UNIVERSITY OF TWENTE.

Graduation project

CogniDecline

Tracking mobile interaction for cognitive assessment

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Contents

Abstract

With our rapidly ageing population, mental disorders associated to ageing are becoming more prevalent. Cognitive impairments, such as dementia can cause severe problems in daily life. Currently diagnosis of cognitive impairment is performed through medical assessments after potential symptoms have been detected. Technical approaches may be able to provide more immediate and continuous assessment which could allow for much earlier diagnosis of mental disorders. However, technical approaches currently focus primarily on biomedical factors which could influence the risk and therefore are difficult to compare to the clinical questionnaire-based approaches in medical assessments. This paper shall provide a way of integrating traditional forms of assessment digitally with technical forms of assessment using biosensory data on a smartphone. This paper is accompanied by the development of a plugin for the AWARE application for Android smartphones, which allows for the digitalisation of clinical cognitive assessment tests.

Acknowledgement

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Chapter 1

Introduction

Recent developments in socio-economic conditions have resulted in a rapidly ageing population [1]. Ageing is associated with cognitive decline, primarily memory loss and declining speed of cognitive operations [2]. If the speed of cognitive decline increases beyond the normal range of age-related cognitive decline and the decline causes impairment in daily life, a mental disorder such as dementia can often be diagnosed [3]. According to the WHO approximately 15% of adults aged 60 and over suffer from a mental disorder [4] and 47.5 million people are affected by dementia, with 7.7 million new cases every year [5]. The Diagnostic and Statistical Manual of Mental Disorders (DSM) describes mental disorders to be “conceptualized as a clinically significant behavioral or psychological syndrome or pattern that occurs in an individual and that is associated with present distress (e.g., a painful symptom) or disability (i.e., impairment in one or more important areas of functioning) or with a significantly increased risk of suffering death, pain, disability, or an important loss of freedom” [3]. An early stage of cognitive decline is called mild-cognitive disorder (MCI), it is often a pre-phase of dementia, especially when the cognitive impairment is not recognised and treated. Most applications for treatment and diagnosis target MCI or an early stage of dementia, because treatment in these cases can often be successfully used to reduce the speed of cognitive decline and allow patients to retain control over their lives as long as possible.

1.1 Cognition and cognitive functioning

In order to gain an understanding of Cognitive Decline, a clear definition of cognitive function and cognition shall be outlined in the following paragraphs. According to Bermúdez [6], “the guiding idea of cognitive science is that mental operations involve processing information, and hence that we can study how the mind works by studying how information is processed." [6]. Reed [7] describes Cognition as the "acquisition of knowledge" [7]; "Psychologists who study cognition are interested in pattern recognition, attention, memory, visual memory, visual imagery, language, problem-solving, and decision making" [7]. In Section 2, several methods for analysing cognition along these areas will be explained, beginning with traditional assessment methods, and continuing with new digital means of assessing cognitive functioning.

The Oxford dictionary describes cognition as "the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses" [8]. Cognitive abilities are therefore required for accomplishing any task of daily activity. While a wide variety of cognitive abilities can be described, most commonly the cognitive abilities of *perception*, *attention*, *memory*, *language skills*, *visuospatial processing*, and *executive function* are differentiated. In the following subsections, a general description of each ability will be outlined.

Cognition can therefore be understood as the study of the mind, and therefore the study of neuroactivity and the brain. A frequently used classification of anatomical, functionally distinct regions in the cerebral cortex was developed by Korbinian Brodmann. Brodmann distinguished regions based on the type and density of cells. Brodmann's areas are shown in figure 1.1. For instance, the primary visual cortex is located in area 17. The primary motor cortex is area 4 [6]. In Broca's area (area 44 and 45) speech and language is produced and in Wernicke's area (area 39 and 40) speech comprehension is localised [9].

Figure 1.2 shows the four lobes of the cerebral cortex. The frontal lobe is responsible for thinking, planning, motor and executive functions. The parietal lobe is mainly responsible for somatosensory perception, that is the general sensations associated with the body. The temporal lobe is associated with long-term memory functions, as well as auditory perception in the superior temporal lobe or Brodmann's areas 41 and 42. Visual perception and spatial processing is performed by the occipital lobe [6, 9].

The next sections will explain a variety of cognitive abilities that are often tested in assessment tests. Following the assumption that the human capacity of processing information at any point in time is finite [10], a test of a specific cognitive domain should assess the maximum capacity of the subjects. The limited capacity model suggests that tasks require a specific cognitive load, unfamiliar tasks require a greater cognitive load than familiar tasks, and the cognitive load that a person is able to perform at any given time must be smaller than their cognitive capacity [11].

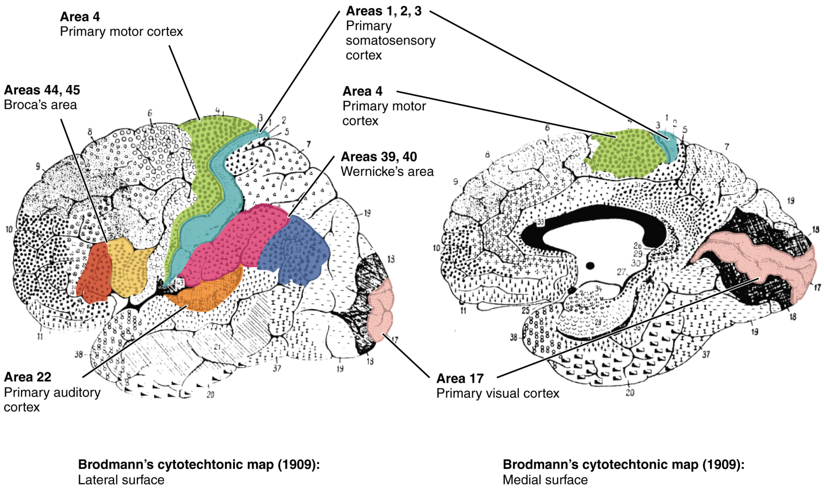


Figure 1.1: Brodmann mapping of functionally distinct regions of the cortex was based on its cytoarchitecture at a microscopic level. Note. Reprinted from [9].

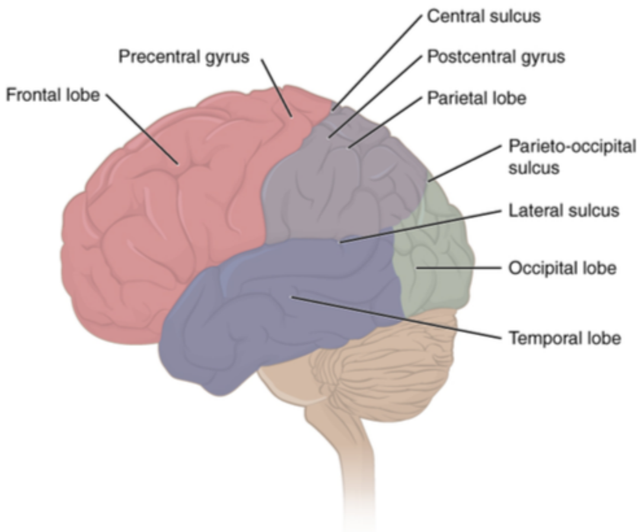


Figure 1.2: The four lobes of the cerebral cortex. Note. Reprinted from [9].

1.1.1 Perception

Perception is defined as "the ability to see, hear, or become aware of something through the senses" [12] and "the neurophysiological processes, including memory, by which an organism becomes aware of and interprets external stimuli" [12]. Jacoby and Brooks [13] describe a view of perception to rely on "abstract representations of knowledge such as schemata and logogens" [13]. This assumption has led to the development of paradigms, such as *priming*, which refers to "the effect of a single presentation of an item on its later speed of processing or probability of correct identification" [13].

One of the first insights into perception came from Weber's law. Weber recognised that the *increment intensity* that allows one to perceive the difference in sensory stimuli is proportional to the *background intensity.* Weber's fraction therefore states: $\frac{\Delta I}{I} = K$ (i.e., the ratio of the intensity change (ΔI) and the background intensity (I) is constant (K)) [14, 15]. This means for instance in a loud, noisy environment, a louder voice is required to communicate compared to a quiet environment. According to Weber's law, the minimum volume required to understand the voice and the volume of the environment are proportional.

The study of perception has led to the ideas of *Gestalt psychology* which gave new insight into perception. Gestalt Psychology originated in the discovery of *phi motion* ("*φ-Phänomen*"), in 1912 by Max Wertheimer. The phenomenon led to insight in the *perception of vision* and the understanding of *apparent movement*, which occurs in the presentation of image frames in rapid succession, which are perceived as a fluent motion. The idea of the *principles of grouping* was first proposed by Gestalt psychologist.

First insight into the view of perception as the recognition of organised patterns, was proposed by Wertheimer (1912):

> „Der spezifische, eindringliche Charakter von Bewegung (...) kann nicht durch Rekurs auf die Art bloßer Wahrnehmung kontinuierlicher Lagen und nicht durch Rekurs auf einen (...) Eindruck der Identität des Objekts, (...) in seinem Wesentlichen gefaßt werden.“ [16]
>
> "[Translation] The specific, vivid character of movement (...) cannot through reference to the mode of pure perception of continuous positions and not through reference to an (...) impression of the identity of the object, (...) be gripped in its essence."

This insight later led to the proposition of the *principles of grouping* ("*Prägnanz*"). The central understanding of Gestalt is that stimuli are perceived as whole.

In the study of visual perception several laws (e.g., proximity, similarity, common fate, closure, symmetry, past experience), that demonstrate perceptual grouping of objects, have been proposed. The central law, *law of Prägnanz*, or *law of good Gestalt* states that patterns that are simple, regular, and consistent, are perceptually grouped [16, 17, 18, 19, 20].

For example, perception is used to interpret the sound of a ringing telephone correctly as such or to recognise smells, touch, and other sensory stimuli.

1.1.2 Attention

Attention is necessary for becoming aware of unitary objects, in normal condition focal attention and top-down processing operate together, however, as shown by Treisman and Gelade [21], in extreme conditions the two ways can operate almost independently [21]. Furthermore, attention is claimed to be "necessary for the correct perception of conjunctions, although unattended features are also conjoined prior to conscious perception" [21]. The results of several experiments on attention by Treisman and Gelade [21] suggest the ability to "detect and identify separable features in parallel across a display", but conjunctions "require focal attention to be directed serially to each relevant location" [21]. The authors conclude that "attention can either be narrowed to focus on a single feature, when we need to see what other features are present and form an object, or distributed over a whole group of items which share a relevant feature" [21].

The clinical model of attention, proposed by Sohlberg and Mateer, illustrates five components of attention: *focused attention*, *sustained attention*, *selective attention*, *alternating attention*, and *divided attention*. This model is based on observations of the attention process in patients with traumatic brain injury [22].

The term *sustained attention* refers to the ability to focus on a specific cognitive activity continuously over a period of time. Sustained attention is a necessary requirement for reading a newspaper for instance [23]. Sohlberg and Mateer [22] describe sustained attention using the subcomponents *vigilance*, necessary for maintaining focus on a task, and *working memory*, used for "manipulating information and holding it in mind" [22].

Selective attention is the ability to select and focus on some specific stimuli for a certain period of time. Hillyard et al. [24] define selective ability as the human ability to "confine their attention to a single auditory message within a noisy environment and to disregard equally intense but 'irrelevant' sounds" [24]. Sohlberg and Mateer [22] define selective attention as the *"freedom from distractibility"*; "Individuals with deficits at this level are easily

Component	Description	Assessment Tools
Focused attention	Response to discrete visual, auditory, or tactile stimuli	Simple orienting and tracking measures
Sustained attention	Vigilance and working memory	Continuous performance tasks, trails A, digit span, brief test of attention
Alternating attention	Set shifting, mental flexibility	Digit symbol, letter number (WAIS-III), consonant trigrams, trails B
Divided attention	Ability to respond to multiple, simultaneous tasks	Paced auditory serial addition test

Table 1.1: Clinical model of attention. Note. Reprinted from [22].

drawn off by extraneous, irrelevant stimuli" [22].

Alternating attention describes the ability to shift focus between multiple cognitive stimuli, and move between different tasks. Alternating attention is necessary for example for shifting between listening and taking notes during a presentation [22].

Divided attention is the ability to focus on multiple cognitive stimuli at the same time. While some models suggest "multitasking" or divided cognitive attention occurs by rapidly alternating attention, research has shown that this alternation would occur so rapidly making measurement very difficult [25, 26]. Sohlberg and Mateer [22] emphasize the importance of modelling divided attention, despite the criticism of cognitive performance under multiple simultaneous stimuli to reflect rapid alternating attention, to "highlight its importance in the rehabilitation context" [22].

Table 1.1 shows the components of the clinical model of attention, as outlined by Sohlberg and Mateer, along with tools for assessment of each component.

1.1.3 Memory

Memory is a crucial requirement for storing information and the learning process. Memory is divided based on the time memory is stored into short-term memory (STM) and long-term memory (LTM). Several architectural models have been developed, whereby multistore models suggest that STM and LTM require distinct representations, and unitary-store models suggest that STM and LTM rely on the same representations [27]. Most models of memory differentiate between LTM and working memory, and explicit and

System	Other terms	Subsystem	Retrieval
Procedural	Nondeclarative	Motor skills Cognitive skills Simple conditioning Simple associative learning	Implicit
PRS	Priming	Structural description Visual word form Auditory word form	Implicit
Semantic	Generic Factual Knowledge	Spatial Relational	Implicit
Primary	Working Short-term	Visual Auditory	Explicit
Episodic	Personal Autobiographical Event memory		Explicit

Table 1.2: Major categories of human learning and memory. Note. Reprinted from [29].

implicit memory [28]. One of the most widely used models of memory is the model by Dr. Endel Tulving, which had a large impact on the current understanding of human memory. This report will focus on the definition of memory components as defined by Tulving [29]. Aside from STM and LTM, Tulving [29] distinguishes memory between: memory and habit, episodic and semantic memory, and procedural and declarative memory [29]. Table 1.2 shows a summary of Tulving's components of memory.

The *procedural* memory is used for motor and cognitive skills. Cohen and Bacdayan [30] described procedural memory as "memory for how things are done that is relatively automatic and inarticulate" [30]. Studies on patients with amnesia, who lack other forms of memory, have shown that, while patients are able to learn and improve their performance in complex tasks, such as "The Tower of Hanoi" or priming experiments, they lack awareness of what they have learned. The rate of decay of procedural memory has been shown to be slower compared to other forms of memory [30].

Motor skills or *muscle memory* refers to the effect of motor learning. The effect results in motor activity that are performed without conscious attention on the task. One definition of Motor skills describes these as the ability to move the body: they "can be considered as based upon the capacity to organise the spatial-temporal and physical aspects of a movement and its different components in relation to - or in correspondence with - the spatial-temporal and physical aspects of a given situation" [31]. Motor skills are a part of procedural memory. However, they are sometimes tested separately when diagnosing for dementia or other cognitive dysfunctions.

The *perceptual representation system* (PRS) is largely non-conscious [32, 33]. "The concept of perceptual memory refers to the neural and cognitive processes underlying the storage of sensory information" [32]. The *input process* has been described by Kinchla and Smyzer [34] as how the stimulus invokes the sensory states, and the decision process determines the observer's reaction [34]. Tulving defines perceptual priming as "a special form of perceptual learning that is expressed in enhanced identification of objects as structured physical-perceptual entities" [29].

For *semantic* memory, Tulving suggests the concept "general knowledge of the world" [29]. The term semantic refers to the meaning of words. Quillan (1966) suggests that "cognitive and memory structure consists of nothing more than an aggregate of associated elements" [35] and asserts that "the issue with which a semantic model hast to come to grips with is not whether to use plans, attributes or simply associations, but rather what particular sorts of these are to be used to represent a word meanings, and exactly how all of them are to be interlinked" [35].

Primary, working or short-term memory is prominent for highly accessible short-term memory. Recent evidence shows that retrieval from STM is a "rapid, parallel, content-addressable process" [27, p. 204]. An important problem to understand STM is that of forgetting. Jonides et al. (2008) have suggested two explanations for the phenomenon of forgetting in STM: *time-based decay* and *similarity-based interference* [27].

Episodic memory is used to remember own past experiences. Tulving (2002) describes episodic memory to make possible "mental time travel through subjective time (...) allowing one to re-experience, through autonoetic awareness [i.e.: the ability of self-awareness over time], one's own previous experiences" [36].

The first evidence of the existence of STM and LTM came from studying patients with memory impairments. Primarily patient H.M., originally studied by Brenda Miller in 1966, who suffered from epileptic seizures due to a severe head injury. The removal of his two hippocampi, shown in figure 1.3 helped his epileptic seizures, but caused severe anterograde amnesia. H.M. showed normal performance in tasks of repetition but showed significant impairment in recalling information over longer periods. This insight led to the conclusion that different systems must be involved when storing information for a short period of time or for much longer periods. [6]

LTM can be differentiated between *explicit* and *implicit* memory. Declar-

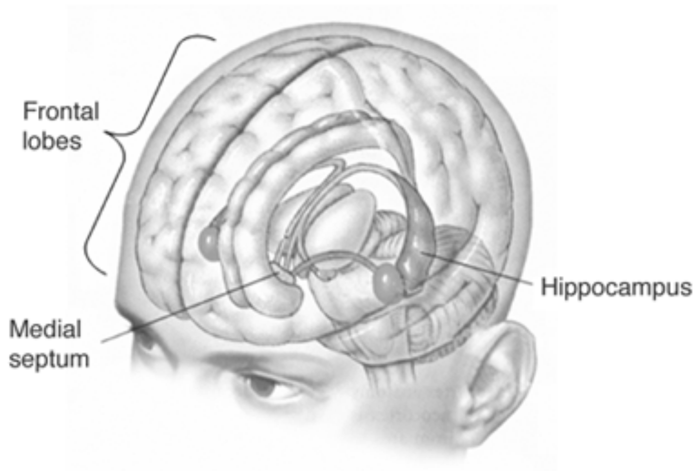


Figure 1.3: Location of the hippocampus, the medial septum, and the frontal lobes. In patient H.M. the two hippocampi where removed. Note. Reprinted from [37].

ative or explicit memory refers to information that is consciously recalled.

1.1.4 Language skills

Language skills are necessary to verbally express and understand words and sentences. Linguistic abilities are the most substantial difference in cognition between humans and other animals [6]. *Human communication* and *talk* can be regarded as a "social accomplishment". Talk can take a wide variety of forms, topics, intentions and means. Semin [38] described *talk* as the process of *choosing* words from a lexicon and *structuring* to form sentences within *real time constraints* [38].

Language skills are often studied through research on the cognitive learning and language development process in children. Epstein and Reilly [39] described the stages of hearing and speech development in children under five years as follows.

From birth to 12 months of age increasing understanding of language can be noted. From birth to 3 months of age, the child will laugh and use voice when played with, and be quite when spoken to in a familiar, friendly voice. At 6 to 9 months understanding of words can be noted; for instance, the child may look at an object when someone is talking about it.

First words appear from 12 to 15 months of age. At 12 to 18 months the child is able to speak 10 to 20 words, at 24 to 30 months 100 to 200, and at 4 to 5 years the child is able to speak at least 1500 words and talk freely, using full sentences [39].

In order to understand human linguistic abilities, artificial intelligence (AI) was used in computer programs to simulate these abilities. One of the first programs developed to simulate conversations is Winograd's SHRDLU program. Winograd argues, that to understand the human language understanding process "we need a program which combines grammar, semantics, and reasoning in an intimate way, concentrating on their interaction" [40]. SHRDLU is able to understand and answer questions about a virtual micro-world, as well as plan, guide and perform actions within this micro-world. In SHRDLU linguistic abilities derive from multiple cognitive processes, that perform specific actions [6, 40].

1.1.5 Visual and spatial processing

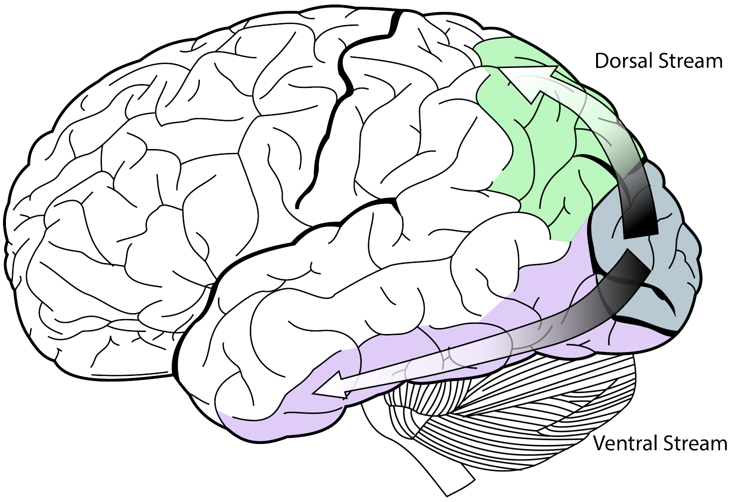
Visual and spatial processing refers to the ability to process visual and spatial information and therefore allows orientation in space and object perception. Fundamental to the understanding of visual processing is the *Two-streams hypothesis*. This model suggests two separate systems for the neural processing of visual information. The *ventral* stream is believed to be primarily used for recognition of shapes and objects, whereas the *dorsal* stream is used for analysing spatial location and orientation of objects [41, 42, 43]. The ventral stream follows a *ventral route* from the primary visual cortex to the temporal lobe, the dorsal stream follows a *dorsal route* from the primary visual cortex to the posterior parietal lobe [6], as can be seen in Figure 1.4.

