ اسم رئيس الولايات المتحدة الأمريكية.....

➢ اسم الحاكم الحالي لبلدك .....

7/1

الطلاقة الشفهية – حرف "م" والحيوانات

الطلاقة اللغة

الحرف [الدرجة 0-7]

قل: سأقوم بإعطائكم حرف من الحروف الأبجدية وأود منك ذكر أكبر عدد من الكلمات التي يمكنك إعدادها والتي تبدأ بهذا الحرف، ولكن تذكر أنها ليست أسماء أشخاص أو أماكن. هل أنت جاهز؟ لديك دقيقة والحرف هو "م"

7	17<				
6	17-14				
5	13-11				
4	10-8				
3	7-6				
2	5-4				
1	3-2				
0	2>				
العدد الصحيح	الإجمالي				

الحيوانات [الدرجة 0-7]

قل: "هل يمكنك ذكر أكبر عدد من أسماء الحيوانات بقدر الإمكان؟ (يمكنك أن تبدأ بأي حرف تشاء). (لديك دقيقة واحدة فقط).

7	21<				
6	21-17				
5	16-14				
4	13-11				
3	10-9				
2	8-7				
1	6-5				
0	5>				
العدد الصحيح	الإجمالي				

اللغة – الإدراك

اللغة

اظهر التعليمات المكتوبة: [الدرجة 0-1]

أغلق عينيك

أمر مكون من ثلاث مراحل: [الدرجة 0-3]

خذ الورقة بيدك اليمنى. قم بطي الورقة نصفين. وضع الورقة على الأرض

اللغة – الكتابة

اطلب من المفحوص إعداد جملة وكتابتها في الفراغ أدناه: [الدرجة 0-1]

قم بتسجيل 1 إذا كانت الجملة تحتوي على بناء صحيح (انظر الدليل للأمثلة)

7/2

اللغة – التكرار

➢ **اطلب من المفحوص تكرار الكلمات التالية (فسيكفيكهم، أسنلزمكموها، فأسقيناكموه، لنستخلفنهم)** [الدرجة 0–2]

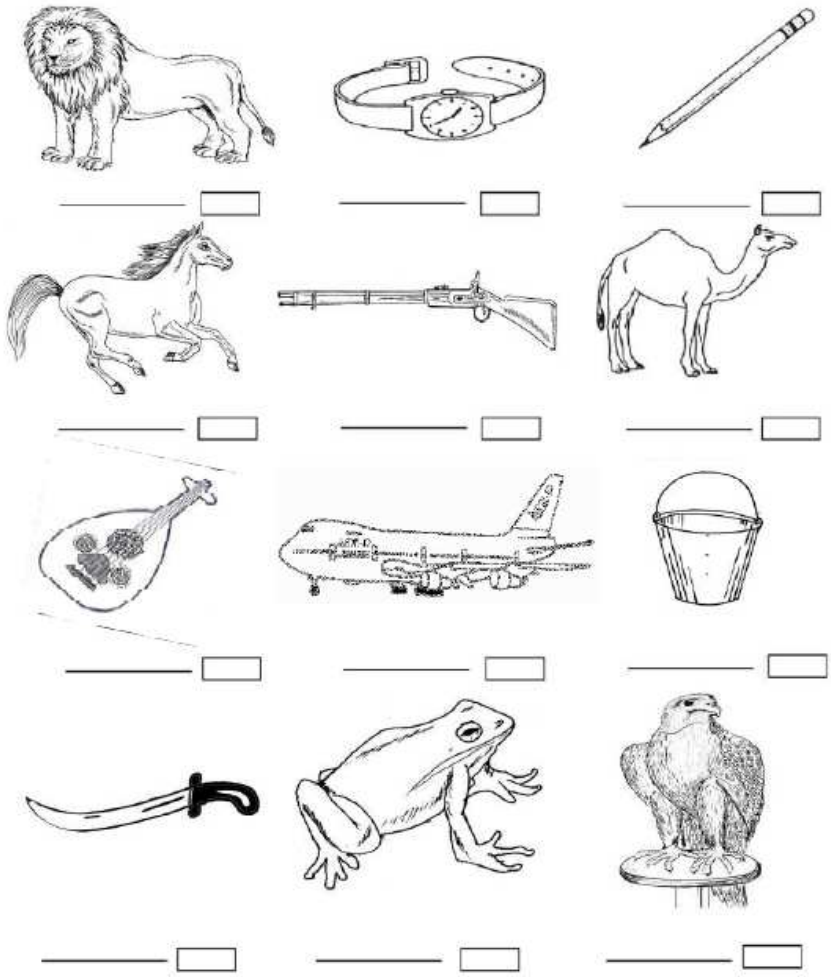
قم بتسجيل نتيجة كلمتين إذا كانت جميعها صحيحة وكلمة واحدة إذا كانت ثلاث كلمات صحيحة، ولا تقم بتسجيل أي نتيجة إذا كانت الكلمات الصحيحة اثنين أو أقل.

➢ * **اطلب من المفحوص تكرار ما يلي:** "فوق، إلى ما بعد، وأسفل" [الدرجة 0–1]

* **اطلب من المفحوص تكرار** "لا إذا أو و أو لكن" [الدرجة 0–1]

اللغة – التسمية

➢ **اطلب من المفحوص تسمية الصور التالية:** [الدرجة 0–2] (قلم مرسم + ساعة)



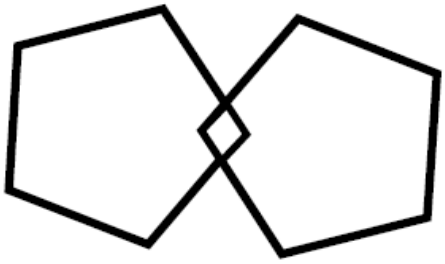
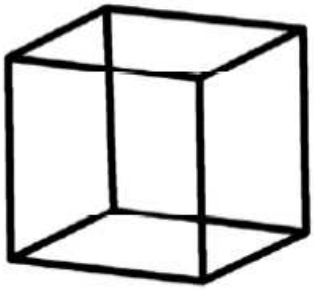
[الدرجة 0–10]

اللغة – الفهم

➢ **باستخدام الصور المذكورة أعلاه اطلب من المفحوص:** [الدرجة 0–4]

- أشر إلى الصورة المرتبطة بإحدى وسائل الحرب القديمة _____
- أشر إلى الصورة المرتبطة بالحيوان الصحراوي _____
- أشر إلى الصورة المرتبطة بالكائن الذي يستخدم للصيد _____
- أشر إلى الصورة المرتبطة بالشيء الذي يستخدم لنقل الماء _____

