



Universidade do Minho
Escola de Medicina

Teresa de Jesus da Costa Castanho

Cognitive functioning from normal aging to mild cognitive impairment: combining rapid cognitive testing and informant reports to improve screening in clinical and research contexts

The work presented in this thesis was performed in the Life and Health Sciences Research Institute (ICVS), University of Minho. Financial support was provided by a PhD grant (SFRH/BD/90078/2012) from the FCT - Foundation for Science and Technology and "SwitchBox" (Contract HEALTH-F2-2010-259772), and co-financed by the Portuguese North Regional Operational Program (ON.2 – O Novo Norte), under the National Strategic Reference Framework (QREN), through the European Regional Development Fund (FEDER), and by the Fundação Calouste Gulbenkian (Portugal) (Contract grant number: P-139977; project "Better mental health during ageing based on temporal prediction of individual brain ageing trajectories (TEMPO)")

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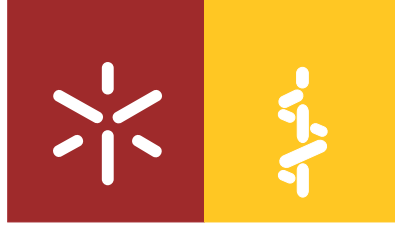
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Teresa de Jesus da Costa Castanho

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aging to mild cognitive impairment:
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in clinical and research contexts**

Tese de Doutoramento em Ciências da Saúde

Trabalho efectuado sob a orientação da

Doutora Nadine Correia Santos

e do

Professor Doutor Nuno Jorge Carvalho Sousa

STATEMENT OF INTEGRITY

I hereby declare having conducted my thesis with integrity. I confirm that I have not used plagiarism or any form of falsification of results in the process of the thesis elaboration. I further declare that I have fully acknowledged the Code of Ethical Conduct of the University of Minho.

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As pessoas sem memória são navegadores sem bússola.

João Lobo Antunes

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Cognitive functioning from normal aging to mild cognitive impairment: combining rapid cognitive testing and informant reports to improve screening in clinical and research contexts

Abstract

The increase in average life expectancy is a worldwide phenomenon responsible for a raise in the older/elderly population, including in Portugal. Of significance, aging is accompanied by a decline in cognitive ability, which has been associated with a decrease in the quality of life. To provide feasible and rapid assessment tools that assist not only in cognitive diagnosis in research and clinical practice, but also to establish thresholds for cognitive impairment, adapted to the Portuguese context, the applicability of rapid cognitive screening and informant instruments (Telephone Interview for Cognitive Status – Modified [TICSM-PT] and Informant Questionnaire on Cognitive Decline in the Elderly [IQCODE] respectively) was explored in this thesis.

Results indicate that the TICSM-PT presents associations not only with global cognitive measures, but also with a number of cognitive and psychological instruments performed in-person. Moreover, it demonstrated to be a practical tool for rapid cognitive assessment, and a valid method of screening cognition by telephone, among older adults with low educational background. Using a different technological approach, but the same instrument, it was further demonstrated that is possible to carry out accurate and reliable cognitive assessments through videoconference. Findings indicate that the videoconference administration method yields comparable results to the traditional face-to-face administration and supports the hypothesis of good acceptability among the older participants. Results also indicate that the IQCODE, when applied in community-dwelling older individuals, may not be an informative tool due to the lack of variability in the informants' responses. Although family members or close companions remain important sentinels in helping in the detection of cognitive impairment, herein the results raise important concerns, regarding their strengths and weaknesses, which prompt for further discussions regarding the weight that health professionals should place on informants' reports to recognize and detect cognitive decline.

Concluding, this thesis demonstrates that telephone and videoconference assessments can provide the opportunity to offer an evaluation to a wider range of people, including those with or without cognitive impairment. Instruments, such as the TICSM-PT, can be of great use to not only detect for cognitive deficits early on but also to monitor cognitive changes across time, in a broad and diverse number of subjects; whereas, the informant questionnaire IQCODE would probably be more useful in clinical situations, rather than in community-dwelling populations.

Funcionamento cognitivo do envelhecimento normal ao declínio cognitivo ligeiro: combinação de instrumentos cognitivos rápidos e relatos de informantes para uma otimização do rastreio em contextos clínicos e de investigação

Resumo

O aumento da esperança média de vida é um fenómeno mundial responsável pelo aumento da população idosa, incluindo em Portugal. De realçar, o envelhecimento é acompanhado por um declínio nas funções cognitivas e tem sido associado a uma diminuição na qualidade de vida. Com o intuito de fornecer instrumentos de avaliação cognitiva fiáveis e rápidos para o contexto português, não só para ajudar na investigação e prática clínica, mas também para estabelecer os limites do que consiste ou não o declínio cognitivo, foi explorada nesta tese a aplicabilidade de um instrumento de rastreio cognitivo rápido e outro baseado no relato de informantes: Entrevista Telefónica para avaliação do Estado Cognitivo – versão modificada (TICSM – PT) e o Questionário do Informante sobre o declínio cognitivo nos idosos (IQCODE).

Os resultados indicam que o TICSM-PT apresenta associações não só com testes de cognição geral, mas também com uma série de instrumentos cognitivos e psicológicos mais específicos aplicados face-a-face. Para além disso, o TICSM-PT demonstrou ser uma ferramenta prática para uma avaliação cognitiva rápida e uma metodologia válida de rastreio cognitivo por telefone mesmo em idosos com baixo nível de escolaridade. Utilizando o mesmo instrumento mas com uma abordagem tecnológica diferente, foi ainda demonstrado que é possível realizar avaliações cognitivas precisas e fiáveis utilizando a videoconferência. Os resultados indicam que o método de administração do TICSM-PT por videoconferência apresenta dados semelhantes à aplicação tradicional (face-a-face) e por telefone e apoia a hipótese de uma boa aceitabilidade desta metodologia entre os idosos. Os resultados também demonstram que o IQCODE, quando aplicado em indivíduos idosos residentes na comunidade, pode não ser um instrumento tão informativo quanto esperado devido à falta de variabilidade das respostas dos informantes. Embora os familiares ou companheiros próximos permaneçam importantes sentinelas ao ajudar na deteção do declínio cognitivo, neste estudo os resultados levantam preocupações importantes, no que respeita aos pontos fortes e fracos deste instrumento, que

incitam a discussões futuras relativamente à importância que os profissionais de saúde devem colocar nos relatos dos informantes no reconhecimento e deteção do declínio cognitivo.

Concluindo, esta tese demonstra que as avaliações por telefone e videoconferência podem oferecer a oportunidade de avaliar um maior leque de pessoas, com ou sem declínio cognitivo e a viver a grandes distâncias dos serviços de saúde ou em meios rurais. Ao utilizar instrumentos como o TICSM-PT, podemos detectar défices cognitivos mais precocemente e acompanhar alterações ao longo do tempo num número amplo e diversificado de pessoas, enquanto que o IQCODE provavelmente será mais útil em contextos clínicos onde o declínio cognitivo é mais prevalente.

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List of Abbreviations

A

AD – Alzheimer’s disease

AD8 – Alzheimer’s disease questionnaire

ADCQ – Alzheimer’s disease caregiver questionnaire

ADL – Activities of daily life

ALFI-MMSE – Telephone version of the mini-mental state examination

AMI – Age-related memory impairment

AUC – Area under the curve

B

BCS – Brief cognitive scale

BDRS – Blessed dementia rating scale

BMI – Body mass index

BOMC – Blessed-orientation-memory-concentration

BSCI – Brief screen for cognitive impairment

BTACT – Brief test of adult cognition by Telephone

C

CBRS – Cognitive behavior rating scale

CDR – Clinical Dementia Rating

CERAD – Consortium to establish a registry for Alzheimer’s disease

CI – Cognitive impairment

CIDS – Concord Informant Dementia Scale

CLTR – Consistent long term retrieval

COGTEL – Cognitive telephone screening test

COWAT - Controlled oral word association test

D

DASS – Depression anxiety stress scale

DAT – Alzheimer’s dementia

DECO – Détérioration cognitive observée

DMT – Double memory test

DQ – Dementia questionnaire

DR – Delayed recall

DSM – Diagnostic and statistical manual of mental disorders

DSST – Digit symbol substitution test

E

EU – European Union

F

FCSRT – Free and cued selective reminding

FTF – face-to-face

G

GDS – Geriatric depression scale

GERRI – Geriatric evaluation by relatives rating instruments

H

HVLT – Hopkins verbal learning test

I

IQCODE – Informant questionnaire on cognitive decline in the elderly

IDD-GMS – Informant interview for the diagnosis of dementia and depression in older adults

L

LTS – Long term storage

M

MATS – Memory and aging telephone screen

MCAS – Minnesota cognitive acuity screen

MCI – Mild cognitive impairment

MIDUS-II – Mid-life in the United States

MIS – Memory impairment screen

MIS-T – Memory impairment screen telephone

MMSE – Mini-mental state examination

MOCA – Montreal cognitive assessment

MQ – Short memory questionnaire

N

NEO-FFI-20 – NEO five-factor inventor-20 items

NF – Not found

NR – Not reported

O

OECD – Organization for economic co-operation and development

P

PFQ – Present functioning questionnaire

PRISMA – Preferred reporting items for systematic reviews and meta-analyses

PRMQ – Prospective and retrospective memory questionnaire

PSS – Perceived stress scale

R

RAGS – Relative's assessment of global symptomatology

ROC – Receiver operating curve

RUDAS – Rowland universal dementia assessment scale

S

SMC – Subjective memory complaints scale

SPMSQ – Short portable mental status questionnaire

SRT – Selective reminding test

STIDA – Structured telephone interview for dementia assessment

T

T-MMSE – 26-point telephone version of the mini-mental state examination

T-MOCA – Telephone montreal cognitive assessment

T3MSE – Telephone adaptation of the modified mini-mental state examination

TCAB – Telephone cognitive assessment battery

TELE – Telephone screening protocol

TIA – Transient ischemic attack

TICS- Telephone interview for cognitive status

TICSM – Telephone interview for cognitive status modified

TIMC – Blessed telephone information-memory-concentration test

V

VC – Videoconference/videoconferencing

W

WAIS-III – Wechsler adult intelligence scale-third edition

WC – Words and colors

WMS-R – Wechsler memory scale-revised

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CHAPTER I

Introduction: Cognitive Decline and Neuropsychological Assessment in Aging

1. Introduction

Our view of aging has changed to a more positive stand over the last few years, largely due to the increase in the number of people who reach advanced ages enjoying good physical and mental condition. However, new concerns are added. Currently, the unprecedented increase in the aging population is a global reality, particularly in western industrialized countries. As such, while when the average life expectancy was low, senility was not a health and/or social concern. Now it is of great care socially, culturally and in politico-economic terms. Just in Portugal, in 2011, there were about 2 million people aged 65 years or more, which corresponds to about 19% of the population (Perista & Perista, 2011). In fact, compared with the other member states of the European Union, Portugal has the fifth highest aging index (Pordata, 2014). Similar to the worldwide trend, also in Portugal the improvements and progress in the health sciences have contributed to people living longer (Governo de Portugal, 2012); but, to optimize well-being throughout aging, this demographic phenomenon must be accompanied by preventive and interventional actions in areas associated with age-related (cognitive) capacities (Tesch-Roemer, 2010).

Aging is not a disease. Instead, it is a normal and universal process, albeit associated with a degeneration of functions and organs over time, rendering systems vulnerable to disease. Thus, as we age, also the brain is not immune to change, and numerous physiological changes can potentiate cognitive decline, adding to other determinants. This cognitive decline, which can associate with (a gradual) loss of quality of life and independence, poses a tremendous challenge for organizations/entities with responsibilities in public health, as well as to the family core, particularly if it goes unnoted. In this context, the necessity to focus on the investment in instruments and cognitive functioning evaluation tests is of need, in order to screen, in a timely manner, for rates of decline, and for possible dementia, and assess the cognitive well-being of the individual and, ultimately, of the overall population.

2. Aging and cognitive trajectories

“I think, therefore I am”, wrote Descartes over 300 years ago. This remains particularly relevant when considering brain function of older individuals. In fact, besides health status,

what people appear to fear most to lose with age is their cognitive ability. Being able to think, process information and remember it, is at the heart of what we are; losing this ability can represent a “cut” from oneself, others and the world, a loss of (self-) identity. From “cell to thought” aging impacts on all body systems (Abdel Kader et al., 2015); but, the chronological age (i.e., the number of years a person has lived since birth) is an insufficient criterion to characterize health or cognitive status. Instead, as age advances, diversity among individuals, regarding health/brain status and performance, increases, and its determination depends on both intrinsic (e.g. genetic) and extrinsic (e.g. socio-economic) factors. Even so, the “normal” aging/getting older process is overall characterized by a functional, progressive and, oftentimes, irreversible decline. This is also associated with an impaired brain structure and function, which is of repercussion in behavior/cognitive phenotype.

Cognition refers to the mental functions involved in attention, thinking, understanding, learning, remembering, solving problems and making decisions. Although the term “cognition” is occasionally interchanged with “memory”, particularly when referring to older individuals, it is a multidimensional concept. It involves a number of interconnected cognitive abilities that depend on brain anatomy and physiology (IOM, 2015), that go from memory, to working memory and executive function. Also, despite the above framework, cognitive aging comprises some cognitive functions that may not change in aging, or may actually improve with age, while others, as stated, may decline. Distinguishing among these abilities is important since they play different roles in the processing of information and, ultimately, in daily functioning (IOM, 2015).

Declines in memory, a function largely controlled by the hippocampus, is one of the most common complaints among older adults. There are many forms of memory; where, some elements are fairly stable in older adulthood, while others decline (Abdel Kadler et al., 2015). For instance, loss of long-term memory does not seem to be a characteristic phenomenon of “normal” aging; while, on the contrary, a loss of short-term memory abilities, such as remembering the location of things, is more susceptible to advancing age. For example, a person may not remember what he/she ate at dinner the day before, but remembers perfectly what ate on his/her wedding day 50 years before. Remote memory or recall of past events, that have been stored over many years, are also relatively maintained in old age; yet, the

capacity to form new memories is more vulnerable to aging. Skills related to semantic memory and verbal abilities, like the use of vocabulary and knowledge acquired previously, may remain stable or even improve through life, declining in already more advanced ages (after 80/85 years) (Welsh-Bohmer & Attix in Steffens et al., 2015). On the other hand, executive functions tend to be impaired in normal aging (that is without pathology); where, executive changes occur gradually until 60 years of age, and are more accelerated when the individual reaches the 70s. One possible explanation may be the natural physiological deterioration of frontal lobes (Banhato & Nascimento, 2007). Declines in executive functioning can affect a person's ability to make decisions and inhibit unneeded/unrequired responses, and to, at the same time, limit the process of distinguishing between relevant and irrelevant information. Importantly, these declines have been linked to impairments in performing instrumental activities of daily life, such as medication management (Abdel Kader et al., 2015).

In fact, several everyday cognitive mechanisms are usually considered to be executive function, such as planning, concept formation and problem solving (Starkstein & Kremen, 2001). Located in the parieto-occipital region, the impairment of spatial ability typically leads to spatial disorientation, in which one can get lost in usual routes or even, in graver cases (normally associated with the presence of pathology), in one's own home (Morales & Lanna, 2008). Moreover, older adults may not perform well on spatial tasks that require mental rotation and/or visualization abilities (Abdel Kader et al., 2015), compared to younger individuals (or their younger self). In turn, declines in attention, or the capacity to ignore irrelevant stimulus, can have wide-reaching effects on one's ability to function properly and efficiently in everyday life (Glisky, 1995). When older, we can show difficulties when dividing or switching attention is required among multiple tasks, such as trying to pay attention to the television and simultaneously talk on the telephone. In fact, the tasks in which older people manifest impairments tend to be those that require flexible control of attention, a cognitive ability related with the frontal lobes (Glisky, 1995). However, as we age we also demonstrate relative preservation of performance on simple or focused attention, such as the ability to view a television program from start to end (e.g. a movie) if it is a dedicated task. In the meantime, one of the hallmarks of cognitive aging is a generalized slowing of processing speed. Generally, it takes longer to process cognitive and motor information and give a response throughout aging. This does not mean that the activities cannot be performed, but rather they just take

more time. Declines in processing speed can affect a person's ability to remember spoken instructions or even attend important information (Abdel Kader et al., 2015).

Despite the normal expected brain decline, there is a tremendous inter- and intra-individual variability in age-related changes in cognitive abilities (IOM, 2015). Thus, it is not easy to pinpoint with certainty when function(s) decline begins. That is, both age and the magnitude of the decline, can be different from person to person, or even intra-individually, across time. The decrease of cognitive functions is not only linked to chronological age, but also aspects such as health, lifestyle and education, must be factored in. Some older individuals maintain admirable cognitive functioning into their 70s and 80s, and can outperform or perform as well as younger ones, while others present relevant signs of decline by age 60. Moreover, decline is not uniform across cognitive abilities; different cognitive dimensions have some “degrees of independence” amongst one another, where some may be more or less prone to aging in different subjects. For instance, some older people have excellent episodic memory function (i.e. memory for personally experienced events) but impaired executive function, whereas others present the opposite pattern (Glisky et al., 1995). This vast heterogeneity among older individuals, thus, increases the challenges associated with understanding cognitive aging, and, ultimately, the approaches to “dealing” with the maintenance and promotion of cognitive abilities.