A study on the visual pathways of patients with Alzheimer's disease (AD) using functional imaging found reduced brain activation in the frontal regions, basal ganglia, thalamus, and left and right superior parietal cortex, therefore less activation in the dorsal stream [44].

Subjects with the reading and learning disability dyslexia, have been commonly associated with deficits or superfluousness of visual-spatial abilities. One study, for instance, found that dyslexic subjects are better able to process visual-spatial information holistically [45].

Spatial orientation and visualisation is often examined through tests which require subjects to perform mental transformation of information, or mental transformation of perspective. For instance, in a test of visual memory, Juhel [47] presented a shape for 1 second to the test subjects, after a delay of 600ms, subjects were required to recognise the shape in a set of 20 items in the same orientation as the presented stimulus. In the second test subject had to mentally transform the shape before recognition [47].

Figure 1.4: Image showing ventral stream (purple) and dorsal stream (green) in the human brain visual system. Note. Adapted from [46].



1.1.6 Executive functions

Executive functions (EF), as defined by Miller [48], refer to the necessity for clear executive decisions, which are required "consequences of behavior in relation to the motivational needs of the whole organism"[48]. Koziol et al. [49] reformulate this definition as "the functions an organism employs to act independently in its own best interest, as a whole, at any point in time, for the purpose of survival"[49]. EFs are therefore necessary when concentrating and paying attention. They are the effortful action of considering and controlling actions and behaviour, and resisting temptations and impulses. [50]

Three core EFs have been outlined by Diamond [50] as: *inhibition*, *working memory* (WM), and *cognitive flexibility*. From these higher-order EFs such as reasoning, problem solving, and planning are constructed [50].

Inhibitory control or inhibition has been described as the ability to control one's attention, behaviour, thoughts, and/or emotions to internal predisposition or external lure. Inhibition therefore creates the possibility of choice. It allows one to focus and selectively attend on some chosen stimuli ("inhibitory control of attention" or "interference control at the level of perception"), while suppressing attention to other stimuli. *Cognitive inhibition* allows one to resist unwanted thoughts and memories, and to intentionally forget. *Self-control* is used to control one's behaviour, resisting temptations, avoiding impulsive behaviour, and keeping focus on the task at hand. [50]

Studies of children with attention-deficit/hyperactivity disorder (ADHD) have revealed impulsive behaviour and difficulties in the ability to inhibit actions, compared to children with no apparent psychopathology [51].

Psychological measures of inhibitory control include the *Stroop task*, *Simon task*, *Flanker task*, *antisaccade tasks*, *delay-of-gratification tasks*, *go/no-go tasks*, and *stop-signal tasks* [50].

Working memory (WM) is used to hold information in mind and work with it. It is necessary for many daily activities, such as understanding language, planning, or solving mathematical problems. WM makes it possible to make sense of information that is expressed over a period of time, by holding and relating past information to new stimuli.

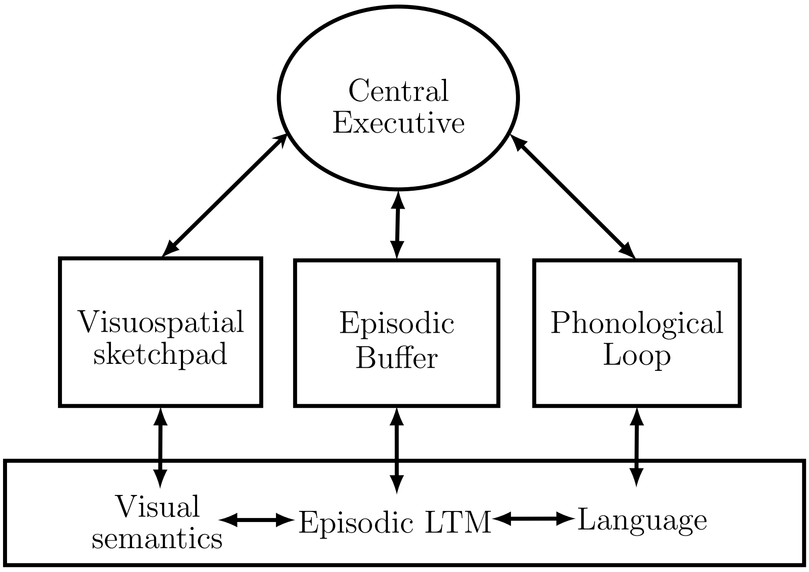
WM is different from STM, and they use separate neural subsystems. STM is used to hold information in mind, whereas WM is also used to manipulate information [50].

The Simon Task and Dots task illustrate the differences between WM and STM. In the Simon task subjects are asked to remember the two rules "for Stimulus 1 press on the right" and "for Stimulus 2 press on the left", this requires only STM. In the Dots tasks however subjects are asked "for Stimulus 1 press on the same side as the stimulus" and "for Stimulus 2 press on the side opposite of the stimulus", accomplishing this task requires holding the information in mind and translating the instruction on which hand to use [50, 52].

One method of explaining the relationship between STM and WM is the *working memory hypothesis* proposed by Alan Baddeley who separated STM into a variety of subsystem, as shown in Figure 1.5. The model consists of the *visuo-spatial sketchpad*, responsible for processing and maintaining visual or spatial information in the short-term, and the *phonological loop* for maintaining verbal information. These subsystems or "slave systems" are controlled by the *central executive* component, which has been described as the system responsible for controlling the flow information in working memory, including the connection to the LTM for storage and retrieval [6, 53]. The *episodic buffer* was added later to serve as an interface for the WM subsystems. In contrast to the previously explained concept of episodic memory by Tulving, the episodic buffer is short term, however, it is thought to play an important role in linking episodic LTM to WM for learning and retrieval [54, 55].

Cognitive flexibility allows mental changing of perspective and adjusting to changing situations [50]. For example in the dimensional change card sort test by Zelazo et al. [56], subjects are asked to sort cards according to one dimension, such as colour, and after several trials, subjects are asked to sort the cards along another dimension, such as shape. This task makes use of cognitive flexibility. In various studies, it has been shown that children at three years of age are unable to accomplish this task successfully, and con-

Figure 1.5: Baddeley's model of working memory



tinue sorting along the first dimension, whereas four to five year old children switch immediately to the new rule [56, 57].

1.1.7 Summary

Cognition has been defined as mental operations in the processing and acquisition of information, based on the definition of Reed [7] and Bermúdez [6]. Cognition has been divided in the cognitive domains: memory, language, perception, attention, language skills, visual-spatial processing, and executive functioning, as well as their relations to cognitive decline, and related mental disorders have been outlined. In the previous sections several means of assessing and treating cognitive decline have been introduced. Depending on the severity, reason for decline or loss, and cognitive abilities that is lost or declining, as well as several other factors, a mental disorder, including MCI, delirium, and dementia syndrome, which includes AD can be diagnosed.

Table 1.3 shows a summary of the cognitive domains, based on cognitive abilities, as well as examples of daily activities for which they are necessary.

1.2 Cognitive decline

In the previous section cognition has been described using the domains: perception, attention, memory, language skills, visuospatial processing, and ex-

Cognitive Domain	used for	exemplary use case
Perception	recognise and interpret sensory input	interpret the sound of a telephone
Attention	focus and become aware of unitary objects	reading & writing
Memory	information storage knowledge retrieval	learning & remembering
Language skills	express and understand words	talking & listening
Visuospatial processing	orientation in space and object perception	understand the layout of a room
Executive Functions	goal oriented behaviour Inhibition; Working Memory; Cognitive flexibility	resisting impulses; understanding mathematical problems

Table 1.3: Domains of cognitive abilities

ecutive functions. Cognitive decline describes the decline of one or multiple of the outlined domains. Most commonly memory or short term memory problems are mentioned when diagnosing or characterising cognitive decline. Most likely because it is the domain where problems are most notable, and easiest to assess. The following section will give an overview of mental disorders most commonly associated with cognitive decline, along with their characteristics, treatment, and assessment.

An important differentiation between cognitive impairment caused by cognitive decline, and pre-existing impairment should be made. Diagnosis for mental disorders related to cognitive decline can only be made if the cognitive impairment follows a previously higher state of cognitive functioning. That is the cognitive impairment cannot be linked to a pre-existing medical condition. Medical tests for the diagnosis of cognitive decline therefore often assess patients multiple times over a period of time. While for the diagnosis of a mental disorder the state has to be severe enough, decline always refers to a decrease from a previously higher state, rather than a comparison of cognitive functioning with the general population or otherwise expected cognitive functioning based on age, education or other factors.

1.2.1 Disorders associated with cognitive decline

Cognitive decline is a normal part of ageing in the elderly, most noticeable in minor memory problems and/or other cognitive functions. Decline is usually more significant in people with high cognitive ability at their normal state (i.e., mostly people with a high level of education) [58]. In people with lower cognitive ability, cognitive decline is proportionally smaller. Significant decline may often cause problems in daily functioning, usually leading to the diagnosis of a mental disorder. There are several mental disorders relating to cognitive decline, common disorders are delirium, dementia, and amnestic disorder.

Decline has been shown to be affected by environmental conditions. A healthy lifestyle and cognitive training have been shown to reduce the speed of decline, and improve cognitive functioning.

Mild Cognitive Disorder (MCI) is characterised by a short-term memory loss, that is greater than normal age-related cognitive decline. Patients with MCI often experience cognitive decline in multiple of the previously outlined cognitive domains, most notably memory, and short-term memory loss [59, 60]. Research often focuses on MCI because of its role as a potential pre-phase to dementia, including Alzheimer's disease (AD), and other cognitive impairments. Studies have shown a progression of MCI to AD of 10% to 15%, while others have found progression to AD as high as 40% to 65% of people with MCI [59]. Mitchell and Shiri-Feshki [61] found in a review of forty-one studies the adjusted annual conversion rate from MCI to dementia to be 9.6% in specialist clinical settings, and 4.9% in community studies [61].

In contrast to dementia, cognitive problems do not cause significant impairment in daily life, and are rather subtle but noticeable changes in cognitive ability. Impairments from MCI may occasionally interfere with daily tasks, and are often variable throughout the day [59, 62].

Although returning to a normal cognitive functioning from dementia is not possible with current methods, studies have shown that early treatment of MCI can lead to improvements of the cognitive state, and sometimes even recovery to normal cognitive levels. Early diagnosis of MCI is therefore crucial, to achieve the greatest possibility of recovery or improvement. Digital tools may offer a way for the diagnosis of MCI and even improvements of the cognitive state. For this reason, diagnosis of MCI shall be a primary focus of this research.

Memory problems often occur due to depression, high amounts of anxiety or stress, and other health or environmental conditions [59], a healthy lifestyle, including good nutrition, physical and cognitive exercising, social activity, etc., has been shown to lead to improvements in patients with MCI [59]. For instance performing cognitively stimulating activities, such as crossword puzzles [63] frequently has been shown to delay cognitive decline [64, 59].

Delirium is identified by changes in cognition developing over a short period of time and fluctuating throughout the day [3]. This acute state of impairment in delirium stands in contrast to dementia in which cognitive impairment can be described as a "chronic confusional state" [65]. Because of these fluctuations in cognitive state in delirium, the disorder is often not recognised by medical professionals [65]. Similarities of cognitive impairment between delirium and dementia also result in delirium to be sometimes confused for dementia, although the two disorders can even coexist [3, 66]. Delirium is however linked to a higher mortality rate than dementia [65, 66].

In addition to a higher risk of mortality in patients with delirium, patients with the disorder are also at increased risk of developing dementia, as for instance shown by Rockwood et al. [67].

Dementia is a syndrome affecting mainly older people and is linked to the development of multiple cognitive deficits, and causes severe impairment in occupational or social functioning. It can be identified by a cognitive decline in relation to previous cognitive functioning. Dementia symptoms can include among others, memory impairment, spatial temporal disorientation, language impairment, apraxia, agnosia, executive dysfunction and perceptual disabilities [68]. In order to diagnose for Dementia, according to the DSM-IV, symptoms have to be severe enough to cause impairment in daily functioning and must be accompanied by memory impairment [3].

Dementia syndrome describes multiple diseases, one of the most prevalent is *Alzheimer's disease* (AD). The symptoms of AD are as earlier described for dementia syndrome, however diagnosis for AD, according to the DSM-IV can only be made if the reason for cognitive impairment or dementia cannot be linked to other etiologies [3]. AD manifests in progressive memory and the loss of other cognitive abilities [69], especially the ability to learn new information. When the brain is learning, information is moved from WM to the LTM. Patients in the early stages of AD suffer primarily from a damage of the hippocampus [69], which has been linked to this function through studies on rodents [70]. In every day tasks the patient with AD will therefore find it easier to remember information that is already stored in LTM or episodic memory, such as memories from their childhood, but will have a bigger problems remembering recent events.

A popular scale for the assessment of dementia is the *Clinical Dementia Rating* (CDR). The CDR assesses six domains memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care. Each domain is assessed and graded based on five levels: 0 (none), 0.5 (questionable), 1 (mild), 2 (moderate), and 3 (severe) [71].

1.2.2 Summary

The mental disorders MCI, dementia, and delirium have been outlined. Diagnosis is currently performed with the help of the knowledge and experience of a medical professional. Assessment usually occurs only at brief intervals, which makes accurate assessment of the decline of cognitive ability difficult. Especially in the case of delirium inaccuracies are frequent, due to the fluctuating nature of the condition, as well as its similarities to dementia. A tool that is able to assess the cognitive state frequently, therefore, has great potential in giving more accurate information on decline, and could potentially more easily differentiate between delirium and dementia or MCI.

1.3 Aims and objectives

As shown in section 1.1, there are a variety of ways to assess cognitive capabilities and incapabilities. The literature research has shown that a variety of variables provide measurable results for the continuous assessment of cognitive decline, however the approach taken by the different studies vary greatly. The most notable difference has been found to be between studies focusing on the technical opportunities to detect cognitive impairment, which focus on indicative variables of cognitive impairment which can be assessed using current technologies, with studies focusing on the medical understanding of cognition and cognitive decline, which focus on developing a more complete overview of the cognitive state of a person through a variety of specific cognitive tests. This study shall introduce a new approach to early detection of cognitive decline associated with the mental disorders dementia and delirium, through a smartphone-based assessment similar to classical assessments, meaning users will be asked to complete specific questions designed to assess their cognitive state, in addition to a discussion on potential additional variables, assessed through smartphone-based sensing technology that can be combined for a more accurate overview of the cognitive state. This paper shall set an example for continuous technology-based assessment of cognitive impairment and lay the ground work for future semi-obtrusive detection of cognitive decline, as well as the recognition of accelerated decline, which could be linked to a mental disorder such as dementia, through the use of digital technologies to analyse user's behaviour in their daily lives.

This paper poses the research question:

> *How can smartphone technologies be used for continuous assessment of cognitive function?*

Several sub-questions have been formulated that shall be answered throughout this report:

- Which implicit sensing technologies and behaviour variables can be used in a smartphone to assess cognitive functioning?
- How can clinical examinations for cognitive impairment be digitalised for a smartphone application?
- How can these means of assessment interoperate for the assessment of cognitive state?
- How can these assessments be used continuously to monitor decline or improvement of cognitive function?

This chapter has introduced cognition and cognitive decline from a medical perspective. Chapter 2 shall introduce common measurements of cognitive assessment used in current clinical settings in comparison to new technologies means of assessment, that work in both unobtrusive ways, that is sensing technology is employed to assess behaviour, and obtrusive ways, that is applications which require user interaction. Chapter 3 shall introduce a new way of integrating traditional testing methods with newer forms of assessing cognitive impairment in a digitalised form. For this the creation of an application for cognitive assessment is described along with its design choices and a description of its specific implementation. Finally, in Chapter 4 the application is tested based on its usability and recommendations are made based on the survey for future use of the application. Chapter 5 will summarise and evaluate this work and provide recommendations for future research using the tool developed for this thesis.

Chapter 2

State of the art

This chapter shall give a general overview of the state-of-the-art in techniques of cognitive assessment and diagnosis of mental disorders related to cognitive decline, discussing both traditional methods that are currently used to diagnose patients, as well as opportunities for technological interventions, based on scientific literature research and commercial applications. The first section will focus on classical, clinical assessment techniques, that are commonly used in the diagnosis of a mental disorder, including dementia syndrome. The outlined techniques have been proven successful due to their intensive use and high correlation of results among the individual tests. The next sections will discuss modern digital techniques which focus on early assessment through an e-health and telemedicine approach. For this, a Literature Review has been conducted in order to explore the state of the art in unobtrusive assessment of cognitive functioning, with a particular focus on cognitive decline and related mental disorders. The research was conducted with the central question "*How can technology be used for unobtrusive assessment of human cognitive functioning?*". The effectiveness of these new methods is usually examined by testing for correlation of the results with proven tests used in clinical settings.

2.1 Clinical cognitive assessment techniques

2.1.1 Informant Questionnaire on Cognitive Decline in the Elderly

The *Informant Questionnaire on Cognitive Decline in the Elderly* (IQCODE) assesses cognitive decline over a span of ten years, through a questionnaire consisting of 26 questions covering aspects of memory and intelligence, that is filled out by an informant of the subject. Items are ranked on a scale from 1 "much better" to 5 "much worse". The IQCODE rating can, therefore, cover both cognitive decline as well as cognitive improvement. While IQCODE has high reliability and studies have shown correlations between the results from IQCODE and other cognitive screening tests, the results are affected by the mental health of the informant and the relationship between the subject and the informant [72, 73, 74].

In contrast to the other cognitive assessment tests and examinations that will be explained in the following subsections, the IQCODE is the only one that is assessed through information given by the informant, rather than a direct assessment of the subject.

The IQCODE is used to give examiners an overview of the cognitive performance of a subject over a longer period of time. While the assessment has several shortcomings, depending on the informant, it offers insights that are difficult to obtain otherwise, such as directly from the cognitively impaired subject.

2.1.2 Benton Temporal Orientation Test

Prior research has shown failures in time orientation are a common feature in these mental disorders [75]. Based on this notion assessment of orientation to time could be useful in diagnosing cognitive impairment in patients [76]. This has led to the development of the *Benton Temporal Orientation Test.* The test assesses temporal orientation, by asking patients to identify the correct time of an event.

The test quantifies the degree of error through a maximum score of 113 and deducts points for deviations from the correct time: 10 points per year, 5 points per month, 1 for date and weekday and 1 per 30-minute deviation [77, 78].

2.1.3 Recall Test

The *recall test* is a test of memory and learning ability. In this test subjects are asked to learn and recall pairs of information in the form of pictures, words, or objects. There are two types of recall tests, the *free recall test*, requires subject to recall items "freely", that is without aid and in no particular order. In the *cued recall test* subjects are given cues to aid the recall process.

Some examiners of cued recall tests ask subjects to learn word combination of a foreign language [79], whereas other tests ask subjects to identify pictures of different objects [80]. Some examination include cued recall tests in the diagnosis of cognitive ability in various forms, which shall be explained in their respective subsections. The tests vary not only in the type of information that is recalled, but also in the number of items to be recalled, studying time and frequency, duration and cognitive activity during the delay task, before subjects are asked to recall the information [80, 79, 78].

For example, Meulen et al. [78] in *"The seven minute screen"* used an *Enhanced cued recall* test, in which subjects were asked to identify 16 pictures, using four at a time. Recall was tested immediately, and after a delay, in which another task is conducted. If the subject is not able to recall the picture spontaneously, the examiner gave a respective semantic cue [78].

2.1.4 Verbal fluency test

The *verbal fluency test* (VF) (also "word generation test") asks participants to list as many words of a given category or beginning with a specific letter as possible within a time frame. It is a commonly used test in neuropsychological evaluation [81]. When participants are asked to generate words that begin with a specified letter, this is called *phonetic fluency*. When participants are asked to generate words of a specific category it is called *semantic fluency*.

2.1.5 Intersecting pentagons

Another tool, that is sometimes used to diagnose for dementia and similar mental disorders, is testing for the inability to *copy intersecting pentagons* (IP). The test is part of the first publication of the Mini-mental state examination (MMSE) [82]. The MMSE asks examiners to draw intersecting pentagons, subjects are then asked to copy it exactly. For successful completion of the task in the MMSE, all 10 angles must be present and 2 must intersect. Tremor and rotations are ignored [82].

This intersecting pentagons copying test examines visuospatial ability and construction [83].

The pentagon copying test is sometimes used to differentiate subjects who have already been diagnosed with a cognitive impairment from related examinations, such as the MMSE, which will be explained later. Ala et al. [83] used it to differentiate between dementia with Lewy bodies (DLB) and Alzheimer's disease (AD), by testing patients with MMSE scores $\geqslant 13$. The researchers assumed the ability of the test to differentiate DLB and AD, because of visuospatial / constructional impairment prominent in DLB. The results from this study of 17 patients with DLB and 27 with AD suggest that the inability to draw intersecting pentagons in patients with MMSE scores

$\geqslant 13$, is more likely a predictor of DLB rather than AD [83].

2.1.6 Clock Drawing Test

The *Clock Drawing Test* (CDT) is a test commonly used by practitioners to screen for dementia. As described by Royall et al. (1998) "the severity of clock drawing failures progresses over time in Alzheimer's disease, and correlates with longitudinal changes in cognitive testing" [84]. The administrative ease, along with its good reliability has resulted in widely accepted use of CDTs. The patient is asked to draw a clock at a specific time, usually 10 minutes after 11 [84, 85]. The CDT has proven very effective, partly due to the simplicity and speed of the test, when compared to others such as the MMSE. Because the clock is a universal symbol the CDT can be administered cross-culturally. The CDT tests for memory, visuoconstructional skills, and executive function [86, 87]. There are many differences in how the CDT is administered and scored. Many studies make use of the CDTs CLOX1 and CLOX2. CLOX1 asks the subject to draw the clock face on a blank sheet of paper, whereas in CLOX2 subjects are asked to copy a clock face [88].