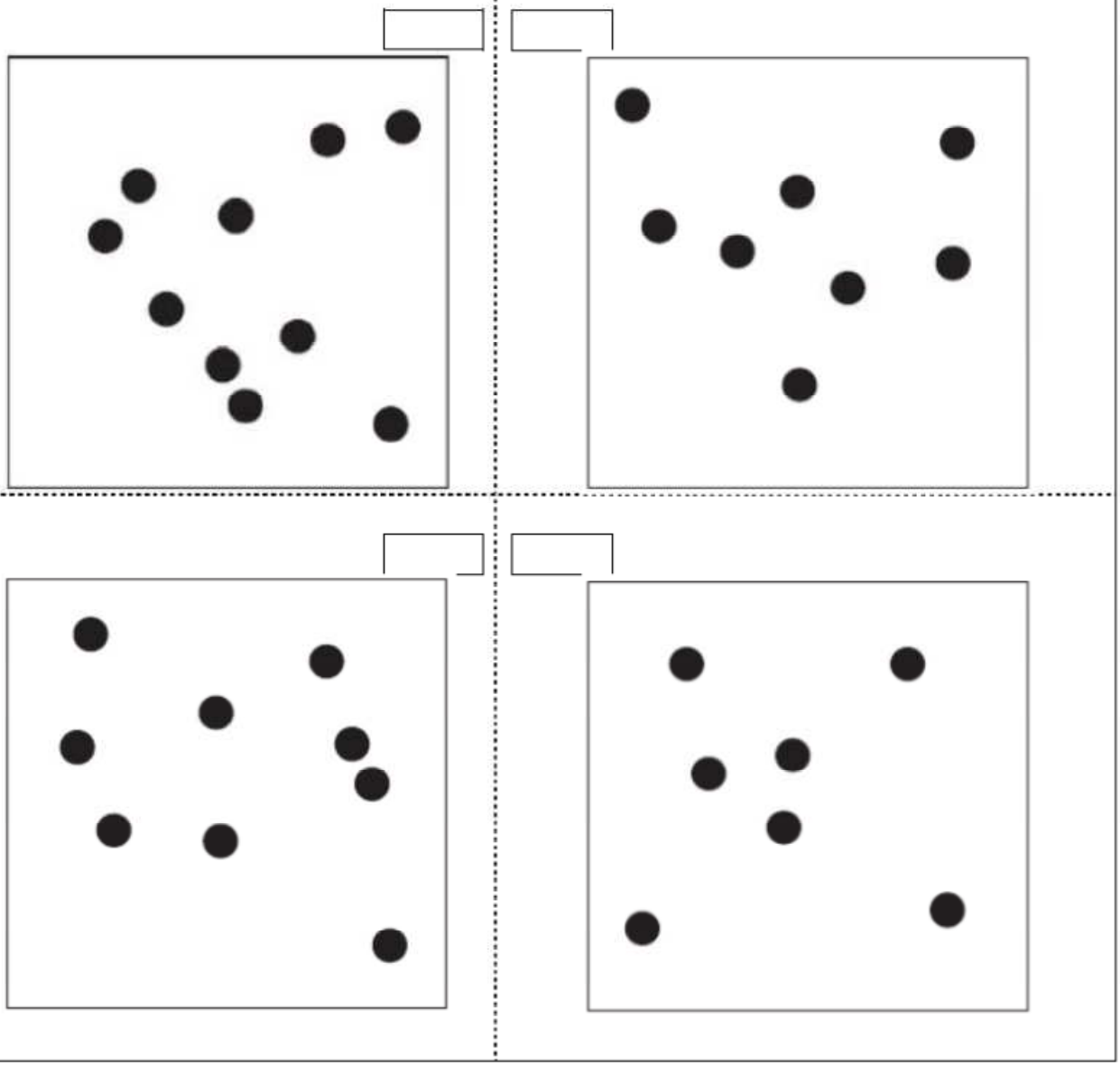
7/3

اللغة		اللغة – القراءة
	[الدرجة 0–1]	➢ اطلب من المفحوص قراءة الكلمات التالية [قم بتسجيل درجات واحدة فقط إذا كانت جميعها صحيحة] فِيمَ عَمَّ يَسَٰ طَاوُس إِلَٰه
إبصاري فراغي		القدرات الإبصارية الفراغية
	[الدرجة 0–1]	➢ شكلين خماسية متداخلة: اطلب من المفحوص نسخ هذا الرسم 
	[الدرجة 0–2]	➢ مكعب سلكي: اطلب من المفحوص نسخ هذا الرسم (لتسجيل الدرجات ، انظر دليل التعليمات) 
	[الدرجة 0–5]	➢ الساعة: اطلب من المفحوص رسم وجه ساعة بها أرقام وتوجد العقارب على الساعة الخامسة وعشر دقائق. (لتسجيل الدرجات انظر دليل التعليمات : الدائرة= 1، الأرقام = 2، العقارب = 2 إذا كانت جميعها صحيحة)

القدرات الإدراكية

- اطلب من المفحوص عد النقاط دون الإشارة إليها:

[الدرجة 0-4]



