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Enhancing cognitive and functional assessment for Alzheimer's Disease

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Declaration

I declare that all work presented in this thesis is my own, except as specified. This work has not been submitted elsewhere for any degree or qualification.

Versions of some chapters have been published in scientific journals, on which I am first author or co-author. The experiment 2 from Chapter 2 was published in the International Journal of Geriatric Psychiatry on which I am second author:

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The part of the review for Chapter 7 was published in in the International Journal of Geriatric Psychiatry on which I am the first author:

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The study in Chapter 4 is under-review in the Parkinsonism and Related Disorders:

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The studies from Chapters 8 and 9 are under-review Psychological Assessment:

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My supervisors Sergio Della Sala, Mario Parra Rodrgues and Tom Booth gave permission to submit these studies for peer-review publication prior to submitting this thesis.

05/11/18

Irina Kozlova

DEDICATION

This work is dedicated to my mum. It wouldn’t have been possible without you.

Thank you.

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Abstract

One major challenge recently recognised by a EU consensus conference is the need of brief, reliable, simple methods to assess Alzheimer's Disease (AD). There is an emphasis on the need for cognitive, behavioural and functional measures that are sensitive and specific for detecting the cognitive impairment earlier of the course of the disease. In my thesis I explore what are these measures. This thesis sought to explore two themes: the first, where I enhance the existing knowledge about Visual Short-Term Memory Binding as a sensitive, specific and early cognitive marker for AD. The second theme is to look at which everyday functional abilities decline first in the trajectory from the healthy ageing to dementia. I argue that everyday financial decline is the earliest functional impairment in the course of the disease.

There are evidences indicating that the Temporal Memory Binding (TMB) reliably detects asymptomatic carriers of the Presenil-1 gene mutation E280A that leads to familial AD and amnestic Mild Cognitive Impairment (aMCI) patients who are at a high risk of conversion to dementia; the test is not affected by healthy ageing and chronic depression; it has been proved culturally unbiased. All these factors make the test a perfect marker for AD. The TMB test has been developed as a computer version. This poses several limitation of using the test globally: it has low mobility, difficulty testing on the older population and patients with AD who have preferences more to conventional paper-and-pencil tests. Therefore, one of the main aims of the thesis was to create a more clinically and user-friendly version of the test. I created a Flash-Card version of the test that contained several modifications from the standard computer version to make the test more clinically oriented: all participants were presented only with two items and the test was presented as a recognition task. The alternative version of the test was presented in the form of the Tablet PC. The first series of experiments (Experiments 1-7) reported in this thesis were dedicated to compare these three formats of testing. I showed that all three methods of testing are equivalent to each other. In these experiments I also have confirmed that the test is unaffected by age in order to serve as a baseline performance on the Flash-Cards and Tablet PC to measure AD performance.

In the following Chapter 3, I focused on addressing the question, what is the neurological reason for older adults to perform as well as younger participants. For that I employed a mobile low-density EEG system that has advantages in its mobility and user-friendliness, which is important in clinical setting and in research with frail older participants. The results

of the study showed increased activity over all electrodes sites suggesting that older participants recruited more neural resources to achieve levels of performance similar to those observed in younger adults.

To show that my Flash-cards TMB task still holds specificity to only AD I recruited patients with aMCI, AD patients and Parkinson's disease (PD) patients with and without cognitive deterioration (Chapter 4). The results of the study showed that only patients with AD presented impaired performance on the TMB task. On the contrary, compared to either cognitively healthy older individuals or PD patients with normal cognition, patients with PD dementia did not show impairment on the TMB.

The other main aim of this thesis was to investigate what functional abilities decline first on the course of the disease and what are those "minimal functional problems". As part of this thesis I conducted a literature review (Chapter 7) that showed that everyday financial abilities represent the most complex and multidimensional functional activities. I coined a term *Acreemagnosia* to highlight the specificity of the symptom. In order to assess this specific symptom I developed *The Acreemagnosia Measurement* (TAM) that is a multi-items measure that inquiries about a person's awareness of financial abilities and examines actual performance on the broad range of everyday financial tasks. On the groups of healthy middle-aged and older people I validated TAM (Chapter 8). I used a two-parameter IRT model to analyse the psychometric properties of TAM and established the best items that would describe financial abilities of participants in different age and gender groups. The analysis suggests that TAM is measuring most reliably at low to average levels of financial ability, meaning that TAM is potentially a good financial measure for people with limited financial proficiency, which is in keeping with the design and intended use of the instrument with elderly retired people and people with cognitive impairment. The results did not reveal any differential item functioning across different gender and age groups in the scale that indicates that tendency to endorse the item reflects the ability level and are not affected by variables such as gender and age.

As TAM is intended for patients with cognitive impairment, I recruited patients with amnestic-MCI and mild-AD (Chapter 9). In this feasibility study I showed that patients with amnestic-MCI are already present with some problems in everyday financial abilities and are unaware of these problems demonstrating that they present with Acreemagnosia, thus confirming the sensitivity of TAM to capture such impairments.

The general findings of this thesis indicate that TMB task and TAM can enhance the assessment of dementia and potentially serve in the detection of cognitive impairment at the pre-clinical level.

Lay Summary

The overarching theme of this thesis is to enhance cognitive and functional assessment of Alzheimer's disorder (AD). The first part of the thesis is dedicated to a cognitive test shown to be very sensitive and specific to detect preclinical cognitive impairment of AD. The Temporary Memory Binding test (TMB) has been shown to be resistant to the effect of age, other than AD types of dementia and geriatric depression, it was also shown to be sensitive to asymptomatic forms of AD. In order for the test to be more affordable and clinically friendly I created a Flash-Card version of the TMB test. I showed that this format of testing is equivalent to the computer version of the test and it retains all diagnostic qualities of the computer test.

The second part of the thesis is dedicated to the functional assessment of AD and detecting the most sensitive tasks to detect early functional difficulties. I argue that financial tasks can fulfil this role. To highlight the specificity of the symptom we have suggested a term: *Acreemagnosia* from the ancient Greek a- ("lack of") and creema ("money"). In order to explore my hypothesis deeper, I design the Acreemagnosia Measurement . In series of experiment on healthy middle- and older adults I explore its psychometric properties and in clinical sample of patients with various cognitive impairment and healthy older controls I show its discriminability.

I argue that the combination of TAM and TMB can aid early detection of preclinical AD.

Abbreviation list

ACE-R	The Addenbrooke's Cognitive Examination – Revised
AD	Alzheimer's disease
ADH	Age-Related Associative Memory Deficit Hypothesis
ADL	Activity of Daily Living
aMCI	Amnestic Mild Cognitive Impairment
BADL	Basic Activities of Daily Living
EEG	Electroencephalogram
ECog	Everyday Cognition Scale
EF	Executive Function
ERC	Enthorhinal Cortex
ERP	Event-Related Potentials
FCAI	Financial Competence Assessment Inventory
FCI	Financial Capacity Instrument
FCSRT	Free and Cued Selective Reminding Test
FIT	Feature Integration Theory
fMRI	Functional Magnetic Resonance Imaging
HC	Healthy Controls

IADL	Instrumental Activity of Daily Living
ICC	Item Characteristic Curve
IRF	Item Response Function
IRT	Item Response Theory
MAFS	The Measure of Awareness of Financial Skills
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
MTL	Medial Temporal Lobe
STAC	Scaffolding Theory of Age and Cognition
STM	Short term Memory
PD	Parkinson's Disease
PAL	Paired Associative Learning
PFC	Pre-Frontal Cortex
RPC	Perirhinal Cortex
RAVL	Ray Auditory Verbal Learning Test
TAM	The Acreemagnosia Measurement
TMB	Temporary Memory Binding
TMT	Trail Making Test
TOPF	Test of Premorbid Functioning

WM	Working Memory
VWM	Visual Working Memory

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Chapter I - Introduction

Part I

In this introduction I will review the current diagnostic criteria for Mild Cognitive Impairment (MCI) and Alzheimer's Disorder (AD) and the difficulties that early diagnosis poses. I will critically appraise the cognitive and functional tests used in clinical setting and in research studies that are claimed to be sensitive and specific to AD. I will also explore what are the current challenges with functional scales and which are the most promising scales and ways of improving their sensitivity. I will review modern diagnostic tools: biomarkers and brain imaging methods. Finally, I will introduce the predominant ideas and aims of the thesis.

Cognitive and functional decline in neurodegenerative disorders: where are we standing?

AD is the most common cause of dementia and the prevalence of the disease increases markedly with age from 14.9% at 65 years to 21.8% at 85 years (Pujades-Rodriguez et al., 2018). In 2017, there were 3.65 million cases of clinical AD in the United States (range, 1.70–7.62 million) (Brookmayer et al., 2018)

The main characteristics of AD were first described by Alois Alzheimer in 1907. Despite all efforts, an effective therapy is still lacking. As AD pathology is already present years before cognitive symptoms appear, diagnosing AD before the disease becomes evident might improve the effectiveness of future therapeutic development options. Early diagnosis is a very challenging undertaking, as symptoms of the disease might resemble those characterising normal ageing or depression in older people. Therefore, researchers were challenged to modify, improve, or create cognitive and functional measures that can be sensitive and specific enough to detect early changes and differentiate AD from other forms of dementia and from normal ageing.

Currently, the diagnosis of dementia in clinical settings is based on the medical history of the patients, on their relatives' concerns about memory deterioration of the patient, and the

outcome of standard neuropsychological tests. If based on this assessment there is a concern about the presence of cognitive deterioration, the patients might be referred to a specialist clinic (if one is available) for a brain scan or for "biomarkers". Therefore, this initial assessment is crucial in order to make the correct referral without over- or underestimating the diagnosis. In clinical practice the most common method of assessment and monitoring of progression are the cognitive scales that would screen for global cognitive function, namely memory, attention, language, perception, orientation, visuo-spatial abilities. The Mini Mental State Examination (MMSE) is one of such scales, designed in the 1970s, is the most widely accepted and used internationally despite its well-acknowledged limitations. It shows good sensitivity to general cognitive deterioration (Nasreddine et al., 2005). It is a very brief but non-specific tool. The other limitation is that it obtains poor scores on the low educational population leading to overestimation of the diagnosis in this group. On the other hand, the test reaches ceiling performance when tested on people with high level of education even if they have some cognitive impairment, resulting in underestimation of the presence of dementia (Nieuwenhuis-Mark, 2010). The same holds for The Montreal Cognitive Assessment (MoCA; Folstein et al., 1975), a brief screening instrument for global cognitive function, and for other more extensive batteries: the Addenbrooke's Cognitive Examination (ACE; Mioshi et al., 2006) and the Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog; Rosen, Mohs, & Davis, 1984). All these screening measures were shown to be non-specific to AD and suitable more for general screening of cognitive impairment. Moreover, they are marred with practice effect and show improvement over repeated tests that can be wrongly interpreted by the clinician as a recovery (Foley et al., 2015). As it was suggested by Costa et al. (2017), these tests batteries are better used only as a first line of screening.

Outside clinical practice, research assessment tools vary dramatically. Different research groups in different countries are striving to develop the most sensitive and specific tool to assist the diagnosis of dementia early on the course of the disease. Fowler et al. (1997) and Swainson et al. (2001) suggested that a test that measures precise cognitive function would be more effective to detect and predict global decline that the measures of global cognitive function. Logie, Parra, & Della Sala (2015) outlined that cognitive markers for AD should (1) be sensitive and specific to AD, (2) not show improvement due to practice effects, (3) not be sensitive to the education or cultural background of the assessed individual, (4) be easy to administer and interpret with minimal training, (5) easily accessible and inexpensive, they

should be (6) theory driven allowing for the alignment of cognitive constructs and the course of AD pathology.

1.1 AD-Specific Markers: Associative memory tests

A well-established finding in dementia research, is that memory impairment, specifically that related to the ability to learn and retain new information is a characteristic feature of AD which seems to appear from the prodromal stages (Petersen et al., 1995; 1999; Albert et al., 2001). Episodic memory deficits have been found to be a strong predictor of incident AD (Flicker et al., 1991; Kluger et al., 1999; Dudas et al., 2005). However, episodic memory impairment is a characteristic of other disorders like depression and also healthy ageing (Jayaweera et al., 2016; Yonelinas, 2001).

Several International Working Groups focused on harmonisation of novel assessments and new conceptual frameworks for early identification of AD propose that the tests related to hippocampal dysfunction and involving list learning and delayed recall (Free and Cued Selective Reminding Test (FCSRT), Paired Associative Learning (PAL) and Ray Auditory Verbal Learning Test (RAVL)) are at the frontline in detecting AD (Costa et al., 2017; Debois et al., 2007; 2014).

Swainson et al. (2001) aimed to identify neuropsychological tests that help to determine the earliest sign of cognitive decline. They used a wide range of neuropsychological tests and showed that associative memory that was determined by PAL is the most effective measure to correctly differentiate AD patients from patients with questionable dementia, depression and healthy controls. In their longitudinal study they showed that PAL deteriorates earlier than non-associative memory, in addition it has high predictive value for progression towards AD. Moreover, they showed that PAL could predict further deterioration in people with MCI. In a similar longitudinal study, Fowler et al. (2002) confirmed that people with questionable dementia who showed impairment in PAL in 2-year period progressed to AD. Notably, performance on the other neuropsychological tests did not deteriorate over the courses of the 2-year follow-up. These were the first attempts to show associative deficits in people with early cognitive deterioration and sensitivity of the test to early AD. In the described studies they used PAL that is a computerised test whereby participants are requested to remember

both the presented pattern and their locations. Therefore, it was concluded that combining object and location was the process affected earlier in the course of cognitive impairment.

The modification of the object/location association and conformation of this associative decline in MCI came from a later study by Dudas et al. (2005). They compared the performance on face/location recognition (by the means of the Face Placing Test (FPT)) of people with AD, MCI and healthy older people. They demonstrated that patients in the predementia stage of AD have deficits in episodic cross-modal associative memory reflecting the poor encoding of new material.

Another popular version of associative memory task is the FCSRT whereby the association between item and context is assessed by the means of free recall and then with a cue. This modified procedure was shown to be sensitive to early preclinical cognitive impairments (Grober et al., 1988; Sarazin et al., 2010). Sarazin et al. (2010) followed their participants, considered at risk of developing dementia, for 3 years and the FCSRT was shown to be sensitive and specific for early AD.

There are ample studies on associative learning repeatedly finding that patients with AD present with deficits regardless of the nature of the stimuli: delayed recall objects-location (Brandt et al., 2005), features-objects (Hoefeijzers et al., 2017), colours-objects (Della Sala et al., 2000; Lloyd-Jones, 2005), faces-location (Dudas et al., 2005; van Geldorp et al., 2015), faces-names (Hodges & Greene, 1998), object parts (Tippett et al., 2003) or pairs of words (Gallo et al., 2004). Tests on associative memory can be very sensitive to the effect of cognitive decline; however, they failed one major requirement for AD cognitive markers (see Logie, Parra, & Della Sala, 2015; Killin, Abrahams, Parra, & Della Sala, 2017) – to be resistant to the effect of age. Indeed, associative memory that relies on object- context interaction is affected by age (Naveh-Benjamin, 2000).

Theory behind the associative memory tests

Naveh-Benjamin (2000) proposed the Age-Related Associative Memory Deficit Hypothesis (ADH) that suggests that memories encompassing complex events are more deteriorated in older adults than memories of single or unrelated events. The theory is based on the extensive literature that shows that long-term associative memory decline is the hallmark of cognitive ageing. In his experiments he tested younger and older adults on associations between words

and semantically unrelated non-words (Experiment 1), pair of words (Experiment 2) and words and contextual information (the font that the words were presented-Experiment 3) and in the Experiment 4 he tested associative memory under different paradigms: free recall, cued recall and recognition. These series of experiments showed that older adults' difficulties in remembering word-word or word-context associations are far greater than their memory difficulties for individual words.

This hypothesis supported an earlier neuropsychological model by Moscovitch (1992) that suggests that memory is underpinned by a network with several components. One component is the medial temporal/hippocampal that binds events together. This system is fairly automatic. The second system is the frontal lobes component that is the effortful system in charge of strategic information processing that helps encode the information. Neither of these systems work at their prime with advancing age: tests that need the hippocampus or the frontal lobes are affected by age.

The other type of the associative memory that is not affected by age is the so-called conjunctive binding (Moses & Ryan, 2006) and the main test used to assess this type of memory is the Temporary Memory Binding Task.

1.2 AD-Specific Markers: The Temporary Memory Binding Task (TMB)

Logie et al. (2015) emphasised that the ideal specific test for cognitive impairment due to AD should be specific only to the effect of the disease; should not be affected by healthy ageing, make a distinction between non-AD dementias and AD. As AD is a progressive disease that takes several years to develop from early symptoms to a full-blown disease the test also should be resistant to repeated testing in order to assess the change over time. In addition, it should be quick to administer, non-invasive, and sensitive to daily living impairment. The body of evidence suggest that the Temporary Memory Binding Task (TMB) satisfies all these criteria. A recent consensus paper recommends *temporary memory binding* - TMB (Costa et al, 2017) as the frontier test for AD diagnosis (see also Rentz et al., 2013).

An approach to find the earliest marker for incipient AD has come from evidence showing that patients with AD have problems dealing with multiple sources of information (e.g., Della Sala et al., 2010; Logie et al., 2004; MacPherson et al., 2012). TMB is a specific form of this

on-line cognitive processing, which defines the processes whereby different features are bound together on a temporary basis as an integrated object. In daily activities, TMB is essential to keep track of, for example, whether the white round pill or the yellow oval pill has just been taken. In laboratory tasks, individual features like colours and shapes are bound to form a coloured shape (Allen, Baddeley & Hitch, 2006; Logie, Brockmole & Vandenbroucke, 2009; Luck & Vogel, 1997; Treisman 2006). The task mostly employs the change detection paradigm whereby the participant should compare initial array of items (study display) and second array (test display) of items after a short retention interval (Wheeler & Treisman, 2002).

This particular TMB task relies on the within-dimension conjunctive binding (e.g., shape and colour) and as such it is different from the binding process discussed above subsuming the association between two different items (e.g., names and faces, names and places) which is known as between-dimension (relational) binding (Isella et al., 2015; Parra et al., 2015) or the binding between feature and location (Peterson et al., 2016; Peich et al., 2013; Liang et al., 2016).

Theories behind development of the TMB test

I will present here a condensed description of how binding is represented in visual working memory and why binding can be impaired in healthy cognitive ageing.

Theories of binding

Feature Integration Theory (FIT) (Treisman, 1996) posits that complex objects are processed in two stages. Initially, in the pre-attentive stage, the complex object is perceived not as a whole object, but as distinctive separate feature maps (i.e., colour, shape etc.). There is no coordination between these maps, and the features are not perceived as elements of objects and attention is needed to bind the different pieces of information. These feature maps are independent from the master map of locations to which feature maps are linked in the secondary stage. Here, features of the object are established through association between master and feature maps by the aid of attention.

The next question is how this complex object is maintained in memory? Does this complex object require more effort than a single feature object? The answer came from the study by Luck and Vogel (1997). In their paper they suggested that the maintenance of the single

feature is compatible to the maintenance of the combined features object. In this series of experiments they showed that the process of binding of features into the object happens automatically. They suggested that visual working memory (VWM) stores almost unlimited number of distinctive features that represent a complex object but limited in the number of objects presented (in their experiment after 4 separate features performance starts to drop) meaning there is no extra effort to maintain integrated features compared to single feature maintenance.

The work by Luck and Vogel was challenged by Wheeler and Triesman (2002). In their experiments they failed to replicate Luck and Vogel findings where different colours were coupled as a single object to increase VWM capacity. Wheeler and Triesman showed reduced performance when bicolored stimuli were presented compared to a single colour object. In the next series of experiments they investigated shape-location and shape colour binding. They showed that in the binding condition performance was worse compared to the single feature condition. They explained it by the existence of parallel stores where each feature has its own limited capacity cache. In addition, they reported that binding depends on the limited attentional recourses that is in line with the FIT theory that postulated that general attention is needed for maintenance of successful binding performance. However, there is another debate whether binding is an attention demanding process or not.

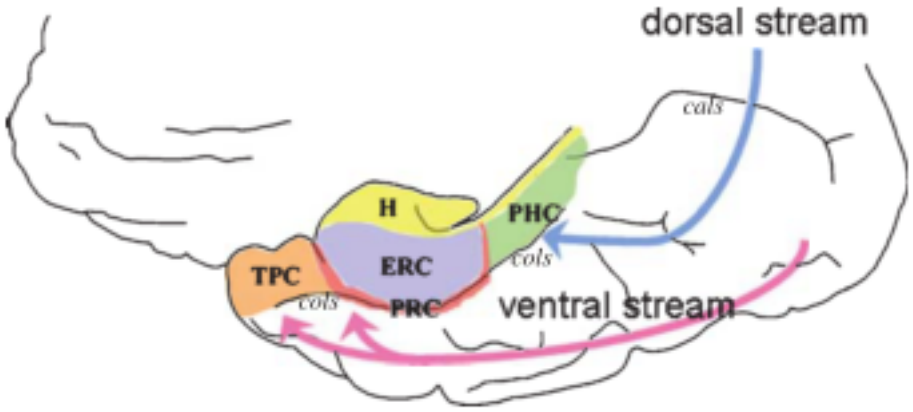
In the revised work on WM model proposed by Baddeley, Allen & Hitch (2011) he highlighted the role of the *episodic buffer* in the binding and this role is in the integration of information from different modality buffers (phonological loop and visuospatial sketchpad). In these series of experiments they found that initial encoding happens automatically and does not require any attentional resources, however the maintenance of the information in VWM requires attention (Allen, Baddeley, & Hitch, 2006). Contrary to Baddeley , Allen & Hitch (2011), Cowan et al. (2005; 2013) attributes attention a central role in the binding process. They concluded that attention is essential to encode several features as well as to encode binding. They proposed that WM can hold a limited number (“about 3”) of features; depending on the individual’s capacity (i.e the number of features one can hold in WM) the number of features that can be retained for each object may differ and therefore the person can partially encode only colour or shape, however still have both shape and colour representation.

Neuroanatomical distinction of relational and conjunctive associative memory

First decline before AD symptoms involve the perirhinal cortex (PRC) and the enthorhinal cortex (ERC) and then spread to the hippocampus (Braak and Braak, 1991) (Figure 1.1).

There is growing evidence that there is an anatomical distinction between conjunctive and relational associative memory. Didic et al (2011) in her hypothesis review proposed the two-stage model of cognitive deterioration in AD, whereby memory tasks that are sensitive to prodromal AD (i.e. before clinical observation) do not depend on contextual information ("context-free memory" for objects, facts and concepts), and are typically associated with pathological lesions in the anterior medial temporal lobe (MTL) network, including the PRC and the ERC. The hippocampus is affected at a later stage, and becomes involved in tasks that do require intact use of contextual ("context-rich memory" like spatial and episodic memory) information. Therefore, memory changes that occur prior in the hippocampus are more promising in detecting AD earlier (Dudas et al., 2005; Wolk et al., 2013; Das et al., 2015). Several lesion data showed that damage into hippocampus leads to impairment in relational memory at long (Moses & Ryan, 2006) and short delays (Olsen et al., 2012), however recognition memory (Holdstock et al., 2005) and conjunctive memory (Mayes et al., 2004) remain intact. Unfortunately, hippocampus lesion is not unique to cognitive impairment due to AD; healthy ageing also shows hippocampal pathology (Balota et al., 2000). Thus, hippocampal atrophy and hippocampal associated tests do not suit as a specific marker for AD.

Figure 1.1 Model of the medial temporal lobe structures.



Note: H: hippocampus; ERC: entorhinal cortex; PRC: perirhinal cortex; TPC: temporopolar cortex; PHC: parahippocampal cortex; cols: collateral sulcus; cals: calcarine sulcus (The picture is taken from Didic et al., 2011)

Conjunctive TMB is shown to engage regions of the ventral visual stream (Figure 1.1) (Mayes et al., 2007; Staresina and Davachi, 2010; Parra et al., 2014) and perirhinal cortex (Staresina & Davachi, 2010; Watson & Lee, 2013; Clarke & Tyler, 2014) known to remain preserved in healthy ageing (Insausti et al., 1998) but affected by AD even earlier than the hippocampus damage becomes overt (Didic et al., 2011; Juottonen et al., 1998). Bastin et al (2014) analysing brain metabolic activity with PET they directly compared both conjunctive and relational associative memory in mild-AD patients and healthy controls. They found hypometabolism in the left parahippocampal gyrus and right anterior extra-hippocampal regions of the MTL predicted patients' recall of colour encoded as part of an object (i.e. intrinsic). Whereas the deficit for recalling colour encoded as context was associated with anterior medial PFC and precuneus, commonly associated with episodic memory.

These important neurophysiological findings imply that TMB shows deterioration earlier on the course of the disease and therefore sensitive to early AD compare to relational associative memory.

Chapter I – Part II

Everyday functional abilities: Measures, Barriers and Suggestions for Improvements.

The process of cognitive decline dramatically impacts not only cognitive but also everyday functional activities. Cognitive abilities have a direct link to everyday functional activities, subtle cognitive deficit is already present years before diagnosis and linked to dependency on carrying out everyday activities (Cahn-Weiner et al., 2007; Frazer et al., 2012). The presence of functional impairment is a strong predictor of progression to dementia not only in individuals with MCI, but also in people performing normally on off-the-shelves neuropsychological tests (Tabert et al., 2002; Peres et al., 2006; Wadley et al., 2008; Okonkwo et al., 2006; Luck et al., 2011; Farias et al., 2013). On the other hand, the absence of functional impairment in people with MCI is suggestive of a lower risk of conversion to dementia, and of an increased chance of reverting to normal functioning (Peres et al., 2006; Luck et al., 2011). Longitudinal data shows that IADL decline in MCI patients is a better predictor of conversion to dementia than neurocognitive testing (Barberger-Gateau et al., 2000; Peres et al., 2006; Luck et al., 2011; Gold et al., 2012).

In this part I review the ADL scales and several important methodological issues that concern ADL scales and studies on functional abilities. Can we improve measurements of functional disability and how? I address cognitive underpinning of functional decline in the next chapter separately for MCI and AD patients as depending on the severity of cognitive impairments different cognitive construct influence everyday functioning.

1.3 Defining ADL scales.

The assessment of activities of daily living (ADL) was introduced by Katz (1963) and further developed by Lawton (1969) to define an individual's ability to complete essential tasks of everyday functioning. The initial proposal was to question whether the individual is independent in the Basic Activities of Daily Living (BADL). These were the fundamental everyday tasks such as dressing, bathing, toileting, grooming, eating, and ambulating. Lawton

proposed to add more complex skills that rely on the higher order cognitive skills: Instrumental Activities of Daily Living (IADL), they encompass tasks like managing bills, using the telephone, driving a car, taking medication, planning a meal, shopping, and working. The scale was also more complex as it provided multiple response options and therefore tease out the level of severity. Activities of daily living are essential in making a diagnosis of dementia; it measures the level of impact of cognitive impairments on everyday functioning, as the presence of functional impairment is a signal of progression to dementia.

Since the performance of IADL requires more cognitive resources, they are more vulnerable to the early effect of cognitive decline (Njegovan, 2001; Wicklund et al., 2007; Peres et al., 2008; Reppermund et al., 2011). Therefore, they have been proposed as aids to the early diagnosis of cognitive decline (Njegovan et al., 2001; Nygard, 2003; Sikkes et al., 2009; De Vriendt et al., 2013), thus in this introduction I will concentrate only on IADL tasks.

1.4 New formats of ADL scales

Traditional ADL-IADL scales are largely ineffective at detecting early stages of disability. The need was felt to develop more sensitive measures of IADL that would detect mild limitation in functioning. To this end, the Complex ADL scale (CADL) was developed by Tabert et al (2002) which addresses issues like the ability to maintain a job, planning a travel, participate in community groups, and play games. With a similar scope, the Advanced ADL (a-ADL) was proposed by De Vriendt (2012). This scale covers activities that are volitional, influenced by cultural and motivational factors, expressing a personal engagement in satisfying activities which are beyond what is needed to be independent (e.g. engagement in organised social life, semi-professional work, self development/self realisation/self educational activities, communication via devices and techniques, etc.).

In order to enhance the diagnostic validity of ADL scales, researchers either upgraded existing scales by including more complex activities (ADCS/MCI/ADL by Pedrosa et al., 2010) or focus on only one ADL in particular (finances by Marson et al., 2000; driving by Wadley et al., 2009; everyday technology by Rosenberg et al., 2009, Malinowsky et al., 2010 and Munoz-Niera et al., 2012; social activities by James et al., 2011; cognitive activities by Geda et al., 2010). Jefferson and colleagues (2008) developed a scale that concentrated not on

everyday activity performance of the individuals, but on errors that they commit when carrying out such activities.

1.5 Self-reported vs. informant reports vs. performance measures

The various scales available differ also in terms of the methods they used: self-reported questionnaires, performance-based assessment (observation or direct assessment) and informant-based questionnaires. Each of these methods of measuring functional abilities has inherent limitations. Self- and informant reports are the most commonly used format; it allows clinicians and researchers to obtain information about the current functional status of the testee relatively fast. Typically, the individuals are given several Likert-type categories to ascertain the level of functional ability. The main criticism of self-reports relates to the fact that the answers tend to be influenced by mood, misjudgement of one own abilities, and misinterpretation of the questions by the responders (Louie & Ward, 2010).

As cognitive impairment impacts patients' insight on their functional ability it hinders the accuracy of their reports, where they mostly overestimate their abilities (Weinberger et al., 1992; Loewenstein et al., 2001; Wadley et al., 2003), researchers and clinicians usually rely on family and carers' information as being more objective measures of patients' performance. However, more and more research indicates that caregivers often underestimate functional abilities of patients (Zanetti et al., 1999; Loewenstein et al., 2001).

Some authors maintain that performance-based scales are a better proxy of the real functional status than questionnaire-based enquiries as they offer a more direct window on the participants ability to enact ADLs and therefore are more objectively valid compared to self- and informant reports (Moore et al., 2007; Tam et al., 2008; Wadley et al., 2008; de Rotrou et al., 2012; Schmitter-Edgecombe et al, 2012). At the same time performance in artificial conditions may not be an accurate reflexion of the true performance in daily life. Performance-based measures do not reflect adaptations made by the person in everyday living situations like avoiding going out if the weather is bad, using reminders, using the same route to go shopping and keeping a standard shopping list, etc.

1.6 Methodological issues

There are a few methodological issues with ADL scales that hamper the adequate measurement of everyday functional activities. First of all, since the introduction of the first ADL scales by Katz and Lawton more and more instruments have been developing every year to measure functional status. These measures differ in a number of items, type of rating scale and difficulties of the items. Some enquires about whether one can or cannot perform a task, other have a different points grade (from 2 (Blessed et al., 1968; Lawton & Browdy, 1969) to 4-points grade (Farias et al., 2008). The other issue is that there is a variety of reference points in time as some of the measures enquire about their activities in the last month (Fieo et al, 2013) others about current performance on the task compared to 10 years ago (Farias et. al., 2008; Fieo et. al., 2013). Most of the scales enquire in general: whether there are any changes or difficulties in daily tasks performance, this hampers the understanding whether there is a decline in performance, or the person always performed poorly or has never done the task. In addition, Sikkes and colleagues (2009) in their systematic review of 12 IADL questionnaires revealed the lack of content validity, internal consistency, and reproducibility of ADL measures. A practical problem in the current use of the available scales, is that most of them were devised decades ago and do not reflect the everyday life challenges that people face nowadays. This applies particularly to technology and financial use (Munoz-Neira et. al., 2012; Marson et. al., 2009). Everyday technologies such as home appliances (microwaves, digital ovens, and coffee machines) or Internet and smart phones services, numerical codes and credit cards become increasingly demanding for older adults and for patients with neurodegenerative disorders (Hedman et. al., 2013), minimising their independence. Saying that, difficulties in performing IADL can not always be considered as a cognitive impairment and succession on the daily task can be a reflexion of a personal preference or previous experience or expertise, as well as age (younger vs older participants vs old-old participant) or gender (some scales are gender sensitive) or cultural effect (urban population vs rural).

After refining MCI criteria (Petersen et al., 2004; Winblad et al., 2004), the major criticism of the new standards was about “minimal impairment IADL scales” (for reviews see Nygard, 2003; Sikkes et. al., 2009; Gold, 2012). The difficulties with the latter are caused by the release of the new classification system that categorises MCI as having two or more cognitive domains impaired and day-to-day functioning with assistance. This allows degrading patients who had very mild and mild forms of AD as having MCI. In the research by Morris (2012) in

a very large cohort of more than 17000 patients he also postulated that the distinction between MCI and AD would be based on the individual judgement of clinicians and therefore nonstandard approaches and moves focus from the earliest stages of cognitive decline. The problems with differentiating between normal aging and MCI is dictated by the notion that present level of functional and cognitive performance should be compared with the previous abilities either by a history of change or by serial cognitive tests, that cannot capture the silent cognitive feature of AD.

1.7 How to overcome ADL challenges

Psychologists have only just began do develop sensitive enough functional instruments to detect early declines and change over time in people who are thought to develop cognitive impairment. Improvement in understanding the progression of the disease and severity of the process may be enhanced by establishing item hierarchy using advanced statistical techniques (e.g. Item Response theory (IRT)). Investigating the hierarchy of disability in ADL and establishing cut-offs for healthy older people, MCI and dementia stages would be useful to determine the level of the disabling process.

The new approach will be to show which changes in day-to-day functioning are present in the current status and to what extent, and include them in the assessment rather than exclude them. There are more and more scales being developed to assess early cognitive impairment. There should be more studies on the specificity of certain tasks to identify early signs of everyday ability impairment. It has been suggested that breaking down components of IADL into subcomponents at every step of an activity rather than evaluating the global task performance allows for more robust assessment of functional ability in dementia (Beck and Frank, 1997).

The new approach is developing scales or tasks with the best sensitivity to the early cognitive decline. These tools ideally should be non-sensitive to gender, age, and being able to be easily adjusted to education level. According to the literature described above, the new instrument should include items from the complex IADL tasks like taking medication, use of new technologies, or financial abilities. These three everyday tasks do not rely on the mobility level or physical fitness, like most others IADL tasks (transportation tasks, climbing stairs, bathe, dress, etc.) (Wilms et.al., 2007).

Ideally the new tool should accommodate all three methods of assessment, as it would allow us to know the level of real performance and awareness of their own performance.

Understanding the level of awareness of one's own performance would add an additional marker of progression towards dementia (Okonkowo et. al., 2009; Amanzio et.al., 2013).

Chapter I – Part III

1.8 Healthy ageing

In this part, I will review the progression of cognitive and functional deterioration from cognitively healthy ageing through MCI to AD. I think it is important to understand that even though we call it "healthy ageing", there are unfortunately cognitive and functional issues that can be already detected. In order not to over-diagnose we need to understand where is this threshold that transfers healthy to pathological ageing.

1.8.1 Cognitive abilities in healthy ageing

Some memory failure is already present in normal ageing that poses a common problem for clinicians, as it can also be a symptom of age-related diseases. In one commonly cited longitudinal study, Wilson et al. (2002) studied 694 healthy adult males and assessed changes in cognitive ability over the course of 6 years. There was a general decline across all tasks including story retention, word retention, digit span, perceptual speed, visuospatial ability, and word knowledge. Studies of cognitive ageing commonly find declines in overall cognitive performance across the lifespan (Deary et. al., 2007; 2009; Lindenberger, Mayr & Kliegl, 1993; Salthouse, 2010a, 2010b). Others argued that there is a complex pattern of decline in healthy ageing. Like that Park et al (2002) demonstrated a decline in tasks related to speed of processing and working memory that began in participants' 20s. This was compensated by an increase in verbal knowledge across the lifespan. Johnson, Logie, & Brockmole (2010) in a large-scale study of 95,000 individuals who had undertaken memory studies identified changes in the level of decline of 5 short-term and working memory tasks across the lifespan in adults aged 18-90. In their study visual short-term memory ability declined at a far greater rate than verbal short-term memory ability. It was also found that older adults relied on more general abilities to complete visual tasks, whilst continuing to demonstrate specific abilities in verbal tasks. Different patterns of decline are also described in studies on associative memory that are presented with conjunctive and relative binding.

1.8.2 Associative memory in healthy ageing

As I mentioned in the Part I, there are two different directions into investigation of the

binding in healthy ageing. One is *item-context* (and its analogous - inter -item or conjunctive) binding that refers to the binding of the object to context (e.g. location) and another is *intra-item binding* (or relational) that implies between surface features from different dimensions (i.e. shape and colour). These different types of memory binding processes seem to be differently affected by age. There is a line of evidence to believe that the binding between objects and location in healthy ageing is more fragile than between surface features binding. Mitchel et al. (2000) were the first to assess the age effect on binding the object to location in WM. In two experiments they showed that compared to a single feature (location alone and object alone), older adults are impaired in performance when the task requires recognising object-location association. They suggested that this impairment is in part due to the encoding problem and also to the "access and evaluation at test" of combined information. This first study was extensively criticised by more recent studies because of its methodological flaws. The experiments used 8.5 sec interval that could have increased the forgetting in older adults. They did not use an articulatory suppression in the task that might have elicited verbal rehearsal that is more prominent in younger adults (Bunce & Macready, 2005). In addition, their age by condition interaction did not reach the significant effect ($p=0.06$) meaning that there was no clear age effect in the object-location binding condition. Aiming to address these methodological errors, Cowan et al. (2006), Peich, Husain, & Bays (2013) and then Read, Rogers, & Wilson (2016) found that the effect of age was clearly larger for relational binding relative to a single feature condition. In more recent experiments Read, Rogers, & Wilson (2016) and Peterson & Naveh-Benjamin (2016) on discriminating objects (shape and color) (Kessels, Hobbel, & Postma, 2007) to location showed that older adults compare to younger adults have clearly committed "mis-binding errors" where they wrongly associated location to a different object. Grober et al. (2008), Frason et. al. (2011) and Killin et. al. (2018) in their studies demonstrated that older adults compare to younger adults performed significantly poorer on free recall of FCSRT, in addition the age effect is also confounded with the level of education and the individual's gender.

On the contrary, research on conjunctive binding using the TMB task specifically has more clearly suggested that it is not affected by healthy ageing (Brockmole et al., 2008; Isella et al., 2015; Parra et al., 2009b; Read, Rogers, & Wilson, 2016; Rhodes, Parra & Logie, 2015; Bastin, 2017; Hoefeijzers, Gonzalez, Magnolia, & Parra, 2017; Rhodes, Parra, Cowan, & Logie, 2017; van Geldorp, Parra, & Kessels, 2014). In healthy ageing conjunctive within-

dimension binding does not seem to be affected even under increased attentional load (Brown & Brockmole, 2010), extended encoding duration (Rhodes et al., 2016) or with interfering information load in the retention interval (Brown et. al., 2017).

The distinction between two types of binding was assessed by several recent studies that directly compared performance on conjunctive and relational binding by younger and older adults. Peterson & Naveh-Benjamin (2016) discovered that intra-item conjunction was impaired in healthy older adults compared to younger adults only when participants performed the task without articulatory suppression, but there was no age effect when young and older adults did the task under articulatory load (i.e repeating one syllable word). They noted that younger adults might have verbalised the relevant features and, in this way, had an advantage over older adults. This advantage disappeared when verbalisation was suppressed by the concurrent task. In the experiments with the item-location binding task they discovered a general impairment on the binding task by older adults regardless whether participants had a concurrent task or not (i.e. counting backwards in the Experiment 2 and repeating one syllable word in the Experiment 3). The other study that directly compared the performance on relational and conjunctive binding (van Geldorp et. al., 2015) did not find a specific decline in relational binding over conjunctive binding, however it showed that articulatory suppression disrupted the former in greater extent than the later, which suggests that more attention is required to the relational binding. These experiments confirm distinction between two types of binding and offer some explanations of this distinction. In accordance to FIT (Triesman, 1996) a feature of the stimuli can be perceived as one object and processed automatically (Luck & Vogel, 1997), however object-location binding is a more resource-demanding task. Conjunctive binding for older adults does not require more attentional resources and the effect of distracting task affects young and older participants' memory comparably confirming once again that that this type of memory is spared in ageing. These evidences make TMB a robust measure for early AD prediction.

1.8.3 IADL in healthy ageing

Rapid changes in the modern world in almost all spheres of our lives impose a great challenge to older people who cannot cope with the pace of the new developments. New technologies, communication, economic and financial systems are shown to be the problem even for healthy older people. The main challenge when assessing ADL performance in

healthy older people is to understand whether the participants cannot perform a certain activity due to cognitive problems or any other factors. Kelly-Hayes (1992) clearly differentiated between functional impairments that make the activity impossible to perform and the actual competence with the activity. The main problems in everyday function for healthy older people are those activities that rely on physical component. That said, there are studies that find a large confounding effect between ADL impairment and mobility level (Wilms et al., 2000; 2007).

It is important to note that Kovar and Lawton (1994) indicated that ADLs were initially formulated to assess the functional status of chronically ill or institutionalised older people. Thus, they may be ineffective when evaluating community dwelling populations in which researchers have to identify very low levels of disability. Currently, traditional ADL-IADL scales are largely ineffective at detecting early stages of disability when applied to community-dwelling persons. This will result in large ceiling effects, with a large proportion of subjects being 'unmeasured'. On the other side, the traditional measures would capture more mobility-related limitations (shopping, transportation, regular outings, etc). Here it may be useful to note that Ng, Niti, Chiam, & Kua (2006) found that some commonly used IADL items (based on exploratory factor analysis) can be differentiated into physical IADLs and cognitive IADLs. Physical are those including housework, laundry and doing grocery shopping. Cognitive ADL included items like finances, managing medication and using telephone. Most physical IADLs items decline prior to cognitive IADLs that support the view that dementia and age related cognitive change result from separate aetiologies. According to Meguro et al. (p. 565, 2001), "dementia is better conceptualised as age-related (occurring within a specific age range) rather than as an aging-related disorder (caused by the aging process itself)".

In Chapter six I investigate what everyday function items healthy older participants fail to perform well and what are the causes of the problems. I also investigate the relationship between cognition and ADLs.

1.9 Mild Cognitive Impairment

1.9.1 Diagnostic Criteria

Mild Cognitive Impairment (MCI) or Mild Cognitive Disorder (MCD) – according to the newly developed DSM-5 – is a transitional stage between normal function and dementia and therefore represents the earliest stage of cognitive decline. A review of the literature suggests that much controversy surrounding the term MCI comes from the fact that diagnostic criteria have been implemented in a variety of ways in research and clinical settings. In addition, most of the research takes MCI as a whole group, however the disorder is more heterogeneous than was originally suggested (Petersen et al., 1995) with different outcomes that depend on the form of MCI. There is a growing amount of studies that support the argument that MCI is a stage between normal aging and Alzheimer's disease, however recently the term MCI started to apply to describe a transition between normal aging and dementia due to Lewy Body and Parkinson's disease (Caviness et al., 2007; Boeve, 2009 (pg.197-212); Goldman & Litvan, 2011). The key challenge is to determine what form of MCI signals to what type of dementia.

The original diagnosis of MCI linked to AD dementia suggested that patients would present with impairment in memory or other cognitive domains and with Activities of Daily Living preserved (Petersen et al., 1995; 1999). From the first published criteria in 1999 by Petersen R.C. the past decades have witnessed a tremendous progress in the characterisation of the early cognitive symptoms of dementia. Diagnostic criteria for Mild Cognitive disorder (or Mild Neurocognitive Impairment in the DSM-4) from DSM-5 are as follows: *evidence of modest cognitive decline (*more specifically in Petersen et al., 2004: 1.5 SD below the mean of the age norm*) from a previous level of performance in one or more cognitive domains* (complex attention, executive function (EF), learning and memory, language, perceptual motor, or social cognition) based on self- or informant report that there has been a mild decline in cognitive function; *and a modest impairment in cognitive performance*, preferably documented by standardised neuropsychological testing or, in its absence, another quantified clinical assessment. Those first Petersen criteria (1999) that specified that for a person to be diagnosed with MCI he/she should demonstrate normal daily functioning, has been reassessed in the later criteria to "minimal impairment" in daily functioning (Petersen, 2004; Winblad et al., 2004; Albert et al., 2011). In DSM-5 it is more specific: *The cognitive deficits do not interfere daily functioning and live independently* (i.e., complex instrumental activities of

daily living such as paying bills or managing medications are preserved, but it is noted that greater effort, compensatory strategies, or accommodation (i.e. adjusting goals and criteria) may be required) (American Psychiatric Association , 2013).

Heterogeneity of the disorder

From a diagnostic perspective, the concept of MCI has been recognised as being heterogeneous (Petersen, 2004). *Amnestic form of MCI (aMCI),* which, as its name implies, represents a primary memory disorder with isolated progressive or static memory deficits (delayed-recall verbal memory, nonverbal memory, or both) and relative preservation of other cognitive domains. aMCI can be subdivided into a *single domain (aMCIsd)* subtype with a pronounced memory deficit or a *multiple domain (aMCImd)* subtype that includes memory impairment along with a progressive or static deterioration in at least 1 cognitive domain (not including memory) such as language, EF, and visuospatial skills, or 1 abnormal test in at least 2 other domains, but who had not crossed the threshold for dementia. The other major subtype of MCI is *non-amnestic (non-aMCI),* which similarly can be subdivided into single and multiple domain subtypes (Petersen, 2006). A purely amnestic syndrome, however, may be relatively uncommon in individuals with MCI within the community (Jagust et al., 2002), and declines in other cognitive functions including naming, orientation, verbal fluency, mental control, EF, visuospatial ability, and general cognition often occur in conjunction and may be important predictors of subsequent dementia (Flicker et al., 1991; Albert et al., 2001).

Despite increased risk of progressing to dementia, a substantial proportion also remained stable or reverted to normal during follow-up (Petersen et al., 1995; Albert et al., 2001; Winblad et al., 2004; Ganguli, 2004). Although patients with MCI may remain non-demented or revert to a cognitively normal state, longitudinal studies of patients with MCI show conversion rates to dementia ranging from 6% to 44% annually (Petersen et al., 1999, 2004), 20% to 66% over 3 to 4 years (Flicker et al., 1991; Kluger et al., 1999), and 60.5% to 100% in 5 to 10 years (Morris et al., 2001). If MCI subtypes were investigated separately, amnestic MCI types had higher conversion rates to dementia than the non-aMCI types (Ganduli et al., 2011; Marcos et al., 2016). It has been proposed that each of the MCI subtypes is associated with an increased risk of developing a particular type of dementia such as AD or PD (Petersen, 2004; 2011). However, research indicates that single-domain aMCI is a rare and unstable condition and can remains either stable or revert to a normal cognitive function (Ganduli et al.,

2011; Mitchell et al., 2009; Saxton et al., 2009). AD was the most common dementia type at follow-up in MCI subtypes. Having aMCImd is the strongest predictor to progression to AD (Forlenza et al., 2009) as they are in the more advanced stages of the cognitive deterioration (Burton et al., 2009). People with non-aMCI–multiple domains were more likely to progress to a non-AD dementia (Busse et al, 2006).

1.9.2 TMB in MCI

To my knowledge, there was only one study that assessed purely behaviourally conjunctive memory binding in MCI. In the recent study by Koppara et al. (2015) people with subjective cognitive decline (SCD) and MCI patients show TMB deficits similar to those observed in asymptomatic presenilin-1 mutation carriers (Parra et al., 2010). In their study SCD did not show any signs of decline on the standard neuropsychological tests, but show decline in TMB. Compared to controls, patients with MCI exhibit worse performance in a single feature condition that imply that MCI patients have STM memory impairment which probably meant that their MCI patients are closer to AD development or converters to AD [see Parra et al., 2016] . This aligns with evidences from hippocampal literature (Moses & Ryan, 2006), it suggests that the hippocampus stores association of the features and features themselves, meaning that in their experiment the hippocampus is already showing signs of decreased activation.

The other recent study examines the electrophysiological attributes of TMB in MCI patients. This study gives an answer to the question about what neural network is affected in early AD and how it disrupts the processing of the complex stimuli. Pietto et al. (2016) in his study he recruited patients with sporadic and familiar MCI (single and multi-domain amnestic and non-amnestic multi-domain MCI and MCI patients with the mutation E280A of the presenilin-1 gene). Behavioural findings of this study are consistent with the results of the Koppara's study. Both MCI patient groups performed significantly worse than controls on the TMB task. Electrophysiologically, MCI patients showed reduced brain activity whilst performing the task in all brain regions, with the most decreased activation over the fronto-central and parieto-occipital in all ERP components.

In the study, N1 and P2 were diminished over the parieto-occipital region and the fronto-central regions respectively that reflects impairments in processing and detection of relevant

stimuli features. Reduction of the Late Post-stimulus Positive component (LPP) over the parieto-occipital region and the fronto-central regions during the retrieval phase suggested uncertainty if the was a change between the study and the test arrays. The overall findings suggest that patients in the early stages of the disease are impaired in early processing stimulus features and detection of the relevant features. Then, during the test stage, patients have difficulties in evaluation and monitoring processes that leads to increase uncertainty if there was a feature change in the Shape-Colour Binding condition and to errors in performing the task. These findings once again support the Feature Integration Theory (Treisman et al., 1996) and ideas of Cowan et al. (2008; 2013) that in order to integrate separate features into a complex object it requires attention. Therefore, a specific attentional mechanism disruption in the parieto-occipital region and the fronto-central regions that require encoding features integration is the early sign of cognitive impairment.

1.9.3 IADL in MCI.

MCI diagnosis was initially formulated as a transitional state between normal cognition and probable dementia and it was characterised by memory impairment and *absence of functional decline* (Petersen et al., 1999). However, the latter criterion has been subsequently criticised. Several studies showed that people at risk of dementia present with impairments that are detectable through the execution of everyday activities even before the formal clinical diagnosis is made (Barberger-Gateau et al., 1999a; Artero et al., 2001; Tabert et al., 2002; Nygard, 2003; Farias et al., 2013). The original definition of MCI (Petersen et al., 1999) was therefore refined by the Working Group on MCI which proposed to include "minimal impairment in more complex ADL" in the diagnostic criteria for MCI (Petersen et al., 2004; Winbland et al., 2004). This modification has been subsequently supported by a considerable number of replications showing that mild impairments in daily functioning are present in people with MCI (Njegovan et.al., 2001; Tuokko, Morris, & Ebert, 2005: Farias et al., 2006; Peres et al., 2006; Perneczky et al., 2006; Giovannetti et al., 2008; Aretouli et al., 2009; Pedrosa et al., 2010; Albert et.al., 2011; Yeh et al., 2011; De Vriendt et al, 2012; Gold et al., 2012). According to Hesseberg and colleagues (2013) only 34% of people diagnosed with MCI reported independent functioning in IADL scales.

A number of studies demonstrate that severity of functional decline aids to track progression from MCI to AD therefore predicts which MCI patients are in more advanced stages and who

will progress to dementia. This way, it was shown that multiple-domain MCI (mdMCI) has greater IADL impairment than single domain MCI (Kim et al., 2009, Pereira et al., 2010, Yeh et al., 2011; de Rotrou et al., 2012). Similarly, amnestic MCI (aMCI) present with more deficits in IADL than non-amnestic MCI (non-aMCI) (Bangen et al., 2010; Tang et al., 2010; Luck et al., 2011).

In my review I focused on performance on IADL by MCI and AD patients as BADL represents a basic set of needs essential for independent living and deteriorates at the advanced stages of dementia. In this part of the introduction I review the current views on IADL performance by MCI. Is it possible to determine which ADL domains are the most complex and therefore show the first signs of deterioration? To what extend this function should be impaired in order to comply with the definition "minimal impairment"?

What are complex ADL?

Complex everyday activities are those that require more neuropsychological capacities and therefore more prone to early impairment triggered by cognitive decline (Njegovan et al., 2001; Peres et al., 2006; Perneczky et al., 2006). However, establishing a unique and the most complex ADL task that in principle will be the most sensitive to the early cognitive deterioration prove to be quite challenging. Just to give an idea on discrepancies between studies, this is what review of the literature on IADL suggests as a complex: some authors have reported that a grocery-shopping task is more demanding and therefore sensitive to cognitive deterioration (Wadley et al., 2008). Others pointed to, that keeping appointments, remembering current events, using the telephone, and finding belongings are the most complex ones (Aretuoli and Brandt, 2010). Managing medication, shopping, planning and cooking meals, but not telephone use and housekeeping was found to be impaired earlier in MCI patients compared to healthy older by Hesseberg and colleagues (2013). According to Reppermund et al. (2011) finding directions and doing two things simultaneously are the tasks with the higher cognitive demands. Barberger-Gateau and colleagues (1999) and then later confirmed by Kim et al. (2009) maintained that the best four IADL tasks predicting dementia conversion were instead, telephone use, medication management, mode of transportation and managing money.

Nevertheless, a common trend can be found: quite a few authors have argued that financial management is a particular complex cognitive task apt to differentiating healthy older people from people with MCI (Fitzgerald et al., 1993; Griffith et al., 2002; Artero et al., 2006; Mariani et al., 2008; Okonkowo et al, 2008; Kim et al., 2009; Pedrosa et al., 2010; Pereira et al., 2010; Luck et al., 2012; Arrighi et al., 2013). The numerous studies on financial abilities show that MCI patients compared to their healthy older counterparts show decrement in financial conceptual knowledge, bank statements, and paying bills (Marson et al., 2001; Griffith et al., 2003; Ozioma et al, 2006). Changes in modern financial systems impose the struggle for healthy older adults and people with cognitive impairment (Marson et al., 1999; Griffith et al., 2003; Van Wiellingen et al., 2004; Kershaw and Webber, 2008; Marson et al., 2014). Rosenberg and colleagues (2009) and Munoz-Neira et al. (2009) found that people with MCI differed from healthy older people in the perceived difficulties in using modern technologies and proposed that the faulty use of modern technologies could be a sensitive indicator of the first signs of MCI. This can be applied to financial systems: mobile banks, self-deposit machines in banks, etc, etc.

"Minimal impairment"

There is a trend that can be drawn from the literature that compare to healthy controls, people with MCI are slower, however do not commit more errors in IADL (Okonkowo et al., 2006; Tam et al., 2008; Wadley et al, 2008; Kim et al., 2009). Tam et al. (2008) referred to subtle changes in MCI and characterised them as having lack of initiation in performing daily activities (without referring to any particular tasks) and need prompts and reminders to carry out these activities. A more comprehensive view on subtle functional problems of people with MCI came later from the explorative study by De Vriendt et al. (2012). Using an "open-minded approach" they asked their participants to describe their typical day and then clustered all activities and problems associated with them according to the International Classification of Functioning, Disability and Health (ICF) (WHO, 2001). All participants reported that they reduced the number of activities due to lack of energy or because of the problems they experienced to perform daily tasks. Participants complained on lack of initiative and perseverance, difficulties in staying focused or going back to the task after being interrupted. They also noted that participants had difficulties adapting to new circumstances and situations and their diminished flexibility to react to unexpected events. They needed external aids,

reminders, or notes in order to successfully perform even some familiar activities (e.g. cooking a complex meal or using a coffee machine).

Cognitive underpinning of functional abilities in MCI

Functional abilities are reported to correlate with cognitive performance in MCI people (Njegovan et al., 2001; Tuokko et al., 2005; Perneczky et al., 2006; Tam et al., 2009; Tan et al., 2009; Farias et al., 2013). There have been numerous attempts to investigate whether a unique cognitive process is associated with functional impairment in people with MCI (see Table 1).

Some researchers argue that measures of global cognitive functioning strongly correlate with functional abilities and explain significantly more variance than tests on executive function, attention, memory, verbal, or visuospatial function (Royall et al., 2007). On the contrary, others posited that functional skills are loaded on a particular cognitive domain. Like that, it has been proposed that memory component and mostly episodic memory supports successful daily activities (Farias et al., 2009). The completion of everyday tasks may, in addition, rely on high-level executive function, in particular, planning and organisation domains (Farias et al., 2009) and inhibition of prepotent responses (Jefferson et al., 2006).

There have been several attempts to link specific cognitive constructs to particular functional subscales. Shmitter-Edgecombe et al. (2009) reported that temporal order memory (i.e., remembering when an event occurred) was a significant and unique predictor of items inquiring about food preparation, while source memory (i.e., remembering how this event happened) was needed for social functioning (keeping track of who said what). They also found that temporal order memory and prospective memory (i.e., remembering to carry out a future action) are needed for successful medication use and household activities. Driving and modes of transportation were associated with both a cognitive component, including planning and inhibition, and a physical component (Peres et al, 2006). However, others showed that it was memory, processing speed, visuo-spatial perception and attention (Barberger-Gateau et al, 1999). In sum, the findings are inconsistent and, consequently, there is no consensus on whether or not a single test or a combination of tests are associated with functional abilities in people with MCI. A few studies explored deficits in financial management in aMCI in more details and showed that the functional impairments were not due to memory deficits, but

rather due to decline in attention, self-monitoring, and integration of information (Okonkowo et al., 2006).

Challenges

Challenges to find a mainstream in IADL impairment due to MCI are manifold. First of all, it is very rare that different studies are using the same IADL, making comparisons across studies challenging. In addition, most of the studies reported performance on the whole scale rather than on itemised tasks making it difficult to detect the relative weight of individual items (see Table 1). More and more research has attempted to design the most sensitive scale for "minimal IADL impairment". Every paper to date that investigates IADL performance on MCI patients emphasises that it is still yet unclear the degree of associated daily function in MCI. There is no consistency on what is considered a complex task. As there is no one "gold standard" IADL, it is very difficult to establish the cut-off scores, where we can say that this function is impaired. The major gap in the characterisation of functional abilities among individuals with MCI is the lack of a definition of what constitutes minimal/moderate/major functional decline and what cognitive attributes accompany these deficits.

There is a large discrepancy in the means of assessment of IADL: informant-based, self-rated, or performance-based measures (Table 1). Some of the studies demonstrated impaired IADL on the performance-based measures when informant-based questionnaires suggested a normal functioning (Goldberg et al., 2010). However, most of the research relies on collateral sources of information, such as a spouse or other relative, and self-rated measures as they are easy to use and do not require special training to obtain the information and there is no consensus regarding which method is the most optimal to approximate real world behaviour. Most of the paper-and-pencil ADL questionnaires that have been devised do not reflect the complexity of real-world challenges. There is evidence that proxies are not always a reliable source of information, as they have a tendency to over- or underestimate IADL deficits (Farias et al., 2005: Okonkwo et al., 2009). In some cases, a proxy is not available or has massive knowledge gaps. Controversy exists about the ability of patients with MCI to adequately rate themselves, as they lack awareness of IADL deficits and overestimate their functional capacity (Tabert et al., 2002; Cramer et al., 2004; Farias et al., 2005; Okonkwo et al., 2009; Suchy et al., 2011). Performance-based assessments despite being more reliable measures,

have better validity and do not have reporter bias, however, it is criticised for allowing observation of only a small excerpt of real-world performance and are quite time-consuming.

Another challenge of the existing literature is in a massive difference in MCI diagnostic criteria (Table 1). In addition, some of the studies recruit MCI patients without differentiating them into the subgroups, other divide them into two or four subgroups. Most of the studies used Petersen criteria, however cut-off scores varied between 1SD and 1.5 SD below age and education norms. Other studies rely only on clinical criteria. MMSE scores range from 22 to 24 which is problematic as it might include undiagnosed dementia, and IADL impairments might be more severe.

There is also a difference in the source of the recruitment. Some studies recruited their patients from the community, others from hospitals. Farias et al., 2009 showed that there is a different conversion rate depending of whether MCI patients were recruited from the clinic or community cohorts. Their clinical sample showed more functional problems than the community one. In addition, at the baseline cognitive and functional measures in these two groups differ significantly.

1.10 Alzheimer's Disease

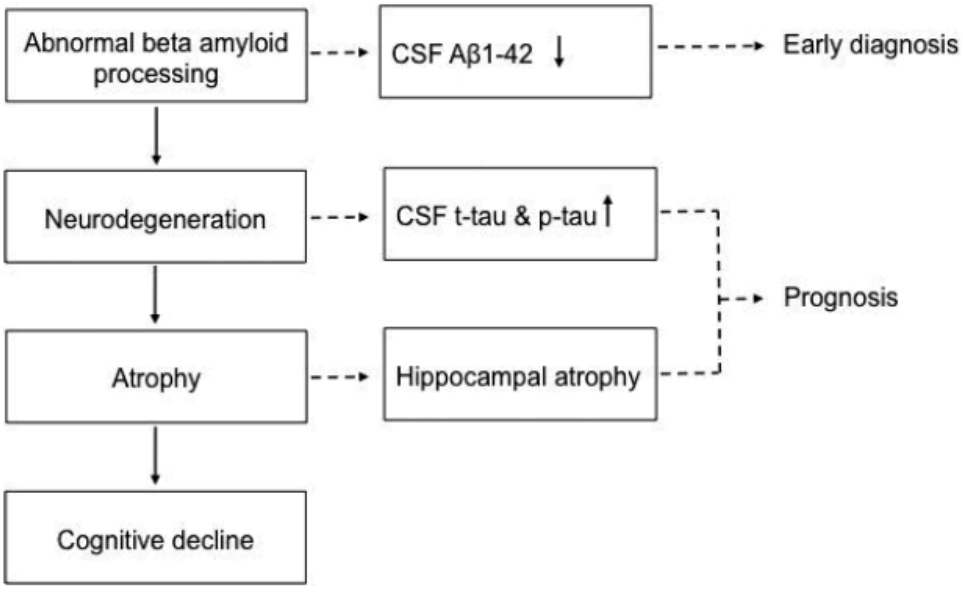
1.10.1 Diagnostic criteria

The diagnostic criteria for AD according to the new classification system (DSM-5) include the family history of AD and genetic testing. Patients with this neurodegenerative brain disorder should display evidences of memory decline and impairment in learning abilities or any other cognitive domains that can be obtain by the detailed history and neurocognitive testing. The primary disorder characteristic is a steadily, progressive and inexorable decline in cognition, without extended plateaus (American Psychiatric Association , 2013). However, definite diagnose is based on the presence of pathological hallmarks of AD such as amyloid plaques and neurofibrillary tangles which appear initially in the mesial temporal lobes and can be detected by the modern neurovisualisation.

Are biomarkers useful for early diagnosis of AD-type dementia?

Neuropathologically, AD is characterised by extracellular deposits of amyloid ("senile plaques") and intracellular accumulation of tau ("neurofibrillary tangles") in the brain. Even though much research has been done since the first discovery of the disease, neuro-patho-physiological mechanisms of AD still remain to be unravelled. Figure 1.2 depicts the widely accepted amyloid cascade hypothesis of AD. According to that, amyloid plaques occur first, followed by neurofibrillary tangles and eventually leading to neuronal loss, specifically of the hippocampus, a brain structure essential for memory performance (Hardy & Higgins, 1992; Jack et al., 2010). In most cases the cause of AD pathology is unclear. Three genes that affect amyloid metabolism are preseniline 1, preseniline 2, and amyloid precursor protein, however they are responsible for only a small percentage of AD cases (Harvey et al., 2003; Goate et al., 1991; Levy-Lahad et al., 1995; Sherrington et al., 1995). Most patients have a sporadic form of the disease, as it was shown in the study by Gatz et al. (2006), who found 80% heritability from AD in twins. The most studied genetic risk factor for AD is the APOE-e4 genotype.

Figure 1.2 The amyloid cascade associated with AD pathology and biomarkers.



Note: The presence of amyloid plaque in the brain is correlated with the reduced level of amyloid beta 1-42 (Aß1-42) in the CSF, and the presence if neurofibrillary tangles in the brain is reflected by increased levels of CSF total tau (t-tau) and tau phosphorylated at threonine 181 (p-tau) (Tapiola et al., 2009).

For decades the diagnosis of probable AD has been based purely on clinical symptoms (McKhann et al., 1984). However, in 2011, the National Institute on Aging and Alzheimer's Association (NIA-AA) (Albert et al., 2011; McKhann et al., 2011; Sperling et al., 2011) created a set of recommendations whereby imaging and cerebrospinal fluid (CSF) should be used in symptomatic individuals to verify AD pathology to detect neurodegeneration and presence of b-amyloid deposition and pathologic tau protein. Amyloid disposition was placed at the apex of the biomarkers hierarchy and AD is already defined not by the clinical consequences of the disease (i.e. signs and symptoms), but its underlying pathologic process documented by in vivo biomarkers (b-amyloid deposition, pathologic tau, and neurodegeneration [AT(N)].).

However, since 2011 there was substantial research showing that MRI, PET, and CSF tau are not specific to AD, but rather nonspecific indicators of brain damage (Wirth et al., 2013). From 10 to 30% of individuals that are clinically diagnosed as AD do not display neuropathological changes that are characteristic to AD (Nelson et al., 2011). Similarly, individuals that at autopsy were present with AD neuropathological changes did not display any signs or symptoms, 30-40% cognitively healthy older adults have AD changes in the brain (Knopman et al., 2003). In addition, none of the biomarkers are as sensitive as direct post-mortem examination of the brain tissue (Jack et al., 2018).

In addition to being non-specific, imaging and biomarkers are expensive, invasive (CSF can be obtained by lumbar puncture) and require speciality clinics and equipment, which restrict their wider use and were recommended to stay as a research tool rather than a widespread clinical diagnostic tool (Sperling & Johnson, 2013; Jack et al., 2018). Moreover, given that the number of AD patients will be only increasing, the cost of these diagnostic methods and resources to cover all needs will be unattainable. Therefore there is a need for alternatives, those tools that are still sensitive and specific, but non-invasive and more affordable that allow identification of the preclinical dementia and also help monitor the progression of the disease.

Many patients with AD pathology have a concomitant medical condition (e.g. vascular disease) that can complicate the diagnosis. Even with the aid of neuroimaging AD brains in some cases prove not to have original AD plagues and tangles; diagnosis may worsen by the

existence of abundant cortical Lewy bodies even without parkinsonism in the patient's history (Mandell & Green, 2011)

The course of the disease goes through three stages: Initial, early, or a stage 1; intermediate, moderate, or a stage II; and advanced, severe, or a stage III. Each stage denotes severity to the cognitive and functional deprivation. However, the individual variations on each stage have occurred.