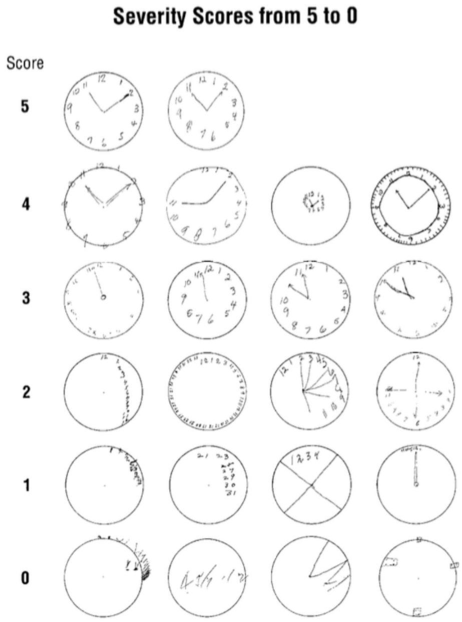
The first attempt of developing a scoring system for the CDT was made by Shulman et al. [89], which consisted of a score ranging from 1 (minor errors) to 5 (no reasonable attempt of drawing a clock) [89]. This score was later reversed in order to award the highest score of 5, when the subject was able to draw an intact clock and the lowest score of 0 to the most impaired subjects [85]. Figure 2.1 shows an example of the severity scores as defined by Shulman [85].

Another method of denoting the score for the CDT is the Clock Drawing Interpretation Score (CDIS), this system awards 3 points for general impression, 12 for 'code number' items, and 5 points for 'code hands' items, resulting in a total of 20 points. In the study on 46 subjects diagnosed with Alzheimer's disease and 26 non-diagnosed control subjects, all control subjects had CDIS scores of 18 or more and only 8.7% of the diagnosed subjects scored 18 or more [90]. This shows the reliability of the CDT along with the CDIS system in analysing presence and severity of dementia.

However, there are many different scoring systems for the CDT which results in a bias in the evaluation results, especially for patients with other physical or mental impairments, such as vision, language or physical disabilities. A commercial approach that tries to reduce this risk of bias, by making the test available worldwide over the Internet, is the Automatic Clock Drawing Test™[1] (ACDT) [86].

[1] available at: http://www.specialtyautomated.com/

Figure 2.1: Severity scores from 5 to 0. Note. Reprinted from [85]



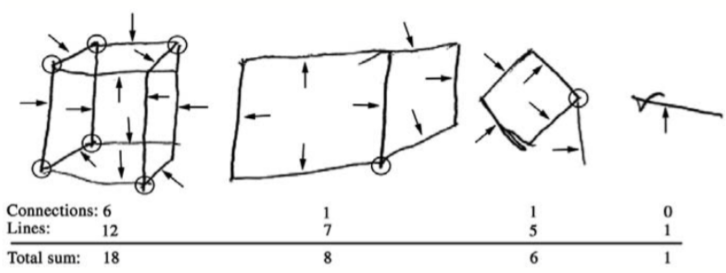
2.1.7 Necker Cube Copying

Necker cube copying is a task to measure visuospatial abilities and to some extent constructional ability. The ability to copy the Necker cube has been shown to deteriorate in patients with AD. The task is therefore used in clinical assessments of dementia [93] and is also part of the Short Test of Mental Status (STMS) [94]. The Necker cube is a three-dimensional, reversible figure defined by the Oxford English dictionary as: "A line drawing of a transparent cube in which the lines of opposite sides are drawn parallel, so that the perspective is ambiguous and the orientation of the cube appears to alternate." [95].

In a study to test the implications of the tasks, Shimada et al. [93] found that half of 15 AD patients with CDR scores of 1 and 2 were unable to draw a three dimensional figure. The researchers concluded: "Copying the Necker cube may be a useful task for the detection of very mild AD." [93].

Other studies showed similar results, such as Palmqvist et al. [92], who were able to show a deterioration the ability to copy a cube for untreated AD patients of the course of 6 months [92]. The authors made use of the assessment developed by Maeshima et al. [91], whereby the connections and lines in the cube are evaluated. For the 8 connections formed at the point where the lines meet, subjects are able to score a maximum of 8 points.

Figure 2.2: Four cube drawings made by different patients and the assessment based on Maeshima et al. [91]. Note. Reprinted from [92]



Deviations of the lines from the connection points must be less than 3 mm to be considered as accurate. The twelve lines of the cube have a maximum score of 12 points. Figure 2.2 shows four cube drawings by subjects of the assessment by Palmqvist et al. [92], in contrast to Maeshima's method, the researchers did not count incorrect lines, the maximum score was therefore 20 points [92].

2.1.8 Mini-Mental State Examination

The *Mini-Mental State Examination*[2] (MMSE) is commonly used to diagnose patients with dementia, but can also be used in the detection of MCI. The MMSE is a ten-minute test covering temporal and locational orientation, repetition, comprehension, attention, reading, writing and drawing. The score is calculated with a maximum of 30 points. A score of 24 or higher indicates normal cognitive functioning [96, 97].

The original MMSE as defined by Folstein et al. [82], consists first of an orientation part awarded with a maximum score of 10 points that assesses spatial and temporal orientation, by asking the patient to correctly identify the current time (year, season, date, day, and month) and location (state, county, town, hospital, and floor). In the *registration* part subjects are asked to repeat three unrelated objects, for a maximum score of 3 points. The next task then assesses *attention and calculation* by asking participants to subtract 7 from 100 five times, or alternatively to spell the word "world" backwards for a maximum of five points, before asking the subjects to *recall* the three objects from the registration part, for a maximum of 3 points. The final part of the MMSE is *language* with a maximum score of 9 points. This part

[2] see: http://www.minimental.com/

consists of multiple tasks that assess the subject's ability of *naming* (subjects are asked to name two objects), *reading* (subject are asked to read and follow a command), *writing* (subjects are to write a sentence of their choosing), *copying* (subjects are asked to copy intersecting pentagons). Finally, the examiner is to assess the level of consciousness of the subject from alert to coma [82].

While the MMSE has shown correlation with other cognitive examination tests, and it is used by approximately 9 out of 10 specialists [98], it has been criticised due to possible correlation of the results to the subject's level of education, age, and literacy [99, 98].

In order to improve the reliability of the MMSE the *Standardized Mini-Mental State Examination* (SMMSE) was developed. The SMMSE provides guidelines on the assessment of the MMSE, that were not available in the original MMSE. The guidelines are related to the set-up, administration, and scoring of the MMSE. For example, the SMMSE introduces explicit time limits, that were not present in the original MMSE [100].

2.1.9 Quick mild cognitive impairment screen

The *Quick mild cognitive impairment screen* (QMCI) is a test specifically developed to differentiate between mild cognitive impairment (MCI) and normal cognition (NC) [101], but is able to assess cognition up to severe dementia, and is more sensitive than the SMMSE [102]. The QMCI consists of six subtests in the domains: orientation, working memory (registration), visuospatial/executive function (clock drawing), semantic memory (verbal fluency), and episodic memory in test of delayed recall for words and logical memory.

The scores for components of the QMCI are as follows: orientation is scored with a maximum of 10 points, 5 points for registration, 15 for the clock drawing test, 20 points each for the registration and verbal fluency tests, and a maximum of 30 points for the test on logical memory [102].

2.1.10 Short Test of Mental Status

The *Short Test of Mental Status* (STMS) was developed as a screening method specifically for mild dementia. The very popular MMSE falls short in early detection of dementia and detection of MCI. The STMS contains a four words delayed recall tasks, that is specifically intended to be sensitive to learning and recall problems in MCI and early dementia [94, 103, 104]. The STMS consists of orientation, attention, learning and immediate recall, calculation, abstraction / similarities, information, construction, and recall.

The maximum score is 38 [94]. In a study comparing the differences between the MMSE, and STMS, it was shown that the STMS performed slightly better in detecting MCI, the two tests were indistinguishable in the detection of dementia [94].

2.1.11 Addenbrooke's cognitive examination

The *Addenbrooke's cognitive examination* (ACE) is a test of memory, language, attention, orientation, verbal fluency, and visuospatial ability [105, 106]. ACE was developed as a method for early detection of dementia syndrome, as well as to differentiate between different dementia subtypes, including AD, and frontotemporal dementia (FTD) [107, 108, 109].

The ACE shares many similarities to the MMSE in terms of testing and scoring. The maximum score for the ACE is 100. The attention and orientation components are equivalent to those of the MMSE, and have a maximum score of 8 and 10 respectively. The memory component has a maximum score of 35, it includes the word recall test from the MMSE, in addition to a "name and address learning and delayed recall" test, and tests for semantic memory. In the language component, for a maximum score of 28, subjects are asked to complete tests of naming, comprehension, repeating, reading, and writing. Finally, the component for visuospatial ability consists of the pentagons (from the MMSE), cube, and clock drawing tests [108].

2.1.12 Cognitive Abilities Screening Instrument

The *Cognitive Abilities Screening Instrument* (CASI) is a test of memory (STM and LTM), attention, language skills, visual construction, list-generating fluency, abstraction, and judgment. The CASI consists of: place and date of birth, age, number of minutes in an hour, direction of sunset, repeating three words, repeating digits backward, first recall of the three words, serial subtractions of 3, temporal orientation, abstracting similarities between pairs of items, judgment, repeating sentences, executing a simple written command, writing a dictated simple sentence, copying two intersecting pentagons, following a three-step oral command, second recall of three words, naming five body parts and five common objects, and recalling the five objects. Furthermore, in order to provide a *universal* experience, it is recommended to account for "cross-cultural applicability", when replacing or modifying items from the test [110].

The CASI is commonly used to assess cognitive functioning in patients with dementia, and to track the progress of dementia in patients [111, 112].

Test	Task	Assesses
Benton Temporal Orientation Test	identify the correct time of an event	temporal orientation
(Cued) Recall Test	learn pairs of information (words, pictures, objects)	memory learning ability (EF)
Intersecting Pentagons	copy a drawing of intersecting pentagons	visuospatial ability construction
Clock drawing test	draw or copy a clock face (at 11.10)	memory visuoconstructional skills executive function
Necker Cube Copying	draw a copy of the Necker cube	visuospatial ability construction
Verbal Fluency Test	List as many words as possible of a category within 60 seconds	verbal fluency semantic memory

Table 2.1: Cognitive Tests used to diagnose dementia and other mental disorders

2.1.13 Summary

Several cognitive assessment tests, commonly used in the professional diagnosis of dementia, MCI, and other cognitive impairments exist. The examinations differ in the cognitive components, and the severity and type of cognitive impairment they assess. Table 2.2 shows a comparison of commonly used examinations, which have been outlined earlier.

Examinations of cognitive impairment consist of a variety of tests for different cognitive domains, and that use different variables, such as the CDT, VF, recall tests, and more. For some digital versions exists, such as the ACDT for the CDT. Many of these tests are part of the professional examinations, for instance, the CDT is part of the MMSE. Figure 2.1 shows a summary of the mentioned cognitive tests. Additionally, a number of tests for digital, remote assessment exist, which will be explained in the next section. The development of digital versions for assessment on a smartphone may be possible.

Prominently mentioned assessment tests for the diagnosis of cognitive functioning and dysfunction, including diagnosis for dementia syndrome are for example: the *Benton Temporal Orientation Test*, the *Clock Drawing Test* (CDT), the *Informant Questionnaire on Cognitive Decline in the Elderly*

Test name	Assessment components	Used or developed for
MMSE	Orientation (temporal & locational) Repetition Comprehension Attention Reading Writing Drawing	Severe cognitive impairment (e.g.: AD)
QMCI	Orientation WM (Registration) Visuospatial/EF (CDT) Semantic memory Delayed recall Logical memory	Mild & severe cognitive impairment (e.g.: MCI, AD)
STMS	Orientation Attention Learning & immediate recall Calculation Abstraction / Similarities Information Construction Delayed recall	Mild & severe cognitive impairment (e.g.: MCI, AD)
ACE	Memory Language Attention Orientation Verbal fluency Visuospatial ability	Early dementia Dementia subtypes
CASI	Memory (STM & LTM) Attention Language skills Visual construction List-generating fluency Abstraction Judgement	Cognitive function (Dementia)

Table 2.2: A selection of tests used by practitioners in the assessment of cognitive ability and diagnosis of mental disorders

(IQCODE), the *Mini-Mental State Examination* (MMSE), and the *Montreal Cognitive Assessment* (MoCA). Cognitive science can be understood as the science of the mind, which is fundamentally linked to brain activity. Therefore neuroimaging of the brain, through technologies such as functional magnetic resonance imaging (fMRI), magnetic resonance elastography (MRE) or positron emission tomography (PET) can grant insights in cognitive functioning and aid in the diagnosis of cognitive impairments [6]. Because of this large number of existing techniques, questionnaires and scales of diagnosing cognitive impairments, several measures combined with the professional opinion of the practitioner are used together in the assessment for dementia and other cognitive impairments [3].

With regards to the characteristics of dementia, as well as its assessment using the aforementioned diagnosis tests, in order to derive at a meaningful diagnosis of mental disorders of cognitive impairments, the outlined cognitive domains play an important role; However, depending on the severity of impairment, and depending on the disorder to be assessed for, the domains have varying weights of importance. In the professional tests this can be noted based on the varying scores for the different domains of assessment. The development of the scoring systems in these tests is usually based on research in the disorders and the severity range the test is designed to assess. For example, in the very early stages of dementia the most cognitive impairment occurs in the memory domain [113], which is why memory is assessed in the majority of tests, and usually has a very high maximum score.

Tests for each cognitive domain vary greatly, for instance in the case of memory distinctions have to be made in the type of memory that is assessed, as well as the specifics of tests, in the case of memory, the nature of the information (verbal, visual), the duration between learning and recall (delayed or immediate recall), and the process of recall (free recall, cued recall, recognition) [114].

2.2 Techniques for digital assessment of cognitive functions

In this section, several newly developed tools and applications for digital assessment of cognitive functioning are introduced. Special focus lies on the assessment of cognitive decline, MCI or early stage dementia. Digital in this case means, that in contrast to traditional assessment methods of cognitive functioning or impairments, the tools introduced in this section rely on assessments through digital measurements and assessment functions.

In addition to digital tools for diagnosing MCI influential developments have been made in the form of specialised applications that are able to prevent or reduce symptoms of dementia and similar cognitively impairing disorders. The techniques and technologies used in these can prove very useful in the development of any tool for dementia patients. The following section will introduce a few of the developed application for the treatment or prevention of dementia at different stages.

Verve *"Vanquishing fear and apathy through E-inclusion"* (Verve)[3] is an EU research project that "aim[s] to develop new technologies to support the treatment of people who are at risk of social exclusion, either because of fear and apathy associated with ageing, or because of a neurological disorder" [115].

One serious game developed by the initiative is *"Kitchen and cooking"*. In this game, participants are asked to cook a variety of virtual recipes. The game consists of an attention and object recognition task, whereby the participants select the right ingredients. The next step is to plan the order in which to perform tasks, a task of executive functioning. Finally, a task of motor skills, in which the subjects perform specific cooking related gestures. The game tracks error and time spent on the individual and total activities. The game was developed for patients with both AD and MCI. The results from the study show that *"Kitchen and cooking"* can be used for both assessment and training of cognitive functioning. The researchers showed that the results of the cognitive assessment based on the time spent on each activity was in line with classical assessment methods. Furthermore, the researchers suggested "Kitchen and cooking" as a training tool based on the results that AD and MCI patients were able to improve their game performance over time [116].

Hagler et al. Hagler et al. [117] developed a passive infrared motion sensor system that measures walking speed. The research has shown a decline in gait velocity prior to cognitive decline. The passive infrared system consists of sensors placed at a short distance apart. The researchers developed a model in order to estimate the velocity of the walking speed [117].

Hayes et al. (2008) Hayes et al. [118] used motion and contact sensors based on the X10 protocol in order to measure in-home activity. Walking speed was estimated based on the speed and order at which different sensors were fired. Based on the sensor firings a model for daily activities could be

[3]http://verveconsortium.eu/

constructed. For instance, the number of times a subject was out of home was calculated based on a lack of sensor firings. Using these sensors, the researchers could demonstrate differences between MCI and non-cognitively impaired subjects, that is in line with literature correlating walking speed with cognitive impairment [118].

Shoval et al. (2011) Shoval et al. [119] collected location data of 41 participants over a course of 28 days, by making use of a device with a global positioning system (GPS) receiver in combination with a Global System for Mobile communications (GSM) modem. Three groups of subjects were formed: those with MCI, those with dementia, and subject without cognitive impairments. The researcher set to answer the question: "does the timing and distance of out-of-home mobility vary with the level of cognitive impairment?" [119, p. 854]. The results show that distances in out-of-home activities were smaller for those with cognitive impairment and that "daily time pattern of those participants with cognitive impairments was less varied and less modulated in comparison with those with higher cognitive function" [119].

Dawadi et al. (2013) Dawadi et al. [120] aimed to "provide automated task quality scoring", as well as, to classify the cognitive state of subjects as "cognitively healthy, MCI or dementia" using machine learning techniques on collected sensor data. The researchers used a smart home environment equipped with a variety of sensors, including motion sensors, door sensors, item sensors, temperature sensor, and electricity consumption. Participants were asked to perform eight activities, namely: sweep the floor, retrieve and fill medicine containers, write a card, setup and watch a video on a DVD, water the plants, answer the phone, cook a soup, and finally select clothes from the closet. The experiment was performed by 263 individuals. Supervised, using a support vector machine (SVM), and unsupervised, using principal component analysis (PCA) machine learning algorithms were used to assess activity quality. For the classification of subjects' cognitive states, a support vector machine and logistic regression classifier algorithms were used. The results show that it is possible to use machine learning techniques for the assessment of task quality and receive a score that correlates with observations by a trained clinician, as the potential of cognitive performance analysis through machine learning techniques [120].

Clustering home activity distributions The study uses unobtrusive sensing technology in homes to detect MCI in older adults. Multiple sensors including infrared motion sensors, bed sensors, and temperature sensors were placed around the home, to detect activity. The researchers found that measuring activity as the total number of sensor firings did not lead to meaningful results. An "inhomogeneous Poisson process to model the presence of subjects within different rooms throughout the day" was constructed. The researchers developed a clustering technique based on 85 subjects, who were administered over the course of three years. The researchers differentiated between non-amnestic mild cognitive disorder (na-MCI) and amnestic mild cognitive disorder (a-MCI). 11 subjects had a-MCI at baseline or developed a-MCI during the monitoring period and 15 subjects had na-MCI at baseline or developed na-MCI during the monitoring period. "The best performance was obtained using a time frame of 20 weeks and a slide size of 4 weeks". The study furthermore found that, "subjects experiencing symptoms of na-MCI had room activity distributions that were significantly different from their room activity distributions when there were cognitively intact.", and that for a-MCI subjects there were no such differences, apart from bedroom activity, which the researchers related to disturbed sleep patterns caused by the a-MCI [121].

COGCAM In *"COGCAM"* cognitive stress is measured based on the subjects' heart rate, breathing rate, and heart rate variability. The researchers captured these parameters using photoplethysmography (PPG), and a camera placed at a distance of 3 meters from the subject. The experiments consisted of a ball control task were subjects were to control a virtual ball using a computer touchpad, and a shortened 64 card version of the *Berg Card Sorting Task*. The researchers developed a model using Naïve Bayes Classifiers for recognising cognitive stress and compared this with answers from a shortened version of the Dundee Stress State Questionnaire. The results show the best reliability for classification based on changes in heart rate variability [122].

ProactiveTasks The study *ProactiveTasks* explores new concepts for interactive smartphone lock screen designs, based on prior research on improving and streamlining the user experience. The researchers classify smartphone interaction into three types: glance, review, engage. *Glance* sessions are described as where the user only looks at information on the lock or home screen, *review* sessions describe when the user interacts with one or two applications for a brief period, and in *engage* sessions the user interacts for a longer period of time with smartphone applications. In a study of 10 participants over a period of 18 to 36 days, assessing smartphone sessions, *glance* and *review* sessions occur most often. The researchers found that users often engage in *glance* sessions to check for new data, and current interfaces have limited diversity for these short sessions. They, therefore, propose a prototype of *ProactiveTasks*, which should proactively suggest review tasks, when the user engages in *glance* sessions. The prototype was evaluated using a study of 30 participants and discussed the aspects of visibility, intrusiveness, efficiency, cognitive and physical demand, multiplicity, security and privacy, and presentation strategy [123].

Kaye et al. (2014) Kaye et al. [124] assessed daily activities and computer use of subject with MCI and compared to subjects without cognitive impairments. Motion and contact sensors placed within the homes were used to unobtrusively assess daily activity, time out of home and walking speed. Computer use was assessed by capturing mouse movement data. The researchers calculated measures for daily computer use and variability or consistency based on the coefficient of variation per month. The results from the study show that "computer use is significantly different over time between independently living older persons with MCI and age-matched, non-cognitively impaired volunteers." The researchers argue that with increasing cognitive decline, individuals "may increasingly keep their sessions brief and less frequent." While the rate of decline for the MCI group was small the researchers conclude that "continuous assessment of computer use is sensitive to subtle early decline in MCI" [124].