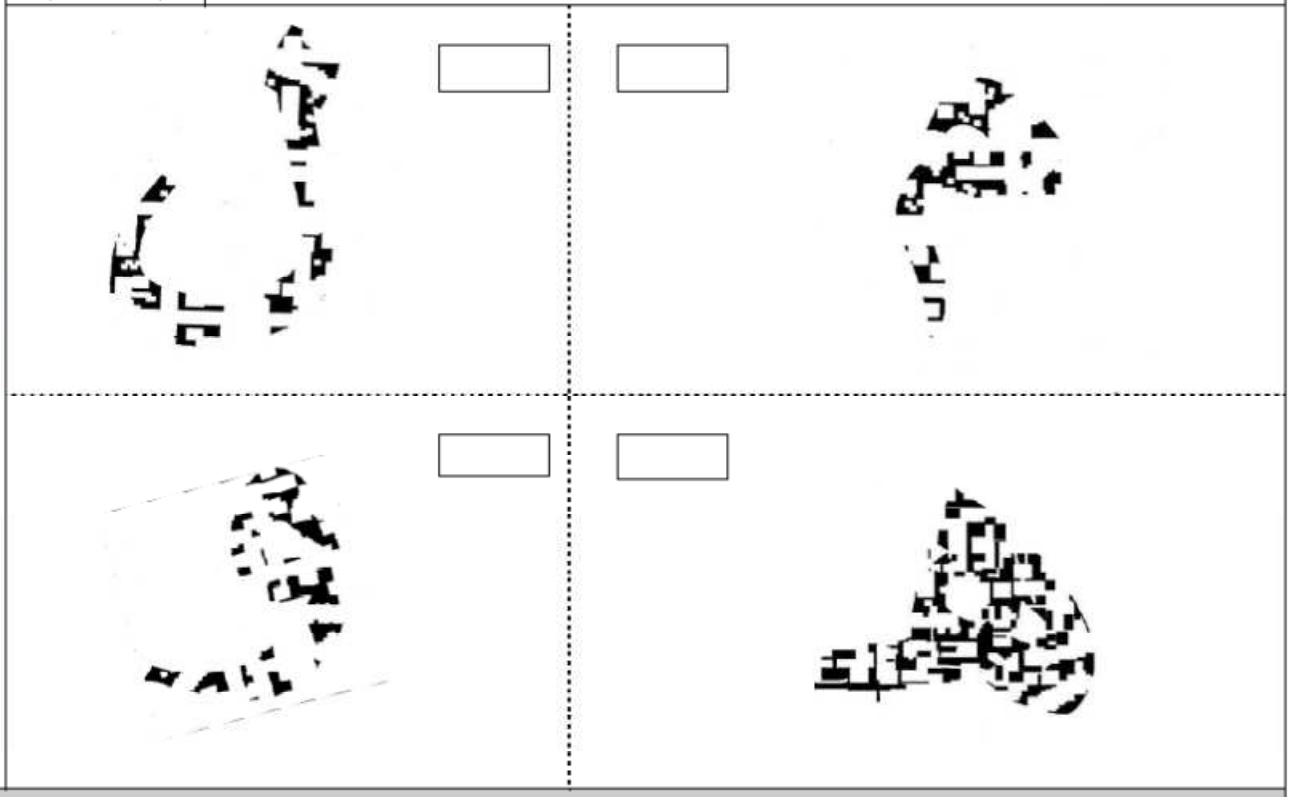
إبصاري فراغي

القدرات الإدراكية

إبصاري فراغي

➢ اطلب من المفحوص التعرف على الحروف:

[الدرجة 0-4]



الاسترجاع

الذاكرة

➢ اسأل "والآن أخبرني ما الذي تتذكره عن ذلك الاسم والعنوان اللذين كنا نكررهما في البداية"

[الدرجة 0-7]

ناصر سعد	....
منزل 24	.....
حي السعادة	.....
ممر النور	....
الدمام	.....

الإدراك

➢ يجب إجراء هذا الاختبار إذا أخفق المفحوص في تذكر عنصر أو أكثر. وإذا تم تذكر جميع العناصر تخطي الاختبار وقم بتسجيل **5**. وإذا تم فقط تذكر جزء ابدأ بوضع العناصر التي تذكرها في الخانة المظللة على الجانب الأيمن. ثم قم بإجراء اختبار حول العناصر التي لم يتم تذكرها بقولك "حسناً" سوف أعطيك بعض التلميحات: هل كان الاسم اكس أو واي أو زد؟ وما إلى ذلك؟ وتكون نتيجة كل عنصر تم تذكره **(1)** والتي يتم إضافتها للنقطة التي تم الحصول عليها بالتذكر.

[الدرجة 0-5]

نادر عبد الله	ناصر سعد	تركي حمد	التذكر	
منزل 42	28	24	التذكر	
حي السعادة	حي الشهادة	حي النفل	التذكر	
ممر النور	شارع النصر	طريق الصخور	التذكر	
حايل	الدمام	أبها	التذكر	

الدرجات العامة لمجموعة المتعلمين:

الدرجات العامة		
اختبار أدنبروكس المعرفي (المنقح)	/100	
الدرجات الفرعية		
الانتباه والتوجيه	/18	
الذاكرة	/26	
الطلاقة	/14	
اللغة	/26	
القدرات الإبصارية الفراغية	/16	

الدرجات العامة لمجموعة الأميين:

الدرجات العامة		
اختبار أدنبروكس المعرفي (المنقح)	/93	
الدرجات الفرعية		
الانتباه والتوجيه	/18	
الذاكرة	/26	
الطلاقة	/14	
اللغة	/23	
القدرات الإبصارية الفراغية	/12	

اختبار أدبروكس المعرفي المنقح

النسخة العربية

يستخدم للأغراض الإكلينيكة فقط

The Arabic Addenbrook's Cognitive Examination - Revised

FOR CLINICAL PURPOSES ONLY

Translated & Adapted By
Ahmed Al Salman, Saeed Wahass, & Jonathan Evans

2013

أختبـار أدنبـروكس المعـرفي المنقـح ACE-R

طريقة التطبيق وتسجيل الدرجات - 2013

أختبار أدنبروكس المعرفي هو أختبار معرفي بسيط يعمل على تقييم خمس قدرات معرفية هي: الانتباه/ التوجه، الذاكرة، الطلاقة اللفظية، اللغة ، والقدرات الإبصارية الفراغية. مجموع الدرجات هو 100. الدرجات العالية تشير إلى قدرات معرفية وظيفية عالية. فكلما كانت الدرجة عالية فوق المعدل كلما دل هذا على أن الأداء المعرفي الوظيفي في أفضل حالاته، وكلما أنخفضت الدرجات عن المعدل دل هذا على تدهور في الأداء المعرفي الوظيفي. عند التطبيق يجب مراعاة بعض التنبيهات مثل:

- تطبيق الاختبار يحتاج حوالي 15 دقيقة.
- هذه التعليمات مصممة بحيث تجعل الفاحصين يطبقون الاختبار ويلقون الأسئلة ويسجلون درجاتها بشكل ميسر ومبسط. لذا الرجاء قراءتها جيدا قبل تطبيق الاختبار على المفحوصين.
- إذا كان ممكنا، اترك تسجيل الدرجات حتى نهاية التطبيق، حتى لا يشعر المفحوص بالارتباك والقلق حين تسجل عليه الإجابت الخاطئة. الأمر الذي قد يؤثر على استجاباته اللاحقة في الأداء.

التوجه – سجل من (0 – 10)

- أسأل المفحوص عن: (اليوم، التاريخ، الشهر، السنة ، أي فصل من فصول السنة). سجل درجة واحدة لكل إجابة صحيحة.
- أسأل المفحوص عن اسم المستشفى (أو المبنى المتواجد فيه حالياً)، الدور (أو الغرفة)، المدينة التي يجرى فيها الاختبار، الدولة التي يقيم فيها. سجل درجة واحدة لكل إجابة صحيحة.
- سجل الاستجابات. يمكن التغاضي عن الأخطاء في التاريخ في حالة كان الخطاء (– 2 أو + 2) يوم. في حالة كان تقييم المفحوص في منزل، اسأل عن اسم المنزل أو من صاحبه. يمكن أن تسأل عن اسم الغرفة لمعرفة إدراك المفحوص لماهية المكان، على سبيل المثال: (مطبخ، غرفة جلوس، غرفة نوم، الخ). لو كان الأمر متعلق
- عندما يجرى الاختبار في وقت يكون الطقس فيه في مرحلة انتقالية بين فصلين، مثلا: نهاية شهر أغسطس الميلادي، ولكن المفحوص أعطى إجابة أنه فصل " الخريف " أسأله إذا ما كان لديه إجابة أخرى؟ إذا قال: " الصيف " فهذا جيد وإذا أصر على الخريف فأعطه درجة هذا السؤال كاملة وهي درجة واحدة، لأنه يجب مراعاة أن الفصل في مرحلة انتقالية بين الصيف والخريف. لكن إذا أجاب المفحوص بأن الفصل في " الربيع " أو " الشتاء "، فلا تعطه أي درجة على هذا السؤال، لأن الإجابة أصبحت بعيدة جداً عن الصحة ولا تمت للمرحلة الانتقالية التي ضربنا لها مثال بأي صلة.
- سوف نعتمد على التقويم الميلادي في معرفة فصول السنة وهي: " الربيع " وأشهره (مارس، ابريل، مايو)، " الصيف " وأشهر (يونيو، يوليو، أغسطس)، " الخريف " وأشهره (سبتمبر، أوكتوبر، نوفمبر)، " الشتاء " وأشهره (ديسمبر، يناير، فبراير).
- وحيث أن الأشهر الميلادية غير مستخدمة في المملكة العربية السعودية من عامة الناس، وحيث أن الأشهر العربية الهجرية تختلف من سنة إلى أخرى وغير متوافقة مع فصول السنة، لذا فإنه الأمر سوف يعود لتقدير وحكم الفاحص عن كون إجابة المفحوص صحيحة أو قريبة للصواب أو بعيدة تماما ولا تمت بصلة نحو احتمالية الصحة.