Evidence suggests that the earliest changes occur in the medial temporal lobe (MTL) structures (hippocampus and entorhinal cortex) that are responsible for episodic memory (Braak and Braak, 1991). This is consistent with the evidences that during ***the initial stage*** memory impairment characterised by the more-than-before forgetfulness and patients themselves are more aware of the decline than sometimes their spouses, family members and colleagues. The episodic memory decline is the most prominent characteristic: individuals have problems with encoding, retaining and retrieval of the new information. At this stage testing on the delayed recall especially with distracting task is poor, as well as brief stories and nonverbal material are poorly recalled (Mesulam, 2000; Small et al., 2000; Mandell & Green, 2011; Lezak, Howieson, & Loring, 2012). Tests involving associative learning and in particular spatial component is shown to be particularly sensitive (Fowler et al., 2002). Semantic encoding does not improve performance on the delay recall compared to healthy adults (Salmon & Bondy, 2009).

Patients experience decreased inhibitory processes and increased sensitivity to interference (Jacobs et al., 1990), selective and divided attention are particularly vulnerable. Sustained attention is the most resistant component (Calderon & Perry, 2001). These intrusion errors and forgetfullness interfere with daily living activities. Individuals can live independent lifes, pay bills and remain socially active, however become more superficial and ineffective and less decisive. (Mandell & Green, 2011; Mesulam, 2000). *Visuospatial and perceptual* dysfunctions occur early. *Aphasia* is an important feature of AD and depends on the severity of dementia and usually occurs in the particular sequence, however it is always fluent (nonfluent aphasia should rise the possibility of alternative diagnosis) (Mesulam, 2000). Word-finding difficulty is the earliest manifestation sign; speech initiation becomes less spontaneous.

On the *second stage* as the pathology spreads from MTL to the associated cortices (temporal, frontal, parietal) (Braak & Braak, 1991) patients have difficulties in storing new information over the brief period of time, as well as maintenance a coherent stream of thoughts. Other cognitive abilities such as language, visuospatial function and EF become apparent. At this point patients have anosognosia and they deny any cognitive and functional difficulties (Mandell & Green, 2011; Mesulam, 2000). With disease progression speech becomes less rich for nouns and then verbs and at the latest stage the lexicon contains mostly words without clear referents such as "thing/it/this" that reduces the meaning of the parlance. Basic language structure remains intact. Eventually patients become disprosodic and fail to discriminate emotional tone; at the terminal stage some patients become mute (Mandell & Green, 2011). As the disease progresses patients become more distractible with impaired planning, goal setting and decision-making (Lefleche & Albert, 1995; Salmon et al., 2009).

Some patients display apathy of a different range of severity from mild passivity to the abulic immobilisation (Mandell & Green, 2011). Depression usually accompanies AD and complicates diagnosis and can be a result of a patient's sense of declining function (Mesulam, 2000).

The *final stage* is characterised by the inability to recognise members of their family, difficulty in feeding and mobility.

1.10.2 TMB in AD

TMB shows a clear and specific effect in AD (Parra et al., 2009). In two experiments Parra et al. showed deficit in memory binding in AD patients compared to healthy ageing. Healthy controls showed deficit neither on memory for a single feature nor on memory for bound features even under high memory load. In addition, AD patients had more pronounced deficit in conditions where they needed to retain bound (i.e. shape and colour) features compare to a single feature objects (i.e. only colour or only object). In their experiments Parra et al. (2009) showed that the binding deficit in AD is not due to overall memory impairment or problems in dealing with perceptual complexity, but represents a specific paramount deficit for bound information. In the further experiments Parra et al. (2011) additionally show that not only binding features between dimensions (e.g. shape and colour), but within dimension (e.g. colour and colour) is impaired in sporadic and familiar AD, but spared in healthy ageing.

TMB detects otherwise asymptomatic carriers of the mutation E280A in the Presenil-1 gene that leads to familial AD and early-onset familial Alzheimer's disease carriers (Parra et al., 2010). Both AD patients groups were impaired in the binding condition of the task. This result is striking, as asymptomatic carriers did not show any signs of cognitive deterioration on the standard neuropsychological test that they performed as well as the control group. It shows that TMB test can help to detect changes in at risk populations, who had not yet developed the disease, where other cognitive tests are not sensitive enough. Compare to the earlier study (Parra et al., 2009) in the current one the researchers were using a version of the same VSTM – visual recognition – as opposed to free recall of verbal features suggesting that conjunctive within features binding is a unique deficit in AD that is not restricted by the retrieval process or the task at hand.

Due to its reliance on simple non-verbal shapes and colours, the TMB test can be used with people with limited language skills. Moreover, it is not affected by repeated testing (Logie et al., 2009), or by the level of education (Parra et al., 2011), so it can be used to test people with low levels of literacy as well as people who are highly educated and in assessing patients with very different socio-cultural backgrounds (Parra et al., 2011).

These main results have been replicated in several contexts and countries including Brazil (Cecchini et al., 2017); Romania (Della Sala et al., 2016), Germany (Koppara et al., 2014), Italy (Della Sala et al., 2012; Parra et al., 2009), Argentina (Pietto et al., 2016), Colombia (Parra et al., 2011) and the UK (Parra et al., 2010), and Russia. As population profiles in most countries become increasingly distinct (Manly, 2005; Grober et al., 2010), neuropsychological tests will have to meet certain requirements in order to be applicable in clinical practice. These include: insensitivity to linguistic, ethnic and cultural influences and easier to use for screening in primary care facilities (Grober et al., 2008; Logie, Parra, and Della Sala, 2015).

1.10.3 IADL in AD.

With the emphasis on the early diagnosis of AD, most of the recent studies are with the patients with MCI and healthy older adults. However, there is a need to distinguish MCI with mild dementia and the latter with the moderate dementia. Most of the time it is difficult to judge where is that line of functional impairment between MCI and mild dementia.

Functional impairment is central to the concept of dementia. In patients affected by AD, decline in functional abilities progresses hierarchically from higher order daily functioning and complex IADL to more basic, routine and overlearned domains that related to BADL (Suh et al., 2004: Arrighi et al., 2013). The latter tends to change in patients from moderately to severe dementia.

Early research showed that finances, telephone, medications, transportation found to be more impaired in AD patients compare to MCI (Barberger-Gateau et al., 1999) this was confirmed by several more recent studies (Njegovan et al., 2001; Arraghi et al., 2013; Hesseberg et al., 2013). However, IADL scores vary over a broader range from MCI and early stages of dementia to moderate dementia severity. Therefore, from this overlap a question can be drawn, what is the difference in performance between MCI and dementia and how much of the impairment should be present in order to draw lines between normal cognitive functioning, MCI and dementia?

Several research groups tried to disentangle these overlapping impairments in daily activities between MCI and mild AD. One of the directions is the direct observation of patients with MCI and AD that showed patients with mild AD committed more total errors on the Naturalistic Action Test (NAT) compared to individuals with MCI (Giovannetti et al., 2008). More specifically, Schmitter-Edgecombe & Persey (2014) using the same task showed that patients with dementia commit more omission and substitution errors, as well as inefficient actions. Patients with dementia are also engaged in more irrelevant tasks compared to MCI. When dressing up mild AD patients the most common errors were unsatisfactory executions and incorrect choices of clothing (Feyereisen, 1999). During the tasks of preparing a hot drink and packing a school bag or picnic basket, omission, sequencing and action addition errors were the most common in AD patients (Ramsden et al., 2008). Mild AD patients were impaired in all domains of financial capacity (Martin et al., 2008), whereas MCI patients had more difficulty with conceptual understanding of finances (e.g., bank statement management, bill payment) and relatively preserved procedural skills (e.g., cash transactions; Okonkwo et al., 2006).

Cognitive underpinning of functional abilities in AD

Cognitive predictors of everyday action performance depend on the severity stage of demented process. Several research groups have initiated longitudinal studies whereby they aim to understand the rate of change in everyday function in each stage of dementia in relation to global cognitive function. Arrighi et al. (2013) using informant-based DAD reported that activities like "organise finances" and "adequately organise correspondence" were lost at the early course of the disease, when median MMSE was 23-24. Then the rest of the subdomains of finance, medication, and outings deteriorate at the median MMSE of 18. The other study reported that an MMSE score of less than 10 is a point of transition to severe AD (Feldman et al., 2005). Jefferson et al., 2006 found that the only measure of global cognition (measured by MMSE) correlated with the IADL scale, interestingly, in addition, they discovered that when MMSE was taken from the regression analysis, object perception was a significant predictor of IADL.

For many years AD was considered as a disease that preliminary affects global cognitive function, then researches accepted that the initial deficit manifests from episodic memory decline, but impairments in other domains of cognitive function were seen as non-specific. More recent clinical observations revealed that patients with AD have been found with predominately executive deficit with relatively preserved episodic memory (Bäckman et al., 2004). It was shown in a number of researches that executive function is a major determinant of disability in dementia and strongly correlates with IADL even before the exact diagnosis is established (Bell-McGinty et al., 2002; Desai, Grossberg, & Sheth, 2004; Boyle & Cahn-Werner, 2005; Burton et al., 2006; Perneczky et al., 2006; Jefferson et al., 2006; Pereira et al., 2008; Mariani et al., 2008; Aretouli and Brandt, 2009, Martyr &Clare, 2012). Royall et al. (2007) have argued that executive function mediates the memory's association with functional decline and questioned the role of memory as a feature of dementia. He showed that memory impairment at the baseline and change rate in memory over three years follow-up did not predict functional decline. However, a low executive function score at the baseline and rate change of executive function over the years are significantly and independently correlated with changes in IADL. Aretouli and Brandt (2009) examined executive functioning components and their association with functional decline and observed that only working memory was associated with daily functioning. Nevertheless, they noted that more variance

was explained by measures of global cognitive functioning that were better predictors of daily functioning.

Farias et al. (2008) proposed that there is a complex relationship between neurocognitive impairment and functional deficit. There are varieties of ways in which different cognitive functions can affect the same everyday functional abilities. She showed that memory and executive function can equally affect Everyday Memory domain of the Everyday Cognition Scale (ECog). This was confirmed by the more recent study (Hsu et al., 2017) where they pointed at the association between global cognitive function, executive function and the ECog scale.

There are several additional confounder variables that explain functional decline in dementia. They are: cognitive impairment, baseline activities, age, sex, race, personality traits, marital status, years of education, and years from the disease onset. Apathy, or the lack of motivation to engage in activities, is not only associated with, but also found to be detrimental for daily functioning and predictive of developing dementia (Fitts et al., 2015; Richard et al., 2012). More importantly, because of the advanced age, the concomitant vascular disorders, depression and parkinsonism contribute to the picture of cognitive decline, making it very difficult to explain what affects functional deterioration.

Challenges

The reasons of the variability in the studies are manifold: the groups of patients recruited for the studies are chosen with different criteria (some of the studies recruit AD patients without distinguishing them into different levels of severity, other take only mild or moderate AD stages). There are different IADL scales that are applied in different studies.

As with patients with MCI, for AD patients there are also no strict criteria for IADL scales. Most of the studies report the overall impairment in IADL overlooking the impairment in individual tasks or types of errors patients commit. Therefore we have only a limited picture of the needs and abilities for mild or moderate dementias.

Another challenge that needs to be pointed is the overlap between different cognitive groups (Munoz-Neira et al., 2012; Nygar, 2003; Rosenberg et al., 2009). These studies pointed at the fact that some subcategories in questionnaires rely on rehearsed and routine everyday habits and intense

practice (e.g. heating water and preparing meal); some tasks are gender sensitive (e.g. laundry, shopping and house work), others display personal interests and previous experience (e.g. computer access and using cell phones) and therefore do not display a decrease or change in performance in formal testing.

In Chapter six I discuss all challenges in IADL research; I seek to identify the everyday task that would be sensitive to early cognitive impartment and propose a new tool to measure this ability and I argue how the new tool would address the limitations of the existent IADL scales.

Differential diagnosis

The episodic memory is known to be particularly vulnerable in AD. Unfortunately, episodic memory problems are not unique to AD. The most widely used tests for the identification of the cognitive deficits associated with AD are based on associative memory (Rentz et al., 2011), list learning or delayed recall (e.g., Fowler et al. 2002; Lowndes & Savage, 2007; Swainson et al., 2001). These tests are failed also by people affected by several other disorders, including chronic depression, making the diagnosis of early AD difficult (Pfennig, Littmann & Bauer, 2007; Wright & Persaud, 2007). Patients in preclinical stages of Vascular Dementia (VD) display strikingly similar cognitive patterns. Patients have difficulties in acquisition of new information and storing and accessing this information.

Recent studies by Stopford et al. (2008; 2012) demonstrated heterogeneity of AD and highlight that episodic memory dysfunction are probably not the earliest symptoms of AD, but working memory deficit, which is coordinated by the frontal lobe functioning and is also a primarily syndrome for FTD. As it was shown, the working memory impairment in these two disorders can be distinguished by the different underlying reason of this deterioration. FTD patients mostly display lack of concerns on their performance and are characterised by inattention, poor response inhibition and sequencing problems. In contrast, AD patients demonstrate short-term memory overload, where they have difficulty holding information or instructions.

Although different types of dementias vary in aetiology and biological triggers there is a clinical overlap of the cognitive and behavioural features among them. All degenerative disorders and depression in older people lead to memory deficits, EF and language impairment, and cause alterations in behaviour, as well as progressive functional decline. In

additional, “text-book” disorders have a particular pattern of impairment. The problem is that most of the time the clinical picture is not typical and AD patients can exhibit more executive symptoms when other dementia types exhibit more episodic memory impairment. An abundant amount of research studies was dedicated to establish the differential diagnosis of various types of dementia. Overlaps in cognitive symptoms of various neurocognitive disorders are a challenge for clinicians to distinguish between dementias especially at the initial stages of neurodegenerative process. In the previous section I showed that the TMB task is the best to distinguish between healthy ageing and cognitive impairment, in other words that TMB is sensitive to cognitive decline. The best marker for AD pathology also should be specific to AD and therefore distinguish AD from other types of dementias.

TMB in non-AD dementias

There is a very limited amount of studies that would investigate TMB in non-AD dementias. Those few show that TMB is specifically impaired in AD compared with other forms of dementia (Della Sala et al., 2012; Cecchini et al., 2017). Della Sala et al., 2012 compared performance of AD patients with that of patients suffering from other types of dementia, such as FTD, VD, LBD and dementia in PD. In their study they use 4 features across all conditions and for the control participants they used 8 features to equate the level of difficulty among the groups. Only AD patients showed significant deficits in recalling object-colours bindings.

Such findings have been recently replicated in a new sample of bv-FTD (Cecchini et al., 2017), as opposed to Della Sala et al (2012), where they were taking semantic and dv-FTD as one group. In their study they used lesser memory load of 6 features per screen for both bound and unbound conditions. In the ROC analysis they showed that bound condition of the task differentiates between bv-FTD and AD and the latter from the healthy controls. Despite different methodologies, they confirmed with the pervious studies that the free recall on the conjunctive binding can be used to diagnose AD and differentiate in from other dementia types.

In these studies, TMB was assessed using a free recall paradigm (Parra et al., 2009a; Della Sala et al., 2012; Cecchini et al., 2017) in which participants are required to verbally recall objects and colours individually or in combinations. In addition, participants performed tasks with different set sizes (Parra et al., 2009; Della Sala et al., 2012) allowing the titration of the

cognitive demand of the task to keep the performance level at baseline conditions (i.e. single features) similar across groups. This procedure, however, may be challenging to use in clinical settings.

Early AD development is clinically characterised not only with cognitive impairment, but also compromised everyday functional activities. Functional activities scales aid to distinguish between MCI and AD patients and also track the progression of the disease. As it is important for the assessment to be accessible and non-invasive, functional scales fulfil these requirements. The development of sensitive and specific tools can enable broader screening for preclinical and early clinical AD. Combined cognitive and non-cognitive measures will serve to discriminate across neurodegenerative disorders as well as between cognitively impaired and healthy older people people. In the next section I will be exploring what are the most sensitive functional abilities for early cognitive decline.

Chapter I – Part IV

Current study.

Several working groups around the world recently raised the concerns about the lack of harmonisation of the assessment tools across the studies in Europe (Diaz et al., 2005; Maruta et al., 2011; Costa et al., 2017) and America (Daffner et al., 2015). They all emphasise that there is a need for cognitive, behavioural and functional measures that are sensitive and specific for detecting the cognitive impairment earlier on the course of the disease. In my thesis I explore what these measures are. I argue that the TMB task and everyday financial abilities are sensitive to early cognitive decline and if used combined can detect the first signs of deterioration.

As Logie et al (2015) proposed, one of the features of the ideal instrument is it should be affordable. At the moment, TMB task only exists as a computer version of the task, which makes it hard to use in the clinical settings. In the Chapter two series of experiments I validate a Flash-Card version of the test and I explore its properties. I argue that it would hold the same psychometric properties as a computer version. In order to investigate and expand on the body of work related to the TMB task, I use a different test paradigm (i.e. recognition task) that has never been explored before in the TMB test and I argue that it will hold the same specificity of the original test. My Flash-Cards were also compared to the other mobile version the test - a Tablet PC version – another affordable and mobile version of the computer TMB task. These two modes of the tests were created for application in clinical settings and had two different features from the computer PC version. In these versions we used two conditions: Shape Only and Shape-Colour Binding Conditions (we did not use Colour Only condition); only two items in each Condition trials that were shown to be sensitive to detect cognitive deterioration in AD patients.

As I argued earlier, the TMB test is not affected by ageing, older adults do not show a disproportional binding cost relative to younger adults. I explore if there is a neurophysiological taxing (i.e. recruitment of additional brain areas) to help performing the task successfully by older people. In Chapter's III experiment I use a mobile EEG system that

is an incredibly desirable tool in clinical and research communities. With the aid of the mobile EEG devices patients and participants can be assessed from home and are very compact and easier to use, compared to stationary EEG recording systems. In addition, the system that I used comprised of fewer electrodes. I show that this system can record clinically meaningful electrophysiological data and this can provide an ideal solution for Mobile Brain imaging Tools (Lau et al., 2012)

In order to show sensitivity and specificity of the newly developed Flash-Cards with the TMB task I recruited patients with AD and Parkinson's disease. In the experiment in Chapter four I show that TMB is a specific test for AD pathology.

The development of dementia is accompanied with not only cognitive impairment, but also with everyday functional problems. Therefore, the other main aim of my thesis was to look at which functional abilities decline first in the trajectory from healthy ageing to dementia. I argue that everyday financial abilities are one of the earliest functional impairments. In the series of experiments I develop and validate the Acreemagnosia Measurement that assess everyday financial abilities in frail older people and patients with cognitive impairment.

In my thesis I introduce a new term to describe everyday financial abilities: "Acreemagnosia" – that is a combination of Ancient Greek words: ἀ- (a-, "not, without"), χρήμα (chreema, "money") and γνωσιακή (gnôsis, "knowledge"). In Chapter seven I review the tools that have been developed to assess financial abilities and argue that there is a need for a new instrument. Taking all strengths and limitations of existing financial assessments I propose that there is a need for a new instrument which should maximise the recognition of early decline in financial knowledge.

In the construction of the measure, that is described in Chapter eight, I use Item Response Theory (IRT) that is more advanced over conservative models in (1) the ability to form item hierarchies; (2) to streamline testing by eliminating items that are much too easy or difficult; (3) examining the characteristics of individual items, and determining if polytomous scoring categories work as intended; (4) to assess the discrimination power of individual items; (5) the ability to test the invariance of items across external groups (i.e., differential item functioning).

In the modest sample of patients I explore the measurement's property and also the most sensitive financial items that would be predictive for early cognitive decline. And finally what

are the cognitive correlates that are responsible for financial abilities. Identifying the cognitive substrates of declining financial abilities would enhance our understanding of the neurological substrates of financial abilities and enrich on the body of work related to Alzheimer's disease.

I argue that the combination of these assessment tools will improve the early diagnosis of AD. The current diagnostic characteristics of MCI as a prodromal stage of AD include memory impairment (i.e. impaired free and delayed recall) and minimal impairment on everyday function. Several Working Groups proposed TMB as one of the tests that can be included in the early diagnosis of AD. I show that everyday financial management abilities as a higher order function can be the first functional marker that declines in patients with MCI. There is a need of such markers which can be incorporated in global trials for AD.

Table 1 Studies assessing IADL in MCI and cognitive underpinning of IADL in MCI

MCI					
Source	**IADL**	**Groups**	**Diagnostic criteria**	**Daily activity impaired**	**Cognitive underpinning**
Albert et al., 1999	self-reported and informant-reported: Pfeffer Functional Activities Questionnaire (FAQ); and Lawton IADL Scale.	MCI and NC	modified MMSE>=40 (equivalent to an MMSE score of>= 22)), CDR of 0 or 0.5	First reported diminished awareness of the functional deficit in MCI patients. First noted that MCI may be associated with greater need for help and restrictions in some daily activities	Was not assessed
Tabert et al., 2002	self-reported and informant-reported: Pfeffer Functional Activities Questionnaire (FAQ); and Lawton IADL Scale.	MCI and NC	modified MMSE>=40 (equivalent to an MMSE score of>= 22)), CDR of 0 or 0.5	Did not assess on the task level, overall score is NC>MCI. A discrepancy index (Informant report - self report) predicts conversion to dementia	Was not assessed

Nygard, 2003	Literature review, IADL/ADLscales of the studies	MCI, AD, and NC	Did not describe it	Everyday functions that are particularly sensitive to cognitive decline include handling finances, taking care of medication, shopping for groceries, managing the telephone, and using public transportation	Was not investigated
Tuokko et al., 2005	Self rated scale: the Older Americans Resources and Services Scale (OARS) (it is a combined Lawton and Brody's IADL scale and Katz's ADL scale.)	NCI, CIND, Dementia	DSM-III criteria	MCI groups to be more impaired on physically demanding IADL.	Poor memory and psychomotor speed were the major contributors to impaired IADL tasks. Participants that performed poorly on memory at the baseline in 5 years show significantly more future impairment in handling finances
Perneczky et al., 2006;	Informant-rate scale: ADCS-MCI-ADL-18; Bayer-ADL, IQCODE	MCI and NC	Petersen 1SD below; CDR 0.5	NC>MCI>AD on finding items at home, Checking bank account, Writing letters or notes, Keeping appointments, using the telephone, preparing meals, travel, talking about recent events, Remembering newspapers, magazines, books, Remembering television shows, shopping, Staying in the home unassisted	They found a strong correlation between patients' level of cognitive performance and their ability to carry out everyday tasks. They inference that memory and complex reasoning affect IADL
Peres et al., 2006	self-reported IADL: 4 items Lawton IADL	MCI, AD, and NC	Petersen 1,5 SD below	All four items: telephone, transport, medication, finances showed decline in people with MCI	Was not assessed

Rozzini et al., 2007	Lawton and Brody's IADL scale and Katz's ADL scale	aMCI	MMSE>=24, CDR 0.5	Patients with aMCI converting to AD during 1 year follow-up was strongly related to the level of worsening in functional ability evaluated with the IADL	Poor global cognitive performance at baseline and worsening executive functioning, but not worsening memory performance, were associated with conversion to Alzheimer's disease (AD) over a 1-year follow-up period.
Jefferson et al., 2008	Informant-rate scale: error-based questionnaire of functional capacity; Lawton IADL scale	MCI and NC	Petersen and clinical criteria	No difference on Lawton scale	Verbal learning was significantly associated with IADL
Tam et al., 2008	Performance based scale: Chinese version of Disability Assessment in Dementia (DAD)	aMCI and milti-MCI	Petersen 1SD below; CDR 0.5	Motor slowness or decreased motivation in IADL may not be benign changes commonly found in older adulthood, but are worthy of clinical evaluation.	Most frequently impaired in the multiple-domains MCI group were those connected to planning and organizing IADL tasks; initiation of tasks was unaffected.
Wadley et al., 2008	Performance based instrument: The Timed Instrumental Activities of Daily Living (TIADL) test	MCI and NC	Petersen and clinical criteria	The performance of persons with MCI was comparable with that of peers without MCI on all five tasks: telephone use, locating nutrition information on food labels, financial abilities, and medication management. Grocery shopping was impaired in MCI. MCI completed the IADL longer but as accurate as NC.	They interfered that errors in grocery shopping are likely associated with decrements in visual search skills, selective attention, and rapid information processing. Individuals in the MCI group who had worse speed or worse accuracy than the comparison group also had worse global mental status

Giovanetti et al., 2008	Performance based instrument: Naturalistic Action Task (NAT)	MCI, AD, and NC	Petersen 1,5 SD below, MMSE>=25	MCI are worse than NC in preparing toast and coffee, wrapping a gift and preparing a lunch box.	They speculate that the high proportion of commission errors in MCI may be secondary to mild executive deficits. Among mild AD participants, the high proportion of omission errors may be caused by episodic and semantic memory deficits
Mariani et al., 2008	Lawton IADL (MCI: informant report, NC: self-report)	aMCI and NC	Petersen 1,5 SD below, MMSE>= 23.8	aMCI showed IADL changes concerning shopping, handling economy, and self-administration of drugs	Executive function is only predictive of IADL
Tan et al., 2009	Informant-reported IADL: modified Scales of Independent Behavior – Revised (mSIB-R), Participants completed Everyday Problem Test (EPT)	MCI and NC	Petersen 1 SD below, MMSE>=24	MCI performed worse than NC	Social engagement was associated with memory and executive processes; executive function is only somewhat predictive of IADL. Episodic memory, executive functions, and speed of processing demonstrated the largest correlations with both IADL.

Kim et al., 2009	Seoul-IADL in a self-rating version	4 types of MCI, AD, and NC	Winblad 1 SD below	MCI to be significantly impaired in using a telephone, keeping appointments, talking about recent events and using household appliances. Worse performance of the MCI group for transportation and finances. After controlling for age, gender, education, and depression, **multi-domain amnestic MCI** was the only subtype to perform significantly more poorly than normal participants in terms of functional abilities.	Was not investigated
Schmitter-Edgecombe et al (2009)	13 ADL-IS	aMCI and nonaMCI		Both groups are significantly impaired in telephone use, organisation, and social function, followed by household and general activities, medication use, conversation and food preparation.	**aMCI** more impaired in content memory (that was linked to the temporal lobes), as well as temporal order memory, source memory, and prospective memory. **nonaMCI** deficit in noncontent memory. Temporal order memory was significant and unique predictor of food preparation, while source memory needed for social functioning (keeping track of who said what). Temporal order memory and prospective memory are needed for successful medication use and household activities. Different cognitive processes, within and between neuropsychological domains, are differentially involved in particular IADL tasks.

Aretouli and Brandt (2009)	Informant report: Activities of Daily Living-Prevention Instrument (ADL-PI), IQCODE	4 types of MCI and NC	Petersen 1.5 SD below; CDR 0.5	Amnestic and non-amnestic MCI patients had similar levels of functional impairment. Major difficulties were reported for keeping appointments, using the telephone, remembering current events and finding things at home, and minor difficulties were reported for driving and using transportation, managing finances, organizing and completing activities, and taking medication.	Executive battery (18 tests): among three executive function components (planning/ problem solving, working memory, and judgment), only working memory was associated with ratings of daily functioning. Measures of global functioning and constructional praxis, the MMSE and the clock drawing test, were better predictors of ADL-PI.
Anh et al., 2009	Seoul-IADL in a self-rating version	MCI and NC	Petersen 1.5 SD below; CDR 0.5	MCI compared with healthy controls in the domains of telephone use, meal preparation, medication intake, management of belongings, keeping appointments, talking about recent events and performing leisure activities and/or hobbies	IADL requiring memory or frontal cortex executive functioning are at particular risk of decline in MCI
Teng et al., 2010	Informant report: FAQ	aMCI, md-aMCI, and NC	Petersen 1,5 SD below, MMSE>=24	**aMCI** had better scores than the **nonaMCI** group on managing bills, preparing taxes, keeping up with current events, attending to media, remembering dates and traveling outside the neighbourhood.	Both memory and executive/processing speed as significant predictors of functional ability, however the correlation is modest.

Goldberg et al., 2010	Performance based instrument: (the University of California San Diego Performance-Based Skills Assessment (UPSA) Informant report: Alzheimer's Disease Cooperative Study/ Activities of Daily Living Inventory	MCI, AD, and NC	Petersen 1,5 SD below, MMSE>=24, CDR 0.5	No difference between MCI and healthy controls on informant report and significant difference between groups on the performance-based IADL	Cognitive scores in speed of processing, episodic memory, and semantic processing and fluency accounted for a significant share of the variance on the UPSA.
Bangen et al., 2010	Performance based instrument: the Managing Money and Health and Safety subscales of the ILS	NC, aMCI, nonaMCI	Petersen 1 SD below age appropriate norms	Nature of the reduced functional abilities varies depending on MCI subtype. **aMCI** performed more poorly relative to the NC participants on the ILS Managing Money subscale. **nonaMCI** group showed a trend toward poorer performance on the ILS Health and Safety subscale.	Decreased functional abilities are associated with decrements in global cognitive functioning, but not specifically memory or executive functioning abilities in MCI.

Pereira et al., 2010	The Informant Questionnaire of Cognitive Disorders of the Elderly (IQCODE), the Blessed Dementia Scale (BDS), and Direct Assessment of Functional Status Scale (DAFS-R)	aMCI, nonaMCI, mdMCI, AD, and NC	Petersen and clinical criteria	Financial and shopping skills were the items that differentiated patients with MCI from healthy controls	Executive dysfunction exerts a negative impact on the ability to perform activities of daily living, stronger than general cognitive deficits. Multiple-domain MCI may be associated with a higher degree of executive dysfunctions with stronger impact on functional status
Pedrosa et al., 2010	Informant report: The Alzheimer's Disease Cooperative Study / Activities of Daily Living scale for MCI patients (ADCS/MCI/ADL) isLawton IADL scale	aMCI, AD, and NC	Petersen 1SD below	Patients with MCI had deficits compared with controls regarding shopping, taking medications and handling finances. Regarding the distinction between aMCI and AD patients on the scale, two groups performed similarly.	Among the ADCS/MCI/ADL questions, those that are highly dependent on memory, planning and sustained attention appeared to be the earliest and most severely affected in aMCI in our study.

Luck et al., 2011	Informant reports: 9 IADL items (Schneekloth and Potthoff, 1993)	aMCA, nonaMCI, and NC	Winblad 1 SD below	Investigated performance on nine IADL items and detected worse performance of patients with MCI compared with healthy controls. Analyses of MCI subtypes revealed that this effect was stronger for amnestic MCI subtypes. Early IADL decrements in particular in individuals with amnestic MCI	Was not investigated
Reppermund et. al 2011	Informant-completed Bayer-Activities of Daily Living Scale (B-ADL).	MCI and NC	Petersen 1,5 SD below, MMSE>=24	The difference between MCI and NC groups was statistically significant for the high cognitive demand factor, but not for the low cognitive demand factor.	Association between neuropsychological measures and functional outcomes is only modest. Small, but statistically significant correlations were found between the B-ADL score and each of the five cognitive domains.
Yeh et al., 2011	Performance based: Disability Assessment in Dementia (DAD)	Single and multi domain aMCI, NC, and AD	Petersen 1,5 SD below, MMSE>=24, CDR<1	Both sd-aMCI and md- aMCI had intermediate IADL scores between normal and mild AD. However, single domain MCI was impaired in less number of items than multi domain MCI	The sd-aMCI group showed impairment in the initiation as well as planning and organization processes, and all 3 executive processes were involved in the md-aMCI group. In addition, measures of memory and language were mildly associated with IADL
de Rotrou et al., 2012	Performance based: Disability Assessment in Dementia with 6 items (DAD-6): instrumental part	Single nonaMCI and multi domain MCI and NC	Petersen criteria without mentioning the cut-off	Single domain MCI were impaired in less number of items than multi domain MCI. The scale differentiate between two MCI types.	Among cognitively impaired subjects, the DAD-6 moderately correlated with the delayed recall. In patients group executive subscores of DAD (initiation, planning, and effective performance) was affected.

Schmitter-Edgecombe et al, 2012	Performance based instrument: The day-out task (DOT); additional informant report: KI-ADL	MCI, AD, and NC	Petersen 1,5 SD below	MCI are worse than NC; it took them more time to complete IADL; they made more errors. MCI participants have knowledge of what to do for the DOT, but were not always capable of using that knowledge to completely and accurately reach the task goals and sub goals.	Retrospective memory was predictive of the number of subtasks left incomplete and inaccurate by the MCI participants.
Reppermund et al., 2013	Informant-rate based IADL: Bayer-ADL	aMCI, nonaMCI and NC	Petersen 1,5 SD below.	Difficulties in more complex IADL with high cognitive demands like finding the way in an unfamiliar place or doing two things at the same time.	Highly cognitively demanding IADL were negatively correlated with performance in five cognitive domains, i.e. memory, attention/processing speed, executive function, language and visuospatial ability.
De Vriendt et al., 2013	Informant rate based for patients and self - report for controls: Katz scale, Lawton IADL and advanced ADL	aMCI, AD, and NC	Winblad 1 SD below	MCI do not have performance problems in b-ADL and i-ADL due to cognitive problems, all participants reported subtle problems in performance when it concerned the more complex ADL such as leisure, self development, or (semi) professional work	Was not investigated
Marshall et al., 2014	Participant and informant rated Ecog	MCI and NC	MMSE>=24, CDR 0.5	Found that worse performance on “remembering a few shopping items”, “remembering appointments”, “developing a schedule in advance of anticipated events” , “balancing checkbook” , and “keeping mail and papers organized” best discriminated MCI from CN.	They inferenced that activities depend primarily on memory and executive function that best distinguished between NC and MCI.

Chapter II

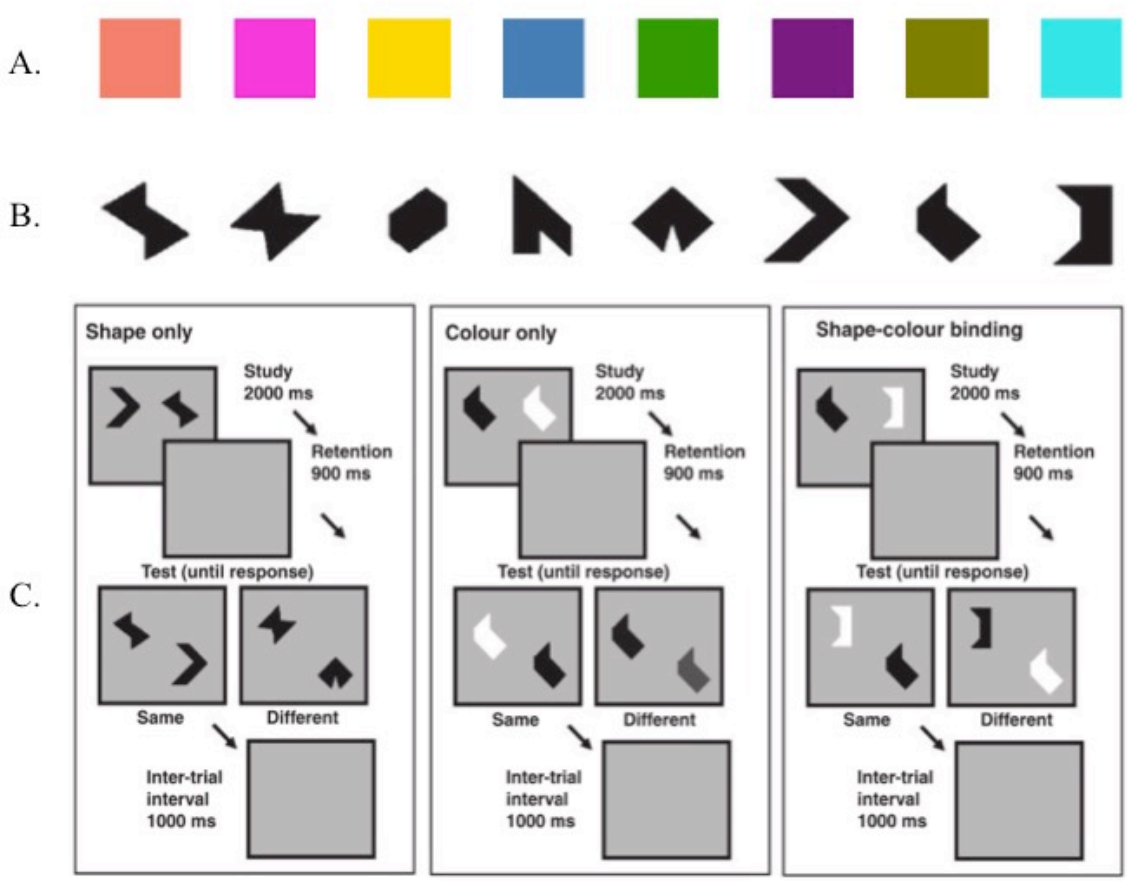
Temporary Memory Binding test.

Introduction

As I have outlined, the TMB task existed as a computerized version that restricts its use in clinical practice to when there is a need for a bedside or at home assessment for frail people or in geographically challenging areas. In this series of experiments I introduce new mobile version of the task: the Flash cards and the Tablet PC. I investigate whether these two modes of the test presentation are comparable. The Flash cards and the Tablet PC were designed on the basis of the Parra et al., 2010 paradigm.

The task assesses visual TMB for arrays of stimuli such as shapes (random polygons), colours, or combinations of shapes and colours. Eight shapes and eight colours were selected so that it is easy to discriminate them visually, but difficult to name them (Parra et al., 2010) (See Figure 2.1).

Figure 2.1 Eight random colours (A) and eight random polygons (shapes) (B) that were used to construct the stimuli. Short-Term Memory Binding Task that Parra et al. (2010) used in his computerized experiment (C).



The task is based on a change detection paradigm. The initial fixation cross is followed by the study display presented for 2 sec. After a very brief unfilled retention interval (about 1 sec) the test display is shown. The participant has to recognise if the items presented in the test display are the same or different from those presented at study, independently of their location. In 50% of the trials the items were the same in both displays (i.e., "same trials") In the other 50%, two items in the test display were different (i.e., "different trials"). Two conditions assess TMB for single features (Shape Only and Colour only) and one assesses the binding of these features (Shape-Colour Binding Condition). A typical TB task is illustrated in Figure 2.1.

Previous versions of the TMB test included two conditions to assess memory for single features (i.e., Shape Only and Colour only) and a condition to assess memory for combined features (i.e., Shape-Colour Binding) (Allen et al., 2006; Parra et al., 2014; Wheeler and Treisman, 2002). To be clinically practical (i.e., shorter) this paradigm has been recently modified to include solely the

condition Shape Only as baseline; this version retains the same psychometric properties of the longer version (Koppara et al., 2015).

In the previous studies (Parra et al., 2009a; 2010a) the number of items has been titrated presented to the individual ability of each participant to minimise unwanted effects simply due to differential response to cognitive demands rather to a fundamental deficits on TMB. In clinical settings this would be challenging. Therefore, in the following experiments trials will be presented with only two items each, which proved to elicit a near ceiling effect in healthy volunteers, yet showing the typical drop in AD patients (Parra et al., 2010a; 2010b).

As the Flash cards and the Tablet PC versions of the test are designed to test on the presence of AD, these TMB versions of the computer test should be resistant to the effect of age and unimpaired when testing other neurodegenerative disorders. The first experiment of this series was set up in order to confirm that there is indeed no age effect of the Computer PC version of the test. This Computer PC version will serve as a mean to compare the Flash cards and the Tablet PC to.

Experiment 1

Is there an age effect on the Temporary Memory Binding Test (TMB). Computerized TMB test.

2.1.1 Aims

In their study, Parra et al. (2009) showed the lack of age-effect on visual short-term memory binding. In this experiment he compared the performance of younger and older group on the single feature condition and feature conjunction, and showed that overall performance on the change detection task by the older group was comparative to the younger group. In the study he used binding within the colour dimension, he noticed that compared to the Shape-Colour Binding from the experiment by Brockmore et al (2008), binding of bicolored objects is more difficult. Given that patients with sporadic and familiar AD have a pronounced deficit in maintaining Shape-Colour Binding (Della Sala et al., 2012; Parra et al., 2010) and following the paradigm used by Parra et al (2010), I aim to replicate this computer experiment to show that the ability to remember a single feature (Shapes) and form a bound representation of different dimension (shapes and colours) in older people is not different than in younger adults.

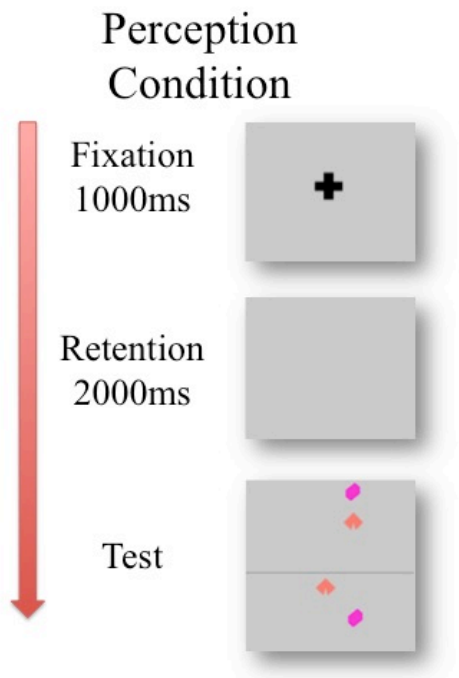
2.1.2 Participants

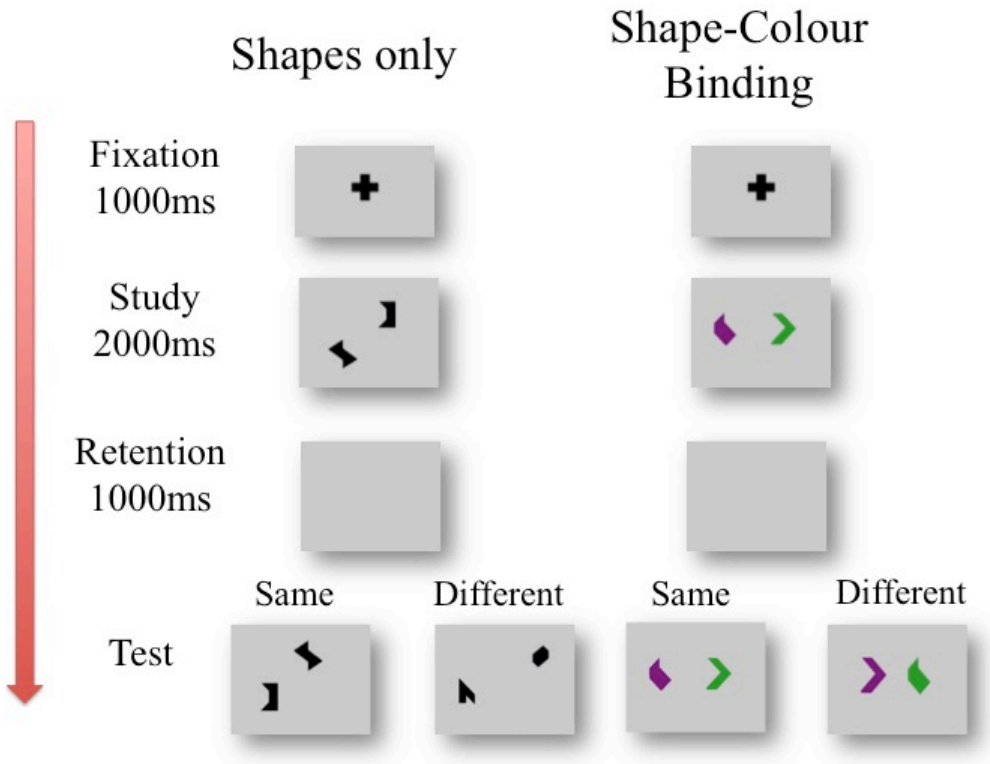
Twenty younger adults (age: M = 27.3, SD = 3.7; 10 males) and 20 older participants (age: M=69.8, SD=7.5; 7 males) were recruited for the experiment. Younger participants were postgraduate psychology students who volunteered for the study. Older participants were members of the Edinburgh Psychology Department panel of volunteers from the healthy general population. Younger and older participants were different in terms of their formal education (younger adults: M= 20.1, SD = 2.8; older adults: M=16.6, SD = 2.7; $t = 4.07$; $p < 0.001$). Ethical approval was granted by the University of Edinburgh Psychology, Philosophy and Language Science Committee. All participants gave their consent on participation in the study. None of the younger or older participants were excluded due to poor colour vision: on the perceptual task all participants performed above the 80% level.

2.1.3 Materials

The computer task consists of three conditions. The conditions procedures are displayed on Figure 2.2.

Figure 2.2 Three parts of the Computer PC version of the test





The TMB test starts with ***the Perception Condition*** (Fig.2.2)**.** The condition is performed to rule out the possibility of poor visual colour perception that can hinder the binding part of the test. It contains 10 trials where participants are presented with two arrays of four coloured shapes on a light gray background. The two arrays are divided by a line: two shapes are below and two above the line. Each object was devised by randomly combining shapes and colours. Half of the trials consist of the same coloured shapes and half of the trials are with the shapes that swap colours. Each object was devised by randomly combining one of eight possible shapes and one of eight possible colours. Shapes and colours were constructed in a way that it is easy to discriminate them visually, but difficult to name them verbally (Parra M.A., 2009). Half of the trials consist of the same coloured shapes and half of the trials are with the shapes that swap colours.

The Shapes Only Condition (Fig. 2.2) consists of 32 trials. Each trial consists of a Study Display with two black shapes presented on a light gray background. On the next Test Display, two black shapes are replaced by two new black shapes. On half of the trials the test array would exactly match the study array and in 50% of the trials the shape of a single object is changed.

In his experiment, Parra et al (2010) used a Colour Only Condition, however he found that healthy older perform this condition with ceiling effect; therefore in my experiment this condition is omitted.

The Shape-Colour Binding Condition (Fig.2.2) consists of 32 trials. Participants are presented with an array of two shapes filled with colours on the study display that is replaced by two shapes on the test display that in 50% of the trials would remain the same colours as on the study display and in 50 % would swap their colours.

2.1.4 Procedures

On the Computer PC the stimuli are presented on a 22" Computer PC screen using a 3x3 virtual grid that subtended 6 cm vertically and horizontally. Each shape is subtended by 1.8 cm vertically and horizontally. Trials on the Computer PC task are fully randomized across participants. Three consecutive conditions were presented to each participant. The experimental procedures are illustrated on the Figure 3.2. Ten trials are for the Perceptual condition and 32 trials for each Shapes Only and the Shape-Condition Binding Conditions. The order of the conditions was always the same: Perceptual condition is followed by the Shapes Only Condition and then the Shape-Colour Binding Condition. All conditions were presented in blocks, before each block the instruction with a verbal explanation and an illustration of the test were presented. Each following condition begins with a fixation cross centered on a light gray background shown for 1000 msec. that is followed by the *study display* for 2000 msec. After the 1000-msec retention interval, the *test display* is followed after which the participants responded.

In the Perceptual Condition participants are asked to detect as accurately and quickly as they can whether the colour-shape combination below and above the line stays the same or shapes swapped their colours. The shapes randomly changed their position within their own half of the screen, but participants were asked not to concentrate on the location of the shapes, but only on the combination of shapes and colours. This ensures that the binding occurs between shapes and colours and not with a location. If the participant performs 8 out of 10 trials correct (80% correct judgments), the next condition will follow. If performance is lower than the threshold, the participant is excluded from the study and may be requested to further test colour perception or visual acuity. Previous studies have shown that scores below 8 are indicative of a colour vision problem as assessed by the Ishihara Colour Vision Test or of perceptual binding deficits (Parra et al., 2009a; Parra et al., 2010a; 2010b).

In the Shapes Only Condition participants were instructed that half of the time the shapes on the test would be the same as on the study display and for the other half of the time a brand new pair of shapes would be introduced. The task is to detect whether the test display contained the same or different shapes than the study display. Objects on the test display were presented in different positions from those in the study display. Like in the Perceptual Condition participants were asked not to concentrate on the location of the shapes.

In the Shape-Colour Binding Condition participants are requested to remember the colour-shape combination on the study display and then ought to detect whether on the test display the colour-shape combinations stayed the same or changed. Only a colour change could occur, shapes stay the same on the study and the test displays.

The response for the condition is given by pressing one of the keys on the computer mouse that would correspond with the answer "same" or "different". Viewing distance was not constrained.

2.1.5 Analysis

The data was analyzed using R-Studio (version 3.2.2) package "stats" (R Core Team, 2017). Performance was analysed with 2 (old young participants) X 2 (Shape Only Condition vs. Shape-Colour Binding Condition) factorial mixed ANOVA. The effect size was calculated using Cohen's d.

2.1.6 Results

Mean performance is shown on a **Table 2.1**. It shows that performance on Shapes only Condition by young and older was at ceiling. Mixed ANOVA confirmed that performance by older and younger adults did not differ: $F(1, 75) = 0.016$; $p = 0.90$; $d = 0.31$. Main effect of condition was significant: $F(1, 73) = 5.22$; $p = 0.02$; $d = 0.43$, however the interaction effect was not significant ($F(1, 73) = 0.73$; $p = 0.39$), confirming that there is no age effect on Shape-Condition Binding.

Table 2.1 Mean performance on TMB test by younger and older adults.

Younger (N = 20)		**Older (N = 20)**	
Shapes	Binding	Shapes	Binding
0.96 (0.05)	0.94 (0.05)	0.97 (0.03)	0.93 (0.09)

The effect of education on tasks performance.

As there was a significant difference in educational level between the two groups, this variable was entered as a covariate into the analysis. As it was already shown by Parra et al. (2011), the current results confirmed that education did not influence performance on the test: $F(1,73) = 1.02$, $p = 0.31$.

All participants were debriefed and asked about how they remembered stimuli. Some participants could not answer and said they "just tried to remember shapes and a combination shape-colour". Some participants gave names to shapes. Other participants on the Shape-Condition Binding Condition remembered only one shape and its colour combination and if on the task trial it was shown with a different colour their response would be "different".

2.1.7 Discussion of Experiment 1

The experiment investigated the effect of age on the TMB test. The aim was to replicate the experiment by Parra M.A. (2009) to show that there is no age effect on the performance on the TMB test. The results of the experiment confirm the previous finding that there is no difference in performance on the Single feature (Shapes) and Shape-colour Biding Condition between young and healthy older adults. Even though the Shape-Colour Binding Condition was more difficult to perform compared to the single feature condition by young and older adults, performance was still at ceiling. Resilience to the age effect of the task can provide a baseline for the performance and cut-off to determine cognitive impairment.

Participants for the experiment had a very high educational level and this could affect the performance on the test (better working capacity on highly educated people (Conway, Kane & Engle 2003), with the positive relationship between education and free recall (Grober et al., 1998)), however Parra et al, 2010 showed that binding is intact in the population with lower education confirming that performance on the TMB test does not depend on education level.

Experiment 2

Temporary Memory Binding Test presented via different means: PC, Flash-cards, or Tablet PC.

Currently the TMB test is available only as a Computer-based test. Alternative forms of this test would facilitate its widespread use. This series of studies was aimed at developing and comparing alternative forms of the TMB test: Flash-cards and a Tablet PC versions of the Computer PC test that would represent more portable alternatives for its use in clinical setting.

Flash cards vs. Computer PC TMB test

The aims of this experiment were to investigate whether the Flash-card version of the TB task results in overlapping outcomes compared to the Computerized version. However, the current experiment was aimed for the first time at introducing the Flash-cards version of the TMB. I therefore opted to relying on Shape-only and Shape-colour Binding for the initial comparison of the two versions of the task but to use all three conditions for validation purposes in the clinical study.

2.2.1. Participants

A total of 32 healthy volunteers entered the experiment. Sixteen were postgraduate psychology students (Mean age = 27, SD = 2.8; 11 males), 16 participants were older adults (Mean age= 70, SD = 7.7; 8 males) recruited from the University of Edinburgh volunteer panel. The two subgroups differed in terms of years of education (younger adults: M= 19.6, SD = 2.5; older adults: M= 14.3, SD = 3.2; $t(22)=5.00$, $p<0.05$). None of the younger or older participants was excluded due to poor colour vision. All participants gave their consent on participation in the study.

2.2.2 Materials

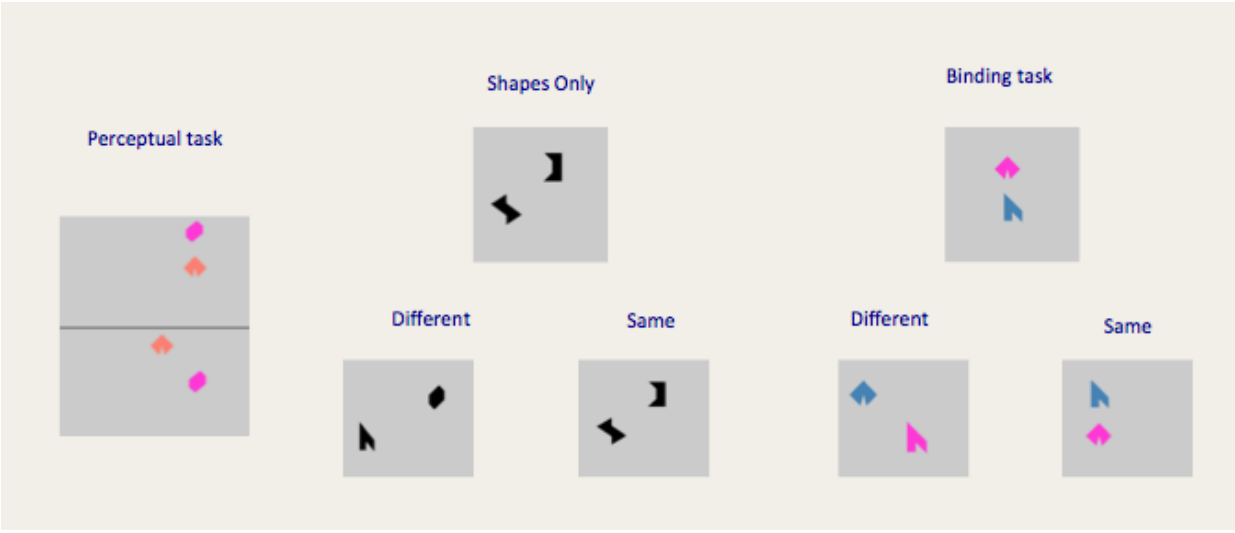
Materials are identical as in the Experiment 1 (See Section 2.1.3).

2.2.3 Procedures

The Computer PC version of the task is described in the Sections 2.1.3 and 2.1.4.

The Flash-cards consist of 118 cards in total that are bound together so each participant receives the same randomized order of the trials as opposed to the Computer PC in which trials are randomized across participants. The conditions and order of the conditions (Perception condition, Shapes only condition, and Shape-Colour Binding Condition) are the same as on the Computer PC (Figure 2.3). The Flash-card version of the TB task consists of 32 trials per condition that is similar to the Computer PC version. Each trial consists of two stimuli to be recognized as either the same or different. The first 10 cards are the stimuli for the perceptual condition and the procedure is similar to the computerized version that is described in section 2.1.3. As on the Computer PC if the participant performs at the 80% level or above the next condition is followed. The second part is the Shapes Only condition which consists of 64 cards: 32 cards for the study trials and 32 for the test trials. The third part with 64 cards consists of the Shape-Colour Binding Condition; half of the cards were for the study trials and the other half were for the test trials. The difference between the Computer PC and the Flash-cards task is that in the flash-cards version visual displays are presented with cards. The cards with trials are flipped over by a researcher with the pause between the study trial and the test trial around 2000 ms in order to give the participant some time to encode the stimuli. The participant gives responses verbally out loud and the experimenter records participant's responses using a scoring sheet.

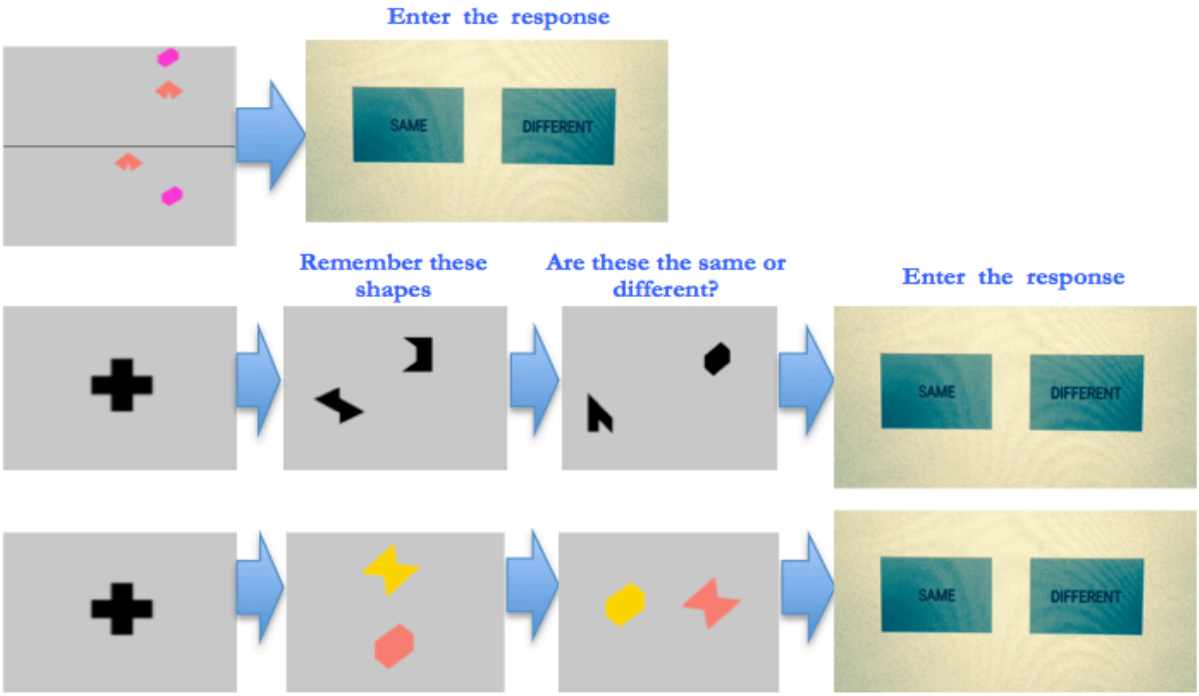
Figure 2.3. Three parts of the Flash-cards experiment.



An android NEXUS 10 Tablet PC is used for the tablet format of the TMB test. The Tablet PC has a 10.1 inches touch-screen display with a resolution of 2560-by-1600 and a pixel density of 330ppi. The conditions and order of the conditions is always the same and identical to the Computer PC experiment. The assessment starts from the perceptual condition, then the Shape

condition followed by the Shape-Colour Binding Condition. Each participant receives the same randomized sequence of trials, this is the difference between Tablet PC and Computer PC version of the experiment. The perceptual condition starts with the instruction display. If the participant performs at the 80% level or above the next condition is followed. There is one common instruction for shapes and binding conditions on the screen before the shape task. On the Shapes only and Shape-Colour Binding Condition the study display is presented for 2000 ms and then followed by the blank display of 1000 msec that is replaced by the test display. On the Tablet PC the responses are given by touching the screen with the option the "same" or "different" on the screen (Figure 2.4).

Figure 2.4. Three parts of the Tablet PC experiment.



On the following experiments I compare the different modes of the TMB test in pairs: the Flash-cards vs. Computer PC, Computer PC vs. Tablet PC, and Tablet PC vs. Flash-cards. The reason I do not present all three modes to the participant at the same time is that I accounted for the length of the experiment and the fact that participants may start to feel fatigue. I also considered the "practice" or learning effect that would occur if the participant performs all three modes of the test at the same time. In the experiments all modes of representation of the test were randomized across participants.

The following three experiments were set up to compare the different formats of the TMB test. I predicted that the mode of the test presentation would not affect the performance of the TMB test and it would retain its cognitive properties as with the Computer PC version of the test.

Participants for the experiment were allocated to each task in a counterbalanced manner: half of the participants received the Computer PC task first and then, after 30 minutes interval that was filled with cognitive tests, they performed the Flash-cards version of the task. The remaining participants received the tests in reverse order. The materials and procedure of the tasks are described in the section 2.1.3, 2.1.4, and 2.2.2.

English version of Addenbrooke's Cognitive Examination Revised Version (ACE-R) (Mioshi et al., 2006) was used to as a screen tool for cognitive impairment.

2.2.4 Analysis

The data was analyzed using R-Studio (version 3.2.2) package "lme4" (Bates, Maechler, Bolker, 2012) to perform linear mixed effect analysis of the impact of different modes of presentation (Flash-cards and Computer PC) on the performance of the TMB test by young and older adults. The model was used to estimate the degree to which age, education, and general cognitive functioning associated with performance. As fixed effects, I entered groups (Young vs. Old), Conditions (Shapes vs. Shape-Colour Binding), and Tasks (Flash-card vs. Computer PC) with interaction terms between these variables. As a random effect the model had intercepts for participants. I run the same set of models, but controlling for the effects of education and general cognitive functioning.

2.2.5 Results

Healthy older participants showed high average performance on the ACE-R ($M = 96.94$, $SD = 3.93$).

Table 2.2 shows proportions of the correct responses across tasks and conditions given by both groups. It shows that for young and older adults performance on the Shape Condition was at ceiling whether it was on the Computer PC or on the Flash-Cards presentation. Mean performance of older participants on Shape-Colour Binding on the Computer PC and Flash –cards was lower than that by younger adults.

Table 2.2 The mean performances (correct responses) by younger and older adults on the Computer PC and Flash-cards tasks

Younger (N = 16)				Older (N = 16)			
Shapes		Binding		Shapes		Binding	
Computer PC	Flash-cards	Computer PC	Flash-cards	Computer PC	Flash-cards	Computer PC	Flash-cards
0.96	0.98	0.95	0.97	0.96	0.98	0.89	0.86
(0.03)	(0.02)	(0.03)	(0.03)	(0.03)	(0.02)	(0.1)	(0.09)

The estimates of fixed effects revealed that mean performance on the Flash-cards and on the Computer PC did not differ. However, older adults performed significantly differently from younger adults on the Shape-Colour Binding Condition: main effects of Group and Condition were significant. Shape-Colour Binding Condition was more difficult to perform for older adults on Flash-cards and Computer PC.

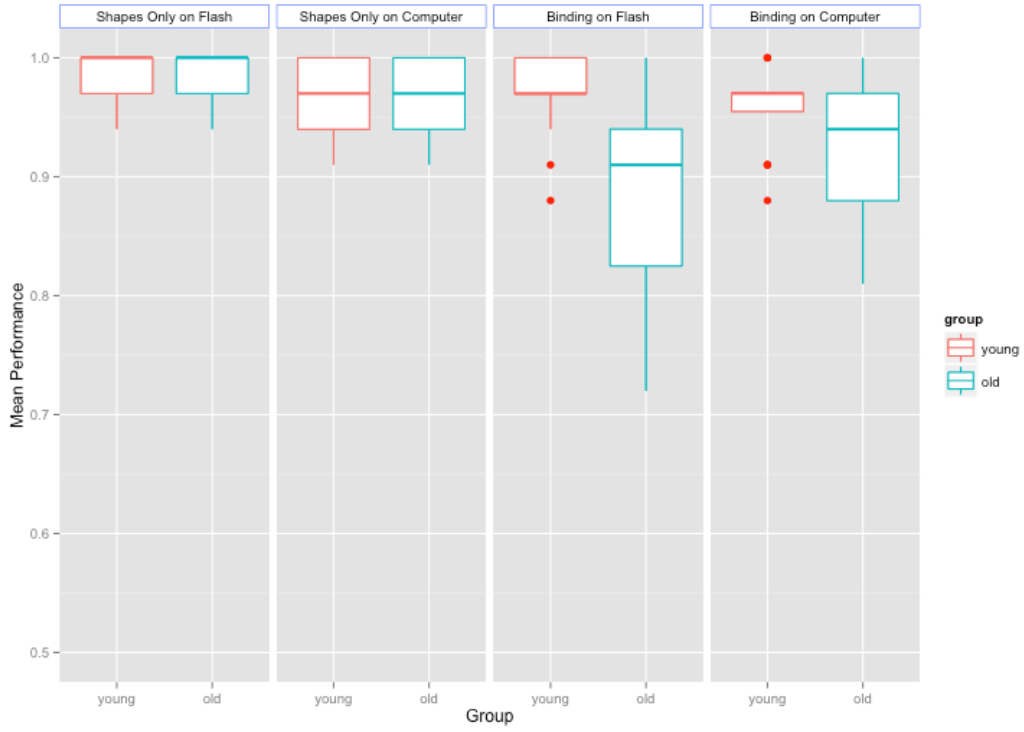
Table 2.3 Estimates of the fixed effects and interaction effects.

	B	Std.Error	DF	t-value	p-value
Flash-Cards	0.013	0.020	30	0.66	0.52
Shapes Only	0.008	0.020	60	0.37	0.7
Old participants	-0.060	0.020	30	-2.88	0.007
Flash x Shapes	0.001	0.028	60	0.33	0.74
Flash x Old	-0.043	0.028	30	-1.52	0.13
Shapes x Old	0.055	0.028	60	1.97	0.053
Flash x Shapes x Old	0.047	0.039	60	1.17	0.24

As there was a difference in years of education between younger and older adults, education was included as a predictor of the performance on the TMB test. Education did not have an effect either on the Task (χ^2 (11)=1.2, p = 0.54) or on the Conditions (χ^2 (12)=0.96, p = 0.32).

Regression model was checked on the influential cases (a value with high leverage on the regression line and Cook's D). There were two participants from the older group, who performed significantly poorer that the rest of the group (cases 22 and 25 with the performance on the Shape-Colour binding Condition 0.63 (on the Flash-cards) and 0.56 (on the Computer PC) respectively). I checked whether exclusion of those cases would change the model prediction. I excluded those cases from the analysis. The mean performance can be seen in the **Fig. 2.5.**

Fig 2.5 Mean performance by the groups with influential cases excluded from the analysis.