Ouchi and Doi (2012) In the study *"Indoor-Outdoor Activity Recognition by a Smartphone"*, the researchers assessed indoor and outdoor activities using smartphone sensors. In order to recognize activities of daily living and classify between activities of daily living (ADL) and Instrumental ADL (IADL) an Android smartphone application was developed, consisting of an indoor and an outdoor activity recognition engine. IADL describes activities that are not fundamental to daily life, such as personal hygiene and eating, but that are often an integral part of independent living, such as cooking, cleaning, shopping. The indoor activity recognition engine classifies movement based on data from the accelerometer when *performing a living activity* was recognized, the microphone was activated and on the basis of the acoustical signal the Mel-frequency cepstral coefficient (MFCC), root mean square (RMS) and zero-crossing rate (ZCR) were calculated. Indoor living activity recognition was performed using an SVM classification approach. For the outdoor migration activity recognition engine data from the accelerometer was used to calculate the direction of gravity and direction of the device, from which classification into *resting*, *walking*, *running*, *boarding* could be performed [125].

BioPhone The researchers behind the *BioPhone* study explored the technical opportunities of Ballistocardiography (BCG) measurements using smartphone accelerometer data. BCG is “a method for obtaining a representation of the heart beat-induced repetitive movements of the human body, occurring due to acceleration of blood as it is ejected and moved in the large vessels” [126].

BCG is often used when unobtrusive measurements are desired. The BCG results can be compared with measurements for heartrate (HR) and breathing rate (BR) from electrocardiography (ECG) equipment. The researchers performed BCG measurement while the smartphone was in various natural positions; in the pocket, in a bag, and in the hand, while the user was engaging in a variety of smartphone-related activities, namely typing, watching a video, and taking a call. The results from the BCG results for HR and BR were compared with measurements from ECG measurements. The results of the study show, that HR and BR data can be measured using smartphone accelerometer, however motions due to usage of the phone has a negative impact on the measurements results. The researchers, therefore, recommend “to provide sporadic assessment during the day when the amount of motion is small (e.g., reading a book, watching TV)” [127].

SmartFABER The SmartFABER system is a “powerful data analysis tool at the service of practitioners”. It is able to recognise abnormal behaviour possibly indicative of MCI. SmartFaber employs a machine learning algorithm for recognising activities in the homes of elderly subjects. SmartFaber is an OWL2 ontology for a variety of IADLs describes as sequences of actions [128].

LOTAR Riboni et al. [129] developed a framework called LOTAR for behavioural analysis and anomaly detection. Sensing devices such as environmental sensors, magnetic sensors, presence sensors and RFID tags were employed and the data was statistically analysed using the SmartFABER algorithm. IADLs were defined a consisting of multiple sequences. For short-term anomalies the researchers differentiated between *omissions*, sequences of an IADL that were not performed, *commissions*, sequences that are performed inaccurately, and *additions*, actions that are performed unnecessarily. According to Riboni et al. [129], “short-term abnormal behaviors are only indicators of possible cognitive issues”, however frequent anomalies over longer periods of time may indicate cognitive impairment, or the progression of MCI [129].

Civitarese et al. (2016) Civitarese et al. developed a system for recognition of activities of daily living (ADL), by using various environmental smart home sensors and creating an object manipulation model from the sensor data. Accelerometer sensors, along with a device for wireless transmission were attached to various items used by the elderly test subjects, namely a liquid bottle, medicine boxes, and a knife. From the sensor data, the researchers used a recognition technique based on supervised machine learning, after omitting irrelevant manipulations, to distinguish between relevant and irrelevant object displacement and object activities (such a drinking or pouring from the bottle). The paper shows a possible method for unobtrusive detection of ADL of elderly people in smart homes, using accelerometers and Bluetooth low energy module, along with a processing method using a machine learning classification approach [130].

Cognitive Research Tools, J. Stone Stone and Towse [131] developed a range of cognitive research tasks for the *Tatool* research tool, including verbal, visuospatial, working memory, processing speed, and others. The tools developed by the researchers are all freely available online[4].

In their study *"A working memory test battery"*, Stone and Towse (2015) differentiate between verbal and spatial WM tasks. Each task consists of a storage and a processing stage. In the storage stage, the subject is asked to store a small chunk of information, such as a numeral, location on a small grid, or the rotation of an arrow. The processing stage consists of a processing task, that is unrelated to the information of the chunk from the storage stage.

The primary differences between the tasks lie in the processing stage; in the *operation* task, the subject is asked to judge on the correctness of a mathematical equation, in the *reading span* task the correctness of a sentence is evaluated, and in the *digit span* task, no processing task is used. In the *spatial WM* tasks, the information chunk is spatial (an object in a grid), rather than a numeral. In the *symmetry* task, the subject is asked to judge on the symmetry of a maze pattern, in the *matrix span* task, the processing stage is again left out. The *rotation span* stage is similar to the previously explained task, but the information from the storage stage is the rotation of an arrow, in the processing stage the user is asked to evaluate whether a rotated letter is mirrored, and in the *arrow span* task the processing stage

[4]see: http://www.cognitivetools.uk/

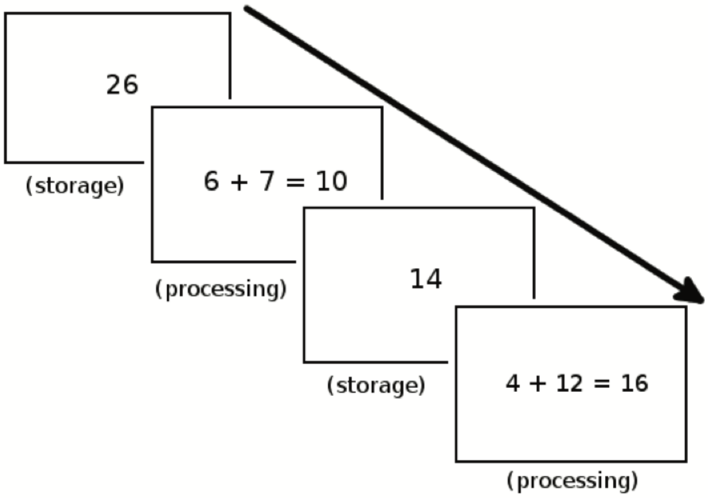


Figure 2.3: Illustration of the operation span task. Note. Reprinted from [131].

is left out again. Figure 2.3 shows an illustration of the *operation span* task, consisting of the different storage and processing stages. The processing-storage order is similar in the other tasks, as outlined. [131]

Tatool Stone and Towse developed their test for the research tool Tatool. *Tatool*[5] is an open-source research tool for psychological experiments written in the Java programming language. The software is extensible, platform-independent, and can be used both online and offline. It is open source and licensed und the GNU Lesser General Public License.

Tatool was developed for the research of cognitive training, and can be used for experiments and questionnaires. Module files for study components can be programmed using Extensible Markup Language (XML). The data is stored in a database and can be exported as a comma-seperated value file (CSV) for analysis using other programs. [132]

Stone offers a variety of Tatool modules for cognitive tasks, including the ones previously outlined online[6].

Tapbrain *Tapbrain* is a serious game consisting of “13 mini-games to stimulate brain exercise and four mini-games to induce physical activity” [68]. The aim of *Tapbrain* is according its developers “to design a game that can stimulate cognitive brain functions by targeting subfactors of the said

[5]available at: http://www.tatool.ch/

[6]available at: http://www.cognitivetools.uk/

two types (those that stimulate the brain and those that induce physical movements) in our mini games" [68]. The researchers propose a game that distinguishes individuals, using quick response (QR) or near-field communication (NFC) technologies and assesses the level of dementia. Initially, the researchers use the MMSE for diagnosis of potential dementia and then start a customised game based on the assessment results. *Tapbrain* examines the performance after gameplay and offers 17 mini-games with 5 difficulty stages for the cognitive domains: memory, attention, problem solving, response / decision making and physical activity games for hand and upper body. [68]

2.3 Commercial applications for cognitive assessment and treatment

The following section will introduce several commercial applications for the assessment and treatment of cognitive decline or cognitive impairment. These commercial applications often offer a variety of games, quizzes, and other methods of assessment in the form of digital platforms. The platforms are usually offered for a variety of devices, usually smartphones, and web-browsers.

The developers of these applications often market their programs using words such as "brain training" or "brain games". Some developers claim effectiveness in terms of cognitive performance of their programs in activities of daily life, and some claim delay, or reduction of cognitive decline caused by mental disorders such as MCI, dementia, including Alzheimer's disease, and others, while providing little scientific evidence to prove their claims.

An important concept in the development of cognitive exercises is cognitive transfer. Transfer can be distinguished in near transfer and far transfer. Training one cognitive domain using one kind of task can often lead to minimal improvements in another task with the same cognitive domain. This kind of transfer is called near transfer. Far transfer refers to improvements of cognitive abilities in other domains than the domains which have been trained. Claims of far transfer have to be carefully regarded as there is usually little evidence showing this kind of transfer, for example Van Muijden et al. [133] found only limited transfer in a video game test with elderly subjects [133].

The applications discussed in this section may offer insights into technologies that can be used for assessment of cognitive impairment, many applications focus on cognitive improvements, through the assumption that cognitive exercising can lead to improve in cognitive functioning and daily activities.

2.3.1 MindMate

MindMate[7] is a mobile platform "to empower people with Dementia, their families & carers"[134]. MindMate is based on the notion that performing mentally challenging task has a positive effect for people with Alzheimer's Disease. The developers of MindMate base this assumption on scientific research, such as Woods et al. (2004) who have shown, that cognitive stimulation therapy for dementia has a positive effect on measures of cognitive function [135]. The ideas behind MindMate are based on the results from the FINGER study, which has shown, that nutrition, physical exercise, cognitive challenges, along with social activity can lead to positive results in reducing the risk for Alzheimer's disease (AD) [136].

2.3.2 Lumosity

Lumosity[8] is a platform offering cognitive training, through games, courses and assessment. Prior research such as the ACTIVE study have demonstrated the effectiveness of cognitive training interventions in older adults [137]. The training program offered by *Lumosity* can be effective, by focusing on several aspects in the development of the *Lumosity* framework, namely: targeting, adaptivity, novelty, engagement, and completeness. Through *targeting*, specific cognitive functions are trained and the training effect, as claimed by its developers, will lead to improvements in tasks of everyday life. *Lumosity* achieves *adaptivity* by adapting the difficulty of the exercises to the user's level. The developers of *Lumosity* describe the importance of novelty in their product as: "working in new ways that are not over-learned is critical for driving nervous system remodeling." [138]. *Engagement* means, that positive encouragement will result in the brain being more open to learning and processing new stimuli. Completeness is the importance of all aspects of cognition in everyday activities [138].

Lumosity offers several brain training games. A few examples are: *"Playing Koi"*, whereby the focus lies in tracking and remember multiple fish across the screen, the game trains the visual attention and working memory cognitive domains; the game *"Familiar Faces"* requires players to associate visual and verbal information, training associative memory; in the game *"By the rules"* players are asked to identify a hidden rule in a card game, the game trains mental flexibility and working memory [138].

[7] http://www.mindmate-app.com/

[8] https://www.lumosity.com/

2.3.3 Sea hero Quest

The serious game *Sea hero quest*[9] has been developed by Deutsche Telecom (Bonn, Germany) in cooperation with the University College London (UCL; London, UK) and the University of East Anglia (Norfolk, UK), as "a quest to save the brain". In Sea hero quest the navigational skills of the player within the game world are analysed through challenges of memory use, spatial recognition, and orientation. The researchers believe the data set created from the games' players can gain insight into the early stage development of dementia. The game is developed for smartphones, and uses common smartphone game mechanics and sensors, in the game players navigate a ship through sea mazes, direct flares and photograph sea monsters [139].

2.3.4 Project: EVO

The company *Akili Interactive Labs*[10] develops a cognitive treatment and measurement platform, with products such as *Project: EVO*. This mobile platform allows customised treatment of mental issues, including AD. The game makes use of the smartphone accelerometer and touch sensor. *Project: EVO* demands multiple cognitive abilities, which can be tracked based on the player's performance. In the game players are asked to steer an alien down a river and recognise and tap specific animals appearing on the screen. [140]

2.4 Summary of the state-of-the-art

Several means of assessing cognitive state have been introduced in the previous sections. Multiple variables have been shown to be potential predictors of cognitive impairment. Clinical assessment tests are based on scientific models of cognition and cognitive domains. The examinations are usually obtrusive, that is subjects are asked to perform a number of tasks and based on their performance a diagnosis of their cognitive state is made. The technical approaches on the other hand work either obtrusively or unobtrusively; Some tests require user interactions, whereas others usually use sensors to analyse behaviour. However, these unobtrusive measurements generally assess the risk for cognitive impairment based on previously identified variables that are potential indicators of a specific mental disorder, or by finding correlations from a dataset of sensor values.

[9] http://www.seaheroquest.com/
[10] http://www.akiliinteractive.com/

Variable	Tool / Sensor	Source
HR (variability) BR	Accelerometer BCG	[127, 126, 141]
HR (variability) BR Cognitive Stress	Camera PPG	[122]
Boredom	Lock / unlock Application use	[123]
Movement (variability)	GPS	[121]
Gait speed	GPS	[117, 118]
ADL	Accelerometer Microphone	[125]
Technology use	Smartphone use	[124]
Out of home activity	GPS	[119]
Clock watching behaviour	Lock / unlock	[142]

Table 2.3: Smartphone Technologies for unobtrusive cognitive assessment

The state-of-the-art research has shown several variables for unobtrusive assessment. Table 2.3 shows a summary of variables and measurements techniques potentially indicative of cognitive impairment. However, currently unobtrusive measurements are not able to provide a comprehensive overview of the cognitive state comparable to clinical tests, and can not be used for diagnosing cognitive impairment. Whereas clinical tests do not yet provide a complete way of continuous assessment of cognitive state in the same way this can be achieved by monitoring sensor data in unobtrusive measurements. Therefore, a technical approach of combining clinical tests with unobtrusive measurements of behaviour is desirable to find new variables and measurements for a more comprehensive overview of cognitive state.

Chapter 3

Method

The goal of this project is to develop a smartphone based assessment that uses a variety of measurements to determine of cognitive functioning. Smartphones provide myriad of ways to measure and assess variables related to cognitive state, as presented in the Chapter 2.

As previously discussed, there are two main approaches to assessing dementia: biosensory assessment, which is data that can be assessed unobtrusively without direct interaction with the user; and questionnaire-based assessments, which require user interaction. In the medical field, the assessment of cognitive impairment is currently performed using face-to-face questionnaire-based approaches. While biosensory information has been found to be indicative of cognitive impairment including dementia, it is currently not commonly used in medical assessments.

In order to be able to create techniques that rely more on unobtrusive sensing data in the future, it is necessary to develop a reliable digital version of the current approach to diagnosing cognitive impairment, namely a digitised version of clinical questionnaires. The accuracy of this digital test should be comparable to that of the validated clinical cognitive assessment test.

The mini-mental state examination (MMSE) has been chosen for digitalisation because it is one of the most commonly used tests when diagnosing for dementia. The MMSE is a short test, that contains several questions that aid in the assessment of cognitive state. As one of the first and most popular tests for dementia, the MMSE is an appropriate choice for the digitalisation of traditional testing using smartphones.

This chapter will explain the various design decisions that were made during the development of a digital test, as well as describe its implementation in a cognitive testing smartphone application.

3.1 Design

Compared to the development of the clinical version of the test, the development of a digital test exhibits several difficulties related to the shortcomings of technology that make it difficult to simulate a clinical environment. Therefore, the design decisions made during implementation can have a significant effect on the performance and effect of the test. The end result should resemble the original testing method as closely as possible in order to avoid the information loss due to the digitalisation process. At the same time, the digital test should allow for remote assessment through a medical professional or even automatic assessment through the application.

This section will outline the difficulties in translating cognitive tests into digital versions and specify a selection of requirements to be taken into consideration during the development phase.

3.1.1 Requirements

The requirements for the newly developed application can be summarised using the MoSCoW approach. The MoSCoW method differentiates between *must have*: specific requirements that are crucial to the success and therefore must be included; *should have*: requirements that should be included, however the application will be successful without them and they may be omitted in case of time constraints; *could have*: requirements that may be included if permitted by time and cost, and *will not have*: requirements that may be included in future work but will not be included in the current project [143].

Must have: The system to be developed must work on most current smartphones and must include specific methods for testing for cognition that are comparable to those used in traditional cognitive tests. The application must be extendable for future research and must include a simple method for the digitalisation of most common cognitive tests. It must be possible to create different components, similar to classical tests, which contain separate tasks. The researcher must also be able to specify a schedule when the application should ask the test questions to the user. Furthermore, the system must allow for future extensibility, specifically the inclusion of unobtrusive testing using sensors values in future use cases. Finally the data must be stored on a central server for analysis and the application must be designed so that tests can be scheduled remotely.

Should have: The system should include a fully developed digital version of the popular MMSE. It should also include text-to-speech functionality, meaning the instructions are read to the user in order to closely resemble the traditional testing environment. The system should also be able to specify separate schedules for the different test components.

Could have: The system could have the option for voice inputs such as speech-to-text functionality in order to closely resemble the traditional testing scenario and avoid issues with typing that some users may experience. It could be possible to allow the researchers to change the order in which test components are run so that the test subjects will be less likely to remember which test components appear next. Combined with the capability to schedule specific test components, this feature could allow components to be easily replaced by similar components, thereby avoiding a learning effect on the test subjects when executing the test multiple times.

Will not have: The system will not include other unobtrusive methods (i.e. biosensory variables) during the testing of the application. This approach will also not further explore the effect of different sensory variables and their relation to traditional or digitised testing methods.

3.1.2 Design choices

As described in subsection 3.1.1, the application will communicate with a central database where the user input will be stored for assessment by the researchers or medical personnel. The researchers will be able to schedule the test remotely. In the MMSE, as in many other clinical assessment tests, the majority of answers involve a user talking to the researchers. For other questions users are asked to write or draw their answers. The smartphone application shall therefore allow for different answer options depending on the question, so that users can speak, type or draw their answers on the smartphone. The architectural diagram of the application is shown in Figure 3.1.

3.1.3 Mini-Mental State Examination

The MMSE, introduced in subsection 2.1.8, is one of the most prominent tests when assessing for AD and other dementias [98]. The original MMSE, developed by Folstein et al. in 1975, has been translated into a variety of languages, and has since been adapted to multiple other versions of the test. In light of this, the original MMSE [82] has been chosen here for this digitised version.

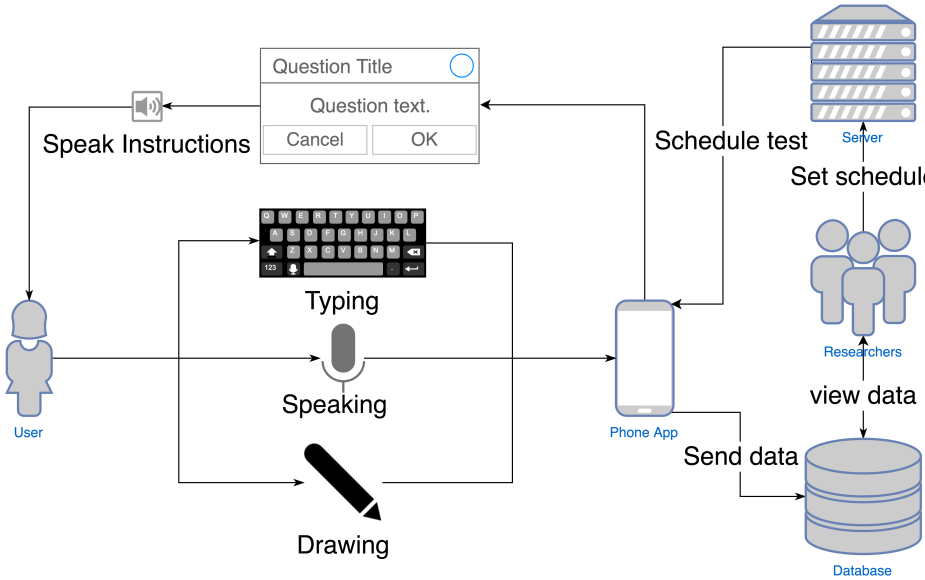


Figure 3.1: Architecture diagram of the application

The MMSE consists of five components: **1)** orientation, **2)** registration, **3)** attention and calculation, **4)** recall, and **5)** language. While the original test is assessed directly in person through the examiner, the test has to be conducted by the application in the digitised version.

Therefore, it was crucial during the development of the application it was crucial to identify possible constraints related to the technology that may cause significant differences when compared to the in-person assessment, as well as possible difficulties users may have when performing the test using a smartphone. First, users may have difficulties reading and understanding the instructions on the smartphone screen. Therefore it is important to include text-to-speech functionality in the application, which allows the application to read the instructions to the user. Second, users may have problems typing on the smartphone. Therefore the application should make use of speech-to-text, which allows the users to speak the answer into the microphone, instead of relying solely on interaction with the smartphone's keyboard.

The digital version of the test should resemble the MMSE by Folstein et al. as closely as possible. A text input and voice field shall be used for the orientation component, closely resembling the face-to-face paper version of the MMSE. The questions of the orientation component will be separated into individual sub-questions to be answered by the user with the following instructions:

Question 1.
What is the (year) (season) (date) (day) (month)?

a) What is the current year?

b) What is the current season?

c) What is the current date?

d) What is the current day of the week?

e) What is the current month?

Question 2.
Where are we: (state) (county) (town) (hospital) (floor)?

a) Which state are you in?

b) Which county are you in?

c) Which town are you in?

d) Which hospital are you in?

e) Which floor are you on?