التسجيل – سجل من (0 – 3)

أجعل المفحوص يعيد نطق الكلمات (ليمون، مفتاح، وكره) واطلب منه أن يتذكرها. تكلم ببطئ وروية وأنت تنطقها له، قبل أن تطلب منه تكرارها وتذكرها. أعد نطقها مره أخرى في حالة الضرورة ولكن (لثلاث مرات فقط). قل للمفحوص أنك سوف تطلب منه هذه تذكر وتكرار هذه المعلومات لاحقاً. سجل عدد المحاولات في الخانة المخصصة، ولكن سجل درجة المحاولة الأولى فقط.

الانتباه والتركيز – سجل من (0 – 5)

- حاصل العملية الحسابية: أسأل المفحوص أن يطرح 7 من 100، سجل النتيجة، بعد ذلك أطلب من المفحوص أن يطرح 7 من نتيجة الطرح الأولى، ثم سجل النتيجة الأخرى. أفعل هذا الأمر 5 مرات. إذا أعطى المفحوص إجابة خاطئة، واصل ولا تتوقف، وتحقق من نتائج الطرح المتتالية في الخمس عمليات. سجل الإجابات الصحيحة فقط. (مثلاً: 92، 85، 79، 72، 65، سجل 3). تذكر أن الهدف من هذا السؤال ليس اختبار القدرة الحسابية للمفحوص ولكن قدرته على التركيز والانتباه.
- التهجئة: أسأل هذا السؤال في حالة أن المفحوص قام بأي خطاء في عملية الطرح الحسابية السابقة. أبدأ بالطلب من المفحوص أن يتهجى كلمة (مدرسة). بعد ذلك أطلب منه أن يتهجى الكلمة بشكل عكسي (بالمقلوب). سجل الاستجابة.
- تسجيل نتيجة التهجئة:
- سجل 1 درجة لكل تهجئة حرف صحيحة. سجل الترتيب الصحيح = م د ر س هـ = 5 درجات.
- عد خطاء 1 لكل تقصير أو إهمال. [تبديل الحروف المتجاورة (تبديل حرف مكان حرف آخر)]، [الإدخال أو الإقحام (إقحام حرف جديد)]، أو [تغيير الموضع (نقل حرف من الحروف لأكثر من مسافة)].
- أنظر للجدول التالي التي يعطيك الطريقة الصحيحة لتسجيل الدرجات حين يكون هناك خطاء في التهجئة:

	الإسقاط	الانتقال	الإدخال	وضع الحروف في غير ملحها
الإسقاط	م د س هـ(4)			
الانتقال	م **س د** هـ (3)	م **ر د** س هـ (4)		
الإدخال	م د **ل** س هـ (3)	**د م م** ر س هـ (3)	م د **ر ر** س هـ (4)	
وضع الحروف في غير ملحها	د م ر **س** (3)	**د ر م** س هـ (3)	هـ م **د** م ر **س** (3)	د ر س هـ **م** (4)

- يوجد بإحدى الإجابة مثل < س هـ م م د > ر ثلاثة أخطاء (ويعد كل من حرفي < م د > أحرف صحيحة، لذا سيتم تسجيل درجتين لهما). وتتضمن تلك الكلمة نقل الحرفين < م د > وإدخال حرف < م > الزائد ووضع حرف < هـ > في غير محله. إذا أضاف المشارك حرف واحد أو أكثر من نفس الحرف في نهاية الكلمة، فاعتبرها كخطأ واحد (على سبيل المثال، يمكن تسجيل < س هـ ر م م م > كخطأين، كعمليتي تحويل وإضافة).
- قم بوضع نقطة واحدة لكل عملية حسابية صحيحة أو على كل حرف تم هجائه بشكل صحيح. وقم فقط بوضع بتسجيل أفضل أداء تم مرة واحدة.

الذاكرة : الاسترجاع – سجل من (0 – 3)

- أسأل المفحوص فيما إذا كان يستطيع أن يسترجع الكلمات التي جعلته من قبل يعيد تكرارها وطلبت منه أن يتذكرها. سجل الاستجابات. سجل درجة 1 لكل إجابة صحيحة.

الذاكرة: الذاكرة التقدمية – سجل من (0 – 7)

- قل للمفحوص: (سوف أقرأ لك اسم وعنوان وأود منك أن تعيد ذكره بعد أن أنتهي. سوف نكرر هذا ثلاث مرات، لذلك سوف يكون لديك فرصة استيعابه جيداً. سوف أسألك عنه لاحقاً). إذا بدأ المفحوص بإعادة العنوان بعد كل مقطع قبل أن تنتهي من ذكر العنوان كاملاً، أخبره أن يتريث حتى تنتهي من ذكر العنوان كاملاً له. سجل الإستجابات لكل محاولة. لكن، فقط المحاولة الثالثة هي التي سوف تسجل كدرجة لهذا السؤال من أجل تقييم حالة المفحوص على اختبار أدنبروكس المعرفي المنقح.

الذاكرة الرجوعية – سجل من (0 – 4)

- أسأل المفحوص الأسئلة التالية :
1) عاصمة الدولة التي يقيم فيها.
2) اسم الحاكم السابق لبلده.
3) اسم رئيس الولايات المتحدة الامريكية.
4) اسم الحاكم الحالي لبلده.
- سجل درجة واحدة لكل جواب صحيح.
- إقبل إجابات تشير إلى اسماء الحكام السابقين لدولة المفحوص، في السعودية يمكن قبول الملك خالد، الملك فيصل، الملك عبد العزيز على سبيل المثال. لأنه ليس بالضرورة ان يكون الحاكم السابق مباشرة. إسأل عن اسم عائلة الحاكم أيضاً.