These two cases were excluded from the analysis. The fixed estimates of the model (**Table 2.4**) show that the mean performance on Shapes Only did not differ from the mean performance on the Shape-Binding Condition. Older participants' performance did not differ from younger participants. The interaction effect was also non-significant: older adults' mean performance on the shapes did not differ from the mean performance on the binding condition.

Table 2.4 Estimates of the fixed effects and interaction effects

	β	Std. Error	DF	t-value	p-value
Flash-Cards	0.006	0.035	17	0.17	0.86
Shapes Only	0.018	0.035	34	0.51	0.61
Old participants	-0.041	0.028	17	-1.42	0.17
Flash x Shapes	-0.006	0.049	34	-0.12	0.9
Flash x Old	-0.054	0.04	17	-1.32	0.2
Shapes x Old	0.03	0.04	34	0.71	0.48
Flash x Shapes x Old	0.073	0.058	34	1.26	0.21

2.2.6 Discussion

The results of the experiment indicate that there is no significant effect of the mode of presentation (Computer PC or the Flash-cards) on the performance between young and older participants. After looking at the errors participants committed during the task and in particular the Shape-Colour Binding, I noticed that the very first trials on the Flash-cards were the most difficult (generated the most mistakes) not only for old, but also for young participant. On the debriefing session participants confirmed that they fully understood the aim of task only after a couple of trials. The instructions for Flash-cards were given verbally by the researcher and there were no written instructions or any visual aids presented to the participants, I hypothesized that if the instruction for the Flash-cards will be displayed on the "run-in cards", performance on the test will improve. To check this hypothesis I introduced the "run-in cards" in the Experiment 3.

Experiment 3

Flash-cards with "run-in cards" vs. Computer PC

Participants are presented with a series of run-in trials until the examiner is satisfied that they fully understood the instructions of the task.

2.3.1 Participants

Thirty-two new participants entered the experiment. Sixteen were postgraduate psychology students (11 male and 5 females) who volunteered for the study and gave their informed consent. Their mean age was 27 (SD = 2.8). The other 16 participants (8 male and 8 females) were older adults recruited from the University of Edinburgh volunteer panel with mean age 70 (SD = 7.7). The two subgroups differed in terms of years of education (young adults: M= 19.6, SD = 2.5; older adults: M= 14.3, SD = 3.2; t (22)=5.00, $p<0.05$).

2.3.2 Stimuli and procedure

In the experiment the "run-in cards" were introduced as an aid to familiarise the participant with the task. Run-in cards were presented as A4 format explanatory cards with the same Conditions as on the Flash-cards: Perceptual, Shapes Only, and the Shape-Colour Binding Condition. Before each condition these cards were presented to the participant with the verbal explanation of each

Condition. If the participant confirmed that he or she understood the instruction the test on the Flash-cards would follow.

2.3.3 Analysis

The data was analyzed using R-Studio (version 3.2.2) package "lme4" (Bates, Maechler, Bolker, 2012) was used to perform linear mixed effect analysis of whether the introduction of the "run-in cards" for the Flash-cards improved the performance of the TMB test. As fixed effects, I entered Group (young vs. old), Condition (Shapes Only vs. Shape-Colour Binding Condition), and Task (performance on the Flash-cards with the "run-in cards" and Computer PC) with interaction term between these variables; as random effect was intercepts for participants.

2.3.4 Results

The mean performance on the task and conditions is summarized in the Table 2.5 it shows that there was a significant improvement in the performance on the test when I introduced the "run-in cards"

Table 2.5. Mean proportion of correct recognition on the TMB test by two groups.

Group	**Computer PC**		**Flash-Cards**	
	Shapes	Binding	Shapes	Binding
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Older (N= 16)	0.96 (0.03)	0.90 (0.1)	0.98 (0.01)	0.96 (0.06)
Younger (N = 16)	0.96 (0.03)	0.95 (0.03)	0.98 (0.02)	0.98 (0.04)

The average mean difference between two modes of the test representation was 0.03 of the scale range. In other words, on a 0 to 1 scale, the mean of the scores from the Flash-card measure was 0.03 points higher than the mean of the scores from the Computer PC version.

Estimates of the fixed effects revealed that mean performance on the Flash-card and on the Computer PC did not differ ($\beta = 0.018$, $P = 0.19$); the Bayes factor (BF) (for a sample difference between Computer PC and the Flash-cards of 0.93, SE = .02) was 0.77 ($1/3 > BF < 3$), which is strong evidence supporting the null versus alternative hypotheses. This indicates that the mode of the presentation of the test did not impact on the performance on TB task. Mean performance on Shapes only was not significantly different from the mean performance on the Shape-Colour

Binding Condition (β = -0.007, P = 0.59), BF = 1.91 (M = .96, SE = 0.6). The older adults' mean performance did not differ from the younger adults' performance on the TB task (β = -0.003, P = 0.79), BF = 1.49 (M =0 .95, SE = 0.65), confirming the lack of age-related effect on the test, independently of the mode of the presentation. All the interactions were far from significance.

2.3.5 Discussion

The aim of the experiment was to check whether inclusion of the "run-in cards" for the Flash-Cards would improve the accuracy on the TMB test. As the experiment shows, inclusion of the cards for the Flash-Cards test improves the understanding of the task and significantly improves TMB performance.

Mean differences between the Flash-card and Computer PC version were small, suggesting equivalence. As predicted from previous experiments (Brockmole et al., 2008; Isella et al., 2015; Parra et al., 2009b; Read et al., 2016; Rhodes et al., 2015), no effect of age emerged and with two items per trial performance was near ceiling in both groups which, should there be a fundamental impairment of TMB in AD, will maximize sensitivity.

During the debriefing session younger volunteers stated that they felt more comfortable with the Computer-based task whereas older participants found the Flash-card version friendlier. Some older participants on the Computer PC version of the tasks noticed their limited computer literacy and questioned their performance. This should be taken into consideration in order to improve compliance in older people. In sum, the Flash-cards version, which is portable, inexpensive, and accommodates clinical needs proved to be a sound alternative to the Computer PC version of the TB task.

Experiment 4

Tablet PC vs. Computer PC

In this experiment the Tablet PC mode of representation of TMB was compared to the computerized TMB test. The aim of the experiment is to test if the two means of TMB assessment produce equivalent scores.

2.4.1 Participants

A new sample of 32 participants entered the experiment. Sixteen participants were postgraduate psychology students (8 males and 8 females) who volunteered for the study and gave their informed consent with mean age of 23.38 (SD = 4.03) and average education of 16.25 years (SD = 3.04). The other 16 participants were older adults (6 males and 10 females) that were recruited from the University of Edinburgh volunteer panel with mean age of 72.44 (SD = 6.68), with the mean of years of education of 17.19 (SD = 5.18). The two subgroups did not differ in terms of years of education (t (22) = -1.27, p = 0.20). Participants also did not differ in general cognitive functioning (ACE for young adults: M = 97.25, SD = 2.43; older adults: M = 95.94, SD = 3.85; t (22) = 1.59, p= 0.12). None of the young or old participants were excluded due to poor colour vision: on the Perceptual Condition on the Computer PC and on the Tablet PC all performed above the 80% level.

2.4.2 Procedure

Participants for the experiment were allocated to each task in a counterbalanced manner: half of participants received the Computer PC task first and then, after a 30 minutes interval that was filled with cognitive tests, they performed the Tablet PC version of the task. The remaining participants received the tests in the reverse order. Before each task participants read the instruction for each task on the Computer PC or Tablet PC screen. The materials and procedure of the tasks are described in the section 2.1.3, 2.1.4, and 2.2.2.

2.4.3 Analysis

The data was analysed using R-Studio (version 3.2.2) package “lme4” (Bates, Maechler, Bolker, 2012) to perform linear mixed effect analysis of the impact of different mode of presentation (Tablet PC and Computer PC) on the performance of the TMB test by young and older adults. As fixed effects were Group (young vs. old), Conditions (Shapes Only vs. Shape-colour Binding Conditions), and Task (Tablet PC vs. Computer PC) with interaction term between those variables, as random effect I had intercepts for participants. I run the same set of models, but controlling for the effects of education and general cognitive functioning.

2.4.4 Results

Table 2.6 shows the proportion of the correct responses on the Tasks and Conditions. Performance on the Computer PC and on the Tablet PC by young adults was at ceiling in both Conditions. For older adults Shape Only Condition was at ceiling on both Computer PC and the Tablet PC, however on the Shape-Colour Binding Condition on both Tablet PC and Computer PC older participants made more mistakes than on the Shapes Condition.

Table 2.6 Mean performance (correct responses) on the Computer PC and on the Tablet PC by younger and older adults

Younger (N = 16)				**Older (N = 16)**			
Shapes		Binding		Shapes		Binding	
Computer PC	Tablet PC	Computer PC	Tablet PC	Computer PC	Tablet PC	Computer PC	Tablet PC
0.96 (0.04)	0.98 (0.03)	0.97 (0.03)	0.97 (0.04)	0.97 (0.03)	0.97 (0.04)	0.92 (0.07)	0.88 (0.12)

Obtaining the estimates of the fixed effects revealed that the mode of representation (Tablet PC or Computer PC) did not affect the performance on the TMB test. Mean performance on the Shape-Colour Binding Condition was not significantly different from the mean performance on the Shape Only Condition. The direction of the association indicated that older participants overall performed worse than younger adults. Performance on the Shapes Only Condition for older adults was easier than on the Shape-Colour Binding condition **(Table 2.7)**.

Table 2.7 Estimates of the fixed effects and interaction effects

	β	**Std.Error**	**DF**	**t-value**	**p-value**
With cards	0.0012	0.019	30	0.66	0.94
Binding condition	-0.004	0.019	60	-0.23	0.81
Old participants	-0.049	0.021	30	-2.35	0.02
Tablet x Shapes	0.0125	0.027	60	0.46	0.64
Tablet x Old	-0.039	0.027	30	-1.44	0.16
Shapes x Old	0.0575	0.027	60	2.13	0.03
Tablet x Shapes x Old	0.0243	0.038	60	0.64	0.52

I checked the regression model on the influential cases (a value with high leverage on the regression line and Cook's D). There were two participants from the older group, who performed significantly poorer than the rest of the group (cases 50 and 89 with the performance on the binding task 0.60 (on the Tablet PC)). I checked whether exclusion of those cases would change the models prediction. When I excluded these two cases from the analysis, the fixed estimates of the models shows that older participants' mean performance was worse than mean performance of younger participants ($\beta = -0.05$, $p < 0.01$). The group – condition interaction effect was significant ($\beta = -0.05$, $p = 0.008$): older adults' mean performance on the Shape-colour Binding Condition was significantly worse that the mean performance of younger adults on the Condition.

I checked if the education level or level of general cognitive functioning influenced the result. When I entered the education level and general cognitive functioning, those variables did not improve the model fit: education level did not affect the performance on the task (Tablet PC vs. Computer PC) (χ^2 (14) = 4.20, p = 0.12) or condition (Shapes Only vs. Shape-Colour Biding) (χ^2 (17) = 1.21, p = 0.74). There was no effect of general cognitive function on performance on the conditions (χ^2 (25) = 1.33, p = 0.85).

2.4.5 Discussion

Results indicate that there is no significant effect of the mean of testing (whether TMB test was on the Computer PC or Tablet PC) and therefore I confirmed that the Tablet PC version of the TMB test is a good alternative to the Computer PC version of the test. When debriefing older adults I noticed that they were more comfortable working with a Computer PC version of the test than with the Tablet PC. In addition, participants pointed out that all the instructions for both Shapes Only and Shape-Colour Binding Conditions on the Tablet PC version were given at the beginning of the test. They had to remember the instructions about the Shape-Colour Binding Condition while performing the Shapes Only Condition. I hypothesized that this could cause the errors on the Shape-Colour Binding Condition.

To address the last issue, I introduced the "run-in cards" to familiarise participants about the task to allow practicing before each condition. I hypothesized that the inclusion of the "run-in cards" would improve the accuracy on the TMB test and specifically on the Shape-Colour Binding Condition.

Experiment 5

Tablet PC with "run-in cards" vs. Computer PC

2.5.1 Participants

Twelve new participants entered the experiment. Six were postgraduate psychology students (2 male and 4 female) who volunteered for the study and gave their informed consent. Their mean age was 23.67 (SD = 2.6). The other 6 participants (3 male and 3 females) were older adults recruited from the volunteer panel with mean age 72 (SD = 5.04). The two subgroups did not differ in years of education (young adults: M= 17.83, SD = 2.2; older adults: M= 20.5, SD = 6.34; t (13.62)=-1.37, p = 0.19). The two subgroups did not differ in terms of their general cognitive function: ACE (young adults: M= 96.83, SD = 1.75; older adults: M= 95.83, SD = 4.57; t (14.15)=0.708, p = 0.49). None of the young or old participants was excluded due to poor colour vision: on the Perceptual Condition on the Computer PC and on the Tablet PC all performed above the 80% level.

2.5.2 Stimuli and procedure

In the experiment I introduced the "run-in cards" that were used in the Experiment 3 that are an aid to familiarise the participant with the task. Stimuli and procedure were explained in the Experiment 2.1.3, 2.1.4 and 2.2.2.

2.5.3 Analysis

The data was analysed using R-Studio (version 3.2.2) package "lme4" (Bates, Maechler, Bolker, 2012) was used to perform linear mixed effect analysis of whether introduction of the "run-in cards" for the Flash-Cards impact performance of the TMB test. As fixed effects, I entered groups (young vs. old), conditions (shapes vs. binding task), and tasks (performance on the Tablet PC with "run-in cards" and Computer PC) with interaction term between those variables. As random effect I had intercepts for participants.

2.5.4 Results

The mean performance (correct responses) on the Tablet PC with "run-in cards" and on the Computer PC can be seen in the **Table 2.8.** The performance means improved and were at ceiling for both groups regardless of the Task and Conditions.

Table 2.8. Mean performance (correct responses) on the Tablet PC with "run-in cards" and on the Computer PC.

	Tablet PC with Cards		**Computer PC**	
	Shapes	Binding	Shapes	Binding
Old (N = 6)	0.98	0.92	0.97	0.95
Young (N = 6)	0.99	0.99	0.98	0.98

Mean performance on the Tablet PC and on the Computer PC did not differ ($\beta = 0.015$, $t = 0.77$, $p = 0.45$); mean performance on the Shapes Only Condition was not significantly different from the mean performance on the Shape-Colour Binding Condition ($\beta = 0.005$, $t = 0.25$, $p = 0.8$). Older adults' mean performance did not differ from the younger adults performance on the TMB test ($\beta = -0.01$, $t = -0.47$, $p = 0.64$).

2.5.5 Discussion

The aim of the experiment was to check whether inclusion of the "run-in cards" would improve the accuracy on the TMB test. As the experiment shows that inclusion of the "run-in cards" to the Tablet PC version of the TMB test significantly improves the TMB test performance.

Experiment 6

Flash-cards vs. Tablet PC

2.6.1 Participants

Thirty-two new participants entered the experiment. Sixteen were postgraduate psychology students (8 male and 8 female) who volunteered for the study and gave their informed consent with mean age of 23.81 (SD = 4.6). The other 16 participants (4 males and 12 females) were older adults that were recruited from the volunteer panel with mean age of 71 years old (SD = 8.65). Younger and older adults did not differ in terms of their years of education (young adults: M= 17.12, SD = 1.5; older adults: M= 16.5, SD = 4.5; $t(126) = 1.08$, $p = 0.28$) and general cognitive

functioning: ACE (young adults: M = 97.35, SD = 2.44: old adults M = 95.50, SD =5.3; t-test (22)= - 0.95, *p*=0.35). None of the young or old participants was excluded due to poor colour vision: on the Perceptual Condition on the Tablet PC and on the Flash-cards all performed above the 80% level.

2.6.2 Procedure

Participants for the experiment were allocated to each task in a counterbalanced manner: half of the participants received the task on the Flash-cards first and then, after a 30 minutes interval that was filled with cognitive tests, they performed the Tablet PC version of the task. The remaining participants received the tests in reverse order. The procedure of the tasks is described in sections 2.1.3 and 2.2.2. We included the "run-in cards" that were designed for the previous experiments in the procedure of the test.

2.6.3 Analysis

The data was analysed using R-Studio (version 3.2.2) packages "lme4" (Bates, Maechler, Bolker, 2012) to perform linear mixed effect analysis of the impact of different mode of presentation (Flash-Cards and Tablet PC) on the performance of the TMB test by young and older adults. As fixed effects, I entered Groups (young vs. old), Conditions (Shapes Only vs. Shape-Colour Binding), and tasks (Flash-cards vs. Tablet PC) with interaction terms between those variables; as random effect I had intercepts for participants.

2.6.4 Results

The mean performance (correct responses) on the task is presented in the **Table 2.9.**

Table 2.9 Proportion of correct responses on the Flash-cards and Tablet PC by two groups.

Young (N = 16)				**Old (N = 16)**			
Shapes		Binding		Shapes		Binding	
Flash-cards	Tablet PC	Flash-cards	Tablet PC	Flash-cards	Tablet PC	Flash-Cards	Tablet PC
-0.98 (0.02)	0.98 (0.02)	0.98 (0.04)	0.98 (0.04)	0.98 (0.01)	0.97 (0.04)	0.98 (0.05)	0.94 (0.10)

The estimates of the fixed effects show that the main effect of the Task was not significant (β = 0.018, t = 0.03; p = 0.97) meaning that these two means of assessment of the TMB test produce the same results. Mean effect of group was not significant (β = -0.02, t = 1.67; p = 0.09), as well as

mean performance on the Shapes Only Condition was not significantly different from the mean performance on the Shape-Colour Binding Condition ($\beta = 0.02$, $t = 0.81$; $p = 0.41$). None of the interaction also did not reached significance.

2.6.5 Discussion

Results of the experiment indicate that there is no effect on the performance between young and older adults on the Tablet PC or Flash-cards. That is supported by our hypothesis that these two forms of assessment are alternatives to each other.

There was no age affect on the performance between two groups. Both young and older adults performed better on the shapes and poorer on the binding task.

Additional Analysis

Flash-cards vs. Tablet PC vs. Computer PC

I combined Experiments 3, 5, and 6 to compare performance on the TMB test across all modes of presentation.

2.7.1 Participants

Thirty-eight participants were postgraduate psychology students (20 male and 18 female) with mean age of 25.05 (4.01) years old and 38 older participants (15 males and 23 females) with mean age of 70.74 (7.58) years old. Younger and older adults differ in terms of their years of education (young adults: M= 18.29, SD = 2.34; older adults: M= 16.24, SD = 4.80; t (1, 74) = 2.37, *p*= 0.02), but not general cognitive functioning: ACE (young adults: M = 97.58, SD = 2.19: old adults M = 96.39, SD = 4.42; t-test (1,74)= 1.48, *p*=0.14).

2.7.2 Analysis

The data was analysed using R-Studio (version 3.2.2) packages “lme4” (Bates, Maechler, Bolker, 2012) to perform linear mixed effect analysis of the impact of different mode of presentation (Computer PC, Flash-Cards and Tablet PC) on the performance of the TMB test by young and older adults. As fixed effects, I entered groups (young vs. old), conditions (Shapes only vs. Shape-

Colour Binding task), and tasks (Computer PC vs. Flash-Cards vs. Tablet PC) with interaction term between those variables; as random effect I had intercepts for participants.

2.7.3 Results

Mean performance (correct responses) on the task can be seen in the **Table 2.10.** The scores on all modes of TMB test presentation were at ceiling with very little variability.

Table 2.10 Mean performance (correct responses) on the Flash-cards, Tablet PC, and Computer PC

Young						Old					
Shapes			Binding			Shapes			Binding		
Flash-cards	Tablet PC	Computer PC	Flash-cards	Tablet PC	Computer PC	Flash-cards	Tablet PC	Computer PC	Flash-Cards	Tablet PC	Computer PC
0.98 (0.02)	0.99 (0.02)	0.96 (0.03)	0.97 (0.02)	0.99 (0.04)	0.95 (0.03)	0.98 (0.01)	0.97 (0.03)	0.96 (0.03)	0.95 (0.05)	0.92 (0.05)	0.91 (0.10)

Obtaining the estimates (Table 2.11) of the fixed effects revealed that there was no difference on TMB performance regardless on which method of assessment the test was performed. Shape Only and Shape-Colour Binding Conditions were equally difficult for young and older adults. None of the interactions reached significance.

Table 2.11 Estimates of the fixed effects and interaction effects

	β	Std.Error	DF	t-value	p-value
Task	0.01	0.02	72	0.65	0.52
Condition	0.04	0.06	72	0.77	0.44
Group	0.002	0.03	72	0.07	0.93
Task x Condition	-0.01	0.03	72	-0.22	0.82
Task x Group	-0.03	0.02	72	-0.19	0.84
Condition x Group	-0.06	0.04	72	-1.52	0.13
Task x Condition x Group	0.01	0.02	72	0.50	0.61

2.7.4 Discussion

Results of the experiment indicate that there is no difference in performance between young and older adults regardless whether the test was performed on the Computer PC, Tablet PC or Flash-

cards. That is supported by our hypothesis that these three forms of assessment are alternatives to each other and can be used in the TMB assessment.

Older adults' performance was near ceiling; this can raise the question on whether an age effect might have been found had I had adapted the task to remove these ceiling effects. There is a considerable amount of research showing that there is no age effect on TMB tasks (Allen et al., 2013; Bastin, 2017; Brockmole et al., 2008; Brown & Brockmole, 2010; Brown et al., 2017; Hoefeijzers et al., 2017; Isella et al., 2015; Parra et al., 2009; Rhodes et al, 2015; Rhodes et al. 2017; van Geldorp et al, 2014). In the studies by Parra et al (2009) and by Rhodes et al (2015), the authors have used an increased memory demand arrays of 3, 4, and 6 coloured shapes. In addition to the increased memory load they manipulated presentation time (Rhodes et al., 2016) and mixed trial types (Rhodes et al., 2017). None of these variables were found to produce an age-related binding deficit. Therefore, the reduction of number of items is unlikely to have produced an age affect once we account for ceiling effect.

General discussion.

The use of Computer PC or other computerised mediums of assessment (i.e. smart phones or Tablet PC) in comparison to the paper version of assessment increasingly attracts research interest. This is not in term of which form would dominate or if I need to replace all paper forms of testing into computerised ones ("paperless office" by Sellen & Harper, 2002) but whether these forms are equivalent to each other. The main aim of the experiments was to show that three methods of assessments of the TMB test (Computer PC, Tablet PC, and Flash-Cards) are alternatives to each other. In the series of experiments I showed that three forms of testing the TMB test yielded the same outcome for a single feature condition and for the Shape-Colour Binding condition. During the debriefing session younger volunteers stated that they felt more comfortable with the computer-based tasks whereas older participants found the Flash-Card version is friendlier for them. Some older participants noticed that they have limited computer literacy and questioned their performance and favoured more conventional forms pencil methods of assessment. This finding should be taken into consideration when testing older people. Tablet PC and Flash-cards are proved to be the alternative to the Computer PC form of assessing of the test and achieve the same outcome. Tablet PC and Flash-card versions have a main advantage over the Computer PC version as these are more portable forms of assessment and therefore can accommodate clinical

needs. In addition to that, Flash-cards are more affordable and cost effective form of assessment. For the future experiments it should be noted that the Flash-cards are required to use the "run-in cards" before each trials that would considerably reduce the amount of errors at the beginning of the tasks. These series of experiments showed that without the cards performance of older adults is poorer on the binding task compared to younger adults.

Even though I showed that these forms of assessment are equal in terms of the test score outcomes, there are advantages and disadvantages of each method. Advantages of the computer-based assessment (Computer PC and Tablet PC) in the standardization of the testing environment. In another way, Conditions of the TMB test are presented in the same way and in the same time. Errors in administration of the test are minimized as well as testing bias. Another benefit is in the accurate timing of the procedure and automatic scoring of the data that is again reducing human error. Storage of the big data set and easy access to it, as well as recording into the "ready-to-analyse format" is another advantage. Additional benefit of the Tablet PC version over the Computer PC version of the test is in its portability that is a great advantage, should the test be performed outside clinical or laboratory settings.

There are number of disadvantages of the computerized methods over the Flash-card one. First of all, this is in the need of the computer proficiency as computer's and tablet's software and hardware can be problematic and a subject of freezing and crushing. The person, who is assessing, should be computer knowledgeable and be able to fix any problems that can arise during the testing. Some of the older participants complained during the test that staring at the screen was tiring and uncomfortable for eyes, that this discomfort jeopardizes their concentration on the test. The other point of concern of the computerized methods is confidentiality, as most computers require Internet access for storage of large data sets. The last disadvantage is the personal preferences. As I already noted, older participants felt that Flash-card version of the test was more comfortable and user friendlier for them. In the contrary, younger participants preferred Tablet PC and Computer PC versions.

Flash-card version immediate benefit is in its affordability and portability. This is very beneficial for clinical and research purposes as it requires minimum financial impact, and can be used outside clinical and research facilities. Flash-cards version would be more advantageous for testing people with cognitive impairment as it will minimize anxiety of computer illiteracy that some of the patients might have.

Chapter III

ERP components of the Temporal Memory Binding (TMB) task in younger and older adults

3.1 Introduction

The general decline of cognitive performance with age is a well-documented and broadly researched phenomenon (Deary et al. 2007; Salthouse, 1996, Johnson, Logie, & Brockmole, 2010). WM capacity is reduced in older adults relative to younger adults (Park et al., 2002; Logie & Maylor, 2009), however Binding within-object features (e.g., shape and colour) is generally unaffected by normal ageing (Brockmole et al., 2008; Parra et al., 2009; Parra, Abrahams, Logie, & Della Sala, 2009; Brown & Brockmole, 2010, Rhodes et al., 2015; Isella, Molteni, Mapelli, & Ferrarese, 2015; Peterson & Naveh- Benjamin, 2016; Rhodes, Parra, & Logie, 2016).

In the previous chapters, I showed that the Binding within-object features process (e.g., shape and colour) is generally unaffected by normal ageing (Brockmole et al., 2008; Parra et al., 2009; Parra, Abrahams, Logie, & Della Sala, 2009; Brown & Brockmole, 2010, Rhodes et al., 2015; Isella, Molteni, Mapelli, & Ferrarese, 2015; Peterson & Naveh- Benjamin, 2016; Rhodes, Parra, & Logie, 2016). This experiment was set up to investigate whether the recruitment of additional areas in older adults aids their ability to perform the task successfully. According to Park and Reuter-Lorenz's (2009) Scaffolding Theory of Aging and Cognition (STAC) as a reaction to the increase task difficulty and in order to maintain their overall task outcome older adults supplement their performance through the recruitment of compensatory neural pathways. If this is true for successful performance on TMB task by older adults, we should observe compensatory recruitment of more areas of the brain compared to younger adults. I will first elaborate on the STAC.

Scaffolding Theory of Cognitive Ageing

More and more research is trying to explain age-related declines in cognitive tasks by behavioural and functional changes in cognition. The Scaffolding Theory of Age and

Cognition (STAC) (Park & Reuter-Lorenz, 2009) postulates that in response to behavioural ageing such as decrease in processing speed, inhibitory process, decline in storage systems, the ageing brain increases frontal activation that is a hallmark of cognitive ageing. The authors suggest that the compensatory recruitment of the areas such as the pre-frontal cortex is a healthy response to the challenge of cognitive ageing that aids successful task completion. STAC is similar to Stern's cognitive reserve theory (2002). Stern suggested a response to brain damage may be the compensatory recruitment of neural structures not normally used for given tasks.

STAC is based on the results of series functional imaging studies of ageing, that is the decrease in brain volume in the caudate, hippocampus, and the cerebellum are compensated for by increased bilateral activation in the pre-frontal cortex (PFC). Cabeza et al. (2004) and Reuter-Lorenz et al. (1999) in their experiments using measures of verbal working and long-term memory examined pre-frontal cortex activation in young and older adults. They demonstrated left-sided pre-frontal activation in the younger adults, whilst the older adults displayed increased bilateral activation of these areas as compensation to the increased demands.

Exploring if in fact in order to complete task successful, older adults recruit more bilateral frontal areas I employed Event-related potentials (ERPs).

Portable low-density EEG

Monitoring human brain activity has great potential in helping us understand the functioning of our brain. Non-invasive surface EEG is the dominant modality for studying brain dynamics and performance in real-life interaction of humans with their environment. ERP provide an affordable measure of neurological functioning.

Published works on EEG-based AD diagnosis have typically relied on EEG setups ranging from 16, 20, 32, 64, or 128 electrodes. Such systems are cumbersome and time consuming to place on the participants, sometimes taking up to one hour only for the EEG headgear preparation. This can have serious outcomes especially for frail elderly and patients with AD diagnosis, as drowsiness, fatigue, stress, and/or alternate mental states may alter EEG patterns, thus deteriorating diagnostic accuracy. Moreover, such medical-grade systems are hard to

transport and expensive to fund in low- and middle-income countries, as well as in remote and rural regions of developed countries.

Over the last few years, the miniaturization of EEG equipment has led to the proliferation of portable wireless headsets. Such headsets have several interesting advantages compared with their research-grade counterparts, such as: (1) reduced hardware-related stress to the user during headset preparation and during recordings, thus reducing distractions and allowing longer recordings in more natural positions or activities, such as book reading or TV watching, (2) since wires are eliminated, transportation of these devices is much easier and recording and processing of EEG signals has become a reality, and lastly, (3) the lower power consumption requirements have allowed for long-term recordings while subjects are performing their daily activities, thus making ambulatory EEG practical.

As such, it is important that we explore the benefits of using low-density portable systems for AD diagnostic purposes. This experiment presents the implementation of the low-density EEG setup comprised of 7 electrodes.

In this experiment the Event Related Potentials (ERP) elicited during a TMB task were analyzed to investigate the hypothesis whether temporarily holding feature bindings is neurally costlier than holding individual features. Previous behavioural studies investigating this hypothesis have yielded negative findings (Allen, Baddeley, & Hitch, 2006; Karlsen, Allen, Baddeley, & Hitch, 2010). Yet biological evidence drawn from fMRI showed a costly binding process relative to single feature processing (Parra et al., 2014). To date, no electrophysiological study has addressed this hypothesis

3.2 Materials and Methods

3.2.1 Participants

Twenty-five young undergraduate students (age M= 26.2, SD=4.2) from the University of Edinburgh and 20 healthy older participants (age M=69.8, SD=7.5) recruited from the University of Edinburgh psychology research volunteer panel and from the community took part in the study. All participants reported no history of neurological or psychiatric diseases. They also reported normal colour vision. All participants provided written informed consent. The Ethics of the National Health Services (NHS-MREC) and Lothian REC (MREC Ref.

06/MRE07/40; Lothian R&D Ref. 2006/P/PSY/22) approved the study.

3.2.2 Neuropsychological assessment

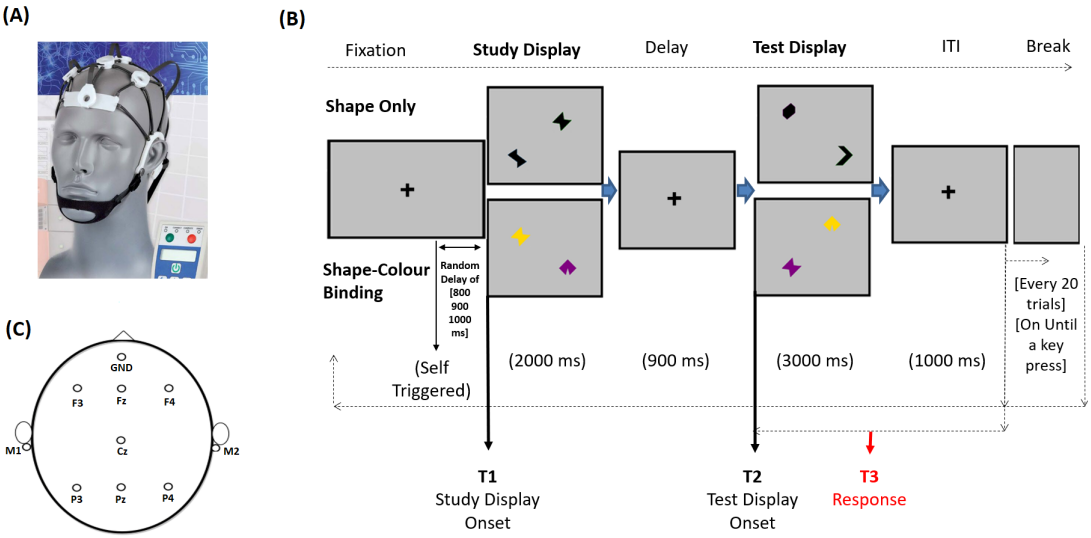
The general cognitive status of participants was examined with the Addenbrooke's cognitive examination-revised (ACE-R) (Mioshi et al., 2006). All participants score on the ACE-R above 95. Years of education differ significantly between groups (Older: M=16.60, SD=2.66; Younger: M =19.40, SD= 2.89), W =114, p=0.002.

3.2.3 The Memory Binding Task

The TMB task is described in the Sections 2.1.3 and 2.1.4. In this experiment I used two Conditions: the first one was a single feature Shape only condition (100 trials) that was followed by feature binding Shape-Colour Binding Condition (100 trials). Trials in both conditions were presented with two items. Before each condition participants were presented with 20 run-in trials so the participants could fully understand the instructions of the task.

Trials in each condition are fully randomized across participants. Each condition begins with a fixation cross-centred on a light grey background shown for 1000 msec. That is followed by the *study display* for 2000 msec. After a 1000-msec retention interval, the *test display* is presented after which the participants responded. Responses are given by pressing one of the keys on the computer mouse that would correspond with the answer "same" or "different" (See Figure 3.1. B).

Figure 3.1. (A) COGNISION® is a portable EEG system aimed at providing EEG-based biomarker evidence. With the support from Neuronetrix, we incorporated the TMB to COGNISION® to undertake the present study. (B) Experimental design. Example of a trial sequence during the Shape Only and Shape-Colour Binding Conditions of TMB test. (C) EEG setup used to collect ERP data.



Electroencephalogram (EEG) recording

Electroencephalographic (EEG) activity was recorded from 7 electrode sites (Figure 3.1.C) of the international 10-20 system using a COGNISION® Headset (Neuronetrix, Figure 3.1.A). Electrodes were referenced to averaged mastoids (M1, M2), and Fz served as the common electrode. The headset used for data collection has been validated to perform reliable ERP recordings (Cassani et al., 2017; Cecchi et al., 2015). Impedance was automatically checked at all electrodes throughout the task and was kept below this limit (<70 kΩ; see Cecchi et al., 2015). The EEG was digitized at 125 Hz and bandpass filtered from 0.3 to 35 Hz. Epochs of EEG data were extract from −200 to 3000ms locked to the onset of the study or test display around the stimuli. An automatic artefact threshold detection limit of ±100 μV was set for the tests. Epoch sets with artefacts exceeding the threshold were rejected in real time and randomly rescheduled thus avoiding trial loss. Trial averaging and extraction of ERP measures were performed offline after exporting the raw data.

3.3 Analysis

3.3.1 Behavioral data

The data were analysed using R-Studio (version 3.3.3) and its build-in package "stats" (R Core Team, 2017). Performance on two conditions by two groups was compared through one-way non-parametric ANOVA. As age and education were significantly different between two groups they were held as covariates.

3.3.2 ERPs

Analyses were performed offline with EEGLAB (Version 13.5) and MATLAB 2016. Data were filtered between 0.3 Hz (high-pass) and 30 Hz (low-pass). EEG activity was referenced to the grand average. Visual inspection of the data was followed by independent component analysis (ICA) to further remove artefacts such as blinks. Continuous EEG data were segmented in epochs of -200 to 2000 ms locked to stimulus onset for both the study and test phase. A baseline correction using -200 to 0 ms window was applied. To each memory phase (encoding and retrieval) we subtracted the "true" baseline (-200 ms prior the study display). Epochs containing artefacts with exceeded threshold of +/- 100 μV were manually removed. Separate grand averages for each participant and each TMB condition (only correct trials were included in the analysis) were generated.

We used a component-free approach, and thus all sensors for both conditions were assessed for significant differences across conditions and groups. To this aim, we used Monte Carlo permutation tests (4000, threshold p=0.01) combined with bootstrapping, as reported in other studies (Hesse et al., 2016; Ibanez et al., 2013; Naccache et al., 2005). This method is a modified version of the permutation test proposed by (Maris & Oostenveld, 2007) which generates a non-parametric estimate of the *p*-value, representing the statistical significance of the originally sample space. Such an analysis offers a straightforward solution for multiple comparison problems and does not depend on multiple comparisons correction or Gaussian assumptions about the probability distribution of the data (Nichols & Holmes, 2002). Time-windows with the significant results were used to extract the averaged ERP activity (amplitude) that entered the next step of analysis. Linear Mixed model was performed to

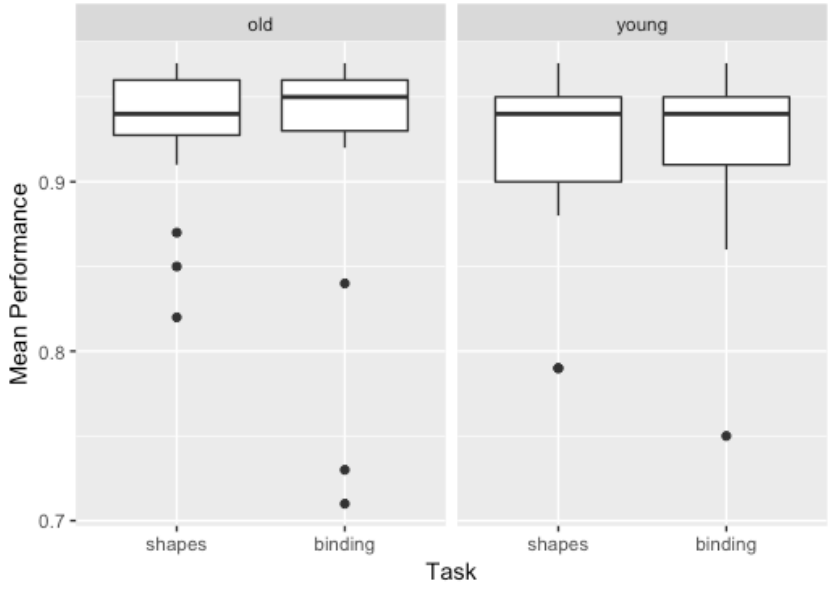
evaluate the association between ERP components and the two conditions of TMB task across the two groups for each electrode.

3.4. Results

3.4.1 Behavioral results

Performance on the TMB task is displayed on the Figure 2. Younger and Older adults performed equally well on the Shape only (Older: M = 0.93, SD= 0.04; Younger M=0.92, SD=0.05) and Shape-Binding condition (Older: M = 0.92, SD= 0.08; Younger: M=0.93, SD=0.05). The main effects of Group and Condition were non-significant (F (1, 84) = 0.011, p = 0.92, d = 0.41 and F (1, 84)=0.02, p = 0.97, d = 0.42 respectively), and neither was the Group x Condition interaction (F (1, 84) = 0.350, p = 0.55). The accuracy for both groups was close to ceiling on both conditions of the TMB task.

Figure 3.2. Mean performance during the TMB task in the shape-only and shape-color binding conditions performed by two groups.



3.4.2 ERP results

From the permutation test Young vs Old (Figure 3.3) during the encoding phase significant difference emerged in the time window between 300 msec and 600 msec in both conditions over all electrode sites.

From the permutation test Shape Only vs Shape-Colour Binding (Figure 3.3) during the encoding phase for younger adults there were no significant difference in encoding phase between Shape Only and Shape-Colour Binding conditions. For older adults, on the other hand, significant difference emerged in the early time window between 50 and 300 msec and late time windows between 450 and 600 msec and 1000-1200 msec over P3 and P4 electrodes sites.

From the permutation test Young vs Old (Figure 3.3) significant difference emerged during all retrieval phase in both conditions over all electrode sites.

From the permutation test Shape Only vs Shape-Colour Binding (Figure 1) during the retrieval significant different is in time windows between 100 and 200 ms and 300 and 600 ms over Cz and P4 electrodes sites. For older adults, on the other hand, there was no significant difference in retrieval during Shape Only and Shape-Colour Binding Conditions.

Figure 3.3. Results from the permutation tests.

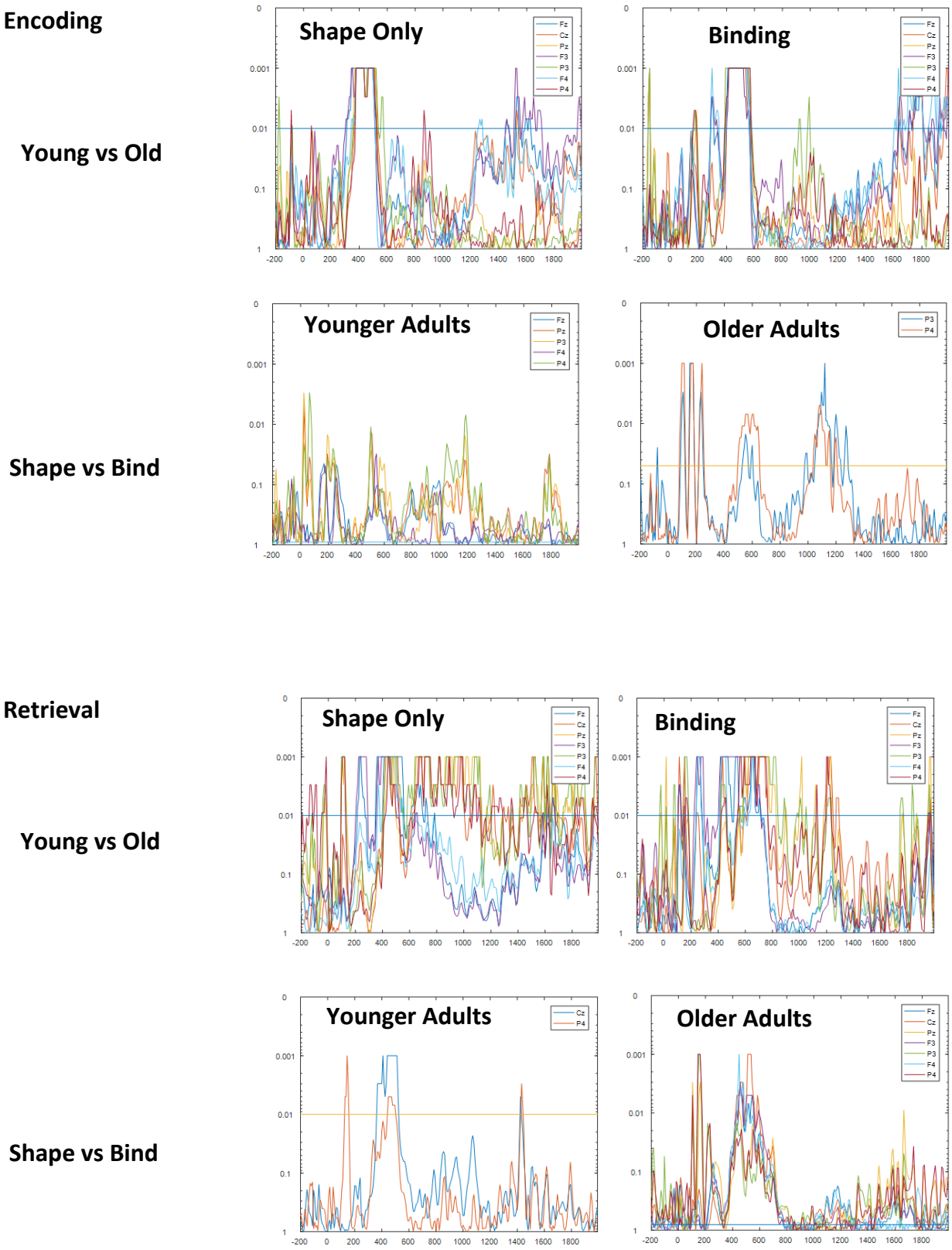
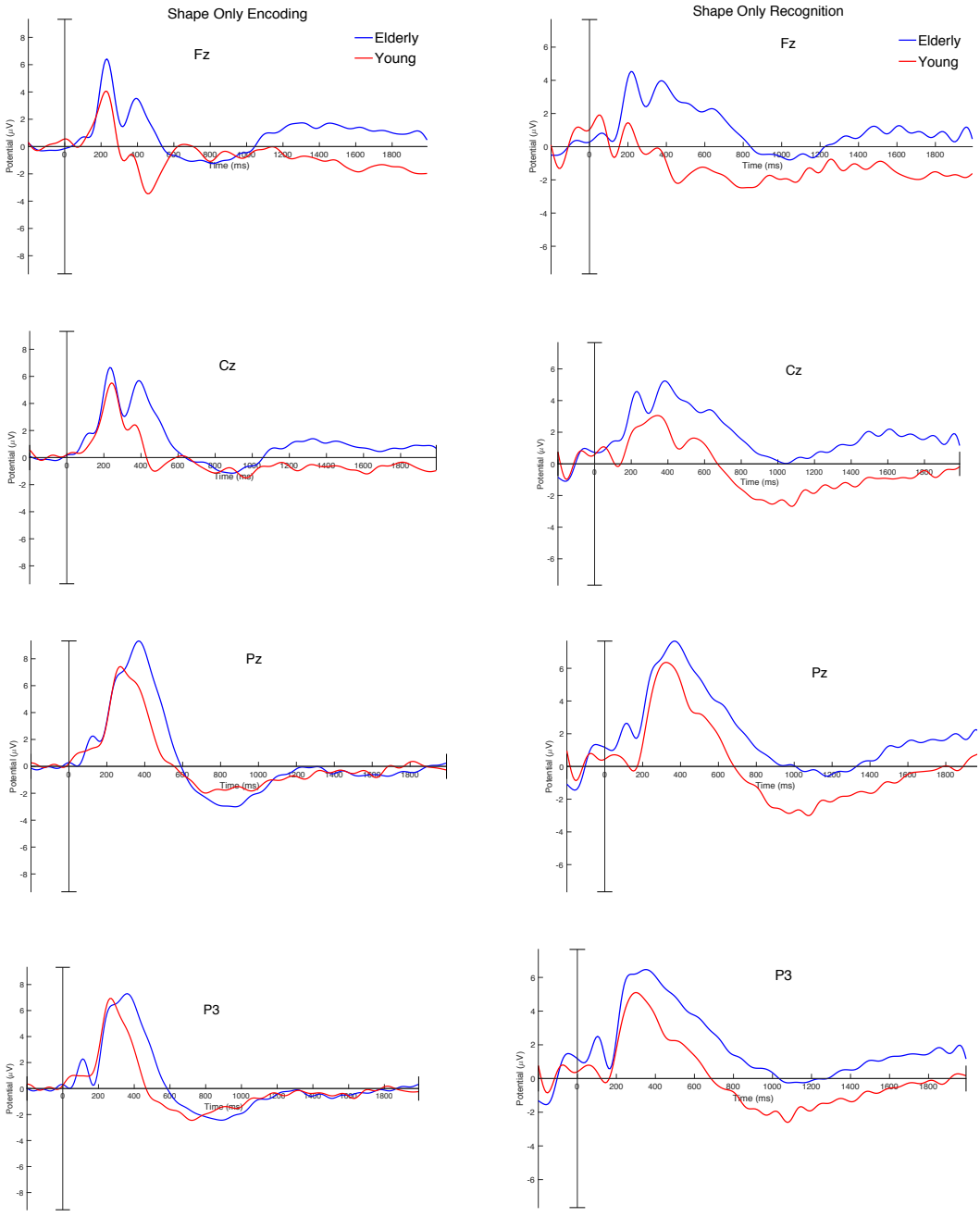
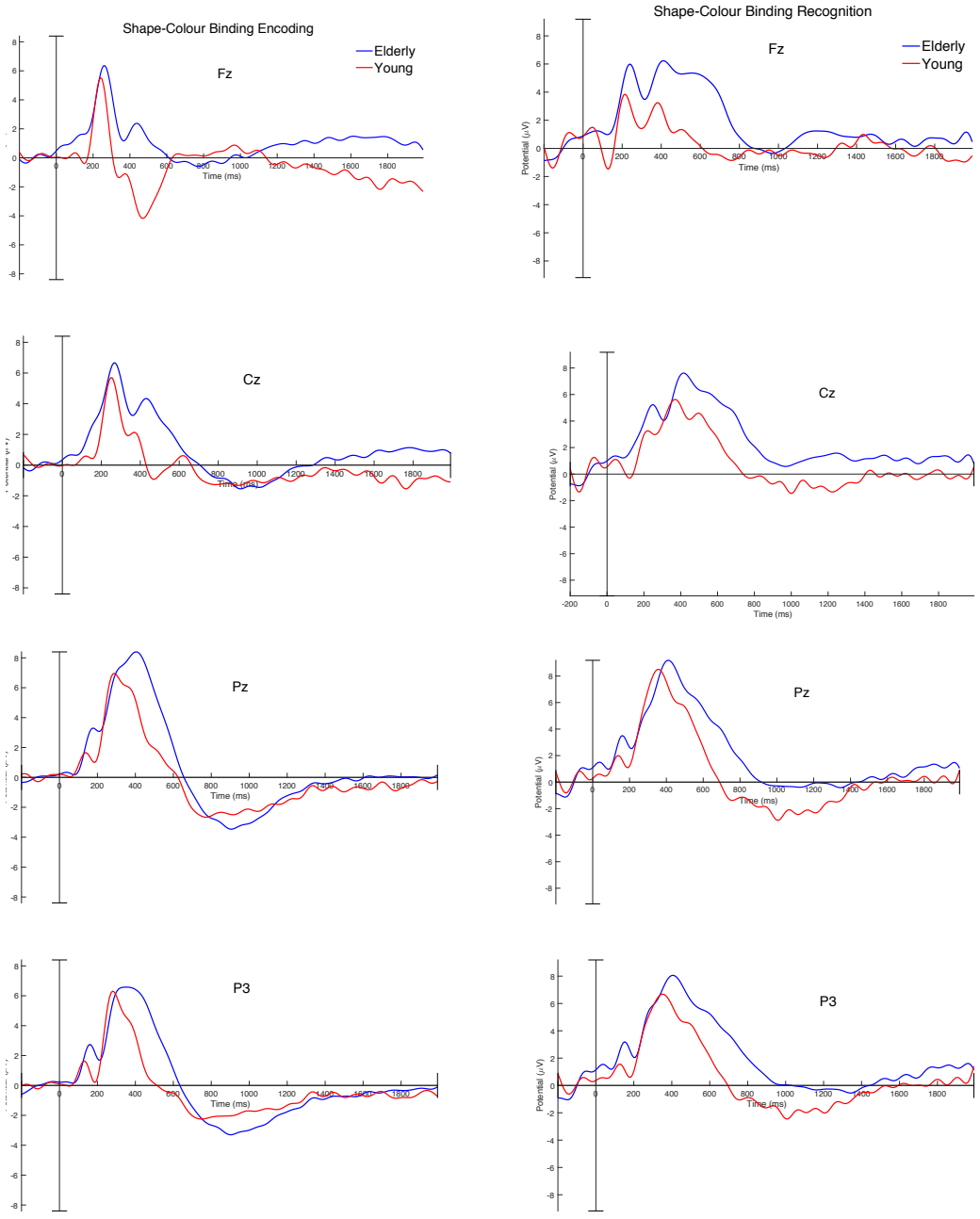


Figure 3.4. Grand average ERPs for Shape only and Shape-Colour Binding Condition in young and elderly participants





The main outcomes from all the linear models are presented in Table 3.1

Table 3.1 Linear Mixed Model Results for Early and Late Components over 7 electrodes For Young and Older Adults

Encoding

	Main effect of Group				Main effect of Condition				Interaction			
Early component (200-800 msec)	F	p	ES	P (%)	F	p	ES	P (%)	F	p	ES	P (%)
Fz	13.54	0.02	0.78	68	0.11	0.74	-	-	0.06	0.82	-	-
Cz	17.46	0.01	0.90	80	0.06	0.80	-	-	0.006	0.59	-	-
Pz	13.34	0.02	0.76	65	0.78	0.39	-	-	0.78	0.39	-	-
F3	10.01	0.03	0.58	44	0.67	0.43	-	-	0.67	0.43	-	-
P3	17.12	0.01	0.88	78	0.19	0.67	-	-	0.19	0.67	-	-
F4	5.89	0.13	-	-	0.09	0.76	-	-	0.008	0.93	-	-
P4	9.67	0.03	0.65	52	0.64	0.44	-	-	0.14	0.74	-	-
Late component (800-1990 msec)												
Fz	5.6	0.14	-	-	3.71	0.05	0.12	7	0.02	0.90	-	-
Cz	4.79	0.16	-	-	6.94	0.01	0.49	33	0.04	0.85	-	-
Pz	0.002	0.96	-	-	3.75	0.05	0.21	10	0.33	0.62	-	-
F3	0.50	0.49	-	-	4.62	0.04	0.46	30	0.04	0.85	-	-
P3	0.72	0.48	-	-	4.36	0.05	0.13	6	0.09	0.78	-	-
F4	5.15	0.15	-	-	4.44	0.04	0.30	17	0.18	0.70	-	-
P4	0.88	0.44	-	-	5.31	0.03	0.19	15	0.43	0.57	-	-

Retrieval

	Main effect of Group				Main effect of Condition				Interaction			
Early component (200-800 msec)	F	p	ES	P (%)	F	p	ES	P (%)	F	p	ES	P(%)
Fz	23.93	0.001	0.99		7.79	0.005	0.58		0.02	0.89	-	-
Cz	22.54	0.001	0.92		10.75	0.001	0.69		0.02	0.87	-	-
Pz	21.00	0.001	0.86		3.87	0.05	0.40		0.21	0.66	-	-
F3	25.83	0.001	1.04		8.58	0.003	0.62		0.44	0.53	-	-
P3	23.49	0.001	0.99		4.30	0.04	0.37		0.25	0.64	-	-
F4	2.62	0.105	-	-	8.00	0.05	0.60		0.09	0.77	-	-
P4	19.43	0.001	0.86		2.98	0.12	-	-	0.13	0.73	-	-
Late component (800-1990 msec)												
Fz	3.49	0.06	-	-	2.19	0.13	-	-	0.18	0.68	-	-
Cz	16.20	0.001	0.75	64	4.54	0.03	0.19	9	0.23	0.65	-	-
Pz	19.72	0.001	0.85	75	4.71	0.06	-	-	0.43	0.51	-	-
F3	2.22	0.21	-	-	1.35	0.24	-	-	0.40	0.55	-	-
P3	18.37	0.001	0.83	73	4.40	0.03	0.20	9	0.39	0.53	-	-
F4	2.62	0.10	-		3.69	0.05	0.35	19	0.12	0.74	-	-
P4	13.79	0.001	0.73	62	4.81	0.02	-	-	0.28	0.62	-	-

3.4.2.1 Encoding Phase. Age effect

During the early time-window (200-800 ms) the main effect that proved significant was that of Group over all electrodes except F4. Linear contrasts showed that older adults had increased amplitude during the early time-window over all electrodes (apart F4) compare to younger adults ($p<0.001$ for all). This suggests that older adults need to allocate more recourses to the visual processing of the stimuli during the encoding phase. During the Late time-window (800-1990ms) the main effect of Group was non-significant.

3.4.2.2 Encoding Phase. Binding Cost

During the early time-window (200-800 ms) neither the main effect of Condition nor the Group x Condition interaction was significant. During the Late time-window (800-1990 ms) the main effect of Condition was significant over all electrodes. Linear contrasts did not reveal significant difference in the late time-window of the encoding phase in both Conditions. The Group x Condition interaction was non-significant. The results show that the encoding phase for Shape-Colour Binding Condition require extra resources compare to the Shape Only condition neither for older adults nor for younger participants.

3.4.2 3 Retrieval Phase. Age effect

During the early time-window (200-800 ms) and the late time-window (800-1990 ms), except F4 for the latter, the main effects of Group were significant. Linear contrasts for both time-windows revealed increased amplitude in older adults over all electrodes (apart F4 during the late time-window) compare to younger adults ($p<0.001$ for all). These results show that the retrieval process, associated with monitoring and evaluation processes, for older adults poses more effort than for younger adults.

3.4.2.4 Retrieval Phase. Binding Cost

During the early (200-800 ms) and late (800-1990ms) time-windows the main effects of Condition were significant over all the electrodes except P4 during the early time-window. Linear contrasts for early and late components revealed that the Shape-Binding Condition has increased amplitude over the Fz, Cz, Pz, F3, and F4 ($p<0.001$ for all). The Group x Condition interaction for both early and late time-windows were non-significant. The results reflect the enhanced electrophysiological brain activity during the whole retrieval phase on the Shape-

Binding Condition mainly over the frontal electrodes as well as central parietal and central electrodes, meaning that decision monitoring and evaluation of bind features is electrophysiologically costlier than of single feature.

3.4.3 P300

As can be seen in Figure 3.4, the ERP effects in the older subjects appear to differ dramatically from those in the young group. The grand average ERPs illustrates higher peaks with later-onsetting across all components over all electrode sites in older people. These effects seem to be more prominent over all parietal electrodes. Even though initially we chose a component-free approach, I wanted to explore if P300 would be more informative than previously selected time-windows. P300 characterises early conscious processes involved in attention and working memory process (Pickton, 1992). This component was shown to behave differently in younger and older adults and in discriminative tasks in younger adults the component picks earlier (around 300 ms) than in older adults (around 500-600 ms) post-stimulus (Tays et al., 2008), suggesting that older adults recruit additional control processing (occurring closer to the point of response selection) to aid performance that is in line with STAC and my initial hypothesis about over-recruitment of frontal recourses that would aid the performance on the challenging tasks.

For the analysis of both P300 latencies (300 to 600 ms post-stimulus) and amplitudes, the mixed linear model was performed. The results of are shown quantitatively in Table 3.2.

Table 3.2 Outcomes from the linear mixed models for P300 component across two groups over the 7 electrodes.

	P300 amplitude		**P300 latency**	
	F	*p*	*F*	*p*
G	8.18	0.005	12.34	<0.001
C	2.27	0.04	45.95	<0.001
E	65.87	<0.001	17.28	<0.001
G x C	0.26	n.s	1.24	n.s
C x E	1.67	0.05	1.97	0.01
G x E	6.94	<0.001	3.83	0.002
G x C x E	1.24	n.s	0.51	n.s

Note: C, condition (Shape-Colour Binding encoding, Shape-Colour Binding retrieval, Shapes Only encoding, Shapes Only retrieval); G, group; E, electrodes

There were significant main effects of group, conditions and electrodes, as well as condition x electrodes and group x electrodes interactions for P300 amplitude and latency.

3.4.3.1 Encoding phase. Age effect

Linear contrasts show that during the encoding phase older participants had more positive going P300 amplitude than younger adults over bilateral frontal and central electrodes, indicating anterior shift of P300 in older participants: Cz ($p = .03$), Fz ($p = .04$), F3 ($p = .05$), and F4 ($p = .05$).

Linear contrasts show that older participants have slower P300 latencies compare to younger adults over central and bilateral parietal electrodes: Cz ($p = 0.01$); Pz ($p < 0.001$); P3 ($p < 0.001$) and P4 ($p < 0.001$).

3.4.3.2 Encoding phase. Biding cost

P300 amplitudes for Shape-Colour Binding Condition was more positively going than during Shapes Only Condition for both groups over Cz ($p = .01$), Fz ($p = .008$), Pz ($p = .03$), F3 ($p = .01$), and F4 ($p = .03$).

During Shape-Colour Binding encoding latency of P300 component was longer, compare to Shapes Only, over Pz ($p = 0.01$); F3 ($p = 0.009$), F4 ($p = .008$), and P4 ($p = .003$) in both groups. This reflects engagement of more attention during Shape-Colour Binding Condition.

3.4.3.3 Retrieval phase. Age effect

Linear contrasts show that older participants have more positive going P300 amplitudes compare to younger adults over Cz ($p = .01$), Fz ($p = .04$), F3 ($p = .002$), and F4 ($p = .02$).

Linear contrasts show that older participants have slower P300 latencies compare to those in younger adults over Cz ($p = .01$), Pz ($p = .002$), P3 ($p = .05$), and P4 ($p = .03$).

Amplitudes of P300 were larger in both conditions during retrieval phase compare to encoding phase in older adults compare to younger adults over F3 ($p = .05$). Latencies of P300 component were longer over all electrodes sites ($p < 0.001$ for all) for both conditions during retrieval phase compare to encoding phase in older adults.

3.4.3.3 Retrieval phase. Binding Cost

Linear contrasts show that during Shape-Colour Binding Condition P300 had more positive going amplitudes compare to Shape Only Condition over Cz (p = .04), Fz (p = .02), F3 (p = .003), and F4 (p = .03).

Linear contrasts show that Shape-Colour Binding Condition has larger P300 latencies compare to Shape Only Condition over all electrodes (apart Fz): Cz (p < .001), Pz (p < .001), F3 (p = .01), P3 (p = .01), F4 (p = .02) and P4 (p < .001) for both younger and older adults.

Amplitudes of P300 were larger during Shape-Colour Binding Condition during retrieval phase compare to encoding phase in both groups over F3 (p = .05). Latencies of P300 component were longer over all electrodes sites (p < 0.001 for all) for both conditions during retrieval phase compare to encoding phase in older adults. During Shapes only Condition neither amplitudes nor latencies differ during the retrieval phase compare to encoding phase between two groups.

3.5 Discussion

This experiment investigated electrophysiological differences in younger and older adults when performing the TMB task. I aimed to investigate the electrophysiological correlates of the TMB in normal ageing. Results showed no behavioural differences for either single feature objects or features bindings between younger and older adults. These results support a fast growing literature and the results of the experiments reported in Chapter 2, confirming that age spares TMB (Allen et al., 2013; Bastin, 2017; Brockmole et al., 2008; Brown & Brockmole, 2010; Brown et al., 2017; Hoefeijzers et al., 2017; Isella et al., 2015; Parra et al., 2009; Rhodes et al., 2017; Rhodes et al., 2015; van Geldorp et al., 2014).

Novel findings from the present study are that despite no behavioural differences between younger and older adult, there were (1) significant electrophysiological differences regardless of task condition. That (2) such effects were more prominent during the retrieval phase of memory than during encoding and (3) were unlikely due to increased task demands. Finally, (4) feature binding was found to be more resource demanding than single feature processing. Yet, such a neurally demanding function remains impermeable to the normal course of ageing.

Insensitivity to normal ageing

In a situation where older adults did not differ behaviourally from younger adults they did so neutrally, whereby they recruited significantly more brain resources as denoted by increased ERP amplitudes. Increased activity over all electrodes sites suggests that older participants recruit more neural resources to achieve levels of performance similar to those seen in younger adults. That was true regardless of task condition suggesting that (1) there are age-related compensatory processes supporting short-term memory (2) which are not specifically necessary to support the condition of the task known to decline rapidly in abnormal ageing variants such as AD. This is the first evidence indicating that neither behaviourally nor physiologically, binding poses differential demands to older people as compared to single feature processing.

These compensatory changes are in line with the tenet of the Scaffolding Theory of Aging and Cognition (Park & Reuter-Lorenz, 2009) which states that in response to behavioural ageing, such as decreasing processing speed, lack of inhibitory process, or a decline in storage systems, the ageing brain increases prefrontal activation in order to aid successful task completion. Such theory rests on abundant evidence from the fMRI literature (Cabeza et al., 2002; Rajah & D'Esposito, 2005) which consistently reports neural over-recruitment in order adults during cognitive tests where little evidence of age-related decline is found. Researchers explain differently this additional prefrontal over-recruitment in older adults. Some supports the Scaffolding theory and state that decreased posterior activation and increase prefrontal activity aids more efficient task performance (Davis et al., 2008; Reuter-Lorenz et al., 2000; Cabeza et al., 2002; Missonier et al., 2004; Grady et al., 1995). However, the recent fMRI study by Morcom & Henson (2018) challenged the idea of age-related re-organisation of functional brain networks and applied a novel multivariate Bayesian analysis of fMRI data also using a standard univariate analysis. They reported on two experiments with long- (LTM) and short-term memory (STM) tasks. During the LTM paradigm, they scanned participants during memory encoding (participants paired objects with background scenes and then recalled the scene that has been paired with the test object). In the STM paradigm participants had to watch moving patterns and the memory load was manipulated by increasing number of pattern to be remembered. Participants were scanned while recalling the direction of motion after a brief delay. They first used standard univariate analysis and compared the activity level in the PFC and in the posterior visual cortex (PVC) during the

performance both STM and LTM experiments. Then they applied a multivariate Bayesian analysis to show if the increased activity in PFC contributes to memory performance. The authors showed additional activation of the prefrontal areas, however, they stressed that this does not mean up-regulation and that this activation did not carry additional information. On the contrary, they showed decreased response in long-term memory (LTM) and increased activity in STM. The researchers interpreted their findings postulating that with age the neural responses become less efficient and less specific and the activity in the prefrontal cortex becomes more task-dependent. They proposed that their findings better support the view of cognitive ageing, whereby intact cognitive function is supported by effective maintenance of a youth-like brain (Nyberg et al, 2012). Even though Morcom and Henson (2018) provided evidence against the Scaffolding theory, they indicated that the task-based network organisation still occurred in the prefrontal cortex. Whether it is occurred due to reserve (Stern, 2002; Barulli & Stern, 2013), maintenance (Nyberg et al, 2012) or adaptive response (Park & Reuter-Lorenz, 2009) is a subject of a large debate and remains unclear, but it adds weight to the hypothesis that the network reorganisation in successful ageing is happening in the prefrontal cortex.

Interestingly, in the current experiment stronger effects of Group and Condition were found in the Retrieval Phase than in the Encoding Phase. This suggests that encoding and storage information is not more recourse demanding for older adults compare to younger adults. Separate analysis of the P300 component confirms that Retrieval Phase is more attention demanding: larger amplitudes in frontal electrodes bilaterally that relates to enhanced engagement of attention in change detection. Older adults compared to younger adults had delayed P300 latencies at parietal sites and increased bilateral frontal amplitudes that can be interpreted as a compensatory function as a reaction on a task load and evidence of cognitive slowness (Grady et al., 1995; Missonier et al., 2004; Tays et al., 2008) due to posterior neural decrements. Other studies have also found decrease posterior activation, however, associated with optimal performance, but only when it was paired with bilateral frontal activation (Davis et al., 2008; Cabeza et al., 1997).