3. Aging and Dementia

With the overall aging of the population being the norm and not the exception, it is inevitable the increase in incidence and prevalence of age-associated chronic diseases. In cognitive abilities and/or brain aging, cognitive impairment and, in a last instance, dementia, are of great concern. In Portugal, it is estimated that the number of patients with dementia is about 153.000, of which 90.000 with Alzheimer's disease. These numbers are expected to duplicate by 2020, since that, according to a recent epidemiological study aiming to provide an estimate of the prevalence of dementia / Alzheimer's disease in Portugal, it is in the age groups above 80 years of age that lie more than 64% of people with dementia (Santana et al., 2016). Interestingly, dementia has been regarded as a pathological process since the 17th century (Kane et al., 2016). A stabilization of the identification of its cores features occurred over the

last century, as reported by Emil Kraepelin: progressive cognitive impairment, with a decline in previous functions, sufficient to affect everyday functioning. At the structural/ morphological level, it is characterized by a loss of neurons and atrophy of brain tissue eventually leading to cognitive limitations (Welsh-Bohmer & Attix in Steffens et al., 2015; Kane et al., 2016). Health professionals frequently use the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) to guide them to determine if a person has dementia or not, and if so, its causes. In the latest edition of the manual, the DSM-5 describes dementia as a cognitive disorder that may be classified as 'major' or 'mild' (American Psychiatric Association, 2013). To meet DSM-5 criteria for a major cognitive disorder, an individual must present significant and accentuated cognitive decline, and it must interfere with the independence and autonomy in everyday tasks (e.g. to need help with tasks such as paying bills and management of medication). In turn, to meet DSM-5 for mild cognitive disorder, one must exhibit modest cognitive decline but the everyday life activities are not disturbed, it only requires greater mental effort to perform them (American Psychiatric Association, 2013).

The knowledge of the risk factors for dementia has, nonetheless, changed/evolved along the past decades (Matthew et al, 2016), and several have been identified including age, genetic susceptibility, various clinical characteristics and family history. Still, care is of note. For instance, although it is true that age is a risk factor for dementia, dementia is not a normal part of aging, thus, it is not because of an old age that someone will unavoidably suffer from dementia (Baltes & Smith, 2003). In fact, curiously, it is described that the "feeling of being older (rather) than the actual age" is the predictor of poor general health; specifically, higher perceived age is related to increased mortality (Uotinen et al., 2005). Beyond the non-modifiable factors (e.g. age in itself), other aspects like lack of physical activity, both low and high BMI, poor(er) sleep, (higher levels of) stress and alcohol consumption, have all been indicated as modifiable lifestyle factors that can play a role in dementia (Aalbers et al., 2016). Furthermore, literature also indicates that those with fewer years of education are at higher risk for dementia (Sharp & Gatz, 2011). This later observation may relate with "cognitive reserve." Some studies indicate that having more years of education builds a "cognitive reserve" that enables individuals to better compensate for alterations in the brain (Stern, 2012). Other authors further indicate for other education-related factors that may contribute to or account for the increased risk of dementia; these include, for instance, being more likely to have

occupations that are less mentally stimulating and/or a lower socio-economic status. The latter one can, for instance, increase one's likelihood of malnutrition and reduce the ability to pay for health care and/or for suggested treatments (McDowell et al., 2007). Even the context or the place where the individual lived/lives can be a risk factor. For instance, it was described that rural living over the course of someone's life could be related to dementia; besides the difference in the potential educational offer in rural areas compared to urban areas, the access to activities that enhance cognition (i.e., libraries, social support), and to medical care, may vary between the contexts (St John et al., 2016).

In summary, since there is no cure for dementia, any action that delays its onset or development acquires an enormous relevance. Hence, it is of great importance to develop methodologies to prevent or to, at least, delay the progression of the disease, which includes necessarily identification of cognitive decline. At present, prevention focuses either in physiologic or psychosocial factors and lifestyle. However, how these factors are involved in the emergence and development of dementia remains poorly known.

4. Neuropsychological evaluation of cognitive performance

The majority of cognitive functions such as memory, executive function, visuospatial abilities and processing speed, are known to be associated to highly sophisticated networks containing tens of millions of neurons. This highlights the need for continued development of refined neuropsychological tests (IOM, 2015). Moreover, the tendency towards the aging of population, and the concomitant increase in cognitive decline/impairment and/or dementia, as previously discussed, justifies an increasing need for reliable and valid neuropsychological instruments, including in Portugal. Neuropsychological evaluations, or cognitive testing, allow for a better characterization of the most affected cognitive "areas", and are important in the early detection of cognitive dysfunction, providing information regarding patient capacities and deficits. This is of importance in selecting intervention approaches and for guiding (future) decision making with respect to competency and safety (Welsh-Bohmer & Attix in Steffens et al., 2015).

The development of translated instruments, and their adaption to the language and cultural context of each individual country, is essential to (i) conduct consistent and relevant

epidemiological studies, and (ii) assist in the diagnostic elucidation of clinical practice and identifying patients at early stages of cognitive impairment (Bustamante et al., 2003). As described by Young et al (2011), the key to a reliable identification of cognitive impairment comprises three components: (1) observation of the patient/participant; (2) results of standardized tests with population-based normative data; and, (3) a collateral report from an informant (Young et al., 2011). These are next briefly considered:

- Observation of the patient: in this regard, the conversation with the patient/participant can be sensitively guided to address intrusions in everyday life, such as forgetting appointments, problems with finances, imprecision with dates and sequence of events, or a tendency to repeat phrases. These clues, associated with the presence of cognitive impairment, may be subtle and overlooked, thus the importance of their observation.
- Collateral report from an informant: it is important to talk not only with the patient but also to someone who knows him/her well. A collateral report from an informant is essential to clarify what symptoms exist, and their timescale and relation(ship) to(with) the patient's previous mental function. Informant-based questionnaires may be useful to structure the conversation. They are supposed to be simple and rapid to complete, either face-to-face or by telephone. This type of questionnaires focus more on long-term changes, in aspects of cognitive functioning and behavior, instead of present function.
- Standardized tests: many brief and standardized tests of cognitive function have been developed, but only a few are properly adapted for use in the Portuguese population. Overall, brief cognitive tests are aimed to screen cognitive impairment. They are useful in the control of the development of cognitive deficits, and in the assessment of the effectiveness of several strategies. However, whether used alone or incorporated into batteries of tests, they require necessarily a further exhaustive evaluation to establish firm conclusions.

In this context, tests should be valid, reliable and culturally sensitive (Young et al., 2011). Validity refers to the extent to which a tool or scale actually measures what is designed to measure. To be considered valid, the interpretation of tests scores must be based on theories and empirical evidence that indicates a relation between the test and what it purports to

measure (Furr & Bacharach, 2013). Reliability is mainly concerned with issues of consistency. This covers stability over time, so that if participants complete a questionnaire at a certain point in time, and repeat it at some point later, the score(s) remain(s) similar. When constructs are not reliably measured, the obtained scores will not approximate a true value regarding the cognitive or psychological variable under evaluation (Geisinger, 2013). If the measure is properly applied and interpreted, the results can help to refine the diagnosis and serve as an indicator of disease development or cognitive decline. Cultural sensitivity refers to the suitability of an instrument to be used with different ethnic groups, or in different countries or socio-cultural backgrounds, to those in which it was first developed.

Besides these considerations, one of the most crucial aspects when administering neuropsychological tests is the selection of the appropriate test(s). This means that the selection of tools must be dependent on the examination of normative data collected with each tool and the population associated to it. Most cognitive tests have normative data that reflect the main demographic characteristics of the population, like age, sex, and ethnic and educational background (Lesak et al., 2012). Other considerations are the setting where they are applied, and/or the amount of time the neuropsychologist, clinician, and/or the person administering the test, has with the individual being assessed. For instance, brief tests, in general, take few minutes to complete, but can provide a way of evaluating mental status that is not too exhausting for people who may be ill. These tests can be administered without the need for extensive training, and are capable of use to identify people whose cognitive function may require further investigation.

The conventional approach to assess cognitive performance involves in-person based administration of neuropsychological tests. It may be a fixed battery, which entails a specific set of neuropsychological tests regardless of the reason for testing or a flexible battery. However, in either instance, for whatever reason, many participants/patients may not have access to the traditional face-to-face and paper-and-pencil neuropsychological assessment (Cowain, 2001). Thus, alternative means of test applications, such as telemedicine, can be a plausible and potentially cost-effective solution (Cowain, 2001). Particularly, older people often demonstrate physical or cognitive disabilities which limit their ability to travel to health care centers. Cognitively impaired individuals can often experience greater confusion and some of them may require a caregiver to accompany them, who may not be always available (Gray in

Fillit et al., 2016). Distance strategies can, thus, represent an important opportunity to overcome in-presence challenges. They encompass various applications of telecommunication technology to provide mental and medical services to, for example, people located in isolated or different geographical areas than the health professional (Jacobsen et al., 2003). There are many technologies available for cognitive evaluation. These include traditional telephones and videoconference equipment, as well as communication technologies such as email to send and receive assessment materials. The internet is also used to administer neuropsychological tests and measures remotely on web pages, and for videoconference by using webcams on personal computers (Luxton et al., 2014). Previous research has also demonstrated that reliable and valid testing of neuropsychological constructs can be done over the telephone (Kliegel et al., 2007). As the current technology continues to develop, and to build infrastructure to support methods to obtain and deliver information, the mechanisms and techniques available for remote assessment of neuropsychological performance will also continue to expand (Mundt et al., 2006). Nevertheless, one has to consider that regardless of the technologies to be adopted, these must have demonstrated usability for older adults with variable cognitive skills.

As cognitive assessment becomes an increasing part of adult's lives, society has a collective interest in ensuring that testing is performed in a responsible and accurate way. The failure to do so may have serious consequences, such as people receiving inadequate labels regarding their cognitive abilities (labels that can lead to stigma and discrimination) or, on the other hand, false reassurance (IOM, 2015). An accurate assessment of cognitive abilities, and their trajectory, is thus one of the great challenges facing health professionals.

5. Objectives

For most individuals, aging contributes to a loss of capacity to perform basic activities of daily life, decreased performance on cognitive abilities and increased health-care costs. Despite the fact that the public health impact of cognitive impairment is clear, this is often under-recognized. Therefore, when considering our current societal shift/population aging, the need for better, faster and more reliable cognitive screening is imperative, and of care, in clinical settings and research. In line, the main focus of this thesis was to investigate the viability of

“rapid screening” instruments and informants reports in the evaluation of cognitive heterogeneity and cognitive impairment in older individuals.

Specifically, the aims were as follows:

1 – Translation/retro-translation and validation of two “rapid-screening” cognitive instruments: the Modified Telephone Interview for Cognitive Status Assessment (TICSM) and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (Chapter III and VII);

2 – Evaluation of the reliability of the validated instruments via specific neuropsychological tests in order to characterize the cognitive functioning of older individuals (Chapters III and VII);

3 – Determination of whether cognitive testing via a videoconferencing approach using the validated tool TICSM would provide comparable results with the face-to-face interview and telephone assessment methodologies (Chapter V).

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CHAPTER II

Teresa Costa Castanho, Liliana Amorim, Joseph Zihl, Joana Almeida Palha, Nuno Sousa,
Nadine Correia Santos (2014)

Telephone-based screening tools for mild cognitive impairment and dementia in aging studies: a review of validated instruments

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Telephone-based screening tools for mild cognitive impairment and dementia in aging studies: a review of validated instruments

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Abstract

The decline of cognitive function in old age is a great challenge for modern society. The simultaneous increase in dementia and other neurodegenerative diseases justifies a growing need for accurate and valid cognitive assessment instruments. Although in-person testing is considered the most effective and preferred administration mode of assessment, it can pose not only a research difficulty in reaching large and diverse population samples, but it may also limit the assessment and follow-up of individuals with either physical or health limitations or reduced motivation. Therefore, telephone-based cognitive screening instruments can be an alternative and attractive strategy to in-person assessments. In order to give a current view of the state of the art of telephone-based tools for cognitive assessment in aging, this review highlights some of the existing instruments with particular focus on data validation, cognitive domains assessed, administration time and instrument limitations and advantages. From the review of the literature, performed using the databases EBSCO, Science Direct and PubMed, it was possible to verify that while telephone-based tools are useful in research and clinical practice, providing a promising approach, the methodologies still need refinement in the validation steps, including comparison with either single instruments or neurocognitive test batteries, to improve specificity and sensitivity to validly detect subtle changes in cognition that may precede cognitive impairment.

Keywords: neurocognitive impairment, early detection, rapid-assessment tools, dementia, telephone-based screening, cognition

1. Introduction

In the past years, improvements and progress in the health sciences have contributed to people living longer lives. In order to optimize physical and mental health, as well as well-being, during aging, appropriate gerontological research addressing changes in cognition is needed. Of note, aging is usually associated with an overall gradual decline in cognitive functioning, particularly in information processing/attention, memory and executive function, which may lead to a decrease in independence of daily living and, thus, of life quality (Salthouse, 2010). However, decline in cognitive domains is not uniform across all individuals, and even in the same individual, throughout aging (Riddle, 2007). For instance, factors that can possibly confer a risk of decline in cognitive performance, other than age in itself, are low(er) level of schooling, institutionalization, female gender, depressive mood, and the presence of “unhealthy” lifestyle factors and/or of clinical pathologies (Ardila et al., 2000; Van Gool et al., 2003, 2007; Wilson et al., 2009; Yamamoto et al., 2009; Paulo et al., 2011; Köhler et al., 2012; Santos et al., 2012; Costa et al., 2013; Viscogliosi et al., 2013). This heterogeneity in cognitive aging, and the need to reach larger population samples, challenges the available instruments that currently exist to efficiently assess global cognition and screen/detect deviations from healthy (“normal”) cognitive aging to cognitive impairments and dementia.

Cognitive impairment is defined as a clinical and transitional condition that spans from age-related memory impairment (AMI) to dementia (Petersen, 2004). Specifically, the American Academy of Neurology includes as criteria for mild cognitive impairment (MCI) the presence of memory complaints (preferably corroborated by an informant) and memory impairment, albeit still presenting normal global cognitive functioning and intact activities of daily life (ADL) (Petersen et al., 2001). Because cognitive impairments diagnosed as MCI are not severe enough to have a significant impact on daily life, individuals with MCI may be easily missed. Therefore, these individuals, who present a cognitive impairment, but without functional deficits, are at higher risk for dementia. Any possible intervention strategies to prevent this transition or, more precisely, the assessment of intervention strategies, requires the availability of valid and reliable screening assessment tools. At present, the gold standard to assess cognitive functioning, and to diagnose MCI and dementia, in older adults, is in-person (face-to-face) evaluation using a battery of standardized and validated cognitive tests (Herr and Ankri, 2013). However, this procedure implies high effort and time for the administration of the

comprehensive cognitive battery by specialized researchers/clinicians. In addition, it holds also the risk of sampling biases because studies tend to comprise healthier and more educated older subjects, and those without limitations of mobility (Pachana et al., 2006). Therefore, cognitive assessment performed by telephone may provide an efficient, practical and valuable alternative and/or complementary strategy to the traditional face-to-face test administration methodology (Kliegel et al., 2007).

In fact, since the introduction of the Telephone Interview for Cognitive Status (TICS), by Brandt et al. (1988), cognitive screening instruments administered by telephone have been shown to provide some key advantages. Foremost, they not only allow a “rapid-administration” protocol that can be utilized by health care professionals, and/or researchers, on a regular basis (albeit being designed in a manner that can also be applied in the course of “normal” face-to-face evaluations if needed). Complementarily, they also serve as a more cost-effective and rapid-screening cognitive tools in medium- to large-scale epidemiological studies (Rabin et al., 2007), providing a means to lower dropout rates in longitudinal studies and overcoming geographical limits (Beeri et al., 2003). Furthermore, their indirect application is more likely to be well accepted by older/elder subjects who may present impediments in their physical mobility or health status, and/or with reduced motivation and, therefore, allow both “cognitive triage” and follow-up assessments in population samples that are difficult to reach (Kliegel et al., 2007). Finally, the practicability and efficiency of use is mainly derived from the instruments' design. The more accessible telephone instruments follow the model of the most widely accepted in-person brief screening measure for dementia diagnosis, the Mini-Mental State Examination (MMSE) (Wolfson et al., 2009).