الطلاقة اللفظية

- **الحروف – سجل (0 – 7)**

- قل للمفحوص: سوف اعطيك حرف من الحروف الهجائية، وأود منك أن تذكر لي اكبر قدر ممكن من الكلمات التي تبدأ بهذا الحرف، على ألا تكون اسماء أشخاص أو أماكن. هل أنت جاهز؟ لديك فقط دقيقة واحدة، والحرف هو حرف الـ (م).
- قد يكرر المفحوص بعض الكلمات ويواظب عليها مثل "مدرسه/ مدراس/ مدرسين". قم بتسجيل تلك الكلمات وقم بإحصائها لإجمالي العدد الكلي للإجابات ولكن لا تضعها في الدرجات النهائية. وبنفس الطريقة، يتم تسجيل المدخلات مثل الكلمات التي تبدأ بحروف أخرى ولكن لا يتم وضع درجات لها. ولا يتم حساب أسماء الأعلام مثل (محمد ومحمدين). وبالنسبة إلى الكلمات مثل "مدن، مدائن" ، يكون المجموع =2، والإجابة الصحيحة =1. قم باستخدام الجدول الموضوع في صفحة الاختبار الإدراكي المنقح لأدنبروك (ACE-R) للحصول على الدرجة النهائية لهذا الاختبار.

- **الحيوانات – سجل (0 – 7)**

- قل للمفحوص: "يمكنك الآن ذكر أسماء العديد من الحيوانات بقدر استطاعتك، والتي تبدأ بأي حرف؟" وقد يقوم المفحوص بتكرار الكلمات. قم بتسجيلهم وإحصاءهم لتسجيل إجمالي العدد الكلي للإجابات، ولكن لا يجب وضعهم في الاعتبار بالنسبة للدرجة النهائية. وقد يسيء المفحوص فهم عملية تسمية الحيوانات التي تبدأ بحرف "م" مثلاً، أو المواظبة عليها. كرر التعليمات في غضون 60 ثانية عند الضرورة.
- إذا قال المفحوص مثلاً "سمكة" ثم قال فيما بعد "سلمون" و "تونة" فقم بإحصاء وتسجيل الإجابات كمجموع إجمالي "3"، ولكن لا تقبل كلمة "سمكة"، على أنها الإجابة الصحيحة (وسجل الدرجات فقط (اثنين من الثلاثة) إذا كانت الإجابة على سبيل المثال "سالمون، وتونة") ولكن إذا ذكر الفصيلة فقط مثل السمك بدون أي أمثلة محددة، فقم بوضع درجة واحدة (1) على كلمة سمكة باعتبارها إجابة صحيحة نهائية. وتطبق نفس الطريقة على التدييات والزواحف والطيور وسلالة الكلاب والحشرات وما إلى ذلك..

اللغة – الفهم – سجل (0 أو 1)

قل للمفحوص: " إقرأ هذه الجملة وأفعل كما تقول". إذا قرأ المفحوص الجملة بصوت مسموع ولم يتبع تعليماتها، يعطى درجة 0.

اللغة – الفهم – (أمر من ثلاث مراحل) سجل (0 – 3)

- أعطي تعليمات للمفحوص وقل: "خذ هذه الورقة بيدك اليمنى واطويها من النصف وضعها على الأرض". ولا تسمح للمتقدم للاختبار بأخذ الورقة قبل أن تنتهي من إعطاء التعليمات كاملة.
- سجل نقطة واحدة لكل أمر صحيح، فعلى سبيل المثال إذا قام المفحوص بأخذ الورقة بيده اليمنى ووضعها على الأرض بدون ثنيها، سجل 2، بينما إذا أخذ المفحوص الورقة بيده اليمنى وطواها عدة مرات وتركها على الطاولة، سجل له 1.

اللغـة – الكتابة – سجل (0 – 1)

- أطلب من المفحوص كتابة جملة.
- الجملة يجب أن تكون مفهومة ومكتوبة بالطريقة المباشرة السهلة، بمعنى يجب أن تكون قواعدها النحوية اللغوية واضحة. إذا كان المفحوص يواجه صعوبة في التفكير في كتابة شيء، قم بحثه بطريقة لطيفة بطرح سؤال عليه مثل "كيف تبدو حالة الجو اليوم؟"

اللغـة – التكرار – سجل (0 – 2)

اطلب من المفحوص تكرار الكلمات بعدك. وقل كلمة واحدة في كل مرة. وقم بعمل دائرة حول الكلمات التي تم تكرارها بطريقة خاطئة. ولا تسجل درجات إلا على المحاولة الأولى. وسجل الإجابات. وتكون الدرجة (2) في حالة إذا كانت جميع الكلمات صحيحة، ويكون مجموع النقاط (1) إذا كان عدد الكلمات صحيحة ثلاثة ،ويكون (0) إذا كان عدد الكلمات الصحيحة إثنتين أو واحدة.

اللغـة – التكرار – سجل (0 – 2)

اطلب من المفحوص تكرار كل جملة. ولا تقبل التكرارات الصحيحة جزئياً، على سبيل المثال "لا تستخدم لا لإذا ولكن" و "فوق وأسفل" باعتبارها إجابات صحيحة،ع بل سجل درجة واحدة لكل جملة كاملة وصحيحة.

اللغـة – التسمية –

تسمية (الساعة وقلم رصاص) سجل (0 – 2)

أطلب من المفحوص تسمية كل صورة. الإجابات الصحيحة: قلم رصاص او قلم مرسم، ساعة يد أو ساعة.

تسمية (5 حيوانات و 5 أشياء) سجل (0 – 10)

أطلب من المشارك وضع اسم لكل صورة. الإجابات الصحيحة: أسد، جمل، بندقية، حصان/فرس/خيل، سطل/دلو/جردل، طائرة، عود، صقر، ضفدع، سيف.

أعط درجة واحدة لكل منهم.

اللغـة – الادراك – سجل (0 – 4)

الادراك:

أطلب من المفحوص أن يشير على الصورة وفقا لقراءة العبارة في هذه المهمة. سجل درجة واحدة لكل عبارة يشير فيها المفحوص إلى الصورة الصحيحة. اسمح بالتصحيحات الذاتية.