Previous studies investigating binding in AD also using EEG based methods have confirmed that poor performance in these patients is accounted for that inefficient encoding mechanism (Parra et al., 2017; Pietto et a., 2016, see also fMRI study by Sperling et al., 2003). The data suggest that older adults encoding abilities are more preserved that their retrieval functions. It

could be due to the fact that retrieval process is more prone to vulnerability to interference leading to greater cognitive efforts, less active recollection with a greater reliance on familiarity what may recruit more cortical resources.

Recent EEG studies suggest TMB impairments in variants of abnormal ageing such as AD are accounted for by limitations during encoding (Parra et al., 2017; Pietto et al., 2016). The data presented here suggest that age would not be a factor accounting for such AD-related effects. Older adults' performance was near ceiling thus suggesting that only healthy older adults could achieve such level of performance. Resilience to the age effect of the task can provide a baseline for the performance and cut-off to determine cognitive impairment. Therefore, should there be a fundamental impairment on TMB performance this would likely signal cognitive deterioration. AD markers which are not affected by the normal course of ageing are highly needed. Here the results provide behavioral and biological evidence supporting the lack of sensitivity of TMB to normal ageing and revealing for the first time the neural underpinning of this.

Binding Cost.

Significant effect of condition was observed during late encoding and throughout retrieval (Binding > Shape). This was true regardless of age. Hence, processing in STM feature bindings does indeed require more neural resources that processing single features, as shown previously using fMRI (Parra et al., 2014). This is interesting as a more neurally challenging task skips the effects of ageing regardless of the task difficulty. Globally reorganised functions supporting STM performance in older age are sufficient to boost this ability of maintaining a high level of performance even during demanding tasks. It will be useful to investigate why and for how long age spares such low-level binding functions necessary to form objects' identity.

Affordable Biomarkers

Developing effective and affordable biomarkers is critical. EEG methods offer promising alternatives to expensive and invasive functional imaging and CSF biomarkers techniques due to their low cost, portability and growing reliability. Compared to studies with high-density arrays of electrodes (Misionnier et al., 2004; Parra et al., 2012; Saliasi et al., 2013) low-density ERP recording of the current study showed comparable quality of the

electrocortical source signal from the performance on the TMB task. This portability can be useful in clinical setting (Mihajlovic et al., 2015) and for researcher and developers who are interested in implementing mobile brain imaging.

In the current study I used EEG equipment that was developed to investigate the P300 and to this aim, it has a fixed arrange of sensors which does not include occipital-temporal electrodes. However, my hypotheses concerned frontal lobe compensation in older adults and due to the portability of the device I decided to use it for the present study. Future studies also using low-density portable devices which are more flexible in terms of sensors location should investigate whether my findings can be generalized to other brain regions.

Chapter IV

Temporary binding is impaired in dementia of the Alzheimer's type but not in Parkinson's dementia

4.1 Introduction

Evidence summarised in Chapter I, suggests that TMB is sensitive to Alzheimer's Disease (AD) (Parra et al., 2009) and even reliably detects otherwise asymptomatic carriers of the Presenil-1 gene mutation E280A that leads to familial AD (Parra et al., 2010b) and amnestic Mild Cognitive Impairment (aMCI) patients who are at a high risk of conversion to dementia (Koppara et al., 2014)). The test is not affected by the healthy ageing as I have showed in Experiment one and by how it was showed in previous studies (Rhodes et al., 2017, 2016; Isella et.al., 2015; Parra et al., 2009; Brockmole et al., 2008), by repeated testing (Logie et al., 2009), level of education (Parra et al., 2011), or by different socio-cultural backgrounds (Della Sala et al., 2016). It is also not impaired by chronic depression (Parra et al., 2010a). Due to these properties, the TMB test has been proposed as a cognitive marker for AD (Logie et al., 2015; Dubois et al., 2016; Costa et al., 2017).

There is however still rather limited research confirming the specificity of the TMB test to AD relative to other dementias. Della Sala et al. (2012) compared the performance of AD patients with that of patients suffering from other types of dementia such as frontotemporal dementia, vascular dementia, Lewy body dementia and dementia in Parkinson's disease (PD). In this study participants were assessed using free recall paradigm in which participants are required to verbally recall objects (common objects like apple, bed, etc.) and colours (common colours, i.e. red, blue, etc.) individually or in combinations. Healthy participants were presented with a larger array of items than patients in order to rule out the effect of difficulty on the performance and keep performance far from ceiling effect for elderly participants and from floor effect for patients. Only AD patients showed significant deficits in recalling object-colours bindings. Short-term memory binding task was unaffected by non-AD dementias. This was the first study that would document specificity of the test to the AD pathology.

Such findings have been recently replicated in a new sample of behavioural variant of Fronto-temporal dementia (bvFTD) (Cecchini et al., 2017). This study was also using a free recall paradigm, however, compared to the previous study, they kept the level of difficulty similar across groups. They confirmed that free recall paradigm of the TMB task is sensitive and specific to AD dementia.

In these earlier studies, TMB was assessed using a free recall paradigm, and participants performed tasks with different set sizes allowing the titration of the cognitive demand of the task to keep performance level at baseline conditions similar across groups.

To uphold such a claim, we need to demonstrate that TMB assessed by other means (e.g., via recognition tests such as the change detection task (Parra et al., 2010a)), retains the same specificity thus confirming that is the function and not the testing procedure that is sensitive to AD.

Recall vs recognition

As I mentioned, the earlier studies with TMB tasks relied on different retrieval mechanisms (i.e. recall). Recall and recognition represent two different systems that rely on different structures and brain network. Recall has been shown to rely on hippocampus and is associated with metabolic rate (Zimmerman et al., 2008; Sarazin et al., 2010). Maintenance of retrieval is dependent on the ventral visual stream (Staresina & Davachi et al., 2010; Parra et al., 2014) and also may rely on the functioning of the perirhinal cortex (Staresina & Davachi et al., 2010; Tyler et al., 2013; Watson & Lee, 2013; Clarke & Tyler, 2014) and entorhinal cortex (Yonekinas et al., 2007). The evidence is that parahippocampal functions are affected earlier in the demented process than hippocampal formations (Didic et al., 2011) that pointed to the fact that recall is affected later than recognition. In addition to that, hippocampus is affected by ageing (Balota et al., 2000; Mitchell et al., 2000), therefore impairment in a recall paradigm is present in healthy cognitive ageing [see Danckert & Craik, 2013]. Recall paradigm is also affected by education level and gender (Grober et al., 1998; Frasson et al., 2011) and therefore can hamper to see the genuine effect of pathological cognitive decline and will be affected by socioeconomic status.

The present study addresses the issue of whether TMB is preserved in PD with and without dementia, when the assessment procedure involves recognition and all the participants are tested with the same memory load (i.e., same set size). We were interested in investigating if under such experimental conditions the reported specificity of TMB for AD would be upheld.

Parkinson's disease

Although PD is mostly characterised primarily as a movement disorder, a large body of evidence now reports the presence of accompanying non-motor symptoms. Progressive cognitive impairment is recognised as one of the non-motor symptoms and a high proportion of patients with PD will develop MCI and dementia. Cognitive dysfunction that patients with PD experienced reflects subcortical syndrome, often termed "executive functions". These include problems with working memory (Gabrieli et al., 1996; Dubois & Pillon, 1997; Beato et al., 2008), procedural learning (Koenig et al., 1999), and attentional shifting (Moustafa et al., 2008) as well as visuospatial deficits (Bradley et al., 1989; Owen et al., 1993; Crucian et al., 2003; Bronnick K. , et al., 2006; Sell al, 2006). Other non-motor symptoms of PD include behavioural impairment such as apathy, mood disturbances, hallucinations, delusions, and excessive daytime sleepiness (Emre et al., 2007).

Throughout the literature, the most commonly reported impairments in PD are those of executive functioning and working memory, however PD patients have been shown to have specific deficits in verbal and visuospatial working memory (Morris et al., 1988; Gabrielli et al., 1996). More specifically, Possin et al. (2008) showed that PD patients have deficit in visual-object and visual-spatial WM. Weintraub et al. (2011; 2012) in a series of experiments showed that patients with PD exhibit a pattern of brain atrophy similar to those in AD patients, which includes volume loss in the hippocampus, and this atrophy predicts global cognitive decline at 2-year follow up. Other neuroimaging studies reinforced this finding and showed that medial temporal lobe atrophy is associated with memory decline in PD patients and present in PD-MCI and PD with dementia (Beyer et al., 2013; Bruck et al., 2004).

Associative memory in Parkinson's disease

There is no clear evidence whether recognition is or not impaired in PD. While EF is a main cognitive substrate for cognitive impairment in PD, it can influence memory problems. Like that, dysfunction during encoding (generation and elaboration of strategies) and retrieval (search strategies and post-retrieval monitoring) is at least in part accounted for by executive deficit. Impaired free recall and intact recognition memory suggest difficulties with executive control of retrieval process (Cohn et al., 2016). Some studies have reported preserved recognition in PD (Flowers et al., 1984) regardless of the presence of medication. This study, however, reported ceiling and floor effects on recognition tasks that may have prevented finding significant differences between patients group and control participants. In this study patients with PD were without cognitive impairment. This is a common pattern of impairment in patients with PD: impaired free recall and reserved recognition, however, all these studies did not recruit patients with MCI and dementia that, as I pointed out earlier, share neuro-pathological substrate with AD (i.e MTL atrophy).

Higginson et al. (2005) aimed to address the question of if the recognition memory deficit was evident in Parkinson's dementia compared to patients without dementia. They reported impaired recognition in PD regardless of whether patients had dementia or not. Whittington et al (2000) in his meta-analysis of 39 studies included patients with PD with and without dementia found that PD patients with dementia demonstrate impaired recognition. PD patients without dementia had much smaller recognition deficit.

Hence, such evidence warrants investigation of TMB using a recognition paradigm. Moreover, titration is a procedure difficult to undertake in clinical settings (Della Sala et al., 2016) therefore here we test our Flash-cards with two items per trial for both our patient groups and healthy controls.

4.2 Methods

4.2.1 Participants

For this experiment all participants were collected from different clinics in Moscow, Russia. I myself collected healthy controls and trained the other two researchers on how

to use the Flash-cards and the scoring system. N.T is a Neurologist who is specialising in Parkinson's disease. She helped in collecting patients with Parkinson's disease. M.G. is a Psychiatrist and the head of a private clinic for patients with AD. She helped in recruiting patients with aMCI and AD.

PD was diagnosed by a neurologist (N.T.) with expertise in movement disorders and familiar with the widely used Queen Square Brain Bank criteria for PD (Hudges et al., 2002; Berardelli et.al., 2013) The diagnosis was based on the presence of at least two of the following symptoms: a) resting tremor; b) bradykinesia; 3) rigidity, the absence of atypical symptoms and positive response to dopaminergic medication. The duration of illness prior to participation was on average 5.97 years (SD=3.53). Two patients were classified as tremor-dominant, 6 were akinetic-rigid, and 25 were mixed (tremor and akinetic-rigid) (Kang et al., 2005). Twenty-eight patients were treated with their normal regimen of dopaminergic medication and 5 were without any medication at the time of testing. None of the patients were taking antipsychotic or antidepressant medications.

PD patients were subdivided into those with no cognitive impairment (N= 11) and those with mild cognitive impairments (PD-MCI, N=14 (Winblad et al., 2004)) or dementia (N=8; PDD (Jessen et al., 2014), total N = 22). PD-MCI and PDD were diagnosed by a certified neurologist (N.T.) with experience in PD and cognitive disorders, based on the clinical interview of the patients and their examination, and in accordance to the MDS (Movement Disorder Society) Task Force recommendations (Litvan et al., 2012; Berg et al., 2015). In addition, as cognitive screening for PD-MCI we used the MoCA cut-off of 26, a MMSE score ≥ 24 and minimal or no impairment in IADL. For PDD the criteria were: MoCA cut-off = 24, MMSE score ≤ 24 and presence of IADL impairments that would interfere with everyday functional activities. The 1-year rule was applied, i.e., PDD was diagnosed only if the dementia process started at least one year after the onset of Parkinson's disease (Aarsland et al., 2017).

Patients with amnestic MCI likely due to AD (aMCI, N = 8) and patients with mild AD dementia (mild-AD, N= 18) were diagnosed by an old age psychiatrist (M.G.) according to the *National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association* (NINCDS-ADRDA) (Albert et al., 2011). Exclusion criterion for all participants was the presence of any concomitant

brain disorder (head injury, tumour or any other neurological or psychiatric disorders). In addition, participants were not recruited for the study if they had a problem with colour vision or failed a perceptual binding test used as a screening tool (Parra et al., 2010).

Control participants were screened for history of significant neurological disease, serious psychiatric disorder, and substance abuse. Control participants were selected so they would not differ from the patients groups in terms of average age and education. They were not recruited into the study if they scored 24 or less on the Montreal Cognitive Assessment (MoCA) (Folstein et al., 1975) or 25 or less on the Mini Mental State Examination (MMSE) (Nasreddine et al., 2005).

Informed consent was obtained from all control participants and PD patients with no cognitive impairment; PD-MCI, PDD, aMCI and mild-AD patients gave their informed consent together with their caregivers. The study was approved by the National Health Services (NHS-MREC) and Lothian REC (MREC Ref. 06/MRE07/40; Lothian R&D Ref. 2006/P/PSY/22).

4.2.2 Procedures

4.2.2.1 Background Neuropsychological tests

All participants underwent a neuropsychological evaluation. Cognitive measures included: MMSE and MoCA. Functional abilities were assessed with the Lawton Instrumental Activities of Daily Living (IADL) (Lawton et al., 1969).

4.2.2.2 Flash-Card Version of the Temporary Memory Binding

The flash-card version of the task is the one that is described in Sections 2.1.3 and 2.2.3.

We additionally timed our participants using the iPhone's stopwatch: a separate time was collected for each condition (Shapes Only and Shape-Colour Binding) and the total time that it took to complete two conditions.

4.3 Analyses

The data were analysed using R-Studio (version 3.2.2) package "psych" (Revelle et al., 2017) by means of mixed ANOVAs (4 Groups x 2 Conditions) to determine whether

performance on the TMB task revealed a group by condition interaction informing on specific TMB impairments in a given group. As a between subject factor we entered patients groups and healthy controls; the within subject factor were the two experimental conditions (Shape Only and Shape-Colour Binding) with interaction terms between these variables. The effect size was calculated using eta-squared (η^2).

A Receiver-operating curve (ROC) analysis was performed to establish the cut-off scores of the Shape Only and Shape-Colour Binding Conditions and their sensitivity and specificity to correctly differentiate AD patients from PD patients with and without cognitive impairment, as well as from controls. The AUC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and per cent correctly diagnosed were calculated for each condition. The optimal screening cut-off point was defined as the lowest value that achieved >80% sensitivity and NPV; the optimal diagnostic cut-off point was defined as the highest value that achieved >80% specificity and PPV. The analysis was carried using the "pROC" package for R (Robin et al., 2011).

4.4 Results

Five groups of patients and a group of healthy volunteers acting as a control group were recruited for the study. The demographic, global cognitive, and functional measures of the four groups of participants are summarized in **Table 4.0.** Performance on the TMB task by these groups is shown in the **Table 4.1**.

As the number of PD patients with cognitive impairment and patients with aMCI and mild-AD is rather small, in order to boost power calculation, we decided to combine PD with MCI and PD with dementia in one group PD-MCI+PDD and aMCI and mild-AD in one group and therefore have 4 groups of patients (Healthy controls, PD with unimpaired cognition, PD-MCI+PDD, and aMCI+mild-AD). The demographic, global cognitive, and functional measures of the four groups of participants are summarized in **Table 4.2.** One-way ANOVA (with Bonferroni-corrected alpha to 0.01) revealed no significant difference in age or years of formal education across the groups (see Table 4.2).

Results of the neuropsychological assessment are shown in Table **4.2**. Post hoc contrasts revealed that PD with normal cognition did not differ from the control groups in their performance on MMSE, MoCA and IADL scales. Performance on the MoCA, MMSE

and Lawton tests did not differ between aMCI+mild-AD and PD-MCI+PDD, however these two groups performed significantly worse than healthy controls and PD with normal cognition in all tests. The PD-MCI+PDD patients scored higher than the controls and aMCI+mild-AD on the Geriatric Depression Scale (GDS 15) (Sheikh et al., 1986).

Table 4.0 Demographic, global cognitive and functional measures for six groups of participants.

	Controls (n =35)		PD (normal cognition) (n = 11)		PD-MCI (n =14)		PDD (n =9)		aMCI (n = 8)		mild-AD (n =18)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age	69.88 (8.48)	59-91	68.27 (8.45)	58-86	69.64 (7.53)	56-80	69.33 (12.06)	54-85	69.88 (8.06)	55-80	73.06 (8.62)	54-88
% Male	34	-	36	-	50	-	75	-	25	-	27	-
Education	14.31 (2.82)	10-20	16.09 (1.76)	10-19	14.82 (2.84)	14-20	15.56 (3.09)	10-19	15.50 (1.41)	13-18	14.56 (3.33)	8-20
MoCA	25.91 (2.05)	22-30	26.36 (1.86)	23-30	23.79 (1.58)	20-26	18.11 (2.26)	14-21	25.75 (2.19)	21-28	17.89 (2.63)	12-22
MMSE	27.51 (1.56)	24-30	27.43 (1.40)	25-29	24.79 (2.29)	21-29	23.33 (3.50)	16-27	24.75 (1.39)	22-27	21.28 (3.81)	16-27
IADL	43.60 (1.87)	39-45	43.1 (2.07)	39-45	40.29 (2.12)	35-45	35.22 (2.57)	30-39	44 (1.93)	42-45	37.83 (5.83)	28-45
GDS15	3.44 (3.03)	0-13	5.55 (2.98)	0-11	5.79 (3.14)	1-11	7.38 (4.78)	1-15	2.88 (1.96)	1-7	3 (1.46)	0-7

Table 4.1 Mean proportion of correct recognition on the TMB Conditions by the six groups.

	Shape Only	Range	Shape-Colour Binding	Range
Controls	0.96 (0.05)	0.84-1.00	0.91 (0.08)	0.75-1.00
PD (normal cognition)	0.97 (0.04)	0.90-1.00	0.91 (0.06)	0.81-1.00
PD-MCI	0.94 (0.04)	0.87-0.97	0.85 (0.10)	0.62-0.97
PDD	0.89 (0.09)	0.75-0.97	0.80 (0.15)	0.59-1.00
aMCI	0.86 (0.14)	0.62-1.00	0.73 (0.09)	0.59-1.00
mild-AD	0.81 (0.16)	0.53-1.00	0.61 (0.13)	0.37-0.84

Table 4.2 Demographic, global cognitive and functional measures of the four groups of participants

	Controls (n =32)		PD (normal cognition) (n = 11)		PD-MCI+PDD (n =22)		aMCI+mild-AD (n =26)		ANOVA	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	F(df)	p-value
Age	69.34 (8.30)	59-91	68.27 (8.45)	58-86	69.68 (9.48)	54-85	72.08 (8.42)	54-88	1.19 (3, 87)	0.17
%Male	35	-	36	-	59	-	73	-	0.028 (1,89)	0.86
Education	14.36 (2.82)	10-20	16.09 (1.76)	14-19	15.16 (2.95)	10-20	14.85 (2.88)	8-20	0.19 (3, 87)	0.66
GDS	3.44 (3.03)	0-13	5.55 (2.98)	0-11	6.36 (3.79)	1-15	2.96 (1.59)	0-7	7.12(3,87)	<0.01
MoCA	26.00 (2.05)	22-30	26.36 (1.86)	23-30	21.73 (3.35)	14-26	20.31 (4.44)	12-28	56.99 (3, 87)	<0.01
MMSE	27.70 (1.40)	25-30	27.82 (1.47)	25-29	24.59 (2.32)	16-29	22.35 (3.71)	16-27	79.21 (3, 87)	<0.01
IADL	43.61 (1.89)	39-45	43.27 (2.15)	39-45	38.28 (3.59)	30-45	39.73 (5.71)	28-45	21.93 (3, 87)	<0.01

Abbreviations: GDS15, Geriatric Depression Scale; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; IADL, Lawton Instrumental Activities of Daily Living.

The mean performance on the Shape Only and Shape-Colour Binding Conditions of the TMB task for the 4 groups is shown in **Table 4.3**. There was a significant main effect of Group [$F(1, 84) = 44.25$, $p < 0.001$, $\eta^2 = 0.38$], Condition, [$F(1, 84) = 47.25$, $p < 0.001$, $\eta^2 = 0.12$], and a significant interaction between Group and Condition, [$F(1, 84) = 5.023$, $p = 0.002$, $\eta^2 = 0.04$].

Eight post-hoc contrasts were carried out to check the performance of the four groups on the two conditions (alpha corrected 0.05/8 = 0.006). Only aMCI+mild-AD patients performed worse than controls (Shapes Only: MD =0.13, p<0.001 and Shape-Colour Binding: MD = 0.13, p<0.001) and both PD patient groups on both conditions of the TMB task (Shapes Only: aMCI+mild-AD vs PD normal cognition: MD = 0.14, p<0.001; aMCI+mild-AD vs PD normal cognition: MD = 0.10, p<0.001; and Shape-Colour Binding: aMCI+mild-AD vs PD normal cognition: MD = 0.14, p<0.001; aMCI+mild-AD vs PD normal cognition: MD = 0.10, p<0.001). There was no significant difference between both PD patient groups and controls on their performance on Shape Only and Shape-Colour Binding Conditions.

Table 4.3 Mean proportion of correct recognition on the Shape Only and Shape-Colour Binding Conditions of the TMB task by the four groups.

	Shape Only	**Range**	**Shape-Colour Binding**	**Range**
Controls	0.96 (0.05)	0.84-1.00	0.92 (0.08)	0.75-1.00
PD (normal cognition)	0.97 (0.04)	0.90-1.00	0.91 (0.06)	0.81-1.00
PD-MCI+PDD	0.93 (0.06)	0.75-0.97	0.83 (0.11)	0.62-1.00
aMCI+mild-AD	0.83 (0.15)	0.53-1.00	0.64 (0.13)	0.37-0.84

The mean time to complete the Shape Only Condition was significantly different across groups [$F(1.89) = 53.75$, $p < 0.001$]: Controls M = 2.11 (0.33) min., PD (normal cognition) M = 2.22 (0.25) min., PD-MCI+PDD M = 2.77 (0.79) min., aMCI+mild-AD M = 3.09 (0.60) min. Performance of PD-MCI+PDD and aMCI+mild-AD was significantly slower than Controls ($p < 0.001$). aMCI+mild-AD completed the Condition significantly slower than PD (normal cognition) ($p<0.001$), but not PD-MCI+PDD (p =

0.25). Performance of PD-MCI+PDD group and PD (normal cognition) did not differ (p = 0.047).

Table 4.4 shows the outcome from the ROC analyses for aMCI+mild-AD and PD-MCI+PDD when performance on the Shape-Colour Binding Condition and Shape Only was used. AUC for aMCI+mild-AD is > 90% (with the cut-off point at 0.83), suggesting that the Shape-colour Binding Condition discriminates mild-AD from controls. The Shape-Colour Binding Condition discriminates between aMCI+mild-AD and PD-MCI+PDD patients (AUC is 90.2% when the cut-off point is 0.70). Low discrimination accuracy was found between PD-MCI+PDD patients and the control group (AUC is 71.2% with the cut-off point of 0.89). The ROC analysis for Shape Only Condition showed a moderate accuracy to discriminate between aMCI+mild-AD and controls (AUC=82.7 % and the cut-off point at 0.96), and it is low between PD-MCI+PDD patients and controls (65.9%, the cut-off point is 0.95), and between aMCI+mild-AD and PD-MCI+PDD (AUC= 63.8 %, the cut-off point is 0.92). It should be noted that the sensitivity for the Shape Only Condition in all contrasts was low (less than 69 %).

Table 4.4 ROC analyses for the Shape-Colour Binding and the Shape Only Conditions.

Shape-Colour Binding	**cut-off**	**AUC**	**sensitivity**	**specificity**	**ppv**	**npv**
Controls vs aMCI+mild-AD	0.83	97.8	0.88	0.87	0.80	0.93
Controls vs PD-MCI+PDD	0.89	71.2	0.62	0.65	0.31	0.87
aMCI+mild-AD vs PD-MCI+PDD	0.70	90.2	0.83	0.87	0.93	0.70
Shape Only	**cut-off**	**AUC**	**sensitivity**	**specificity**	**ppv**	**npv**
Controls vs aMCI+mild-AD	0.96	82.7	0.78	0.68	0.58	0.85
Controls vs PD-MCI+PDD	0.95	65.9	0.75	0.68	0.37	0.91
aMCI+mild-AD vs PD-MCI+PDD	0.92	63.8	0.66	0.50	0.75	0.40

Abbreviations: AUC - Area under the curve, PPV – positive predictive value, NPV – negative predictive value

4.5 Discussion

This experiment was set out to investigate whether TMB is affected by PD when the assessment procedure involves recognition and no titration procedures. Moreover, it investigated if TMB differentiates between AD and PDD using a clinically suitable version of the task based on Flash-cards. The results show that only patients with AD present with impaired performance on the TMB task. Compared to either cognitively healthy elderly individuals or PD patients with normal cognition, patients with PDD did not show impairment on the TMB. This finding supports the findings of previous studies showing a specific TMB deficit in AD compared to healthy elderly individuals and other types of dementias (Della Sala et al., 2012; Cecchini et al., 2017) and also patients with depression (Parra et al., 2010). ROC analyses confirmed that the Shape-Colour Binding Condition yielded the best discrimination between AD patients, controls and patients with PD.

Compared to the study of Della Sala et al., 2012, whose subjects had mild and moderate stages of AD dementias and mild and moderated stages of non-AD dementias, in this experiment we were using aMCI and AD patients with mild stage of severity. The experiment is therefore reinforcing the fact that binding deficit occurs early in preclinical AD and can distinguish even between mild forms of other dementias from AD.

Earlier studies demonstrating the specificity of binding deficits in AD compared to other dementia (Della Sala et al., 2012; Cecchini et al., 2017) used a free recall paradigm and did not consider the cognitive continuum of PD from normal to dementia. Therefore, the current experiment provides novel evidence on (1) preserved TMB functions along the continuum of PD, (2) that such preserved function is task-independent, and (3) that a clinically friendly version of the TMB task can aid in the differential diagnosis between AD and PDD.

It is worth noting that the PD-MCI+PDD sample also had mild clinical depression as indicated by the GDS scores. This would make the diagnosis of these individuals more challenging as both depression and PD can cause cognitive decline. Our results show that the TMB task holds specificity for AD under these conditions, making the test a suitable marker for the early diagnosis and differential diagnosis of these forms of dementia (Della Sala et al., 2016).

4.5.1 Preserved TMB function in PD is task-independent

This is an important finding, especially if we consider that earlier studies have shown discrepant findings in PD samples during assessments of similar cognitive constructs using different tasks (Flowers et al., 1984; Higginson et al., 2005). In the context of TMB, the current experiments have shown that in cases of AD the specific binding impairments are found regardless of the task used (i.e., verbal free recall (Parra et al., 2009; Della Sala et al., 2012; Cecchini et al., 2017) or visual recognition (Dalla Sala et al., 2016; Parra et al., 2010a; 2010b)). The outcomes of the present experiment demonstrate that the lack of such impairments in PD is also task-independent (i.e., verbal recall, or visual recognition as shown here). Such evidence confirms that TMB is affected by AD and not by other neurodegenerative diseases. In addition, in the current experiment the TMB task was presented on the clinically and user-friendly Flash-cards. There is evidence that populations with low literacy or poor cultural backgrounds find verbal recall tasks more challenging than visual recognition tasks (Boivin et al., 2010). For instance, the Free and Cued Selective Reminding Test has been produced in "Word" and "Picture" versions and while both versions have been shown to be sensitive to AD the visual version yields higher scores than the verbal version (Delgado et al., 2016). That is not an issue with the TMB task.

It should be noted that one person from the PD-MCI and two patients form the PDD group showed a deficit on the task, even though the group as a whole did not differ in the comparison of means from the controls. I would like to stress that the findings are robust regardless of the presence of these three impaired patients as the PD with cognitive impairment as a group performed as well as the control group. An account for these outliers' performance could be traced back to the fact that a task can be failed for many different reasons. Parkinson's disease could give rise to a gamut of cognitive symptoms, including disturbances in attention, motivation, accessing and manipulating knowledge and psychomotor slowness (Cummings & Benson, 1984); the presence of any of these symptom may have affected performance, independently of the main cognitive function tested.

Finally, some limitations should be noted to this experiment. The sample of the current study was rather small; we combined MCI and patients with dementia to boost power of our analyses, thus limiting the generalization of the results.

Chapter V

Discussion of the part on the development of a new version of the TMB test

The TMB test is an ideal cognitive test to aid the diagnosis of AD: it has proved to be a sensitive and specific test for AD (Parra et al., 2010), it is not affected by healthy ageing (Rhodes et al., 2017, 2016; Isella et.al., 2015; Parra et al., 2009; Brockmole et al., 2008) and chronic depression (Parra et al., 2010a). The TMB test was initially designed as a computer version. This mean of test presentation offers a number of advantages: 1) standartisation of the testing environment; 2) automatic randomisation of the stimuli; 3) easy automatic scoring; 3) reduction of the testing bias. Despite all these benefits, there are also some drawbacks. This touches on characteristics of the testing population that TMB task has been designed: frail elderly and patients with dementia that may impede the assessment completed on the computer. Older people and patients with dementia that have little computer experience might have more difficulty responding to the test, resulting in jeopardised results. In addition, computerised tests are difficult to use in the remote areas when there is a need in testing at home. There is also a need in more affordable testing forms. The aim of this first part of the study was to address all these disadvantages of the computer test presentation and create a mobile and more clinically and user -friendly version of the TMB test.

5.1 A new version of the test.

I created a Flash-Card version of the test. The other alternative version of the test was presented in the form of the Tablet PC. The first series of experiments (Experiments 1-6 and additional analysis) reported in this thesis was dedicated to compare these three formats. The aim was to demonstrate that the scores derived from the computerised version of the test, the Flash Cards and the Tablet PC version of the test do not differ.

When performing the experiments, older participants noticed that they completely understood the procedures of the Flash-Cards and Tablet PC versions only sometime after the starting of the test. The problem was in the method of delivery of the instructions. For Flash-Cards the

instructions were only oral. For Tablet PC all instructions were given on the screen before all conditions. Therefore, by the time of testing with the Shape-Colour Condition they had already forgotten the instructions. To counter these problems, a set of the "run-in cards" was created. These cards are explanatory A4 format cards presenting conditions: Perceptual, Shape Only and Shape-Colour Binding. Before each condition these cards were shown to the participant with a verbal explanation for each Condition. If the participant confirmed that he or she understood the instructions, the proper test with the Flash-cards would follow. This method allowed us to eliminate all errors that were due to misunderstanding of the instructions.

There were several further modifications to the test presentation from the standard PC version to the more clinically oriented version that I have proposed in my experiments: on the Flash-Cards and Tablet PC version all participants were presented only with two items. On previous experiments (Parra et al., 2009) patients were assessed with two items per Conditions, whereas healthy elderly participants were given three items per Condition. The number of items in the previous experiments was titrated in order to avoid an unwanted ceiling effect by older participants. This is a valid procedure in the laboratory settings; however, in the clinical practice it could be challenging and time consuming. Therefore, our clinically versions of the test are presented with the fixed number of items.

The other difference is the method of testing: previous studies have been using a free recall paradigm, on the Flash-Cards we employed a recognition test. This was dictated by the fact that recall and recognition are function of different brain systems. If free recall relies mostly on hippocampus, recognition tasks would depend on parahippocampal areas that are known to be affected earlier in the course of the disease (Didic et al., 2011).

There was no difference in performance between the PC, Flash-Cards, and Tablet versions. The new modes of the test presentation replicated the ceiling effect of the visual recognition of the Computer PC form of the TMB test. It shows the high degree of scores overlapping between different testing methods therefore it shows good comparability of all three methods of testing. In addition, frail older participants noted that they preferred a paper format of the task, as they felt less confident using computers.

5.2 Age effect

This series of experiments have confirmed that there is no age effect, replicating previous studies (Rhodes et al., 2017, 2016; Isella et.al., 2015; Parra et al., 2009; Brockmole et al., 2008). Healthy older adults performed as well as younger adults on the recognition version of the TMB task. Given that one of the aims of the thesis is to show an early cognitive marker for AD, this is necessary to show that the proposed recognition paradigm is unaffected by age in order to serve as a baseline performance on the Flash-Cards and Tablet PC to measure AD performance. Older adults performed at ceiling on the task which therefore creates a perfect baseline condition for testing patients with cognitive impairment as performance off ceiling would indicate abnormality.

5.3 ERP correlates with TMB

Having confirmed that there is no age effect during the performance on the TMB task, my next aim was to address the question about what is the neurological reason for older adults to perform as well as younger participants. According to the Scaffolding Theory of Age (Park & Reuter-Lorenz, 2009) older adults recruit more brain areas when confronted with difficult and complex tasks. The aim of the experiment was to see if this held true for TMB task.

Compared to other neuroimaging methods (PET, MRI, fMRI), electroencephalography (EEG) is a low-cost procedure that provides highly sensitive measures of cognitive functions. In my Experiment 8, I have used a mobile low-density EEG system. The main advantage of this system is its mobility and user-friendliness which is important in clinical setting and in research with frail older participants. EEG was reordered from the COGNITION® Headset (Neuronetrix) 7 electrodes system (Fz, Cz, Pz, F3, P3, F4, P4). Compare to the standard laboratory EEG recorders that contain 64 to 128 electrodes, the low-density layout (7 electrodes) recording can pose some questions on if it is enough to adequately detect and assess cortical activity during the performance on the task. TMB task relates to the activity in the frontal and parietal areas of the brain (Parra et al., 2014). These regions engage when attention is required into encoding and maintaining feature representation (Parra et al., 2012; Parra et al., 2014). In addition, P300 wave that is shown to be altered in AD and proposed to be a potential biomarker for early detection of cognitive deterioration is more prominent in

central parietal and frontal regions (Parra et al., 2012; Parra et al., 2013). Therefore, our 7 electrodes set-up is sufficient for the research aims we were pursuing.

The results of the study confirmed that there are no behavioural differences in performance between older and younger adults, both groups perform equally well on the task. Electrophysiologically, however, a difference emerged. Increased activity over all electrodes sites suggests that older participants recruited more neural resources to achieve levels of performance similar to those observed in younger adults. This complies with the Scaffolding theory: neural over-recruitment of prefrontal areas in order adults during cognitive tests where little evidence of age-related decline is found.

The initial computerised TMB task and the Flash-Card version of the task identical in the number of trials per condition. In the ERP experiment, TMB task presents 100 trials per condition. Despite this, the behavioural results that we obtained are comparable with the task with fewer trials and thus granting reliability (internal validity) of this version of the task.

5.4 TMB specificity to AD

In order to be conceived as a marker for AD, the test should be sensitive and specific to AD. Study in Chapter 4 was set up to see if only patients with AD show deficits performing the TMB task. To this end, I recruited patients with AD and PD that performed the task on the Flash-Cards version of the test.

There is a very little research that would determine specificity of the task to AD. Two studies could be found in the literature: one by Della Sala et al. (2012) on patients with AD, FTD, and PD; the other by Cecchini et al. (2017) on patients with FTD and AD. In both these two studies a free recall paradigm has been employed and participants performed tasks with different set sizes.

In my study a recognition test paradigm has been used in order to show that TMB test retains the same specificity thus confirming that it is the function and not the testing procedure that is sensitive to AD. I used the Flash-Cards version of the TMB test that I validated in Experiments 1-6 with two items per testing trial. For this experiment, I recruited amnestic MCI patients, patients with mild AD, and patients with PD with and without cognitive deterioration. Some previous studies showed that patients with PD are not impaired in

recognition, but impaired in free recall tasks (Cohn et al., 2016; Flowers et al., 1984). However other studies assessing PD with and without dementia showed a different pattern. Higginson et al. (2005) and Whittington et al. (2000) showed that regardless of the presence of dementia, PD patients are impaired in recognition tasks.

As PD patients show volume loss in hippocampus (Schneider et al., 2017; Cohn et al., 2016) tasks that are supported by hippocampus should be difficult to perform for these patients; whereas tasks that are supported by parahippocampal complex should be preserved. In Experiment 9 I hypothesised that the recognition paradigm of TMB task should not affect performance by PD patients regardless whether they have cognitive decline or not.

The results of the experiment showed that only patients with AD presented with impaired performance on the TMB task. On the contrary, compared to either cognitively healthy older individuals or PD patients with normal cognition, patients with PD dementia did not show impairment on the TMB.

5.5 Implication

The results of the experiments have demonstrated that the TMB task presented with Flash-Cards is more clinically and user friendly and does not require titration for patients and healthy controls. At the same time it obtains the same results as the computer version of the test. This series of experiments has shown that there is no age effect of the TMB task regardless of the task used (i.e., verbal free recall or visual recognition) that makes it a perfect baseline for detection cognitive deterioration. The outcomes have confirmed that TMB is affected only by AD and not by other neurodegenerative diseases thus confirming its sensitivity to AD.

The creation of the Flash-cards was directed by the fact that TMB was existed as a computer version and it was difficult to use in the remote areas, in the situations where there is a need of assessment participants at home. In addition, computerised version of the test requires a special training in setting-up and testing and storage of the big data (that requires the Internet connection that in the clinical setting would be difficult to do). Furthermore, population under investigation are frail older people and patients with cognitive impairment who have limited computer knowledge and might develop “computer anxiety” that would affect the performance on the test. The Flash-Cards successfully address all these issues.

While traditional EEG devices are expensive and hard to transport, advances in the manufacturing of electronic devices have led to the recent appearance of affordable portable wireless EEG devices, opening the doors to EEG-based AD diagnosis in developing countries and geographically remote regions. The Flash Cards and the EEG system that I have been using in my experiments represent mobile and affordable means of testing patients.

5.6 What next?

As the early diagnosis of AD is based not only on the basis of the presence of cognitive impairments, but also "minimal functional problems" (Albert et al., 2011), I aimed to investigate what functional abilities decline first on the course of the disease and what are those "minimal impairment".

Dealing with AD, MCI patients and their caregivers I, during my clinical career as a forensic psychiatrist, have observed how often they lack financial competence and are unaware of this impairment. Literature review on the most complex and multidimensional functional activities, financial abilities has been found (along with transportation and using medication) showed to be more advanced and conceptually distinct from other everyday activities (like household, meal preparation or shopping) that comprise the range of different abilities and being purely "cognitive" meaning that it does not rely on the physical fitness like most other daily abilities. Financial abilities are crucial for functional independence and personal autonomy.

In my following chapters I also argue that they might serve as a functional marker of early dementia. I review current tools that were developed to assess everyday financial abilities and reason that there is a need of a new instrument that would help to detect the level of impairment. To highlight the specificity of the symptom we have suggested a term to define it: ***Acreemagnosia*** (Kozlova et al., 2018), from the Ancient Greek ἀ- (a-, "lack of"), χρήμα (creema, "money") andγνωσιακή (gnôsis, "knowledge").

In the next series of experiments I investigate financial capacities in older adults and patients with cognitive impairment. I research if these abilities indeed different from other everyday abilities and if they can help to distinguish between healthy and pathological ageing. As there are no accessible financial scales, I developed the measurement that aided me to investigate my research questions. I describe the development and validation of the Acreemagnosia

Measurement (TAM) and on a number of patients I show that this is a promising tool for the measurement of the everyday financial abilities in frail older people and patients with cognitive impairment.

Chapter VI

Importance of improving IADL

6.1 Introduction

The distinction between healthy ageing, MCI, and early AD is difficult especially with regard to Activity of Daily Living (ADL). There is a growing body of studies showing that functional impairment in ADL already exists in MCI (Bengen et al., 2010; De Vriendt et al., 2012; Farias et al., 2005; Hedman et al., 2013; Luck et al., 2011; Mariani et al., 2007; Morris, 2012; Nygard et al., 2012; Pedrosa et al., 2010; Perneczky et al., 2006; Peres et al., 2006; Sikkes et al., 2009; Schmitter-Edgecombe et al, 2011; Tuokko et al., 2005). Moreover, there is evidence that functional decline in ADL is detectable also in cognitively healthy older people, who later are going to develop MCI (Farias et al., 2013; Marshall et al., 2014; Peres et al., 2008; Suchy et al., 2011; Schmitter-Edgecombe & Parsey, 2014). Those healthy older people with functional impairments are four-fold more likely to develop dementia over the ensuing few years (Lau et al., 2015). Several studies (Schmitter–Edgecombe et al., 2011; Lafirtune & Balestat, 2007) showed that individuals over 75 years of age are at great risk of limitations in everyday functioning and low functioning (low educational and/or occupational statuses) non-demented older people show functional decline on average in their 60s (Willis, 1996). Schmitter-Edgecombe & Parsey (2014) observed that performance accuracy of functional activities decreased with increased age and level of cognitive impairment. Therefore, this period of time when cognitively unimpaired older adults exhibit some functional impairment but remain independent is a critical opportunity for intervention practice that can help to delay conversion to dementia. Consequently, clinical practice would benefit of sensitive behavioural measures that would detect these subtle functional problems.

These early functional impairments occur first in Instrumental Activity of Daily Living (IADL) tasks, as they are complex tasks, requiring motor, cognitive, and psychological

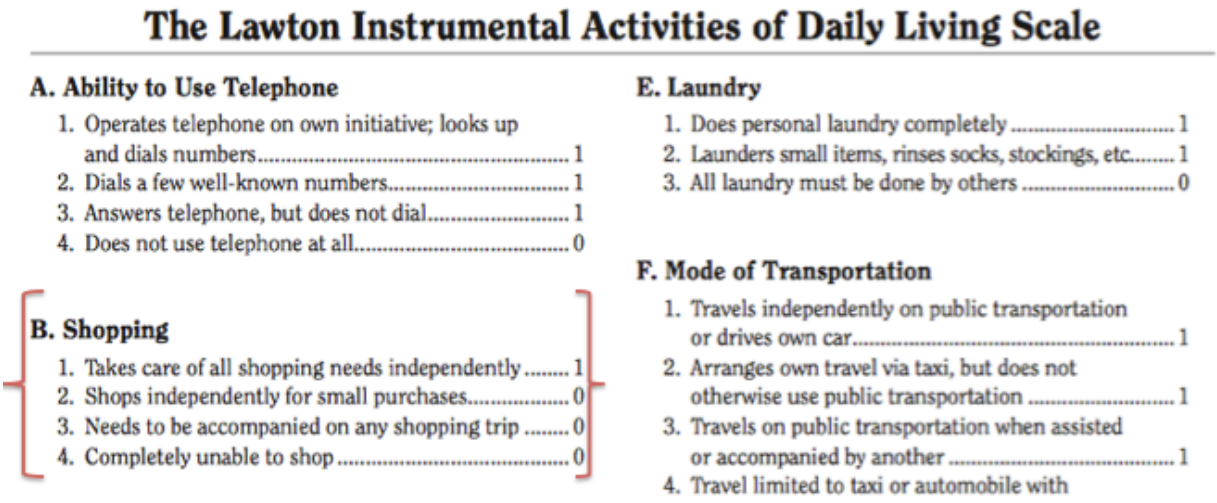
skills, as well as appropriate environmental conditions (World Health Organization, 2001). This makes them very susceptible to the initial effects of cognitive impairment. Therefore, the assessment of IADL can prove valuable in the detection of early dementia (Desai et al., 2004; Morris et al., 2912). Several studies consider handling finances, shopping, transportation, and managing medication among the most demanding cognitive activities (Aretouli & Brandt, 2009; Bangen et al.; Barberger-Gateau et al., 1999; Gold, 2012; Kim et al., 2009; Njegovan et al., 2001; Nygard, 2003; Reppermund et al., 2011; Willis et al., 1995).

However, typically in clinical practice a patient's function is examined not by looking at the performance on each individual task, but by summing up their responses in a total score. While this is a quick and easy method, it yields quite inaccurate estimates of underlying functional abilities or functional impairments. Total scores do not take into account important differences in item characteristics and different possible pattern of responses. The items within the most functional scales differ in terms of physical and cognitive difficulties and two responders can achieve the same score on a scale, however interpretation can be completely different. For example, frail older people without cognitive impairment can have difficulties with physical items and no problems with cognitive items; on the other hand, physically sound patients with dementia may have no problems with physical items, but fail complex cognitive items. Classifying participants with the same total score as having the same degree of functional impairment could be inaccurate and misleading.

Most of the scales do not give enough response variance to allow one to see if there is a problematic task/s within a given ability. For instance, shopping ability can have many subtasks like getting to the shops, remembering what items one intended to buy, knowing the prices and estimate what would be the cost, as well as physical effort of the errands. The most widely used scales enquire very broadly about shopping abilities. **Figure 6.1** gives some examples of how the most common ADL scales enquire about shopping abilities. Most of the scales inquire vaguely and broadly about independence on certain abilities without probing more comprehensively on different aspects of everyday life.

In this experiment, I aimed to investigate how MCI patients differ in performance on the most common functional scales from healthy older people. I aim at assessing whether the sensitivity of different scales used to detect early functional changes differ in patients with MCI. I investigate whether or not standard functional scales accurately differentiate between healthy controls from patients with cognitive impairment and if some tasks are more sensitive to detect early functional problems than others. This way the most sensitive tasks can be used to build more sensitive IADL scales targeting preclinical dementia, assessing early IADL changes and screening for asymptomatic dementia or older individual who are at risk of dementia. In addition, I aimed to examine the neuropsychological predictors of functional abilities in healthy controls and patients with MCI and mild-AD. The other purpose of the experiment to examine if there is indeed a diminished awareness of functional difficulties among individuals with MCI.

Figure 6.1 Examples of questions about shopping abilities from the most common ADL scales.



The Lawton Instrumental Activities of Daily Living Scale

A. Ability to Use Telephone

1. Operates telephone on own initiative; looks up and dials numbers 1
2. Dials a few well-known numbers 1
3. Answers telephone, but does not dial 1
4. Does not use telephone at all 0

B. Shopping

1. Takes care of all shopping needs independently 1
2. Shops independently for small purchases 0
3. Needs to be accompanied on any shopping trip 0
4. Completely unable to shop 0

E. Laundry

1. Does personal laundry completely 1
2. Launders small items, rinses socks, stockings, etc. 1
3. All laundry must be done by others 0

F. Mode of Transportation

1. Travels independently on public transportation or drives own car 1
2. Arranges own travel via taxi, but does not otherwise use public transportation 1
3. Travels on public transportation when assisted or accompanied by another 1
4. Travel limited to taxi or automobile with

BLESSED DEMENTIA-SCALE

Patient Name: _____
Rater Name: _____
Date: _____

Instruction
One point for each correct answer unless otherwise indicated. **Score**

CHANGES IN PERFORMANCE OF EVERYDAY ACTIVITIES

A Inability to perform household tasks	_____
A Inability to cope with small sums of money	_____
A Inability to remember shortlist of items; for example, in shopping list	_____

Functional Activities Questionnaire

Administration
Ask informant to rate patient's ability using the following scoring system:

- Dependent = 3
- Requires assistance = 2
- Has difficulty but does by self = 1
- Normal = 0
- Never did [the activity] but could do now = 0
- Never did and would have difficulty now = 1

1.	Writing checks, paying bills, balancing checkbook	
2.	Assembling tax records, business affairs, or papers	
3.	Shopping alone for clothes, household necessities, or groceries	
4.	Playing a game of skill, working on a hobby	
5.	Heating water, making a cup of coffee, turning off stove after use	
6.	Preparing a balanced meal	
7.	Keeping track of current events	
8.	Paying attention to, understanding, discussing TV, book, magazine	
9.	Remembering appointments, family occasions, holidays, medications	
10.	Traveling out of neighborhood, driving, arranging to take buses	
	TOTAL SCORE:	

14. COMMUNICATION

a. Able to hold appropriate conversation [ ]
b. Shows understanding and attempts to respond verbally with gestures [ ]
c. Can make self understood but difficulty understanding others [ ]
d. Does not respond to or communicate with others [ ]
e. Not applicable [ ]

15. TELEPHONE

a. Uses telephone appropriately, including obtaining correct number [ ]
b. Uses telephone if number given verbally/visually or predialled [ ]
c. Answers telephone but does not make calls [ ]
d. Unable/unwilling to use telephone at all [ ]
e. Not applicable [ ]

16. HOUSEWORK/GARDENING

a. Able to do housework/gardening to previous standard [ ]
b. Able to do housework/gardening but not to previous standard [ ]
c. Limited participation even with a lot of supervision [ ]
d. Unwilling/unable to participate in previous activities [ ]
e. Not applicable [ ]

17. SHOPPING

a. Shops to previous standard [ ]
b. Only able to shop for 1 or 2 items with or without a list [ ]
c. Unable to shop alone, but participates when accompanied [ ]

Scoring

d. Unable to participate in shopping even when accompanied [ ]
e. Not applicable [ ]

18. FINANCES

a. Responsible for own finances at previous level [ ]
b. Unable to write cheque but can sign name and recognizes money values [ ]
c. Can sign name but unable to recognize money values [ ]
d. Unable to sign name or recognize money values [ ]
e. Not applicable [ ]

19. GAMES/HOBBIES

a. Participates in pastimes/activities to previous standard [ ]
b. Participates but needs instruction/supervision [ ]
c. Reluctant to join in, very slow, needs coaxing [ ]
d. No longer able or willing to join in [ ]
e. Not applicable [ ]

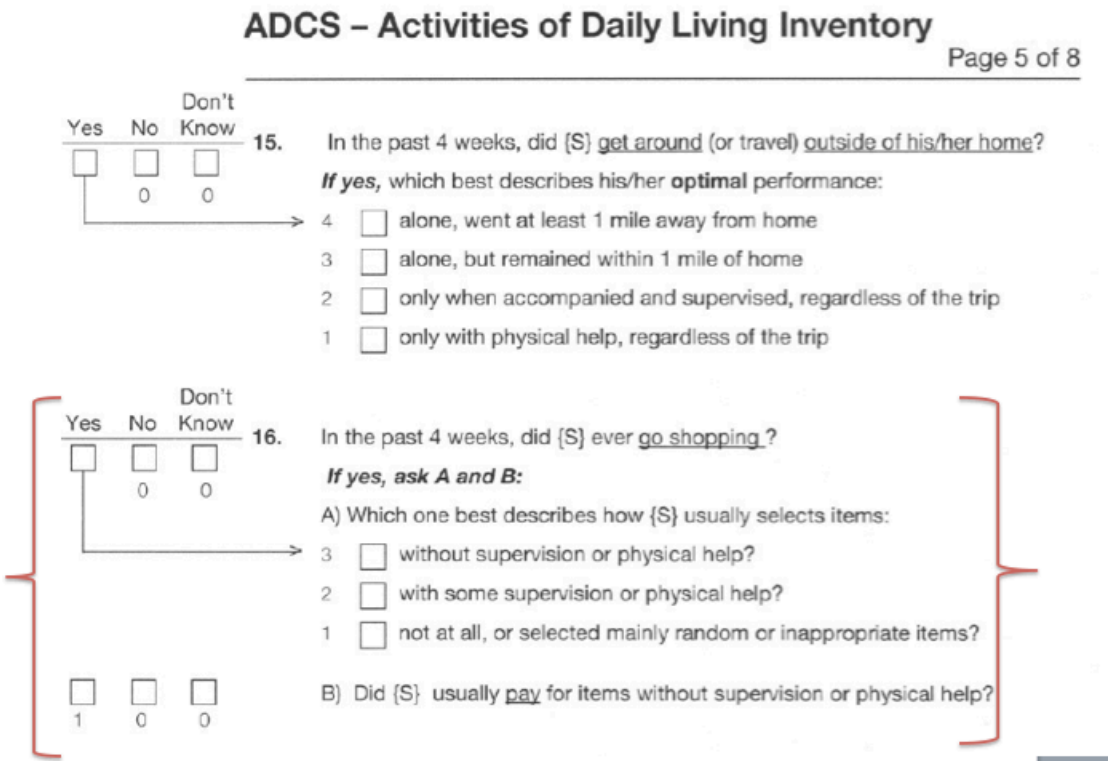
20. TRANSPORT

a. Able to drive, cycle or use public transport independently [ ]
b. Unable to drive but uses public transport or bike etc [ ]
c. Unable to use public transport alone [ ]
d. Unable/unwilling to use transport even when accompanied [ ]
e. Not applicable [ ]

Thank you for taking the time to complete this questionnaire.

Bayer Activities of Daily Living Scale

Does the person have difficulty....			Not applicable	Unknown	SCORE
1.	...managing his/her everyday activities?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
2.	...taking care of him/herself?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
3.	...taking medication without supervision?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
4.	...with personal hygiene?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
5.	...observing important dates or events?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
6.	...concentrating on reading?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
7.	...describing what he/she has just seen or heard?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
8.	...taking part in a conversation?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
9.	...using the telephone?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
10.	...taking a message for someone else?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
11.	...going for a walk without getting lost?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐
12.	...shopping?	never ①②③④⑤⑥⑦⑧⑨⑩ always	☐	☐	☐



ADCS – Activities of Daily Living Inventory

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Yes No Don't Know

15. In the past 4 weeks, did {S} get around (or travel) outside of his/her home?

☐ ☐ ☐

0 0

If yes, which best describes his/her **optimal** performance:

→ 4 ☐ alone, went at least 1 mile away from home

3 ☐ alone, but remained within 1 mile of home

2 ☐ only when accompanied and supervised, regardless of the trip

1 ☐ only with physical help, regardless of the trip

Yes No Don't Know

16. In the past 4 weeks, did {S} ever go shopping ?

☐ ☐ ☐

0 0

If yes, ask A and B:

A) Which one best describes how {S} usually selects items:

→ 3 ☐ without supervision or physical help?

2 ☐ with some supervision or physical help?

1 ☐ not at all, or selected mainly random or inappropriate items?

☐ ☐ ☐

1 0 0

B) Did {S} usually pay for items without supervision or physical help?

6.2 Methods

6.2.1 Participants

Eighty-five healthy older controls (HC), 14 patients with amnestic Mild Cognitive Impairment (a-MCI) and 14 patients with mild-Alzheimer's disease (mild-AD) (Haxby et al., 1992) entered the study. The diagnosis was made by an Old Age Psychiatrist who followed the guidelines proposed by Albert et al. (2011) to diagnose MCI relying on core clinical criteria and those of the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (DSM-V) (American Psychiatric Association, 2005) and the *National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association* (NINCDS-ADRDA, McKhann et al., 1984) to detect AD. HC were recruited from the volunteer panel of the University of Edinburgh. Informed consent was obtained from control participants, MCI and AD patients, and their carers. The study was approved by the Psychology Research Ethics Committee, University of Edinburgh and by the West Midlands MREC.

6.2.2 Measures

6.2.2.1 Cognitive functions

General Assessments:

The Addenbrooke's Cognitive Examination Revised (ACE-R; Mioshi et al., 2006). This is a brief measure of global cognitive function which incorporates five sub-domain scores (orientation/attention, memory, verbal fluency, language and visuo-spatial). The maximum score is 100 with the 88-82 cut-off score that signalling about cognitive impairment (Mioshi et al., 2006).

The Test of Premorbid Function (TOPF; Pearson assessment, 2009), which is a reading test as an estimate of the premorbid functioning in neurodegenerative brain disorders. The test consists of 70 words that are presented in the ascending difficulty order with regular words at the beginning with the following further more irregular and complex words. The maximum raw score is 70.

Executive functions: Participants completed two measures of executive function. The *Trail Making Test* (TMT parts A & B) (Reitan, 1992) was used to assess simple and complex visual scanning. The simple version of the task required participants to draw a line between circles according to a sequence (numbers). The complex version of the task required participants to alternate between two sequences (numbers and letters) while drawing lines to connect circles.

Memory: *Free and Cued Selective Reminding Test* (FCSRT) (Buschke et al., 1984) was used to assess the ability to learn and recall a list of words after a delay. The participant was presented with written words on cards, 4 words at a time on one card, with 16 words in total. The participant was asked to point and name a word (e.g., "Please point and name a fruit"). Once all of 4 items on a card were identified, the card was removed and the participant would complete an immediate free recall of the seen words, then, if some of the words were not recalled, the participant was given a cue for the missing words (e.g., "What was the fruit") in the same order they were encoded. Then, when all 16

items were seen, the participants were asked to freely recall all items without any order and them with the cue if some of the words were not recalled. This process was repeated three times. Following a delay of approximately 20 minutes, the participant was asked to recall words again freely and cued. Memory for free, cued and total recall was measured at the end by summing up all the words recalled freely of with cues.

Temporary Memory Binding Test (TMB). See Chapter 1-Part 1 and Chapter 2.

6.2.2.2. Functional tests

*Lawton Instrumental Activities of Daily Livin*g (Lawton IADL; Lawton and Brody, 1969). This is one of the earliest self-report scales developed to assess self-maintenance and lifestyle. It assesses 8 activities: the ability to use the telephone, to shop, prepare food, handle finances, do housework, managing medications, do laundry and to travel. Each task is scored dichotomously as either 1 (can perform task) or 0 (cannot perform or requires some assistance), providing a total IADL score ranging from 0 (significant impairment) to 8 (no impairment). This is the most popular and widely used functional scale in clinical practice.

Extended Instrumental Activities of Daily Living (E-IADL; Fieo et al., 2014). It is a brief 9 items scale that assesses complex and more cognitively demanding everyday tasks (shopping, house chores, find a way around the neighbourhood), they also incorporated leisure activities that are more stimulating and more challenging than traditional IADL (attending classes, doing community or volunteer work, take part in activities, going to movies, restaurant etc., visit friends/relatives). The score ranges from 0 (significant impairment) to 36 (no impairment).

Everyday Cognition (ECog; Farias et al., 2006) is an informant rated functional scale that assess six domains: Everyday Memory, Everyday Language, Everyday Visuospatial abilities, and three everyday executive domains including Everyday Planning, Everyday Organization, and Everyday Divided Attention. There are 39 items in total and the informant compare the participant's current level of functioning to 10 years earlier. The rating is the following: 1 = better or no change, 2 = questionable/occasionally worse, 3 =

consistently a little worse, 4 = consistently much worse. The total score ranges from 39 (no impairment) to 156 (significant impairment).

ECog and EIADL include more "advanced" items like social life and new scoring system that assesses changes in functional activities over time. Prior studies show that ECog effectively differentiate between MCI and healthy older people and also between MCI and AD dementia (Farias et al., 2011).

6.3 Analyses

The data were analysed using R-Studio (version 3.2.2) package "psych" (Revelle et al., 2017) by means of non-parametric Wilcox tests were used to compare HC and two patients groups on all demographic and functional measures. The effect size was calculated using eta-squared (η^2) for significant results.

In order to test if patients were aware of their functional difficulties I calculated Discrepancy Index (DI) scores using formula: self-rating minus proxi-rating test outcome (Farias, Mungas, & Jagus, 2005; Tabert et al., 2002). Those who overestimated their abilities would have a negative DI scores and those who underestimated their abilities would have a positive DI scores.

To examine what are the cognitive abilities that determine a successful functional performance in older adults and impairment in what cognitive function correlate with decline in everyday function a series of univariate analyses were performed to identify the bivariate association between each neurocognitive domain and functional scales and tasks.

6.4 Results

Table 6.1 shows the results of group comparisons on demographic and neuropsychological variables. There was no age difference in between patients with MCI and HC, however AD patients were significantly older than both MCI and HC. There was no difference between groups in their years of education.

As expected by the virtue of the diagnosis, MCI and AD differed significantly from the controls on ACE-R and specifically the two patient groups were significantly different from their healthy counterparts on memory and fluency domains. AD patients' performance on other domains of ACE-R was significantly worse than both MCI and HC. Memory total free and total delayed recalls on FCSRT and executive TMT A-B also differentiated the three groups.

Table 6.1 Demographic and neuropsychological measures for the three groups of participants.

Group	**Healthy (n = 85)**	**MCI (n = 14)**	**AD (n = 12)**	**Sig**		η^2
Gender (%Male)	29	79	50	<0.001	HC<MCI=AD	0.09
Age	71.8 (7.41)	74.71 (8.25)	78.92 (5.33)	<0.001	MCI=HC<AD	0.12
Education	15.74 (3.90)	14.04 (3.01)	13.67 (2.99)	n.s		-
TOPF	65.98 (5.25)	62.93 (4.83)	55.42 (9.94)	<0.001	HC=MCI<AD	0.17
ACE-R	96.33 (3.97)	87.58 (6.14)	70.82 (10.46)	<0.001	HC<MCI<AD	0.52
ACE-R subscales:						
Attention	17.65 (0.90)	17.00 (1.04)	13.91 (2.17)	<0.001	HC=MCI<AD	0.34
Memory	24.46 (2.88)	19.67 (4.05)	14.55 (3.80)	<0.001	HC<MCI<AD	0.42
Fluency	12.64 (1.61)	10.25 (2.05)	8.00 (2.79)	<0.001	HC<MCI<AD	0.32
Language	25.85 (0.42)	25.50 (0.67)	21.27 (3.98)	<0.001	HC=MCI<AD	0.29
VSP	15.79 (0.56)	15.33 (0.89)	13.27 (2.49)	<0.001	HC=MCI<AD	0.23
FCSRTtotalfree	46.45 (2.01)	37.20 (11.55)	25.40 (12.41)	<0.001	HC<MCI<AD	0.53
FCSRTdelayfree	9.80 (2.57)	4.10 (1.97)	1.70 (1.70)	<0.001	HC<MCI<AD	0.55
TMT A-B	50.55 (37.24)	112.16 (126.13)	152.04 (114.00)	<0.001	HC<MCI<AD	0.19
Binding	0.92 (0.09)	0.79 (0.13)	0.74 (0.10)	<0.001	HC<MCI=AD	0.30

Note: ACE-R - The Addenbrooke's Cognitive Examination – Revised (Mioshi et al., 2006), TOPF - Test of Premorbid Functioning (Wechsler et al., 2011); FCSRT – Free and Cued Selective Reminding Test – total score (Grober et al., 2009), ECog – Everyday Cognition (Farias et al., 2008), TMT A-B - Trial Making Test (Army Individual Test Battery, 1944); Lawton - the Lawton Instrumental Activities of Daily Living (Lawton and Brody, 1969), EIADL - Extended IADL (Fieo et al., 2014), Binding – Temporary Memory Binding test (Parra et al., 2014; 2015).

Examination of group differences in performance measures of functional abilities (**Table 6.2**) revealed that the performance of the two patient groups was comparable to each other and significantly worse in most of the functional scales compare to HC. The only items that distinguished the two patient groups were the financial domain on the Lawton scale and the balancing chequebook on the ECog scale.

Table 6.2 Difference on measures of functional abilities across three groups of participants

Group	Healthy (n=85)	MCI (n = 14)	AD (n = 14)	Sig	η^2
Lawton	7.95 (0.26)	6.29 (1.54)	7.08 (1.16)	HC<MCI=AD	0.25
Telephone	0.99 (0.11)	1.00 (0.00)	1.00 (0.00)	n.s	
Shopping	0.99 (0.15)	0.67 (0.49)	0.50 (0.52)	HC<MCI=AD	0.23
Food prep	0.99 (0.15)	0.67 (0.49)	0.58 (0.51)	HC<MCI=AD	0.29
House	1.00 (0.00)	1.00 (0.99)	0.92 (0.29)	n.s	-
Laundry	0.99 (0.00)	0.75 (0.45)	0.58 (0.51)	HC<MCI=AD	0.31
Transport	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	n.s.	
Medical	1.00 (0.00)	0.83 (0.39)	0.67 (0.49)	HC=MCI<AD	0.16
Finances	1.00 (0.00)	0.92 (0.29)	0.75 (0.45)	HC=MCI<AD	0.11
EIADL	10.36 (8.45)	23.54 (5.70)	21.25 (4.41)	HC<MCI=AD	0.25
Ecog	39.28 (12.64)	50.21 (23.04)	45.18 (18.80)	n.s	
Everyday memory	16.58 (4.94)	20.29 (6.07)	21.80 (9.99)	**HC<AD=MCI**	0.16
Everyday Language	4.61 (1.29)	6.36 (1.91)	5.40 (2.67)	HC<MCI=AD	0.14
Everyday Planning	8.45 (2.04)	6.57 (4.16)	7.80 (5.87)	n.s	
Everyday organisation	5.44 (1.43)	6.43 (2.59)	5.00 (3.16)	n.s	
Everyday Divided attention	2.81 (1.06)	2.50 (0.85)	3.60 (1.90)	n.s	
Assessing Finances	1.19 (0.42)	1.31 (0.63)	1.40 (0.55)	n.s	
Balancing Cheque book	1.05 (0.22)	1.08 (0.29)	1.67 (1.03)	HC=MCI<AD	0.16
Organising finances	1.13 (0.33)	1.45 (0.69)	1.60 (0.55)	HC<MCI=AD	0.12

Note: on the Ecog higher mean scores mean more impairment

There is ample research showing that patients with cognitive impairments often cannot assess their functional abilities adequately. **Table 6.3** presents the results from the analysis of the DI. The discrepancy between self- and proxy-report was significantly greater for patients groups compare to HC. MCI and AD patients had grater overestimation of their functional performance on Lawton and EIADL. Patient groups

overestimated their abilities of everyday planning, organisation and attention. However, there was little power to detect the difference, as the sample size is small with a large within group variability. Financial tasks of the Ecog scales fared better in detecting the difference between the groups. MCI patients and moreover AD patients overestimated their abilities to assess finances. Abilities on the tasks like balancing chequebook and organising finances were overestimated by AD patients, when MCI patients on these tasks accurately estimated their abilities.