The goal of this review is to provide a compiled base of the available telephone-based instruments for neurocognitive screening. Information is provided on the instrument purpose, authors, validation sample, and gold standard. Furthermore, characteristics regarding administration time, number of items, maximum score, cut-off threshold for cognitive impairment, and sensitivity and specificity measures are also provided. It is also reported if the instrument has been applied in other cohorts and/or translated to languages other than the original. Finally, an overall critical analysis is provided, informing on strengths and weakness of the instruments.

2. Literature review

The systematic search of the literature was conducted in the EBSCO, Science Direct, and PubMed databases, using a combination of the search terms “telephone assessment,” “aging” (or “ageing”), “cognitive evaluation,” “MCI,” “dementia,” “telephone interview (for) cognitive status,” “validation questionnaire” and/or names of the specific instruments as these were identified. The search was limited to articles published in English and to instruments that allow discriminating between “normal” cognitive aging and cognitive impairment/dementia. Instruments/batteries administered by telephone to assess for cognitive function, and/or impairment, in non-aging cohorts, and/or designed for specific clinical cohorts [such as, for example, used to assess cognitive function in patients with pulmonary arterial hypertension (Taichman et al., 2005) or with chronic fatigue syndrome (McCue et al., 2002)], were not considered. Exceptions were for MCI, dementia, Alzheimer's disease, stroke and/or other cognitive-related disorders. Titles and abstracts were evaluated as a first step and then full-text articles were read for their relevance to this review. Two separate researchers conducted the search and the lists were cross-compared to generate a compiled list. The literature search was conducted between September 2012 and April 2013, with a total final of 19 separate telephone-administered screening tools identified. The search procedure is summarized in Figure 1, following the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)” flow diagram template (Moher et al., 2009). Table 1 summarizes the instruments, including number of elements/items and time of administration, and reporting on measures of validity. Furthermore, for each instrument, overall characteristics, usefulness and applicability, in clinical and research contexts, are next described.

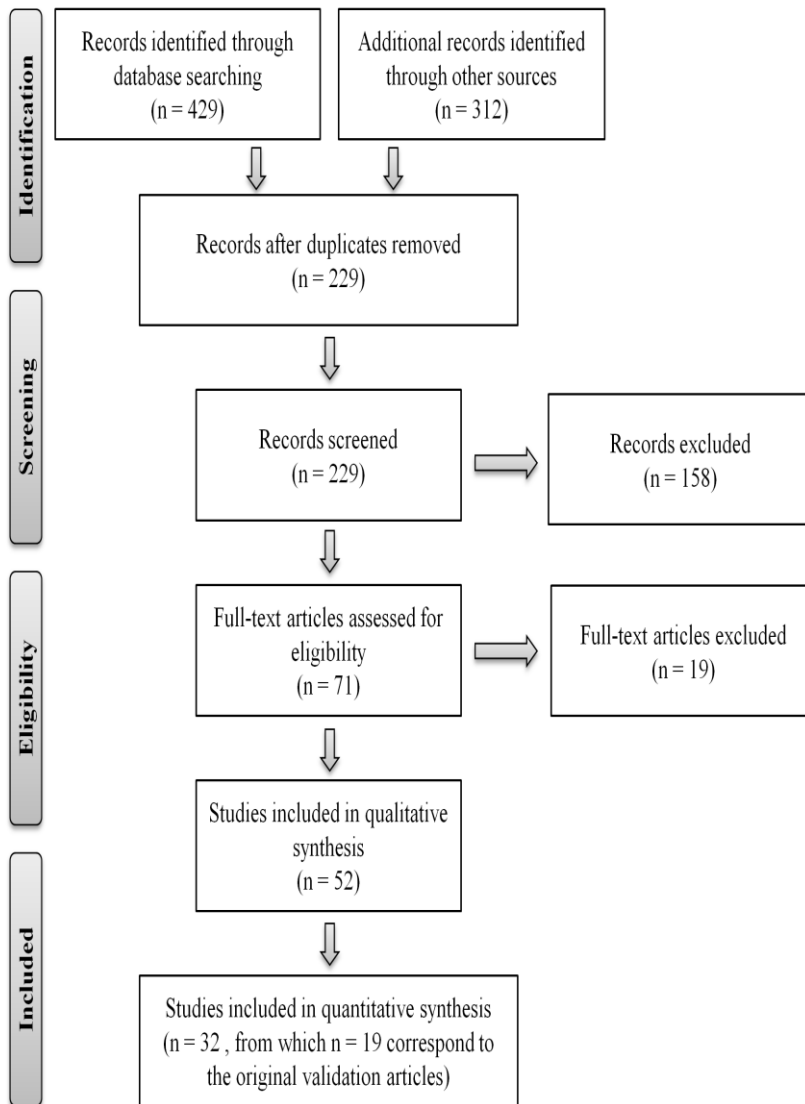


Figure 1. Flow diagram of the literature review. Depiction of the flow of information through the different phases of the review. PRISMA flow diagram template (Moher et al., 2009).

3. Telephone-Based Neurocognitive Screening Instruments

Telephone Interview for Cognitive Status (TICS) and Telephone Interview for Cognitive Status—Modified (TICSM)

The TICS instrument was originally purposed for the evaluation of cognitive functions in patients with Alzheimer's disease (Brandt et al., 1988; Brandt, 1991). Surpassing its original intent, it is now the most frequently used telephone-based cognitive screening test in medium- to large-scale studies and epidemiologic surveys (Herr and Ankri, 2013). Briefly, it assesses orientation to time and place, attention, short-term memory, sentence repetition, immediate recall, naming to verbal description, word opposites and praxis. The TICSM is the TICS modified version, adding a measure of delayed verbal recall. Both instruments have been translated into several languages, including Finnish, French, German, Hebrew, Italian, Japanese, and Spanish, serving an important role in clinical and research contexts. In clinical trials, TICS discriminated carefully diagnosed Alzheimer's disease patients from healthy controls, and in a sample of stroke patients TICS and TICSM were found valid instruments for evaluating cognitive function (Brandt et al., 1988; Barber and Stott, 2004). In epidemiological studies, both instruments detected a range of mild to moderate cognitive disorders and appeared to have comparable sensitivity and specificity as cognitive screening instruments for dementia and Alzheimer's disease (Welsh et al., 1993; Smith et al., 2008; Wolfson et al., 2009). There is, however, relatively little information concerning its use in longitudinal studies (Lopez and Kuller, 2010) and with older individuals (Baker et al., 2013). Both the TICS and TICSM' scores are highly correlated ($r = 0.94$, $p < 0.001$ and $r = 0.57$, $p < 0.05$, respectively), with the MMSE (Brandt et al., 1988; Jager et al., 2003). Furthermore, TICSM scores are adjusted to subjects' educational level (Gatz et al., 2002) and it is assumed to distinguish reliably between normal cognition, MCI and dementia (Knopman et al., 2010). Despite its wide use, the only information reported on its application is indicated in the TICSM validation study, in which psychometricians applied the instrument.

The original study indicates some key strengths of the instrument, including: cost-effectiveness for use in large-scale studies; little evidence of ceiling and/or practice effects; and greater acceptability by participants, who appear to find the telephone interview less threatening than if conducted in a face-to-face clinic assessment. These indicate for the possibility of lower dropout rates in trials and longitudinal studies. Another strength relates with the fact that it addresses the lower end of the cognitive ability spectrum (dementia). Still, the authors also report on some important instrument limitations, namely: individuals with hearing impairment may be unable to complete the test or make errors; certain words are more difficult for participants to distinguish clearly and require careful attention to pronunciation; concentration

and recall repetition may be hindered if words are not clearly heard. Finally, the authors also note that the instrument must be validated in preclinical populations, so to assess for the positive predictive value in healthy or mildly impaired or “ambiguous” cases.

Telephone Version of the Mini-Mental Status Examination (ALFI-MMSE) and the 26-Point Adaptation of the ALFI-MMSE (T-MMSE)

This telephone-based version of the MMSE was originally administered as part of the Adult Lifestyles and Function Interview (ALFI) (Roccaforte et al., 1992). It has been recommended as an instrument to examine cognitive function in patients with Alzheimer's disease, mainly regarding orientation, attention, memory recall, and calculation, and as means to reassess individuals who have been evaluated in person, allowing to assess cognitive stability or estimating decline. The ALFI correlated significantly with other face-to-face screening tests, specifically the MMSE ($r = 0.85$; $p < 0.001$) and the Brief Neuropsychiatric Test (correlation and p-values not reported) (Roccaforte et al., 1992). The ALFI-MMSE has been used in several studies including stroke patients (Longstreth et al., 2010), post-myocardial infarction patients (Thomas et al., 2011), and older adults with different levels of nutritional risk (Roberts et al., 2007), as a practical assessment tool when face-to-face assessments were difficult to obtain. Subsequently, a 26-point adaptation of the ALFI-MMSE was constructed (the T-MMSE), which in addition comprised a three-step action-based response (“say hello, tap the mouthpiece of the phone three times, then say I'm back”) and the request to provide the phone number. The T-MMSE was validated in a group of patients with probable Alzheimer's disease (Newkirk et al., 2004), although the authors mentioned that future research using a randomized test order would be necessary to better estimate the effect of previous exposure to the test (test–retest). For both tests, the ALFI-MMSE and the T-MMSE, a clinical nurse specialist conducted the phone interviews.

Short Portable Mental Status Questionnaire (SPMSQ)

The SPMSQ is a 10-item test that measures the presence and severity of cognitive impairment regarding orientation to time and place, memory for personal information and serial subtraction (Roccaforte et al., 1994). It is a brief and easy instrument to administer that allows discriminating between subjects with dementia or without dementia. The SPMSQ telephone version was found to significantly correlate ($r = 0.81$, $p < 0.001$) with face-to-face MMSE

(Smith et al., 2008). Regarding test application, no information was provided concerning specific qualifications and/or skills required.

Blessed Telephone Information-Memory-Concentration Test (TIMC)

The telephone version of the Blessed IMC consists of a 27-item list to evaluate verbal memory and orientation to time and place, which highly correlated with its face-to-face version (Spearman rank = 0.96, $p < 0.001$) (Kawas et al., 1995). The telephone-version has a greater acceptance by participants, compared with its face-to-face form, since the time needed for assessment is shorter. Despite being a potential instrument for epidemiological and longitudinal cognitive research, the authors recommend its administration in a broader and more varied population sample for further validation. No information is provided regarding specific qualifications recommended for test applicants and/or interviewers.

Table 1. Telephone-based neurocognitive screening instruments.

Original Instrument

Name and author	Validation sample	Country of validation	Statistical methods for analysis and validation	Gold standard	Number of items; Administration time	Cut-off for cognitive impairment/Maximum possible score	Sensitivity; Specificity	Validation in other countries
Telephone Interview for Cognitive Status (TICS) (Brandt et al., 1988)	100 patients with mild DAT (mean age: 71 yrs), 33 healthy individuals (mean age: 67 yrs)	USA	Pearson correlation between MMSE and TICS scores; test-retest reliability; intraclass correlation coefficient.	MMSE	11 items; 10 minutes	28/41	94%; 100%	Finland: 30 Alzheimer's disease patients, 26 healthy individuals (Järvenpää et al., 2002); Italy: 45 Alzheimer's disease patients, 64 healthy individuals (Dal Forno et al., 2006); Japan: 49 Alzheimer's disease patients, 86 healthy individuals (Konagaya et al., 2007); Spain: 36 stroke patients, 36 healthy individuals (Gude et al., 1994); Holland: 51 individuals (Kempen et al., 2007); Germany: 63 individuals (Loerbroks et al., 2008)
Hopkins Verbal Learning Test (HVL) (Brandt, 1991)	129 healthy individuals (65 women and 64 men; aged 19 to 77 yrs)	USA	Cochran's C to calculate variances of the total recall scores; Pearson test to test correlations. Statistical tests of significance involving the amnesic group were not performed because of small sample size.	Clinical assessment of dementia	12 items; 10 minutes	16/36	83%; 83%	France: 180 individuals (Rieu et al., 2006); China: 631 individuals (Shi et al, 2012)
Telephone version of the MMSE (ALFI-MMSE) (Roccaforte et al., 1992)	100 outpatients in a geriatric evaluation program (76 women and 24 men; aged ≥65 yrs)	USA	Pearson's correlation coefficients to compare the total scores of ALFI-MMSE and MMSE; McNemar's χ^2 test to measure bias between the individual items and the two test versions; paired t-test to compare scores from participants with and without perceived hearing impairment and for the 22-item scores of the two test versions.	MMSE and Brief Neuropsychiatric Screening Test	22 items; NR	17/22	68%; 100%	Brazil: 37 Alzheimer's disease patients, 36 healthy individuals (Kochhann et al., 2009); Italy: 104 Alzheimer's disease patients (Metitieri et al., 2001)

Telephone Assessed Mental State (TAMS) (Lanska et al., 1993)	30 individuals with DSM-III-R criteria for dementia (22 women and 8 men; aged 59 to 88 yrs)	USA	Spearman rank correlation and linear regression to assess the relation between TAMS and other instruments scores.	MMSE	4 items; NR	4/17	NR; NR	NF
Modified Telephone Interview for Cognitive Status (TICSM) (Welsh et al., 1993)	209 individuals (aged 67 to 94 yrs)	UK	Kruskal-Wallis statistic to assess differences between groups (normal, presumed normal, questionable and demented); Receiver Operating Characteristic (ROC) analysis to determine TICSM performance.	MMSE	13 items; 5-10 minutes	27-30/39	99%; 86%	Israel: 576 individuals (Beeri et al., 2003); France: 120 women (Vercambre et al., 2009)
Short Portable Mental Status Questionnaire (SPMSQ-T) (Roccaforte et al., 1994)	100 individuals meeting DSM-III-R criteria for dementia (76 women and 24 men; aged ≥ 65 yrs)	USA	K statistic to evaluate the reliability of individual items; McNemar's χ^2 test to assess bias between the two routes of administration; Pearson's correlation to evaluate agreement between the two SPMSQ versions and the construct validity of the telephone SPMSQ in comparison to the face-to-face version and the MMSE; criterion validity measured by comparing sensitivity and specificity of SPMSQ versions to the clinical diagnosis of dementia.	In-person evaluation	10 items; NR	NR/10	74%; 79%	NF
Blessed Telephone Information - memory - concentration test (TIMC) (Kawas et al., 1995)	84 individuals (31 men and 45 women; aged 50 to 98 yrs)	USA	Spearman's rank correlation coefficient to assess correlation between in-person and telephone assessment; Paired t-tests to determine differences; Multiple regression analysis to determine the covariates that could predict the model.	Blessed Information Memory (IMC)	27 items; 5-10 minutes	NR/NR	NR; NR	NF

Telephone Screening Protocol (TELE) (Gatz et al., 1995)	30 outpatients, 26 individuals randomly selected (aged ≥55 yrsb)	USA	Standard receiver operating characteristic (ROC) analysis.	Mental State Questionnaire (MSQ)	10 items; NR	15-16/20	86%; 90%	NF
Structured Telephone Interview for Dementia Assessment (STIDA) (Go et al., 1997)	15 individuals with cognitive impairment, 13 healthy individuals (22 women and 8 men; aged 60 to 88 yrs)	USA	Internal consistency measured using correlation between each STIDA subscale with the total STIDA score using the Informant/Subject STIDA (no information regarding the type of correlation test or its name was given by the authors); ROC curves contrasting the behavior of three tests, using clinician-based CDR as the gold standard, were generated.	CDR rating scale for dementia	6 subscales; 10 minutes (if no medical information is collected)	NR/NR	93%; 77%	NF
Telephone Cognitive Assessment Battery (TCAB) (Debanne et al., 1997)	40 patients with DAT, 40 healthy individuals (48 women and 32 men; mean age 75 and 71 yrs, respectively)	USA	Shapiro Wilk's test to evaluate normality of data; T tests to compare means of independent and paired samples; Kappa statistic to assess interrater reliability; Discriminant analysis techniques to evaluate the TCAB's ability to classify individuals according to cognitive status.	Expert opinion	6 neuropsychological tests; 15-20 minutes	NR/NR	97.5% (cases) and 92.5% (controls); 85.0% (cases) and 97.5% (controls)	NF
Memory Impairment Screen Telephone (MIS-T) (Buschke et al., 1999)	27 individuals with dementia, 273 healthy individuals (≥ 65 yrsb)	USA	Receiver operating characteristic (ROC) curves for each screening measure were generated to plot the advantage/ disadvantage of sensitivity and specificity; For each of the screening measures, discriminative validity was assessed by calculating the sensitivity and specificity for detecting dementia for various test cut-cores given different base rates; Area under the ROC curve (AUC) to	DSM-III-R	4 items; 4 minutes	4/8	78%; 93%	NF

			compare screening tests; McNemar test to determine statistically significant differences in specificities between tests at constant values of sensitivity; ROC curves to evaluate the sensitivity-specificity for all dementias versus no dementia.					
Telephone adaptation of the Modified Mini – Mental State Exam (T3MS) (Norton et al., 1999)	263 community dwelling elderly (aged 65 to 93 yrsb)	USA	Repeated measures ANOVA to assess telephone and in-person administrations; Regression techniques to develop a model of translation of T3MS to 3MS scores; Pearson correlation coefficients to assess 3MS – T3MS agreement with 10 cognitive domain categories and the agreement of the overall tests scores and 3 subscales.	Modified MMSE version (3M)	34 items; NR	NR/100	91%; 97%	NF
Minnesota Cognitive Acuity Screen (MCAS) (Knopman et al., 2000)	99 mild to moderate dementia, 129 community-dwelling elderly individuals (aged 55 to 85 yrsb)	USA	Analysis of variance to determine overall group differences in demographic characteristics, in-office neuropsychological test performance, and performance on the MCAS subtests; Pearson product-moment correlations between MCAS total score and in-office neuropsychological measures; Receiver operator characteristic (ROC) curves to evaluate overall classification accuracy; Ordinal logistic regression with adjacent category logits to generate predicted probabilities for MCAS total scores using age and education as covariates and then regenerated covariate-specific ROC curves to identify whether sensitivity and/or specificity could be improved after controlling of these factors.	NR	9 subtests; 15 minutes	NR/60	98%; 99%	NF