The smartphone will use text-to-speech functionality to read the instructions to the user and give the option for keyboard or voice input for answering these questions. A list of options instead of keyboard or voice input should be avoided in order to reduce the risk of providing the participants with contextual clues and thereby influencing their answers. A numeric keyboard can be used for questions where numeric input is expected, such as the date or the questions measuring attention and calculation.

In the registration component of the MMSE, the patient is asked to recall three objects. This section will be digitised in a similar manner as the orientation component. The user will be introduced to the test using a dialog box reading the following instructions:

> "In the following dialog boxes three random items will appear. Please remember them well. You will be asked to recall them later."

The following dialog boxes will introduce the words "table", "chair", and "house" in written and auditory form. These words could potentially be replaced by any other object as well, since the MMSE does not specify any particular words to use. As in the orientation component, a text dialog box with a keyboard or voice input can be used to closely resemble the MMSE. The face-to-face MMSE allows the patient to try recalling the words multiple times until the correct words is recalled. However, the user is only asked once in the digitised version. This choice was made because recalling an answer multiple times would have required verifying that the answer is correct, which was not the goal of this application. However, there is no time limit for answering this question, allowing users to wait before entering the answer until they know the correct answer.

The attention and calculation component of the MMSE consists of either a Serial 7's test, whereby the patient is asked to count backwards by 7 starting with 100, or alternatively a test asking the patient to spell the word "world" backwards. The spelling test will not be digitised because of difficulties regarding the visual cues that would be given on the smartphones screen from the instruction text or the keyboard. The Serial 7's test shall be digitised through multiple dialog boxes. The first dialog will ask the user to subtract 7 from 100, and in the proceeding dialog boxes the patient will be asked to subtract 7 from their previous answer. The dialog boxes for these questions will be designed to allow users to more easily enter the numbers.

The recall component of the MMSE asks patients to recall the items from the registration component. The digital version for this component therefore resembles the dialog boxes explained in the registration component.

The language component of the MMSE poses the largest challenge for digitalisation. Its individual components are digitised in the following form:

Name a pencil, and a watch
: In the paper version of the MMSE the examiner shows the participant a a pencil and a watch and asks to identify the objects. This task is digitised using two dialog boxes with images of a pencil, and a wrist watch respectively, in place of the actual objects. The patient is able to use the keyboard or text-to-speech input to answer the question.

Repeat the following: "No ifs, ands or buts."
: Subjects with cognitive impairment have difficulty saying the sentence "No ifs, ands or buts". This task is digitised using a dialog box with text or voice input options for answering the question.

Follow a three-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor".

This task can unfortunately not be directly performed on a smartphone. The importance of this task is that participants are asked to remember three different steps that they have execute to complete the task. An alternative three-stage command has been designed in the digitised version. The screen will show three circles of different colours at seemingly random positions. The patient will be asked to align them in a vertical line in a specified order without overlaps. The patient is asked to remember the positions of the circles by showing a dialog box with instructions before the task begins.

Read and obey the following: "Close your eyes"

This one-stage command task is also difficult to digitise. Similar to the three-stage command, the user is asked to move a single circle from the centre of the smartphone screen to the right. This tasks requires the patient to read the instructions. The text-to-speech functionality is therefore disabled for this task.

Write a sentence

This task ask the patient to write a sentence of their choosing. The sentence must not be given by the examiner. In order to complete this task, the sentence must contain a subject and verb and must be sensible, grammar and punctuation are disregarded. In the digitised version, similar to several other tests, the user is presented with a text input field in which to write a sentence.

Copy design

The original MMSE asks the patient to copy intersecting pentagons on a piece of paper. In the smartphone application, the user is presented with an image of intersecting pentagons, and asked to copy the drawing in the field below. The patient can use his or her finger to draw on the smartphone.

Score The scoring system for this smartphone-based MMSE is equivalent to that of the paper version of the MMSE. While the smartphone performs as much of the evaluation as possible independently, the scoring should be performed by a professional evaluator who is familiar with the MMSE scoring system. When only one answer is possible, as in the calculation tasks, the answer should be supplied along with the test in order to make evaluation as simple as possible. However, many questions allow for solutions that may be difficult to encode and do not apply to every test (e.g. the current time and the location). These variables could be retrieved from other information such as when the test was executed or location data from the phone. When assessing written tasks, spelling mistakes should not lead to a deduction of the score. Because it would be very difficult for an automated system to account for all these factors, evaluation in this case is mostly left to the human evaluator. This process is designed to be as simple as possible.

3.1.4 Summary

When developing digital versions of face-to-face medical assessment tests, the differences have to be carefully assessed and considered during the development in order to provide a comparable evaluation. Because of its popularity and relevance for this project, the MMSE by Folstein et al. has been chosen for digitalisation. The test is commonly performed and evaluated in person and on paper by a medical professional. The digital version is conducted using a smartphone.

The digital test uses text- and audio-based instructions that resemble the method of the face-to-face assessment. A variety of text input methods exist, such as speech-to-text or the keyboard. For input where numeric input is expected, a numeric keypad will allow the user to more easily input numbers.

The main differences between the paper version of the MMSE and this smartphone based assessment method primarily lie in the questions from the language component, which were not directly translatable to the smartphone delivery method. In the digital version of the MMSE, the patient or a caregiver, friend or family member is required to operate a smartphone to input. As in the paper version the digital results of the new test require evaluation by a professional. The digital results are therefore sent to a database for evaluation.

3.2 Implementation

The Android[1] platform was chosen for the digitisation of the MMSE. Android is a popular operating system primarily developed for mobile computing devices including smartphones and tablets. Applications for Android are programmed using the Android software development kit (SDK) and the Java programming language. The digitalisation of the MMSE was performed using the Android Mobile Context Instrumentation Framework (AWARE)[2] framework for Android. The AWARE framework can already assess a variety of different information from the smartphone sensors, it is designed as

[1] see: https://www.android.com/
[2] available at: http://awareframework.com/

a research tool, and stores all information on a central server. Therefore, AWARE forms the ideal foundation for the intended developments.

That said, in order to develop the application described in section 3.1, certain changes to the core AWARE framework had to be made. This allows for future independent use of the improvements, without relying on the Cognitive Experience Sampling plugin, which was developed specifically for the execution of cognitive tests. The plugin was developed to execute a test definition of a cognitive assessment test. For example, as described in section 3.1, the MMSE was digitised. However, the plugin was designed so that future digitalisations of other cognitive tests will be very simple.

The focus of this implementation was primarily on the future extensibility of the plugin, that is the possibility of the plugin to be easily altered and extended for future use cases in similar cognitive tests. For this reason an XML test definition, that follows a defined schema, can be used to digitise cognitive tests. The XML schema has been designed to allow tests to be scheduled at a specific time and day and even allows specific components to be scheduled separately.

3.2.1 AWARE Framework

Android Mobile Context Instrumentation Framework (AWARE) is a framework available for iOS and Android that can be used to track a variety of information from the smartphone's sensors, as well as setup questionnaire based tests. AWARE is an open-source development that is freely available online, licensed under the Apache Software License 2.0 [144].

The framework uses a server-client approach. Researchers are able to set up a server running AWARE, and test subjects can then join a study using the AWARE smartphone application using their own smartphones. Once running the application will then periodically send data from its plugins to the server. AWARE allows researchers to develop their own plugins, but also provides a variety of plugins already. For instance, data from the smartphone's accelerometer, battery, or temperature sensor can be easily assessed.

The operation of the application based on the AWARE framework is illustrated in Figure 3.2, which shows the AWARE framework's reliance on a database to store user data. AWARE plugins allow the collection and storage of information about the device, as well as data from its sensors which are stored in the database. The Cognitive Experience Sampling Plugin collects information about the MMSE questionnaire and other digitised cognitive tests, which AWARE stores in this database. In comparison to traditional assessments, the data can be easily made accessible to multiple researchers and medical professionals for analysis. The application communicates with

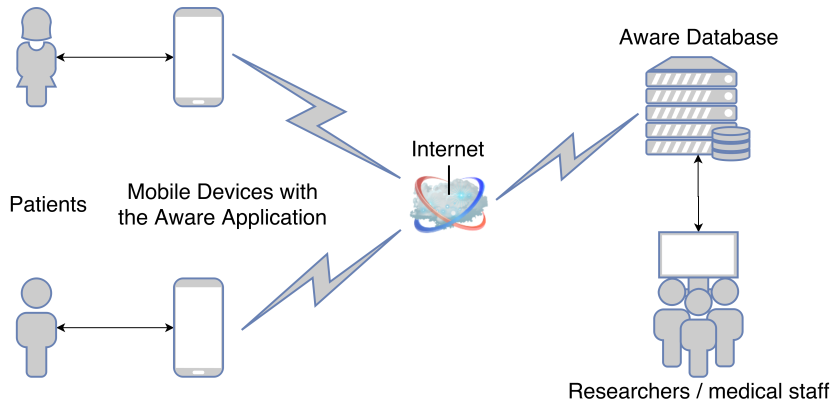


Figure 3.2: Operation of the AWARE application.

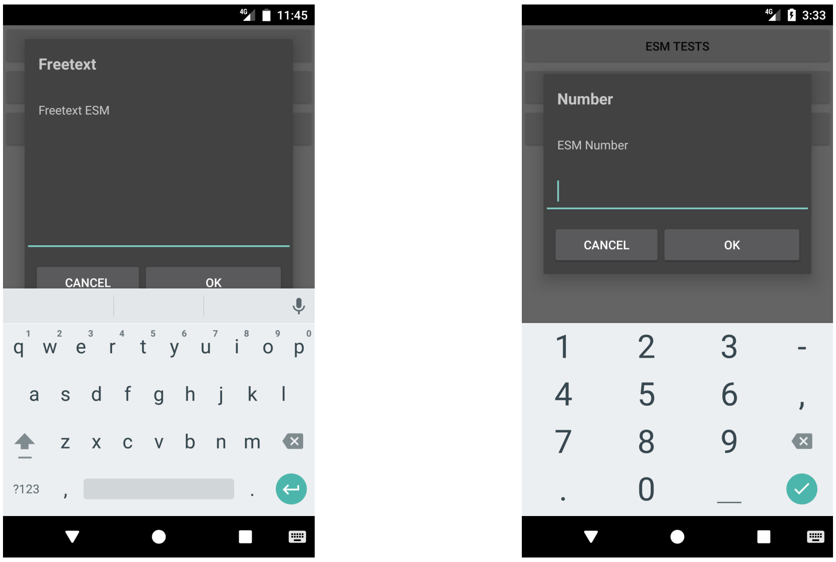
the database over the internet.

Experience Sampling Method In addition to the unobtrusive sensing methods of AWARE, researchers are able to trigger the mobile experience sampling method (ESM) questionnaires remotely or schedule ESMs using the AWARE Dashboard or from within the AWARE plugin. AWARE provides a variety of ESM types, including free text, radio buttons, checkbox, Likert scale, quick answer, scale, and numeric types. AWARE ESMs primarily consist of a title, the instruction text, the submit button text, and the user answer as a string once it has been answered. Additionally, it is possible to specify for how long the notification should be active for and how much time the user has to answer the question. The following ESMs are offered by the AWARE framework and are used in the application:

ESM_Freetext: This ESM is used for text input and text-based instructions. It consists of a title, an instruction text and an input field. Figure 3.3a shows an example of a free text ESM in AWARE.

ESM_Number: This ESM is used when the input is a number and text-based instructions are required. In contrast to the ESM_Freetext dialog, this dialog contains an input field that only allows numeric characters. The Android system will therefore open a keyboard with numeric input options only. Figure 3.3b shows an example of an ESM dialog with numeric input.

The ESM dialogs provided by the AWARE framework already provide a variety of different input methods. However, while many other ESM dialogs could have been used for the realisation of the digital MMSE, they



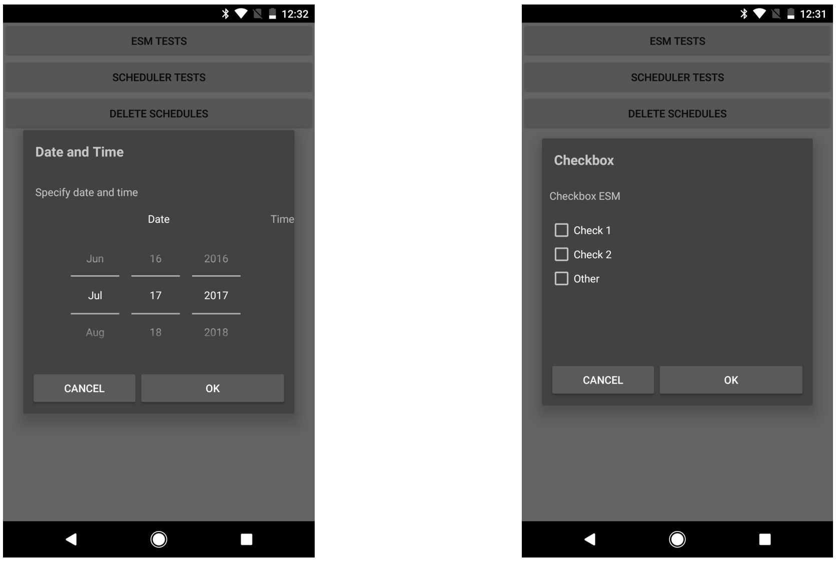
(a) Example of a free text ESM (b) ESM with numeric input

Figure 3.3: Example of the ESM_Freetext and ESM_Number from the AWARE Framework.

have been avoided, in order to minimise the contextual clues provided to the user that could influence the decision-making process and therefore provide inaccurate results. For example, `ESM_DateTime.class` could have been used instead for the orientation component question of the MMSE. An example of the `ESM_DateTime` ESM dialog is shown in figure 3.4a. However, the use of this dialog could have influenced the user's solution by showing a specific date, therefore, this question was broken into multiple smaller individual questions about the day, month, and year. Similarly the `ESM_Radio` or the `ESM_Checkbox`, as shown in Figure 3.4b, could have provided an easier method of inputting answers, by allowing the user to select from a variety of options, such as selecting from a set of answers for the current season. However, providing the user with multiple choice answers was not desired as this does not accurately represent the MMSE. It could influence the user's decision-making process, and therefore could have lead to significantly different results.

3.2.2 Development of the AWARE plugin

The development of the digital MMSE consisted of changes to the core AWARE framework, as well as the development of the AWARE Cognitive Experience Sampling plugin. This plugin uses an altered form of the core



(a) ESM_DateTime dialog example (b) ESM_Checkbox dialog example

Figure 3.4: ESM_DateTime and ESM_Checkbox examples which were not used in the application.

AWARE framework, designed to schedule and construct ESM-based tests that are provided in XML form. The following paragraphs will illustrate the changes that have been made to the core AWARE framework.

First, in order to allow dialogs to give auditory feedback of the instructions, a new Boolean variable has been implemented in the ESM_Question class. If set to 'true', a new Android intent will be started, that uses the existing AWARE class `Aware_TTS` in order to give text-to-speech instructions about the task instructions.

While many of the existing ESM dialogs could be used to digitise the MMSE, several other ESM classes had to be constructed in order to allow for alternative input methods and instructions and to fully digitise the MMSE and other tests.

ESM_DRAW: This class is used to create an ESM dialog with drawing functionality. The user can use their finger to draw on the screen's canvas in the colour black. When the submit button is pressed the bitmap image is retrieved and converted into a base64 string using the `ESM_ImageUtils` class. This class also contains a function with the ability to convert the string back into a bitmap image. The string is added as the "esm_user_answer" to the JSON (JavaScript Object Notation) response of the ESM. Figure 3.6a shows an example for the ESM_DRAW dialog.

ESM_IMAGE_Freetext: The `ESM_IMAGE_Freetext` class has been constructed to allow for image instructions. The instructions that are passed to this class are in the form of a JSON object that has been converted to string via the `.toString()` function. The JSON object that should be passed should contain either a bitmap image that was converted into base64 string using the `ESM_ImageUtils.bitmapToString(Bitmap bitmap)` function, or a URL string. Listing 1 shows the basic instructions to create this JSON object. An example of an ESM_IMAGE_Freetext dialog is shown in Figure 3.6b.

ESM_Notice: The `ESM_Notice` class has been created to allow for instructions that do not require user input. It can for instance be used to test the user's ability to recall information by including an `ESM_Notice` instance with instructions before the actual test ESM dialog. Upon submission, the class returns a 'success' JSON response with an empty string user answer. Figure 3.6c shows an example notice dialog.

ESM_IMAGE_DRAW: The `ESM_IMAGE_DRAW` class combines the functionality of the `ESM_DRAW` and `ESM_IMAGE_Freetext` class by creating a dialog box with image-based instructions and drawing input. This class is useful for questions in which the user is asked to copy an image, as shown in Figure 3.6d. Similar to the `ESM_IMAGE_Freetext` class the instruction is a string created from a JSON object that follows the format displayed in Listing 1.

ESM_ImageManipulation: The `ESM_ImageManipulation` class is defined specifically for tasks that require the execution of step-by-step commands, as in the three-step command of the MMSE. The class is able to draw circles on a canvas that have been defined in the instructions. The instruction should be in the form of a JSON object converted to string as shown in Listing 2. This JSON instructions should contain an array of shapes to be drawn on the canvas. This call is easily extended, for instance in order to allow for custom evaluation of the output. By using the `ESM_Question.setESM_Class(String className)` function on the class instance with the `OverridingClass.class.toString()` as input, it is possible for the `ESM_Factory` to create an instance of the new class at runtime. The output for this class is a JSON object converted to

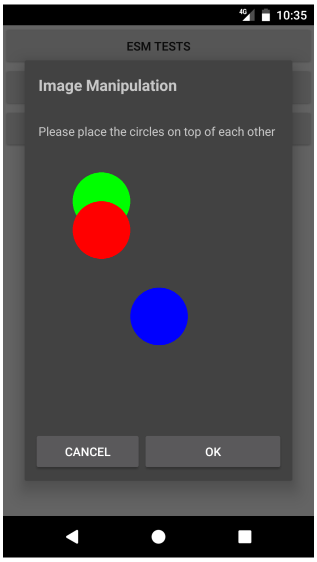


Figure 3.5: ESM for multi-step command instructions in cognitive tests (shape manipulation).

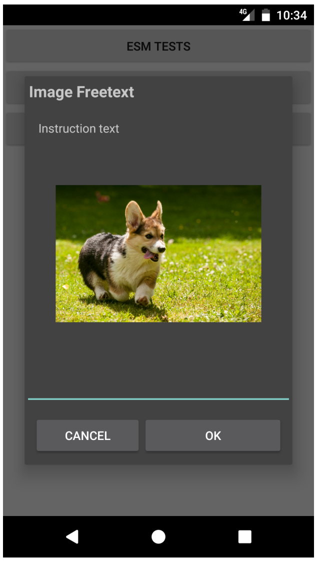
string with a variable ("Image") that contains the bitmap image retrieved from the canvas converted to base64 string. An example of the dialog for three circles, using the instruction string, as outlined in Listing 2, is shown in Figure 3.5.

```
{
  "Text" : "The instruction text",
  "ImageUrl" : "Url to the image",
  "encodedImage" : "The base64 encoded image"
}
```

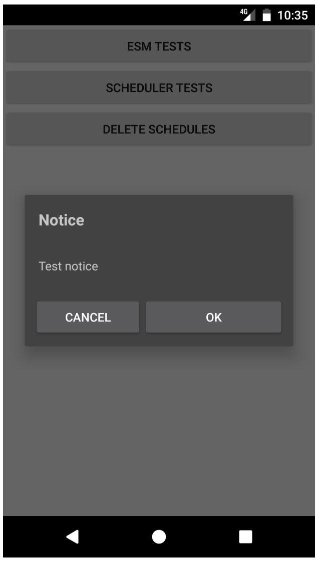
Listing 1: JSON object for the Image based instruction esms. Only one of "ImageUrl" or "encodedImage" should be included

The AWARE plugin contains the functionality of creating an AWARE ESM questionnaire and setting a schedule based on a definition in an XML file that follows the XML schema. This will be explained in greater detail subsection 3.2.3. As described earlier, the plugin contains ESMs that extend the `ImageManipulation` class for the functionality of the MMSE and other similar tests.

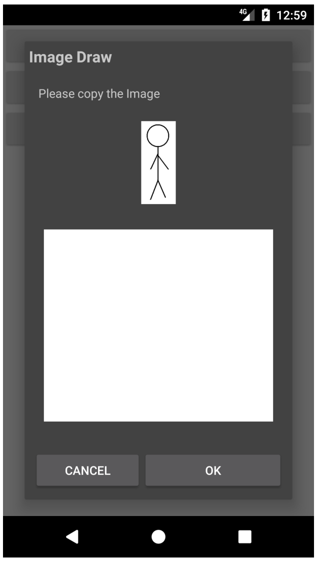
(a) ESM with drawing input.



(b) ESM with image instructions.



(c) ESM notice without user input.



(d) ESM for copying tasks.

Figure 3.6: Examples of the new created ESM dialogs for the AWARE framework.

```json
{
  "Text" : "The instruction text",
  "Shapes" : [
    {
      "type" : "Circle",
      "xPos" : 200,
      "yPos" : 200,
      "radius" : 100,
      "color" : -65536
    },
    {
      "type" : "Circle",
      "xPos" : 200,
      "yPos" : 100,
      "radius" : 100,
      "color" : -16711936
    },
    {
      "type" : "Circle",
      "xPos" : 400,
      "yPos" : 500,
      "radius" : 100,
      "color" : -16776961
    }
  ]
}
```

Listing 2: JSON object for the `ImageManipulation` instructions.