Table 6.3 Discrepancy Index (DI) across functional scales and functional domains

	Healthy (SD) (n = 27)	**MCI (SD) (n = 9)**	**AD (SD) (n = 9)**	**Sig**	**η^2**
Lawton	-0.03 (0.96)	0.93 (1.44)	1.44 (2.30)	0.001	0.31
Telephone	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	n.s.	-
Shopping	0.00 (0.00)	0.29 (0.47)	0.25 (0.45)	0.03	0.09
Food prep	0.00 (0.00)	0.14 (0.36)	0.25 (0.62)	0.03	0.10
House	0.00 (0.00)	0.07 (0.27)	0.17 (0.39)	n.s	-
Laundry	-0.04 (0.20)	0.29 (0.47)	0.42 (0.51)	0.001	0.23
Transport	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	n.s.	-
Medical	0.00 (0.00)	0.14 (0.36)	0.33 (0.49)	0.006	0.14
Finances	0.00 (0.00)	0.00 (0.00)	0.33 (0.49)	0.007	0.14
EIADL	0.52 (0.94)	0.33 (2.60)	2.00 (7.81)	0.009	0.002
ECog	2.96 (4.87)	-0.86 (32.34)	-10.00 (40.91)	0.69	-
Everyday memory	0.86 (6.19)	-2.29 (13.54)	-4.40 (13.89)	0.94	-
Everyday Language	-0.11 (1.69)	-0.14 (4.88)	-3.40 (5.55)	0.09	0.12
Everyday Planning	0.42 (5.67)	-1.43(8.00)	-5.60 (9.91)	0.003	0.04
Everyday organisation	-0.06 (3.82)	0.00 (5.80)	-3.20 (4.60)	<0.001	0.05
Everyday Divided attention	0.61 (2.11)	-1.29 (2.93)	0.60 (3.05)	<0.001	0.01
Assessing Finances	0.04 (0.68)	-0.33 (0.58)	-2.85 (1.00)	<0.001	0.30
Balancing Chequebook	-0.09 (0.29)	0.00 (0.00)	-3.00 (0.00)	<0.001	0.42
Organising finances	0.04 (0.36)	0.00 (0.00)	-1.00 (0.00)	<0.001	0.06

Note: On the **Ecog** negative DI means overestimation of the functional abilities as higher mean scores on the Ecog mean more impairment, on the contrary, for **Lawton and EIADL** positive DI means overestimation of the functional abilities as higher mean scores on the scales mean lesser impairment.

Cognitive underpinnings of functional abilities.

In Healthy Controls the Lawton scale was associated with gender variance, β = 1.18, $\chi 2(1) = 7.08$, p = .008. ECog total score, as it was expected, was associated with memory test performance (FCSRT free recall: β = -0.88, $\chi 2(1) = 14.92$, p < .001) and general cognitive function (ACE-R: β = -2.19, $\chi 2(1) = 3.36$, p = .02). Everyday memory and everyday language subscales of the ECog correlated with the FCSRT free recall task, β = -0.34, $\chi 2(1) = 9.20$, p = .003 and β = 1.18, $\chi 2(1) = 13.45$, p < .001. Everyday planning subscale of the Ecog associated with the FCSRT free recall task (β = -0.34, $\chi 2(1) = -2.10$, p = .03) and visuospatial abilities (β = -0.34, $\chi 2(1) = 2.10$, p = .03). Everyday divided attention subscale of the Ecog correlated with attention (β = -0.50, $\chi 2(1) = -2.68$, p = .001).

Assessment of finances of the Ecog test in healthy controls showed that it depends on attention (β = 1.19, $\chi 2(1) = -2.68$, p = .01) and fluency (β = -0.12, $\chi 2(1) = -2.59$, p = .01). Balancing chequebook proved to be another complex task that in healthy controls depends on general cognitive function (β = 0.06, $\chi 2(1) = 2.65$, p = .01), attention (β = -0.1, $\chi 2(1) = -2.23$, p = .02), memory (β = -0.4, $\chi 2(1) =- 2.23$, p = .02), fluency (β = -0.08, $\chi 2(1) =-3.04$, p = .003), and visuospatial abilities (β = -0.42, $\chi 2(1) = -3.63$, p =<.0001). Organising finances relied on fluency component (β = -0.1, $\chi 2(1) = -2.28$, p = .02). Lawton task domains and EIADL in healthy older controls did not correlate with any of the cognitive abilities.

In the *MCI group,* the Lawton's subscale of telephone use was associated with free recall variable (β = 0.1, $\chi 2(1) = 2.28$, p = .02) and finances was associated with language (β = 0.35, $\chi 2(1) = 9.45$, p = .01). Total score of the ECog and EIADL scales correlated with free recall (β = 0.65, $\chi 2(1) = 3.49$, p = .05; β = 0.65, $\chi 2(1) = 2.45$, p = .05). All other associations were non-significant.

In *the AD group* Lawton's subscale of finances and shopping was associated with premorbid function that was measured by TOPF (β = 0.48, $\chi 2(1) = 3.84$, p = .002). All other associations were non-significant. TMB task was associated with managing

medication ($\beta = 0.62$, $\chi2(1) = 4.00$, $p = .001$) and performance on the ECog Scale ($\beta = 0.49$, $\chi2(1) = 3.90$, $p = .002$).

6.5 Discussion

In this experiment I aimed to investigate which items are the best to distinguish between patients with different levels of cognitive impairments (MCI and AD dementia) and that would detect early functional problems in patients with cognitive impairment. The reason in setting-up this experiment is in the on-going discussion about the MCI criteria (Petersen et al., 2014; Morris, 2012). The differentiation between early, mild and major cognitive impairment lies in the extent to which cognitive impairment interferes with everyday functioning. In MCI and mild-AD individuals may remain autonomous with some functional problems in complex everyday activities (Farias et al., 2006; Geda et al., 2010; Giovanetti et al., 2008). Moderate AD patients have already a pronounced functional deficit (Morris et al., 2013; Hesseberg et al., 2013; Reppremund et al., 2012). Consequently, it is paramount to know which functional deficit underpins early cognitive decline and the degree of impairment of everyday functioning so that we can establish an accurate level of cognitive impairments (MCI, mild-AD or moderate-AD).

In clinical practice, the level of functional impairment is ascertained by asking the caregiver or the patient to complete a report-based questionnaire assessing the overall everyday functioning. This approach gives an imprecise estimation of the individual's functioning, as it does not take into account differences in item characteristics and different possible pattern of responses. The items in the scales have different level of complexity (finances items are very complex, whereas self-care and household items are less so). Moreover, the total scores often employed assume that all items carry the same weight. In addition, some of the items are gender unbalanced (e.g., laundry, food preparation), other rely on physical components (e.g., transportation, getting in and out of the car).

The current study showed that performance on individual items in the Lawton's and ECog scales could differentiate between different groups better than the total score of the

scales. The results of the experiment show that Lawton's, EIADL and ECog total score could not distinguish between the two groups of patients assessed, namely MCI and AD, however they could differentiate between healthy controls and two groups of patients with cognitive impairment. However, items assessing finances could detect functional differences between MCI and AD. Moreover, single items like food preparation, shopping and laundry and organizing finances could detect cognitive impairment (i.e., MCI and AD patients performed worse than HC). These results show that using the total score of the performance as a mean of measuring functional decline can be misleading and underestimate functional problems. Therefore, prospective new functional tools that would enquire deeper into the essence of the everyday functional tasks, asking questions that would break down the components of each task would have more potential in detecting early functional problems. In addition, these tasks should rely only on the cognitive component and be gender indifferent.

In this study, I also examine awareness of patients with MCI and AD of their functional difficulties. It was important to establish as the first part of this experiment was based on the self-report of functioning. Investigating the accuracy of self-report of functional abilities is a critical scientific and clinical undertaking. I found that patients with MCI were significantly more likely than healthy controls to overestimate their functional abilities and more so patients with AD. This was seen mostly in the estimation of their performance on the tasks assessing financial abilities (in Lawton's scale and ECog) and also managing medication item of the Lawton scale. Specifically, patients with MCI and patients with AD tended to overestimate their abilities on these items. Similar findings were observed in several prior studies (Okonkowo et al., 2007; Peres et al., 2006; Tuokko et al., 2005; Clare at al., 2013). An important consideration of the study is in the heterogeneity of the anosognosia in patients with cognitive impairment: patients with MCI and AD are not as accurate on estimation of their financial abilities as they are in other everyday functional abilities. Interestingly, Clare et al. (2013) have shown that the nature of memory awareness is a heterogeneous phenomenon which can be differently impacted by the level of cognitive impairment. They reported that patients with MCI showed normal performance on monitoring task (performance monitoring while

completing a memory task), but had an impaired general evaluative judgment (evaluative judgment about the use of memory in everyday situation). The researchers suggested that evaluative judgment reflects a general difficulty with judgement and relies on episodic and autobiographical memory whilst performance monitoring relies on the ability to detect errors in memory tests performance and relates to executive functioning. These dissociable aspects of memory awareness are more than just an academic interest as awareness of cognitive deficits may be a be a more direct predictor of specific outcomes, The identification of distinct awareness phenomena would be interesting to investigate further in the development of the new performance-based scales, whereby awareness indices derived from the evaluative judgment scores and performance monitoring scores can ascertain different degree of awareness loss to derive a fuller picture when exploring patients differences.

Neurocognitive studies have the potential to improve our understanding of the relationship between cognitive function and functional loss in MCI and AD patients by highlighting specific cognitive processes that are essential for functional abilities. The current study shows that in healthy controls Lawton's scale was associated with gender variable that confirms once again a gender associative nature of the scale. Financial abilities have proved to be a complex cognitive construct that relies on composite measures of several cognitive domains. However, although memory is a cardinal deficit in MCI and AD, language was the only cognitive function associated with financial performance in MCI patients. This can be explained with the small sample size and large within group variability that was the major limitation of the current study.

There is a very interesting finding of the study: the Shape-Colour Binding Condition was associated with managing medication in patients with AD. This is the first study that would show this association. It has an important clinical implication as patients with AD will have troubles associated certain coloured pills

The other limitation of the study is the large proportion of males in the patient groups. This could skew the results and display as impairment in gender associated items (e.g., laundry, food preparation, house chores). It is very difficult to judge in the modern world

about gender specific items in functional scales and the roles of females and males have drastically changed. Nevertheless, Hesseberg et al (2013) in their study have also showed that primarily in IADL scale (Lawton's Scale) there were no gender specific items except laundry.

Chapter VII

Acreemagnosia (Loss of financial knowledge): a symptom of functional and cognitive loss in frail older people

More and more research argues that the most cognitively demanding items in functional scales requiring more sophisticated cognitive and psychological organisation are better than cognitive assessments at identifying community dwelling older people who are at risk of developing dementia (Brodaty et al. 1998; Cromwell et al. 2003; Kempen and Suurmeijer 1990; Peres et al. 2006; Schmitter-Edgecombe et al. 2011; Schmitter-Edgecombe and Persey 2014). It has been argued that deficits in ADL/IADL are capturing the earliest deficiencies experienced in everyday life beyond those measured by standardised neuropsychological tests (Luck et al. 2011; Peres et al. 2006; Sikkes et al. 2011). Indeed, functional scales may be less biased by education than cognitive scales (Juva et al.1997) and they rely on multiple cognitive domains (Farias et al. 2006; Gold 2012; Peres et al. 2008). Several longitudinal studies (Peres et al. 2008; Purser et al. 2005) examining trajectory of decline from the cognitively healthy individuals to dementia showed that in healthy individuals and MCI patients that reported IADL restriction, researchers were able to predict incipient dementia within ten years time than those who were independent in IADL.

The ability to maintain one's own finances is a complex function which relies on several cognitive constructs (Aretouli and Brandt 2010; Arrighi et al. 2013; Griffith et al. 2003; Hesseberg et al. 2013; Marson et al. 2000). Its decline is argued to be an early symptom of dementia (Marson et al. 2000, Wills 1996) and a strong predictor of future cognitive decline (Chiong et al. 2014; Peres et al. 2008). The impairment in financial abilities and the lack of awareness of such deficits carry considerable social and legal impact, and are believed to be among the primary factors precluding independent life and requiring legal assistance (Cramer et al. 2004; Kershaw and Webber 2008; Wills 1996). Despite its relevance, little attention has been paid to this common symptom. In this chapter I will discuss the relevance of assessing everyday financial management abilities in frail older people and people with cognitive decline and will critically appraise the available assessments tools. To highlight the specificity of the symptom we have suggested a term to define it: ***Acreemagnosia***, from the Ancient Greek ἀ- (a-, "lack of"), χρήμα (creema, "money") andγνωσιακή (gnôsis, "knowledge").

I begin by arguing that the financial items included in Activities of Daily Living (ADL), in particular in Instrumental Activities of Daily Living scales (IADL), are the most complex self-management items in those scales. I then address the importance of assessing financial abilities which could potentially offer the earliest window for the detection of ADL/IADL impairments. I critically appraise the proposed tools to assess Acreemagnosia, and conclude by making some propositions as to what a valid instrument to assess financial competence should encompass.

7.1 Everyday financial abilities as the most complex items of ADL/IADL Scales.

Njegovan et al. (2001) showed a hierarchy of functional losses associated with cognitive decline in older people at higher order functional activities, such as housework, shopping, and finances decline first. Other studies that evaluated hierarchical relationships across the different items encompassed within the ADL/IADL scales found a fair degree of overlap across them, though confirmed that, using phone, self-medication and handling money were the most "complex self-management tasks" (Thomas et al. 1998, p.318). Studies aimed at differentiating healthy ageing from MCI using ADL/IADL scales demonstrated that activities such as shopping, transportation, managing medication and handling finances were the best suited for the purpose (Aretouli and Brandt 2010; Bangen et al. 2010; Barberger-Gateau et al. 1992; Barberger-Gateau et al. 1999b; Gold 2012; Kim et al. 2009; Njegovan et al. 2001; Nygard 2003; Pedrosa et al. 2010; Reppermund et al. 2011; Willis 1996). The identifications of problems with these four above mentioned activities has been claimed to be a predictor of dementia 3-5 years prior to the onset of clinically detectable dementia (Barberger-Gateau et al. 1999a; Cromwell et al. 2003). Some of the studies investigating the multidimensionality of IADL/ADL scales have shown a clear hierarchy across the different items composing the scales. Kempen and Suurmeijer (1990) in their study on the development of the Hierarchical ADL-IADL that incorporated ADL and IADL items for non-institutionalised elders reported that shopping was one of the most difficult items to perform. Managing finances and shopping were confirmed to be the most difficult items for non-demented older by more recent studies reporting invariant item ordering using Item Response Theory (IRT). This analysis enables to consider the formal hierarchy of the scales with more accuracy (Spector and Fleishmen 1998; Fortinsky et al. 2003). Sikkes et al. (2011) in a multicentre longitudinal study on the IADL scales' ability to predict future dementia showed that two of the most discriminating items between normal and pathological ageing were handling money and understanding personal financial affairs. Peres et al. (2008) in their prospective population-based study showed that decline in managing finances was the strongest predictor of cognitive decline up to 10 years before the onset of dementia. Data from recent studies suggest

that managing finances is among the earliest IADL impairments in MCI (Gold 2012; Griffith et al. 2003; Kim et al. 2009; Marson et al. 2000). Bangen et al. (2010) found that patients with different MCI subtypes report a dissociation in the Managing Money Subscale of the Independent Living Scale (ILS), a performance-based IADL scale (Loeb 1996): amnestic MCI showed more impaired abilities of handling finances that non-amnestic MCI (the two groups did not differ from each other on the Dementia Rating Scale (DRS) scores). These findings suggest that investigating financial skills may be useful also in differentiating between subtypes of MCI.

Given the considerations above, assessment of financial abilities is of paramount importance not only because it appears to be a sensitive and early functional marker of incipient dementia, but also because a reduced competence to look after one's own finances is a major risk of being financially exploited or abused, hence losing independence (James et al. 2014; Smith 2000; Tueth2000). In Chapter 6, I showed that patients with MCI already present with unawareness in acreemagnosia: only answers to the questions related to their financial abilities differed between MCI patients and their proxies. The clustering, resulting from item analysis of the output from ADL/IADL scales suggests that Acreemagnosia is a deficit in its own right, and as such should be recognized, offering a conceptual frame within which to devise appropriate assessing instruments.

7.2 Assessment of financial knowledge in current clinical practice

The reason why the assessment of financial competence has received little attention probably resides in the lack of a framework to assess financial management abilities in older people and patients with cognitive impairment, a lack of guidelines, but also a lack of standardised assessment tools. Clinicians routinely check for financial competence by relying on clinical interviews, neuropsychological tests, and ADL/IADL scales, which do not thoroughly explore financial abilities (Kershaw and Webber 2008). This introduces variability to the outcome of such assessment and increases the likelihood of incorrect judgments about financial competence. There is growing concern that general cognitive assessment tests are unsuitable for evaluating financial ability (Kershaw and Webber 2008; Stebnicki 1997). Indeed, there is evidence that people who perform well on psychometric tests may still perform poorly on financial competence tests (Bechara et al. 1994).

Most ADL/IADL scales include only a few items inquiring about financial competence. These items investigate global financial abilities rather than specific underlying constructs. For

example (see **Table 7.1**), one of the most widely used such scales in clinical setting, the Lawton IADL scale (Lawton and Brody 1969), enquires about one's own independence in carrying out financial matters and in managing day-to-day purchases. This was confirmed by my experiment in Chapter 6: the most difficult items to perform were financial items and in addition patients with cognitive impairment was unaware of these difficulties. Instruments with the best psychometric properties (Sikkes et al. 2009), like the Disability Assessment for Dementia (DAD) (Bucks et al. 1996) and the Bristol ADL (Gelinas et al. 1999), lack a unifying conceptual model of financial abilities. The DAD enquires about interests and organisation of personal affairs and correspondence whereas the Bristol ADL asks about the level of responsibility of one's own finances hence inquiring about different areas in everyday financial life and therefore measuring different aspects of the concept.

Table 7.1 Examples of ADL/IADL items enquiring about financial abilities

Lawton IADL (Lawton et al. 1969)	Bristol ADL (Gelinas et al. 1999)	DAD (Bucks et al. 1996)
1. Manages financial matters independently (budgets, writes checks, pays rent, bills, goes to bank), collects and keeps track of income. 2. Manages day-to-day purchases, but needs help with banking, major purchases, etc. 3. Incapable of handling money	1. Responsible for own finances at previous level 2. Unable to write cheque but can sign name and recognizes money values 3. Can sign name but unable to recognize money values 4. Unable to sign name or recognize money values 5. Not applicable	1. Shows an interest in his/her personal affairs such as his/her finances and written correspondence 2. Organizes his/her finance to pay his/her bills (cheques, bankbook, bills) 3. Adequately organizes his/her correspondence with respect to stationery, address, stamps 4. Handles adequately his/her money (make change)

Moreover, the few items incorporated into IADL scales that enquire about financial management knowledge are rather dated. Technological advances (computers, smart phones, tablets), changes in shopping styles (online shopping, food order online or ticket bookings), financial affairs (more complex banking and investment systems, ATM machines and online banking) can impose new challenges to older people, especially to those experiencing cognitive decline. These various technological, financial, and cultural advances of modern life are not considered in ADL/IADL scales (Munoz-Neira et al. 2012; Rosenberg et al. 2009).

Assessment of everyday financial ability and awareness of older peoples' financial knowledge can help reduce the probability of financial exploitation and scams. There is an alarming rate of financial exploitations of older people (Aciernoet al. 2010). Financial victimisation is a serious problem as it can result in loss of independence and security, and devastating emotional distress (James et al. 2014; Tueth 2000). A growing number of articles highlighting the need for research to portrait a financial scam victim emerging from empirical research (Acierno et al. 2010; James et al. 2014; Tilse et al. 2005; Tueth 2000). Kemp and Mosqueda (2005) in their study of financial abuse of older people also stress the lack of assessment instruments available for these needs.

A standardised assessment tool focusing on the most complex aspect of everyday life - financial abilities – would play an important role not only in the early identification of Acreemagnosia but would inform clinical judgment on the ability of the individual to live independently as well as in the type of support that should be given to families to avert financial, legal, and psychological problems.

7.3 Available tools specifically assessing financial competence

There are three instruments specifically developed to evaluate financial abilities (**Table 7.2**). Most of the tools that have been specifically designed to assess financial competence came from the work of the group led by Daniel Marson. Other instruments have not been fully validated and standardised and have not been used outside research environments. Below we review the status of these instruments.

Table 7.2 Instruments that are specifically aimed to assess financial management abilities

Test	Components	Population	Validation	Reliability	Strength	Limitations
Financial Capacity Instrument (FCI) *(Marson et al. 2000)* 170 citations according to the Scopus.com (date of retrieval 29/08/18)	112 items, 20 tasks within 9 domains •Basic monetary skills •Financial conceptual knowledge •Cash transactions •Check-book management •Bank statement management •Financial judgment •Personal financial knowledge (assets and estate) •Bill payment •Investment decision	FCI (6 domain) 23 healthy older controls 30 mild AD 20 moderate AD FCI (8 domain) 23 healthy older controls 20 mild AD FCI (9 domain) 21 healthy older controls 21 amnestic MCI 22 mild AD	**•Discriminant Validity:** significant differences in FCI scores between healthy older controls, MCI, mild AD, moderate AD; mild AD patients show rapid decline over a year, MCI patients converting to AD show selective decline over a year **•Convergent Validity:** Overall financial capacity (FCI-9) in controls, MCI, and mild AD strongly predicted by written arithmetic, and also executive skills **•Factor Validity:** Factor analysis of FCI-9 tasks revealed 6 factor structure with eigenvalues ≥0.96, and factor loadings = 0.39-0.60 [n = 322]	**•IC:** α = 0.85–0.98 for FCI-6 domains. α = 0.81–0.93 for core FCI-8 domains **•IR:** % agreement = 81.0-100.0 for FCI-6, and = 90.6–100.0 for FCI-8 **•T-RT:** Pearson r range = 0.85–0.98 for FCI-6 domains (P < .001), and = 0.78-0.92 for core FCI-8 domains	• Direct, standardised, and quantified assessment; • Global overview score; • Multi-dimensional; • Includes functional component; • Clinically relevant and useful; • Conceptually well-grounded; • Research-based	• 40 min for older controls, 60 min for AD patients (time consuming); • The instrument is not accessible for free use; • Doesn't account for previous expertise and financial knowledge; • Relevancy only established with people with dementia and MCI; • Small sample size, thus limiting the extent to which findings can be generalised; • There is no rationale provided for what are "simple" and "complex" tasks; • Difficulty of the tasks did not correlate with severity of dementia; • Pioneer-stage research; some of the items are outdated eg check-book management; • No information to date, results have not been published yet • The measure is based on

						the legal and monetary system in America. •Limited use outside the country
The Financial Capacity Instrument – Short Form (FCI-SF) (Gerstenecker et al., 2016) 3 citations according to the Scopus.com (date of retrieval 29/08/18)	A short version of FCI 37 Items measure • Coin/currency knowledge • Financial conceptual knowledge • Problem Solving • Understanding/using a check-book • Understanding/using a bank statement	No information to date, results have not been published yet	No information to date, results have not been published yet	•**IC:** α = 0.90 •**IR:** % agreement = 96 across two raters •**T-RT:** Pearson r range = 0.91, p <0.001	Brief assessment (15 minutes)	

Test	Components	Population	Validation	Reliability	Strength	Limitations
Semi-structured Clinical Interview for Financial Capacity (SCIFC) *(Marson et al. 2009)* 49 citations according to the Scopus.com (date of retrieval 29/08/18)	• **Shares same 8 domains with FCI.** • Interview format and specific test items • Examines competence in each of FCI -8 • 3 level scoring: capable, marginally capable, incapable	75 healthy controls; 58 patients a-MCI; 97 mild-AD; 31 moderate AD	**Discriminant Validity:** significant differences in FCI scores between healthy older controls, MCI, mild AD, moderate AD.	**•IC, IR, T-RT** was not assessed	Brief assessment (25 minutes)	• Potential for considerable variability, bias and subjective interpretation of the outcomes; • The measure is based on the legal and monetary system in America. Limited use outside the country
Prior Financial capacity Form (PFCF) and Current Financial capacity Form (CFCF) *(Wadley et al. 2003)* 54 citations according to the Scopus.com (date of retrieval 29/08/18)	• **Shares same 8 domains with FCI.** • Provides comparison between premorbid (PFCF) and current (CFCF) financial capacity • Global judgment and judgment about current functioning in 8 domains and 20 associated tasks • 3 level scoring: capable, marginally capable, incapable	• 20 AD and their family caregivers; • 23 healthy controls and their family informants	On CFCF patients self-reports differed significantly from caregiver report. Control CFCF self-report did not differ from control informant.	**•IC, IR, T-RT** was not assessed	• Functioning is appraised over time in everyday life settings; • First tool to address relevance of premorbid functioning to current abilities	• Risk of bias and errors because information is obtained via collateral sources; • 40-60 min. administration; • In developmental stage; • High level of stability over 1 month period in controls and their informants, however low level of stability in AD patients and their caregivers; • The measure is based on the legal and monetary system in America. Limited use outside the country

Test	Components	Population	Validation	Reliability	Strength	Limitations
Financial Competence Assessment Inventory (FCAI) *(Kershaw and Webber 2008)* 14 citations according to the Scopus.com (date of retrieval 29/08/18)	•38-items •6 domains •Everyday financial abilities •Financial judgment •Estate management •Debt management •Cognitive functioning related to finances •Support resources	36 Acquired brain injury 29 Schizophrenia 22 probable AD 32 Intellectual disability 59 healthy controls	•**Discriminant Validity:** Significantly worse FCAI scores for patients with global cognitive impairment (AD, intellectual disability), P < .01 •**Convergent Validity:** Correlated with Money Management subscale of ILS, the Financial Decision Making scale of the Hopemont Capacity Assessment Interview •**Factor Validity:** No information	•**IC:**Cronbach α = 0.96 (range 0.54-0.91) •**IR**: Percent agreement on 10 pairs of raters range, 83 to 98%, average 89% Cohen's k = 0.86 •**T-RT:** overall Pearson correlation coefficient = 0.93, range 0.57-0.98	• Multi-dimensional approach • Tested on 4 different cognitive impairment groups • Being able to distinguish between groups • High internal consistency reliability	• Time to administer the questionnaire is not indicated; • Moderate validity: some of the questions are low internal consistency and test-retest reliability (0.54 and 0.57 respectively); •The instrument is not accessible to use; • Minimal research to date; • The measure is based on the legal and monetary system in Australia. Limited use outside the country

Measure of Awareness of Financial Skills (MAFS) *(Cramer et al. 2004)* 18 citations according to the Scopus.com (date of retrieval 29/08/18)	• Participant self-rating • Informant parallel questions • Performance on 6 financial tasks to parallel the questionnaire • 32 questions related to financial management	6 experts experienced in helping people manage their finances 25 well-functioning older adults and their informants 10 dementia (7 probable AD; 1 possible AD; 2 vascular dementia).	•**Discriminant Validity:** unawareness scores were much lower for well-functioning participants, $P < .01$. •**Convergent Validity:** Level of cognitive functioning (3MS) correlated significantly with unawareness scores; the amount of control participants felt they have over their life did not correlate with unawareness scores •**Factor Validity:** No information	•**IC:**Cronbach $\alpha = 0.92$ for participants questionnaire; $\alpha = 0.97$ for informant questionnaire •**IR** and **T-RT** no information is given	•Can compare self-reports, informant reports and objective performance • Research-based	• 1.5 hours participants administration, 20 minutes informant administration; • The awareness scores rely on participants and informar reports that can be biased; •The instrument is not accessible for free use •Minimal research to date • Validated on the Canadian population

Abbreviations: IC, internal consistency; IR, inter-rater reliability; T-RT, test retest; 3MS - Modified Mini Mental State Examination; ILS - the Independent Living Scale; AD - Alzheimer's Disease; MCI - Mild Cognitive Impairment; a-MCI - amnestic Mild Cognitive Impairment

7.3.1 Financial Capacity Instrument (FCI)

Seminal research on financial abilities in people with dementia was carried out by Marson and his colleagues at the University of Alabama, Birmingham (Marson et al. 2000). They argued that financial competence is a multidimensional concept comprising at least three components: (i) *Conceptual knowledge* - the established store of semantic and episodic facts, concepts and events related to financial knowledge (for example, naming coins, understanding bank transactions);(ii) *Pragmatic knowledge*– automatic skills and routines that are based on overlearned practical performance (for example, counting coins/currency, writing a cheque, simple cash transactions);(iii) *Judgment abilities*- the ability to predict the consequences of financial decisions in novel situations (for example, detecting mail fraud). Following this tenet, they developed the "Financial Capacity Instrument" (FCI) to assess financial abilities in people with dementia. The only financial instrument that has been fully validated and standardised. However, this instrument remains unpublished and is not available for use.

These researchers showed that patients with mild Alzheimer Disease (AD) performed as well as healthy older controls on simple tasks (naming and counting coins, recognizing parts of a check book, detecting risk of mail fraud) and performed worse than controls on more complex tasks like those requiring to apply financial concepts, obtaining exact change, understanding and using bank statements, and making investment decisions (Marson et al. 2000). They also found a considerable variability in performance of people with mild AD (as measured by MMSE), meaning that patients with the same level of cognitive impairment performed differently on the same financial tasks. Performance on tasks that were defined as 'simple' or 'complex' was not found to correlate with severity of dementia. However, the boundaries between "simple" and "complex" tasks are left unclear. In a one-year longitudinal study from the same research group that had a more homogeneous, compared to the previous study, group of patients with only mildly impaired AD had a more consistent result. Patients showed further decline, the greatest of which was on the more complex tasks, such as bank statements management, investment decisions, financial judgments, and cash transactions (Martin et al. 2008). The results from these studies confirm the notion that by breaking down ADL/IADL into more specific functions it is possible to unveil deficits that otherwise would go unnoticed when probed by general questions.

There are three other tools resulting from the work by Marson and colleagues, both strongly based on the FCI (details see in the Table 2). FCI was the first instrument specifically designed

to assess financial abilities; however, the tool has a very limited clinical utility as it encompasses more than 100 items and takes more than an hour to administer. To address this issue Marson and his colleagues have devised two shorter versions of the instrument. The Semi-structured Clinical Interview for Financial Capacity (SCIFC) (Marson et al. 2009), proposed as a brief (25 minutes) financial clinical assessment tool, comprises the same 8 domains of the FCI scale. The other one is the Financial Capacity Instrument – Short Form (FCI-SF) which is also a brief (less than 15 minutes) clinical screening tool (Gerstenecker et al., 2016) assessing financial competence and calculation. A further instrument based on the FCI Includes two components, the Prior Financial Capacity Form and the Current Financial Capacity Form (Wadley et al. 2003) also addressing the same 8 FCI domains and proposed to evaluate the prior and current financial abilities of AD patients. The reference point for the prior functioning was assumed to be when the examinee was best at managing personal financial affairs. The FCI and its descendent tools, which are all based on the US monetary system, have been validated and standardised on MCI and AD patients, however they have not been used outside research. These instruments have not been tested or validated on other patient groups or on individuals with diverse cultural and ethnic backgrounds, which is also limits its use. None of these different versions of the FCI are available for use.

7.3.2 Financial Competence Assessment Inventory (FCAI)

Another questionnaire reported in the literature is the "Financial Competence Assessment Inventory" (FCAI) by Kershaw and Webber (2008) from the Deakin University in Australia. This questionnaire is aimed at investigating the legal criteria used in the United States and Australia; this tool is also unavailable for public use. The instrument was never published in full; only a brief description of the subscales was given in the manuscript about the validity of the tool without detailing the actual questions for each of the domains. According to Kershaw and Webber, financial competence is a multidimensional ability that includes everyday financial abilities (e.g., paying bills), financial judgment (e.g., financial goals), cognitive functioning related to financial tasks (e.g., basic reading, writing, and numeracy), estate management (e.g., understanding Power of Attorney), debt management, and support resources (e.g., knowing where to look for help in managing finances). The instrument was developed to assess legal financial competence for patients with different types of cognitive impairment: acquired brain injury, schizophrenia, AD, intellectual disability and also for people without overt cognitive impairments.

The scale was aimed at determining competence in four legal fields: “understanding”, “appreciation”, “reasoning”, and “expressing a choice”. The FCAI comprises 41 items (tasks and questions) related to financial abilities and consists of 6 subscales. The degree of impairment in all subtests was more serious in people with dementia and intellectual disability. The groups with more “localized” impairment (acquired brain injury, schizophrenia) performed worse on the specific item of financial judgment. Performance of patients with more “diffused” impairment (dementia and intellectual disability) was poor across all domains of the scale. People with acquired brain injury and schizophrenia showed better overall scores on the scale than people with dementia and intellectual disability. The authors noticed that the groups with more “localized” impairment (which included schizophrenia and acquired brain injury) showed better overall scores on the scale than people with "diffuse" impairment, which included patients with dementia or intellectual disability. However, the authors’ grouping is questionable, as schizophrenia is hardly a localized impairment (Karlsgodt et al., 2010). The similarities of performance across different groups with different cognitive profiles, severity of cognitive impairment, and onset of the disease (people with intellectual disabilities who have had a disorder from early age might have never been exposed to financial tasks to the same extent as a person with dementia) were not discussed in the paper despite indicating the lack of specificity of this assessment tool. The scope of the study’s outcomes is further limited by the lack of group matching in terms of education and age. Moreover, prior financial knowledge was not considered, which could have affected the results (Marson et al. 2000). This instrument has never been used outside research, has not been fully validated and is unavailable to use. There is also a question about whether this instrument can be used outside the legal and monetary Australian and American systems.

7.3.3 Measure of Awareness of Financial Skills (MAFS)

Cramer et al. (2004) suggested that awareness in finances abilities is a central component of competency and unawareness would relate to the severity of cognitive impairment. Accordingly, they devised the Measure of Awareness of Financial Skills (MAFS) that comprises three parts: one given to the participant, a parallel part is for the informant or caregiver, and a performance measure (see Table 2). The instrument contains 34 questions about different financial tasks; participants are asked to rate, on a four-point scale, the amount of difficulty they experience when performing each of these tasks and the amount of help they would need to perform them correctly. The results show that performance on the tests was

related to awareness scores (calculated as the discrepancy between the self-report and the informant's report); that is the poorer the financial competence the lower the awareness of one's own deficit. However, the size of the sample was rather small (25 healthy volunteers acting as controls and 10 participants with different types of dementia) and encompassed different types of dementia, the severity of which was not reported.

Cramer et al. (2004) hypothesized that awareness across different financial skills relates to higher order cognitive abilities such as executive functions. Contrary to their prediction, they found no or very little correlation between performance on different tests assessing executive functions, global cognitive function, and degree of financial awareness. They suggested that decline in executive functions and cognition is not uniform throughout the disease progression and attributed this lack of correlation to the heterogeneity of dementia in their sample. Another suggestion made by authors is that different levels of difficulties on the tasks could contribute to the discrepancies in awareness. That is, mildly demented patients will be more aware of their performance level on simple tasks than on complex tasks (Van Wielingen et al. 2004). The researchers however did not provide a solid rationale to distinguish between "simple" and "complex" tasks. Cramer et al.'s (2004) concept of lack of awareness of one's own financial incompetence is relevant; hence it is embedded as a possible component of Acreemagnosia.

All the studies reporting on the development of financial competence assessment tools recognise that traditional neuropsychological instruments are inappropriate to assess financial abilities. They also emphasise that financial competence is a multidimensional construct and suggest the need to break it down into separate components hence requiring a broad set of cognitive and procedural skills.

7.4 Cognitive underpinnings of Acreemagnosia

It is debated whether financial impairment precedes or follows clinically observable cognitive impairments or whether there is a link between specific cognitive constructs and financial abilities. Indeed, Silberfeld et al. (1995) maintained that there is little correlation between specific cognitive impairments and the ability to make financial decisions. Earnst et al. (2001) suggested that working memory deterioration is associated with financial abilities loss in people with mild AD. It must be noted that this study did not use any other cognitive measures except working memory (all measures were taken from the Wechsler Adult Intelligence Test (WAIS)-III: arithmetic, digits forward and backward, and letter-number sequencing). Okonkwo

et al. (2006) in their study using FCI together with a comprehensive neurocognitive battery, demonstrated that executive deficits (assessed by means of WAIS-III, Trial Making Test A, and visuo-motor sequencing) and impairments of attention (assessed by means of the Dementia Rating Scale (DRS)-2, Attention and Wechsler Memory Scale (WMS)-III, Spatial Span Forward) were the only cognitive impairments associated to the financial abilities decline of people with amnestic MCI. Sherod et al. (2009) supported this conclusion. They showed that performance on the FCI was mediated by similar neurocognitive predictors in healthy controls, MCI patients, and mild AD patients. These predictors were a measure of written arithmetic skills (the Wide Range Achievement Test (WRAT)-3 Arithmetic), tasks assessing executive functions (using visuo-motor sequencing; Trial Making Test A and B) and verbal memory (immediate and delayed story recall).

Other studies however have questioned the correlation between scores in cognitive tests and financial management competence (Silberfeld, et al.1995; Spector and Fleishman 1998). Basset (1999) in her study with mild and moderate AD patients found no correlation between general cognitive function (as measured by the MMSE) and scores on five financial competence questions (Basset 1999). She also questioned that intelligence test scores can reflect everyday financial competence. However, in the same study she showed that performance on a simple attention measure (Trial Making Test A) was the only significant predictor for AD patients' performance accounting for over 80% of variance. Kershaw and Webber (2008) in their study for scale validation used MMSE. They had mixed results that were depended on the population. That is, they showed that MMSE has no or low correlation with their FCAI scale in people with brain injury and cognitive healthy control groups; they had positive correlation between FCAI and MMSE performance on other three groups (schizophrenia, AD, and intellectual disability). They concluded that MMSE is not a reliable measure of financial capacity in healthy older and people with brain injury. Bechara, Damasio, Damasio, and Anderson (1995) in their study on patients with ventromedial prefrontal lesions reported on the cases of patients unable to make real-life financial decisions in spite of their normal performance on a battery of cognitive tests.

In sum, the data culled from the literature shows that severity of cognitive impairment is a relevant variable for financial incompetence to emerge, yet the precise cognitive profile associated to it remains elusive.

7.5 The need for a new instrument

Assessing the possible presence of Acreemagnosia is important as older people are at greater risk of functional dependence (De Vriendt et al. 2012; Schmitter-Edgecombe et al. 2011) and are prone to different types of financial frauds (Acierno et al. 2010; James et al. 2014; Reiboldtand Vogel, 2003; Tilse et al. 2005; Tueth 2000). Ad hoc scales assessing financial abilities are not fully validated, have psychometric limitations, are old fashioned, and, importantly, are not available for use. Therefore, there is the unmet need for a new instrument, which could aid the diagnosis of Acreemagnosia and quantify its severity.

Ideally, such an instrument should take into account the limitations and the strengths of the existing scales in order to maximize the sensitivity to recognize early decline in financial knowledge. It should incorporate various financial domains and contain sufficient financial items to adequately represent various financial ability constructs. The instrument should be devised to be informative also when assessing financial competence in normal ageing, avoiding ceiling effects by means of enclosing tasks with different levels of complexity (easy, moderate and difficult items). This would also allow clinicians and researchers to establish a natural history of financial decline and monitor the development of the disease, the capacity to live independently, and importantly identify those potentially vulnerable to financial scams.

In order to improve construct validity and consider the risk of bias and proneness to underestimation in caregivers' appraisals of patients' functional abilities (Cramer et al. 2004; Loewensteinet al. 2001) such a tool should incorporate informant-based, self-report and performance-based measures that would complement each other. To achieve a better measurement precision and establish particularly sensitive items to differentiate among cognitively healthy older people, MCI and early dementia, sound psychometric techniques should be employed (e.g., Item Response Theory Analysis) to cluster different items of the scale upon an individual level (Fieo et al. 2011). A new instrument should refine conceptual aspects underlying both simple and complex items not addressed in the existing scales. A psychometrically valid tool should incorporate unidimensional items which measure specific constructs as well as items which measure more than one construct, referred to as complex (Reckase 2009, pg. 63).

As financial involvement and interests change after retirement, the ideal instrument should also take these changes into account and reflect everyday financial abilities and needs of retired

people. Finally, the ideal instrument assessing financial competence will have to be culturally valid. Financial matters greatly vary from country to country so any instrument assessing financial abilities should rely on similar constructs but incorporate them in a way that truly reflects contextual challenges. A simple translation into a different language of an instrument devised for a particular cultural group would not suffice.

7.6 Conclusions

Financial management is a complex everyday functional ability that requires a high order of cognitive function (Griffith et al., 2013). In this Chapter I highlighted the rationale for incorporating assessment of everyday financial knowledge into routine clinical assessment, and how this would aid the early detection of early behavioural changes in frail older. In order to assess financial knowledge, researchers and clinicians are currently using ADL/IADL scales that do not sufficiently address the intricacy of everyday financial requirements. There are several financial scales that have been devised to particularly look at financial abilities, competence, and awareness. Unfortunately, these scales are unavailable for use and are not fully validated.

Dealing with AD, MCI patients and their caregivers we, as several others, are observing how often they lack financial competence and are unaware of this impairment. We coined the term Acreemagnosia to label this symptom in order to frame it as a specific cognitive difficulty which could hamper the independent daily life of people at different levels of cognitive competence. Importantly, often also the carers are not fully aware of the patient's impaired financial knowledge. There are a numbers of unanswered questions about Acreemagnosia.

To address them and further explore the symptom, a proper instrument is needed. This instrument should combine subjective, objective and performance-based measures and should reflect everyday financial involvement of the post-retirement person and account for financial proficiency. Such an instrument would serve not only in diagnosing early impairments but would also help health care professionals (i.e. general practitioners, nurses, clinical psychologists) and other relevant professionals (i.e. social workers, financial or family counsellors) making the correct and objective judgment about the person's everyday financial knowledge. In order to make it more accessible for clinical, research, and public use we propose that this new instrument should be made freely available. In the next Chapter, I report on such tool. I describe the development and validation of the Acreemagnosia Measurement

(TAM). In Chapter 9, with a small sample of patients I investigate if TAM can help distinguishing between healthy older people and patients with cognitive impairment.

Chapter VIII

The Acreemagnosia Measurement: Psychometric evaluation of a new assessment of the loss of financial knowledge.

8.0 Introduction

Based on the literature reviewed and the need for a new measure of everyday functional abilities, the aim of the following two studies was to develop a new tool to evaluate financial abilities as a multi-dimensional concept, the first stage of which was done in a healthy, middle age and elderly population.

In the next two experiments, I aim to show the rationale behind the construction of the scale. As financial ability is a multi-dimensional construct, I wanted to build the instrument that reflects this complexity. During this part of the study I consulted various professionals in the financial area: financial advisors, economists, financial psychologists, lawyers, pension advisors in order to help me to refine all parts of the measurement, questions and tasks within these parts. The aim was to build the instrument that would reflect the financial life of the retired person. Different people have a different financial involvement: some people have a particular interest in finance or previous experience or expertise, whereas other might have a very limited understanding of difficult concepts and their financial experience is limited to everyday grocery purchase and bill payments.

To reflect this complexity and address the fact that within the financial abilities there are tasks that are very complex and difficult and other tasks that are simple, I relied on the Item Response Theory (IRT). To ensure understanding of the ensuing sections of the chapter, I devote its initial section to the description of core features of this analysis.

Item response theory

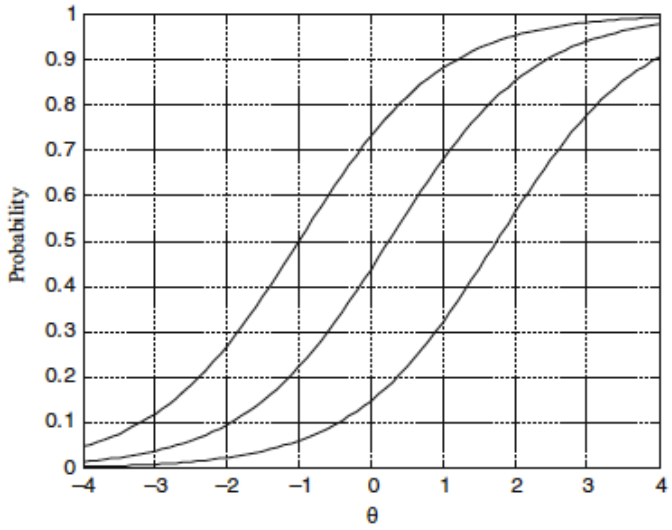
It is a model-based measurement in which the trait level estimate is dependent on both the individual's response and the properties of the item within the test (Embretson &

Reise, 2013). IRT describes the relationship between the individual's trait level and the probability of a given response to an item using a nonlinear monotonic function (Embretson & Reise, 2013). The individual's ability or trait level in IRT is denoted with theta (θ) and describes each respondent's item and test performance (latent trait level) (see more detailed description in the section 8.3.3.2).

IRT models are based on the probability of responding correctly to any given test item and based on individual ability and item parameters. This probability is referred to as the Item Response Function (IRF) or graphically through the Item Characteristic Curve (ICC) (see more detailed description in the section 8.3.3.2). IRF or ICC reflects the behaviour of the item in relation to the latent trait. The IRF is a non-linear regression on ability of the probability of a correct response to an item (Mungas & Reed, 2000).

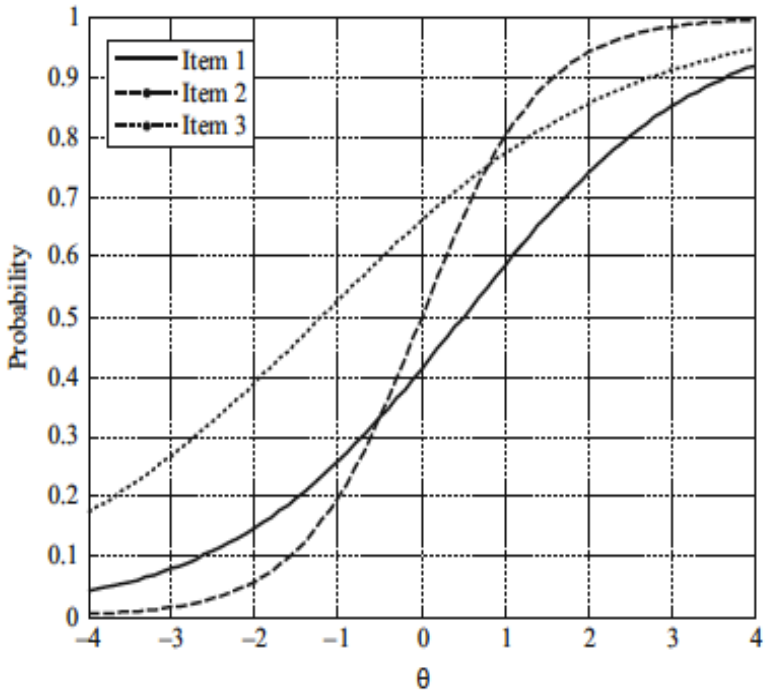
The simplest and most popular IRT model is the one that specifies only a single latent trait (e.g. Rasch model). Items within the test would vary on the difficulty level and this affects response probability. In this model a person with the high level of ability will correctly respond to an item with the high *difficulty* (a_i) level. This *difficulty* parameter requires for a respondent to have a 50% probability of a correct answer to an item. For example, for an item difficulty level of 1.0, the respondent with a corresponding trait level of 1.0 would have a 50% chance of correctly responding to the item.

Figure 8.1 One-parameter logistic model (1PL). Three ICC with different location (*difficulty*). A picture is taken from Reckase, 2009.



In my study, I was using a two-parameters logistic model (2PL) that allows different degrees of association between the test or an item and the latent trait. It requires a different discrimination and difficulty of the item. The slope parameter reflects item *discrimination* (*bi*j) and the steeper the slope the more accurately this item can differentiate between the latent traits (In the Figure 8.2 the Item 2 will be the best to discriminate between high and low latent traits). In 2PL model each item's score is weighted and the more this item has discrimination power, the more weight will be assigned. This is the same with the difficulty of the item. In the Figure 8.2 at the $\theta = 1$ the Items 2 and 3 are much easier that the Item 1 and the probability of the correct response will be for Items 2 and 3. This model is thought to be more precise and accurate than the 1PL model (Embretson & Reise, 2002).

Figure 8.2 Two-parameters logistic model (2PL). Three ICC with different location (*difficulty*) and different slopes (*discrimination*). A picture is taken from Reckase, 2009.



8.1 Initial Instrument Development

Development of the modules of The Acreemagnosia Measurement (TAM)

TAM is designed to combine participants' reports and direct assessment of the financial abilities, which jointly, would provide a more objective and accurate approach. TAM is comprised of three parts.

In the ***first part of TAM*** ('Awareness'), participants rate their current financial abilities compared to the same abilities 10 years before the interview. The first part is a self-assessment section, through which participants will evaluate their own current financial management abilities. This part will also be completed by a relative or caregiver in order to obtain complementary information on the participant's financial skills. Everyday financial management abilities are grouped in 8 general domains which cluster upon neuropsychological constructs of memory, organisation, planning, anticipating the future, prioritising, language, calculation, divided attention, judgment, and decision making. This structure of the responses is similar to that proposed by Farias et al. (2008) who emphasize that everyday functional abilities can be accurately mapped onto these cognitive domains.

For the Awareness part of TAM I identified 10 possible questions within each domain, yielding a selection of 80 questions in total. The initial pool of the potential items was created after surveying existing financial and functional scales as well as reviewing the existing literature on financial matters to identify activities important for successful financial functioning of older people.

The second part ('Background') gathers the background financial information, including one's own family and socio-economical status; it also comprises questions regarding demographic characteristics and one's everyday financial life. This part will help understanding the level of financial activity and whether the participant has a prior competence, knowledge or interest in finances. It looks at what banking methods and bill paying the participant normally uses or used. It explores where people turned for help or advice when struggling with financial management. This information is needed to understand the level of the everyday financial involvement of the participant. If the participant has been never involved in, for example, financial

investments or does not have a bank account, it can be expected that performance on the items of the Skills Section that require these abilities would be poor. Hence, knowledge about background experience in financial affairs would help interpret and correctly weight such poor performances.

For the Background part of TAM I created a list of common questions about their demographic characteristics and socioeconomic status, as well as simple questions in regards to their financial involvement (e.g. do you have a credit or debit card, do you have investments or shares).

The third part ('Skills') is a practical financial skills section whereby an individual will complete a series of tasks mimicking everyday financial management designed to mirror as closely as possible those performed in real-life. This part will provide insight to the real performance on the specific financial tasks. The Skills part has initially comprised of 30 multiple-choice questions as well as practical financial tasks.

To devise and select the most relevant and useful items for each part of the instrument I consulted with subject matter experts from various fields (i.e., business, finances, economics, neuropsychology and law). They answered the following questions: i) whether the item or the question reflects everyday financial management activity, ii) which everyday financial management activity the question or the task reflects, iii) whether the question or the task was clearly and correctly formulated, and iv) whether the activity can be affected by MCI and dementia. After such consultations I retained 33 questions to build the first part of the instrument and 23 for the third part.

8.2 Pilot study towards the refinement of the instrument

8.2.1 Objectives

The aim of the pilot study was to ensure that all items were clear and unambiguous, to ensure that all questions were interpreted as intended (face validity).

8.2.2 Participants

A group of 25 older people were recruited from the Volunteer Panel of the Psychology Department of the University of Edinburgh. Mean age of the participants

was 71 (SD = 8.65) and the mean of their years of education was 16.5 (SD = 4.5). All participants were community dwelling, financially active retired older adults who were cognitively unimpaired at the time of testing (mean ACE-R of 97.35, SD = 2.44). Informed consent was obtained from all participants following a protocol that was approved by the Psychology Research Ethic Committee, University of Edinburgh.

8.2.3 Method and Results

An initial pool of 12 participants were assessed with TAM and were asked during a debriefing session about comprehensibility, ambiguity or sensitivity of the questions and tasks, and to make sure that the questions would not disclose the participant's identity. Following this, adjustments to TAM were made, and the process was repeated with a second sample of 13 participants. Based on feedback from these respondents, a number of further alterations to the questions and response formats of items were made.

Following these adjustments, the second wave of the pilot study was conducted, where the next 13 participants received the amended version of the questionnaire and were asked, as with the previous participants, to provide feedback for each question and the scale as a whole.

In the ***first part of TAM*** ('Awareness'), participants rated their current financial abilities compared to the same abilities 10 years before the interview. Each ability was rated using an 8-point Likert's scale (0: never did before; 0: did it before, no longer necessary; 1: better; 2: no change; 3: questionable or occasional problems; 4: consistently a bit worse; 5: consistently much worse; 6: did it before unable to do it anymore). This allowed capturing the current level of one's financial abilities. Responses falling within these categories would not affect the final score.

With respect to the distribution of the questions across the eight theoretical domains, there are three questions related to memory, 7 questions related to organisation, 5 questions related to planning and anticipating the future, 3 questions related to prioritizing, 4 questions related to language and calculation, 2 questions related to divided attention (these 2 questions were taken from the Everyday Cognition Scale

ECog scale, Farias et al. 2008), 4 questions relate to judgment, and 8 questions relate to financial decision making.

The third part ('Skills') comprises questions as well as tasks. Correct answers are given a score of "1", wrong or don't know answers are given a score of "zero". All questions varied in the difficulty level. At the beginning there are two questions regarding simple financial calculations (e.g., give the correct change from a "purchase"), ability to make up the certain amount of money (e.g., make 25p from the given coins and identify the value of 10 pound banknotes, what can you afford with this?) intertwining with financial conceptual knowledge (e.g., what is a mortgage?). The next series of questions is on the ability to recognize a financial scam from investment offers scenarios, whereby the participant after reading a financial offer should decide whether this is a scam or a fair deal. The final section includes tasks on the ability to handle financial documents such as recognize a bill and the amount of money that is to be paid, fill a deposit slip. In constructing the questions and tasks I was aiming to design them with various difficulty levels in order to reflect the fact that people have different levels of financial involvement. The other reason was in tracking the progression of cognitive decline that would reflect in deterioration of financial abilities.

There are two questions that were taken from the financial literacy questionnaires on the fundamental economic concepts for saving decisions and on basic financial numeracy. These items were previously shown to be highly informative in evaluating the financial literacy of retired people (Lusardi & Mitchell, 2005[1]). The item wording was not modified for any of these questions, but a number of additional response options were added.

No further changes were identified in consultation with the second set of participants, and the resultant item set was carried forward to the psychometric validation study.

[1]These two questions are marked as * in Appendix #A and #B

8.2.3.1 Scoring procedure

Awareness. The participant's total score and the informant's total score is calculated by adding scores from each of the 33 items. These scores (participant and informant) ranged from 0 (never been involved in finances) to 198 (completely unable to perform any more). By taking the participant's total score away from the total score of the informant's evaluation of the participant's financial performance we can calculate the discrepancy score. In combination with the Skills part, this will confirm whether the discrepancy is due to the participant's unawareness of the financial decline or due to the caregiver's misestimation of the participant's actual performance.

Background. As noted above, this section contains a variety of demographic questions and questions on everyday financial involvement. The response formats provide nominal category data which require no specialist scoring.

Skills. A Performance score is obtained by summing up the tasks scores within each domain. If the item is performed correctly, the participant receives 1 point; if the response is incorrect or deficient (answers "don't know"), the score is 0 with a possible maximum score of 23.

8.3 Investigating the psychometric properties of the Skills part of TAM

8.3.1 Objectives

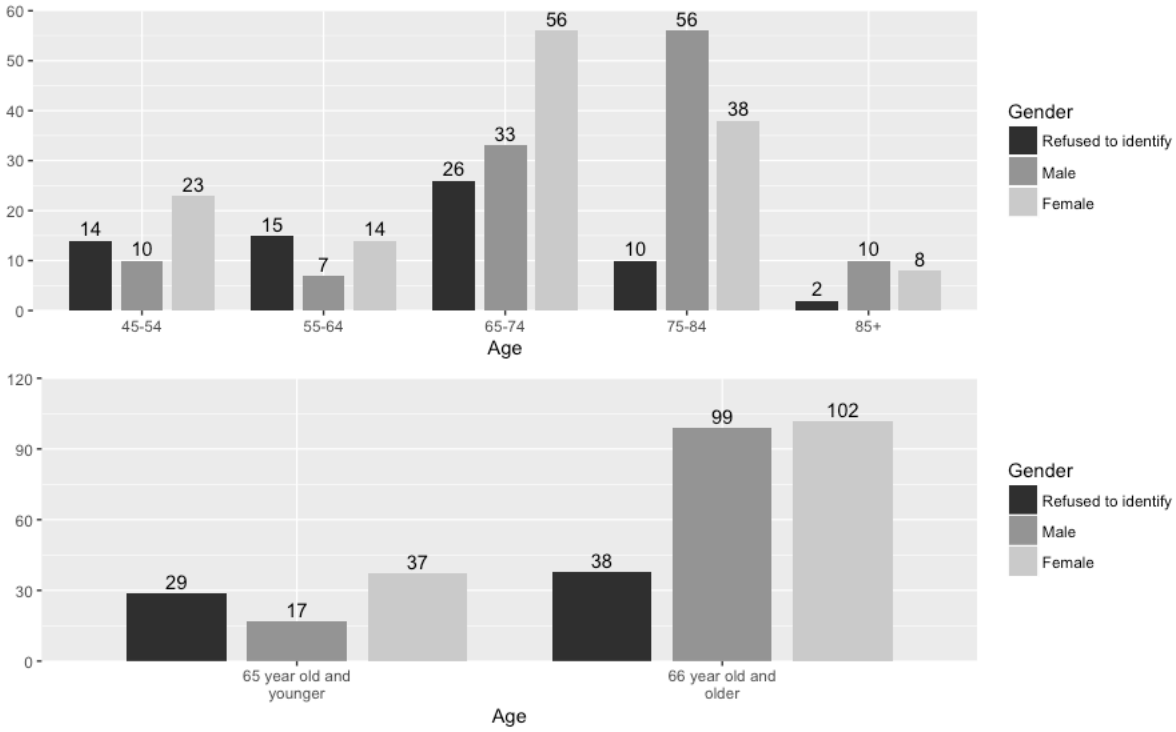
The primary aim of the Experiment was to investigate the psychometric properties of the TAM scale. In particular, analyses focussed on scale dimensionality, item performance in the whole sample, differences in performance across key demographic splits (gender and age), and scale reliability. The goal was to identify those items which may be reasonably removed or modified in later scale developments.

8.3.2 Participants

Three hundred and twenty-two participants recruited online and from the university volunteer panel completed TAM online. For the analysis we partitioned out participants sample into younger than 65 years old and above 65 (see **Figure 8.3**).

The partition of younger and older respondents was based on both theoretical considerations of key ages for MCI and dementia (Geda, 2012) and on practical limitations in order to maintain sufficient sample sizes in both groups.

Figure 8.3 Participants distribution according to age and gender



8.3.3 Analyses

The psychometric evaluation of the scale followed a series of steps to evaluate item performance using Item Response Theory (IRT) models. IRT models are ideally suited to scale development in clinical settings (Reise & Waller, 2009).

8.3.3.1 Step 1. Establishing unidimensionality

Dimensionality refers to understanding whether all items load onto a single latent dimension (unidimensionality), or whether subsets of items load onto different latent dimensions (multi-dimensional). Unidiemsnionality is a key assumption for a number of IRT models (Embretson & Reise, 2013). Understanding item structure allows the selection of the correct item response model.

Here, the unidimentionality of the item set was established according to the combined evidence across a number of indices. First, I considered the results from parallel analysis (PA; Horn, 1965) and Velicer's minimum average partial (MAP: Velicer, 1976) test. Both tests have performed well in simulation studies investigating methods for scale dimensionality. I used PA and MAP to define a plausible range for the appropriate dimensionality of the data, where PA would set the upper bound, and MAP the lower bound.

Next, I considered model fit comparisons based on exploratory factor analytic solutions. I considered both overall fit, using empirically supported guidelines (Hu & Bentler, 1998), and the difference in fit between models with a sequentially increasing number of factors. Specifically, a model fits well if the root-mean-square error approximation index (RMSEA, Steiger & Lind, 1980) is <0.06 and the Tucker-Lewis fit index (TLI; Tucker & Lewis, 1973) is ≥ 0.95. I also considered the improvement in fit demonstrated by the addition of an extra factor. Alongside model fit, the ratio of the first and the second eigenvalues were considered, with ratio's more than 3.0 providing indicative support for unidimensionality (Slocum-Gori & Bruno, 2011). Finally, I considered the theoretical coherence of factor solutions with more than one factor, versus the theorized structure of TAM.

Once an appropriate dimensionality had been established, I used the results from these factor models to remove items which did not appear to relate to any other items. This was assessed based on low item factor loadings, with items loading below 0.30 considered for removal from subsequent IRT analysis.

All analyses were performed using R version 3.3.3 (R Core Team, 2017) using the packages 'psych' (Revelle, 2016) and 'mirt' (Chalmers, 2012).

8.3.3.2 Step 2. Fitting 2PL model and assessment of item characteristic and test information curves

After establishing latent trait unidimensionality, item performance was analysed using the two-parameter logistic model (2PL) that assumes that items differ both with respect to how difficult they are to answer (*difficulty parameter* (a_i)), and how well they differentiate levels of the latent trait (θ) (*discrimination parameter* (*bi*j)). Individual items were assessed for fit based on the S-χ2 proposed by Orlando and

Thissen (2000). It is based on a comparison of observed and predicted by the model item responses given an individual's level of the latent trait (θ). Poorly fitting items were inspected with ICC. ICC is a non-linear regression line that expresses a subject's probability of a correct response to each item. The slope of the ICC characterizes the discriminability of the item; item difficulty was characterized as the point along the theta continuum with a 50% chance of correctly answering the item. In the context of evaluating item performance of TAM, items that have large discrimination parameters and which span a range of difficulty levels will be retained.

Item difficulty and discriminability parameters, standard errors, and summary statistics were obtained using maximum-likelihood estimation. The characteristic curves for each item were plotted for visual inspection. I calculated 2PL models using the mirt() R package (Chalmers, 2012), and item characteristic using irtoys() R package (Partchev, 2016).

A second purpose of our IRT analyses was to explore the reliability of the total score on TAM. Reliability in IRT differs from conventional reliability metrics such as Cronbach's alpha as with IRT models, reliability is assessed across levels of the latent ability factor (θ). For a given level of θ, if the amount of information is large, it means that an individual's ability at that level can be estimated with higher precision and thus is more reliable. If the amount of information is small, it means that an individual's ability at that level cannot be estimated with precision and the estimates will be widely scattered about the true ability.

In order to investigate information across the range of measured ability, I computed the test information curve by plotting the amount of test information against ability. The curve will allow to identify how robust the test is in estimating ability over the whole range of ability scores. In evaluating TAM, I will calculate the range of ability levels that can be reliably assessed by identifying the range within which test information is greater than 10. This approximately corresponds to a classical test theory reliability (Cronbach's alpha) of .90.

8.3.3.3. Step 3. Evaluation of differential item functioning by age and sex

Finally, I used Differential Item Functioning (DIF) analyses to identify differences in item parameters across groups. DIF occurs when individuals who have the same standing on the latent trait do not have the same probability of item endorsement (Edelen et al, 2006). In other words, DIF analyses identifies items which perform differently in different groups of individuals. Failure to identify items which show DIF can result in biased tests. Given the proposed use of the current measure, I investigated DIF across sex (Male vs. Female) and across age group (Younger vs. Older).

The mirt() R package (Chalmers, 2012) was used to assess DIF. I set no anchors a priori; all items were tested for DIF by adding item constraints one item at a time. In the analysis by sex, the male group was my reference group, with the mean and standard deviation of the female group estimated (focal group). In the analysis by age group, the younger participants group was my reference group, with the mean and standard deviation of the older participants estimated (focal group). The test compares parameter estimates (difficulty level and discriminability of each item) across the reference and focal group. Wald tests based on the procedure proposed by Lord (1977), providing separate chi-square statistics for the discrimination and threshold parameters for each studied item, which are used to evaluate the presence of DIF. When DIF is detected, effect sizes for the threshold and/or slope parameters will aid the description and interpretation of the group differences (Steinberg & Thissen, 2006).

8.3.3.4. Step 4. Item selection

Based on the results of the whole sample and DIF analyses, items were selected for removal. Items which show DIF across either group, or which have poor discrimination in the total sample or sub-groups, were removed. Once items were removed, I re-calculated the test information in order to assess whether the removal of items impacts on test reliability.

8.3.4 Results

8.3.4.1 Step 1. Establish unidimensionality

Eigenvalues suggest one general factor: eigenvalues for first four factors were 7.83, 1.71, 1.47 and 1.28, with a large ratio between the first and the second eigenvalues (4.5) when compared to the second and third (1.16). MAP suggested a single factor, whilst PA suggested 3 factors (See **Figure 8.4 and 8.5**).