The 26-point telephone version of the Mini-Mental Status Examination (TMMSE) (Newkirk et al., 2004)	46 patients with DAT (24 women and 22 men; aged 55 to 90 yrs)	USA	Correlation coefficients computed (tests used not reported); Linear regression with predictor variables centered and interaction terms included; 2-tailed paired t-test to test whether scores were higher on one version than the other; McNemar's chi-square test with the exact function to identify inconsistencies for individual items.	MMSE	26 items; 5-10 minutes	NR/26	NR; NR	China: 34 Alzheimer's disease patients, 31 healthy individuals (Wong et al., 2009)
Brief Screen for Cognitive Impairment (BSCI) (Hill et al., 2005)	35 individuals with dementia; 35 healthy individuals (34 women and 36 men; aged 65 to 89 yrs)	USA	Comparisons of the differences between cases and controls in BSCI scores; Comparisons of the correlations between patient scores on BSCI; Comparisons of the areas under the receiver operating characteristic (ROC) curves.	MMSE and Alzheimer's Disease Assessment Scale (ADAS)	3 items; 80 seconds	NR/NR	77%; 97%	NF
Brief Test of Adult Cognition by Telephone (BTACT) (Tun et al., 2006)	84 healthy community-dwelling individuals (aged 23 to 80 yrsb)	USA	Test scores were excluded for outliers that were >2.5 SD from the age-group mean or failure to follow instructions; Kolmogorov-Smirnov tests; ANOVA for testing differences; Tukey tests; To examine the effects of age after controlling for education effects, educational level included as a covariate.	NR	6 subtests; 15-20 minutes	NR/NR	NR; NR	NF
Cognitive Telephone Screening Instrument (COGTEL) (Kliegel and Martin, 2007)	81 younger adults (40 women and 41 men, 19 to 37 yrs;) and 83 older individuals (41 women and 42 men,	Germany	Significance level of .05; ANOVA to test variance effects of age and administration mode; Effect sizes calculated; Factor analyses to assess factorial structures; Extraction of principal component factors using an eigenvalue of less than 1; Factors orthogonally rotated with the Varimax procedure; Confirmatory factor	Wechsler Memory Scale-Revised (WMS-R) and Wechsler Adult Intelligence Scale-Revised (WAIS-R)	6 subtests; 13-14 minutes	NR/NR	NR; NR	NF

	59 to 75 yrs)		analysis; To evaluate concurrent validity correlations between COGTEL scores, age and education, and external cognitive indicators were computed; Kolmogorov-Smirnov test to determine distribution.					
Memory and Aging Telephone Screen (MATS) (Rabin et al., 2007)	120 older individuals with MCI and/or memory complaints (75 women and 45 men; aged ≥60 yrs)	USA	Skew and kurtosis statistics to determine asymmetry and peakedness in the distribution of MATS scores; Parametric tests two-tailed tests, and nonparametric equivalents, utilized in analyses involving discrimination scores; ANOVA to evaluate group differences in MATS scores on the subjective memory test; Post-hoc comparisons using the Tukey HSD correction; One-way analysis of covariance (ANCOVA) to evaluate mean differences; MANOVA to evaluate group differences in MATS scores; Pearson correlation coefficients.	Consensus between neuropsychologists and a geropsychiatrist	12 items (subjective memory questionnaire) and 10 items (learning test); 20 minutes (subjective memory questionnaire and learning test combined)	30/50	NR; NR	NF
Telephone Montreal Cognitive Assessment (T-MoCA) and Short version of Telephone Montreal Cognitive Assessment (T-MoCA-Short) (Pendlebury et al., 2013)	91 patients with minor stroke or transient ischemic attackb	UK	Differences between MoCA face-to-face and T-MoCA evaluated through the Wilcoxon signed rank test. Area under the receiver – operating characteristic curve to predict mild cognitive impairment by T-MoCA.	Montreal Cognitive Assessment (MoCA)	22 items (T-MoCA) and 12 items (T-MoCA-Short); NR (T-MoCA and T-MoCA-Short)	18-19/22 (T-MoCA) and 10-11/22 (T-MoCA-Short)	81% and 89% (cut-off 18 and 19, respectively, T-MoCA) and 70% and 96% (cut-off 10 and 11, respectively, T-MoCA-Short) c; 59% and 46% (cut-off 18 and 19, respectively, T-MoCA) and 51% and 39% (cut-off 10 and 11, respectively, T-MoCA-Short) c	NF

CDR = Clinical Dementia Rating; DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, third edition, revised; DAT: Alzheimer's dementia; MMSE: Mini-Mental-State Examination; yrs: age in years; MCI: Mild Cognitive Impairment; NF = Not Found, unable to find any published peer-reviewed articles regarding instrument translations and/or validations in other countries; NR = Not Reported, information not provided by the authors.

a Gold Standard: empirical frame of reference against which an individual's test performance is compared.

b No information provided regarding gender and/or age.

c Sensitivity and specificity for the cut-off values; however, authors also provide sensitivity and specificity values for other scores.

Telephone Screening Protocol (TELE)

The TELE was introduced by Gatz et al. (1995) and it is based on the 10-item Mental Status Questionnaire (Kahn et al., 1960), with an additional 11 items concerning attention, verbal short-term memory and cognitive abstraction, and health issues. Clinical psychologists, registered nurses or other professionals with medical background carried out the screening in the validation process (Gatz et al., 2002). On sensitivity and specificity measures it discriminated reliably between Alzheimer's disease patients and healthy cognitively normal individuals (Gatz et al., 2002), particularly in the verbal working memory (digits backwards), 3-word recall, and indication of current month (Jarvenpaa et al., 2002). Initially designed to address the lower end of the cognitive ability spectrum, which is considered an advantage, it is consequently not as suitable in studies addressing normal cognitive aging (Kliegel et al., 2007), perhaps due to ceiling effects.

Telephone Cognitive Assessment Battery (TCAB)

The TCAB was designed to evaluate elderly cognitive status, which can discriminate between mild cognitively impaired and cognitively normal individuals (Debanne et al., 1997). It comprises six categories concerning mental status, semantic memory, reasoning, executive ability and language. This instrument requires administration by a well-trained professional, preferably from the field of neuropsychology. It is noted by the original authors that further work is needed to indicate for its applicability in wider community settings.

Structured Telephone Interview for Dementia Assessment (STIDA)

Developed for the NIMH Genetic Initiative Alzheimer's Disease Study Group, and administered by skilled clinicians, the STIDA is a brief telephone screening instrument designed to discriminate people with normal cognitive functioning from those with cognitive changes due to early Alzheimer's disease (Go et al., 1997). It comprises items from the MMSE and from the Blessed-Oriented-Memory-Concentration (BOMC), and consists of six subscales including memory, orientation to time and place, judgment, and community and home activities. A much-abbreviated version of STIDA has been developed that contains questions on cognitive abilities and functional status (Go et al., 1997); however, no published studies regarding its application were found.

Memory Impairment Screen Telephone (MIS-T)

Based on the well-known in-person Memory Impairment Screen (MIS), this test contains the same semantic memory elements as the Free and Cued Selective Reminding (FCSRT) and the Double Memory Tests (DMT) (Lipton et al., 2003). The MIS-T was originally designed to measure episodic memory (Buschke et al., 1999) in a validation sample of randomly selected older individuals, and has been applied in cross-sectional studies. In the validation study individuals were evaluated by a neurologist, a neuropsychologist and a social worker student (Lipton et al., 2003). Used independently and in conjunction with the Category Fluency Test (semantic memory), and with other telephone cognitive screening tests, namely the TICS, the MIS-T demonstrated to be more robust than the TICS in discriminating dementia from normal cognitive functioning (Smith et al., 2008).

Minnesota Cognitive Acuity Screen (MCAS)

The MCAS comprises nine cognitive domains, including orientation to time and place, attention, delayed word recall, comprehension, sentences repetition, naming, computation, judgment, and verbal fluency (Knopman et al., 2000). The analysis of each domain score can be used to discriminate individuals with cognitive impairment due to MCI or Alzheimer's disease from cognitively normal subjects. The MCAS has also been proven an effective screening instrument for memory disorders (Tremont et al., 2011). Regarding the test administration, no information is provided regarding applicants' qualifications.

Hopkins Verbal Learning Test (HVLТ)

The HVLТ questionnaire assesses various aspects of verbal memory: short and long delay recall and recognition (Brandt, 1991). Six distinct forms of HVLТ are available, each containing a 12-item unique word list, which can be used to avoid practice effects due to repeated administration. Although it was designed for face-to-face application, the HVLТ can also be administered by telephone (Brandt, 1991). The reliability and validity of the instrument has been verified in patients with traumatic brain injuries, schizophrenia and in most common subtypes of dementia (Alzheimer's disease and vascular dementia) (Kuslansky et al., 2004). No information is provided concerning specific skills recommended for test applicants.

The HVLTL has as main advantages its appropriateness for serial testing as part of longitudinal studies, with the possibility for alternative forms to be used to circumvent practice effects (test–retest). Also, the results were independent of the effects of demographic variables, and as such it may be more appropriate for identifying memory deficits associated with dementing processes than the MMSE. As shortcomings of the instrument, the authors refer to its validation in samples of convenience (patients referred to geriatric psychiatry and for neuropsychological evaluation); therefore, the authors indicate for the necessity of further research in other community settings. It is also noted that the HVLTL performance is compromised in persons with low reading ability (perhaps, as a proxy of education), as well as in individuals diagnosed with clinical depression. Further research is also recommended in order to develop shorter, efficient versions, or in combination with other tools to improve the sensitivity of the instrument.

Telephone Adaptation of the Modified Mini-Mental State Exam (T3MS)

The T3MS is a modified version of the 3MS for the assessment of orientation to time and place, verbal memory, mental flexibility, abstract reasoning and language. The outcome of the T3MS correlates with the 3MS ($r = 0.82$; p -value not reported). The T3MS can distinguish between patients with MCI and individuals without cognitive impairment, with a sensitivity of 82% and a specificity of 100%, and was found a reasonable substitute for its face-to-face version (Alexopoulos et al., 2006). This instrument was used in the Cache County Study, designed to examine factors associated with the risk of Alzheimer's disease and other forms of dementia (Norton et al., 1999). No information is provided regarding qualifications of the interviewers, and no comments are made regarding how it compares with other instruments. The authors recognized that more studies are necessary to extrapolate the results to individuals with moderate to severe cognitive impairment, as well as studies with a more homogeneous population.

Brief Screen for Cognitive Impairment (BSCI)

The BSCI consists of a three-item test (delayed verbal recall, frequency of help with planning everyday activities, and frequency of help remembering to take medications), which is also suitable to detect dementia (Hill et al., 2005). The target sample of the original study comprised demented patients and cognitively healthy individuals. Compared with other

screening tests, the BSCI has the advantage of being very brief and presenting no difficulties in its administration and scoring. However, the authors recommend that an experienced interviewer should conduct the evaluation. In addition, it should not be used in a stand-alone evaluation of MCI or dementia (Fillit et al., 2003). The main advantage of the instrument is that it was designed to be included in initiatives targeted to the elderly population, including comprehensive disease management and geriatric case management programs. Specifically, as described by the original authors, the BSCI can be incorporated into larger telephonic health risk assessments (in the original study those conducted by Medicare-managed care plans). No information is available regarding its application in other studies and/or cohorts.

Brief Test of Adult Cognition by Telephone (BTACT)

The BTACT is a brief test that covers several domains of adult cognition (Tun and Lanchman, 2006). Specifically, it assesses speed of processing, verbal working and long-term memory, executive function, and reasoning. Notably, the instrument can be paired with an optional computerized task-switching test, yielding further information on reaction time and executive function. The items are based on laboratory research and telephone versions of well-known psychometric testing instruments (these were not, however, specified). Furthermore, it was used as a part of the MIDUS-II (Mid-Life in the United States) study, which consisted of a sample of 7000 healthy individuals between 35 and 85 years of age (Tun and Lanchman, 2005). One important feature of this test is its applicability in well-functioning younger and middle-aged individuals as well as older people, from a range of educational backgrounds, and also in face-to-face evaluations, providing versatility in aging studies that span different age intervals (Tun and Lanchman, 2006). The authors recommend recording of the telephone interview and that, as hearing loss can compromise performance, a brief screening on hearing should be conducted at the beginning of the interview. No information is provided concerning specific characteristics and/or qualifications of the applicants and/or interviewers.

Memory and Aging Telephone Screen (MATS)

Developed and designed purposely by Rabin et al. (2007) for longitudinal assessment, the MATS consists of a subjective cognitive complaints questionnaire on subjects' perceived cognitive decline (onset, course, severity and impact on functioning), and 10 cognitive items assessing verbal memory (list-learning). The instrument was not modeled after the MMSE and

excluded items known to lack sensitivity in preclinical groups (e.g., orientation to person or place, basic expressive language, praxis), being designed to screen individuals with MCI and/or significant cognitive complaints. It provides a key advantage over other instruments by including both objective and subjective memory assessments, and also by not showing a ceiling effect (even in cognitively intact controls). It is also reported that education, gender, and depressive symptoms did not significantly influence the results. Still, it is noted by the authors the relatively high education level of the participants in the validation sample, and that the instrument may be less sensitive to early cognitive impairment presented primarily in the form of nonamnestic deficits. Sensitivity and specificity were not determined, which limits the interpretation and utility of the test. It is indicated that longitudinal follow-ups are necessary to confirm the instrument's diagnostic value, to monitor rates of cognitive progression, and to identify which test variables best predict clinical conversion. The MATS can be also administered face-to-face by trained researchers/clinicians and it can be applied to individuals who cannot read and/or write and/or are visually impaired.

Cognitive Telephone Screening Instrument (COGTEL)

The COGTEL is a six components screening instrument that covers working, long-term verbal and prospective memory, verbal fluency and inductive reasoning (Kliegel et al., 2007). Its purpose is to assess cognitive-function domains across adulthood. The scores of the subtests can be analyzed one by one or be combined to a total score. Studies suggest that the COGTEL can be administered in large samples, including in cross-sectional, longitudinal and/or epidemiological (Kliegel et al., 2007), allowing for the global assessment of cognitive function among healthy younger and older adults test without being constrained by ceiling effects. The ongoing epidemiological study “Estrogen and Thromboembolism Risk (ESTHER)” represents an example of where it has been applied (Breitling et al., 2010). No information is provided concerning specific characteristics and/or qualifications of the applicants and/or interviewers.

Telephone Montreal Cognitive Assessment (T-MoCA)

In order to reduce missing data for patients that cannot be physically present in a clinical context, Pendlebury et al. (2013) developed a telephone version of the Montreal Cognitive Assessment (MoCA), a widely recognized brief screening test for milder forms of cognitive impairment (Nashreddine et al., 2005). The T-MoCA includes items that do not require the use

of a pencil and paper or a visual stimulus, with the exception of the sustained attention task where subjects have to tap the side of the telephone with a pencil, instead of tapping on the desk. This tool, combined with the TICSM, was tested in a sample of community-dwelling patients 1 year after they had a transient ischemic attack (TIA) or a mild stroke. Overall, although abstraction, verbal fluency and repetition items may have been affected by telephone administration (patients performed worse), the T-MoCA proved to have sufficiently good accuracy to detect MCI among stroke/TIA patients (Pendlebury et al., 2013). The authors have also developed a shortened version of the T-MoCA (T-MoCA-Short) that includes only verbal fluency, verbal recall and orientation domains (Pendlebury et al., 2013). No information was provided regarding administration time or the T-MoCA (-Short) application in “healthy/normal” cognitive aging studies. Optimal cut-offs for the T-MoCA (and of the TICSM) will vary with different definitions of MCI.