ThreeStepCommand The `ThreeStepCommand` class has been specifically designed to evaluate the tree-step command of the MMSE. In the traditional MMSE, the patient is instructed to "Take a paper in your right hand, fold it in half, and put it on the floor". In the digital version, three circles are to be moved and positioned in a vertical line without overlapping. This class extends the `ImageManipulation` and overrides the `createJsonOutput(CanvasView feedback)` function to create an output converted to string, where the output has been evaluated programmatically. This is shown in Listing 3. The evaluation is performed based on a predefined threshold of 10 pixels.

```
{
  "image" : "base64 encoded image string",
  "test passed" : false,
  "evaluation" : {
    "x-values" : "Do the circles align on the x-axis?",
    "y-values" : "Do the circles align on the y-axis?",
    "overlap"  : "Are the circles not overlapping?"
  }
}
```

Listing 3: JSON response from the `ImageManipulation` class. The `"test passed"` variable will evaluate to 'false' if one condition has not been fulfilled. The evaluation response shows where issues have been detected.

OneStepCommand: The `OneStepCommand` class has been designed for the task in the MMSE, for which the participant is asked to read a single command and perform its action. In the traditional MMSE, the participant is asked to read and obey the command, "Close your eyes". In the smartphone application, however, the user is asked to move a circle to the right of the screen. Since in the MMSE this task requires understanding of written information the speech-to-text functionality is disabled for this test in the digitised MMSE. The implementation is similar to that of the `ThreeStepCommand`. Similarly, the `OneStepCommand` class extends the `ImageManipulation` class, however only one circle should be used in this case. The evaluation function determines whether the circle has been moved to the right side of the screen.

Table 3.1: Start component of the test

MMSE	**Screenshot**	**AWARE**

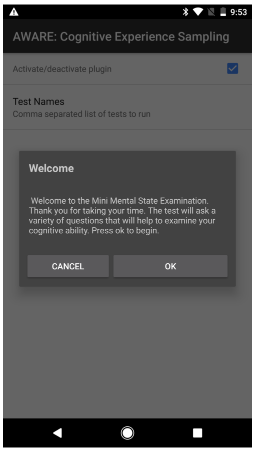
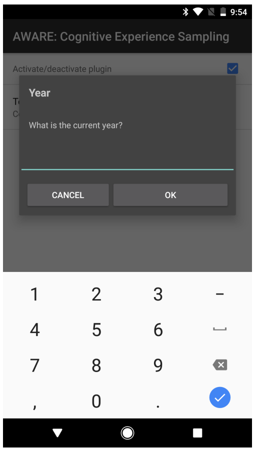
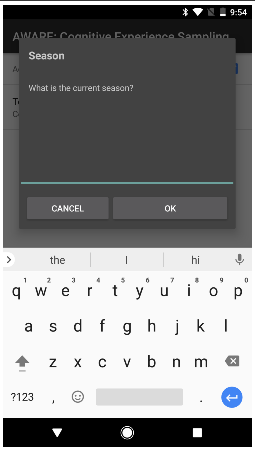
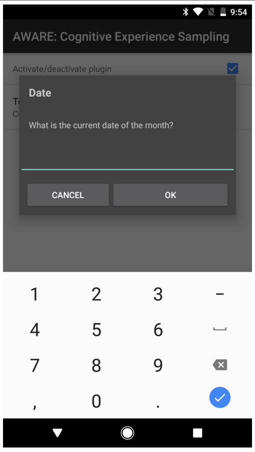
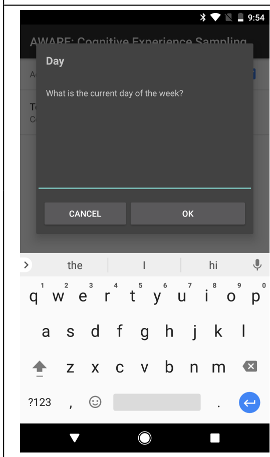
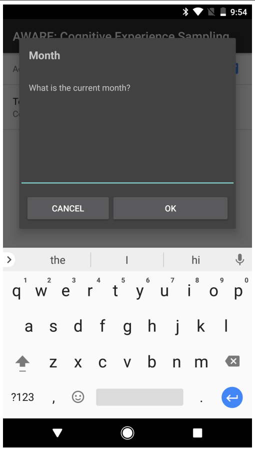
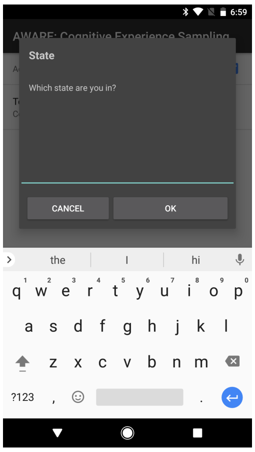
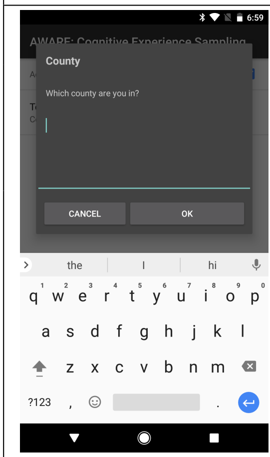
none		**ESM_Type:** ESM_Notice **Instructions:** Welcome to the Mini Mental State Examination. Thank you for taking your time. The test will ask a variety of questions that will help to examine your cognitive ability. Press ok to begin. **Input methods:** none

Table 3.2: Orientation component of the test

MMSE	Screenshot	AWARE
question: What is the (year) (season) (date) (day) (month)? **score:** 5		**ESM_Type:** ESM_Number **Instructions:** What is the current year? **Input Methods:** numeric keyboard

		**ESM_Type:** ESM_Freetext **Instructions:** What is the current season? **Input Methods:** keyboard, microphone
		**ESM_Type:** ESM_Freetext **Instructions:** What is the current date of the month? **Input Methods:** keyboard, microphone
		**ESM_Type:** ESM_Freetext **Instructions:** What is the current day of the week? **Input Methods:** keyboard, microphone

		**ESM_Type:** ESM_Freetext **Instructions:** What is the current month? **Input Methods:** keyboard, microphone
question: Where are we: (state) (county) (town) (hospital) (floor) **score:** 5		**ESM_Type:** ESM_Freetext **Instructions:** Which state are you in? **Input Methods:** keyboard, microphone
		**ESM_Type:** ESM_Freetext **Instructions:** Which county are you in? **Input Methods:** keyboard, microphone

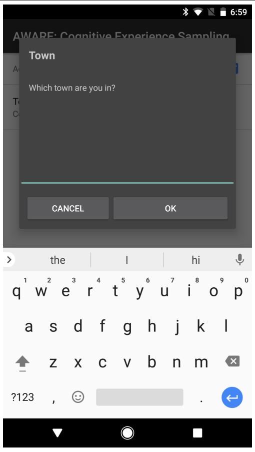
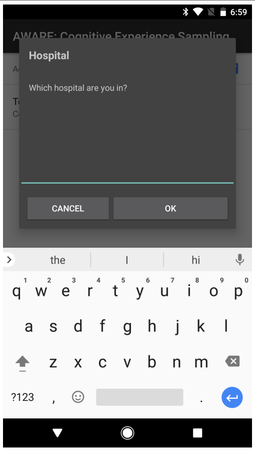
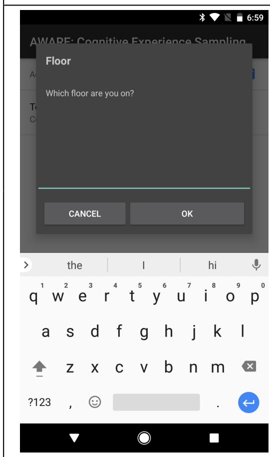
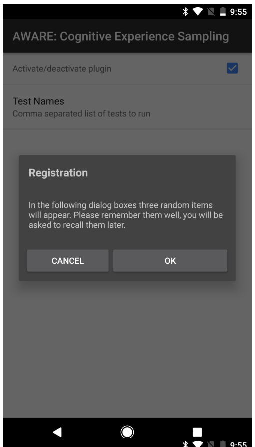
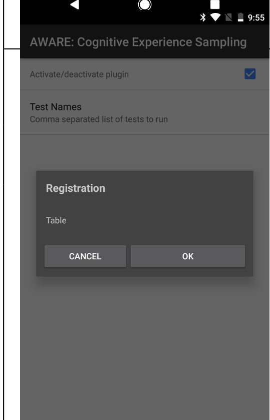
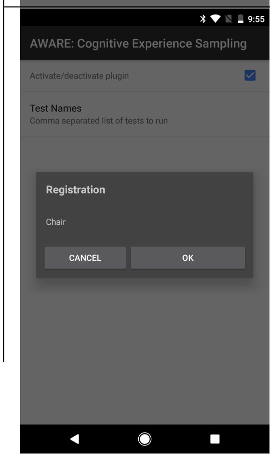
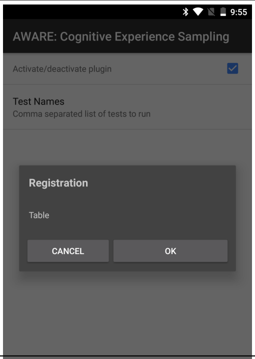
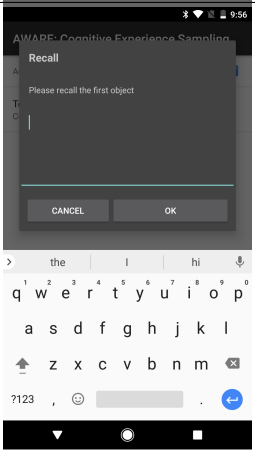
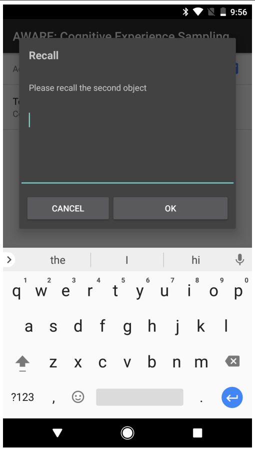
		**ESM_Type:** ESM_Freetext **Instructions:** Which town are you? **Input Methods:** keyboard, microphone
		**ESM_Type:** ESM_Freetext **Instructions:** Which hospital are you in? **Input Methods:** keyboard, microphone
		**ESM_Type:** ESM_Freetext **Instructions:** On which floor are you? **Input Methods:** keyboard, microphone

Table 3.3: Registration component of the test

MMSE	Screenshot	AWARE
question: Recall three random objects **score:** 3		**ESM_Type:** ESM_Notice **Instructions:**In the following dialog boxes three random items will appear. Please remember them well, you will be asked to recall them later. **Input Methods:** none
		**ESM_Type:** ESM_Notice **Instructions:** table **Input Methods:** none
		**ESM_Type:** ESM_Notice **Instructions:** chair **Input Methods:** none

		**ESM_Type:** ESM_Notice **Instructions:** house **Input Methods:** none
		**ESM_Type:** ESM_Freetext **Instructions:** Please recall the first object **Input Methods:** keyboard, microphone
		**ESM_Type:** ESM_Freetext **Instructions:** Please recall the second object **Input Methods:** keyboard, microphone

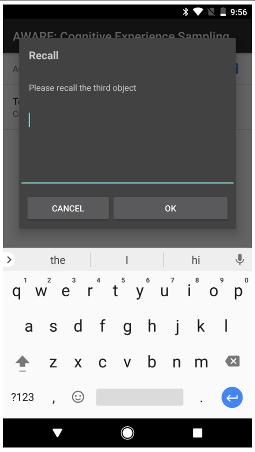
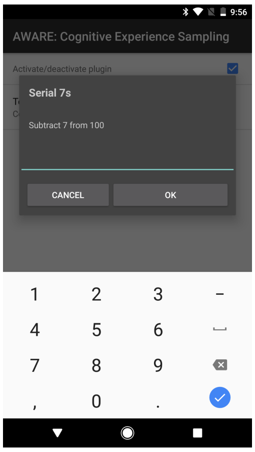
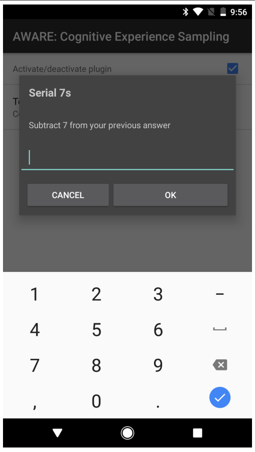
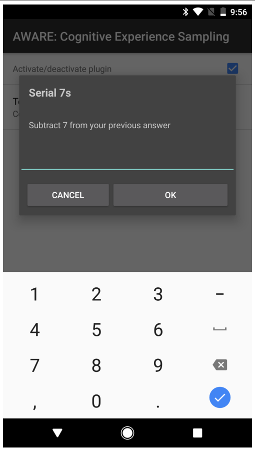
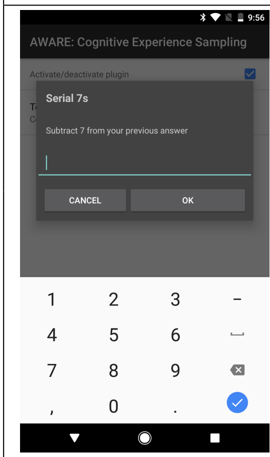
		**ESM_Type:** ESM_Freetext **Instructions:** Please recall the third object **Input Methods:** keyboard, microphone

Table 3.4: Attention and Calculation component of the test

MMSE	**Screenshot**	**AWARE**
question: Subtract 7 from 100, stop after five answers. **score:** 5		**ESM_Type:** ESM_Number **Instructions:** Subtract 7 from 100 **Input methods:** numeric keyboard

		**ESM_Type:** ESM_Number **Instructions:** Subtract 7 from your previous answer **Input methods:** numeric keyboard
		**ESM_Type:** ESM_Number **Instructions:** Subtract 7 from your previous answer **Input methods:** numeric keyboard
		**ESM_Type:** ESM_Number **Instructions:** Subtract 7 from your previous answer **Input methods:** numeric keyboard

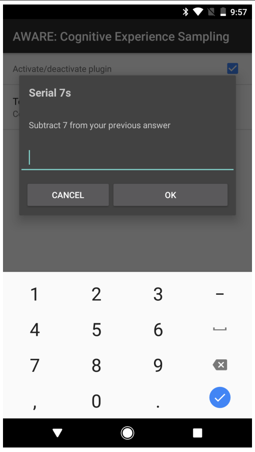
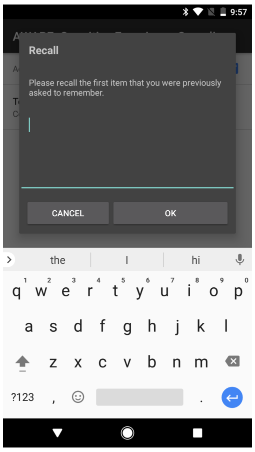
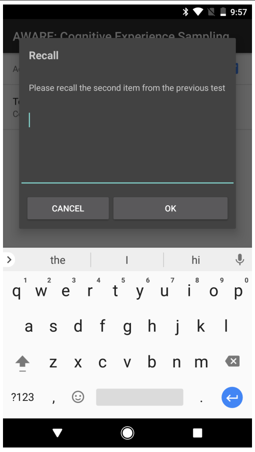
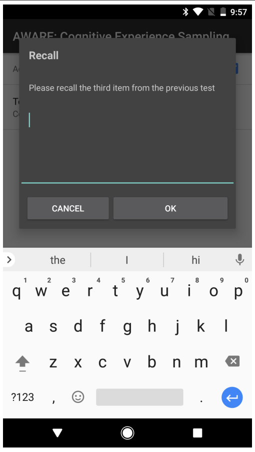
		**ESM_Type:** ESM_Number **Instructions:** Subtract 7 from your previous answer **Input methods:** numeric keyboard

Table 3.5: Recall component of the test

MMSE	**Screenshot**	**AWARE**
question: Repeat the 3 objects from above. **score:** 3		**ESM_Type:** ESM_Freetext **Instructions:** Please recall the first item that you were previously asked to remember. **Input methods:** keyboard, microphone

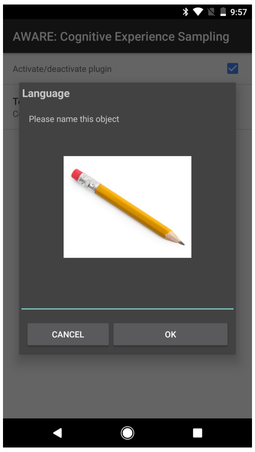
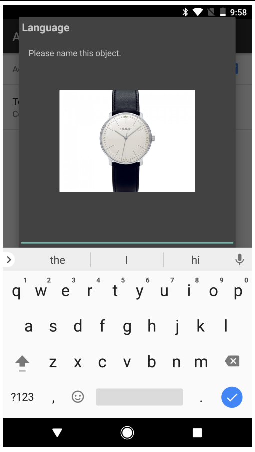
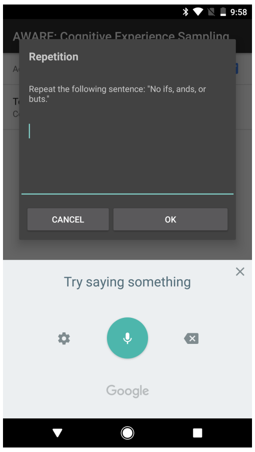
<table>
<tr><td></td><td>
</td><td>ESM_Type: ESM_Freetext
Instructions: Please recall the second item from the previous test

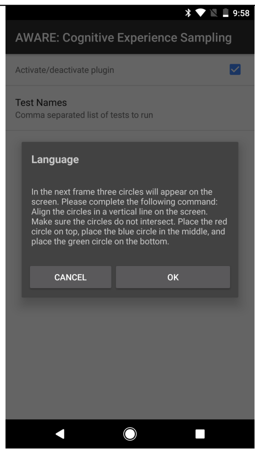
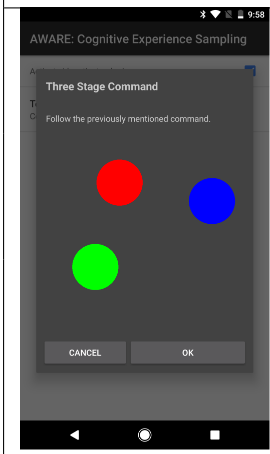
Input methods: keyboard, microphone</td></tr>
<tr><td></td><td>
</td><td>ESM_Type: ESM_Freetext
Instructions: Please recall the third item from the previous test

Input methods: keyboard, microphone</td></tr>
</table>

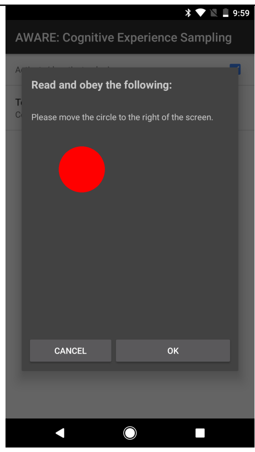
Table 3.6: Language component of the test

MMSE	Screenshot	AWARE

question: Name a pencil and a watch. **score:** 2		**ESM_Type:** ESM_Freetext **Instructions:** Please name this object. **Input methods:** keyboard, microphone
		**ESM_Type:** ESM_Freetext **Instructions:** Please name this object. **Input methods:** keyboard, microphone
question: Repeat the following sentence: “No ifs, ands, or buts.” **score:** 1		**ESM_Type:** ESM_Freetext **Instructions:** Repeat the following sentence: ”No ifs, ands, or buts.” **Input methods:** keyboard, microphone

<table>
<tr>
<td rowspan="2">question: Follow a 3-stage command: “Take a paper in your right hand, fold it in half, and put it on the floor”
score: 3</td>
<td>
</td>
<td>ESM_Type: ESM_Notice
Instructions: In the next frame three circles will appear on the screen. Please complete the following command: Align the circles in a vertical line on the screen. Make sure the circles do not intersect. Place the red circle on top, place the blue circle in the middle, and place the green circle on the bottom.
Input methods: none</td>
</tr>
<tr>
<td>
</td>
<td>ESM_Type: Command: ThreeStageCommand

Instructions: Follow the previously mentioned command.

Input methods: finger</td>
</tr>
<tr>
<td>question: Read and obey the following: CLOSE YOUR EYES
score: 1</td>
<td>
</td>
<td>ESM_Type: Command: OneStageCommand

Instructions: Please move the circle to the right of the screen.