Figure 8.4 Scree plot

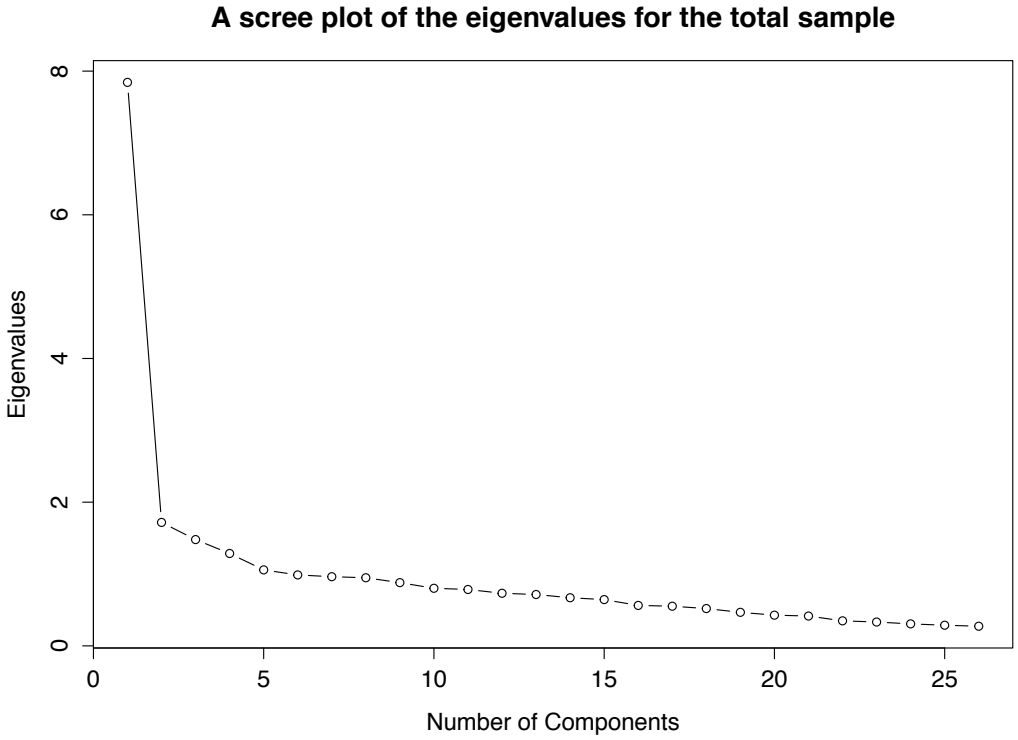
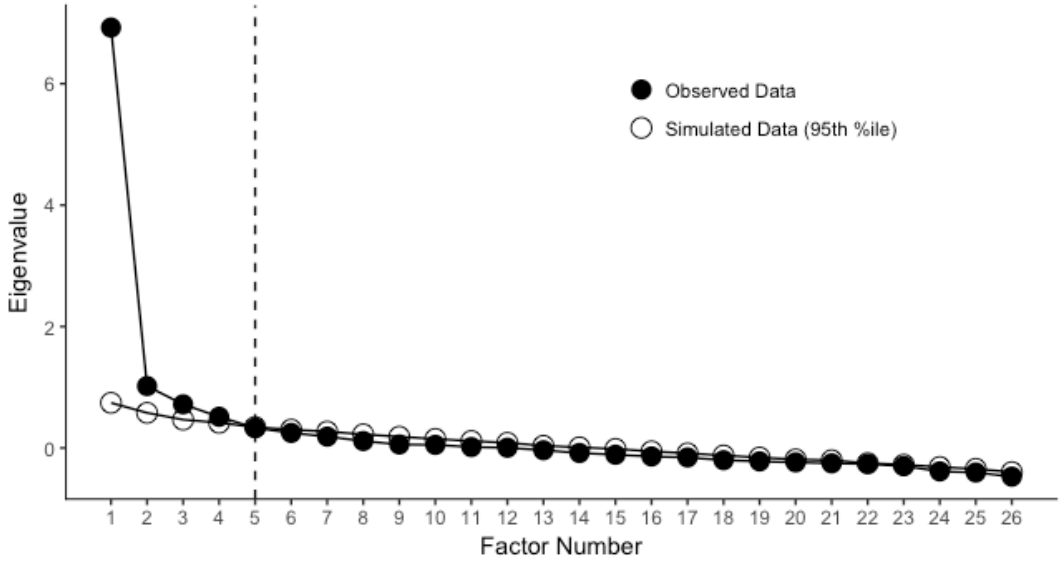


Figure 8.5 Parallel Analysis Scree Plot



Examination of model fit across the one (RMSEA = .076, TLI = .795), two (RMSEA = .064, TLI = .852) and three (RMSEA = .040, TLI = .91) factor models suggested, as expected, that fit improved as the number of factors increased. All models met minimum criteria for the RMSEA, and no models reached the minimum criteria according to the TLI. The difference in fit across models was significant ($p < .001$) according to the chi-square tests. Thus collectively, the suite of test of dimensionality suggested between one and three factors.

In order to select between the solutions, I explored the item factor loadings. All items from the scale loaded significantly on one general factor with loadings above 0.3 for all items, except for three items (items 36, 37, and 38) with factor loading 0.03, 0.14, and -0.11 respectively. In the two-factor solution, 4 items loaded on the second factor (items 36, 37, 38, and 46), and on the 3-factor model items 38, 39, 40, and 41 formed the third factor. Neither 2 nor 3 factor-model seem to reflect a coherent theoretical interpretation. We inspected these items more closely.

Taking all the above information into account, we retained a single factor model, primarily driven by the theoretical coherence of the model. Due to the low loadings noted above, items 36, 37 and 38 were excluded from subsequent analyses.

8.3.4.2 Step 2. 2PL model. Test reliability. Item characteristics.

Items characteristics

Table 8.1 reports item parameter (difficulty and discrimination) estimates and their standard errors for the 2PL model. Item discrimination parameters were between 0.53 and 4.38. Discrimination parameters greater than 1.70 are considered large and therefore have excellent discrimination capacity (Baker, 2001, pg. 34). Most of the items in the scale have an excellent discrimination. Item difficulty estimates were distributed between -1.80 and 0.19. This indicates that a majority of items are positioned at below, or just above average (theta= 0) levels of performance. Item 41 has large and significant S-χ2, meaning that this item does not fit into a predicted response model. Inspecting its ICC and item discrimination, however, revealed that the item has an excellent discrimination capacity (a = 2.3) that is why I decided to retain item 41 for further inspection.

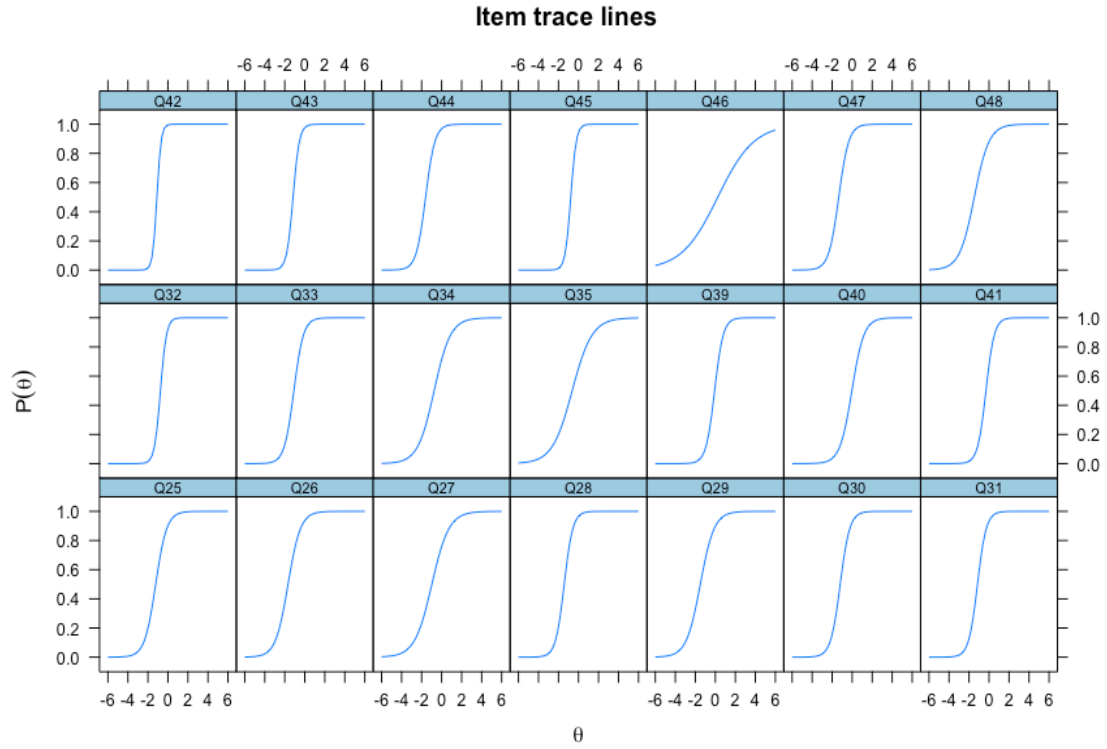
Inspection of ICC (**Figure 8.6**) and parameter estimates indicates that Item 46 had a near-zero discrimination parameter (slope is 0.14) and subsequently a flatter ICC, suggesting that this item was poor in discriminating between respondents and thus yielded minimal psychometric information. Based on these findings, item 46 was identified as a potential item for removal from the final version of TAM.

Table 8.1 Item fit statistics and Item parameter estimates (SE) of a Two-parameter Unidimensional Item Response Model listed in ascending *difficulty* order

Item	Mean	S_X2	p	a	SE	d	SE
Q46 (Judgmental financial knowledge, financial scheme)	0.52	5.71	0.93	0.53	0.14	0.19	0.24
Q40(Conceptual financial knowledge)	0.53	6.82	0.74	1.61	0.26	-0.08	0.1
Q39(Application of conceptual financial knowledge)	0.55	10.68	0.30	2.25	0.35	-0.12	0.09
Q41(Judgmental financial knowledge, financial scheme)	0.61	23.3	0.003	2.3	0.36	-0.37	0.09
Q35(Application of conceptual financial knowledge)	0.66	13.71	0.32	0.96	0.17	-0.71	0.1
Q32(Conceptual financial knowledge)	0.79	5.87	0.75	3.11	0.48	-0.84	0.09
Q34(Application of conceptual financial knowledge)	0.70	8.4	0.75	1.17	0.19	-0.84	0.16
Q45(Judgmental financial knowledge, financial scheme)	0.79	6.35	0.70	3.45	0.55	-0.87	0.09
Q27(Mental calculation)	0.74	10.83	0.54	1.13	0.19	-1.07	0.18
Q33(Mental calculation)	0.82	3.27	0.97	2	0.31	-1.2	0.13
Q42(Judgmental financial knowledge, financial scheme)	0.85	4.3	0.37	4.38	0.88	-1.23	0.09
Q31(Knowledge the value of the item)	0.84	7.61	0.66	2.18	0.34	-1.27	0.13
Q30(Knowledge the value of the item)	0.84	11.61	0.31	2.02	0.32	-1.3	0.14
Q43(Judgmental financial knowledge, financial scheme)	0.85	6.96	0.54	2.95	0.5	-1.3	0.11
Q25(Conceptual financial knowledge)	0.83	9.31	0.59	1.71	0.27	-1.34	0.16
Q47(Recognising parts of financial documents)	0.86	13.53	0.19	1.94	0.32	-1.45	0.16
Q28(Conceptual financial knowledge)	0.87	8.39	0.39	2.22	0.38	-1.55	0.15
Q48 (Recognising parts of financial documents)	0.83	14.71	0.19	1.32	0.23	-1.57	0.21
Q29(Naming coins)	0.85	5.44	0.90	1.38	0.23	-1.62	0.21
Q44(Judgmental financial knowledge, financial scheme)	0.90	14.07	0.08	2.09	0.38	-1.72	0.18
Q26(Naming notes and understanding the value)	0.89	17.19	0.07	1.54	0.27	-1.8	0.22

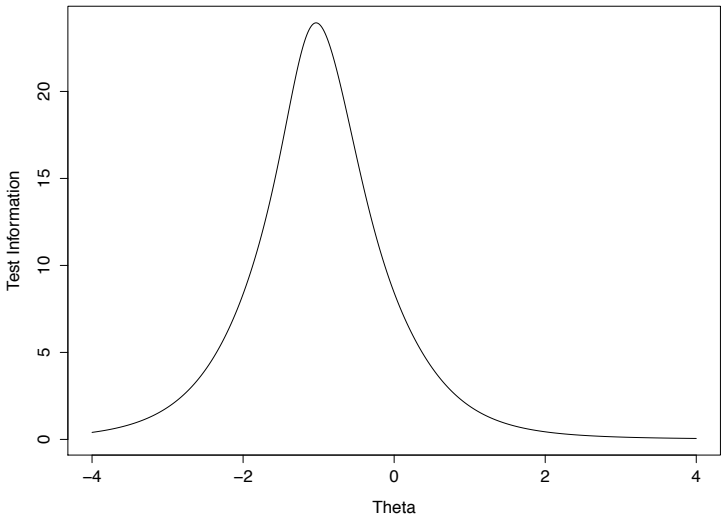
Note: S_X2 = goodness of fit index ,a = item *discrimination* with higher scores indicating higher *discrimination*, d = item *difficulty* with higher scores indicating lower *difficulty*, SE= standard error

Figure 8.6 Item Characteristic Curves (ICC)



Maximal information in the whole sample for the final scale (23.92) is at the trait level (θ) of -1.04, with the reliable range of measurement (information > 10) for the ability range between -1.89 and -0.14 (See **Figure 8.7**). Therefore, TAM is best capturing moderately low to average levels financial abilities.

Figure 8.7 Test Information Curve on dichotomously scored scale



8.3.4.3 Step 3. Establish DIF by age and gender– remove any items which do not have DIF by age and by gender

Parameters estimated for the 2PL model across younger and older groups individually are provided in **Table 8.2**. Most of the items were found to have very good discrimination abilities, with discriminating parameters ranging from 1.30 to 4.45. Items 42-45 in the younger sample were found to have very high difficulty and discriminating parameters (d = 16.56, 10.56, 10.15 and 13.24 respectively and a = 12.52, 9.00, 7.38, 15.56) meaning that only those in the younger group at very high levels of the latent trait get these items correct. Generally, difficulty level for most of the items on the scale for younger participants was higher than for older participants. However, despite this, based on the Wald statistics, no DIF was identified across age groups in either the discrimination or difficulty parameters (**Table 2**).

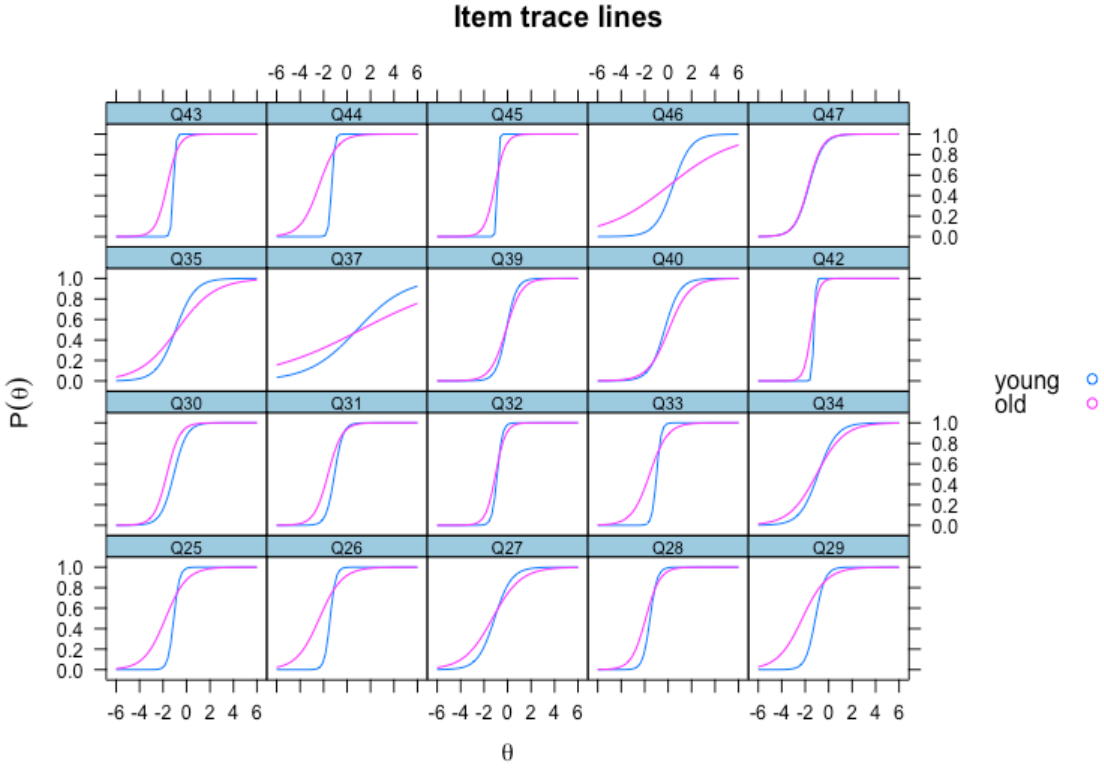
Table 8.2 Item parameters estimates and DIF results for different Age groups in ascending difficulty order

	<65 (n=83)						**>65 (n=239)**				
Item	Mean	a	d	Totalχ2	p	Item	Mean	a	d	Total χ2	p
Q46	0.41	1.3	-0.55	0.98	0.32	Q40	0.49	1.14	-0.05	-0.2	1
Q39	0.55	2.12	0.25	-0.27	1	Q46	0.49	0.38	-0.03	-0.06	1
Q40	0.55	1.49	0.45	-0.29	1	Q39	0.53	1.51	0.2	-0.32	1
Q41	0.66	1.71	0.91	0.14	0.71	Q35	0.6	0.63	0.5	-0.18	1
Q34	0.72	1.22	1.13	-0.35	1	Q41	0.6	1.83	0.68	-0.065	1
Q35	0.72	1.24	1.13	0.09	0.76	Q34	0.66	0.85	0.86	-0.29	1
Q27	0.77	1.41	1.55	-0.072	1	Q27	0.7	0.81	1.06	-0.19	1
Q30	0.8	1.92	2.01	-0.21	1	Q48	0.82	0.84	1.87	-0.03	1
Q47	0.88	1.58	2.69	-0.08	1	Q25	0.81	1.09	1.96	0.45	0.5
Q29	0.84	2.36	2.7	0.33	0.56	Q33	0.8	1.31	2.05	0.21	1
Q48	0.84	2.58	2.85	0.96	0.32	Q29	0.84	0.97	2.15	-0.17	1
Q31	0.84	2.81	2.99	-0.16	1	Q45	0.75	2.27	2.41	1.22	0.27
Q32	0.82	4.46	3.92	0.001	0.97	Q26	0.86	1.03	2.43	1.16	0.28
Q25	0.86	4.06	4.43	1.27	0.26	Q32	0.75	2.43	2.44	-0.16	1
Q33	0.85	4.96	4.86	0.98	0.32	Q31	0.83	1.74	2.78	-0.24	1
Q28	0.92	3.19	5	0.095	0.75	Q47	0.84	1.7	2.9	-0.17	1
Q26	0.92	4.04	5.94	1.43	0.23	Q30	0.84	1.82	3.04	-0.34	1
Q44	0.92	7.35	9.78	2.41	0.12	Q44	0.89	1.3	3.05	1.85	0.17
Q43	0.89	9.14	10.36	2.3	0.13	Q28	0.86	1.63	3.11	-0.02	1
Q45	0.84	12.48	10.65	2.19	0.14	Q43	0.85	2	3.3	1.56	0.21
Q42	0.92	11.35	14.59	1.57	0.21	Q42	0.84	3.19	4.66	1.33	0.24

Note: a = item *discrimination* with higher scores indicating higher *discrimination*, d = item *difficulty* with higher scores indicating lower *difficulty*

Visual inspection of the item curves (**Figure 8.8**), and inspection of the item parameters in Table 8.2, reveals again that Item 46 has low difficulty level for both age groups and has very low discrimination.

Figure 8.8 Item Characteristic Curves (ICC) for different age group



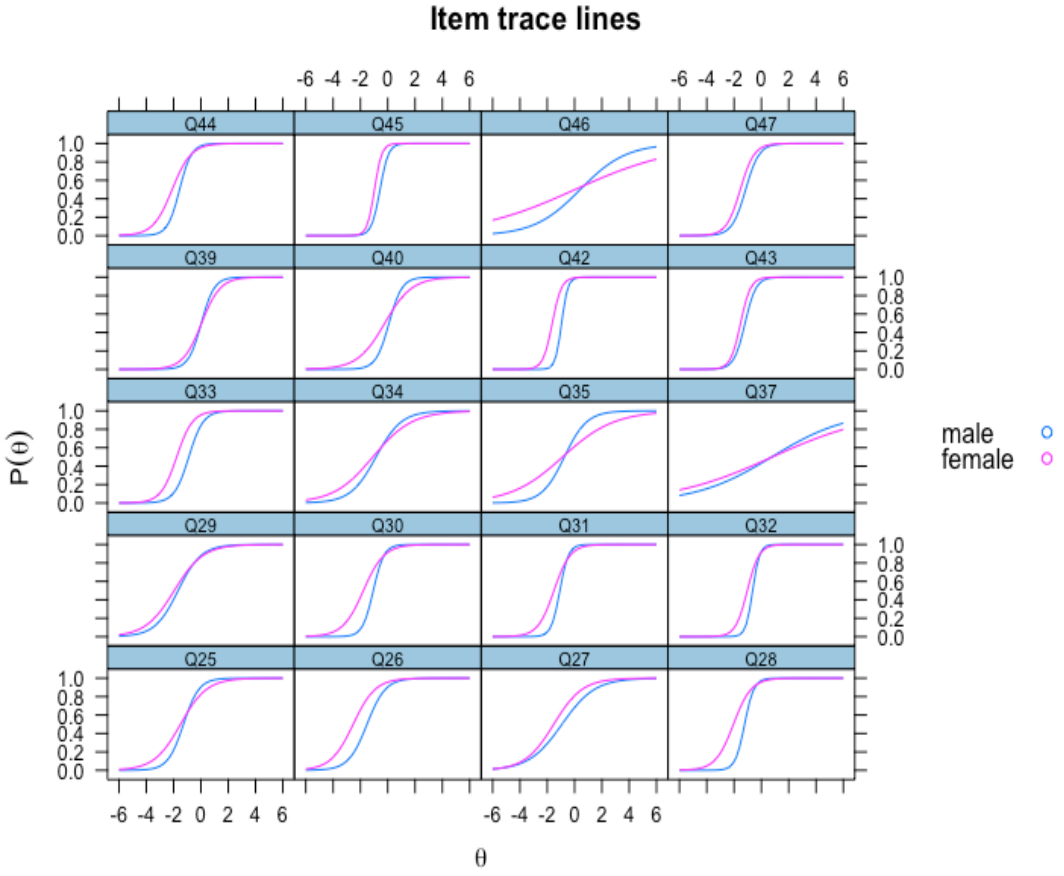
Parameters estimated for the 2PL fit for different gender groups individually are provided in **Table 8.3** and ICC for the parameters in **Figure 8.9**. Most of the items were found to have high discrimination parameters ranging from 0.80 to 4.18. Again, Item 46 was found to have the lowest discrimination parameter in both gender groups. Generally, difficulty level for most of the items on the scale for male participants was higher than for female participants. However, despite this, based on the Wald statistics, no DIF was identified across gender in either the discrimination or difficulty parameters (**Table 8.3**).

Table 8.3 Item parameters estimates and DIF results for different gender groups (excluding th who refused to identify their gender (n = 67)) in ascending *difficulty* order

MALE (n = 116)						***FEMALE (n = 139)***					
Item	Mean	a	d	**Total χ2 a (df)**	p	Item	Mean	a	d	**Total χ2 a (df)**	p
Q46	0.44	0.59	-0.24	0.36	0.55	Q39	0.54	1.46	-0.07	0.01	0.93
Q40	0.47	2.11	-0.19	0.17	0.68	Q46	0.51	0.26	-0.01	0.23	0.63
Q39	0.49	2.13	-0.06	0.05	0.81	Q40	0.58	1.01	0.22	0.03	0.87
Q41	0.55	3.55	0.37	0.35	0.55	Q41	0.62	1.32	0.37	0.02	0.9
Q27	0.66	0.83	0.76	0.05	0.82	Q35	0.63	0.53	0.46	0.13	0.72
Q35	0.67	1.22	0.9	0.29	0.64	Q34	0.68	0.69	0.76	0.05	0.82
Q34	0.68	1.08	0.92	0.07	0.78	Q27	0.78	0.95	1.45	0.02	0.89
Q33	0.74	1.89	1.67	0.02	0.89	Q25	0.79	1.04	1.55	0.07	0.79
Q45	0.69	3.26	1.84	0.06	0.81	Q29	0.83	0.95	1.85	0.02	0.89
Q29	0.83	1.18	1.98	0.06	0.8	Q48	0.87	1.23	2.3	0.04	0.85
Q48	0.84	1.4	2.19	0.03	0.87	Q30	0.86	1.33	2.36	0.05	0.82
Q25	0.82	1.76	2.24	0.12	0.72	Q32	0.8	2.34	2.41	0	1
Q26	0.84	1.48	2.24	0.05	0.82	Q31	0.85	1.7	2.56	0.08	0.78
Q47	0.81	2.02	2.32	0.003	0.95	Q44	0.9	1.44	3.04	0.07	0.78
Q32	0.72	3.99	2.54	0.11	0.74	Q47	0.87	1.96	3.04	0.01	0.9
Q30	0.81	2.56	2.71	0.14	0.7	Q33	0.88	1.73	3.06	0.01	0.92
Q43	0.84	2.49	2.98	0.02	0.88	Q26	0.92	1.23	3.1	0.04	0.84
Q31	0.83	3.2	3.44	0.15	0.7	Q28	0.9	1.53	3.14	0.09	0.77
Q44	0.89	2.3	3.6	0.08	0.78	Q45	0.81	3.78	3.67	-0.01	1
Q28	0.86	2.94	3.61	0.18	0.67	Q43	0.88	2.73	4.16	0.02	0.88
Q42	0.81	4.39	4.17	0.13	0.71	Q42	0.9	2.99	4.87	0.09	0.76

Note: a = item *discrimination* with higher scores indicating higher *discrimination*, d = item *difficulty* with higher scores indicating lower *difficulty*

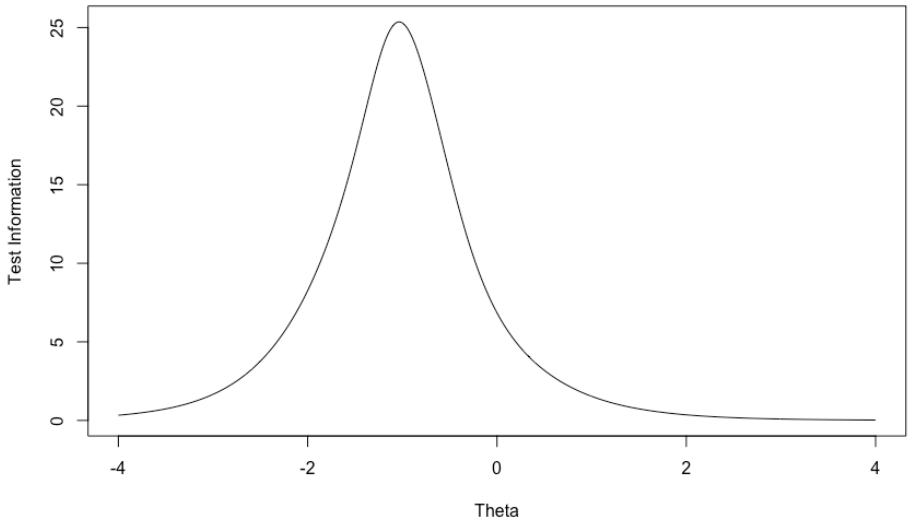
Figure 8.9 Item Characteristic Curves (ICC) for different gender group



8.3.4.5 Step 4. Item selection

I eliminated all the poorly fitted items and items with poor discriminability (Items 36, 37, 38 after the first step and Item 46 after initial reliability analysis) and analysed the final, shorter scale. Maximal information in the whole sample for the final scale (25.28) is at theta = -1.07, with the reliable range of measurement (information > 10) for the ability range between -1.89 and -0.14 (See **Figure 8.10**) which is not very different from the test information curve that I had initially (See Figure 8.7). As removing these items added little value in improvement of the test information, I decided to retain all the items to explore further on clinical population to ensure their performance to be robust, discriminative and responsive.

Figure 8.10 Test Information Curve



8.4 Discussion of steps towards the development of TAM

I used a two-parameter IRT model to analyse the psychometric properties of the Skills part of TAM and establish the best items that would describe financial abilities of participants in different age and gender groups. First, I found evidence of multidimensionality due to item clustering, but this multidimensionality did not distort the primary dimension. A unidimensional model was therefore sufficient to describe financial ability, as measured by TAM. This multidimensionality of the financial construct was supported by studies carried by Marson et al (2000) and Kershaw and Webber (2008).

Secondly, the analysis suggests that TAM measures most reliably at low to average levels of financial ability, meaning that TAM is potentially a good financial measure for people with limited financial proficiency, which is in keeping with the design and intended use of the instrument with elderly retired people and people with cognitive impairment. In addition, all the items in TAM proved to have a good discrimination capacity and were distributed with respect to difficulty level within this specific discriminability range. Collectively the results suggest that TAM has initially promising psychometric properties.

Third, I assessed item functioning across different gender and age groups. Results did not reveal any DIF in the scale. If there were items that would perform differently across different groups the results from the scores from males and females and from young and old adults would be incompatible. The results indicate that tendency to endorse the item should only reflect the ability level and should not be affected by variables such as gender and age.

TAM was constructed in a way to address different level of financial abilities and financial knowledge and also to track progression of cognitive impairment over time, the tasks and questions were designed with various levels of difficulties. There were several main domains in TAM: recognising coins and notes and understanding the value, mental calculation, conceptual financial knowledge and its application, judgmental financial knowledge and abilities to recognise scams, and recognising parts of financial documents and being able to feel them in. Each domain contains easy and difficult items. The most difficult items (40 to 79 % correct answers) disregard the age and gender were judgmental financial knowledge (Q41 and Q46), conceptual financial knowledge (Q 32 and Q40) and its application (Q35 and Q39). Items with medium difficulty (80 to 90 % correct answers) were items on judgmental financial knowledge (Q45), application of financial knowledge (Q34) and tasks on mental calculation (Q27 and Q33). Easy items (82 to 92% correct responses) judgmental financial knowledge (Q42, Q43 and Q44), conceptual financial knowledge (Q25 and Q 28), naming coins and notes and understanding the value (Q26, Q 29, Q30, and Q31) and recognising parts of the financial documents and being able to fill them in (Q47 and Q48).

Nevertheless, these results should be interpreted with caution as they were drawn from relative small samples and thus the statistical power to detect DIF was low. IRT models are very sensitive to sample size. For 2PL model, sample sizes of 500-1000 participants are sufficient (Tsutakawa & Johnson, 1990), Similarly, Reise & Yu (1990) recommended approximately 500 participants, which in the scope of my PhD was unfortunately very difficult to achieve. Another limitation of this part of the study is that the data was gathered online and participants were self-selected; this may restrict generalizability.

Chapter IX

Financial abilities in people with cognitive impairment (feasibility study)

9.1 Introduction

Everyday financial abilities, as I already stated throughout this thesis, are considered a higher order cognitively mediated functional activity (Marson et al., 2013) and therefore ***sensitive to early cognitive decline***. In the pioneering research (see Section 7.3.1) by Marson et al. (2000) they demonstrated that Healthy Controls (HC) performed better than mild-AD patients that in turn performed better than patients with moderate AD on Financial Capacity Instrument (FCI) and that in all financial domains except basic monetary skills these two patient groups were equivalently good. In this study he noted that there is a great deal performance variability in mild-AD patients that imply that there are other factors that affect financial abilities. In a follow up study by Griffith et al. (2003) from Marson's group their aMCI patients performed worse than HC, but better than mild AD suggesting that financial ability decline already exists early in the course of the disease. In the one-year follow-up study they showed a similar pattern of decreased financial abilities, in addition, patients with aMCI decline more on cheque-writing task, but not in their understanding of the concept. Patients with mild-AD declined in their abilities to detect fraud (Martin et al., 2008; 2013). FCI was also shown to be sensitive to decline of financial abilities in patients with Parkinson's disease and dementia (Martin et al., 2013). Another domain specific tool – Financial Competence Assessment Inventory (FCAI), developed by Australian research group (Kershaw & Weber, 2008), was able to discriminate between HC and patients with cognitive impairment (See Section 7.3.2).

AD patients are known to frequently minimise, fail to recognise or deny all together their cognitive and functional problems (Vasterling et al., 1995). This symptom that was coined by Babinski (1914) as anosognosia is very common even in the early stages of AD (Sevush, 1999; Farias et al., 2005) and the degree of unawareness grows with the disease progression (Vasterling et al., 1997). Diminished awareness of functional difficulties strongly predicts progression from MCI to AD (Albert et al.,

2002; Tabert et al., 2002). If this is also true for everyday financial abilities, unawareness of financial impairment or Acreemagnosia can be a very early functional symptom of AD. There is only one study, conducted by Cramer et al. (2004, see also Section 7.3.3), which addresses this question. They developed the Measure of Awareness of Financial Skills (MAFS) and in a sample of HC and patients with various types of dementia show the lack of awareness of the financial deficit in patient groups. As I stated in the Section 7.3.3, their patients' sample was very heterogeneous and in addition they did not have a group of patients that would show mild impairment.

In my last experiment, I aimed to explore how financial abilities decline in a group of patients with various degrees of cognitive impairment and older healthy controls. I also had an interest in unveiling which tasks are the most susceptible to cognitive decline. I hypothesised that financial abilities of patients with cognitive impairment will be compromised in comparison to those of healthy older adults and in addition they will be unaware of this deficit. The tasks that require more complex cognitive organisation would be impaired in patients with MCI compare to HC.

The other aim of this experiment was to investigate the neurocognitive basis of the financial impairment in patients with cognitive impairment. Previous study by Okonkowo et al. (2006) using the FCI showed that despite the fact that memory is a primary deficit in MCI patients; attention and EF (See Abbreviation List) were the primarily cognitive domains that significantly correlated with FCI performance. If EF function deficit is a robust predictor of financial decline, in my study this cognitive domain should be also associated with performance on TAM.

9.2 Methods

9.2.1 Participants

To evaluate the validity of TAM to discriminate between different levels of cognitive impairment we recruited 24 healthy control volunteers (HC), 14 patients with amnestic Mild Cognitive Impairment (a-MCI) and 14 patients with mild-Alzheimer's disease (mild-AD) (Haxby et al., 1992). The diagnosis was made by an old age psychiatrist who followed the guidelines proposed by Albert et al. (2011) to diagnose

MCI and those from the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (DSM-V) (American Psychiatric Association, 2005) and the *National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association* (NINCDS-ADRDA, McHann et al., 1984) to detect AD. T

HC were recruited from the volunteer panel of the University of Edinburgh. Informed consent was obtained from control participants, MCI and AD patients, and their carers. The study was approved by the Psychology Research Ethics Committee, University of Edinburgh and by the West Midlands MREC.

9.2.2 Procedures

9.2.2.1 Background Neuropsychological tests

General cognitive functions: *The Addenbrooke's Cognitive Examination Revise* (ACE-R; Mioshi et al., 2006). A brief measure of global cognitive function which incorporates five sub-domain scores (orientation/attention, memory, verbal fluency, language and visuo-spatial). The maximum score is 100 with the 88-82 cut-off score that signaling about cognitive impairment (Mioshi et al., 2006).

The Test of Premorbid Function (TOPF; Pearson assessment, 2009) is a reading test as an estimate of the premorbid functioning in neurodegenerative brain disorders. The test consists of 70 words that are presented in the ascending difficulty order with regular words at the beginning following on with further, more irregular and complex words. The maximum raw score is 70.

Executive functions: Participants completed two measures of executive function. The *Trail Making Test* (TMT parts A & B) (Reitan, 1992) was used to assess simple and complex visual scanning. The simple version of the task required participants to draw a line between circles according to a sequence (numbers). The complex version of the task required participants to alternate between two sequences (numbers and letters) while drawing lines to connect circles.

Memory: *Free and Cued Selective Reminding Test* (FCSRT) (Buschke et al., 1984) was used to assess the ability to learn and recall a list of words after a delay. The

participant was presented with written words presented on cards, 4 words at a time on one card with 16 items in total. The participant was asked to point and name a word (e.g., "Please point and name a fruit"). Once all of the 4 items on a card were identified, the card was removed and the participant would complete an immediate free recall of the seen words, then, if some of the words were not recalled, the participant was given a cue for this/these words (e.g., "What was the fruit") in the same order they were encoded. Then, when all 16 items were seen, the participants were asked to freely recall all items without any order and then with the cue if some of the words were not recalled. This process was repeated three times. Following a delay of approximately 20 minutes, the participant was asked to recall words again freely and cued. Memory for free, cued and total recall was measured at the end by summing up all the words recalled freely or with cues.

Temporary Memory Binding Test (TMB). See Sections 2.1.3 and 2.2.2.

9.2.2.2. Background Functional test

Functional abilities were assessed with several functional ADL scales: the Lawton Instrumental Activities of Daily Living (IADL) (Lawton et al., 1969), Everyday Cognition (ECog) (Farias et al., 2008), and Extended IADL (EIADL) (Fieo et al., 2014) (See Section 6.2.2.2 for description).

The Acreemagnosia Measurement (TAM) (See Section 8.2.3 for description of the parts and 8.2.3.1 for scoring procedure, also See Appendix #A for all tasks included in TAM).

9.3 Analyses

All analyses were performed using R version 3.3.3 (R Core Team, 2017) using the packages 'psych' (Revelle, 2016) and 'mirt' (Chalmers, 2012).

Scores from two sections of TAM (the Skills part and the Awareness part) were compared across the three groups using one-way analysis of variance controlling for age, followed by Bonferroni-corrected post-hoc tests. Post hoc comparisons were carried out across groups for each part of the test (3x1 = 3 contrasts for Skills and Awareness part), the Bonferroni-corrected alpha level was set at 0.01.

To check if age and education has influence on TAM performance and to delineate the relationship between different cognitive domains and financial abilities, Pearson product correlations were calculated between scores on TAM, age, education and cognitive tests for each group. The Bonferroni-corrected alpha level was set at 0.01

9.4 Results

The demographics and neuropsychological profiles of HC and the two groups of patients are shown in **Table 9.1**.

Table 9.1 Demographic, neuropsychological and functional measures for the three groups of participants.

	HC (N =24)		**MCI** (N =14)		**AD** (N = 14)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age	72.50 (4.52)	64-81	74.00 (7.40)	55-84	76.75 (9.21)*	56-88
Education (years)	14.65 (3.48)	10-20	14.69 (2.93)	10-18	13.67 (2.99)	09-18
TOPF	63.44 (8.14)	49-86	62.54 (4.79)#	55-68	55.57 (10.20)*	37-68
ACE-R	95.3 (3.24)^	89-100	88.27 (5.93)#	81-98	73.07 (10.69) *	54-90
FCSRT	29 (6.98)^	20-35	17.33 (7.55)#	06-32	7.08 (4.46)*	01-15
ECog	36.81 (6.48)	29-51	45.00 (9.95)	30-68	49.08 (26.31)*	20-89
TMT B-A	47.86 (47.99)	12.02-176	102.2 (125.99)#	-17.35-493.55	120.53 (85.06) *	1.02-358.56
EIADL	26.81 (4.58)	20-34	24.54 (5.39)#	12-32	19.29 (4.51)*	10-24
Lawton	7.88 (0.49)^	06-08	6.69 (1.49)#	04-08	6.79 (1.37)*	04-08
Binding	0.90 (0.12)^	0.65-1.00	0.82 (0.13)#	0.50-1.00	0.70 (0.09)*	0.50-0.84

Note: ACE-R - The Addenbrooke's Cognitive Examination – Revised (Mioshi et al., 2006), TOPF - Test of Premorbid Functioning (Wechsler et al., 2011); FCSRT – Free and Cued Selective Reminding Test – total score (Grober et al., 2009), ECog – Everyday Cognition (Farias et al., 2008), TMT A-B - Trial Making Test (Army Individual Test Battery, 1944); Lawton - the Lawton Instrumental Activities of Daily Living (Lawton and Brody, 1969), EIADL - Extended IADL (Fieo et al., 2014), Binding – Temporary Memory Binding test (Parra et al., 2014; 2015).
^ HC significantly different between HC and both MCI and mild-AD
# MCI differ significantly from mild-AD
* mild-AD differ significantly from both HC and MCI

Table 9.2 shows overall performance on the different parts of TAM for each group. There was no discrepancy in the answers in the TAM Awareness part between healthy

older adults and their relatives. AD patients' awareness score was very low compared to the score of the MCI people and older adults.

On the Skills part of TAM the main effect of Group (HC, MCI, AD) was significant, F (2, 42) = 6.7, $p < 0.01$. MCI patients scored significantly worse than HC on both the Awareness and Skills parts of TAM, and patients with AD scored worse than both HC and MCI.

Table 9.2 Performance on TAM achieved by the three groups

	HC (N =24)		**MCI** (N =14)		**AD** (N = 14)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
TAM Self	58.09 (11.21)	41-74	58.21 (10.02)	45-80	58.09 (14.63)	54-87
TAM Informant	58.09 (11.21)	41-74	51.21 (49.20)	0-158	72.64 (54.15)	0-158
TAM Awareness	0 (0.00)	0	-7 (52.85)[#]	-65-112	14.55 (54.76)*	-87-96
TAM Skills section	0.85 (0.09)	0.71-1.00	0.82 (0.07)	0.71-0.96	0.62 (0.15)*	0.42-0.88

***Note*:** TAM Self – TAM Awareness part completed by the participant; TAM Informant – TAM Awareness part completed by proxies; TAM difference – difference between TAM Self and TAM Informant that shows the level of participant's awareness of financial skills.

[#] MCI differ significantly from HC

* mild-AD differ significantly from HC and MCI

Table 9.3 shows the performance of the HC and the patients on the individual items of the TAM. The aim of this analysis was to investigate which test components of TAM show larger between-group (HC and people with cognitive impairment) discrepancies. Patients with mild-AD had an impaired performance on the judgmental knowledge and recognition items of financial documents. Both patient groups performed significantly worse than the controls on complex mental calculations.

Table 9.3 Performance on the different items of TAM by the three groups

	HC (N =24)	**MCI** (N =14)	**AD** (N = 14)
Item	Mean	Mean	Mean
Q25 (Conceptual financial knowledge)	0.7	0.64	0.43
Q26 (Naming notes and understanding the value)	0.94	0.93	0.93
Q27 (Mental calculation)	0.82	0.93	0.64
Q28 (Conceptual financial knowledge)	1	0.78	0.57*
Q29 (Naming coins)	1	1	1
Q30 (Knowledge the value of the item)	1	0.93	0.93
Q31 (Knowledge the value of the item)	0.94	1	1
Q32 (Conceptual financial knowledge)	0.88	0.92	0.71
Q33 (Mental calculation)	1	0.57#	0.64*
Q34 (Application of conceptual financial knowledge)	0.82	0.78	0.78
Q35 (Application of conceptual financial knowledge)	0.47	1#	0.43
Q36 (Mental calculation)	1	0.86	0.86
Q37 (Conceptual financial knowledge)	0.65	0.86	0.93
Q38 (Application of conceptual financial knowledge)	0.71	0.71	0.43
Q39 (Application of conceptual financial knowledge)	0.59	0.78	0.5
Q40 (Conceptual financial knowledge)	0.76	0.78	0.21*
Q41 (Judgmental financial knowledge, financial scheme)	0.70^	0.21	0.21
Q42 (Judgmental financial knowledge, financial scheme)	0.88	0.78	0.43*
Q43 (Judgmental financial knowledge, financial scheme)	0.88	0.85	0.28*
Q44 (Judgmental financial knowledge, financial scheme)	0.82	0.78	0.43*
Q45 (Judgmental financial knowledge, financial scheme)	0.94	0.78	0.43*
Q46 (Judgmental financial knowledge, financial scheme)	0.94	0.93	0.86
Q47 (Recognising parts of financial documents)	1	0.92	0.78*
Q48 (Recognising parts of financial documents)	1	0.92	0.57*

^HC significantly different from both MCI and mild-AD

#MCI differ significantly from mild-AD

*mild-AD differ significantly from HC and MCI

Pearson product correlations between scores on TAM and cognitive tests are presented in Table 9.4. Age and education have weak non-significant relationship

with both parts of TAM for healthy controls and MCI patients, but not for mild-AD patients where education has a very strong and highly significant correlation with the Skill Part. In the healthy control group all correlations with cognitive measures are non-significant and weak for both sections of TAM. On the contrary, moderate to strong significant correlations are found with some cognitive measures and specifically with the memory tests in MCI group. Fluency test and total free recall of FCSRT correlate strongly and significantly with TAM skills part in AD patients.

Table 9.4 Correlations between scores on TAM and demographics and cognitive tests

	HC		**MCI**		**Mild-AD**	
	TAM Skills	TAM Awareness	TAM Skills	TAM Awareness	TAM Skills	TAM Awareness
Age	-.12	.25	-.12	.18	.24	-.10
Education	.34	-.07	.34	.40	.99*	.09
TOPF	-.35	.18	.40	-.03	.21	-.10
ACE-R	-.15	.38	.52*	-.20	.30	.64
ACE-R subscale:						
attention	-.05	.00	.36	-.05	.52	.38
memory	-.20	.48	.62**	-.22	.57	.83
fluency	-.15	.07	.39	-.09	-1.00***	-.20
language	.13	-.11	.40	-.30	-.12	-.55
VSP	.16	-.12	.19	-.13	.49	-.69
FCSRTtotalfree	-.84	-.13	.72**	.03	.76*	.60
FCSRTtotalREC	.16	.06	.43	.00	.91	.14
TMT A-B	.15	.31	.22	-.04	-.24	.46
Binding	.02	-.14	.25	-.13	.47	.53

Note: p< .001****; p<.001***; p<.01 **, p< .05 *

The relationship between TAM and measures of daily functions is displayed in Table 9.5. Positive moderate correlations emerged between TAM and subscales of IADL that measures similar skills, namely finances, and social skills for MCI patients but not for healthy controls or for mild-AD patients. As there is no variability in the Awareness part for HC (HC and their proxy did not differentiate in their answers in the Awareness part of TAM) it accounts for absence of the correlations between this part and other functional scales.

Table 9.5 Correlations between scores on TAM and functional scales

	HC		MCI		Mild-AD	
	TAM Skills	TAM Awareness	TAM Skills	TAM Awareness	TAM Skills	TAM Awareness
Ecog	.26	-	.24	.37	.44	-.55
EIADL	.04	-	.47*	-.23	-.10	.49
Social activity	.46	-	.60**	-.19	-.19	-.08
Lawton	.30	-	.03	-.21	-.26	-.52
Finances	-	-	.48*	-.12	.25	.23
Shopping	.30	-	.30	.12	.28	.47
TAM Awareness	-.44	-	.18	1.00	.29	1.00

Note: p< .001****; p<.001***; p<.01 **, p< .05 *

9.5 Discussion of the feasibility study

In order to assess financial abilities researchers and clinicians are currently using ADL/IADL scales that do not sufficiently address the intricacy of everyday financial requirements. There are several financial scales that have been devised to particularly look at financial abilities, competence, and awareness. Unfortunately these scales are unavailable for use (see my review of these scales in Section 7.3).

Dealing with AD, MCI patients and their caregivers we, as several others, are observing how often they lack financial competence and are unaware of this impairment. The term ***Acreemagnosia*** was created to label this symptom in order to frame it as a specific cognitive difficulty which could hamper the independent daily life of people at different levels of cognitive competence. Importantly, often also the carers are not fully aware of the patient's impaired financial knowledge. There are numbers of unanswered questions about Acreemagnosia. To address them and further explore the symptom we developed the Acreemagnosia Measurement that combines subjective, objective and performance-based measures and reflect everyday financial involvement of the post-retirement person and account for financial proficiency.

One of unresolved questions that this experiment aimed to address is whether Acreemagnosia is already present in patients with MCI. To my knowledge, there are no studies that would include healthy older controls and MCI patients against which to compare AD patients' financial abilities.

In this experiment I showed that practical skills associated with financial abilities are impaired in AD that corresponds to the findings by Marson et al. (2000) and Kershaw and Webber (2008). My analysis demonstrates that patients with mild-AD performed equivalently to healthy people on TAM's tasks such as naming coins and knowing the value of the item, that are easy to perform ("easy" and "difficult" TAM items see Section 8.4). Difficult items such as financial judgment, conceptual financial knowledge, and mental calculation (medium difficulty items), showed impaired performance of mild-AD patients relative to both healthy controls and MCI patients. In addition, comparing healthy older controls with MCI patients showed worse performance on financial judgment and mental calculation. The outcome of this feasibility experiment is limited by the small sample size. Despite this limitation, the results indicate that mild-AD patients, and to a lesser degree MCI patients, show impairment in everyday financial abilities and this impairment starts from the declining financial judgemental knowledge.

The other unanswered question that the experiment was aiming to resolve is if patients with early cognitive impairment are already presenting with Acreemagnosia. Analysis shows that there was no discrepancy between HC and their relatives' answers in TAM, indicating that these participants are fully aware of their financial abilities. However, there was a discrepancy in the patient groups which grew from MCI to dementia stages. Therefore, patients with MCI and mild-AD are often unaware of their financial difficulties, demonstrating that they present with Acreemagnosia, thus confirming the sensitivity of TAM to capture such impairments. According to Vasterling et al. (1995), unawareness of the impairment in AD patients depends on the disease progression and starts with the functioning that requires more advanced cognitive processing, my experiment fully supports this statement.

TAM has several advantages over the existing scales. Firstly, it is individual-centred tool that is designed to assess financial abilities in people with various degree of financial knowledge. Secondly, it incorporates several constructs: awareness of

financial abilities and actual financial knowledge. While proxy-reports may provide useful information, they may be inaccurate and biased due to their subjective nature. The same holds for self-assessment measures and even more so for patients with cognitive impairment that start to experience a degree of anosognosia early in the course of the disease. The use of objective performance-based measure is of much advantage. As the Practical Part of TAM contains tasks from various financial spheres, clinicians and researchers can detect which part of financial abilities the patients is in much disadvantage and advise to their carers. In addition, the deterioration progress from the most complex financial task to the easy tasks can signal of disease progression. In addition to that, TAM assesses awareness of financial abilities. As I stated before, anosognosia can be the first symptom of cognitive decline. In the experiment, some MCI patients were not fully aware of the difficulties they experience with regards to financial abilities. This is important in clinical and practical ways. Firstly, anosognosia of Acreemagnosia can be the first functional sign of cognitive decline and the assessment of Acreemagnosia should therefore become an integral part of the assessment of patients with cognitive decline. Reduced awareness of financial abilities can pose a challenge on families and carers of patients, as they can be a target of financial scams, exploitation and unintentional self-impoverishment.

Unfortunately, in the experiment reported here due to the time constrains and difficulties with the access to patients, the sample size of MCI patients was rather small and very heterogeneous: some of the patients had prior expertise on finances and two of the patients were current accountant advisors for charity shops. Other patients had no prior or very little financial experience.

Chapter X

Discussion of the part on the development and validation of TAM

During this study and in my previous clinical work as a forensic psychiatrist I have observed when dealing with AD, MCI patients and their caregivers, how often they lack financial competence and are unaware of this impairment. In order to assess financial knowledge, researchers and clinicians are currently using ADL/IADL scales that do not sufficiently address the intricacy of everyday financial requirements. Almost every IADL scale has a question on everyday financial abilities. However, these questions are usually very general inquires of the participant's problems to deal with everyday financial tasks. Another limitation across IADL scales is that they are not providing information on whether there is a decline in performance or if the testee has always had problems with finances. Lastly, commonly used ADL/IADL questionnaires inquire if the person is capable of preforming a particular task, in other words require the assumption of ability to perform. Standard scales cannot answer that question on whether the person can actually perform the task. There are a few financial scales devised to look particularly at financial abilities, competence, and awareness. Unfortunately, these scales are unavailable for use and are not fully validated.

We coined the term ***Acreemagnosia*** to label this symptom in order to frame it as a specific cognitive difficulty which could hamper the independent daily life of people at different levels of financial competence. Importantly, often also the carers are not fully aware of the patient's impaired financial knowledge. There are numbers of unanswered questions about Acreemagnosia; in order to address them and further explore the symptom, I developed TAM that reflects everyday financial involvement of frail older people and accounts for their financial proficiency.

A multi-domain approach.

Usually functional scales are presented either as self- or proxi-questionnaires or performance-based tools. I constructed TAM by combining these methods of assessments. The reason for that was mainly two-fold. Firstly, TAM assesses awareness of the participant of one's financial abilities by calculating the discrepancy between self- and proxy questionnaire scores. Unawareness of functional limitations is one of the symptom of cognitive decline *(*Okonkowo et. al., 2008; Amanzio et.al., 2013*)* and unawareness of financial limitations in addition to that can lead to exploitation of the person with cognitive decline and leads to family burden and hamper independent living.

Secondly, reliability and validity of the information obtained from report-based is dependent on the accuracy of the reporter, that is most of the time prone to bias. TAM is assessing an actual performance rather than perception of one own performance. It enables participant to enact financial tasks and therefore more objectively measure the level of financial abilities.

Multi-dimensional concept

The pioneer research by Marson et al. (2000) showed that financial abilities are a multi-dimensional construct that incorporates several domains (See more on that in the Section 7.3.1). I aimed to support and incorporate this idea, inquire deeper and in more detail about the financial abilities. After consultation with the professionals in the area, we constructed items and tasks that would reflect this multi-dimensionality and the complexity of real-world financial challenges; and to approximate post-retirement financial behaviour. Based on that TAM evaluates the following financial tasks: 1) Being able to recognise different notes and coins and know what you can buy with a certain amount of money, 2) Ability for mental calculation, 3) Know financial concepts and being able to apply them, 3) knowing the main financial forms, being able to recognise them and fill them in, 4) clear reasoning and financial judgment abilities.

Hierarchy of the items

To my knowledge, TAM is the first measure that was constructed in order to apply it for people with different levels of financial knowledge. TAM reliably measures peoples' financial abilities at average and low financial proficiency. This was exactly the aim of the measure as it was intended for people after retirement and patients with cognitive impairment.

This other methodological issue that TAM addresses is to show a formal hierarchy of the financial items: what are the "easy ", "moderate" and "difficult" items by using the IRT model. This was not addressed in the existing scales. The most difficult items were shown to be financial judgment, knowledge in financial concepts and applying these concepts (e.g. knowing what is the profit and maximum of the profit you can get, you make more weighted decision on the investment).

Gender and age non-specific

Differential Item Functioning analysis showed that TAM performance is not affected by age or gender. This is a very interesting finding and might reflect a change in social norms, lifespan development (or a cohort effect). Financial strategies and decisions naturally change over the course of the lifespan, which makes comparisons between working middle-aged adults and retirees difficult. Adults in the middle age range often face with important financial decisions that have long-term consequence, such as those related to retirement, investing, and insurance. However, older adults after retirement nowadays are usually still quite active in financial life and actively use all modern technologies and innovations.

Gender was often hypothesised to be an important moderator of financial abilities. Early studies stated that in general, women tend to report lower levels of financial knowledge and make overly conservative financial choices, resulting in lower earnings and return on investments (Gecas, 1989). Nowadays the picture is different and women have a very active financial position where they have equal access to investments, they participate in the financial life equally with males and make most of the major financial decisions.

MCI patients are already present with Acreemagnosia

Finally, in the last experiment with patients with cognitive impairment I showed that Acreemagnosia is already present in patients with early cognitive decline and patients with MCI demonstrate lower accuracy in their estimation of their financial abilities. Acreemagnosia starts from the diminished ability in financial judgment; they had difficulties detecting fraud scenarios. Mild-AD patients, apart from being impaired in the financial judgment domain, had difficulty with financial conceptual tasks and in manipulating these concepts.

In summary, financial ability is shown to be vulnerable to early effects of cognitive decline. I designed TAM in order to address the limitations of the existing ADL/IADL scales that cannot detect financial abilities decline. TAM is a multi-items measure that enquires about a person's awareness of financial abilities and examines actual performance on a broad range of everyday financial tasks. The present data indicates that TAM is a promising tool for the measurement of the everyday financial abilities in frail older people and patients with cognitive impairment. It would serve not only in detecting early impairments but it would also help health care professionals (i.e., general practitioners, nurses, clinical psychologists) and other relevant professionals (i.e., social workers, financial or family counsellors) to make an evidence-based decision about the person's everyday financial knowledge and it would allow them to follow up the patients' performance. In order to make TAM easily accessible for a clinical, research, and public use it is made freely available.

Chapter XI General discussion

11.1 Aims of the thesis

AD pathology is already present years before cognitive symptoms appear and early diagnosis is crucial (for an early therapeutic intervention) and challenging (as early symptoms resemble those in normal ageing and patients with depression). Therefore, researchers were challenged to modify, improve, or create cognitive and functional measures that can be sensitive and specific enough to detect early changes and differentiate AD from other forms of dementia, depression and from normal ageing. Therefore the central aim of the thesis was to design and explore sensitive and specific cognitive and functional markers for early detection of AD.

In my thesis I investigate and expand on the body of work related to Visual Short Term Memory Binding tasks that was shown on the number of studies around the world to be sensitive to the effect of AD regardless of educational level and cultural differences. The restriction of using TMB task in the clinical practice was in the fact that the test only existed as a form of a computer test. In the field work (e.g. assessing patients at home) and in the situation where it is difficult to use computers (e.g. outpatient clinic office) there was a need of a more mobile version of the test that would hold the same psychometric properties as the computer version.

1. I created a Flash-Card version of the test (Chapter 2) and tested another mobile version of the test – Tablet PC version of the test on healthy older and younger adults.
2. I also aimed at investigating why TMB task is generally unaffected by normal ageing (Chapter 3). I explored if there are any electrophysiological differences in TMB performance between healthy older and younger adults. The experiment was driven by the Scaffolding theory of ageing that postulates that older adults recruit more neural resources in order to perform challenging tasks successfully.
3. I tested the sensitivity and specificity of the Flash-Card version of TMB to detect binding deficit in AD patients. For that I recruited patients with AD and Parkinson's disease (Chapter 4).

As dementia diagnosis is based not only cognitive impairment, but also everyday functional deficit, I aimed to look at the functional abilities that would deteriorate early on the course of the disease.

4. In Chapter 6 I investigated if commonly used clinical functional scales can distinguish between healthy older adults and patients with cognitive impairment and which items are the most sensitive to cognitive decline.
5. I argue that everyday financial abilities are one of the earliest functional impairments and introduce the new term that would describe this symptom: "Acreemagnosia" – that is a combination of Ancient Greek words: ἀ- (a-, "not, without"), χρήμα (chreema, "money") and γνωσιακή (gnôsis, "knowledge") (Chapter 7).
6. In order to explore this symptom and test my hypothesis of early deterioration of financial abilities in people with cognitive impairment I designed an instrument: The Acreemagnosia Measurement. I explore its psychometric properties on healthy adults (Chapter 8).
7. In the group of patients with different level of cognitive impairment and healthy older adults I explore if TAM can differentiate between these groups and which financial tasks are the most sensitive to early cognitive deterioration (Chapter 9). I explore neuropsychological predictors of financial difficulties in healthy older adults and patients with various level of cognitive impairment.

11.2 Main findings of the cognitive part of the study

1. The current work expands on and confirm the findings from a fast growing literature that TMB task resistant to the effect of age. Older and younger adults performed equally on the TMB task. The results of the first series of experiments show that two clinically friendly versions of the TMB test (the Flash-Card version and the Tablet PC version) equivalent to each other. I also showed that older adults have a preference to the Flash-Card version of the test as opposed to two electronic versions (i.e. Computer PC and Tablet).

In order to make it more clinically friendly the Flash-card version of the test contains only two items per trial for healthy participants and patients with dementia. In the computer version the number of items was titrated in order to avoid ceiling effect and for healthy adults

it was three items, whereas patients were given two items. The Flash-Cards are therefore more user-friendly for clinical settings.

2. The ERP study reviled that in order to successfully perform the TMB task, older adults recruited significantly more neural resources than younger adults.

The effect of over-recruitment of brain recourses was more prominent during the retrieval phase confirming previous findings (Parra et al., 2017; Pietto et a., 2016) that older adults encoding abilities are more preserved than their retrieval functions and in older adults retrieval process is more prone to vulnerability to interference leading to greater cognitive efforts.

In addition, the study showed that regardless of age, binding process requires more neural recourses than processing of single features.

4. The results of the study confirm specificity and sensitivity of the TMB test to the effect of AD.

Only patients with AD showed decline performing TMB task compare to patients with Parkinson's disease. On the contrary, performance on the TMB task is not affected by Parkinson's disease regardless of the level of cognitive impairment.

11.2 Implications of the clinically oriented versions of the TMB test

The main implication of the Flash-Cards is to detect biding impairment in patients with AD. Despite different testing method the TMB task on the Flash-Cards showed sensitivity and specificity to AD and resistant to the effect of age. The main implications of the Flash-Card version are in its affordability and portability. The creation of the Flash-cards was directed by the fact that TMB was existed as a computer version and it was difficult to use in the remote areas, in the situations where there is a need of assessment participants at home. In addition, computerised version of the test requires a special training in setting-up and testing and storage of the big data (that requires the Internet connection that in the clinical setting would be difficult to do). Furthermore, population under investigation are frail older people and patients with cognitive impairment who have limited computer knowledge and might develop "computer anxiety" that would affect the performance on the test. The Flash-Cards successfully address all these issues.

11.3 Main findings of the functional part of the study

4. The results of the study revealed that individual items on the Lawton's and ECog scales could differentiate between different groups better than the total score of the scales. More specifically, items assessing finances could detect functional differences between MCI and AD. In addition, patients with cognitive impairment are less aware of these functional difficulties than healthy older adults.

5. I designed the Acreemagnosia Measurement that reflects the complexity and multi-dimentionality of the financial abilities. The measurement reflects post-retirement financial behaviour. It consists of self- and proxi-questionnaires, and performance-based tasks. TAM is the first measure that was constructed in order to apply it for people with different levels of financial knowledge. TAM reliably measures peoples' financial abilities at average and low financial proficiency. This was exactly the aim of the measure as it was intended for people after retirement and patients with cognitive impairment. The other advantage of the measure is that it is gender and age non-specific.

6. TAM showed a good discriminability between patients with different level of cognitive impairment and healthy older adults. TAM shows that Acreemagnosia is already present in patients with early cognitive decline and patients with MCI demonstrate lower accuracy in their estimation of their financial abilities. Acreemagnosia starts from the diminished ability in financial judgment; patients with MCI had difficulties detecting fraud scenarios.

11.4 Implication of the results from everyday functioning study

Typically, in clinical practice the functional level of patients with cognitive impairment is examined by summing the responses on individual items to reach the total score. This is a quick and easy method to ascertain if there is a functional decline, however it may yield quite imprecise estimates of functional abilities. In the study I confirmed that total score cannot detect the difference between early cognitive impairment and dementia and only individual items that are more complex in nature (rely on several cognitive constructs) could detect this difference. Based on these findings and in order to avoid underestimation of functional decline and enhance the sensitivity of the functional scales, I suggested that the new tools should include the ability to establish a formal hierarchy of functional decline (i.e include

complex cognitive tasks with various difficulty level). This would also allow clinicians and researchers to detect functional limitations early, establish a natural history of functional decline and monitor the development of the disease.

The other important finding from the study is reliability of the self-rated scales. I demonstrated lower accuracy in perception of the functional abilities by patient groups. Patients with cognitive impairment tended to overestimate their performance especially on financial and managing medication tasks. This finding highlights the fact that awareness is a heterogeneous phenomenon and it preserved for some tasks, but not another.

11.5 Implication of TAM

The results of the validation of TAM show that it is a promising tool for the measurement of the everyday financial abilities in frail older people and patients with cognitive impairment. It would serve not only in detecting early impairments but it would also help health care professionals (i.e., general practitioners, nurses, clinical psychologists) and other relevant professionals (i.e., social workers, financial or family counsellors) to make an evidence-based decision about the person's everyday financial knowledge and it would allow them to follow up the patients' performance.

Assessing the loss of awareness of financial decline with TAM has an important implication for patient's safety as it is a predictor of the likelihood that they might engage in behaviours that pose significant risk and harm to themselves and their families as they can fail to judge the situation correctly and adequately, be involve in financial scams, fraud and exploitation.

In order to make TAM easily accessible for a clinical, research, and public use it is made freely available.

11.6 Limitations

The major limitation throughout the thesis is small sample size. The results from the study on the psychometric property of the scale (Chapter 8) should be interpreted with with caution as they were drawn from relative small samples and thus the statistical power to detect DIF was low. IRT models are very sensitive to sample size. For 2PL model, sample sizes of 500-1000 participants are sufficient (Tsutakawa & Johnson, 1990), Similarly, Reise & Yu (1990)

recommended approximately 500 participants, which in the scope of my PhD was unfortunately very difficult to achieve and in future studies should be addressed.

The analysis from the study with patients (Chapter 9) should be interpreted as a proof of the concept that need further investigation. This issue is due to the number of patients that were enrolled for the study. The evidences that was born from the study need to be confirmed with the larger cohort of patients.

In addition, the problematic issue with the sampling for all the experiments as healthy older participants were drawn from the University volunteer panel. These control participants are frequent to the psychological experiments and the results of the current studies would be difficult to generalise on the general population.

Another limitation the study from Chapter 8 on psychometric properties of the financial tool is that the data was gathered online and participants were self-selected; this may also restrict generalizability.

11.7 Future directions

In the future studies the sound number of patients and control participants driven from the general population would aid to replicate and confirm the results of the thesis and address all the issues with the sampling error.

Future studies should consider the impact of other variables on financial abilities and financial awareness. The factors such as age, gender, education, race, medical comorbidity in MCI and AD. In addition it would be interesting to ascertain if different types of dementia would show different endorsement on TAM. Would TAM or its items differentiate between different types of dementia?

11.8 Concluding words

There is a challenge to detect AD early, researchers are drawn to design the tools and markers that can aid to detect the disease at the preclinical stage. The current state-of-the-art diagnostic biomarkers are expensive, invasive and not specific to AD. Therefore it limits it use for the specialty clinics. The same with cognitive and functional measures: clinicians use episodic memory impairment and general functional decline as clinical diagnostic markers of

the disease. However cognitive and functional measures should be more precise and more specific to the disorder.

The thesis drew attention to TMB task that is considered as a reliable cognitive marker of the disease and making the task more mobile ad available for use can enhance its application and further analysis.

I argue that financial abilities are one of the first functional decline on the course of the disease and design the tool that would help to detect the symptom and therefore become an integral part of the assessment of patients with cognitive decline.

References

Aarsland, D., Creese, B., Politis, M., Chaudhuri, K.R., Ffytche, D.H., Weintraub, D., Ballard, C. (2017). Cognitive decline in Parkinson disease. *Nature Reviews Neurology*, 13(4), 217–231.