4. Concluding Remarks

Screening for cognitive impairment is a relevant issue in clinical neuroscience and geriatrics. The use of cognitive assessments provides an important basis for diagnosing cognitive disorders and monitoring cognitive decline and, hence, disease progression. Specifically, the evaluation of cognition in healthy older/elderly individuals can help define the extent of alterations in cognition associated with normal aging, thus allowing a valid differentiation of “normal” (healthy cognitive aging) from “abnormal” (pathology-related cognitive decline/impairment) cognitive changes (Rapp et al., 2012). Here, culling from the available literature, we provide a compiled base of the available telephone-based instruments for neurocognitive screening, giving information on the instrument, its main characteristics, and validation measures (Table 1). Based only on published and peer-reviewed studies, a total of 19 validated instruments were identified, with 26.5% of which further validated in countries (and/or languages) other than the original. A summary of the instruments is shown in Figure 2, reporting on main advantages and limitations.

Screening Target	Instruments	Strong Points	Limitations
Normal cognitive aging	<ul style="list-style-type: none"> • BTACT • COGTEL • HVL • MATS • STIDA • TCAB • T3MS 	<ul style="list-style-type: none"> • Of interest for medium/large-scale epidemiological studies, longitudinal designs or clinical follow-ups. 	<ul style="list-style-type: none"> • Hearing problems can be exacerbated; • Background noise may interfere with the respondent clearly understanding the interviewer or failing to concentrate; • The respondent may write words during a memory test or list down notes (cheating); • Lack of possibility to control external aids (e.g. calendars or aid from other individuals); • Some cognitive domains are not evaluated (e.g., visual, spatial or sensorimotor); • Potential effects of age, education and ethnicity/cultural background on test performance; • Psychological confounders (e.g., depression); • If used cross-sectional cannot alone assess cognitive trajectory.
AMI	<ul style="list-style-type: none"> • MCAS • STIDA • TCAB • T-MOCA • T3MS 	<ul style="list-style-type: none"> • Low expense, less time-consuming; • Access a wider, more diverse range of individuals, from varied geographical zones, health and socioeconomic status, age, racial/ethnic background, and educational level; • Comfort of the respondent, because do not have to face an interviewer if performing poorly; • Administration times averages 10-minutes; • Data obtained over the telephone seem to be as valid and reliable as information obtained face to face (validity measures). 	
MCI	<ul style="list-style-type: none"> • ALFI-MMSE • BSCI • HVL • MCAS • MIS-T • SPMSQ • STIDA • TAMS • TELE • TICS • TICSM • TIMC • T-MMSE 	<ul style="list-style-type: none"> • Good sensitivity and specificity in the screening for Alzheimer's disease and/or dementia. 	
Dementia			

Figure 2. Summary of the instruments for different screening goals. Key advantages and limitations of each set of instruments are identified. The choice of an appropriate screening measure depends on the question being asked and the sample studied.

From the literature review, the TICS was identified as the most widely translated and validated instrument, which may be considered as a possible indicator of the extent of its applicability. Regarding the validation sample, most studies (31.6%) used a “mixed cohort” design; that is, instruments were applied in cohorts composed of both “healthy” individuals and those diagnosed with MCI, dementia, minor stroke, TIA, Alzheimer's disease (and/or Alzheimer's dementia, DAT) or dementia. These are altogether, hereafter, referred as “cognitively impaired.” A similar percentage of studies (31.5%) conducted either a random (21%, community-dwellers) and/or convenience (10.5%, geriatric outpatient programs) sampling, for which, in both cases, no previous cognitive performance diagnosis was known regarding if participants were “healthy” or “cognitively impaired”. The remaining studies focused either

only on “healthy” (15.8%) or only on “cognitively impaired” (26.3%) individuals, with already previous indication for the cognitive status. From the total of $n = 2315$ patients/participants assessed, in the total of the 19 studies considered, a ratio of 2.62:3.04:4.34 was noted, respectively, “healthy”：“cognitively impaired”：“cognitively unknown” individuals. Largely, the instruments were applied in aging cohorts, with only the BTACT and the COGTEL having also been administered to younger cohorts.

Perhaps as one of the overall major shortcomings, several instruments lacked direct comparison with more extensive cognitive batteries and/or validation in other cohorts. In fact, regarding the former, only 15.8% of the studies used a combination of gold standards strategies for validation, with only one-fifth having conducted clinical assessment (or use of the CDR or the DSM-III-R) criteria to confirm assessment (“healthy” vs. “cognitive impairment”), and one-third using validated scales/instruments (other than the MMSE/3M) for the same purpose. It is particularly disturbing that 10% of the studies did not use (or reported) any type of gold standard for comparison or measure of validity, and a similar percentage did not describe the validation strategy utilized. The MMSE (or the 3M) was used as the gold standard in the majority of the studies (36.8%). This may warrant some considerations. Despite the fact that the MMSE is the most commonly used instrument for global cognitive screening (Molloy and Standish, 1997), possessing good reliability indexes, some of its limitations have been identified particularly in detecting subtle memory losses (Small, 2002). For instance, a subject with a low educational level may score poorly in the absence of cognitive impairment, while a subject with a higher educational level may score above threshold despite having cognitive impairment and/or respective decline in cognition (Brayne and Calloway, 1990; Tombaugh and McIntyre, 1992). As such, telephone-based cognitive screening tools have been mainly used to obtain a global cognition score and/or to address the lower end of the cognitive ability spectrum, but are unable to detect or indicate MCI onset and/or early phases of dementia, or indicate functional and psychological status. This is probably due to the fact that most instruments were at first developed to either detect dementia in normal samples (Crooks et al., 2005), and/or to facilitate Alzheimer's disease studies, rather than to identify at-risk individuals in diverse contexts (Crooks et al., 2005).

Feasibly, for validation purposes, and/or to guarantee the efficiency of the instrument in each subsequent study, a strategy to overcome the above mentioned shortcomings could be to

conduct a “triage” screening assessment using a telephone-based tool and, in a parallel manner, accompany this with an in-person standard assessment using a comprehensive neurocognitive test battery. This battery should comprise domains from global cognition to information processing/attention, memory and executive function. This could be conducted in at least a percentage of the cohort, so to provide continued measures of internal validity. Some authors further suggest that telephone cognitive assessments could be preceded by an initial selection of subjects of interest made by postal questionnaires, providing further “triage” points depending on the research question of interest (Van Uffelen et al., 2007).

Interestingly, only for the MATS a longitudinal assessment was conducted in the validation study. This handicap should be addressed. The applicability of telephone assessment instruments should, after an initial assessment in a cross-sectional design, also be considered in a longitudinal approach if to better evaluate the sensitivity of the instrument for cognitive changes over time. A useful indication of the degree of cognitive decline can be gained by a combination of different methods in order to discriminate validly and reliably between healthy and “abnormal” mental aging across time (Mackinnon and Mulligan, 1998). For example, a combined approach of a telephone-based cognitive-screening instrument with a questionnaire based on informant reports [such as the Informant Questionnaire on Cognitive Decline in the Elderly, IQCODE (Jorm, 1994)] could be applied. Given their complementary characteristics, the combined use of telephone cognitive screening and informant reports, in cognitive evaluations, is expected to yield promising results in indicating for cognitive trajectories (Knafelc et al., 2003).

All studies considered reported on the statistical methodology used in the data analysis, with 68.4% reporting on both sensitivity and specificity measures. On average, the size of the cohorts was $n = 121$ individuals. Given that, on average, the number of items per instrument was 15, and considering that sample size should be 10 times the number of items for analysis (Nunnally, 1978; Comery and Lee, 1992; Tabachnik and Fidell, 1992), overall the studies considered lacked by 15% in sample size for proper validation. When considered separately, approximately 50% of the studies had sample sizes that were too small for validation, with these on average needing to double participant number for full validation. Nonetheless, it should also be noted that while “10 subjects per item” is recommended when examining individual items, it is less clear if this applies when using the global score. Still, as some of the

samples were small, making meaningful conclusions regarding some of the tests is difficult. A total of nine studies included cut-off scores indicative of “cognitive impairment.” This may overall be one of the most practical goals for the use of these instruments, placing them on similar ground with the rapid assessment tools already extensively used face-to-face. The average time of administration for the instruments considered was 10.8 min, with no administration time reported in six of the studies. Finally, common limitations were reported. The administration procedure could be particularly difficult for severely demented individuals, for those who had poor telephone communication skills or were hearing impaired and/or who were more easily distracted (shorter attention spans). Also, as tasks are instructed and solved verbally, those that involve visual, spatial, or sensorimotor skills cannot be evaluated. Finally, individuals may ask for the help of those nearby (or use external cues/aids) while performing the assessment (Smith et al., 2008). It is also overall recommended that future studies should evaluate for the test–retest and parallel-test reliabilities of the instruments.

As discussed, the current shift in population demographics has been accompanied by a need to develop brief and accurate cognitive screening instruments, with the potential to be applied in different research and clinical contexts for the cognitive assessment in medium to large-population samples (Petersen et al., 2001; Jager et al., 2003). As face-to-face administration tools require individuals to be physically present, telephone instruments have been developed as an alternative. If developed, used and validated properly, despite intrinsic limitations, telephone-based cognitive assessment can considerably contribute to increase sample sizes by reaching more individuals, and can also provide a mean for minimizing costs and participants' burden and accessibility. Furthermore, several studies demonstrated that the outcome in cognitive assessments administered by telephone is similar to that conducted in face-to-face settings (Wilson and Bennett, 2005). Furthermore, it is also noted that telephone-based tools can reduce selection bias in epidemiology studies by allowing covering large areas and facilitating follow-up (Herr and Ankri, 2013). A final comment concerns the use of telephone cognitive assessment for clinical diagnosis. Telephone-based cognitive instruments can be used as screening tools, but are inadequate tools for a diagnostic decision about the presence of MCI or dementia. Results warrant the same care in interpretation as if using face-to-face assessment with “rapid assessment” instruments (e.g., the MMSE). Telephone tools can be used for provisional early diagnosis, with later evaluation by accurate clinical examination,

neuropsychological assessment, sources of information based on informant reports, and laboratory and imaging methods. In conclusion, telephone-based instruments should continue to be further developed and evaluated, and/or improved-on (namely in an era where distant video connection is emerging), in order to be utilized by health care professionals and researchers, serving as a viable complementary and/or alternative tool for cognitive screening in clinical and epidemiological settings.

5. References

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CHAPTER III

Teresa Costa Castanho, Carlos Portugal-Nunes, Pedro Silva Moreira, Liliana Amorim, Joana Almeida Palha, Nuno Sousa, Nadine Correia Santos

Applicability of the Telephone Interview for Cognitive Status (Modified) in a community sample with low education level: association with an extensive neuropsychological battery

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Applicability of the Telephone Interview for Cognitive Status (Modified) in a community sample with low education level: association with an extensive neuropsychological battery

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Abstract

Objective: To explore the applicability of a Portuguese (PT) version of the Telephone Interview for Cognitive Status (TICS), with a delayed recall item (modified, M), here termed TICSM-PT, against an extensive (in-person) battery of neuropsychological instruments, in a sample of older individuals with low educational level and without clinically manifest/diagnosed cognitive impairment.

Methods: Following translation/back-translation and pilot testing in 33 community-dwellers, 142 community-dwellers aged 52 to 84 years (mean = 67.45, SD = 7.91) were selected from local health care centers for the study (convenience sampling; stratified age and gender). Cronbach's alpha was used to assess internal consistency and convergent validity was evaluated through the correlation between TICSM-PT and the Mini Mental State Examination (MMSE), as well as with a comprehensive battery of cognitive instruments. Divergent/discriminant validity was assessed through a battery of psychological instruments. The ROC curve was determined for TICSM-PT to classify participants with and without possible indication of cognitive impairment (CI).

Results: TICSM-PT showed a satisfactory internal consistency (Cronbach's alpha=.705), convergent validity and discriminant validity. TICSM-PT presented a positive association with the global cognitive measures MMSE and the Montreal Cognitive Assessment (MoCA), and also with most neuropsychological parameters. ROC curves present a sensitivity=90.6% and specificity=73.7%. The AUC statistic yielded a threshold score equal or below 13.5 for CI.

Conclusion: TICSM-PT is a practical tool for rapid cognitive assessment among older individuals with low educational background.

Keywords: telephone screening; rapid screening; cognition; psychological morbidity; ageing; education

1. Introduction

In ageing research, the possibility of interactions between factors that impact on cognition has gained interest throughout the years. On this, it has been shown that individuals with more school years seem to present better overall test performance (e.g. Santos et al. 2014) and that cognitive test performance is strongly influenced by cultural factors (e.g. Hedden et al., 2002; Park and Gutchess, 2002; Christofolletti et al., 2007; Weissberger et al., 2013), with psychological morbidity and/or mood also playing a mediator/effector role across educational groups (e.g. Austin et al., 2001; Santos et al. 2014). However, in the “front-lines” (clinics), as well as in population-based epidemiological research on cognitive performance throughout ageing, it is often difficult (if not impossible) to apply an extensive battery of tests that allow for an integrative and/or comprehensive neuropsychological assessment. Thus, rapid-administration of standardized tools has recently raised great interest. Research indicates that cognitive function assessment over the telephone may be as reliable and valid as a traditional face-to-face evaluation, providing a useful/practical approach [see for review, (Castanho et al., 2014)]. Among other strengths, these instruments allow screening of large-scale populations and to reach individuals with limited mobility, poor motivation and/or who live in rural areas or at great distances from clinical/evaluation centers.

So far, to our knowledge, no telephone cognitive-screening instrument has been applied in the Portuguese population, and/or in the Portuguese-Portuguese (PT-PT) language, despite Portugal being one of the most rapidly ageing countries, with estimates indicating that 40% of its total population will be aged 60 years or over by 2050 (United Nations, 2012), and Portuguese being one of the top spoken languages in the world. Furthermore, the current and forecasted educational attainment of the Portuguese population is similar to the average current and forecasted of that worldwide and, thus, of interest in population-based ageing studies [although its older population is lower educated than those in North-American/Western European countries, it is similar to most other more newly developed and/or developing countries (Samir et al., 2010)].

Here, the purpose of the current study was to explore the applicability of the most widely used telephone-based cognitive screening tool, the Telephone Interview for Cognitive Status (TICS), here with a delayed recall item of the Modified version (TICSM), against a broader and detailed (in-person) assessment using a neuropsychological battery, in a cohort of older individuals with

low educational background and without clinically manifest and/or diagnosed neuropsychiatric or neurodegenerative disorder and/or cognitive impairment.

2. Methods

Description of the instrument

The Telephone Interview for Cognitive Status assessment [TICS; original instrument (Brandt et al., 1988)] is the most popular instrument among telephone-based rapid-screening instruments (Castanho et al., 2014). It was developed (and adapted) from the Mini Mental State Examination (MMSE), the “gold standard” among rapid-screening tests, presenting a high validity and reliability on the screening of cognitive impairment. Albeit modelled after the MMSE, the TICS has less ceiling effects, being recognized as a sensitive cognitive measure for detecting mild cognitive impairment (MCI) and early Alzheimer’s disease (AD) (Seo et al., 2011), and to document progressive cognitive decline in population samples (Plassman et al., 1994). The original validation study indicates that the TICS has a good sensitivity (99%) and specificity (86%) for distinguishing demented individuals from those without dementia, as well as cognitively impaired from cognitively normal individuals (Welsh et al., 1993; Plassman et al., 1994). Summarily, it assesses working and recent memory, orientation, attention, sentence repetition, conceptual knowledge and nonverbal praxis (Seo et al., 2011). With the inclusion of a delayed recall task, the TICS-Modified [TICSM; original instrument (Welsh et al., 1993)] is a further refinement of the TICS. TICSM is a 13-item test and has a scoring range of zero to 39 (in the original instrument), with higher scores representing better cognitive performance. It comprises the following items: subject’s age, telephone number; present date (month, day and year), day of week and season; counting backwards from 20 to one; 10-word immediate recall list; subtraction calculation; phrase repetition; stating the country’s president and prime-minister names (first and last); word opposites enumeration; and 10-word delayed recall list. Although the education level of the subjects can influence the TICS(M) scores, studies have indicated that scores can be adjusted for this (Brandt et al., 1988; Welsh et al., 1993; Gatz et al., 2002; Dennett et al., 2013).

Translation, back-translation and pilot study

Based on the original TICS version [(Brandt et al., 1988); and later modifications by (Welsh et al., 1993) and (de Jager et al., 2003) for the recall item (TICSM)], the instrument was translated to PT-PT by two psychologists and a biochemist with expertise in neurosciences, and then back translated by another psychologist and a linguist to establish the linguistic integrity of the version. Translation and back-translation was enhanced by multidisciplinary group discussions and the refined draft was shown to be acceptable in a preliminary pilot survey, with the process resulting in minor modifications. The pilot study was conducted to establish whether the PT-PT version of the TICS(M) (hereby referred as TICSM-PT) could be understood by the target participants (community-dwellers, 50+ years of age) and if it was overall well accepted. A total of n=33 community-dwelling older individuals participated in the pilot study. A trained psychologist conducted the assessment. After completion of the TICSM-PT, participants were asked to comment on whether any parts of the evaluation were difficult to comprehend and to provide their own insights for culture/language adjustments. Test results (scores) from the pilot cohort were not included in the remaining analysis.