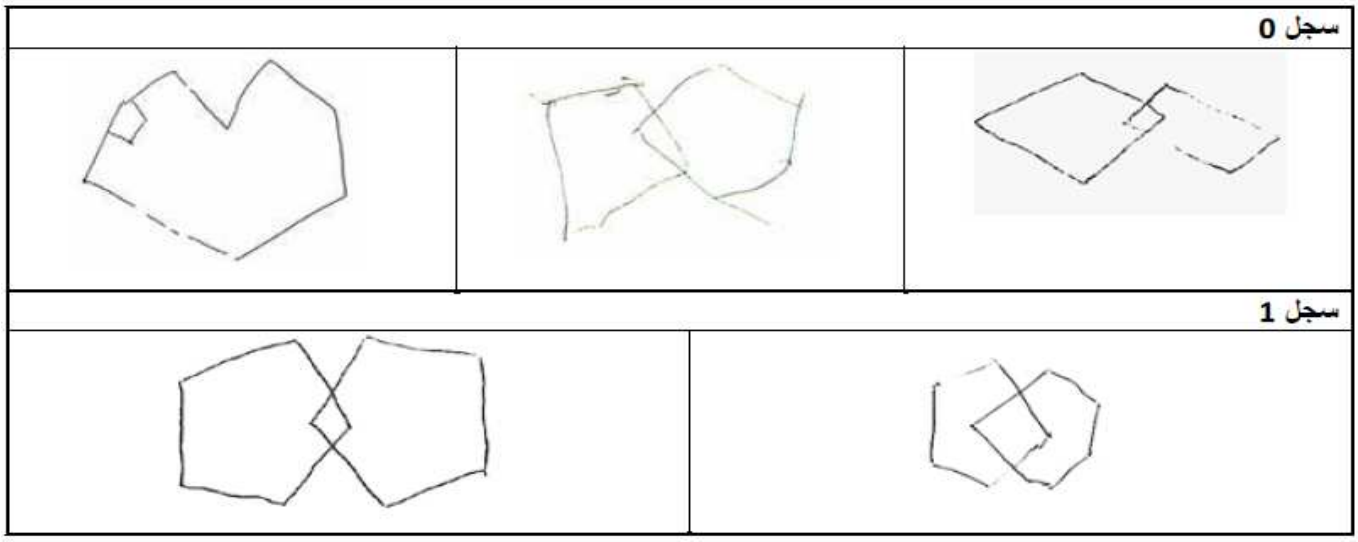
اللغـة – القراءة - سجل (0 – 1)

أطلب من المفحوص قراءة الكلمات بصوت مسموع. سجل درجة واحدة فقط لمجموع الكلمات الخمس إذا لفظت بشكل صحيح. سجل الأخطاء اللفظية للتهجئة قدر الإمكان.

القدرات الإبصارية الفراغية

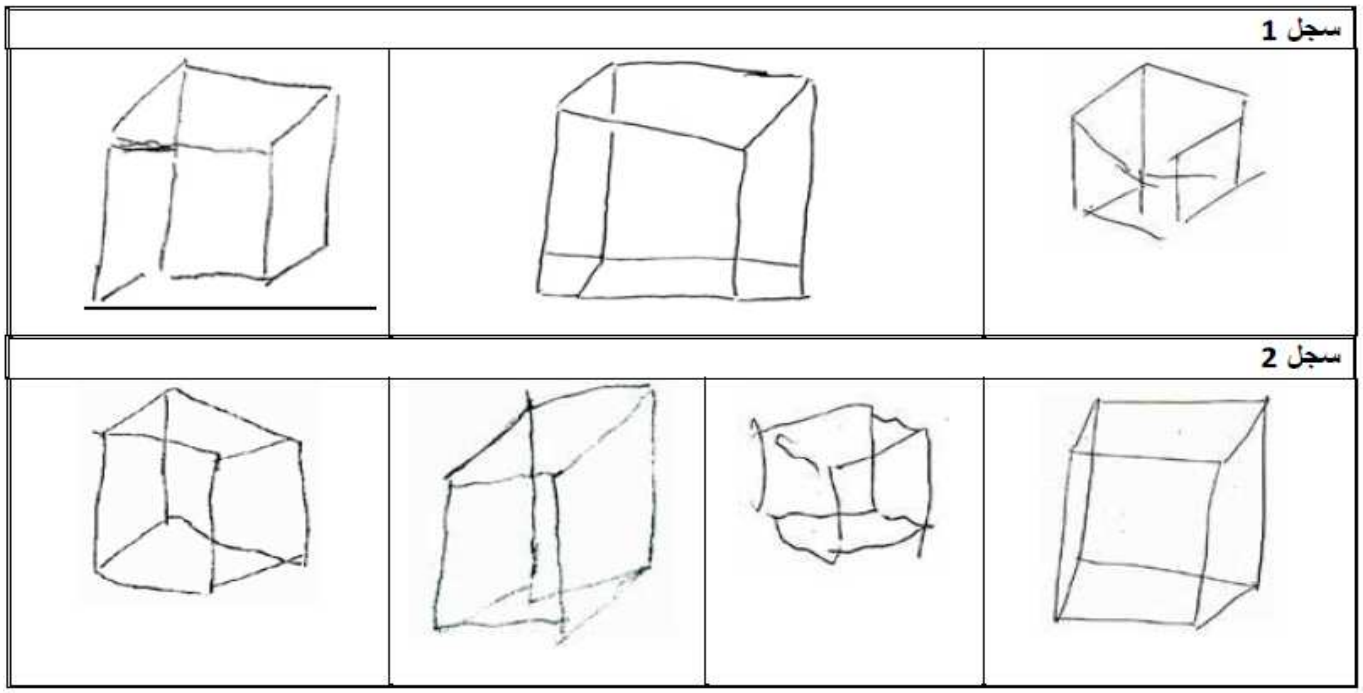
– الشكلان الخماسيان المتداخلان – سجل (0 أو 1)

الشكلين الخماسيين ينبغي أن تتوفر فيهما الخمسة جوانب بشكل واضح بالإضافة إلى التداخل بشكل جلي



– المكعب السلكي – سجل (0 – 2)

الكعب ينبغي أن يتكون من 12 ضلع مما يقدر بمجموع نقاط 2، حتى وإن كانت النسب غير تامة. ويبلغ مجموع النقاط (1) في حالة إذا تكون المكعب من أقل من 12 ضلع، ولكن يتم الاحتفاظ بشكل المكعب العام. انظر الأمثلة أدناه.



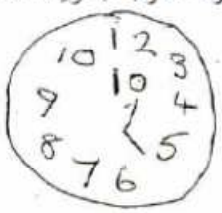
القدرات الإبصارية الفراغية – الساعة – سجل (0– 5)

اطلب من المفحوص رسم وجه ساعة مع كتابة الأرقام عليها. عندما ينهي أو تنتهي من ذلك، اطلب منهم وضع العقارب على "الخامسة وعشرة دقائق".