Input methods: finger</td>
</tr>
</table>

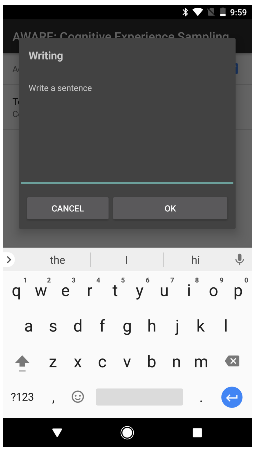
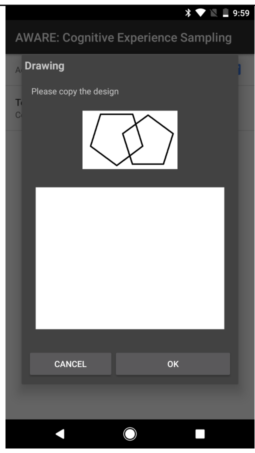
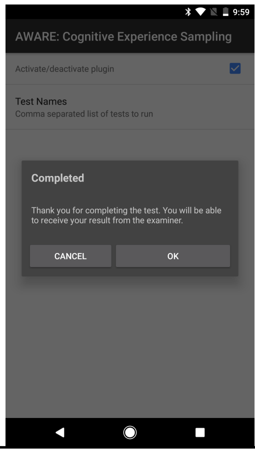
question: Write a sentence **score:** 1		**ESM_Type:** ESM_Freetext **Instructions:** Write a sentence **Input methods:** keyboard, microphone
question: Copy design **score:** 1		**ESM_Type:** ESM_Image_Draw **Instructions:** Please copy the design **Input methods:** finger

Table 3.7: Final component of the test

MMSE	**Screenshot**	**AWARE**

none		**ESM_Type:** ESM_Notice **Instructions:** Thank you for completing the test. You will be able to receive your result from the examiner. **Input methods:** none

3.2.3 Extensible Markup Language (XML)

Extensible Markup Language (XML) is popular language to store and transmit information. It is designed to be both human- and machine-readable and is therefore appropriate for encoding digitised cognitive tests. The XML Schema definition (XSD) is an XML schema language recommended by the World Wide Web Consortium. An XML schema with XML version 1.0 and the "http://www.w3.org/2001/XMLSchema" namespace has been defined that allows future tests to be encoded and read by the AWARE plugin. The decision to use XML to encode test has the advantage that it is easily possible to change or translate the test without requiring changes to the Java code. By defining a test in a single XML file, it is possible to easily read the test and transmit the file, compared to requiring programming in the Java language. A test following the schema can be directly used in the AWARE plugin.

The Test XML file is defined by the TestDefinition.xsd file. Figure 3.7 shows the structure of the XML Schema. By following this schema, it is possible to digitise cognitive test for the use with AWARE. It is possible to set up different test components and include different tasks for each component. Each task is defined by a single question in the paper version of the test. Furthermore, it is possible to create multiple AWARE ESM dialogs for each question. This allows for the inclusion of instructions before the user executes the task, for instance to test the participant's ability to recall information. One way this can be done is by creating an `ESM_Notice` element before an `ESM_Freetext` element.

Additionally, it is possible to create schedules for the test to be activated. The hours, minutes, weekdays, and months when the schedule should be activated can all be defined. By default, the plugin will schedule all test

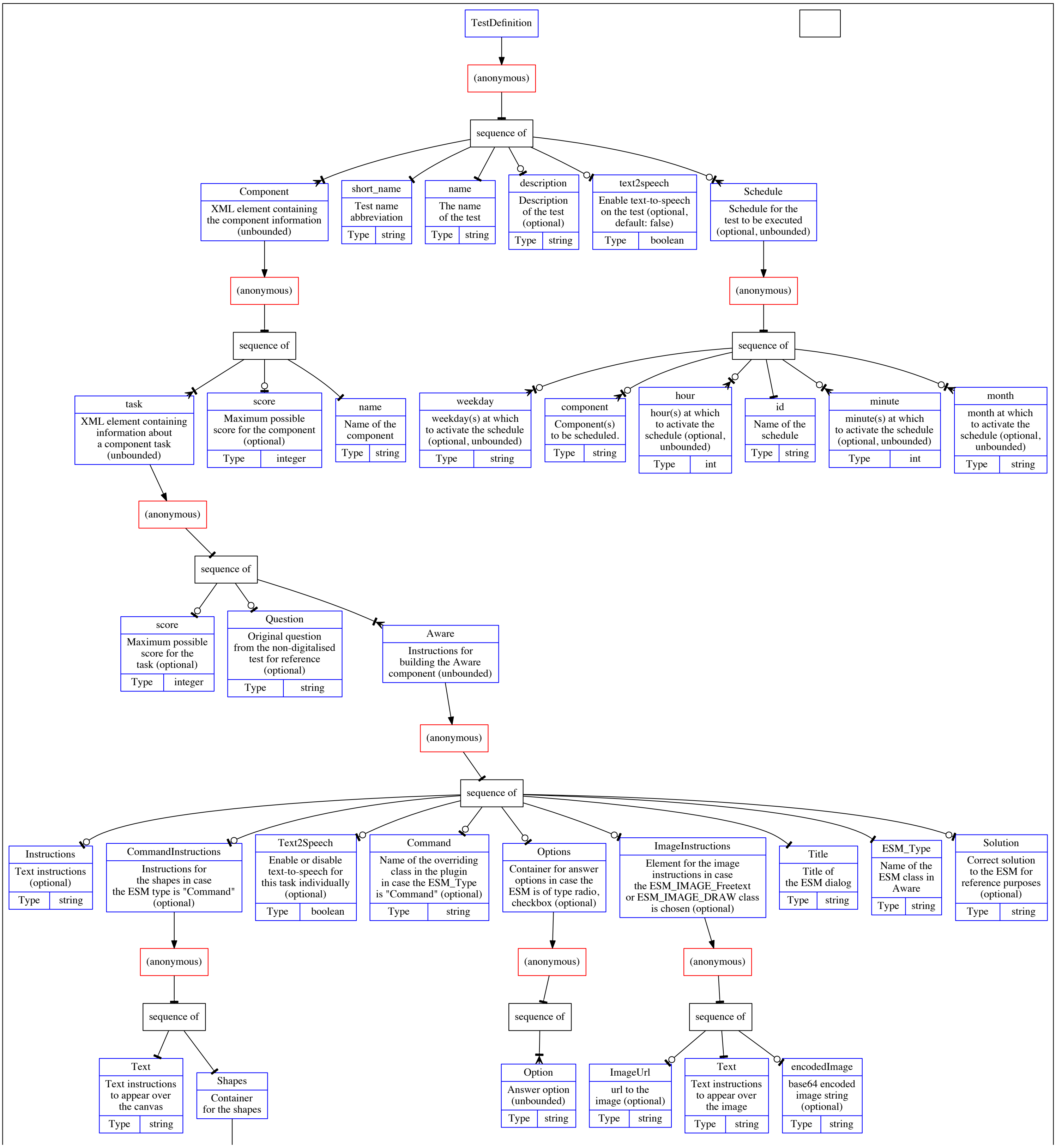


Figure 3.7: Structure of the TestDefinition XSD

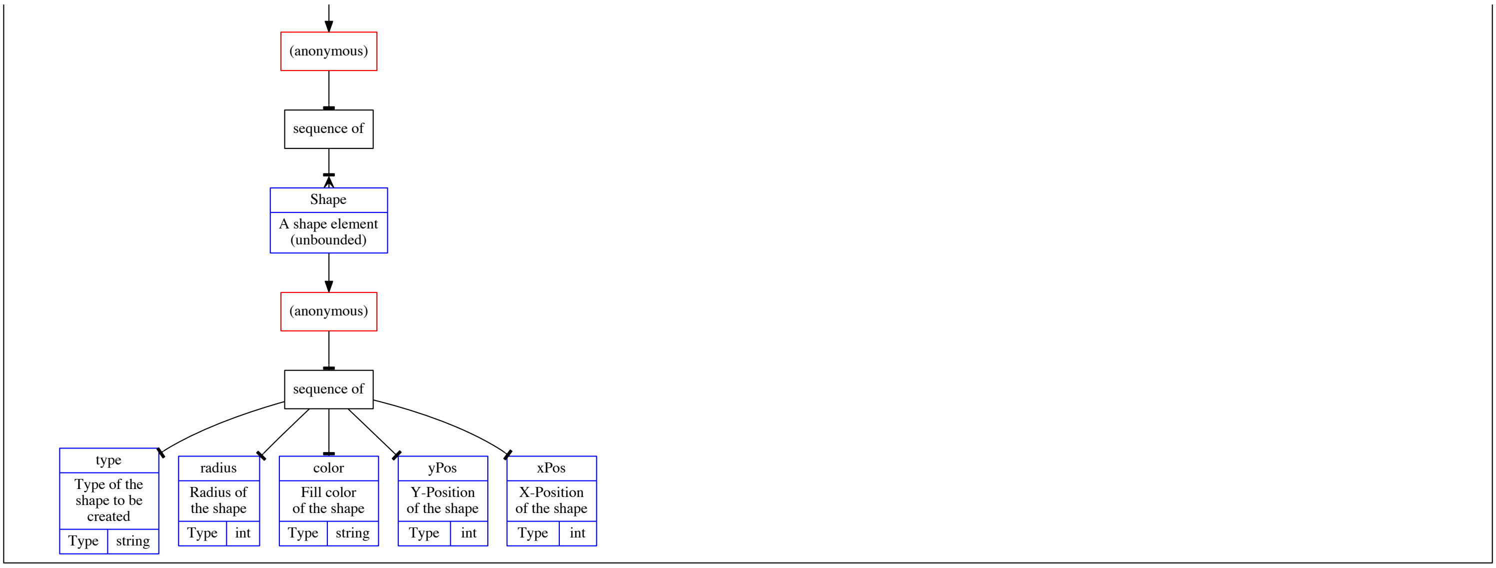


Figure 3.7: Structure of the TextDefinition XSD (continued)

components in the order defined by the test. However, it is even possible to only trigger specific test components, or change the order in which the test components are run, by specifying the components in the Schedule element of the XML file.

The digitised version of the clock drawing test following the XML schema is shown in Listing 4. The test is scheduled to trigger every Monday at 11:10. The test uses the `ESM_DRAW` class to create an ESM dialog with the drawing input method. The components "score", "description", and "solution" are not used by AWARE, however they are designed to make it easier to create and read cognitive tests based on the schema.

For storing data, the AWARE application maintains a local database with all information about the study, as well as the data collected from the plugins. Researchers performing studies with AWARE have to setup a SQL database server where the collected data from all participants can be stored. The AWARE application will periodically update the data on the server with the new user answers. The data for ESMs is stored in the 'esms' table of the SQL database for AWARE. The structure of the 'esms' table is defined by AWARE, as shown in Table 3.8. The data contains the 'device_id', which is unique for each device partaking in the study. The 'esm_json' field shows the specific question from the cognitive tasks that was executed. The answer is given in the 'esm_user_answer' field and is a string. However, as described in subsection 3.2.2, some of the newly developed ESM dialogs use JSON objects converted to strings that contain additional information, such as the encoded image that was drawn in the drawing dialogs.

Field	Type	Null	Key	Default	Extra
_id	int(11)	NO	PRI	NULL	auto_increment
timestamp	double	YES	MUL	0	
device_id	varchar(150)	YES			
esm_json	text	YES	NULL		
esm_status	int(11)	YES		0	
esm_expiration_threshold	int(11)	YES		0	
esm_notification_timeout	int(11)	YES		0	
double_esm_user_answer_timestamp	double	YES		0	
esm_user_answer	text	YES	NULL		
esm_trigger	text	YES	NULL		

Table 3.8: SQL esms table structure in AWARE

3.2.4 Technical requirements

The android application has been programmed using Android studio Version 2.3. The changes to the AWARE Framework where performed on AWARE Version 4.0.700.selfie, which runs on Android SDK Version 11 (Android 3.0) or higher. The same requirements apply to the AWARE Plugin. The final application was tested on the following smartphones and software versions:

- Android Emulator version 26 (Android 8.0) emulating Google Pixel
- Android Emulator version 25 (Android 7.1.1) emulating Google Pixel
- Samsung Galaxy S7 Edge (Android 7.0)
- Samsung Galaxy S7 (Android 6.0.1 and Android 7.0)
- LG G5 (Android 6.0.1 and Android 7.0)
- Google Pixel (Android 7.1.1 and Android 7.1.2)
- Huawei P9 (Android 6.0)

```xml
<?xml version="1.0" encoding="utf-8"?>
<TestDefinition
↪  xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
↪  xsi:noNamespaceSchemaLocation="TestDefinition.xsd">
  <name>Clock Drawing Test</name>
  <short_name>CDT</short_name>
  <description>Participants are asked to draw a clock
   ↪  face.</description>
  <text2speech>true</text2speech>
  <Component>
    <name>CDT Component</name>
    <task>
      <Question>Draw a clock face at 11.10</Question>
      <score>10</score>
      <Aware>
          <ESM_Type>ESM_DRAW</ESM_Type>
          <Title>Clock Drawing Test</Title>
          <Instructions>Please draw a clock face at
           ↪  11.10</Instructions>
      </Aware>
    </task>
  </Component>
  <Schedule>
    <id>ScheduleName</id>
    <hour>11</hour>
    <minute>10</minute>
    <weekday>Monday</weekday>
  </Schedule>
</TestDefinition>
```

Listing 4: The clock drawing test digitalised by following the test definition schema with a Schedule that triggers every Monday at 11:10.

Chapter 4

Results

4.1 Usability Evaluation

Traditional questionnaire-based assessments are aimed at patients in early, mild or severe stages of cognitive impairment. This application, on the other hand, was primarily designed for users who currently do not suffer from a mental disorder, though may develop a cognitive impairment in the future. The application therefore should be able to differentiate between the cognitively fit and cognitively impaired states. The target users for this application are approximately 50 to 60 years old, with no specifications about gender, level of education, or employment status.

In order to test the usability of the application a user evaluation was performed with the goal of answering the following questions:

- Is the CogniDecline application a useable approach for continuous cognitive assessment?
- Are potential users able to use CogniDecline ?
- Do they see any advantages of using CogniDecline?
- Do people experience the effort of using CogniDecline as worthwhile, given its advantages?
- How frequently would people make use of CogniDecline?

The System Usability Scale (SUS) [145, 146] was used for the evaluation. The SUS is a ten-item questionnaire used to evaluate the usability of a system. The answers rank on a five-point scale from “strongly agree” to “strongly disagree”. The SUS is easy to administer, performs reliably on small sample

$$SUSScore = 2.5 \times \sum_{n=1}^{10} \Big(\big(\frac{2n}{n} \in \mathbb{Z}) \rightarrow (5 - Q_n) \big) \wedge \big((\frac{2n+1}{n} \in \mathbb{Z}) \rightarrow (Q_n - 1) \big) \Big)$$

Figure 4.1: SUS score formula

sizes, and can effectively differentiate between usable and unusable systems [145].

The questions of the SUS are as follows:

1. I think that I would like to use this system frequently.
2. I found the system unnecessarily complex.
3. I thought the system was easy to use.
4. I think that I would need the support of a technical person to be able to use this system.
5. I found the various functions in this system were well integrated.
6. I thought there was too much inconsistency in this system.
7. I would imagine that most people would learn to use this system very quickly.
8. I found the system very cumbersome to use.
9. I felt very confident using the system.
10. I needed to learn a lot of things before I could get going with this system.

The usability scores are calculated by subtracting one from the score of all odd-numbered questions and subtracting the score for even-numbered questions from five. This process scales all scores from 0 to 4, whereby 4 represents the highest usability and 0 represents the lowest. The final score is calculated by summing all scaled scores and multiplying the total by 2.5. This results in a final score from 0 to 100. A final score above 68 is considered above average. The formula for calculating the SUS score is shown in Figure 4.1.

For the evaluation, an Android smartphone with the Aware application and Cognitive Experience Sampling Plugin installed was provided to the participants. Participants where provided with one of the following phones, which are very similar in regards to size and functionality:

- Google Pixel
- Samsung Galaxy S7
- LG G5
- Huawei P9

To start the test, the participants where asked to click on the smartphone notification to start the digitised MMSE questionnaire. The Android phone would then open the first dialog box with the Aware ESM of the digitised MMSE. The digitised MMSE was performed as outlined in subsection 3.2.2. After completing all steps of the digitised MMSE, participants where asked to fill out the SUS questionnaire form. In addition to the SUS, the goal of the usability evaluation was to explore user experiences specific to the application and to gain an understanding about potential users' willingness to frequently answer questions from the plugin. The application must be usable by older people who very often have very little experience with technology and smartphones. The degree to which this was achieved was measured with a number of demographic questions, as well as questions about technology use in addition to the SUS. The questions, asked alongside the SUS were as follows:

Comments

1. Did you have any specific difficulties using the application?

2. Did you find the speech-to-text functionality useful?

- ○ Very important
- ○ Moderately important
- ○ Not important

3. How did you find the quality of the formulation of the questions?

- ○ Very good
- ○ Good
- ○ Acceptable
- ○ Poor

- Very Poor

4. How did you experience the amount of questions asked?

- Too much
- About right
- Too little

5. Did you have any difficulties reading or understanding the questions?

6. How often would you be willing to answer a questionnaire from the application?

- Small questions, multiple time a day
- Small questionnaire, once a day
- Questionnaire, once a week
- Full questionnaire, once a month
- I would not use the application.
- Other . . .

7. Do you have any other comments?

Technology use

Participants where then asked to indicate their familiarity with smartphones by indicating how often they use their smartphone and what they use it for:

8. How familiar are you in the use of smartphones?

- I don't have a smartphone.
- I own a smartphone, but I rarely use it.
- I use smartphones for a few limited functions (e.g. texting, news, navigation, ...).
- I use a smartphone everyday for many different functions.

9. What do you use your smartphone for?

- texting
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- calling
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- email
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- reading the news, weather, etc.
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- surfing the web
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- playing games
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- watching videos
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- navigation
  - ○ never ○ rarely ○ occasionally
  - ○ frequently ○ very frequently
- taking photos

- ○ never ○ rarely ○ occasionally
- ○ frequently ○ very frequently

– banking

- ○ never ○ rarely ○ occasionally
- ○ frequently ○ very frequently

Demographic

Finally the following demographic questions where asked:

10. What is your age?

- ○ 19 or younger
- ○ 20 - 24
- ○ 25 - 34
- ○ 35 - 44
- ○ 45 - 54
- ○ 55 - 64
- ○ 65 - 74
- ○ 75 or older

11. What is your gender?

- ○ Female
- ○ Male
- ○ Other ...

12. What is the highest degree or level of school you have completed?

- ○ No schooling completed
- ○ High school graduate
- ○ Completed some college, no degree
- ○ Trade / technical / vocational training
- ○ Associate degree (e.g AA, AS)
- ○ Bachelor's degree (e.g.: BA, BS)
- ○ Master's degree (e.g. MA, MS, MEd)
- ○ Professional degree (e.g. MD, DDS, DVM)
- ○ Doctorate (e.g. PhD, EdD)

13. What is your marital status?

- ○ Single, never married
- ○ Married, or domestic partnership
- ○ Widowed
- ○ Divorced
- ○ Separated

14. What is your current employment status?

- ○ Employed full time
- ○ Employed part time
- ○ Unemployed and currently looking for work
- ○ Unemployed and not currently looking for work
- ○ Student
- ○ Retired
- ○ Self-employed

- Unable to work

The test was conducted at the University of Twente in the Netherlands with primarily native Dutch- or German-speaking subjects of different ages without regards to gender or current employment status. In order to accommodate the specific differences of the testing environment in the experiment compared to the typical assessment of the MMSE, some changes had to made to the phrasing of several questions. The questions of about locational orientation in the MMSE were replaced to accommodate the fact that the experiment did not take place in a hospital in the United States, but rather at a University in the Netherlands. The following questions about locational orientation in the MMSE were removed:

- Which state are you in?
- Which region are you in?
- Which county are you in?

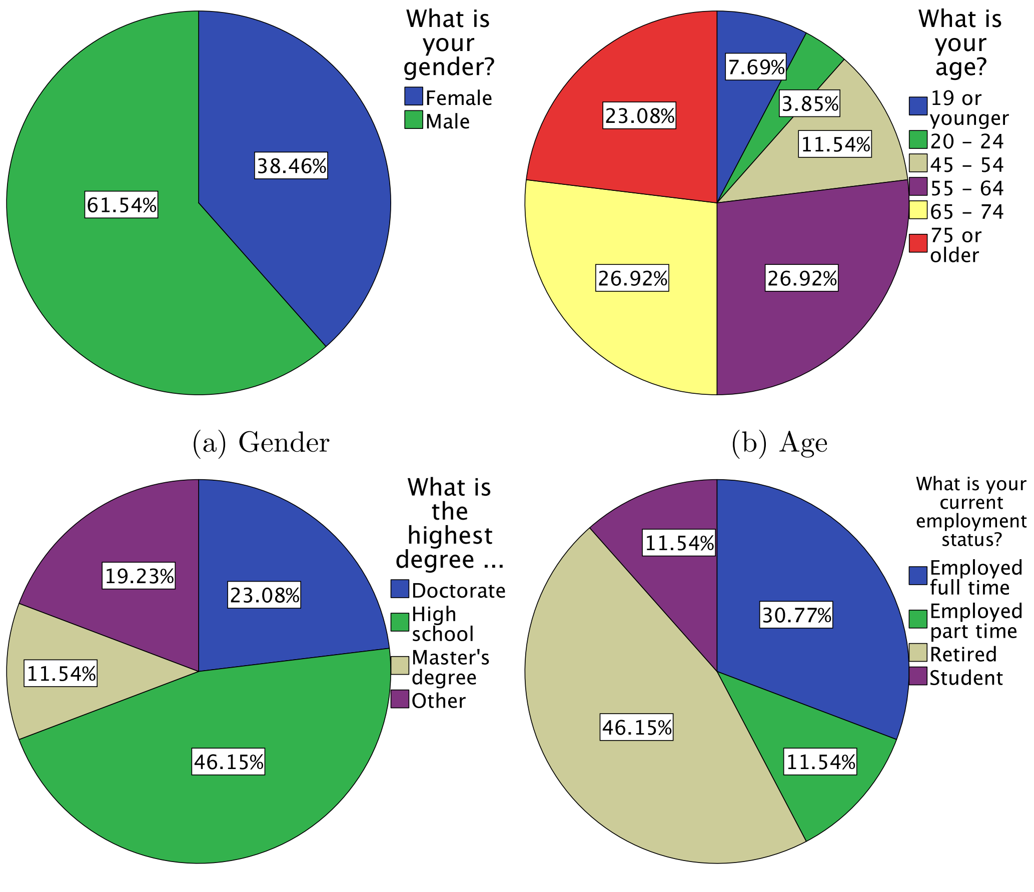
For conducting the survey in the Netherlands the questions were replaced with more appropriate alternatives:

- Which region are you in?
- Which country are you in?
- Which building are you in?