The final version of the TICSM-PT comprised 13 items with a maximum score of 39 points. Minor modifications were introduced to account for cultural and language/sonority specificities. Specifically, item 9 (“Who is the reigning monarch now?”) was altered to ask for the President’s name (“Who is the President of the Republic now?”). Semantic/language issues were also taken into consideration in terms of verbs and adjectives (item 5 “Please subtract 7 from 100” to “Now I will ask you to calculate 100 minus 7”; item 8 “What do you call the prickly green plant that lives in the desert?” to “What is a green plant with thorns which is in the desert?”). As there were many difficulties in understanding word enunciation/overall sentence sonority, a few questions were replaced based on other options suggested by the original authors or those in translated versions in other Latin languages (item 11 “What is the opposite of East?” to “What is the opposite of generous?”; item 12 “Please say this ‘Methodist Episcopal’/ to “No ifs, ands or buts”). No changes were made to the scoring system and the rating criteria from the original instrument. The TICSM-PT comprised questions evaluating temporal and spatial orientation (7 points), the recall task of the 10-word list (10 points), the attention and calculation tasks (subtraction and spell backwards) (6 points), five questions

evaluating semantic memory (5 points), a task involving language (repetition of a sentence) (1 point) and a delayed recall of the 10-word list (10 points).

Sample and data collection for the TICSM-PT study

Potential participants were directly contacted in-person at the local health care center in Póvoa de Varzim, Braga and Guimarães (Portugal) while in the waiting area for their annual check-up (sample of convenience, stratified sampling for gender and age). A total of n=142 community-dwellers agreed to participate. Largely, all Portuguese individuals are automatically attributed a local Health Care Center at birth. The sample was representative of the Portuguese population with respect to gender (62 males, 43.7%), age (M=67.5, SD=7.91, range: 52-84 years) and formal years of formal education (median=4, range: 0-17). Presently, primary/basic grade school education mainly characterizes the middle-aged and older Portuguese population, with low percent scores having completed preparatory, secondary and tertiary levels. The participants were equally distributed between urban (city or city outskirts) and rural (villages) areas. The exclusion criteria for participation included inability to understand informed consent, inability to read or write, choice to withdraw from the study, dementia, diagnosed neuropsychiatric, neurodegenerative disorder and/or clinically manifest/diagnosed cognitive impairment. The study was conducted in collaboration with the participants' general practitioner(s), who provided the clinical information.

After establishing acceptance for the telephone testing, subjects completed the extended neuropsychological battery of tests in an in-person evaluation session. Face-to-face examinations (for the neuropsychological battery) and telephone interviews (for the TICSM-PT) were conducted between May 2013 and June 2014. Specifically, within one month after the neuropsychological examination, each participant underwent the telephone interview. So to reduce interviewer and participant bias, both the interviewer and the subject were blind to the previous evaluation scores in the neuropsychological battery. Before beginning the TICSM-PT evaluation, the participant was asked if he/she was in a quiet room, and with no pen or pencil or temporal information within easy reach (e.g., a newspaper or a calendar). The TICSM-PT required approximately 7/8 minutes for administration. All participants completed the instrument. The same psychologist conducted all assessments.

The study was conducted in accordance with the Declaration of Helsinki (59th Amendment) and approval was obtained from the national and local ethics committees. Written consent was provided from all participants prior to participation.

Permission was obtained from the Psychological Assessment Resources, Inc. (PAR, Inc.) for the use of the TICS with a delayed recall item (TICSM).

Neuropsychological assessment

A total of $n=97$ individuals completed the comprehensive face-to-face neuropsychological assessment. Instruments were always applied in the same order. The remaining participants did not sit the entire neuropsychological session due to the long nature of the independent evaluation (the battery required approximately 90 minutes for completion), albeit agreeing to and later completing the TICSM-PT instrument applied via the telephone-interview. All participants ($n=142$) completed the MMSE. The face-to-face assessment followed previously established methodologies for similar cohorts [(Santos et al, 2014), and neuropsychological tests' references therein], designed to assess a wide range of cognitive abilities. Specifically, attention was assessed with the Digit Span forward test and working memory with the Digit Span backward, from Wechsler Adult Intelligence Scale – Third Edition (WAIS III); verbal fluency with the Controlled Oral Word Association tests (COWAT, letters F-A-S); executive function and processing speed with the Digit Symbol Substitution Test (DSST) from the WAIS III and with the Stroop Word-Color test; and, memory storage, retention and recall with the Buschke Selective Reminding Test (SRT). Global cognitive functioning was evaluated with MMSE and the Montreal Cognitive Assessment (MoCA). Subjects were also evaluated regarding memory difficulty complaints with the Subjective Memory Complaints Scale [SMC; (Ginó et al., 2008)], and the retrospective and prospective memory slips in the everyday life with the Prospective and Retrospective Memory Questionnaire [PRMQ; (Benites and Gomes, 2007)]. Personality traits were assessed with the NEO Five-Factor Inventor-20 items [NEO-FFI-20; (Bertoquini and Pais-Ribeiro, 2006)]. The Geriatric Depression Scale [GDS, long-version; (Barreto et al., 2003)] was administered to assess depressive symptoms, the Perceived Stress Scale [PSS; (Cohen et al., 1983)] to evaluate everyday stress, and the Anxiety Subscale of the Depression Anxiety Stress Scale [DASS; (Pais-Ribeiro et al., 2004)] to screen anxiety symptoms. Two trained psychologists conducted the in-person assessment during the pilot

study, following guidelines previously established and conjoint training in order to reduce interviewers' bias. Only one psychologist performed the evaluations for the main study.

3. Statistical analyses

The internal consistency of the TICSM-PT was assessed with Cronbach's alpha and inter-item correlation matrix. Convergent validity was evaluated through the bivariate correlation between the TICSM-PT and MMSE (both at the total-score and at the domain-score levels), MoCA (total score), SRT [consistent long term retrieval (CLTR), long term storage (LTS), delayed recall (DR) and intrusions parameters], Stroop [Words, Colors, Words and Colors (WC) parameters], DSST (total score), Digits Span (Forward and Backward parameters), and COWAT [admissible (Ad) and non-admissible words (NAd)]. Divergent validity was assessed by testing the correlation matrix between TICSM-PT and NEO-FFI scales (Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness), DASS-21-anxiety subscale, SMC, PRMQ, GDS and PSS (total scores). The relationship between TICSM-PT and cognitive and psychological dimensions were adjusted for education using partial correlations analyses. A receiver operating curve (ROC) analysis was conducted in order to evaluate the discriminative ability of the TICSM-PT to distinguish between normal and cognitive impairment (CI). A more conservative cutoff for CI of MMSE total score <23 was used as test variable to perform the ROC analysis of TICSM-PT for classifying participants with and without possible CI. This follows the threshold for a similar population (Santos et al, 2014) and the validation study for the Portuguese population (Guerreiro et al., 1994). All the statistical analyses were performed using SPSS version 22 (IBM SPSS Statistics). Statistical significance was defined at the $p < .05$ level (two-tailed).

4. Results

Table 1 displays the descriptive statistics for the scores on TICSM-PT and MMSE by gender, age and education, and Table 2 the descriptive statistics for the neuropsychological tests. A significant association was noted between the TICSM-PT and education ($r = .564$, $p < .001$), indicating that better performance on the TICSM-PT was associated with higher education level. A negative significant association was found between the TICSM-PT and age ($r = -.243$, $p < .001$), indicating lower test performance with increasing age.

Table I. Descriptive statistics of the TICSM-PT and MMSE total scores by gender, age and education.

		N (%)	TICSM-PT	MMSE
Gender	Men	62 (43.7)	20.9 (5.2)	26.7 (2.4)
	Women	80 (56.3)	18.2 (5.3)	25.6 (3.6)
Age (yrs)	<70	94 (66.2)	20.2 (5.3)	26.9 (2.6)
	≥70	48 (33.8)	18.3 (5.4)	25.0 (3.6)
Years of education	<4	99 (69.7)	17.6 (4.9)	25 (3.3)
	≥4	43 (30.3)	23.4 (4.2)	28 (1.6)

Values presented as Mean (SD)

MMSE, Mini Mental State Examination; TICSM-PT, Telephone Interview for Cognitive Status Modified-Portuguese-Portuguese

The instrument revealed a satisfactory internal consistency ($\alpha=.705$). Only the exclusion of the language item, which had the lowest correlation coefficients (Table 3), could improve the internal consistency of the instrument (Supplementary Table S1). However, since the magnitude of the increment was not large, the original structure was maintained.

Table II. Descriptive statistics for the cognitive and psychological tests.

	Mean (SD)	Min	Max
TICSM-PT	19.36 (5.37)	8	34
MMSE	26.06 (3.19)	11	30
MoCA	19.02 (5.509)	5	30
SRT LTS	23.67 (15.072)	0	57
SRT CLTR	16.27 (14.534)	0	52
SRT Delayed Recall	4.54 (3.20)	0	12
SRT Intrusions	3.66 (4.15)	0	19
GDS	9.19 (6.74)	0	28

Stroop Words	63.27 (21.906)	0	108
Stroop Colors	48.42 (14.569)	11	77
Stroop WC	28.03 (14.281)	0	58
DSST	32.2 (16.692)	0	78
Digits Forward	7.31 (1.859)	3	12
Digits Backward	4.3 (1.92)	0	8
COWAT Ad	21.13 (12.575)	0	54
COWAT NAd	0.58 (1.142)	0	6
SMC	6.6 (4.287)	0	18
PRMQ	31.33 (9.451)	16	55
PSS	18.94 (7.068)	4	37
DASS	2.45 (2.829)	0	15
NEO-FFI Neuroticism	6.31 (2.852)	0	13
NEO-FFI Extraversion	9.92 (2.605)	3	16
NEO-FFI Openness	7.85 (3.471)	0	14
NEO-FFI Agreeableness	10.26 (2.054)	4	15
NEO-FFI Conscientiousness	12.32 (1.656)	7	16

TICSM-PT, Telephone Interview for Cognitive Status Modified-Portuguese-Portuguese; MMSE, Mini Mental State Examination; MoCA, The Montreal Cognitive Assessment; SRT LTS, Selective Reminding Test Long-Term Storage; SRT CLTR, Selective Reminding Test Consistent Long-Term Recall; GDS, Geriatric Depression Scale; Stroop WC, Stroop Word Color Test; DSST, Digit Symbol Substitution Test; Digit Span Forward; Digit Span Backward; COWAT Ad, Controlled Oral Word Association test Admissible; COWAT NAd, Controlled Oral Word Association test Non-Admissible; SMC, Subjective Memory Complaints Scale; PRMQ, Prospective and Retrospective Memory Questionnaire; PSS, Perceived Stress Scale; DASS, Depression Anxiety Stress Scale; NEO-FFI, NEO Five-Factor Inventory-20.

Table III. Correlations, variances and covariances of TICSM-PT domains.

	TICSM-PT Orientation	TICSM-PT Registration	TICSM-PT Attention/ Calculation	TICSM-PT Comprehension	TICSM-PT Language/ Repetition	TICSM-PT Delayed Recall
TICSM-PT Orientation	.735	.251	.696	.211	.016	.273
TICSM-PT Registration	.184	2.513	1.050	.777	.072	1.951

TICSM-PT Attention/ Calculation	.396 ^{**}	.323 ^{**}	4.198	.950	.123	1.203
TICSM-PT Comprehension	.191 [*]	.381 ^{**}	.360 ^{**}	1.658	.043	.867
TICSM-PT Language/ Repetition	.070	.169 [*]	.224 ^{**}	.124	.072	.049
TICSM-PT Delayed Recall	.192	.745 ^{**}	.356 ^{**}	.408 ^{**}	.111	2.728

* $p < .05$; ** $p < .01$ The top half of the table represents the covariance between the different domains. The bottom half of the table represents the Pearson correlation coefficients between the different domains of TICSM. The diagonal line represents the variance within each domain.
TICSM-PT, Telephone Interview for Cognitive Status Modified-Portuguese-Portuguese

Concerning the convergent validity, the TICSM-PT presented a positive relationship with the MMSE total score ($r = .660$, $p < .001$). At the domain-level, Orientation, Attention/Calculation and Delayed Recall were significantly associated between tests (Table 4). Interestingly, the TICSM-PT Registration score (which was not significantly related between tests) was significantly associated with the Attention/Calculation and Language domains in the MMSE (Table 4).

Table IV. Correlations between the TICSM-PT and the MMSE domains.

	MMSE Orientation	MMSE Registration	MMSE Attention/Calculation	MMSE Recall	MMSE Language
TICSM-PT Orientation	.324 ^{**}	-0.06	0.151	0.138	.185 [*]
TICSM-PT Registration	0.121	-0.019	.187 [*]	.400 ^{**}	.389 ^{**}
TICSM-PT Attention/ Calculation	.327 ^{**}	0.114	.458 ^{**}	.361 ^{**}	.380 ^{**}
TICSM-PT Delayed recall	.179 [*]	-0.005	.233 ^{**}	.358 ^{**}	.391 ^{**}
TICSM-PT Language/Repetition	.206 [*]	-0.024	0.161	0.099	0.041

* $p < .05$; ** $p < .01$

TICSM-PT, Telephone Interview for Cognitive Status Modified-Portuguese-Portuguese; MMSE, Mini Mental State Examination

Given that the MoCA is considered to be more sensitive (albeit less specific) than the MMSE it was also considered in the analysis (Nasreddine et al., 2005). The results indicate a positive correlation between the TICSM-PT total score and the MoCA total score ($r=.750$, $p<.001$). In addition, significant positive associations were found between the TICSM-PT and most cognitive measures, with the exception of those constituting errors (intrusions on SRT and NAd words on COWAT) (Table 5). With respect to the psychological measures, the TICSM-PT was significantly associated with PRMQ, DASS (only Anxiety subscale), GDS and NEOFFI (Openness dimension). Whereas education level did not impact on the significance of the associations between TICSM-PT and cognitive measures, the correlation with DASS, GDS and NEOFFI (Openness dimension) was lost after adjusting for school years (Table 5). The AUC statistic (Figure 1) equalled .870 (95% confidence intervals: 79% - 98%). The calculated optimal TICSM-PT cutoff score for CI was 13.5. Using this threshold, the sensitivity and specificity were 90.6% and 73.7%, respectively. Fifteen participants (10.6%) of the total sample were classified below this threshold.

Table V. Correlations between the TICSM-PT total score and cognitive and psychological dimensions from the neuropsychological test battery.

	TICSM-PT	
	<i>r</i>	Covariance
SRT LTS	0.544 (0.38)	45.979
SRT CLTR	0.564 (0.401)	45.983
SRT DR	0.463 (0.303)	8.318
SRT Intrusions	0.071 (0.089)	1.079
MoCA	0.75 (0.729)	23.177
Stroop Words	0.653 (0.443)	82.948
Stroop Colors	0.64 (0.443)	53.762
Stroop WC	0.663 (0.511)	54.573
DSST	0.764 (0.672)	71.973
Digits Forward	0.565 (0.453)	5.927

Digits Backward	0.743 (0.647) ^{··}	8.235
COWAT Ad	0.606 (0.608) ^{··}	42.978
COWAT NAd	-0.197 (-0.06) ^a	-971
GDS	-0.235 (-0.138) ^{·b}	-9.007
SMC	-0.094 (-0.149)	-2.275
PRMQ	-0.247 (-0.339)	-13.158
PSS	-0.118 (0.082)	-4.717
DASS	-0.377 (-0.257) ^{··a,b}	-6.637
NEO-FFI Neuroticism	-0.05 (-0.009)	-819
NEO-FFI Extraversion	-0.093 (0.023)	-1.401
NEO-FFI Openness	0.461 (0.278) ^{··b}	9.210
NEO-FFI Agreeableness	-0.002 (-0.039)	-018
NEO-FFI Conscientiousness	-0.169 (-0.102)	-1.615

[·] $p < .05$; ^{··} $p < .01$; ^r Unadjusted (and adjusted for education level) correlation coefficient; [·]Non-parametric correlations (Spearman coefficients) were calculated for variables with non-normal distribution. ^aThese associations are no longer significant when controlling for education level.