الدائرة	• نقطة واحدة كحد أقصى في حالة أن تكون الدائرة مقبولة
الأرقام	• نقطتين في حالة وجود جميع الأرقام وفي حالة توزيعها بطريقة جيدة • نقطة واحدة في حالة وجود جميع الأرقام ولكنها موزع بشكل غير جيد
العقارب	• نقطتين إذا تم رسم العقارب بشكل جيد، بأطوال مختلفة وموجهة للأرقام الصحيحة (وقد تتساءل أيهما الأصغر وأيهما الأكبر • نقطة إذا تم توجيه العقارب للأرقام الصحيحة ولكن كانت الأطوال خاطئة. أو • نقطة واحدة إذا تم توجيه عقرب واحد للرقم الصحيح وكان طوله صحيح أو • نقطة واحدة إذا تم رسم عقرب واحد فقط وتم توجيهه للرقم الصحيح على سبيل المثال 5 بالنسبة لـ "الخامسة وعشر دقائق"

الدرجة 2

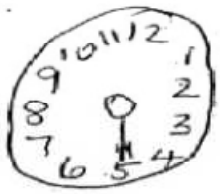
دائرة (1): عقرب واحد موجه بطريقة صحيحة



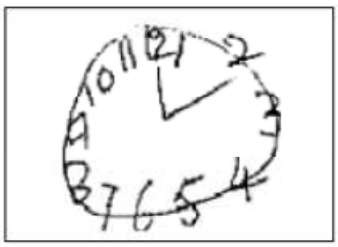
دائرة (1): جميع الأرقام متواجدة ولكنها غير موضوعة داخل الدائرة (1)

الدرجة 3

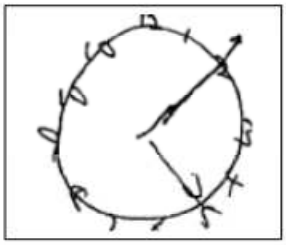
دائرة (1): جميع الأرقام متواجدة ولكنها غير موزعة بنسب صحيحة (1)، مع وجود عقرب واحد موجه بطريقة صحيحة (1)



دائرة (1) جميع الأرقام متواجدة ولكنها غير موضوعة داخل الدائرة (1)، عقرب واحد موجهة بطريقة صحيحة

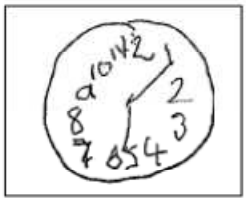


دائرة (1) لاحظ أن الأرقام خارج الدائرة وتحتوي الساعة على رقم 10 مكرر مرتين (0). والعقارب موجهة بطريقة صحيحة

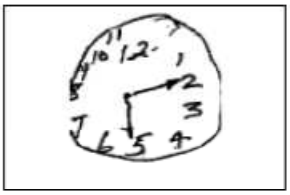


الدرجة 4

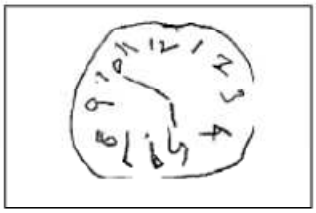
دائرة (1): الأرقام موزعة بدقة (2)، وعقرب واحد موجه بطريقة صحيحة



دائرة (1) جميع الأرقام متواجدة ولكنها غير موزعة بدقة (1): والعقارب موجهة بطريقة صحيحة

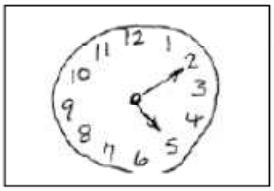


دائرة (1) الأرقام موزعة بدقة (2) وعقرب واحد موجه بطريقة صحيحة



الدرجة 5

دائرة (1) الأرقام موزعة بدقة كلا أنصاف وجه الساعة (2): والعقارب موجهة بطريقة صحيحة (2)



القدرات الحسية الإدراكية – الدرجة (0 – 4)

عد النقاط :

لا يسمح للمفحوص بالإشارة إلى الصورة. سجل نقطة واحدة لكل إجابة صحيحة. الإجابات الصحيحة من أعلى اليسار باتجاه عقارب الساعة: 8 ، 10 ، 9 و 7

القدرات الحسية الإدراكية – الدرجة (0 – 4)

التعرف على الحروف :

يسمح للمتقدم للاختبار بالإشارة إلى الصورة. سجل نقطة واحدة لكل إجابة صحيحة. الإجابات الصحيحة، من أعلى اليسار لاتجاه عقارب الساعة: **ل ، م ، هـ ، و**

الاسترجاع – الدرجة (0 – 7)

قل للمفحوص: "والآن أخبرني بما تتذكر من الاسم والعنوان الذين تم تكرارهم من البداية". ضع إشارة وسجل نقطة واحدة لكل عنصر تم استرجاعه باستخدام دليل الدرجات المقدم في الاختبار. يجب الإنتباه إلى أن شارع مختلف عن طريق او ممر. فلو كان في السؤال كلمة شارع فهي تعني شارع فإذا قال المفحوص طريق أو ممر فيجب ان يسجل له درجة (0) صفر.

احمد خالد	1+1
منزل 73	1
شارع المتنبي	1+1
حي الأمل	1
الرياض	1

مثال 1

أحمد عبد الله	0+1	
منزل رقم 78	0	
شارع المتنبي	1+1	مجموع النقاط 7/3
حي النهاني	0	
.....		

يقوم الفاحص بسؤال المفحوص كالآتي:

- **هل كان اسم الشخص حمد عايد أو أحمد خالد أو أحمد عبد الله؟**
- **هل كان رقم المنزل 37 أو 73 أو 76؟**
- **هل كان اسم الحي هو حي الأماني أو حي النهاني أو حي الأمل؟**

مثال 2

أحمد خالد	1+1	
منزل رقم 73	1	
طريق المتنبي	1+0	مجموع النقاط 7/5
.....	0	
الرياض	1	

يقوم الفاحص بسؤال المفحوص كالآتي:

- **هل كان شارع المتنبي أو طريق الأمانة أو شارع السعادة؟**
- **هل كانت المدينة الرياض أو الجوف أو الخرج؟**

مثال 3

أحمد عايد	0+1	
منزل 33	0	
طريق الأمانة	0+0	مجموع النقاط 7/2
حي السعادة	0	
الرياض	1	

يقوم الفاحص بسؤال المفحوص كالآتي:

- **هل كان اسم الشخص حمد عايد أو أحمد خالد أو أحمد عبد الله؟**
- **هل كان رقم المنزل 37 أو 73 أو 76؟**
- **هل كان اسم الحي هو حي الأماني أو حي التهاني أو حي الأمل؟**

☆ الادراك– سجل (0 – 5)

لا يتم تقديم عملية التمييز إلا في حالة فشل المتقدم للاختبار في استرجاع عنصر أو أكثر من مهمة الاسترجاع.

ينبغي تقديم هذا العمل لإعطاء المفحوص فرصة لتذكر الفقرات التي لا يستطيع هو أو هي استرجاعها. وفي حالة استرجاع المفحوص للاسم والعنوان بطريقة صحيحة، يكون هذا الاختبار غير ضروري ويكون مجموع نقاط المفحوص (5). وبالرغم من ذلك فسيسترجع العديد من المفحوصين أجزاء فقط. ابدأ بتحديد العناصر التي تم تذكرها بطريقة صحيحة في العمود المظلل (في الجهة اليمنى) ثم أخبرهم "دعوني أقدم لكم بعض التلميحات. هل الرقم (أو أيا كان العنصر المنسي أو غير الصحيح) س أو ص الخ؟ وهكذا. ويتم تسجيل درجة واحدة لكل عنصر يتم تذكره. ويكون الحد الأقصى للدرجات المحرزة هو 5. وبإضافة العناصر المسترجعة لتلك العناصر التي تم تذكرها يظهر مجموع النقاط النهائي لهذا الجزء من الاختبار.