The study was conducted with 26 male and female subjects. Most subjects were over the age of 55, however the study also included some younger subjects. The demographic information for the test is shown in Figure 4.2. The test results were evaluated using the statistical software SPSS version 24.

The responses for the ten questions of the SUS are shown in Figure 4.3. The answer rank from 1 "strongly disagree" to 5 "strongly agree".

The SUS results were evaluated using the formula described in Figure 4.1. The final scores of the SUS ranged between 25 and 97.5, with a mean score of 71.25 and a standard deviation of 17. The descriptive statistics for the SUS score can be observed in Figure 4.4. The Shapiro-Wilk test for the 26 test scores reported a significance of 0.363, therefore the SUS scores are normally distributed. The histogram with a normal curve is shown in Figure 4.5. The box plot shown in Figure 4.6 reveals one outlier, with a score of 25.



(a) Gender

(b) Age

(c) Education

(d) Employment

Figure 4.2: Test Demographics

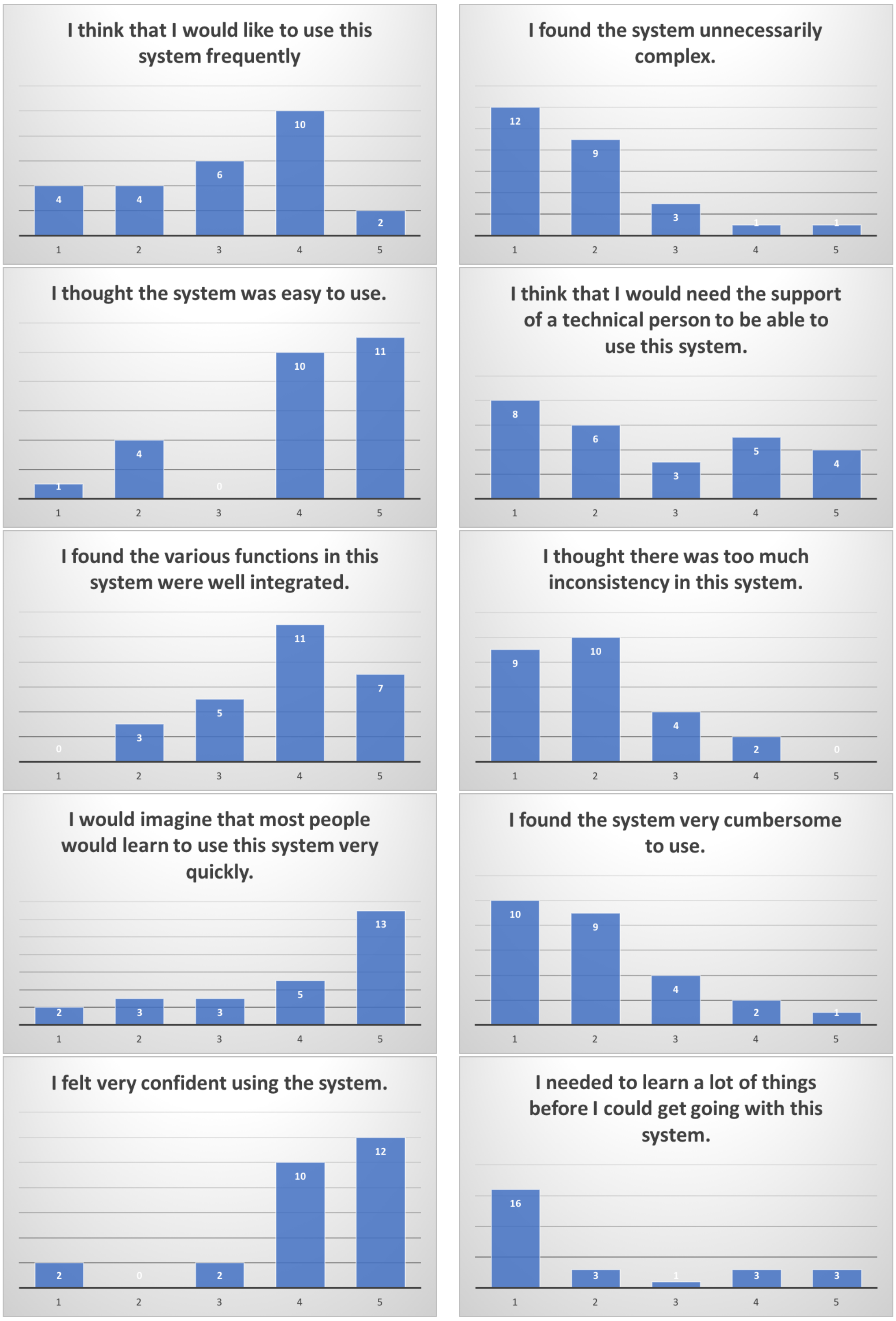


Figure 4.3: Responses for the questions of the SUS.

Descriptives

			Statistic	Std. Error
SUS Score	Mean		71.250	3.3862
	95% Confidence Interval for Mean	Lower Bound	64.276	
		Upper Bound	78.224	
	5% Trimmed Mean		72.073	
	Median		72.500	
	Variance		298.125	
	Std. Deviation		17.2663	
	Minimum		25.0	
	Maximum		97.5	
	Range		72.5	
	Interquartile Range		23.8	
	Skewness		-.701	.456
	Kurtosis		.530	.887

Figure 4.4: Descriptive statistics for the SUS scores.

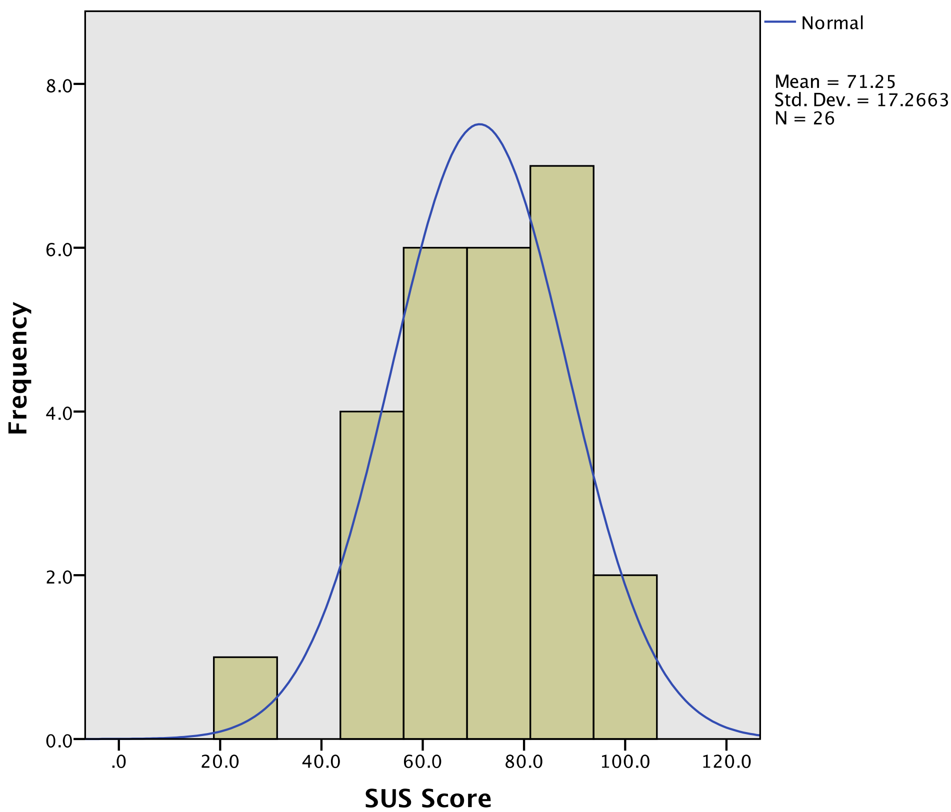


Figure 4.5: Histogram with normal curve for the SUS scores.

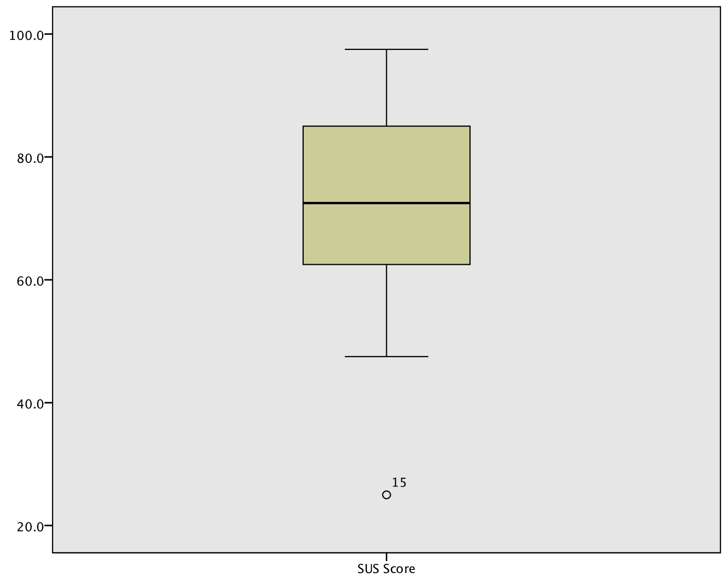


Figure 4.6: Boxplot for the SUS scores

In addition to the SUS, participants were asked about their smartphone use. As shown in Figure 4.7, 50% of respondents reported using their smartphones every day for many different functions, whereas almost 20% reported that they do not own a smartphone. When analysing the relation between the SUS scores and other variables such as age, education, or reported smartphone use no statically significant relationship could be found.

The primary goal of the application is ultimately to gain a better understanding of the user's cognitive state through frequent questionnaires and other assessments. Regarding the response relating to how often potential

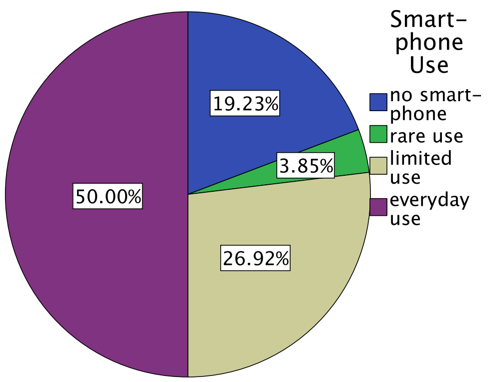
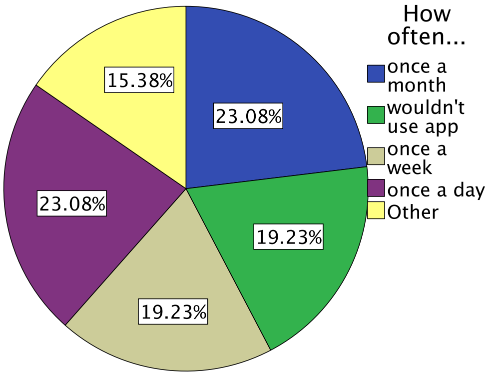
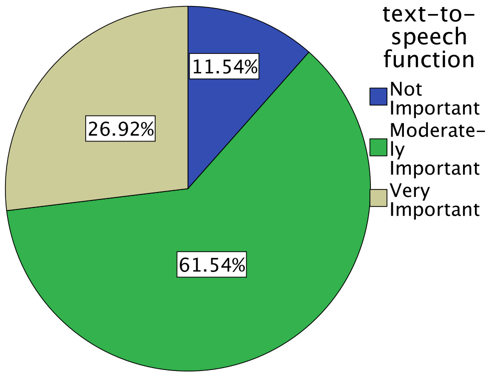


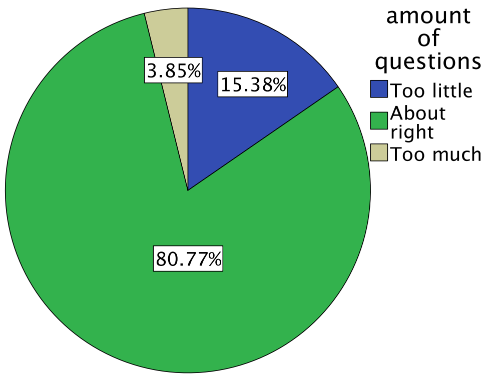
Figure 4.7: Reported smartphone use.



(a) Reported frequency users would answer questionnaires from Aware.



(b) Perceived usefulness of the text-to-speech functionality.



(c) Perceived amount of questions of the questionnaire.

Figure 4.8: Additional questions about the application

users would be willing to answer questions from the application (shown in Figure 4.8a) the usability test showed that only approximately 40% of the respondents would be willing to use the application on a weekly or daily basis. However, the response about how users experienced the amount of questions asked in the digitised MMSE (shown in Figure 4.8c) shows that the majority were satisfied with the amount of questions to be too much. In further comments, some users even stated that they were expecting a longer questionnaire. Therefore, regarding the response for frequency and amount of questions, future applications should aim at less frequent but slightly longer questionnaires, if they want to achieve higher likability by a similar target group.

The results of the usability study show that the plugin is indeed usable by non-cognitively impaired older subjects, even if they are not very familiar with the use of smartphones. While it is currently unclear how much cognitive impairment will influence the perceived usability of the application, and how much the application is capable to indicate the performance differences between cognitively impaired and non-impaired subjects, the results from the study indicate its potential use for tracking of very early cognitive impairment, especially when starting with non-impaired subjects.

Chapter 5

Conclusion and future work

5.1 Summary

This thesis outlines a plugin for the AWARE Framework for Android smartphones has been created that allows for the execution and creation of digitised cognitive tests, designed to resemble those found in traditional assessment methods. For this application the MMSE was selected to be digitised. The AWARE framework with the Cognitive Experience Sampling plugin allows for continuous cognitive assessment through the use of AWARE ESM dialogs in combination with the smartphone sensors.

The plugin developed in this project allows for the digitisation of cognitive assessment questionnaires, which are commonly used by medical professionals to diagnose cognitive impairment. This project aims to combine traditional assessment methods, which currently provide a validated method of diagnosing cognitive impairment, with newer research into technical solutions for assessing risk and protective factors found to influence dementia, especially physical factors that can be assessed using smartphone sensors, explained in Chapter 2. The AWARE framework in combination with the Cognitive Experience Sampling plugin therefore provides a method of linking traditional questionnaires and biographical data, assessed using AWARE's ESM dialogs with biosensory data, assessed from the smartphone's sensors and other AWARE plugins.

The XML schema allows for a quick and easy method of developing similar digital cognitive questionnaire assessments. The schema was designed to be simple, easy to understand, and comparable to the original questionnaire.

The schedules of the questionnaire through the application allow for continuous research into the cognitive state. Schedules make it possible to assess the questionnaire and track its performance over time. The data is thereby stored on a central server together with a timestamp and device ID. It is even possible to specify selected test components in the schedules, thereby creating the option for smaller selective tests, which could be executed more frequently.

5.2 Discussion

A usable smartphone plugin for the AWARE Android application was developed which allows for the digitisation of cognitive assessment tests. The development was lead by the definition of requirements using the MoSCoW approach. As explained in detail in section 5.2, it was possible to successfully fulfil these requirements through the development of the Cognitive Experience Sampling plugin for the AWARE application.

The plugin makes it possible to digitise and set up cognitive tests. These tests can use a variety of input types, which have been discussed in greater detail in . For the digitisation of the MMSE, free text and speech-to-text, drawing, and numeric input types were used. Schedules define when the test is executed by also allow the different test components to be scheduled separately or rearranged. This feature could be important for future continuous assessment with shorter questionnaires. For instance, future research could track the progression of a specific cognitive domain that is tested of the cognitive examination separately over the course of the day, or to differentiate between cognitive impairments. Further, some questionnaires could be designed so that they can be answered by users in a short, non-interruptive manner.

The application was tested with potential target users. This evaluation showed that the plugin is usable by cognitively non-impaired users. However, the usability evaluation indicated several problems related to the usability of the smartphone, the underlying Android operating system, and the AWARE framework that should be taken into account in future research of cognitive impairment using the Plugin. Some subjects were unfamiliar with the use of the Android system, and therefore it is advised that subjects be introduced to the Android smartphone and taught how to use the Cognitive Experience Sampling questionnaire.

As for technical issues, it is important to instruct the user to click on the AWARE notification and that they know how to use the keyboard to enter the solution. Furthermore, the execution of the drawing and copying tasks have been tested using the finger as input, whereas in the original questionnaires these tasks are performed using a pencil. The results from the evaluation test showed that it is very difficult even for non-impaired subjects to achieve clear and accurate results, therefore a stylus should be the used as the preferred input method for this test. Additionally, the application could be used on tablets or larger phones, since many subjects had difficulties typing on the small keyboards of the smartphones provided.

Based on the results from the usability evaluation, many users prefer performing tests that are challenging and engaging based on their specific age and cognitive state. Age-specific testing may result in a more enjoyable and engaging experience for users. For example, subjects in the early stages of cognitive impairment often have problems with memory, and it may be possible to detect these issues very early through cognitive assessment. There is also the potential to improve their ability through regular cognitive training.

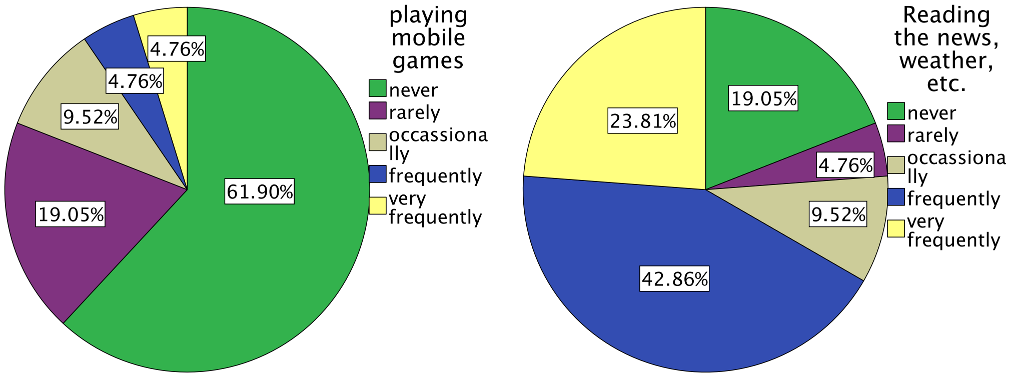
The success in terms of usability and adoption rate of commercial mobile platforms for tracking cognitive function through gaming, may indicate the potential usability advantage of the gamification of the MMSE. Younger subjects without cognitive impairment in particular may prefer more implicit methods of detecting cognitive decline and more engaging experiences could be achieved through gamification. Older subjects, on the other hand mentioned during the usability study, that they might not be interested in learning about their cognitive state and knowing of potential indications of cognitive impairment. Therefore, as with the younger group, a more implicit method may achieve a higher usability rate for future applications.

The percentage of people playing games on smartphones in the evaluation was very low, as shown in Figure 5.1a. The percentage of people reading the news on smartphones, on the other hand, was much higher, as shown in Figure 5.1b. This may indicate that future applications for cognitive improvement and assessment could be more related to the topics of interest of the specific user. For example, short questions about a recently read news article or other factual questions could be incorporated into the assessment. However, this was beyond the scope of developing CogniDecline, whose objective was to resemble the MMSE as close as possible.

The primary research question was:

> How can smartphone technologies be used for continuous assessment of cognitive function?

This question has been answered through a discussion on potential indicative variables that can be assessed on the smartphone. Smartphones are equipped with a variety of sensors that allow for the assessment of biomedical data, however medical examiners currently rely primarily on questionnaire to diagnose cognitive impairments. Therefore this project was accompanied by the development of a smartphone application for continuous cognitive assessment, designed to resemble medical questionnaires.



(a) playing mobile games (b) reading news, etc.

Figure 5.1: Reported frequency smartphones owners in the usability study use their phone to read the news and play games.

5.3 Future work

While the tool developed in this paper does not yet provide a validated method of diagnosing dementia or other cognitive impairments, the similarities to traditional methods of diagnosis make comparisons easier, and help to lay the groundwork for comparing long-term studies using continuous cognitive assessment of biosensory variables with more traditional assessment methods. Comparisons of the results for tests such as the MMSE performed through the plugin with the traditional face-to-face version of the same test are necessary to fully understand the implications of the technology-related differences between two forms of conducting cognitive tests, and to develop validated smartphone-based assessments for diagnosing cognitive impairment in the future.

Future research could incorporate the methods developed here with technical measurements of non-intrusive sensory indicators provided by the AWARE framework. For example, to the influence of gait speed, movement and out-of-home variability could be explored using data from the GPS sensor, accelerometer, or the activity recognition plugin. The influence of smartphone use or clock watching behaviour can be measured using lock and unlock frequency and application use. The influences of heart rate and breathing rate variability and stress can be measured using the accelerometer, or camera data, or dedicated heart rate sensors. By comparing these measurements with long-term studies of continuous cognitive assessment questionnaires that use the Cognitive Experience Sampling plugin, it may be possible to develop more unobtrusive and immediate techniques for diagnosing cognitive impairment.

When using the cognitive experience sampling plugin, it is important to consider potential cognitive impairments that may affect the performance of participants in the tasks and the difficulty of performing the tasks in relation to the usability of the application. The status of impairment could influence the potential of the application to accurately track differences in performance as cognitive functioning declines. The questions in the ESM questionnaire have to be specific to the cognitive state of the test subjects and sensitive to the specific changes in cognitive potential.

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