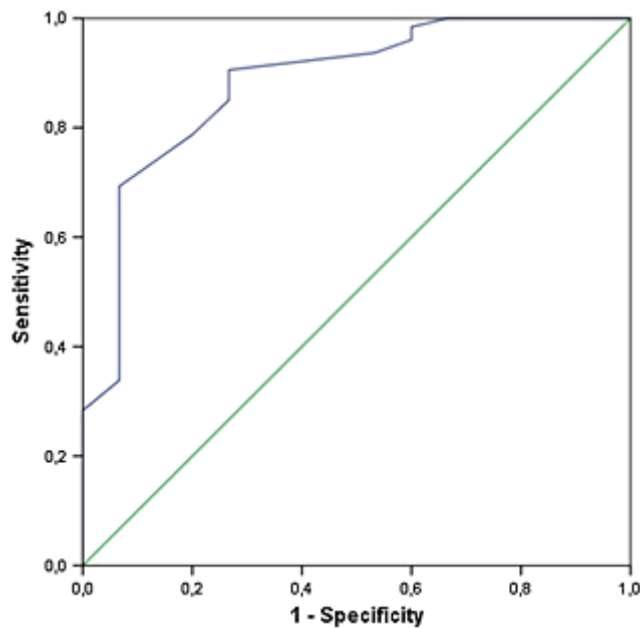


Figure 1. ROC curve of TICSM-PT. The area under the curve was 87% (95% CI: 79% - 98%).

5. Discussion

The purpose of the present study was to explore the applicability of a PT-PT version of the TICS(M) in a cohort with low education level, against a large battery of neuropsychological tests. Results indicate a linear correlation between the TICS-M-PT and the MMSE with a moderate concurrent validity, despite the distinct administration modalities (telephone versus face-to-face). Thus, the TICS-M-PT can possibly be effectively used in place of the MMSE in situations where the TICS-M-PT would be more practical to administer. More so, the TICS-M-PT exhibited moderate to high correlations with the cognitive instruments administered. In a broad sense, the significant association of the TICS-M-PT total score with tests that assess for specific cognitive domains indicates that it overall successfully assesses multiple cognitive domains, yielding an overall cognitive score. Interestingly, the strongest associations were observed between the TICS-M-PT total score and tests that evaluate executive function (namely, the DSST) and working memory (namely, the Digit span backward), which are functions particularly vulnerable to decline due to ageing or dementia (Salthouse, 2010). Nonetheless, associations were also noted for most of other domains, including (verbal) memory and attention measures, which are also of consideration in cognitive ageing.

Although in older individuals (co)morbidities with depressive and anxiety symptoms are frequent, cognitive neuroscience research focusing on the unique and mixed consequences of depression and anxiety on test performance is still surprisingly scarce (Dotson et al., 2014). On this, the present results, which are novel in exploring the association between these dimensions and telephone-administered rapid-screening instruments, indicate that higher levels of trait anxiety and depressive symptoms associate with lower levels of performance on the TICS-M-PT. This follows studies showing that negative mood measures associate with worse cognitive outcomes [for example, (Santos et al., 2014)]. In fact, it is recommended that depression must be always examined since it can possibly mimic dementia, or be a precursor of it, or even be co-morbid with it (Kuslansky et al., 2004). Furthermore, in older people, besides manifestations of depression, personality traits can often impact on performance in cognitive tasks. These personality traits seem to be somewhat influenced by cultural and sociodemographic characteristics, as well as by the effort that each individual puts in the resolution of the task (Mortensen et al., 2014). As reported by several authors (e.g. Soubelet

and Salthouse, 2010; Graham and Lachman, 2012), but again novel for telephone-based instruments, the present findings corroborate a positive association between cognitive ability and the openness trait measure of personality, that was weakened when controlled for education. Trait openness reflects a sustainable approach toward the types of cognitive activities over a lifetime that have been associated with increased cognitive reserve and reduced risk of MCI and dementia in late life (Schretlen et al., 2010). Additionally, despite the higher prevalence of subjective memory complaints in our sample (evaluated to be greater than 25%), no associations were found between this measure and the TICSM-PT score. In fact, the correlation between memory complaints and cognitive performance remains controversial. Studies have demonstrated that memory complaints cannot be taken as a definitive indicator for cognitive impairment since they can reflect depressive disorders and other psychological morbidity aspects (Aguiar et al., 2010). Interestingly, we found a negative association between the TICSM-PT and the PRMQ. This might indicate that individuals with higher performance in the TICMS-PT present fewer difficulties in evoking intentions that must be performed within a short or long period of time and previous events and situations.

Finally, analysis of the ROC curves demonstrated satisfactory discriminant validity with the AUC statistic pointing for a threshold score of equal or below 13.5 for possible CI. Of note, however, the appropriate cut-off of a neurocognitive instrument depends on its purpose and the effects of false positive and false negative results. Here the determined CI cutoff was lower than that of the original study (Welsh et al., 1993 reported a MCI threshold of 27, and a sensitivity and specificity of 99% and 96%, respectively) as well as in other TICSM studies found in the literature (Beeri et al., 2003; Moylan et al., 2004; Vercambre et al., 2010; Knopman et al., 2010). This may be possibly explained when noting that CI cut-off scores can be influenced by the socio-economic and/or educational characteristics, adding to the discussion on considering appropriate thresholds for the study samples being considered, including in telephone-based instruments (which has not yet been fully addressed, probably due to their more recent use).

This work adds to the research on telephone-based rapid cognitive screening by addressing relevant aspects often missing in similar studies: pilot testing; comparison with an extensive battery of neuropsychological measures; inclusion of a sufficiently large sample for instrument validation and/or applicability/utility studies ("10 subjects per item" is recommended when examining individual items, although it is less clear if this applies when using the global score);

methodological clarity on the validity measures used; and, finally, addressing for lower educational settings (vastly similar studies have been conducted in countries with higher educational attainment levels) [for review see (Castanho et al., 2014)]. Nonetheless, there are some disadvantages inherent to the telephone assessment that should be addressed and are also of consideration for the present study. These include the limited control over environmental factors, the potential impact of hearing impairment and the elimination of the examiner's ability to directly observe the participant's behaviour [for review see (Castanho et al., 2014)]. Here, although instructions were given for participants to turn off their TV's or radios and to move any papers or pencils away from where they were, it was not possible to completely control for environmental variables. These may include, for example, the participant referring to a calendar when asked for the date, or the presence of handy notes or of a helpful spouse. Furthermore, the study sample was of convenience and was recruited from the community; therefore, findings may not be extended to a clinical setting and/or be necessarily generalizable. It would also be of interest to (i) assess for performance in individuals that may have already been exposed to telephone assessments, therefore removing any inherent anxiety to the method itself, and (ii) randomize participants to take the TICS(M)-PT before or after in-person testing. Nevertheless, data adds to previous studies demonstrating that the TICS(M) is a reliable and valid alternative to an in-person evaluation in community-dwelling subjects. More so, it is also of note that in some domains the TICS(M) may be a more difficult test compared to the MMSE and the MoCA. In the TICS(M)-PT, the repetition and memorization of 10 words is required, whereas in the MMSE and in the MoCA, 3 and 5 words are required, respectively. Thus, it is here suggested that it may be advantageous to introduce the possibility of repeating the 10 words by the researcher a few times (and/or across trials), which provides the individual with the opportunity to repeat them, also allowing to better investigate the learning process (Knopman et al., 2010). Thus, future studies are needed in order to focus on validating this suggestion and on developing adequate normative data. Here the test administration experience also suggests that certain words were more difficult for participants to distinguish clearly over the telephone and required careful attention to pronunciation. It may be prudent to not only first check the participant's hearing ability with a short pre-test over the telephone before starting the assessment, but possibly also throughout the assessment.

6. Conclusion

The TICS-M-PT demonstrated to be a practical tool for cognitive assessment and a valid method of screening multiple cognitive domains in an older community sample characterized by low education level. The results may have broader implications given that, on measures of literacy, (un)employment rates, positive experience/mental health, and other socio-demographic characteristics, Portugal ranks close to the OECD (Organisation for Economic Co-operation and Development; www.oecd.org/) average. Following this study, future work should address longitudinal assessment and applicability in clinical- and institutional-based settings, and should consider for a randomized sampling.

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Supplementary data

Supplementary Table S1. Internal Consistency (Cronbach's alpha) of the TICSM-PT items.

	Cronbach's Alpha if Item Deleted	Item total correlation
All Items	0.707	
TICSM-PT Orientation	0.699	0.335
TICSM-PT Registration	0.607	0.605
TICSM-PT Attention/Calculation	0.674	0.480
TICSM-PT Comprehension	0.657	0.476
TICSM-PT Language/Repetition	0.727	0.212
TICSM-PT Delayed Recall	0.597	0.628

CHAPTER IV

Teresa Costa Castanho, Nuno Sousa, Nadine Correia Santos

When new technology is an answer for old problems: the use of videoconferencing in cognitive ageing assessment

Manuscript to be submitted

**When new technology is an answer for old problems: the use of videoconferencing
in cognitive ageing assessment**

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Abstract

People living with cognitive impairment and dementia require regular screening of their symptomatology and needs. Brief cognitive screening is crucial for assessing these conditions. Such screening can give health professionals a snapshot of the patient's cognitive abilities and help in their monitoring and adaptation. An appropriate administration of brief cognitive screening using telemedicine technology, such as videoconference, can improve access to care and treatment planning. Moreover, the burden that rural and underserved communities often suffer because of limited access to specialty mental health services is also of concern. Herein, in this report, we describe the existing and relevant research regarding the administration of neuropsychological instruments via videoconferencing, and suggest methodological improvements for further studies. To date, only a handful of scientific studies have been published documenting the feasibility and acceptability of videoconferencing among older people and health professionals. Varying in their assessment tools, the studies demonstrate the reliability of cognitive testing and clinical diagnosis of dementia via videoconferencing, as noted by the associations between results of several cognitive tests using it as compared to face-to-face interviews. Further research is required to replicate findings of studies found and bring new solutions for their adaptation to a wide range of individuals, health professionals, areas of practice and settings.

Keywords: telemedicine; cognitive testing; dementia; neuropsychology

1. Introduction

Over the last two centuries, the human specie has experienced an impressive progress in health and life expectancy. In fact, currently no country in the world has a lower life expectancy compared to those with the highest ones in 1800, and since 1900 the global average life expectancy has more than doubled. However, one of the societal and clinical challenges associated with an aged population is the increased incidence and prevalence of cognitive impairment, imposing the need for convenient, valid and reliable methods to monitor cognitive functions in the older population. This is a must in order to aid in the detection, prevention and/or early intervention, of cognitive decline and/or cognitive (impairment) disorders (Eyre et al., 2015).

In older individuals, standardized neuropsychological evaluations are generally used to screen, characterize and quantify cognitive decline. It is the prime criterion of diagnosis, treatment and follow-up, of patients with or at-risk for dementia (Cullum et al., 2006). However, despite of its potential significant benefits, neuropsychological testing has been limited by its need for in-person/face-to-face (FTF) contact and also by the costs with travel, overhead, visits and missed visits (Cullum et al., 2006). For instance, patients who live in rural communities, or remote distances from medical centers and geriatric services, have difficulties to be screened or evaluated for cognitive performance/status (Shores et al., 2004; Morgan et al., 2009). Also, it has been described that those that are depended on caregivers may be deprived of this resource (Vestal et al., 2006). To overcome such limitation(s) there has been a call for increased use of information and communication technologies to render remote cognitive assessment more readily available (Tyrrell et al., 2001; Lee et al., 2000), including use of instruments that allow users to see visual stimuli, rather than simply hear, during communication (Jastrzembski et al., 2006; Martin-Khan et al., 2011).

In this background, besides the use of the telephone, videoconferencing (VC) (Weiner et al., 2011) is thought to potentially complement and/or offer potential advantages over FTF assessment (Hildebrand et al., 2004). VC has been used to carry out cognitive assessments, to conduct psychiatric interviews and consultations, and to help in management of conditions such as stroke, diabetes mellitus, chronic illness, cancer, depression and post-traumatic stress (Harrell et al., 2014). Besides improving the assistance to (older) individuals who already have

(mild) cognitive impairment, it can also reach those that still without deficit and/or professionally active, avoiding time and money loss due to travel and time missed at work. VC may also improve the capacity to reach a great number of individuals located at multiple stations in a short period of time, offering timely responses and aiding in epidemiological data collection.

Herein we describe the existing and relevant studies regarding the administration of neuropsychological tests via VC, and suggest methodological improvements for future research.

2. Accuracy of cognitive testing in cognitive impairment using videoconferencing

In cognitive impairment care, telemedicine has been used in the areas of patient diagnosis/assessment. The evaluation of cognitive functioning via VC using standardized assessment tools has been shown to correlate well with FTF testing (e.g. Cullum et al., 2006; Shores et al., 2004; Saligari et al., 2002; Loh et al., 2004; Barton et al., 2011). Some of cognitive instruments frequently used include the Mini-Mental State Examination (MMSE), Standardized MMSE, Clock Drawing test, Short Blessed test, Rowland Universal Dementia Assessment Scale (RUDAS), Digit Span, Hopkins Verbal Learning test – Revised (HVLTR) and tests of verbal fluency. The accuracy of a range of cognitive tests that are commonly used in dementia evaluations was tested by Cullum *et al.* in 14 patients with mild cognitive impairment and 19 patients with mild to moderate Alzheimer’s disease (Cullum et al., 2006). The study demonstrated the comparability of VC-based and traditional in-person testing conditions, indicating robust correlations between the two modalities [e.g. MMSE ($r = 0.89$), Boston Naming test ($r = 0.88$), digit span ($r = 0.81$), category fluency ($r = 0.58$), and letter fluency ($r = 0.83$)], providing a good indicator that cognitive assessment via VC may to be a valid and reliable means to conduct neuropsychological evaluations in older individuals with cognitive impairment. In a study that focused on the effectiveness of language evaluation in mild Alzheimer’s disease patients, Vestal *et al.* compared VC with in-person language assessments (Vestal et al., 2006). Findings from the Wilcoxon signed rank test revealed no significant differences in performance on each of the 5 language tests between VC and in-person

modalities, and, altogether, VC proved to be promising for speech and language evaluation services in dementia (Vestal et al., 2006).

Other studies have focused on specific cognitive tests, such as the Mini-Mental State Examination (MMSE; Saligari et al., 2002; Ciemins et al., 2009; Loh et al., 2007). Applying the MMSE via telemedicine, Loh *et al.* aimed to determine the inter-rater reliability of this instrument through VC, as compared to FTF administration, in 20 geriatric patients with diversified diagnoses (normal, dementia and depression) (Loh et al., 2004; Loh et al., 2007). Data indicated that assessments performed at distance with the MMSE using VC yielded similar results to direct evaluations. Timpano *et al.*, whose study validated an Italian version of the 28-item VC-based MMSE (VMMSE) in cognitively impaired and healthy subjects, also concluded that VC is a valid method for clinical and research screening (Timpano et al., 2013). The results demonstrated that the VMMSE has high levels of sensitivity and specificity for the optimal cutoff identification and an accuracy of 0.96. Moreover, VC was preferred over FTF, as it allowed real time communication between the health professional and the patient. Ciemins and colleagues examined the reliability of MMSE administration via remote way in a sample of 72 patients with diabetes (Ciemins et al., 2009). The main focus was to assess the auditory and visual components of the administration. Findings revealed that 80% of individual items demonstrated remote to FTF agreement of $\geq 95\%$ and all items were $\geq 85.5\%$. However, due to the study design only the differences between the scores of the two methods were documented.

3. Dementia diagnostic services in clinical settings using videoconferencing

Barton *et al.* described a VC neuropsychological assessment in a clinical setting (Barton et al., 2011). Using VC, a comprehensive battery of tests comprising clinical and neurologic assessments was performed to 15 veterans. Results indicated that VC is a feasible method to provide consultation and care to people who would otherwise not have access to it. It was also possible to reach a working diagnosis and recommend relevant treatments for each patient. Additionally, with a clinical sample, Harrell and colleagues demonstrated that the majority of patients evaluated by them via telemedicine had an inaccurate diagnosis at the time of the FTF consultation (Harrell et al., 2014). With the administration of a neuropsychological battery of tests via VC, the investigators identified missed and unrecognized mental health treatments

needs in over 77% of the patients referred. Telemedicine proved to be a valuable resource to clarify cognitive and psychiatric diagnoses. Moreover, a study by Martin-Khan and colleagues designed to validate the diagnosis of dementia via VC using a sample of 205 patients demonstrated a significant agreement for the primary outcome “Does the patient have dementia?” between VC and in-person testing conditions (Martin-Khan et al., 2012).

4. Users’ and cultural acceptability of videoconferencing

Research on VC-based neuropsychological assessment has been promising in terms of subject satisfaction and acceptability. Parikh *et al.* indicate that when asked about their preference 98% of the individuals evaluated in the traditional FTF condition and via VC expressed high satisfaction with both test modalities, and 60% indicated no preference for a test condition (Parikh et al., 2013). After completing a questionnaire that evaluated the usefulness of the VC interaction, its efficacy compared to FTF or telephone testing modalities and willingness to try VC again, the same high satisfaction level was seen in the study of Shores *et al.* with a group of veterans (Shores et al., 2004). In addition to the good acceptability, there was 100% agreement in dementia diagnoses between in-person and VC assessments. In another study, Grosch and colleagues documented that the individuals did not experience any difficulties in adapting to the testing environment or procedures, and they expressed satisfaction with the VC assessment (Grosch et al., 2015). In turn, with a sample of healthy volunteers, the study of Hildebrand and colleagues revealed a preference for in-person testing (44%) but 39% of the individuals indicated no preference, leading the authors to conclude good acceptance of VC-based assessments (Hildebrand et al., 2004).