بيانات معيارية

هناك أربعة مجموعات شاركت في الدراسة وهم كالآتي:

فئة المتعلمين:

1) من فئة الأصحاء المتعلمين كان تعداد المشاركين هو (147) مشارك، والمدى العمري بين (50- 85).
2) من فئة المرضى المتعلمين كان تعداد المشاركين هو (44) مريض مشخص إكلينيكيا أنهم مصابين بالخرف من نوع الزهايمر، ومداهم العمري بين (52- 80). بينما بلغ عدد المشاركين المشخصين إكلينيكيا على أنهم مصابين بالتلف المعرفي البسيط (10)، ومداهم العمري بين (56- 80).

فئة الأميين:

3) من فئة الأصحاء الأميين كان تعداد المشاركين هو (283)، والمدى العمري بين (50-80).
4) من فئة المرضى الأميين كان تعداد المشاركين هو (123) مريض من المشخصين إكلينيكياً على أنهم مصابين بالخرف من نوع الزهايمر، ومداهم العمري بين (54- 82). بينما بلغ عدد المشاركين المشخصين إكلينيكياً على أنهم مصابين بالتلف المعرفي البسيط (46)، وومداهم العمري بين (51-80).

- **الجدول 1 :** الحد المنخفض من (الدرجات القياسية المكونة لحد معين) لإجمالي الاختبار الإدراكي المنقح لأدنبروكس والدرجات الفرعية وفقاً لمدى عمري مختلف (لكامل العينة، 50 – 59، 60+) يظهر الوسيط لمجموعة الأصحاء **المتعلمين** ناقص درجتين إنحراف معياري.

		اختبار أدنبروكس المنقح	لانتباه والتوجه	الذاكرة	الطلاقة اللفظية	اللغة	الإبصاري الفراغي
كامل العينة	الوسيط	86	18	23	7	25	13
	المدى الربعي	90-82	18-17	2-22	9-6	24-25	15-10
	%5	73	14	19	4	21	6
59 - 50	الوسيط	89	18	24	7	25	14
	المدى الربعي	92-87	18-17	25-23	9-7	25-24	15-13
	%5	83	16	21	4	22	9
60+	الوسيط	82	17	23	7	24	11
	المدى الربعي	86-77	18-16	24-21	9-6	25-23	13-9
	%5	71	13	18	4	20	6

- **الجدول 2 :** الحد المنخفض من (الدرجات القياسية المكونة لحد معين) لإجمالي اختبار أدنبروكس الإدراكي المنقح والدرجات الفرعية وفقاً لمدى عمري مختلف (لكامل العينة، 50 – 59، 60 – 69، 70+) يظهر الوسيط لمجموعة الأصحاء **الأميين** ناقص درجتين إنحراف معياري.

		اختبار أدنبروكس المنقح	الانتباه والتوجه	الذاكرة	الطلاقة اللفظية	اللغة	الإبصاري الفراغي
كامل العينة	الوسيط	76	17	23	6	21	9
	المدى الربعي	79-74	18-17	24-22	7-5	22-21	10-8
	%5	69	14	19	4	19	5
59 - 50	الوسيط	77	17	24	6	21	10
	المدى الربعي	80-75	18-17	24-22	7-5	22-20	11-8
	%5	72	15	20	4	19	6
69 – 60	الوسيط	76	16	23	6	21	9
	المدى الربعي	78-73	17-16	24-22	7-5	22-20	10-8
	%5	69	14	19	4	19	5
70+	الوسيط	73	17	21	5	21	8
	المدى الربعي	76-70	17-16	23-19	6-5	21-20	9-6
	%5	66	13	16	4	18	4

- **الجدول 3 :** الحساسية، التخصيص والقيم التنبوئية الإيجابية (PPV) على مختلف معدلات إنتشار الخرف في **عينة المتعلمين** من مجموع النقطتين القطعية لدرجات إختبار أدنبروكس المعرفي المنقح، بينما القيم السفلية تمثل كل منها القيم التنبؤية السلبية (NPV).

القيم التنبؤية الإيجابية على مختلف معدلات إنتشار الخرف					الخرف		النقط القطعية	العمر
%50	%40	%20	%10	%5	التخصيص	الحساسية		
1.000	1.000	1.000	1.000	1.000	1.000	0.929	68/69	50 – 59
0.949	0.926	0.825	0.677	0.498	0.947	1.000	69/70	60+
0.953	0.931	0.836	0.695	0.519	0.960	0.821	65/66	
القيم التنبؤية السلبية على مختلف معدلات إنتشار الخرف					الخرف		النقط القطعية	العمر
%50	%40	%20	%10	%5	التخصيص	الحساسية		
0.933	0.954	0.982	0.992	0.996	1.000	0.929	68/69	50 – 59
1.000	1.000	1.000	1.000	1.000	0.947	1.000	69/70	60+
0.842	0.889	0.955	0.979	0.990	0.960	0.821	65/66	

- **الجدول 4 :** الحساسية، التخصيص والقيم التنبوئية الإيجابية (PPV) على مختلف معدلات إنتشار الخرف في **عينة الأميين** من مجموع النقطتين القطعية لدرجات إختبار أدنبروكس المعرفي المنقح، بينما القيم السفلية تمثل كل منها القيم التنبؤية السلبية (NPV).

القيم التنبؤية الإيجابية على مختلف معدلات إنتشار الخرف					الخرف		النقط القطعية	العمر
%50	%40	%20	%10	%5	التخصيص	الحساسية		
0.968	0.954	0.886	0.776	0.621	0.968	1.000	67	50 – 59
0.991	0.987	0.966	0.928	0.859	0.992	0.930	64	
0.984	0.976	0.939	0.872	0.764	0.984	0.989	65	60 – 69
1.000	1.000	1.000	1.000	1.000	1.000	0.857	64	70+
القيم التنبؤية السلبية على مختلف معدلات إنتشار الخرف					الخرف		النقط القطعية	العمر
%50	%40	%20	%10	%5	التخصيص	الحساسية		
1.000	1.000	1.000	1.000	1.000	0.968	1.000	67	50 – 59
0.934	0.955	0.982	0.992	0.996	0.992	0.930	64	
0.988	0.992	0.997	0.998	0.999	0.984	0.989	65	60 – 69
0.874	0.912	0.965	0.984	0.992	1.000	0.857	64	70+

References:

- Al Salman, A., Wahass, S., Altahan, A., Balubaid, H., Algereshah, F., Evans, J.J. (2011) Validation of an Arabic Version of Addenbrooke's Cognitive Examination – Revised. Abstracts of the International Neuropsychological Society Mid-Year Meeting. Brain Impairment, 12, 24.

- Al Salman, A., Wahass, S., Altahan, A., Balubaid, H., Algereshah, F., Evans, J.J. (2012) Reliability of an Arabic Version of Addenbrooke's Cognitive Examination – Revised. Abstracts of the International Neuropsychological Society Mid-Year Meeting, Journal of the International Neuropsychological Society, 18, Supplement S2, 30-31.