Acierno, R., Hernandez, M. A., Amstadter, A. B., Resnick, H. S., Steve, K., Muzzy, W., & Kilpatrick, D. G. (2010). Prevalence and correlates of emotional, physical, sexual, and financial abuse and potential neglect in the United States: The national elder mistreatment study. *American Journal of Public Health*, 100 (2), 292-297.

Ahn, I. S., Kim, J. H., Kim, S., Chung, J. W., Kim, H., Kang, H. S., & Kim, D. K. (2009). Impairment of instrumental activities of daily living in patients with mild cognitive impairment. *Psychiatry investigation*, *6*(3), 180–184.

Albert, M.S., De Kosky, S.T., Dickson,D., Dubois, B., Feldman,H.H., Fox, N.C., Gamst, A., Holzman, D.M., Jagust, W.J., PetersenR.C., Snyder P.J., Carillo, M.C., Thies, B., Phelps,C.H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia*, 7(3), 270–279.

Allen, R. J., Baddeley, A. D., & Hitch, G. J. (2006). Is the binding of visual features in working memory resource-demanding? *Journal of Experimental Psychology: General*, *135*(2), 298-313.

Amanzio, M., Vase, L., Leotta, D., Miceli, R., Palermo, S., & Geminiani, G. (2013). Impaired awareness of deficits in alzheimer's disease: The role of everyday executive dysfunction. *Journal of the International Neuropsychological Society*, *19*(1), 63–72.

American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth edition. Washington, DC: American Psychiatric Association.

Artero, S., Touchon, J., Ritchie, K. (2001). Disability and mild cognitive impairment: a longitudinal population-based study. International Journal of Geriatric Psychiatry, 16, 1092–1097.

Luck, S. J. & Vogel, E. K. (1997). The capacity of visual working memory for features and conjunctions. *Nature*, 390, 279-281.

Allen, R. J., Brown, L. A., Niven, E., Allen, R. J., Brown, L. A., & Niven, E. (2013). Aging and visual feature binding in working memory. In H. Clair-Thompson & H. Clair-Thompson (Eds.), *Working Memory*

Amieva, H., Le Goff, M., Millet, X., Orgogozo, J. M., Pérès, K., Barberger-Gateau, P., Jacqmin-Gadda, H., Dartigues, J. F. (2008). Prodromal Alzheimer's disease: successive emergence of the clinical symptoms. *Annals of Neurology*, *64*(5), 492–498.

Appelbaum, P.S. & Grisso, T. (1995). The MacArthur Treatment Competence Study. I: Mental illness and competence to consent to treatment. *Law Human Behav*, 19, 105-126.

Aretouli, E. & Brandt, J. (2010). Everyday functioning in mild cognitive impairment and its relationship with executive cognition. *International Journal of Geriatric Psychiatry*, 25, 224–233.

Aretouli, E., Okonkwo, O.C., Samek, J., & Brandt, J. (2011). The fate of the predictors of 2-year outcome in mild cognitive impairment. *Journal of the International Neuropsychological Society*, 17(2), 277–288.

Army Individual Test Battery (1944). *Manual of Directions and Scoring*. Washington, DC: War Department, Adjutant General's Office.

Arrighi, H. M., Gélinas, I., McLaughlin, T. P., Buchanan, J., & Gauthier, S. (2013). Longitudinal changes in functional disability in Alzheimer's disease patients. *International Psychogeriatrics/IPA*, *25*(6), 929–937.

Bäckman, L., Almkvist, O., Andersson, J., Nordberg, A., Winblad, B., Reineck, R., & Långström, B. (1997). Brain activation in young and older adults during implicit and explicit retrieval. *Journal of Cognitive Neuroscience,* 9 (3), 378-391.

Bäckman, L., Jones, S., Berger, a-K., Laukka, E. J., & Small, B. J. (2004). Multiple cognitive deficits during the transition to Alzheimer's disease. *Journal of Internal Medicine*, *256*(3), 195–204.

Baddeley, A. D., Allen, R. J., & Hitch, G. J. (2011). Binding in visual working memory: The role of the episodic buffer. *Neuropsychologia,* 49 (6), 1393–1400.

Baker F. (2001). *The basics of items response theory.* Portsmouth, NH: Heinemann

Balota, D. A., Dolan, P. O., & Duchek, J. M. (2000). Memory changes in healthy older adults. In E. Tulving & F. I. M. Craik (Eds.), The Oxford handbook of memory (pp. 395- 409). Oxford: Oxford University Press.

Baltes, P. B., & Lindenberger, U. (1997). Emergence of a powerful connection between sensory and cognitive functions across the adult life span: a new window to the study of cognitive aging? *Psychology and Aging*, 12(1), 12.

Bangen, K. J., Jak, A. J., Schiehser, D. M., Delano-Wood, L., Tuminello, E., Han, S. D., Delis, D.C., Bondi, M. W. (2010). Complex activities of daily living vary by mild cognitive impairment subtype. *Journal of the International Neuropsychological Society : JINS*, *16*(4), 630–639.

Barberger-Gateau, P., Commenges, D., Gagnon, M., Letenneur, L., Sauvel, C, & Dartigues, J. F. (1992). Instrumental activities of daily living as a screening tool for cognitive impairment and dementia in elderly community dwellers. *Journal of the American Geriatrics Society*, 40, 1129-113

Barberger-Gateau, P., Rainville, C., Letenneur, L., & Dartigues, J.F. (2000). A hierarchical model of domains of disablement in the elderly: A longitudinal approach. *Disability and Rehabilitation*, 22(7), 308-317.

Barberger-Gateau, P., Fabrigoule, C., Helmer, C., Rouch, I., Dartigues, J.F. (1999a). Functional impairment in instrumental activities of daily living: An early clinical sign of dementia? *Journal of American Geriatric Society*, 47, 456–462.

Barberger-Gateau, P., Fabrigoule, C., Rouch, I., Letenneur, L., & Dartigues, J. F. (1999b). Neuropsychological correlates of self-reported performance in instrumental activities of daily living and prediction of dementia. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*, *54*(5), P293–303.

Barulli, D. & Stern, Y. (2013) Efficiency, capacity, compensation, maintenance, plasticity: emerging concepts in cognitive reserve. *Trends in Cognitive Science*, 17, 502–509.

Bassett, S. (1999). Attention: Neuropsychological Predictor of Competency in Alzheimer's Disease. *Journal of Geriatric Psychiatry and Neurology*, 12, 200–205

Bastin, C., Bahri, M. A., Miévis, F., Lemaire, C., Collette, F., Genon, S., … Salmon, E. (2014). Associative memory and its cerebral correlates in Alzheimer's disease: Evidence for distinct deficits of relational and conjunctive memory. *Neuropsychologia*, 63 (1), 99-106.

Bastin, C. (2017). Differential age-related effects on conjunctive and relational visual short-term memory binding. *Memory*, 26 (9), 1181-1190.

Beato, R., Levy, R., Pillon, B., Vidal C., Du Montcel, S.T., Deweer,B. . . . Cardoso F. (2008). Working memory in Parkinson's disease patients: Clinical features and response to levodopa. *Arquivos De Neuro-Psiquiatria, 66*(2a), 147-151.

Beck, C.K. & Frank, L.B. (1997). Assessing functioning and self-care abilities in Alzheimer disease research. *Alzheimer Disease and Associative Disorders*, 11(Suppl 6), 73–80.

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition,* 50 (1-3), 7-15.

Bell-Mcginty, S., Podell, K., Franzen, M., Baird, A. D., & Williams, M. J. (2002). Standard measures of executive function in predicting instrumental activities of daily living in older adults, *International Journal of Geriatric Psychiatr*y, 17, 828–834.

Berardelli, A., Wenning, G. K., Antonini, A., Berg, D., Bloem, B. R., Bonifati, V.,… Vidailhet, M. (2013). EFNS/MDS-ES recommendations for the diagnosis of Parkinson's disease. *European Journal of Neurology, 20*, 16–34.

Berg, D., Postuma, R.B,. Adler, C.H., Bloem, B.R., Chan, P., … Deuschl, G (2015). MDS research criteria for prodromal Parkinson's disease. *Movement Disorders*, 30, 1600-1611

Besthorn, C., Zerfass, R., Geiger-Kabisch, C., Sattel, H., Daniel, S., … Förstl, H. (1997). Discrimination of Alzheimer's disease and normal aging by EEG data. *Electroencephalography and Clinical Neurophysiology,* 103 (2), 241-248.

Braak, H. & Braak, E. (1991). Neuropathological stageing of Alzheimer-related changes. *Acta Neuropathologica*, 82 (4), 239-259.

Blessed, G., Tomlinson, B.E., & Roth, M. (1968). The association between quantitative measures of senile change in the cerebral grey matter of elderly subjects. *British Journal of Psychology*, 114, 797–811.

Boeve, B. F. (2009). Early clinical features of the parkinsonian-related dementias. In B. L. M. & B. F.Boeve (Ed.), *The Behavioral Neurology of Dementia* (pp. 197–212).

Boivin, M. J., Bangirana, P., & Smith, R. C. (2010). The Relationship between Visual-Spatial and Auditory-Verbal Working Memory Span in Senegalese and Ugandan Children. *PLoS One, 5*(1),E8914

Boyle, P., & Cahn-Weiner, D. (2005). Functional impairment in vascular dementia. In and S. S. Paul R.H., Cohen R., Ott B.R. (Ed.), *Vascular dementia: Cerebrovascular Mechanisms and Clinical Management* (pp. 171–177). Totwa, NJ: Humana Press Inc.

Brown, L. A., & Brockmole, J. R. (2010). The role of attention in binding visual features in working memory: Evidence from cognitive ageing. *The Quarterly Journal of Experimental Psychology,* 63 (10), 2067-2079.

Brown, L. A., Niven, E. H., Logie, R. H., Rhodes, S., & Allen, R. J. (2017). *Visual feature binding in younger and older adults: encoding and suffix interference effects*. Paper presented at the Memory.

Brown, M. W. & Warburton, E. C. (2006). Association and dissociation in recognition memory systems. In H. D. Zimmer, A. Mecklinger, & U. Lindenberger (Eds.), Handbook of binding and memory, perspective from cognitive neuroscience (pp. 413-443). New York: Oxford University Press.

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 & Associated Disorders*, *12*(1), 1–13.

Brockmole, J.R., Parra, M.A., Della Sala, S., & Logie, R. (2008) Do binding deficits account for age-related decline in visual working memory? P*sychonomic Bulletin & Revew*, 15, 543–547.

Brockmole, J. R. & Logie, R. H. (2013). Age-related change in visual working memory: a study of 55,753 participants aged 8–75. *Frontiers in Psychology*, 4, 1-5.

Brookmeyer, R., Abdalla, N., Kawas, C.H. & Corrada, M.M. (2018). Forecasting the prevalence of preclinical and clinical Alzheimer's disease in the United States. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 14*(2), 121-129.

Bruck, A., Kurki, T., Kaasinen, V., Vahlberg, T., Rinne, J.O. (2004) Hippocampal and prefrontal atrophy in patients with early non- demented Parkinson's disease is related to cognitive impairment. *Journal of Neurology, Neurosurgery and Psychiatry*, 75(10), 1467-1469.

Bucks, R.S., Ashworth, D.L., Wilcock, G.K, Siegfried, K. (1996). Assessment of activities of daily living in dementia: development of the Bristol Activities of Daily Living Scale. *Age Ageing*, 25, 113–20.

Bucur B., Madden D.J., Spaniol J., Provenzale J.M., Cabeza R., White L.E., Huet- tel S.A. (2008). Age-relatedslowingofmemoryretrieval: Contributions ofperceptualspeed and cerebral whitematter integrity, *Neurobiology of Aging* 29, 1070–1079.

Burton, C. L., Strauss, E., Hultsch, D. F., Hunter, M. A., Burton, C. L., Strauss, E., … Hunter, M. A. (2007). Cognitive Functioning and Everyday Problem Solving in Older Adults, *The clinical Neuropsychologist*, 20(3), 432-452.

Buschke, H., Sliwinski, M.J., Kuslansky, G., Lipton, R.B. (1997). Diagnosis of early dementia by the Double Memory Test: Encoding specificity improves diagnostic sensitivity and specificity. *Neurology*, 48, 989–997.

Busse, A., Hensel, A., Guhne, U., Angermeyer, M.C., Riedel-Heller, S.G. (2006). Mild cognitive impairment : long-term course of four clinical subtypes, *Neurology,* 67, 2176–2185.

Cabeza, R., Grady, C. L., Nyberg, L., McIntosh, A. R., Tulving, E., Kapur, S., … Craik, F. I. (1997). Age-related differences in neural activity during memory encoding and retrieval: A positron emission tomography study. *Journal of Neuroscience*, *17*(1), 391–400.

Cabeza R., Anderson N.D., Locantore J.K., McIntosh A.R. (2002). Aging gracefully: Compensatory brain activity in high-performing older adults. *Neuroimage,* 17, 1394-1402.

Cahn-Weiner, D. A., Farias, S. T., Julian, L., Harvey, D. J., Kramer, J. H., Reed, B. R., … Chui, H. (2007). Cognitive and neuroimaging predictors of instrumental activities of daily living. *Journal of the International Neuropsychological Society*, *13*(5), 747–757.

Calderon, J., & Perry, R. (2001). Perception, attention, and working memory are disproportionately impaired in dementia with Lewy bodies compared with Alzheimer's disease. *Journal of Neurology,* 70, 157–164.

Cassani, R., Falk, T. H., Fraga, F. J., Cecchi, M., Moore, D. K., & Anghinah, R. (2017). Towards automated electroencephalography-based Alzheimer's disease diagnosis using portable low-density devices. *Biomedical Signal Processing and Control, 33*, 261-271.

Caviness, J. N., Driver-dunckley, E., Connor, D. J., Sabbagh, M. N., Hentz, J. G., Noble, B., … Adler, C. H. (2007). Defining Mild Cognitive Impairment in Parkinson ' s Disease, *22*(9), 1272–1277.

Cecchi, M., Moore, D. K., Sadowsky, C. H., Solomon, P. R., Doraiswamy, P. M., . . . Fadem, K. C. (2015). A clinical trial to validate event-related potential markers of Alzheimer's disease in outpatient settings. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 1*(4), 387-394.

Cecchini, A.M., Yassuda, M.S., Santoro, V., Leonardo, B., Souza, C. De, … Mario, S. (2017). Recalling feature bindings differentiates Alzheimer ' s disease from frontotemporal dementia. *Journal of Neurology*, *264*(10), 2162–2169.

Chalmers P. (2012). mirt: A Multidimensional Item Response Theory Package for the R Environment. *Journal of Statistical Software,* 48, 1-29.

Chiong, W., Hsu, M., Wudka, D., Miller, B. L., Howard, J., Rosen, H.J. (2014). Financial errors in dementia: Testing a neuroeconomic conceptual framework. *Neurocase*, *20*(4), 389–396.

Clare, L., Whitaker, C.J., Roberts, J.L., Neils, S.M., Martyr, A, …Morris R.G. (2013). Memory awareness profiles differentiate mild cognitive impairment from early-stage dementia: evidence from assessments of performance monitoring and evaluative judgement. *Dementia and Geriatric Cognitive Disorders*. 35, 266–279

Clarke, A., & Tyler, L. K. (2014). Object-Specific Semantic Coding in Human Perirhinal Cortex. *The Journal of Neuroscience*, 34 (14), 4766-4775.

Colzato, L. S., Raffone, A., & Hommel, B. (2006). What do we learn from binding features? Evidence for multilevel feature integration. *Journal of Experemental Psychology: Human Perception and Performance, 32,* 705-716.

Costa, A., Bak, T., Caffarra, P., Caltagirone, C., Ceccaldi, M., Collette, F., … Cappa, S. F. (2017). The need for harmonisation and innovation of neuropsychological assessment in neurodegenerative dementias in Europe: Consensus document of the Joint Program for Neurodegenerative Diseases Working Group. *Alzheimer's Research and Therapy*, *9*(1), 1–15.

Cowan, N., Blume, C. L., & Saults, J. S. (2013). Attention to attributes and objects in working memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 39 (3), 731–747.

Cowan, N., Elliott, E. M., Saults, J. S., Morey, C. C., Mattox, S., Hismjatullina, A., & Conway, A. R. A. (2005). On the capacity of attention: Its estimation and its role in working memory and cognitive aptitudes. *Cognitive Psychology*, 51 (1), 42–100.

Cowan, N., Naveh-Benjamin, M., Kilb, A., & Saults, J. S. (2006). Life-span development of visual working-memory: When is feature binding difficult? Developmental Psychology, 42 (6), 1089–1102.

Cramer, K., Tuokko, H. A., Mateer, C. A., & Hultsch, D. F. (2004). Measuring awareness of Financial skills: Reliability and validity of a new measure. *Aging and Mental Health*, *8*(2), 161–171.

Cromwell, D.A., Eagar, K.P., & Poulous, R.G. (2003) The performance of instrumental activities of daily living scale in screening for cognitive impairment in elderly community residents. *Journal of Clinical Epidemiology*, 56 (2), 131-137.

Cummings, J. L., & Benson, D. F. (1984). Subcortical dementia: Review of an emerging concept. *Archives of Neurology*, *41*(8), 874-879.

Daffner, K. R., Gale, S. A., Barrett, A. M., Boeve, B. F., Coslett, H. B., Esposito, M. D., … Pietras, A. C. (2015). Improving clinical cognitive testing Report of the AAN Behavioral Neurology Section Workgroup. *Neurology*, *85*(10), 910–918.

Danckert, S. L., & Craik, F. I. (2013). Does aging affect recall more than recognition memory? *Psychology of Aging, 28*(4), 902-909.

Das, S. R., Mancuso, L., Olson, I. R., Arnold, S. E., & Wolk, D. A. (2016). Short-Term Memory Depends on Dissociable Medial Temporal Lobe Regions in Amnestic Mild Cognitive Impairment. *Cerebral Cortex, 26 (5), 2006-2017*.

Dauwels, J., Vialatte, F., Cichocki, A. (2010) Diagnosis of Alzheimer's disease from EEG signals: where are we standing? *Current Alzheimer Research*, 7, 487–505.

Davis, S. W., Dennis, N. A., Daselaar, S. M., Fleck, M. S., & Cabeza, R. (2008). Qué PASA? the posterior-anterior shift in aging. *Cerebral Cortex*, *18*(5), 1201–1209.

Deary, I. J., Corley, J., Gow, A. J., Harris, S. E., Houlihan, L. M., Marioni, R. E., … Starr, J. M. (2009). Age-associated cognitive decline. *British Medical Bulletin*, *92*(1), 135–152.

Deary, I. J., Gow, A. J., Taylor, M. D., Corley, J., Brett, C., Wilson, V., et al. (2007). The Lothian Birth Cohort 1936: A study to examine influences on cog- nitive ageing from age 11 to age 70 and beyond. BMC Geriatrics, 7, 28.

Desai, A. K., Grossberg, G. T., & Sheth, D. N. (2004). Activities of daily living in patients with dementia: clinical relevance, methods of assessment and effects of treatment. *CNS Drugs*, *18*(13), 853–875.

Dubois, B., Feldman, H. H., Jacova, C., Hampel, H., Molinuevo, J. L., Blennow, K., … Cummings, J. L. (2014). Advancing research diagnostic criteria for Alzheimer's disease: The IWG-2 criteria. *The Lancet Neurology*, *13*(6), 614–629.

Della Sala, S., Parra, M. A., Fabi, K., Luzzi, S., & Abrahams, S. (2012). Short-term memory binding is impaired in AD but not in non-AD dementias. *Neuropsychologia,* 50 (5), 833-840.

Della Sala, S., Kinnear, P., Spinnler, H., Stangalino, C. (2000) Color-to-figure match- ing in Alzheimer's disease. *Archive of Clinical Neuropsychology*, 15, 571–85.

Delgado, C., Munoz-Neira, C., Soto, A., Martinez, M., Henriquez, F., Flores, P., & Slachevsky, A. (2016). Comparison of the Psychometric Properties of the "Word" and "Picture" Versions of the Free and Cued Selective Reminding Test in a Spanish-Speaking Cohort of Patients with Mild Alzheimer's Disease and Cognitively Healthy Controls. *Archive of Clinical Neuropsychology, 31*(2), 165-175.

de Rotrou, J; Wu Y-H, Hugonot-DienerL, T.-A. (2012). DAD-6 : A 6-Item Version of the Disability Assessment for Dementia Scale Which May Differentiate Alzheimer ' s Disease and Mild. *Dementia and Geriatric Cognitive Disorders*, *33*, 210–218.

De Vriendt, P., Gorus, E., Cornelis, E., Velghe, A., Petrovic, M., Mets, T. (2012). The process of decline in advanced activities of daily living: a qualitative explorative study in mild cognitive impairment. *International Psychogeriatrics / IPA*, *24*(6), 974–986.

Didic, M., Barbeau, E. J., Felician, O., Tramoni, E., Guedj, E., Poncet, M., & Ceccaldi, M. (2011). Which memory system is impaired first in alzheimer's disease? *Journal of Alzheimer's Disease*, *27*(1), 11–22.

Dudas, R. B., Clague, F., Thompson, S. a, Graham, K. S., & Hodges, J. R. (2005). Episodic and semantic memory in mild cognitive impairment. *Neuropsychologia*, *43*(9), 1266–1276.

Earnst, K., Wadley, V., Aldridge, T., Streenwyk, A. B., Hammond, A. E., Harrell, L. E. et al. (2001) Loss of financial capacity in Alzheimer's disease: the role of working memory. *Aging, Neuropsychology, and Cognition,* 8,109–119.

Ebly, E.M., Hogan, D.B. & Parhad, I.M. (1995). Cognitive impairment in the nondemented elderly. Results from the Canadian Study of Health and Aging. *Archive of Neurology*, 52, 612–619.

Edelen, M. O., Thissen, D., Teresi, J., Kleinman, M., & Ocepek-Welikson, K. (2006). Identification of differential item functioning using item response theory and the likelihood-based model comparison approach. Application to the Mini-Mental State Examination. *Medical Care*, *44*(11 Suppl 3), S134-42.

Embretson, S. E. (2002). Generating abstract reasoning items with cognitive theory. In S. H. Irvine, & P. C. Kyllonen (Eds.), Item generation for test development. New Jersey 7 Lawrence Erlbaum Associates.

Embretson, S.E., & Reise, S.P. (2013). Item response theory for psychologists. Psychology Press.

Emre, M., Aarsland, D. , Brown, R. , Burn, D. J., Duyckaerts, C. , … Dubois, B. (2007). Clinical diagnostic criteria for dementia associated with Parkinson's disease. *Movement Disorders*, 22, 1689-1707.

Farias, S.T, Cahn-Weiner, D. a, Harvey, D. J., Reed, B. R., Mungas, D., Kramer, J. H., Chui, H. (2009). Longitudinal changes in memory and executive functioning are associated with longitudinal change in instrumental activities of daily living in older adults. *The Clinical Neuropsychologist*, *23*(3), 446–61.

Farias, S. T., Chou, E., Harvey, D. J., Mungas, D., Reed, B., Decarli, C., … Beckett, L. (2013). Longitudinal Trajectories of Everyday Function by Diagnostic Status. *Psychology of Aging*, *28*(4), 1070–1075.

Farias, S.T., Mungas, D., Reed, B., Harvey, D., Cahn-Weiner, D., DeCarli, C. (2006). MCI is associated with deficits in everyday functioning. *Alzheimer Disease and Associated Disorders,* 20, 217–223.

Farias, S. T., Mungas, D., & Jagust, W. (2005). Degree of discrepancy between self and other-reported everyday functioning by cognitive status: Dementia, mild cognitive impairment, and healthy elders. *International Journal of Geriatric Psychiatry*, 20, 827–834.

Feyereisen, P. (1999). Disorders of Everyday Actions in Subjects Suffering from Senile Dementia of Alzheimer's Type: An Analysis of Dressing Performance. *Neuropsychological Rehabilitation*, 9, 169–188.

Fieo, R., Austin, E. J., Starr, J. M., & Deary, I. J. (2011). Calibrating ADL-IADL scales to improve measurement accuracy and to extend the disability construct into the preclinical range: a systematic review. *BMC Geriatrics*, *11*(1), 42.

Fieo, R., Manly, J.J., Schupf, N., Stern, Y. (2014). Functional Status in the Young–Old: Establishing a Working Prototype of an Extended-Instrumental Activities of Daily Living Scale, *The Journals of Gerontology: Series A*, 69 (6), 766–772.

Fitts, W., Weintraub, D., Massimo, L., Chahine, L., Chen-Plotkin, A. …Dahodwala, N. (2015). Caregiver report of apathy predicts dementia in Parkinson's disease. *Parkinsonism Related Disorders*, 21(8), 992–995.

Flicker, C., Ferris, S., & Reisberg, B. (1991). Mild cognitive impairment in the elderly: Predictors of dementia. *Neurology*, 41, 1006–1009.

Forlenza, O.V., Diniz, B.S., Nunes, P.V., Memoria, C.M., Yassuda, M.S., Gattaz, W.F. (2009) Diagnostic transitions in mild cognitive impairment subtypes. *International Psychogeriatrics*, 21, 1088-1895.

Foley, J., Cocchini, G., Logie, R., & Della Sala, S. (2015). No dual- task practice effect in Alzheimer's disease. *Memory*, 23, 518- 528.

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, 189–98.

Fortinsky, R.H., Garcia, R.I., Sheehan, J.T., Madigan, E.A., Tullai-McGuinness, S. (2003). Measuring disability in Medicare home care patients: application of Rasch modelling to outcome and assessment information set. *Medical Care*, 41, 601-661

Fowler, K. S., Saling, M. M., Conway, E. L., Semple, J. M., & Louis, W. J. (1997). Computerized neuropsychological tests in the early detection of dementia: prospective findings. *Journal of the International Neuropsychological Society*, 3(2), 139-146.

Fowler, K. S., Saling, M. M., Conway, E. L., Semple, J. M., & Louis, W. J. (2002). Paired associate performance in the early detection of DAT. *Journal of the International Neuropsychological Society*, 8,58–71.

Frasson, P., Ghiretti, R., Catricalà, E., Pomati, S., Marcone, A., Parisi, L., … Clerici, F. (2011). Free and cued selective reminding test: An Italian normative study. *Neurological Sciences*, *32*(6), 1057–1062.

Frazer, S.M., Oyebode, J.R., & Cleary, A. (2012). How older women who live alone with dementia make sense of their experiences: An interpretative phenomenological analysis. *Dementia,* 11(5), 677-693.

Gabrieli, J.D.E., Singh, J., Stebbins, G.T. & Goetz, C.G. (1996). Reduced working memory span in Parkinson's disease: Evidence from a front-striatal system in working and strategic memory. *Neuropsychology*, 10, 322-332.

Gallo, D.A., Sullivan, A.L., Daffner, K.R., Schacter, D.L., Budson, A.E. (2004) Associative recognition in Alzheimer's disease: evidence for impaired recall-to-reject. *Neuropsychology,* 18, 556–63.

Ganguli, M., Snitz, B. E., Saxton, J. A., Chang, C.-C. H., Lee, C.-W., Vander Bilt, J., … Petersen, R. C. (2011). Outcomes of Mild Cognitive Impairment by Definition. *Archives of Neurology*, *68*(6), 761–767.

Gatz, M., Reynolds, C. A., Fratiglioni, L., Johansson, B., Mortimer, J. A., Berg, S., … Pedersen, N. L. (2006). Role of genes and environments for explaining Alzheimer disease. *Archives of General Psychiatry*, 63 (2), 168-174.

Geda, Y. (2012). Mild Cognitive Impairment in older adults. *Current Psychiatry Reports,* 14, 321-327.

Geda, Y. E., Roberts, R. O., Knopman, D. S., Christianson, T. J., Pankratz, V. S., Ivnik, R. J., … Rocca, W. A. (2010). Physical exercise, aging, and mild cognitive impairment: a population-based study. *Archives of Neurology*, *67*(1), 80–86.

Gelinas, I., Gauthier, L., McIntyre, M., & Gauthier, S. (1999). Development of a functional measure for persons with Alzheimer's disease: the disability assessment for dementia. *American Journal of Occupational Therapy*, 53,471–481.

Gerstenecker, A., Eakin, A., Triebel, K., Martin, R., Swenson-Dravis, D., Petersen, R.C., Marson, D. (2016). Age and Education Corrected Older Adult Normative Data for a Short Form Version of the Financial Capacity Instrument. *Psychological Assessment*, 28, 737–749.

Giovannetti, T., Bettcher, B. M., Brennan, L., Libon, D. J., Burke, M., Duey, K., . . . Wambach, D. (2008). Characterization of everyday functioning in mild cognitive impairment: A direct assessment approach. *Dementia and Geriatric Cognitive Disorders,* 25, 359–365.

Goate, A., Chartier-Harlin, M. C., Mullan, M., Brown, J., Crawford, F., Fidani, L., … Hardy, J. (1991). Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease. *Nature*, 349, 704-796.

Gold, D. A. (2012). An examination of instrumental activities of daily living assessment in older adults and mild cognitive impairment. *Journal of Clinical and Experimental Neuropsychology*, *34*(1), 11–34.

Goldberg, T.E., Koppel, J., Keehlisen, L., …DaviesP. (2010). Performance-Based Measures of Everyday Function in Mild Cognitive Impairment. *American Journal of Psychiatry,* 167 (7), 845-853.

Goldman, J. G., & Litvan, I. (2011). Mild cognitive impairment in Parkinson's disease. *Minerva Medica*, *102*(6), 441–459.

Grady, C.L., McIntosh, A.R., Horwitz, B., Maisog, J.M., Ungerleider, L.G., et al. (1995) Age-related reductions in human recognition memory due to impaired encoding. *Science,* 269, 218–221.

Grady, C. L. (1998). Brain imaging and age-related changes in cognition. *Experimental Gerontology, 33*(7-8), 661-673.

Grady, C. L. (2008). Cognitive neuroscience of aging. *Annals of the New York Academy of Sciences,* 1124, 127-144.

Grady, C. L., & Craik, F. I. (2000). Changes in memory processing with age. *Current Opinion in Neurobiology,* 10, 224-231.

Griffith, H. R., Belue, K., Sicola, A., Krzywanski, S., Zamrini, E., Harrell, L., Marson, D.C. (2003). Impaired financial abilities in mild cognitive impairment: A direct assessment approach. *Neurology*, *60*(3), 449–457.

Grober, E., Buschke, H., Crystal, H., Bang, S. and Dresner, R. (1988). Screening for dementia by memory testing. *Neurology*, 38, 900–903

Grober, E., Hall, C., McGinn, M., Nicholls, T., Stanford, S., Ehrlich, A., … Lipton, R. B. (2008). Neuropsychological strategies for detecting early dementia. *Journal of the International Neuropsychological Society*, 14, 130–142.

Grober, E., Sanders, A. E., Hall, C., & Lipton, R. B. (2010). Free and cued selective reminding identifies very mild dementia in primary care. *Alzheimer Disease and Associated Disorders*, *24*(3), 284–290.

Hardy, J.A. & Higgins, G.A. (1992). Alzheimer's disease: the amyloid cascade hypothesis. *Science,* 256, 184-185.

Harvey, R. J., Skelton-Robinson, M., & Rossor, M. N. (2003). The prevalence and causes of dementia in people under the age of 65 years. *Journal of Neurology, Neurosurgery and Psychiatry*, 74 (9), 1206-1209.

Haxby, J.V., Raffaele, K., Gillette, J., Schapiro, M.B., Rapoport, S.I. (1992). Individual trajectories of cognitive decline in patients with dementia of the Alzheimer type. *Journal of Clinical and Experimental Neuropsychology,* 14, 575-592.

Hebert, L. E., Scherr, P. A., Bienias, J. L., Bennett, D. A., & Evans, D. A. (2003). Alzheimer disease in the US population: Prevalence estimates using the 2000 census. *Archives of Neurology*, 60 (8), 1119-1122.

Hedman, A., Nygård, L., Almkvist, O., & Kottorp, A. (2013). Patterns of functioning in older adults with mild cognitive impairment: a two-year study focusing on everyday technology use. *Ageing and Mental Health*, 17(6), 697-688.

Hesse, E., Mikulan, E., Decety, J., Sigman, M., Garcia Mdel, C., Silva, W., ... Ibanez, A. (2016). Early detection of intentional harm in the human amygdala. *Brain, 139*(Pt 1), 54-61.

Hesseberg, K., Bentzen, H., Ranhoff, A. H., Engedal, K., Bergland, A. (2013). Disability in instrumental activities of daily living in elderly patients with mild cognitive impairment and Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders*, *36*(3-4), 146–53.

Higginson, C. I., Wheelock, V. L., Carroll, K. E., & Sigvardt, K. A. (2005). Recognition memory in Parkinson's disease with and without dementia: Evidence inconsistent with the retrieval deficit hypothesis. *Journal of Clinical and Experimental Neuropsychology*, *27*(4), 516–528.

Hodges, J.R. & Greene, J.D. (1998). Knowing about people and naming them: can Alzheimer's disease patients do one without the other? *Quarterly Journal of Experimental Psychology*, 51, 121–34

Hoefeijzers, S., Gonzalez, H. A., Magnolia, R. A., & Parra, M. A. (2017). Feature Binding of Common Everyday Items Is Not Affected by Age. *Frontiers of Aging in Neuroscience, 9*, 122.

Holdstock, J. S., Mayes, A. R., Gong, Q. Y., Roberts, N., & Kapur, N. (2005). Item recognition is less impaired than recall and associative recognition in a patient with selective hippocampal damage. *Hippocampus*, 15, 203–215.

Horn, J.L. (1965). A rationale and test for the number of factors in factor analysis. *Psychometrika*, 30, 179-185.

Hsu, J. L., Hsu, W. C., Chang, C. C., Lin, K. J., Hsiao, I. T., Fan, Y. C., Bai, C. H. (2017). Everyday cognition scales are related to cognitive function in the early stage of probable Alzheimer's disease and FDG-PET findings. *Scientific Reports*, *7*(1), 1–10.

Hu, L.T. & Bentler, P.M. (1998). Fit indices in covariance structure modeling: Sensitivity to underparameterized model misspecification. *Psychological Methods, 3,* 424–453.

Hughes, A.J., Daniel, S.E., Shlomo Y.B., & Lees A.J. (2002). The accuracy of diagnosis of parkinsonian syndromes in a specialist movement disorder service, *Brain*, 125(4), 861–870.

Ibanez, A., Cardona, J. F., Dos Santos, Y. V., Blenkmann, A., Aravena, P., Roca, M., . . . Bekinschtein, T. (2013). Motor-language coupling: direct evidence from early Parkinson's disease and intracranial cortical recordings. *Cortex, 49*(4), 968-984.

Insausti, R., Juottonen, K., Soininen, H., Insausti, A.M., Partanen, K., Vainio, P., . . . Pitkänen, A. (1998). MR volumetric analysis of the human entorhinal, perirhinal, and temporopolar cortices. *American Journal of Neuroradiology, 19*(4), 659-671.

Isella, V., Molteni, F., Mapelli, C., & Ferrarese, C. (2015). Short term memory for single surface features and bindings in ageing: A replication study. *Brain and Cognition, 96*(0), 38-42.

Jack, C. R., Bennett, D. A., Blennow, K., Carrillo, M. C., Dunn, B., Haeberlein, S. B., … Silverberg, N. (2018). NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimer's and Dementia*, *14*(4), 535–562.

Jack, C. R., Jr, Knopman, D. S., Jagust, W. J., Shaw, L. M., Aisen, P. S., Weiner, M. W., … Trojanowski, J. Q. (2010). Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *The Lancet. Neurology*, *9*(1), 119–128.

Jacobs, D., Salmon, D.P., Tröster, A.I., Butters, N. (1990). Intrusion errors in the figural memory of patients with Alzheimer's and Huntington's disease. Archives in Clinical Neuropsychology, 5, 49–57.

James, B.D., Boyle, P.A. & Bennet, D.A. (2014). Correlates of Susceptibility to Scams in Older Adults Without Dementia. *Journal of Elder Abuse and Negligence*, 26, 107–122.

James, B.D., Boyle, P.A., Buchman, A.S., Barnes, LL.., Bennett, D.A. (2011). Life space and risk of Alzheimer disease, mild cognitive impairment, and cognitive decline in old age. *American Journal of Geriatric Psychiatry*, 19(11), 961–969.

Jayaweera, H. K., Hickie, I. B., Duffy, S. L., Mowszowski, L., Norrie, L., Lagopoulos, J., & Naismith, S. L. (2016). Episodic memory in depression: The unique contribution of the anterior caudate and hippocampus. *Psychological Medicine, 46*(10), 2189-2199.

Jefferson, A.L., Byerly, L.K., Vanderhill, S., Lambe, S., Wong, S., Ozonoff, A., Karlawish, J.H. (2008). Characterization of activities of daily living in individuals with mild cognitive impairment. *The American Journal of the Geriatrics Psychiatry,* 16, 375–383.

Jefferson, A. L., Paul, R. H., Ozonoff, A., & Cohen, R. a. (2006). Evaluating elements of executive functioning as predictors of instrumental activities of daily living (IADLs). *Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists*, *21*(4), 311–320.

Jekel, K., Damian, M., Wattmo, C., Hausner, L., Bullock, R., Connelly, P.J., Dubois, B… Frolich, L. (2015). Mild cognitive impairment and deficits in instrumental activities of daily living: a systematic review. *Alzheimer's Research & Therapy*, 7(1), 17.

Jessen, F., Amariglio, R. E., van Boxtel, M., Breteler, M., Ceccaldi, M., Chételat, G., … Wagner, M. (2014). Subjective Cognitive Decline Initiative (SCD-I) Working Group. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimer's & Dementia : The Journal of the Alzheimer's Association*, *10*(6), 844–852.

Johnson, W., Logie, R. H., & Brockmole, J. R. (2010). Working memory tasks differ in factor structure across age cohorts : Implications for dedifferentiation. *Intelligence*, *38*(5), 513–528.

Juottonen, K., Laakso, M.P., Insausti, B.M., Lehtovirta, M., Pitkänen, A., Partanen, D. & Soininen, H. (1998). Volumes of the Entorhinal and Perirhinal Cortices in Alzheimer's Disease. *Neurobiology of Aging, 19*(1), 15-22.

Juva, K., Makela, M., Erkinjuntti, T., Sulkava, R., Ylikoski, R., Valvanne, J., Tilvis, R. (1997). Functional assessment scales in detecting dementia. *Age & Ageing*, 26, 393–400.

Kang, G., Bronstein, J., Masterman, D., Redelings, M., Crum, J., & Ritz, B. (2005). Clinical characteristics in early Parkinson's disease in a central California population based study. *Movement Disorders, 20*(9), 1133-1142.

Karlsen, P. J., Allen, R. J., Baddeley, A. D., & Hitch, G. J. (2010). Binding across space and time in visual working memory. *Memory & Cognition, 38*(3), 292-303.

Karlsgodt, K. H., Sun, D., & Cannon, T. D. (2010). Structural and functional brain abnormalities in schizophrenia. *Current Directions in Psychological Science*, 19 (4), 226-231.

Katz, S., Ford, A. B., Moskowitz, R. W., Jackson, B. A., & Jaffe, M. W. (1963). Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *Journal of the American Medical Association*, 185, 914-919.

Kelly-Hayes, M. & Odell, P. (1992). Functional limitations and disability among elders in the Framingham study. *American Journal of Public Health, 82*, 841-845.

Kemp, B. J., & Mosqueda, L. A. (2005). Elder financial abuse: An evaluation framework and supporting evidence. *Journal of the American Geriatrics Society,* 53, 1123-1127.

Kempen, G. & Suurmeijer, T. (1990). The Development of a Hierarchical Polychotomous ADL-IADL Scale for Non institutionalized Elders. *Gerontologist*, 30, 497-502.

Kershaw, M. M., & Webber, L. S. (2008). Assessment of financial competence. *Psychiatry, Psychology and Law*, 15, 40-55.

Kessels, R. P. C., Hobbel, D., & Postma, A. (2007). Aging, context memory and binding: a comparison of "what, where and when" in young and older adults. *International Journal of Neuroscience, 117*(6), 795-810.

Killin, L., Abrahams, S., Parra, M. A., & Della Sala, S. (2018). The effect of age on the FCSRT-IR and temporary visual memory binding. *International Psychogeriatrics, 30*(3), 331-340.

Kim, K. R., Lee, K. S., Cheong, H. K., Eom, J. S., Oh, B. H., Hong, C. H. (2009). Characteristic profiles of instrumental activities of daily living in different subtypes of mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders*, *27*(3), 278–285.

Kluger, A., Ferris, S. H., Golomb, J., Mittelman, M. S., & Reisberg, B. (1999). Neuropsychological prediction of decline to dementia in nondemented elderly. *Journal of Geriatric Psychiatry and Neurology,* 12 (4), 168-179.

Koenig, O., Thomas-Anterion, C & Laurent, B (1999). Procedural learning in Parkinson's disease: Intact and impaired cognitive components, *Neuropsychologia,* 37, 1103-1109.

Koppara, A., Frommann, I., Polcher, A., Parra, M. A., Maier, W., Jessen, F., … Wagner, M. (2015). Feature Binding Deficits in Subjective Cognitive Decline and in Mild Cognitive Impairment. *Journal of Alzheimer's Disease*, *48*(S1), S161–S170.

Kovar M.G. & Lawton P. (1994). Functional disability: Activities and instrumental activities of daily living. *Annual Review of Geriatric Gerontology*, 14, 57–75.

Knopman, D., Boeve, B., & Petersen, R. (2003). Essentials of the proper diagnoses of mild cognitive impairment, dementia, and major subtypes of dementia. *Mayo Clinic Proceedings*, 78, 1290-1308.

Lafortune, G., & Balestat, G. (2007). Trends in Severe Disability Among Elderly People: Assessing the evidence in 12 OECD countries and the future implications. *OECD Health Working Papers,* (26), 0_1-7,9-79.

Lau, T. M., Gwin, J. T., & Ferris, D. P. (2012). How Many Electrodes Are Really Needed for EEG-Based Mobile Brain Imaging? *Journal of Behavioral and Brain Science*, 2, 387-393.

Lau, K. M., Parikh, M., Harvey, D. J., Huang, C.-J., Farias, S. T. (2015). Early Cognitively Based Functional Limitations Predict Loss of Independence in Instrumental Activities of Daily Living in Older Adults. *Journal of the International Neuropsychological Society*, *21*(09), 688–698.

Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: self- maintaining and instrumental activities of daily living. *Gerontologist,* 9, 179–186.

Lefleche, G., Albert, M.S. (1995). Executive function deficits in mild Alzheimer's disease. *Neuropsychology*, 9, 313–20.

Levy-Lahad, E., Wasco, W., Poorkaj, P., Romano, D. M., Oshima, J., Pettingell, W. H., … Tanzi, R. E. (1995). Candidate gene for the chromosome 1 familial Alzheimer's disease locus. *Science,* 269, 973-977.

Lezak, M., Howieson, D., & Loring, D. (2012). *Neuropsychological assessment* (fifth edit). OUP USA.

Lloyd-Jones, T. J. (2005). The role of color in the implicit memory performance of healthy older adults and individuals with Alzheimer's disease. *Neuropsychology,* 19(1), 44-53.

Liang, Y., Pertzov, Y., Nicholas, J. M., Henley, S. M., Crutch, S., Woodward, F., . . . Husain, M. (2016). Visual short-term memory binding deficit in familial Alzheimer's disease. *Cortex* , 78, 150–164.

Lindenberger, U., Mayr, U., & Kliegl, R. (1993). Speed and intelligence in old age. Psychology and Aging, 8, 207–220.

Litvan, I., Goldman, J.G., Tröster, A.I., Schmand, B.A., Weintraub, D., Petersen, R.C., Mollenhauer, B., Adler, C.H., Marder, K., Williams‐Gray, C.H., Aarsland, D.,

Kulisevsky, J., Rodriguez‐Oroz, M.C., Burn, D.J., Barker, R.A., Emre. M. (2012) Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Movement Disorders, 27, 349-356.

Loeb, P. (1996). Independent living scales. San Antonio: Psychological Corporation.

Loewenstein, D.A., Arguelles, S., Bravo, M., Freeman, R.Q., Arguelles, T., Acevedo, A., et al. (2001). Caregivers' judgments of the functional abilities of the Alzheimer's disease patient: a comparison of proxy reports and objective measures. *Journal of Gerontology*, 56B, 78–84.

Logie, R. H., Brockmole, J. R., & Vandenbroucke, A. R. (2009). Bound feature combinations in visual short-term memory are fragile but influence long-term learning. *Visual Cognition,* 17 (1-2), 160-179.

Logie, R., Cocchini, G., Sala, S., Baddeley, A., & Becker, James T. (2004). Is There a Specific Executive Capacity for Dual Task Coordination? Evidence From Alzheimer's Disease. *Neuropsychology, 18*(3), 504-513.

Logie, R. H. & Maylor, E. A. (2009). An Internet study of prospective memory across adulthood. *Psychology and Aging,* 24, 767−774

Logie, R. H., Parra, M. A., & Sala, S. Della. (2015). From Cognitive Science to Dementia Assessment. *Policy Insights from the Behavioral and Brain Sciences*, *2*(1), 81–91.

Lord, F. M. (1977). A study of item bias, using item characteristic curve theory. In Y. H. Poortinga (Ed.), Basic problems in cross-cultural psychology (pp. 19-29). Amsterdam: Swets and Zeitlinger.

Louie, G. H. & Ward, M. M. (2010). Association of measured physical performance and demographic and health characteristics with self-reported limitations. *Health & Quality of Life Outcomes*, 8, 1-13.

Lowndes, G., & Savage, G. (2007). Early detection of memory impairment in Alzheimer's disease: a neurocognitive perspective on assessment. *Neuropsychological Review*, 17, 193–202.

Luck, T., Luppa, M., Angermeyer, M. C., Villringer, a, König, H.-H., & Riedel-Heller, S. G. (2011). Impact of impairment in instrumental activities of daily living and mild cognitive impairment on time to incident dementia: results of the Leipzig Longitudinal Study of the Aged. *Psychological Medicine*, *41*(5), 1087–1097.

Luck, S. J. & Vogel, E. K. (1997). The capacity of visual working memory for features and conjunctions. *Nature,* 390 (6657), 279-281.

Lusardi, A., & Mitchell, O. (2005). Implications for Retirement Wellbeing. *Michigan Retirement Research Center*, *Working Pa* (November 2016).

MacPherson, S. E., Parra, M. A., Moreno, S., Lopera, F., & Della Sala, S. (2012). Dual task abilities as a possible preclinical marker of Alzheimer's disease in carriers of the E280A presenilin-1 mutation. *Journal of the International Neuropsychological Society,* 2 (18), 234-241.

Malinowsky, C., Almkvist, O., Kottorp, A. and Nygard, L. (2010). Ability to manage everyday technology: a comparison of persons with dementia or mild cognitive impairment and older adults without cognitive impairment. *Disability and Rehabilitation Assistive Technology*, 5, 462–469.

Mandell, A. M., & Green, R. C. (2011). Alzheimer's disease. In Andrew E. Budson and Neil W.Kowalll (Ed.), *The handbook of Alzheimer's disease and other dementias* (first, pp. 1–90).

Manly, J.J., Bell-McGinty, S., Tang, M.-X., Schupf, N., Stern, Y., Mayeux, R. (2005) Implementing diagnostic criteria and estimating frequency of mild cognitive impairment in an urban community. *Archives of Neurology,* 62, 1739-1746.

Marcos, G., Santabárbara, J., Lopez-Anton, R., De-la-Cámara, C., Gracia-García, P., Lobo, E., … Lobo, A. (2016). Conversion to dementia in mild cognitive impairment diagnosed with DSM-5 criteria and with Petersen's criteria. *Acta Psychiatrica Scandinavica*, *133*(5), 378–385.

Maris, E., & Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *Journal of Neuroscince Methods, 164*(1), 177-190.

Marshall, G. A., Zoller, A. S., Kelly, K. E., Amariglio, R. E., Locascio, J. J., Johnson, K. A., … For The Alzheimer's Disease Neuroimaging Initiative. (2014). Everyday cognition scale items that best discriminate between and predict progression from clinically normal to mild cognitive impairment. *Current Alzheimer Research*, *11*(9), 853–861.

Mariani, E., Monastero, R., Ercolani, S., Rinaldi, P., Mangialasche, F., Costanzi, E., Vitale, D.F., Senin, U., Mecocci, P. (2008). Influence of comorbidity and cognitive status on instrumental activities of daily living in amnestic mild cognitive impairment: Results from the ReGAl project. *International Journal of Geriatric Psychiatry*, 23, 523–530.

Marson, D.C., Sawrie, S.M., Snyder, S., McInturff, B., Stalvey, T., Boothe, A., Chatterjee, A., Harrell, L. E. (2000). Assessing financial capacity in patients with Alzheimer's disease. A conceptual model and prototype Instrument. *Archive of Neurology*, *57, 877-884*.

Marson, D. C., Martin, R. C., Wadley, V., Randall, H., Snyder, S., … Harrell, L. E. (2009). Clinical Interview Assessment of Financial Capacity in Older Adults with Mild

Cognitive Impairment and Alzheimer's disease. *Journal of American Geriatric Society*, *57*(5), 806–814.

Marson, D.C., Sawrie, S.M., Snyder, S., McInturff, B., Stalvey, T., Boothe, A., Aldridge, T., Chatterjee, A., Harrell, L. (2000). Assessing financial capacity in patients with Alzheimer's disease. A conceptual model and prototype Instrument.

Martin, R., Griffith, H. R., Belue, K., Harrell, L., Zamrini, E., Anderson, B., … Marson, D. (2008). Declining financial capacity in patients with mild Alzheimer disease: a one-year longitudinal study. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry*, *16*(3), 209–219.

Martyr, A. & Clare, L. (2012). Executive function and activities of daily living in Alzheimer's disease: a correlational meta-analysis. *Dementia and Geriatric Cognitive Disorders*, 33, 189–203.

Mayes, A., Holdstock, J. S., Isaac, C. L., Montaldi, D., Grigor, J., Gummer, A., et al. (2004). Associative recognition in a patient with selective hippocampal lesions and relatively normal item recognition. *Hippocampus,* 14, 763–784.

Mayeux R & Stern Y (2012). Epidemiology of Alzheimer disease. Cold Spring Harb Perspect Med, 2.

Meguro, K., Shimada, M., Yamaguchi, S., Ishiizaki, J, Yamadori, A., & Sekita, Y. (2001). Five-year interval changes of cognitive screening tests performances in the elderly: a community-based study. *Journal of Gerontology: Psychological Science,* 56, 314-318.

Mcdonald, R. J., & White, N. M. (2013). A triple dissociation of memory systems: Hippocampus, amygdala, and dorsal striatum. *Behavioral Neuroscience,* 107 (1), 3-22.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group* under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology,* 34, 939-944.

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Kawas, C. H., … Phelps, C. H. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia,* 7(3), 263-269.

Mesulam, M., 2000. Attentional Networks, Confusional States and Neglect Syndromes. In Mesulam, M., Ed. Principles of Behavioral and Cognitive Neurology. Oxford University Press, New York, pp 174–239.

Mihajlovic, V., Grundlehner, B., Vullers, R., & Penders, J. (2015). Wearable, wireless EEG solutions in daily life applications: What are we missing? *IEEE Journal of Biomedical and Health Informatics*, *19*(1), 6–21.

Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., & Hodges, J. (2006). The Addenbrooke's Cognitive Examination Revised (ACE‐R): A brief cognitive test battery for dementia screening. *International Journal of Geriatric Psychiatry, 21*(11), 1078-1085.

Missonnier, P., Gold, G., Leonards, U., Costa-Fazio, L., Michel, J. P., Ibáñez, V., & Giannakopoulos, P. (2004). Aging and working memory: Early deficits in EEG activation of posterior cortical areas. *Journal of Neural Transmission*, *111*(9), 1141–1154.

Mitchell, K. J., Johnson, M. K., Raye, C. L., & D'Esposito, M. (2000). fMRI evidence of age-related hippocampal dysfunction in feature binding in work- ing memory. *Cognitive Brain Research*, 10, 197–206.

Moore, D. J., Palmer, B. W., Patterson, T. L., & Jeste, D. V. (2007). A review of performance-based measures of functional living skills. *Journal of Psychiatric Research*, *41*(1–2), 97–118.

Morcom, A. M. & Henson, R. N. A. (2018). Increased prefrontal activity with aging reflects nonspecific neural responses rather than compensation. *The Journal of Neuroscience*, *38*(33), 1701–17.

Morris, J. C. (2012). Revised criteria for mild cognitive impairment may compromise the diagnosis of Alzheimer disease dementia. *Archives of Neurology*, *69*(6), 700–708.

Moses, S. N. & Ryan, J. D. (2006). A comparison and evaluation of the predictions of relational and conjunctive accounts of hippocampal function. *Hippocampus,* 16 (1), 43-65.

Moscovitch, M. (1992). Memory and working-with-memory: A component process model based on modules and central systems. *Journal of Cognitive Neuroscience*, 4 (3), 257–267.

Moustafa, A.A., Sherman, S.J., & Frank, M.J. (2008). A dopaminergic basis for working memory, learning, and attentional shifting in Parkinson's disease. *Neuropsychologia*, 46, 3144-3156.

Mungas, D. & Reed, B. R. (2000). Application of item response theory for development of a global functioning measure of dementia with linear measurement properties. Statistics in Medicine, 19(11-12), 1631-1644.

Muñoz-Neira, C., López, O. L., Riveros, R., Núñez-Huasaf, J., Flores, P., & Slachevsky, A. (2012). The technology - activities of daily living questionnaire: a version with a

technology-related subscale. *Dementia and Geriatric Cognitive Disorders*, *33*(6), 361–371.

Naccache, L., Gaillard, R., Adam, C., Hasboun, D., Clemenceau, S., Baulac, M., . . . Cohen, L. (2005). A direct intracranial record of emotions evoked by subliminal words. *Procedeengs of the National Academy of Science of the USA, 102*(21), 7713-7717.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., … Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695-699.

Naveh-Benjamin, M. (2000). Adult age differences in memory performance: Tests of an associative deficit hypothesis. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 26 (5), 1170–1187.

Nichols, T. E., & Holmes, A. P. (2002). Nonparametric permutation tests for functional neuroimaging: a primer with examples. *Human Brain Mapping, 15*(1), 1-25.

Nieuwenhuis-Mark, R. E. (2010). The death knoll for the MMSE: Has it outlived its purpose? *Journal of Geriatric Psychiatry and Neurology, 23 (3), 151-157.*

Njegovan, V., Hing, M. M., Mitchell, S. L., & Molnar, F. J. (2001). The hierarchy of functional loss associated with cognitive decline in older persons. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *56*(10), 638–643.

Nyberg L., Lovden M., Riklund K., Lindenberger U., Backman L. (2012) Memory aging and brain maintenance. *Trends in Cognitive Science*, 16, 292–305.

Nygård, L. (2003). Instrumental activities of daily living: a stepping-stone towards Alzheimer's disease diagnosis in subjects with mild cognitive impairment? *Acta Neurologica Scandinavica*, *179*, 42–46.

Ng, T.-P., Niti, M., Chiam, P.-C., & Kua, E.-H. (2006). Physical and cognitive domains of the Instrumental Activities of Daily Living: validation in a multiethnic population of Asian older adults. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *61*(7), 726–735.

Okonkwo, O. C., Wadley, V. G., Griffith, H. R., Ball, K., Marson, D. C. (2006). Cognitive correlates of financial abilities in mild cognitive impairment. *Journal of the American Geriatrics Society*, 54(11), 1745–50.

Okonkwo, O. C., Griffith, H. R., Vance, D. E., Marson, D. C., Ball, K. K., & Wadley, V. G. (2009). Awareness of functional difficulties in mild cognitive impairment: A multidomain assessment approach. *Journal of the American Geriatrics Society*, *57*(6), 978–984.

Olsen, R. K., Moses, S. N., Riggs, L., & Ryan, J. D. (2012). The hippocampus supports multiple cognitive processes through relational binding and comparison. *Frontiers in Human Neuroscience,* 6 (146).

Orlando, M., & Thissen, D. (2000). Likelihood-based item-fit indices for dichotomous item response theory models. *Applied Psychological Measurement, 24 (1), 50-64*.

Owen, A. M., Milner, B., Petrides, M., & Evans, A. C. (1996). Memory for object features versus memory for object location: a positron-emission tomography study of encoding and retrieval processes. *Proceedings of the National Academy of Sciences, 3 (Suppl 3), S552*.

Partchev, I. (2016). *irtoys: A Collection of Functions Related to Item Response Theory (IRT)*. R package version 0.2.0.

Parra, M. A., Abrahams, S., Logie, R. H., & Della Sala, S. (2009). Age and binding within-dimension features in visual short-term memory. *Neuroscience Letters*, 449,1–5.

Parra, M. A., Abrahams, S., Logie, R. H., & Della Sala, S. (2010). Visual short-term memory binding in Alzheimer's disease and depression. *Journal of Neurology, 257*(7), 1160-1169.

Parra, M. a, Sala, S. Della, Abrahams, S., Logie, R. H., Méndez, L. G., & Lopera, F. (2011). Specific deficit of colour-colour short-term memory binding in sporadic and familial Alzheimer's disease. *Neuropsychologia*, *49*(7), 1943–1952.

Parra, M. A., Ascencio, L. L., Urquina, H. F., Manes, F., & Ibáñez, A. M. (2012). P300 and neuropsychological assessment in mild cognitive impairment and alzheimer dementia. *Frontiers in Neurology*, *3 DEC*(December), 1–10.

Parra, M. A., Della Sala, S., Logie, R. H., & Morcom, A. M. (2014). Neural correlates of shape-color binding in visual working memory. *Neuropsychologia, 52*(0), 27-36.

Parra, M. A., Fabi, K., Luzzi, S., Cubelli, R., Hernandez Valdez, M., & Della Sala, S. (2015). Relational and conjunctive binding functions dissociate in short-term memory. *Neurocase,* 21 (1), 56–66.

Parra, M. A., Fernandez-Guinea, S., Sanchez, L., Suarez, B., Frank, A., Olazaran, J., & Della Sala, S. (2016). *When is short-term memory binding selectively impaired in Mild Cognitive Impairment?* Paper presented at the Alzheimer's & Dementia: The Journal of the Alzheimer's Association.

Parra, M. A., Mikulan, E., Trujillo, N., Sala, S. D., Lopera, F., Manes, F., . . . Ibanez, A. (2017). Brain information sharing during visual short-term memory binding yields a memory biomarker for familial Alzheimer's disease. *Current Alzheimer Research, 1-46*.

Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging, 17(2), 299-320.*

Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: Aging and neurocognitive scaffolding. *Annual Review of Psychology*, 60, 173–196.

Pedrosa, H., De Sa, A., Guerreiro, M., Maroco, J., Simoes, M. R., Galasko, D., de Mendonca, a. (2010). Functional evaluation distinguishes MCI patients from healthy elderly people--the ADCS/MCI/ADL scale. *The Journal of Nutrition, Health & Aging*, *14*(8), 703–709.

Peich, M.-C., Husain, M., & Bays, P. M. (2013). Age-related decline of precision and binding in visual working memory. *Psychology and Aging,* 28 (3), 729–743.

Pérès, K., Chrysostome, V., Fabrigoule, C., Orgogozo, J. M., Dartigues, J. F., Barberger-Gateau, P. (2006). Restriction in complex activities of daily living in MCI: impact on outcome. *Neurology*, *67*(3), 461–6.

Pérès, K., Helmer, C., Amiela, H., Orgogozo, J.-M., Rouch, I., Dartigues, J.-F., Barberger-Gateau, P. (2008). Natural history of decline in instrumental activities of daily living performance over the 10 years preceding the clinical diagnosis of dementia: A prospective population- based study. *Journal of the American Geriatric Society*, 56, 37–44

Pereira, F. S., Yassuda, M. S., Oliveira, a M., & Forlenza, O. V. (2008). Executive dysfunction correlates with impaired functional status in older adults with varying degrees of cognitive impairment. *International Psychogeriatrics / IPA*, *20*(6), 1104–1115.

Pereira, F.S., Yassuda, M.S., Oliveira, A.M., Diniz, B., Radanovic, M., Forlenza, O. (2010) Profiles of functional deficits in mild cognitive impairment and dementia: benefits from objective measurement. Journal of the International Neuropsychological Society, 16, 297-305.

Perneczky, R., Pohl, C., Sorg, C., Hartmann, J., Komossa, K., Alexopoulos, P., … Kurz, A. (2006). Complex activities of daily living in mild cognitive impairment: Conceptual and diagnostic issues. *Age and Ageing*, 35(3), 240–245

Persson, J., Nyberg, L., Lind, J., Larsson, A., Nilsson, L. G., Ingvar, M., & Buckner, R. L. (2006). Structure–function correlates of cognitive decline in aging. *Cerebral Cortex*, 16(7), 907-915.

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

Petersen, R. C., Caracciolo, B., Brayne, C., Gauthier, S., Jelic, V., & Fratiglioni, L. (2014). Mild cognitive impairment: A concept in evolution. *Journal of Internal Medicine, 275 (3), 214-228*.

Peterson, D. J., & Naveh-Benjamin, M. (2016). The role of aging in intra-item and item-context binding processes in visual working memory. *Journal of Experimental Psychology: Learning, Memory, and Cognitio*n, on-line ahead of print, 42 (11), 1713-1730.

Petersen, R.C., Smith, G. E., Ivnik, R.J., Tangalos, E.G., Schaid, D.J., Thibodeau, S.N., Kokmen, E., Waring, S.C., Kurland, L.T. (1995). Apolipoprotein E status as a predictor of the development of Alzheimer's disease in memory-impaired individuals. *JAMA, The Journal of the American Medical Association, 273*(16), 1274-1278.

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

Pietto, M., Parra, M. A., Trujillo, N., Flores, F., Garcia, A. M., Bustin, J., . . . Baez, S. (2016). Behavioral and Electrophysiological Correlates of Memory Binding Deficits in Patients at Different Risk Levels for Alzheimer's Disease. *Journal of Alzheimer's Disease, 53*(4), 1325-1340.

Pfennig, A., Littmann. E., & Bauer, M. (2007). Neurocognitive impairment and dementia in mood disorders. *Journal of Neuropsychiatry and Clinical Neuroscience*, 19, 373–382.

Purser, J. L., Fillenbaum, G. G., Pieper, C. F., & Wallace, R. B. (2005). Mild cognitive impairment and 10-year trajectories of disability in the Iowa established populations for epidemiologic studies of the elderly cohort. *Journal of the American Geriatrics Society,* 53 (11), 1966-1972.

Rajah, M. N., & D'Esposito, M. (2005). Region-specific changes in prefrontal function with age: A review of PET and fMRI studies on working and episodic memory. *Brain*, 128, 1964–1983.

Pujades-Rodriguez M, Assi V, Gonzalez-Izquierdo A, Wilkinson T, Schnier C, Sudlow C, et al. (2018) The diagnosis, burden and prognosis of dementia: A record-linkage cohort study in England. PLoS ONE 13(6): e0199026.

Ramsden, C.M., Kinsella, G.J., Ong, B., & Storey, E. (2008). Performance of everyday actions in mild Alzheimer's disease. *Neuropsychology,* 22(1), 17-26.

Read, C. A., Rogers, J. M., & Wilson, P. H. (2016). Working memory binding of visual object features in older adults. Aging, Neuropsychology, and Cognition, 23 (3), 263–281.

Reckase (2009) *Multidimentional item response theory*, Dordrecht, New York, Springer

Reiboldt, W., & Vogel, R. E. (2003). A critical analysis of telemarketing fraud in a gated senior community. *Journal of Elder Abuse & Neglec*t, 13(4), 21–38.

Reitan, R.M. (1992). Trail making test: Manual for administration and scoring. Reitan Neuropsychology Laboratory, Tucson, AZ.

Rentz, D.M., Amariglio, R.E., Becker, J.A., Frey, M., Olson, L.E., …Sperling, R.A. (2011). Face-name associative memory performance is related to amyloid burden in normal elderly. *Neuropsychologia*, 49, 2776-2783.

Rentz, D., Parra, M. A., Amariglio, R., Stern, Y., Sperling, R., & Ferris, S. (2013). Promising developments in neuropsychological approaches for the detection of preclinical Alzheimer's disease: a selective review. *Alzheimer's Research & Therapy, 5*(6), 58.

Reppermund, S., Sachdev, P. S., Crawford, J., Kochan, N. a, Slavin, M. J., Kang, K., … Brodaty, H. (2011). The relationship of neuropsychological function to instrumental activities of daily living in mild cognitive impairment. *International Journal of Geriatric Psychiatry*, *26*(8), 843–852.

Reuter-Lorenz, P.A, Stanczak, l. & Miller, A. (1999). Neural recruitment and cognitive aging: Two hemispheres are better than one especially as you age. *Psychological Science,* 10, 494-500.

Revelle, W. (2017) psych: Procedures for Personality and Psychological Research, Northwestern University, Evanston, Illinois, USA.

Rhodes, S., Parra, M. A., Cowan, N., & Logie, R. H. (2017). Healthy Aging and Visual Working Memory: The Effect of Mixing Feature and Conjunction Changes. *Psychology and Aging, 32 (4), 354-366*.

Rhodes, S., Parra, M. A., & Logie, R. H. (2016). Ageing and feature binding in visual working memory: The role of presentation time. *Quarterly Journal of Experimental Psychology, 69 (4), 654-668*.

Robin, X., Turck, N., Hainard, A., Tiberti, N., Lisacek, F., Sanchez J-C. & Müller, M. (2011). pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC *Bioinformatics, 12*, p. 77.

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

Rosenberg, L., Kottorp, A., Winblad, B., &Nygård, L. (2009). Perceived difficulty in everyday technology use among older adults with or without cognitive deficits. *Scandinavian Journal of Occupational Therapy*, *16*(4), 216–226.

Reuter-Lorenz, P.A., Stanczak, L., Miller, A. (1999). Neural recruitment and cognitive aging: two hemispheres are better than one especially as you age. Psychol. Sci. 10:494–500

Saliasi, E., Geerligs, L., Lorist, M. M., & Maurits, N. M. (2013). The Relationship between P3 Amplitude and Working Memory Performance Differs in Young and Older Adults. *PLoS ONE*, *8*(5).

Salmon, D. P., & Bondi, M. W. (2009). Neuropsychological Assessment of Dementia. *Annual Review of Psychology*, *60*(1), 257–282.

Salthouse, T. A. (2010a). *Major Issues in Cognitive Aging* (M. D'Esposito, J. Driver, T. Robbins, D. Schacter, A. Treisman, & L. Weiskrantz Eds. Vol. 49). New York: Oxford University Press.

Salthouse, T. A. (2010b). Relations between Age and Cognitive Functioning. New York: Oxford University Press. (Reprinted from: Not in File).

Sarazin, M., Chauvire, V., Gerardin, E., Colliot, O., Kinkingnehun, S., de Souza, L. C., . . . Dubois, B. (2010). The amnestic syndrome of hippocampal type in Alzheimer's disease: an MRI study. *Journal of Alzheimer's Disease,* 22 (1), 285-294.

Sarter, M., Givens, B., & Bruno, J. P.Schmitter-Edgecombe, M., Parsey, C., & Cook, D. J. (2011). Cognitive correlates of functional performance in older adults: comparison of self-report, direct observation, and performance-based measures. *Journal of the International Neuropsychological Society : JINS*, *17*(5), 853–864.

Saxton, J., Snitz, B.E., Lopez, O.L., Ives, D.G., Dunn, L.O., Fitzpatrick, A., Carlson, M.C., DeKosky, S.T. (2009). GEM Study Investigators. Functional and cognitive criteria produce different rates of mild cognitive impairment and conversion to dementia. *Journal of Neurology, Neurosurgery and Psychiatry*, 80(7), 737-743.

Schmitter-Edgecombe, M., McAlister, C., & Weakley, A. (2012). Naturalistic assessment of everyday functioning in individuals with mild cognitive impairment: the day-out task. *Neuropsychology*, *26*(5), 631–41.

Schmitter-Edgecombe, M., Parsey, C., & Cook, D.J. (2011). Cognitive correlates of functional performance in older adults: comparison of self-report, direct observation, and performance-based measures. *Journal of International Neuropsychological Society,* 17, 853–864.

Schmitter-Edgecombe, M., & Parsey, C. M. (2014). Cognitive correlates of functional abilities in individuals with mild cognitive impairment: comparison of questionnaire, direct observation, and performance-based measures. *The Clinical Neuropsychologist*, *28*(5), 726–746.

Schneider-Garces, N. J., Gordon, B. A., Brumback- Peltz, C. R., Shin, E., Lee, Y., Sutton, B. P., … Fabiani, M. (2010). Span, CRUNCH, and beyond: Working memory capacity and the aging brain. *Journal of Cognitive Neuroscience*, 22, 655–669

Sellen, A., & Harper, R. (2002). *The myth of the paperless office*. Cambridge, Mass; London: MIT Press.

Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. *Clinical Gerontologist, 5*, 165-173.

Sherrington, R., Rogaev, E. I., Liang, Y., Rogaeva, E. A., Levesque, G., Ikeda, M., … St George-Hyslop, P. H. (1995). Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease. *Nature,* 375 (6534), 754-760.

Sherod, M. G., Griffith, H. R., Copeland, J., Belue, K., Krzywanski, S., Zamrini, E. Y. et al. (2009). Neurocognitive predictors of financial capacity across the dementia spectrum: Normal aging, mild cognitive impairment, and Alzheimer's disease. *Journal of the International Neuropsychological Society: JINS*, 15, 258–267.

Sikkes, S. a M., de Lange-de Klerk, E. S. M., Pijnenburg, Y.L., Scheltens, P., Uitdehaag, B. M. J. (2009). A systematic review of Instrumental Activities of Daily Living scales in dementia: room for improvement. *Journal of Neurology, Neurosurgery, and Psychiatry*, *80*(1), 7–12.

Sikkes, S. A. M., Visser, P. J., Knol, D. L., De Lange-De Klerk, E. S. M., Tsolaki, M., Frisoni, G. B., … Uitdehaag, B. M. J. (2011). Do instrumental activities of daily living predict dementia at 1- and 2-year follow-up? Findings from the development of screening guidelines and diagnostic criteria for predementia Alzheimer's disease study. *Journal of the American Geriatrics Society, 59 (12), 2273-3381*.

Silberfeld, M., Corber, W., & Checkland, D. (1995). Acknowledgement of limitations and understanding of their consequences in mental capacity assessments. *Behavioral Sciences and the Law*, 13, 381–390.

Slocum-Gori, S. & Bruno, Z. (2011). Assessing the unidimensionality of psychological sclaes: using multiple criteria from factor analysis. *Social Indicators Research,* 102, 443-461.

Small, J.A., Geldart, K., & Gutman, G. (2000). Communication between individuals with Alzheimer's disease and their caregivers during activities of daily living. *American Journal of Alzheimer's disease*, 15 (5), 291-302.

Smith, R. (2000). Fraud and financial abuse of older persons. *Current Issues in Criminal Justice*, *11*(3), 273–291.

Smith, K., Ricaud, B., Shahid, N., Rhodes, S., Starr, J. M., Ibáñez, A., . . . Vandergheynst, P. (2017). Locating Temporal Functional Dynamics of Visual Short-Term Memory Binding using Graph Modular Dirichlet Energy. *Scientific Reports, 7, 42013*.

Spector, W.D. & Fleishman, J.A. (1998). Combining activities of daily living with instrumental activities of daily living to measure functional disability. *Journal of Gerontology: Social Science,* 53 (Suppl 1), S46-S57.

Sperling, R. A., Aisen, P. S., Beckett, L. A., Bennett, D. A., Craft, S., Fagan, A. M., … Phelps, C. H. (2011). Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia*, *7*(3), 280–292.

Sperling, R. A., Bates, J. F., & Chua, E. F. (2003). fMRI studies of associative encoding in young and elderly controls and mild Alzheimer's disease *Journal of Neurology*, *74*, 44–50.

Sperling, R., & Johnson, K. (2013). Biomarkers of alzheimer disease: Current and future applications to diagnostic criteria. *CONTINUUM Lifelong Learning in Neurology*, *19*(2), 325–338.

Staresina, B. P., & Davachi, L. (2010). Object unitization and associative memory formation are supported by distinct brain regions. *The Journal of Neuroscience*, 30 (29), 9890-9897.

Stebnicki, M. A. (1997). A conceptual framework for utilizing a functional assessment approach for determining mental capacity: A new look at informed consent in rehabilitation. *Journal of Rehabilitation*, *63*(4), 32–37.

Steiger, J.H. & Lind, J.C. (1980). *Statistically based tests for the number of factors. Paper presented athte annual spring meeting of the Psychometric Society*, Iowa City, IA.

Steinberg, L., & Thissen, D. (2006). Using effect sizes for research reporting: Examples using item response theory to analyze differential item functioning. *Psychological Methods*, *11*(4), 402–415.

Stephan, B. C. M., Hunter, S., Harris, D., Llewellyn, D. J., Siervo, M., Matthews, F. E., & Brayne, C. (2012). The neuropathological profile of mild cognitive impairment (MCI): a systematic review. *Molecular Psychiatry*, *17*(11), 1056–76.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society*,8(03), 448-460.

Stopford, C.L., Snowden, J.S., Thompson, J.C., & Neary, D. (2008) Variability in cognitive presentation of Alzheimer's disease. *Cortex*, 44(2), 185e195.

Stopford, C.L., Thompson, J.C., Neary, D., Richardson, A.M.T., Snowden, J.S. (2012). Working memory, attention and executive function in Alzheimer's disease and frontotemporal dementia. *Cortex*, 48, 429–446.

Suchy, Y., Kraybill, M. L., & Franchow, E. (2011). Instrumental activities of daily living among community-dwelling older adults: discrepancies between self-report and performance are mediated by cognitive reserve. *Journal of Clinical and Experimental Neuropsychology*, *33*(1), 92–100.

Suh, G., Ju, Y., Yeon, B. K., & Shah, A. (2004). A longitudinal study of Alzheimer ' s disease : rates of cognitive and functional decline. *International Journal of Geriatric Psychiatry*, (19), 817–824.

Swainson, R., Hodges, J. R., Galton, C. J., Semple, J., Michael, A., Dunn, B. D.,Iddon, J. L. et al. (2001). Early detection and differential diagnosis of Alzheimer's disease and depression with neuropsychological tasks. *Dementia and Geriatric Cognitive Disorders*, 12, 265-280.

Tabert, M. H., Albert, S. M., Borukhova-Milov, L., Camacho, Y., Pelton, G., Liu, X., … Devanand, D. P. (2002). Functional deficits in patients with mild cognitive impairment: Prediction of AD. *Neurology*, *58*(5), 758–764. http://doi.org/10.1212/WNL.58.5.758

Tapiola T, Alafuzoff I, Herukka SK, et al. (2009). Cerebrospinal fluid {beta}-amyloid 42 and tau proteins as biomarkers of Alzheimer-type pathologic changes in the brain. *Archive of Neurology*, 66, 382-389.

Tam, C. W. C., Lam, L. C. W., Lui, V. W. C., Chan, W. C., Chan, S. S. M., Chiu, H. F. K., & Chan, W. M. (2008). Clinical correlates of functional performance in community-dwelling Chinese older persons. *International Psychogeriatric*, 1059–1070.

Teng, E., Becker, B. W., & Cummings, J. L. (2010). Subtle Deficits in Instrumental Activities of Daily Living in Subtypes, *Dementia and Geriatric Cognitive Disorders*, 30, 189–197.

Tilse, C., Setterlund, D., Wilson, J., & Rosenman, L. (2005). Minding the money: A growing responsibility for informal carers. *Ageing and Society, 215-227*.

Tippett, L.J., Blackwood, K., Farah, M.J. (2003) Visual object and face processing in mild-to-moderate Alzheimer's disease: from segmentation to imagination. *Neuropsychologia,* 41, 453–68.

Treisman, A. (1996). The binding problem. *Current Opinion in Neurobiology*, 6 (2), 171–178.

Treisman, A. (2006). Object tokens, binding, and visual memory. In H. D. Zimmer, A. Mecklinger, & U. Lindenberger (Eds.), Handbook of binding and memory: perspectives from cognitive neuroscience (pp. 315–338). New York, NY: Oxford University Press.

Thomas, V.C., Rockwood, K., McDowell, I. (1998). Multidimensionality in instrumental and basic activities of daily living. *Journal of Clinical Epidemiology*, 51(4), 315–21.

Tucker, L.R. & Lewis, C. (1973). A reliability coefficient for maximum likelihood factor analysis. *Psychometrika, 38*, 1-10.

Tueth, M. J. (2000). Exposing financial exploitation of impaired elderly persons. *American Journal of Geriatric Psychiatry, 8 (2), 104-111*.

Tuokko, H., Morris, C., & Ebert, P. (2005). Mild cognitive impairment and everyday functioning in older adults. *Neurocase,* 11, 40–47.

van Geldorp, B., Parra, M. A., & Kessels, R. P. (2014). Cognitive and neuropsychological underpinnings of relational and conjunctive working memory binding across age. *Memory*, 1-11.

van Geldorp, B., Heringa, S. M., van den Berg, E., Olde Rikkert,M.G., Biessels,G.J.and Kessels,R.P. (2015). Working memory binding and episodic memory formation in aging, mild cognitive impairment, and Alzheimer's dementia. *Journal of Clinical and Experimental Neuropsychology*, 37, 538–548.

Van Wielingen, L. E., Tuokko, H. a, Cramer, K., Mateer, C. a, &Hultsch, D. F. (2004). Awareness of financial skills in dementia. *Aging & Mental Health*, *8*(4), 374–380.

Velicer, W.F. (1976). Determining the number of components from the matrix of partial correlations. *Psychometrika,* 41, 321-327.

Vermeij, A., van Beek, A. H. E. A., Olde Rikkert, M. G. M., Claassen, J. A. H. R., & Kessels, R. P. C. (2012). Effects of aging on cerebral oxygenation during working-memory performance: A functional near-infrared spectroscopy study. PLoS ONE, 7, e46210.

Wadley, V.G., Harrell, L.E., Marson, D.C. (2003). Self- and informant report of financial abilities in patients with Alzheimer's disease: Reliable and valid? *Journal of the American Geriatric Society,* 51, 1621-1626.

Washington testimony (April 27, 2016). Retrieved November 18, 2018, from https://pennmemorycenter.org/in-washington-testimony-karlawish-calls-for-federal-whealthcare-action/.

Wadley, V. G., Okonkwo, O., Crowe, M., & Ross-Meadows, L. a. (2008). Mild Cognitive Impairment and Everyday Function: Evidence of Reduced Speed in Performing

Instrumental Activities of Daily Living. *The American Journal of Geriatric Psychiatry*, *16*(5), 416–424.

Wadley VG, Okonkwo O, Crowe M, et al. (2009) Mild cognitive impairment and everyday function: An investigation of driving performance. *Journal of Geriatric Psychiatry and Neurology,* 22(2), 87–94.

Watson, H. C., & Lee, A. C. (2013). The perirhinal cortex and recognition memory interference. *The Journal of Neuroscience*, 33 (9), 4192-4200.

Webber, L. S., Reeve, R. a., Kershaw, M. M., & Charlton, J. L. (2002). Assessing Financial Competence. *Psychiatry, Psychology and Law*, *9*, 248–256.

Wechsler, D. (2011). *The Test of Premorbid Functioning (TOPF*). San Antonio TX: The Psychological Corporation.

Weinberger, M., Samsa, G.P., Schmader, K., Greenberg, S.M., Carr, D.B. & Wildman, D.S. (1992). Comparing proxy and patients' perceptions of patients' functional status: results from an outpatient geriatric clinic. *Journal of the American Geriatrics Society*, 40, 585–588.

Weintraub, D., & Burn, D. (2011). Parkinson's disease: The quintessential neuropsychiatric disorder. *Movement Disorders, 26*(6), 1022-1031.

Weintraub, D., Dietz, N., Duda, J., Wolk, D., Doshi, J., Xie, S., . . . Siderowf, A. (2012). Alzheimer's disease pattern of brain atrophy predicts cognitive decline in Parkinson's disease. *Brain, 135*(1), 170-180.

Wheeler, M. E., & Treisman, A. M. (2002). Binding in short-term visual memory. *Journal of Experimental Psychology: General*, 131 (1), 48–64.

Whittington, C. J., Podd, J., & Kan, M. M. (2000). Recognition memory impairment in Parkinson's disease: Power and meta-analyses. *Neuropsychology*, *14*(2), 233–246.

Wicklund, A. H., Johnson, N., Rademaker, A., Weitner, B. B., & Weintraub, S. (2007). Profiles of decline in activities of daily living in non-Alzheimer dementia. *Alzheimer Disease and Associated Disorders*, 21(1), 8–13.

Willis, S.L. (1996). Everyday cognitive competence in elderly persons: conceptual issues and empirical findings. *Gerontologist,* 36, 595–601.

Wilms HU, Riedel-Heller SG, Angermeyer MC (2007). Limitations in activities of daily living and instrumental activities of daily living capacity in a representative sample: disentangling dementia- and mobility-related effects. *Comprehensive Psychiatry,* 48, 95–101.

Wilson R.S., Bennet D.A., Bienias J.L., Aggarwal N.T., Mendes de Leon C.F., Morris M.C., Evans D.A. (2002). Cognitive activity and incident AD in a population-based sample of older persons. *Neurology*, *59*(12), 1910–1914.

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., Fratiglioni, L., Wahlund, L.-O., … 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*(3), 240–246.

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., Fratiglioni, L., Wahlund, L.-O., et al. (2004). Mild cognitive impairment-beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *Journal of Internal Medicine*, 256(3), 240–246.

Wirth, M., Villeneuve, S., Haase, C.M., Madison, C.M., Oh, H., Landau, S.M., Jagust, W.J. (2013). Associations between Alzheimer disease biomarkers, neurodegeneration, and cognition in cognitively normal older people. JAMA Neurology, 70, 1512–1509.

Wolk, D. A., Mancuso, L., Kliot, D., Arnold, S. E., & Dickerson, B. C. (2013). Familiarity-based memory as an early cognitive marker of preclinical and prodromal AD. *Neuropsychologia,* 51, 1094-1102.

World Health Organization (2001). International Classification of Functioning, Disability and Health (ICF). Geneva.

Wright, S.L. & Persad, C. (2007). Distinguishing between depression and dementia in older persons: neuropsychological and neuropathological correlates. *Journal of Geriatric Psychiatry and Neurology*, 20,189–198.

Yeh, Y., Lin, K., Chen, W., & Lin, C. (2011). Functional Disability Profiles in Amnestic. *Dementia and Geriatric Cognitive Disorders*, *31*, 225–232.

Yonelinas, A. P., Hopfinger, J. B., Buonocore, M. H., Kroll, N. E. A., & Baynes, K. (2001). Hippocampal, parahippocampal and occipital-temporal contributions to associative and item recognition memory: An fMRI study. *NeuroReport, 12 (2), 359-363*.

Zanetti, O., Geroldi, C., Frisoni, G. B., Bianchetti, A., & Trabucchi, M. (1999). Contrasting results between caregiver's report and direct assessment of activities of daily living in patients affected by mild and very mild dementia: The contribution of the caregiver's personal characteristics. *Journal of the American Geriatrics Society, 47 (2), 196-202*.

Zimmer HD, Mecklinger A, &Lindenberger U. (2006). Leves of binding: types,mechanisms, and functions of binding.In H.D. Zimmer, A. Mecklinger, & U. Lindenberger, editors. Handbook of binding and memory, perspective from cognitive neuroscience (p. 3-25). New York: Oxford University Press.

Zimmerman, M. E., Pan, J. W., Hetherington, H. P., Katz, M. J., Verghese, J., Buschke, H., … Lipton, R. B. (2008). Hippocampal neurochemistry, neuromorphometry, and verbal memory in nondemented older adults. *Neurology*, *70*(18), 1594–1600.

APPENDIX A ORIGINAL SET OF ITEMS

Self-assessment part

	OVER THE LAST 10 YEARS					
Financial management Items	Doesn't Apply	Better or no change	Always was bad	Questionable or occasional problems	Consistently a little worse	Consistently much worse
Memory						
1. Remembering to pay bills on time (phone, utility bills, loans)/Pay bills twice	0	1	2	3	4	5
2. Remembering pin-codes and passwords for cards and accounts	0	1	2	3	4	5
3. Remembering where you keep copies of bills/statements	0	1	2	3	4	5
Organization						
4. Able to keep track on your spendings (bills, debts, incoming cash flow)	0	1	2	3	4	5
5. Able to keep track on your savings	0	1	2	3	4	5
6. Assembling business, tax or financial records*	0	1	2	3	4	5
7. Able to keep track on your investments	0	1	2	3	4	5
8. Organizing your financial records, tax forms	0	1	2	3	4	5
9. Balancing the chequebook without error*	0	1	2	3	4	5
10. Carry monthly credit card balances	0	1	2	3	4	5
Planning, anticipating future						
11. Planning your budget ahead and stick to the plan	0	1	2	3	4	5
12. Planning your expenses	0	1	2	3	4	5
13. Choosing to spend on the things that are important while cutting back on the things that aren't.	0	1	2	3	4	5
14. Planning to maximize savings	0	1	2	3	4	5
15. Working on you retirement account	0	1	2	3	4	5
Prioritizing						

16. Prioritising purchases and spendings by importance	0	1	2	3	4	5
17. Making impulsive purchases	0	1	2	3	4	5
18. Deciding on your short- and long-term savings goals	0	1	2	3	4	5
Financial management Items	Doesn't Apply	Better or no change	Always was bad	Questionable or occasional problems	Consistently a little worse	Consistently much worse
Language and calculation						
19. Difficulties understanding parts of bills, bank statement, tax forms (identifying parts of it)	0	1	2	3	4	5
20. Difficulties writing cheques, filling in tax forms (enters information)	0	1	2	3	4	5
21. Difficulties with banking activities (money deposits, withdrawals)	0	1	2	3	4	5
22. Calculation change or tips	0	1	2	3	4	5
Divided Attention						
23. The ability to do 2 things at once*	0	1	2	3	4	5
24. Returning to a task after being interrupted*	0	1	2	3	4	5
Judgment						
25. Buying items trough the Internet or TV	0	1	2	3	4	5
26. Being able to identify financial scams	0	1	2	3	4	5
27. Being able to identify a good offer (sales, discounts)	0	1	2	3	4	5
28. Being able to identify good investment offers	0	1	2	3	4	5
Decision making						
29. Making investment decisions	0	1	2	3	4	5
30. Making decision about your financial matters	0	1	2	3	4	5
31. Buying what you want instead what you need.	0	1	2	3	4	5
32. Funnel your saving into investment account	0	1	2	3	4	5
33. Playing bingo or casino	0	1	2	3	4	5
34. Making a decision between several choices in a store	0	1	2	3	4	5
35. Buying things on the spur of the moment	0	1	2	3	4	5
36. Buying things after long considerations	0	1	2	3	4	5

Background information

I. Age group
1. Younger than 40.
2. 40-49
3. 50-59
4. 60-69
5. 70+

II. City/Town you live in.
_____

III. How many years of education do you have?
_____

IV. What is the highest level of education do you have?
_____

V. Family status
1. I live alone
   a) Divorced
   b) Widowed
   c) Separated
   d) Never been married
   e) Other
2. I live with a spouse
3. I live with kids
4. Other
   If Other, please specify_____

VI. Work status
1. Employed
2. Unemployed (how many years)
   ---
3. Retired (how many years)
   ---
4. Retired, but still working

5. Other

VII. How do you usually pay your bills?

1. In person
2. Writing and mailing paper checks
3. Pay at a store that accepts bill payments for other companies
4. With technologies
    a) Online
    b) ATM machines
    c) Using applications for smart phones/tablets
    d) Over the phone using automated telephone service
5. Direct Debit

VIII. Do you have a credit card?

1. No
2. Yes

If yes, do you…

a) Carry a full monthly balance payment
b) Carry less than monthly balance payment
c) Carry a minimum monthly payment
d) Other

If Other, please specify_____

IX. Which of the following banking methods are you using?

1. Banking in person
    a) Checking account balances
    b) Making deposits
    c) Making withdrawals
2. Online or phone banking
    a) Checking account balances
    b) Making transaction
    c) Setting-up direct debits
    d) Setting-up standing orders
3. I don't have a bank account
4. Other

If Other, please specify_____

X. Do you have a mortgage?

1. Yes
2. I don't have a mortgage, I am an owner of the house
3. I don't have a mortgage, I rent

XI. Do you have a loan?

1. I don't have any loans
2. I have a loan (please, specify)

XII. Are you confident to prepare your tax returns?

1. Extremely
2. Quite
3. Somewhat
4. A little
5. Not at all
6. I don't do that (someone else is doing that for me, ex. Financial advisor/spouse)

XIII. Financial decision making

1. I have an Individual Saving account (ISA)
2. I have investments/I have an annuity
3. I hold shares in a company
4. Other
   If Other, please specify_____

XIV. Do you need help in everyday money management:

1. No
2. I never needed any help with money management, but over the last few years I feel I need help (**or** Compare to 10 years ago, do you need more help now with money management?).
   a) I need a help only with big purchases
   b) With small and big purchases
3. I've always been bad with money
   a) To make big purchases
   b) With small and big purchases

XV. How would you pay £1000 pound unexpected expense?

1. Pay from my account
2. Borrow from a friend
3. I will loan money from the bank
4. I will save money by spending less on other items
5. I will withdraw from my retirement account
6. I would not pay at all
7. Other
   If Other, please specify_____

XVI. Where do you usually get help with your finances?

1. I have someone from the family members to help me
2. I rely on help of non-family members
3. I ask professionals
4. Other

If Other, please specify_____

XVII. Have you ever been asked to invest in something that you believed, suspected, or later found to be fraudulent?

1. I've never been a victim of any kind of fraud
2. I've been a victim of a financial fraud
3. There was/were attempt(s) to contact me, but I detected a fraud.
4. Other

If Other, please specify_____

XVIII. When you receive a call from the organisation you are not familiar with, how often do you think it is a call that may be fraudulent?

1. Almost all time
2. Most of the time
3. Less than half of the time
4. Hardly ever
5. Don't know

XIX. Retirement planning

1. I've planned my pension plan myself
2. I've planned my pension plan with professional help
3. I've never planned my pension
4. Other

If Other, please specify_____

XX. Do you have power of attorney?

1. Yes
2. No
3. I had it, but cancelled it
4. I've never considered to have one, but now I will
5. I've never planned for someone to make these decisions for me and newer will.
6. I have an alternative plan (e.g. joint account, other_____)

XXI. Do you have a will written?

1. Yes
2. I had a will, but cancelled it
3. No
3. Other

   If Other, please specify_____

XXII. Confidence in financial decision making

1. I've always been confident
2. I became more confident over the last few years (3, 5, 10)
3. I've never been confident
4. I was always confident, but over the last few years (3, 5, 10) became less confident

XXIII. Do you play bingo or casino?

1. I've always played
   a) Once a month
   b) More than once a month
2. I've never played
3. I've started playing a few years ago.
   a) Once a month
   b) More than once a month

XXIV. Have you in the last 3, 5 years made a major financial transaction (grater than £1000) that you later regret?

1. Yes
2. No
3. Other

   If Other, please specify_____

XXV. Why did you regret this transaction?

1. I couldn't afford it
2. I paid more than I should have
3. I responded to a strong sales pitch
4. Fraud/theft/scam

5. I didn't need it
6. Other

XXVI. Have you used Internet for:

1. Paying bills
2. Buying tickets (movie, travel, etc)
3. Buying or selling something using the Internet
4. Play lottery
5. None of the above.

Practical part.

1. **What is money?**
   a) A measurement of wealth
   b) A unit of account, a store of value, and a medium of exchange
   c) A unit of debt

2. How much money is that? What could you buy?

   a) Lunch
   b) TV
   c) I can't afford to buy anything with this money.

3. If you have £39.50 and want to buy trousers that cost £24 what would you do?
   a) I don't have enough money to buy trousers
   b) I will buy trousers and will have a change of £15.50
   c) I' borrow £15.50 to pay for the purchase.

4. **What is savings?**
   a) The portion of income not to spend on current expenditures.
   b) An outflow of money to another person or group to pay for an item or service
   c) I don't know

5. You have these coins:

Could you give me 27p from the coins?

6. What is more expensive – lunch at the local café or a computer?

a) Lunch
b) Computer
c) They are about the same

7. What costs less – a pint of milk or a packet of cigarette?

a) Milk
b) Cigarette
c) They are about the same

8. What is a credit?

a) An agreement that someone receives something now and agrees to repay the lender in the future.
b) Immediate payment
c) Cash that you currently have.

9. If you buy 1 pint of milk that cost £0.79 and bread that worth £1.30 and you have a £5 note, how much change do you expect to receive?

a) £2.91
b) £1.91
c) Non of the above

10. Suppose you have £100 in a savings account earning 2 percent interest a year. After five years, how much would you have? (a question is taken from Lusardi and Mitchell, 2011)

a) More than £102
b) Less than £102
c) Exactly £102
d) Don't know

11. If I invest £100 per month starting at the age 21, and that money earns a 7% return,

how much will I have after 70 years?

a) £130, 957
b) Between £150,000 and £225,000 depending on life expectancy
c) More than 1.5 million pounds
d) None of the above

12. Imagine that the interest rate on your savings account is 1 percent a year and inflation is 2 percent a year. After one year, would the money in the account buy more than it does today, exactly the same or less than today? (a question is taken from Lusardi and Mitchell, 2011)

a) More
b) Same
c) Less

13. What is a mortgage?

a) A loan to finance the purchase of your home
b) A thing that is borrowed, usually a sum of money, that is expected to be paid back with interest
c) An agreement under which one party agrees to rent property from another party.

14. If someone else's name is on your bank account, can they take all of the money in your account and use it like it is their own money? (a question is taken from Bassett, 1999 (p.201))

a) Yes
b) No
c) Don't know

15. A 15-year mortgage typically requires higher monthly payments than a 30-year mortgage but the total interest over the life of the loan will be less.

a) True
b) False
c) Don't know

16. Which of the following financial products can help you lower your personal risk?

a) Insurance
b) Mutual funds
c) National insurance contribution or private pension plan
d) None of the above

17. If you don't have a written long-term financial plan, which of the following you might experience

a) Being unable to afford fun activities you want to enjoy
b) Having a freedom to live the lifestyle you want
c) Both 'a' and 'b'

18. How do I decide how much coverage do I need when selecting car insurance?

a) Do online research to find out the minimum coverage requirement
b) Ask sales people from several different insurance companies
c) Ask a friend or mentor with a high level of insurance experience
d) All of the above

19. Which of these has priority:

a) Paying the bill
b) Going out with your friends
c) Buying something that you were craving for some time
d) Going to the local pub?

20. From the following list, choose the two best suggestions for building and maintaining a good credit rating

a) Have money in savings and protect against identity theft
b) Keep your debt low and pay your bills on time
c) Make safe investments and set clear financial goals
d) None of the above

21. NEXT DAY company offers you the best opportunity to invest money without any risks. You can take 5% of her pension in cash now and the rest will be invested in UK property developments, which will generate a guaranteed 8% return for her savings. This will assure you the prospect that the investment will grow quickly.

a) Yes, I will definitely go for this offer.
b) No, I think that I can't benefit from it.

22. The TRUST company offers you fast loan and will have your application approved regardless of your credit history. Before you receive the loan, you must pay an upfront fee of 75 pounds to cover insurance for the loan.

a) Yes, I will definitely go for this offer.
b) No, I think that I can't benefit from it.

23. A letter form the TNTB company asks if you are interested in making easy money by working from home, or setting up your own online business. The scheme allows you to choose when you work and enables you to fit your work around your other responsibilities. The work itself could involve filling envelopes, assembling products or selling goods or services through your own website. You will receive all instruction manuals that you need. In addition you will be given a fully developed web site that you can advertise. You have to pay 125 pounds money up front to register with the scheme, buy customer leads, and buy products to sell on.

a) Yes, I will definitely go for this offer.
b) No, I think that I can't benefit from it.

24. You have a phone call from **the British Rarity Company** saying that today is the last day of their special promotion. They are offering a free Sacagawea Golden Dollar, the highly sought after, newly minted dollar offered by the UK mint. These coins are in big demand and there are only a few left in our inventory. They are promising to send you out your free coin and an information packet today with no obligation whatsoever, just for being willing to review some valuable financial information about investing (Your Name, address, and bank details).

a) Yes, I will definitely go for this offer.
b) No, I think that I can't benefit from it.

25. You have a telephone call from a company you are not familiar with and trying to get you to BUY something, enter a sweepstakes or contest, or make an investment. What would you do in this situation?

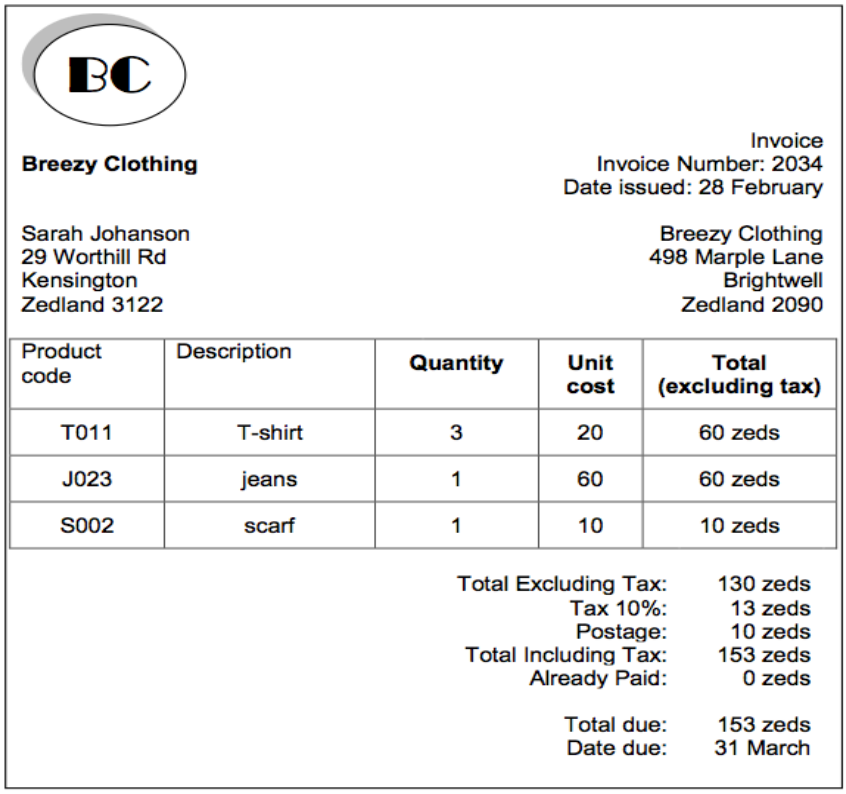
a) Hang up immediately or and the call at a convenient pause
b) I'd respond positively if I feel that the offer is sound.
c) Other

26. You have a telephone call from a British Allegiance Organisation saying that you won one of the four prizes: a cruise tour, a TV set, a shopping spree, or a cash. You guarantee to win at least one of the prizes, and all you have to do is to provide you correct address and the bank details. You response:

a) I'd respond positively as I feel that the offer is sound.
b) I would hung up, it is not sound as a good offer.

27. A situation takes place in the fictional country of Zedland, where the Zed is the unit of currency (a question is taken from the PISA2012 financial literacy questionnaire for 15-years olds).

Sarah receives this invoice in the mail:



Breezy Clothing

Invoice
Invoice Number: 2034
Date issued: 28 February

Sarah Johanson
29 Worthill Rd
Kensington
Zedland 3122

Breezy Clothing
498 Marple Lane
Brightwell
Zedland 2090

Product code	Description	**Quantity**	**Unit cost**	**Total (excluding tax)**
T011	T-shirt	3	20	60 zeds
J023	jeans	1	60	60 zeds
S002	scarf	1	10	10 zeds

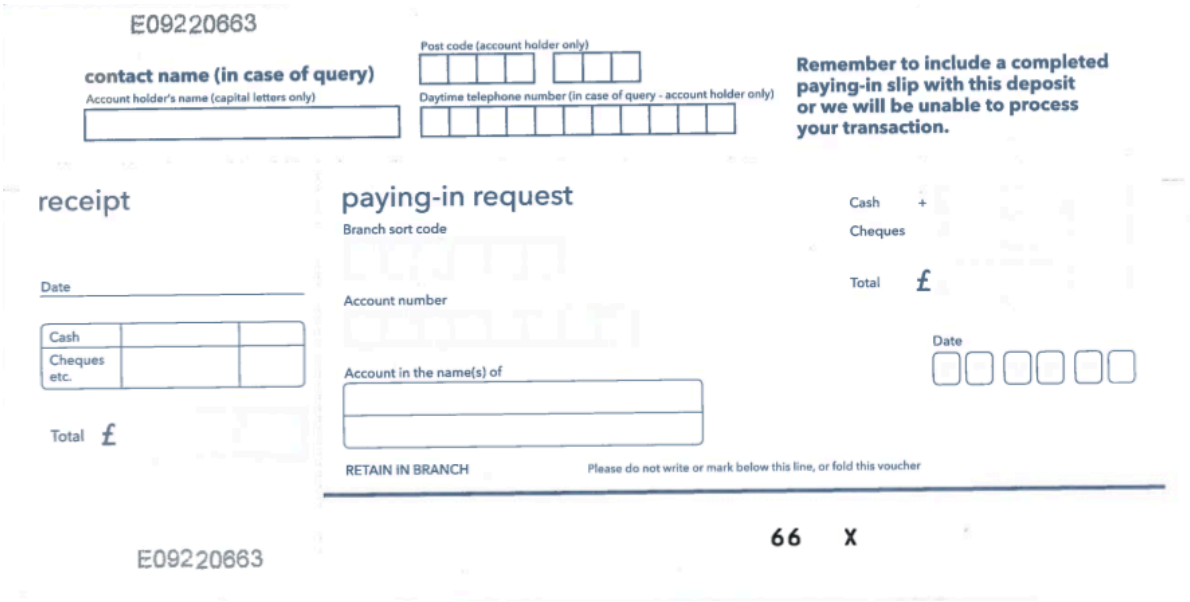
Total Excluding Tax:	130 zeds
Tax 10%:	13 zeds
Postage:	10 zeds
Total Including Tax:	153 zeds
Already Paid:	0 zeds
Total due:	153 zeds
Date due:	31 March

Why was this invoice sent to Sarah?

a) Because Sarah has paid the money to Breezy Clothing.
b) Because Breezy Clothing has paid the money to Sarah.

28. How much has Breezy Clothing charged for delivering the clothes? Delivery charge in zeds: .....

29. Please, fill the deposit slip for the amount of 200 pounds from the account number 0102030405, sort-code 01-02-03.



30. Mr. J Smith received energy and gas bills. How much Mr. J Smith should pay for his gas and electricity?.....

SCOTTISHPOWER

page **3** of 3

Energy charges this period

Electricity

	Meter number	
Start reading End reading	**56678 Customer read** 22 Aug 13 **57821 Actual** 09 Nov 13	
Units used	**1143 = 1143 kWh (kilowatt-hrs) used**	
22/08/13 to 08/11/13 22/08/13 to 08/11/13	Consumption charge, secondary **949 kWh x 11.449p =** Consumption charge, primary **194 kWh x 23.498p =**	£108.65 £45.59

NSC Option	**Meter number**	
Start reading End reading	**57821 Actual** 09 Nov 13 **58230 Customer Read** 03 Dec 13	
Units used	**409 = 409 kWh (kilowatt-hrs) used**	
09/11/13 to 02/12/13 09/11/13 to 02/12/13	Consumption charge, secondary **350 kWh x 11.449p =** Consumption charge, primary **59 kWh x 23.498p =**	£40.07 £13.86

S | 00 | 000 | 000 | 00 | 0000 0000 | 000 |

Total electricity charges **£208.17**

Gas

	Meter number	
Start reading End reading	**21960 Customer read** 22 Aug 13 **22209 Actual** 09 Nov 13	
Units used	**249 = 2773 kWh (kilowatt-hrs) used**	
22/08/13 to 08/11/13 22/08/13 to 08/11/13	Consumption charge, secondary **2193 kWh x 3.359p =** Consumption charge, primary **580 kWh x 7.564p =**	£73.66 £43.87

	Meter number	
Start reading End reading	**22209 Actual** 09 Nov 13 **22360 Customer Read** 03 Dec 13	
Units used	**151 = 1681 kWh (kilowatt-hrs) used**	
09/11/13 to 02/12/13 09/11/13 to 02/12/13	Consumption charge, secondary **1505 kWh x 3.359p =** Consumption charge, primary **176 kWh x 7.564p =**	£50.55 £13.31

Your gas meter point reference number

Total gas charges **£181.39**

Total energy charges this period **£389.56**

Discounts

Gas & Electricity discount	credit	-£4.51
	Total discounts	**-£4.51**

Other charges

DD BONUS 08/13		-£1.90
	Total other charges	**-£1.90**

VAT

VAT at 5.00% on £385.05 VAT at 5.00% on -£1.90		£19.25 -£0.10
	Total VAT	**£19.15**

.....

31. You need to set up a new standing order for the dental medical service in BCBIOMEDICAL (account number 12345678, sort code 55-44-33) for the sum of 250 pounds monthly for the 12-month period starting from the 1th of February 2015. Your bank details: account number 09876543, sort code 77-88-66. Please, fill in the form below:

BARCLAYS

Regular Payments form

Please tick relevant box

☐ Set up a new Standing Order (please complete section A)
☐ Amend an existing Standing Order (please complete section B)
☐ Cancel an existing Standing Order or Direct Debit (please complete section C)

Please complete all boxes in BLOCK CAPITALS and tick when necessary.

Customer Account Details

Account Name
Sort code ☐☐-☐☐-☐☐
Account number ☐☐☐☐☐☐☐☐

Section A - Set up a new Standing Order (Who do you want to pay?)

Beneficiary Name
Sort code ☐☐-☐☐-☐☐
Account number ☐☐☐☐☐☐☐☐
Reference
Amount of first payment — Date of first payment ☐☐/☐☐/☐☐
Amount of usual payment — Date of last payment ☐☐/☐☐/☐☐
Frequency of Payment (Weekly/Monthly/Annually) — Date of Usual payment ☐☐/☐☐/☐☐

☐ Or please continue until further notice

Section B - Amend an existing Standing Order (Who you are paying?)

Beneficiary Name

Amend payment amount	from		to	
Amend payment date	from		to	
Amend payment frequency	from		to	
Amend date of first payment	from		to	
Amend reference number	from		to	

Section C - Cancel an existing Standing Order or Direct Debit (Who you no longer want to pay?)

Beneficiary/Originator Name
Amount
Usual payment date
I wish to cancel with effect from ☐☐/☐☐/☐☐

(For Direct Debit details you should also advise the originator of your cancellation).

All relevant sections must be fully completed for your request to be processed.

PLEASE ENSURE YOU SIGN AND DATE THE FORM.

(Where signing mandate is 'both' or 'all'; all relevant parties must sign to authorise.)

Customer Signature(s)
Contact Telephone Number — Date ☐☐/☐☐/☐☐

Please either post this completed form to Barclays Bank Leicester LE87 2BB or hand in at any Barclays branch.

Barclays Bank PLC Regulated by The Financial Services Authority.
Registered in England. Registration No. 1026167. Registered Office: 1 Churchill Place, London E14 5HP

APPENDIX B FINAL SET OF ITEMS

Background information

XXVII. Age group

6. Younger than 40.
7. 40-49
8. 50-59
9. 60-69
10. 70+

XXVIII. City/Town you live in.

_____

XXIX. How many years of education do you have?

_____

XXX. What was your profession?

_____

XXXI. Family status

5. I live alone
   f) Divorced
   g) Widowed
   h) Separated
   i) Never been married
   j) Other
6. I live with a spouse
7. I live with kids
8. Other
   If Other, please specify_____

XXXII. Work status

6. Employed

7. Unemployed (how many years)
   ---
8. Retired (how many years)
   ---
9. Retired, but still working
10. Other

XXXIII. How do you usually pay your bills?

6. In person
7. Writing and mailing paper checks
8. Pay at a store that accepts bill payments for other companies
9. With technologies
   e) Online
   f) Direct Debit
   g) ATM machines
   h) Using applications for smart phones/tablets
   i) Over the phone using automated telephone service

XXXIV. Do you have a credit card?

4. No
5. Yes

   If yes, do you…

e) Make a full monthly balance payment
f) Make less than monthly balance payment
g) Make a minimum monthly payment
h) Other

If Other, please specify_____

XXXV. Which of the following banking methods are you using?

5. Banking in person
   d) Checking account balances
   e) Making deposits
   f) Making withdrawals
6. Online or phone banking
   e) Checking account balances
   f) Making transaction
   g) Setting-up direct debits
   h) Setting-up standing orders
7. I don't have a bank account
8. Other

   If Other, please specify_____

XXXVI. Do you have a mortgage?

4. Yes
5. I don't have a mortgage, I am an owner of the house
6. I don't have a mortgage, I rent

XXXVII. Do you have a loan?

3. I don't have any loans
4. I have a loan (please, specify)

XXXVIII. Are you confident to prepare your tax returns?

7. Extremely
8. Quite
9. Somewhat
10. A little
11. Not at all
12. I don't do that (someone else is doing that for me, ex. Financial advisor/spouse)

XXXIX. Financial decision making

5. I have an Individual Saving account (ISA)
6. I have investments/I have an annuity
7. I hold shares in a company
8. Other
   If Other, please specify_____

XL. Do you need help in everyday money management:

4. I never needed any help with money management, but over the last few years I feel I need help.
   c) I need a help only with big purchases
   d) With small and big purchases
5. No
6. I've always been bad with money
   c) To make big purchases
   d) With small and big purchases

XLI. How would you pay £1000 pound unexpected expense?

8. Pay from my account
9. Borrow from a friend
10. I will borrow money from the bank
11. I will save money by spending less on other items
12. I will withdraw from my retirement account
13. I would not pay at all
14. Other
    If Other, please specify_____

XLII. Where do you usually get help with your finances?

5. I have someone from the family members to help me
6. I rely on help of non-family members
7. I ask professionals
8. Other

    If Other, please specify_____

XLIII. Have you ever been asked to invest in something that you believed, suspected, or later found to be fraudulent?

5. I've never been a victim of any kind of fraud
6. I've been a victim of a financial fraud
7. There was/were attempt(s) to contact me, but I detected a fraud.
8. Other
    If Other, please specify_____

XLIV. When you receive a call from the organisation you are not familiar with, how often do you think it is a call that may be fraudulent?

6. Almost all time
7. Most of the time
8. Less than half of the time
9. Hardly ever
10. Don't know

XLV. Retirement planning

5. I've planned my pension plan myself
6. I've planned my pension plan with professional help
7. I've never planned my pension
8. Other
    If Other, please specify_____

XLVI. Do you have power of attorney that names someone else to act on your behalf?

7. Yes
8. No
9. I had it, but cancelled it
10. I've never considered to have one, but now I will
11. I've never planned for someone to make these decisions for me and newer will.
12. I have an alternative plan (e.g. joint account, other_____)

XLVII. Do you have a will written?

4. Yes
5. I had a will, but cancelled it
6. No

XLVIII. Confidence in financial decision making

5. I've always been confident
6. I became more confident over the last few years (3, 5, 10)
7. I've never been confident
8. I was always confident, but over the last few years (3, 5, 10) became less confident

XLIX. Do you play bingo or casino?

2. I've always played
4. I've never played
5. I played in a past, not any more
6. I've started playing a few years ago.

L. Have you in the last 3, 5 years made a major financial transaction (greater than £1000) that you later regret?

4. Yes
5. No
6. Other

If Other, please specify_____

LI. If you answer was 'YES' on the previous question, why did you regret this transaction?

7. I couldn't afford it
8. I paid more than I should have
9. I responded to a strong sales pitch
10. Fraud/theft/scam
11. I didn't need it
12. Other

LII. Have you used Internet for:

6. Paying bills
7. Buying tickets (movie, travel, etc)
8. Buying or selling something using the Internet
9. Play lottery
10. None of the above.

Practical part.

1. What is money?

d) A measurement of wealth
e) A unit of account, a store of value, and a medium of exchange
f) A unit of debt

2. How much money is that (a picture below)? What could you buy with it?

a) Lunch
b) TV
c) I can't afford to buy anything with this money.

3. If you have £39.50 and want to buy trousers that cost £24 what would you do?
   d) I don't have enough money to buy trousers
   e) I will buy trousers and will have a change of £15.50
   f) I'd borrow £15.50 to pay for the purchase.

4. What is savings?

d) The portion of income not to spend on current expenditures.
e) An outflow of money to another person or group to pay for an item or service
f) Neither 'a' nor 'b'

5. You have these coins:

   Could you tick 27p from the coins?

6. What is more expensive – lunch at the local café or a computer?
   d) Lunch
   e) Computer
   f) They are about the same

7. What costs less – a pint of milk or a pack of cigarettes?
   d) Milk
   e) Cigarettes
   f) They are about the same

8. What is credit?
   d) An agreement that someone receives something now and agrees to repay the lender in the future.
   e) Immediate payment
   f) Cash that you currently have.

9. If you buy 1 pint of milk that cost £0.79 and bread that worth £1.30 and you have a £5 note, how much change do you expect to receive?

   d) £2.91
   e) £1.91
   f) None of the above

10. Suppose you have £100 in a savings account earning 2 percent interest a year. After five years, how much would you have?

   e) More than £102
   f) Less than £102
   g) Exactly £102

h) Don't know

11. Imagine that the interest rate on your savings account is 1 percent a year and inflation is 2 percent a year. After one year, would the money in the account buy more than it does today, exactly the same or less than today?
    d) More
    e) Same
    f) Less

12. You are planning to buy a TV. You came to a shop where the cost of a TV is £500 and there is a discount of 20% on it. In another store the same TV would cost you £350. Where would you buy the cheapest TV?
    a) The first with the sale of 20% is cheaper
    b) The second where the cost £350
    c) They are the same price.

13. What is mortgage?
    d) A loan to finance the purchase of your home
    e) A thing that is borrowed, usually a sum of money, that is expected to be paid back with interest
    f) An agreement under which one party agrees to rent property from another party.

14. If someone else's name is on your bank account, can they take all of the money in your account and use it like it is their own money?
    d) Yes
    e) No
    f) Don't know

15. A 15-year mortgage typically requires higher monthly payments than a 30-year mortgage but the total interest over the life of the loan will be less.
    d) True
    e) False
    f) Don't know

16. From the following list, choose the **two best** suggestions for building and maintaining a good credit rating
    e) Have money in savings and protect against identity theft
    f) Keep your debt low and pay your bills on time
    g) Make safe investments and set clear financial goals
    h) Borrow large amount of money, but pay on time

17. NEXT DAY company offers you the best opportunity to invest money without any risks. You can take 5% of your pension in cash now and the rest will be invested in UK property developments, which will generate a guaranteed 8% return for your savings. This will assure you the prospect that the investment will grow quickly.
    c) Yes, I will definitely go for this offer.
    d) I'd consider after further research
    e) No, I think that I can't benefit from it.
    f) It's definitely a scam

18. The TRUST company offers you fast loan and will have your application approved regardless of your credit history. Before you receive the loan, you must pay an upfront fee of 75 pounds to cover insurance for the loan.
    c) Yes, I will definitely go for this offer.
    d) I'd consider after further research
    e) No, I think that I can't benefit from it.
    f) It's definitely a scam

19. A letter from the TNTB company asks if you are interested in making easy money by working from home, or setting up your own online business. The scheme allows you to choose when you work and enables you to fit your work around your other responsibilities. The work itself could involve filling envelopes, assembling products or selling goods or services through your own website. You will receive all instruction manuals that you need. In addition you will be given a fully developed web site that you can advertise. You have to pay 125 pounds money up front to register with the scheme, buy customer leads, and buy products to sell on.
    a) Yes, I will definitely go for this offer.
    b) I'd consider after further research
    c) No, I think that I can't benefit from it.
    d) It's definitely a scam

20. You have a phone call from **the British Rarity Company** saying that today is the last day of their special promotion. They are offering a free Sacagawea Golden Dollar, the highly sought after, newly minted dollar offered by the UK mint. These coins are in big demand and there are only a few left in our inventory. They are promising to send you out your free coin and an information packet today with no obligation whatsoever, just for being willing to review some valuable financial information about investing (Your Name, address, and bank details).
    a) Yes, I will definitely go for this offer.
    b) I'd consider after further research
    c) No, I think that I can't benefit from it.
    d) It's definitely a scam

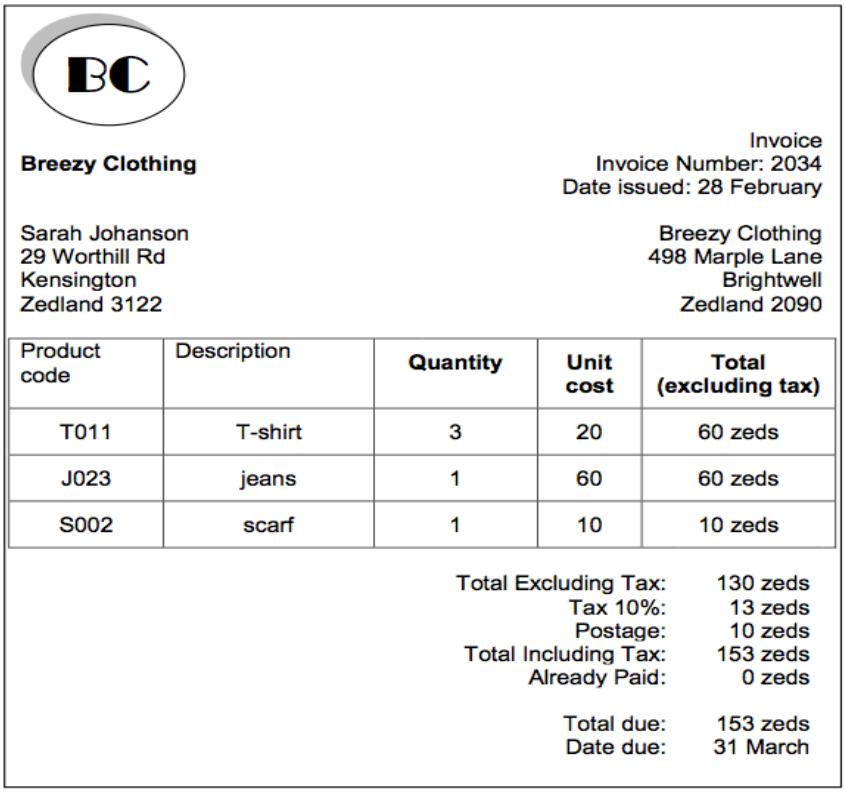
21. You have a telephone call from a company you are not familiar with and trying to get you to BUY something, enter a sweepstakes or contest, or make an investment. What would you do in this situation?
    d) Hang up immediately or end the call at a convenient pause
    e) I'd respond positively if I feel that the offer is sound.
    f) Other

22. You have a telephone call from a British Allegiance Organisation saying that you won one of the four prizes: a cruise tour, a TV set, a shopping spree, or a cash. You guarantee to win at least one of the prizes, and all you have to do is to provide you correct address and the bank details. You response:
    c) I'd respond positively as I feel that the offer is sound.
    d) I would hang up; it is not sound as a good offer.

23. A situation takes place in the fictional country of Zedland, where the Zed is the unit of currency.

    Sarah receives this invoice in the mail. **Why was this invoice sent to Sarah?**

    c) Because Sarah owes the money to Breezy Clothing.
    d) Because Breezy Clothing owes the money to Sarah.



Breezy Clothing

Invoice
Invoice Number: 2034
Date issued: 28 February

Sarah Johanson
29 Worthill Rd
Kensington
Zedland 3122

Breezy Clothing
498 Marple Lane
Brightwell
Zedland 2090

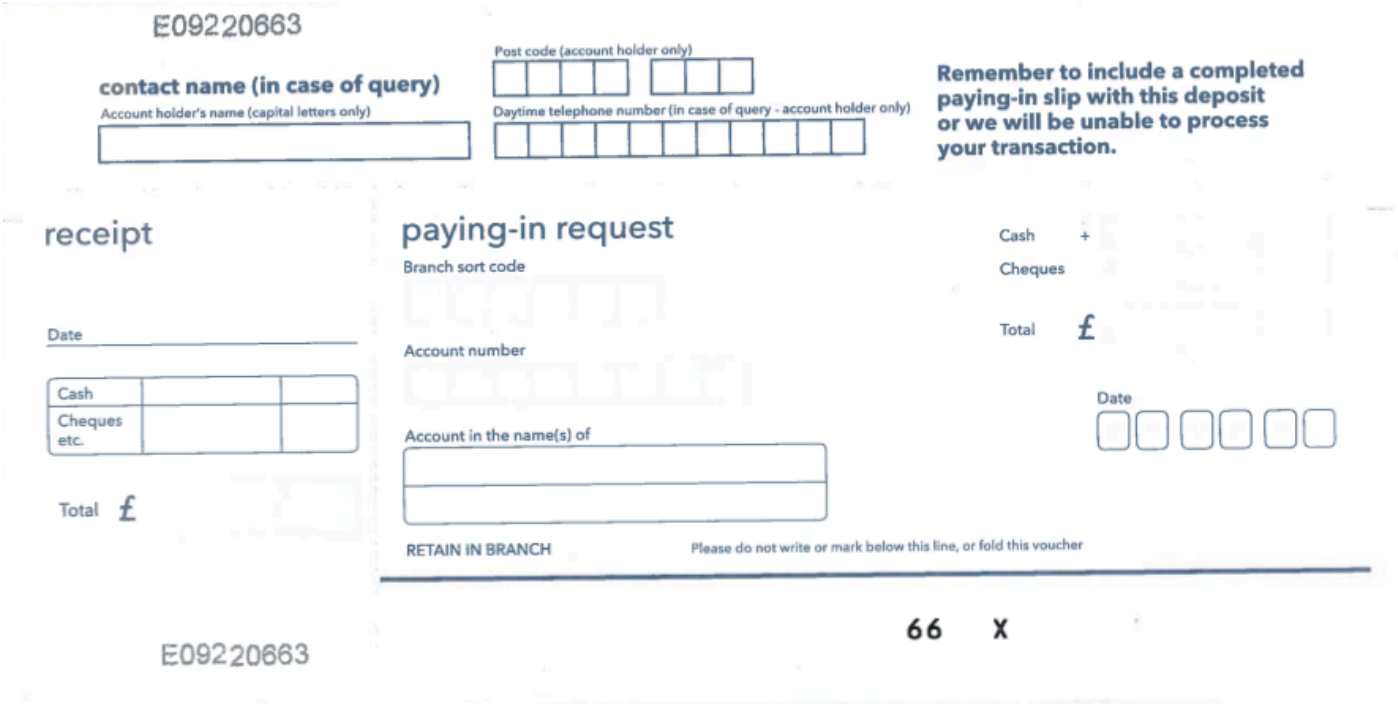
Product code	Description	Quantity	Unit cost	Total (excluding tax)
T011	T-shirt	3	20	60 zeds
J023	jeans	1	60	60 zeds
S002	scarf	1	10	10 zeds

Total Excluding Tax:	130 zeds
Tax 10%:	13 zeds
Postage:	10 zeds
Total Including Tax:	153 zeds
Already Paid:	0 zeds
Total due:	153 zeds
Date due:	31 March

24. How much has Breezy Clothing charged for delivering the clothes? Delivery charge in zeds:
    .....

25. Please, fill the deposit slip for the amount of 200 pounds in cash to the account

01020304, sort-code 01-02-03.


E09220663

contact name (in case of query)

Account holder's name (capital letters only)

Post code (account holder only)

Daytime telephone number (in case of query - account holder only)

Remember to include a completed paying-in slip with this deposit or we will be unable to process your transaction.

receipt

Date

Cash

Cheques etc.

Total £

paying-in request

Branch sort code

Account number

Account in the name(s) of

RETAIN IN BRANCH

Please do not write or mark below this line, or fold this voucher

Cash +

Cheques

Total £

Date

66 X

E09220663

26. Mr. J Smith has received the Energy and Gas bill. How much should Mr. J Smith pay for his gas and how much for the electricity?

SCOTTISHPOWER

Energy charges this period

Electricity

	Meter number	
Start reading End reading	**56678 Customer read** 22 Aug 13 **57821 Actual** 09 Nov 13	
Units used	**1143 = 1143 kWh (kilowatt-hrs) used**	
22/08/13 to 08/11/13 22/08/13 to 08/11/13	Consumption charge, secondary **949 kWh x 11.449p =** Consumption charge, primary **194 kWh x 23.498p =**	£108.65 £45.59

NSC Option	**Meter number**	
Start reading End reading	**57821 Actual** 09 Nov 13 **58230 Customer Read** 03 Dec 13	
Units used	**409 = 409 kWh (kilowatt-hrs) used**	
09/11/13 to 02/12/13 09/11/13 to 02/12/13	Consumption charge, secondary **350 kWh x 11.449p =** Consumption charge, primary **59 kWh x 23.498p =**	£40.07 £13.86

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	00	0000 0000	000

Total electricity charges **£208.17**

Gas

	Meter number	
Start reading End reading	**21960 Customer read** 22 Aug 13 **22209 Actual** 09 Nov 13	
Units used	**249 = 2773 kWh (kilowatt-hrs) used**	
22/08/13 to 08/11/13 22/08/13 to 08/11/13	Consumption charge, secondary **2193 kWh x 3.359p =** Consumption charge, primary **580 kWh x 7.564p =**	£73.66 £43.87

	Meter number	
Start reading End reading	**22209 Actual** 09 Nov 13 **22360 Customer Read** 03 Dec 13	
Units used	**151 = 1681 kWh (kilowatt-hrs) used**	
09/11/13 to 02/12/13 09/11/13 to 02/12/13	Consumption charge, secondary **1505 kWh x 3.359p =** Consumption charge, primary **176 kWh x 7.564p =**	£50.55 £13.31

Your gas meter point reference number

Total gas charges **£181.39**

Total energy charges this period **£389.56**

Discounts

Gas & Electricity discount	credit	-£4.51
	Total discounts	**-£4.51**

Other charges

DD BONUS 08/13		-£1.90
	Total other charges	**-£1.90**

VAT

VAT at 5.00% on £385.05 VAT at 5.00% on -£1.90		£19.25 -£0.10
	Total VAT	**£19.15**

27. You need to set up a new standing order for the dental medical service in BCBIOMEDICAL (account number 12345678, sort code 55-44-33) for the sum of 50 pounds monthly for the 12-month period starting from the 1st of February 2017. **Your bank details**: account number 09876543, sort code 77-88-66. Please, fill in the form below:

BARCLAYS

Regular Payments form

Please tick relevant box

☐ Set up a new Standing Order (please complete section A)
☐ Amend an existing Standing Order (please complete section B)
☐ Cancel an existing Standing Order or Direct Debit (please complete section C)

Please complete all boxes in BLOCK CAPITALS and tick when necessary.

Customer Account Details

Account Name
Sort code ☐☐-☐☐-☐☐
Account number ☐☐☐☐☐☐☐☐

Section A - Set up a new Standing Order (Who do you want to pay?)

Beneficiary Name
Sort code ☐☐-☐☐-☐☐
Account number ☐☐☐☐☐☐☐☐
Reference
Amount of first payment — Date of first payment ☐☐/☐☐/☐☐
Amount of usual payment — Date of last payment ☐☐/☐☐/☐☐
Frequency of Payment (Weekly/Monthly/Annually) — Date of Usual payment ☐☐/☐☐/☐☐

☐ Or please continue until further notice

Section B - Amend an existing Standing Order (Who you are paying?)

Beneficiary Name

Amend payment amount	from		to	
Amend payment date	from		to	
Amend payment frequency	from		to	
Amend date of first payment	from		to	
Amend reference number	from		to	

Section C - Cancel an existing Standing Order or Direct Debit (Who you no longer want to pay?)

Beneficiary/Originator Name
Amount
Usual payment date
I wish to cancel with effect from ☐☐/☐☐/☐☐

(For Direct Debit details you should also advise the originator of your cancellation).

All relevant sections must be fully completed for your request to be processed.

PLEASE ENSURE YOU SIGN AND DATE THE FORM.

(Where signing mandate is 'both' or 'all'; all relevant parties must sign to authorise.)

Customer Signature(s)
Contact Telephone Number — Date ☐☐/☐☐/☐☐

Please either post this completed form to Barclays Bank Leicester LE87 2BB or hand in at any Barclays branch.

Self-assessment part	OVER THE LAST 10 YEARS							
Financial management Items	Never did before	Did it Before No longer necessary but could do it if needed	Better	No change	Questionable or occasional problems	Consistently a bit worse	Consistently much worse	Did it Before Unable to do it anymore
Memory								
4. Remembering to pay bills on time (phone, utility bills, loans)/Pay bills twice	0	0	1	2	3	4	5	6
5. Remembering pin-codes and passwords for cards and accounts	0	0	1	2	3	4	5	6
6. Remembering where you keep copies of bills/statements	0	0	1	2	3	4	5	6
Organization								
19. Able to keep track on your spendings and savings (bills, debts, incoming cash flow)	0	0	1	2	3	4	5	6
20. Assembling business, tax or financial records	0	0	1	2	3	4	5	6
21. Able to keep track on your investments	0	0	1	2	3	4	5	6
22. Organizing your financial records, tax forms	0	0	1	2	3	4	5	6
23. Balancing the credit/debit cards without error	0	0	1	2	3	4	5	6
Planning, anticipating future								
24. Planning your budget ahead and stick to the plan	0	0	1	2	3	4	5	6
25. Choosing to spend on the things that are important while cutting back on the things that aren't.	0	0	1	2	3	4	5	6
26. Planning to maximize savings	0	0	1	2	3	4	5	6
27. Working on your retirement account	0	0	1	2	3	4	5	6
Prioritizing								
28. Prioritising purchases and spendings by importance	0	0	1	2	3	4	5	6
29. Making impulsive purchases	0	0	1	2	3	4	5	6
30. Deciding on your short- and long-term savings	0	0	1	2	3	4	5	6

goals								
	OVER THE LAST 10 YEARS							
Financial management Items	Never did before	Did it Before No longer necessary, but could do it if needed	Better	No change	Questionable or occasional problems	Consistently a bit worse	Consistently much worse	Did it Before Unable to do it anymore
Language and calculation								
31. Difficulties understanding parts of bills, bank statement, tax forms (identifying parts of it)	0	0	1	2	3	4	5	6
32. Difficulties writing cheques, filling in tax forms (enters information)	0	0	1	2	3	4	5	6
33. Difficulties with banking activities (money deposits, withdrawals)	0	0	1	2	3	4	5	6
34. Calculation change or tips	0	0	1	2	3	4	5	6
Divided Attention								
35. The ability to do 2 things at once	0	0	1	2	3	4	5	6
36. Returning to a task after being interrupted	0	0	1	2	3	4	5	6
Judgment								
22.Buying items through the Internet or TV	0	0	1	2	3	4	5	6
23. Being able to identify financial scams	0	0	1	2	3	4	5	6
24. Being able to identify a good offer (sales, discounts)	0	0	1	2	3	4	5	6
25. Being able to identify good investment offers	0	0	1	2	3	4	5	6
Decision making								
26. Making investment decisions	0	0	1	2	3	4	5	6
27. Making decision about your financial matters	0	0	1	2	3	4	5	6
28. Buying what you need instead what you want.	0	0	1	2	3	4	5	6
29. Funnel your saving into investment account	0	0	1	2	3	4	5	6
30. Playing bingo or casino	0	0	1	2	3	4	5	6
31. Making a decision between several choices in a store	0	0	1	2	3	4	5	6
32. Buying things on the spur of the moment	0	0	1	2	3	4	5	6
33. Buying things after long considerations	0	0	1	2	3	4	5	6