Telemedicine diagnosis and assessment have also been welcomed in Spanish-speaking and Native American populations from remote and rural settings where access to specialized care is restricted (Weiner et al., 2011; Vahia et al., 2015). Using a Spanish-language battery of cognitive tests via VC, Vahia and colleagues compared it to in-person and found no significant differences between cognitive scores (Vahia et al., 2015). Additionally, the study of Weiner *et al.*, in a sample of individuals with dementia of the Choctaw Nation, suggested that the use of VC to diagnose and treat cognitive disorders was a feasible alternative to the traditional FTF examination (Weiner et al., 2011). High levels of acceptability of VC use were found amongst

this specific sample, with only 3% not showing for VC meetings and 2 individuals refusing to be examined afterwards.

5. Implications, limitations and recommendations

The state of the art described here provides evidence that VC is feasible and acceptable among many older people and health professionals. Studies demonstrated the reliability of cognitive testing via video-telemedicine, as noted by the correlations between results of various cognitive tests using VC as compared to in-person interview. Specifically, MMSE via telemedicine (e.g. Loh et al., 2004; Ciemins et al., 2009; Loh et al., 2007) can be as accurate as FTF, as well as particularly useful in documenting cognitive stability or decline. Other studies compared the results of several neuropsychological tests through FTF and VC in patients cognitively intact and with dementia. These studies did not find any significant difference between the two testing modalities and showed that patient acceptance and satisfaction with telemedicine is high. Moreover, comparisons of diagnosis made FTF and via VC suggested that clinical diagnosis of dementia via telemedicine consultation is valid and reliable (Shores et al., 2004; Loh et al., 2007).

Although VC increases access to particular services, there are inherent challenges specific to its use. Concerning the administration of neuropsychological tests, the ones that are the standard of care for assessment of older adults include measures that are sometimes not feasible for VC administration (Harrell et al., 2014). Also, participants tested by the same health professional in both conditions (VC and FTF) may inflate test-retest correlations. Using and learning new technology often demands keen perceptual and cognitive abilities which tend to decline as we get older. Therefore, the use of VC can be limiting for patients with significant sensory and auditory problems or those with more severe confusion or communication difficulties (McEachern et al., 2008). Additionally, it should be kept in mind that results can't be extrapolated because, to date, most studies have been conducted in small and non-randomized samples, and in specific settings.

Taking into account VC limitations, some recommendations are necessary for its use. First, before incorporating an instrument into a VC assessment, its reliability in the administration needs to be confirmed in the population setting attending to factors such as education level,

cultural aspects and exposure to technology. Those who administer neuropsychological testing should also guarantee competence in the practice of cognitive assessment via telemedicine, including appropriate educational background, and proper training (Ciemins et al., 2009). It should also be carried out an evaluation of the possible effects of sensory impairment and presence of psychiatric disorders on performance and subject's reactions to VC, previous to the assessment itself. A critical factor in acceptance of technology is its ease of use. Telemedicine through video should be simple and appropriate for the individual's competence. This is especially pertinent for people with dementia who usually have reduced processing speed, less manual dexterity and low visual acuity. At last, future studies should consider the use of larger and mixed diagnostic samples, as well as focus on subjective assessment of satisfaction/acceptability of telemedicine and not only administering cognitive tests. Further research is thus still warranted to fully establish the feasibility of conducting remote cognitive assessments and dementia diagnosis in real-life than experimental settings.

6. Conclusion

With the increase of older individuals requiring care it is imperative to develop new solutions to assist in remaining cognitively healthy and postpone the development of dementia. Telemedicine represents an excellent approach in the incorporation of technology, such as videoconferencing, in bridging the distance between health professionals and patients. On this, VC can be a useful tool in the screening and signaling patients with specific needs for further examination or follow-up. Moreover, the use of 'telemedicine' in cognitive assessment has the potential to support people with dementia while improving patients' quality of life and reducing health care costs (Bossen et al., 2015). The current state-of-the-art indicates for its use being as effective as an in-person evaluation, and an acceptable approach to assess those in underserved and remote areas. Still, despite the promising results, further research is required to replicate findings and bring a new solution to an old problem: to reach all individuals.

7. References

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CHAPTER V

Teresa Costa Castanho, Liliana Amorim, Pedro Silva Moreira, José Mariz, Joana Almeida
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Assessing cognitive function in older adults using a videoconference approach

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Assessing cognitive function in older adults using a videoconference approach

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Abstract

Background: The use of communication technologies is an emerging trend in healthcare and research. Despite efficient, reliable and accurate neuropsychological batteries to evaluate cognitive performance in-person, more diverse and less expensive and time consuming solutions are needed. Here we conducted a pilot study to determine the applicability of a videoconference (VC, Skype®) approach to assess cognitive function in older adults, using The Telephone Interview for Cognitive Status-Modified – Portuguese version (TICSM-PT).

Methods: After inclusion and exclusion criteria, 69 individuals (mean age = 74.90 ±9.46 years), selected from registries of local health centers and assisted-living facilities, were assessed on cognitive performance using videoconference, telephone and in person approaches.

Findings: The videoconference administration method yielded comparable results to the traditional application. Correlation analyses showed high associations between the testing modalities: TICSM-PT VC and TICSM-PT telephone ($r=.885$), TICSM-PT VC and MMSE face-to-face ($r=.801$). Using the previously validated threshold for cognitive impairment on the TICSM-PT telephone, TICSM-PT VC administration presented a sensitivity of 87.8% and a specificity of 84.6%.

Interpretation: Findings indicate for the range of settings where videoconference approaches can be used, and for their applicability and acceptability, providing an alternative to current cognitive assessment methods. Continued validation studies and adaptation of neuropsychological instruments is warranted.

Keywords: cognitive instruments; telemedicine; epidemiological studies: ageing

1. Introduction

Demographic ageing is a worldwide phenomenon that presents new socio-economic and health challenges, with an increasing need for proficient healthcare services to meet the needs of older adults. Most relevant, ageing is accompanied by cognitive decline; (Ciemins et al., 2009) thus, an efficient assessment process to determine cognitive status in aged individuals is of uttermost need. However, a comprehensive neuropsychological testing is a lengthy ordeal that goes well beyond several hours of physical presence in a healthcare institution.

With the broad availability and diffusion of the Internet, computer-based cognitive assessment can provide the greatly needed renewed impetus on cognitive function assessment (Wild et al., 2008). In fact, videoconferencing (VC) has been used to carry out clinical consultations of older people (Hildebrand et al., 2004). Such approach minimizes, for example, the burden of travel for seniors who live in remote/rural areas (Shores et al., 2004). Regarding cognitive testing it can also be a cost-saving methodology and may be suited for broad screening strategies (Wild et al., 2008, Castanho et al., 2015). In fact, good agreement between face-to-face versus non face to face methodology has been reported (Timpano et al., 2013, Weiner et al., 2011). For example, Hildebrand and colleagues (Hildebrand et al., 2004) administered via in person and by videoconference a battery of neuropsychological tests to 29 cognitively intact older adults; multiple cognitive measures demonstrated high degree of concordance between the two methods of evaluation. A feasibility study in older subjects with Mild Cognitive Impairment (MCI) and with mild to moderate Alzheimer's disease (AD) found correlations between 0.5 and 0.8 on a brief battery of neuropsychological instruments administered in-person and via videoconference (Cullum et al., 2006). There are also some studies on the use of videoconference to diagnose and treat cognitive disorders in the elderly, such as brain injury and other neurological disorders (Shores et al., 2004, Lott et al., 2006). In fact, work has demonstrated good correlations between various cognitive tests using other technologies compared with face-to-face interview, most often using telephone-based instruments (Castanho et al., 2015). Among these, the Telephone Interview for Cognitive Status (TICS; original instrument) (Brandt et al., 1988) is the most commonly used tool used by telephone for screening of cognitive status in older/elderly individuals. Still, the establishment of a practical assessment of cognition through videoconference is unexplored. On this, the most practical

solution could be the addition of video to validated telephone instruments, allowing to create a social presence and by pass problems posed by telephone methods (Menon et al., 2001, Castanho et al., 2015).

Here, addressing this need, the purpose was to use a videoconference approach of the TICSM in different settings: (i) full-time community-dwellers, (ii) those resorting to assisted-living during the daytime (day care centers), and (iii) full-time residents in nursing homes with diagnosed Alzheimer's Disease. To our knowledge, there are no studies that compare three separate administration methodologies of cognitive screening in the same individual and across different settings/groups.

2. Materials and Methods

Participants

A convenience sample was selected from Braga and Paços de Ferreira (Portugal) local health centers, assisted-living day-care centers and nursing homes. After inclusion/exclusion criteria, the final sample was composed of 69 subjects (40.6% men), with ages between 57 and 95 years (mean = 74.33, SD = 9.46). Formal education level ranged between 0 and 17 years. All participants from the local health centers (n = 20) were community-dwellers and all participants from the day care centers (n = 30) attended the center on a partial basis (afternoon and/or morning period, night time at family residence). The remaining participants (n = 19) were residents in a licensed skilled nursing facility with 24-hours care. The sample characterization is summarized in Table 1 and the participant flow chart in Fig. 1. Portuguese citizens are registered in local health centers since birth and are automatically assigned a family/general practitioner. Individuals requesting assisted-living support (partial or full-time) are allocated to their local centers. On measures of literacy, (un)employment rates, positive experience/mental health, and other socio-demographic characteristics, Portugal ranks close to the OECD (Organization for Economic Co-operation and Development; www.oecd.org/) average.

Table I. Sample characterization.

Gender		
	Male	28 (40.6%) ^a
	Female	41 (59.4%) ^a
Age		74.3 (9.46), [57-95] ^b
Years of formal education		4 (3.29), [0-17] ^b
Group		
	Healthy	50 (72.5%) ^a
	AD	19 (27.5%) ^a
Provenience/Setting		
	Community	20 (29%) ^a
	Day care center	30 (43.5%) ^a
	Nursing home	19 (27.5%) ^a

^aData presented as n (% of total sample)

^bData presented as mean (SD), [range]

The primary exclusion criteria included inability to understand informed consent, choice to not participate or withdraw from the study, incapacity and/or inability to perform or complete each of the cognitive screening assessment sessions. Nursing home residents were previously diagnosed with early Alzheimer's disease by the psychologist of the institution or by a psychiatrist. Clinical information for all participants was obtained from medical records and through neuropsychological evaluations and/or neuroimaging exams. The study was conducted in accordance with the Declaration of Helsinki (59th Amendment) and approval was obtained from the national and local ethics committees. Written informed consent was obtained from all volunteer participants prior to participation and recording of the evaluations. Because patients with Alzheimer's disease may be impaired in their ability to give adequate informed consent, which may be the case even in the disease's earliest, their primary caregiver and/or surrogate decision maker also signed the informed consent.

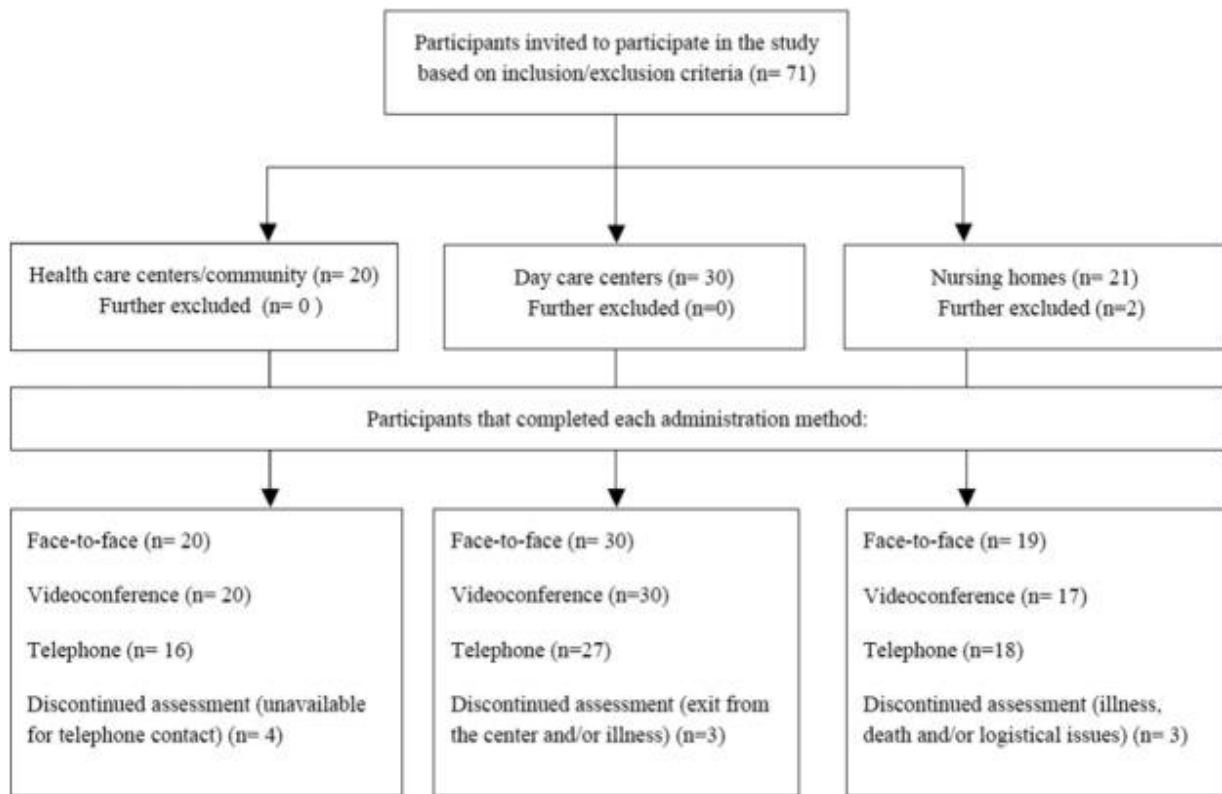


Figure 1. Participants flow diagram.

Procedure

The testing set-up included two laptops, one running Microsoft® Windows 7® (i5 M450, 2.40 GHz, 4GB RAM) for participants' use, and a second running Microsoft® Windows 7® (Intel Pentium® B950, 2.1Ghz, 6GB RAM) for the psychologist's use. Both laptops had built-in microphones and web cameras. The TICSMS administration took place through real-time videoconference carried out with the free video-call software Skype® v6.16 on both computers. Audio, video and connection settings were adjusted in each evaluation session in order to achieve good quality of communication.

At the start of the videoconference evaluation, the psychologist gave each participant a brief introduction regarding the VC-Skype® testing procedure and explained that would only appear on a screen but that another psychologist would be readily available in person if necessary. For all assessments, the psychologist in the room was out of the participant's line of sight, and primarily assessed for the testing conditions and took note of any difficulty or (internet) connection problem. Otherwise could not intervene. For safety concerns, and well care of the

study participants/patients, in the day care centers and nursing homes there was always a health professional of the institution outside the closed door. Among the individuals diagnosed with early Alzheimer's disease this is an established safety measure in order to prevent patients from leaving the room unattended. For the full-time community-dwellers testing took place at the Clinical Academic Center-Braga (2CA, Braga, Portugal); for all other participants testing took place at an adequate room of the day care center or nursing home. Each evaluation by telephone took 7 to 8 minutes, and by videoconference took on average 2 minutes longer to administer when also accounting for computer/video connection setup time. No confusion regarding who was at the other end of the telephone and videoconferencing was noted throughout the assessment for any of the participants.

To indicate for the acceptability, anxiety and ease of the participants, an informal guided discussion was previously held in a small group, for individuals of each of the settings (community, day care center and nursing home). Feedback on the quality of connection (sound and image) in order to particularly address for potential difficulties for those with hearing or visual impairment was obtained. The pilot sample was not considered/included in the study, but a similar informal discussion, which addressed the same parameters, also followed each videoconference assessment for the study participants (Table 6).

Instruments

Originally developed from the MMSE, the TICSM has a high validity and reliability on the screening of cognitive impairment (Welsh et al., 1993). Summarily, it consists of 13 items that assess different domains of cognitive function (orientation, learning, attention/calculation, language and delayed recall) (Castanho et al., 2014). The instrument has been validated in the Portuguese (PT) population (TICSM-PT) (Castanho et al., 2015) showing satisfactory internal consistency and convergent and divergent validity. All participants went through the assessments in the same order: face-to-face, videoconference and telephone. The TICSM-PT via videoconference was applied 1 month after the MMSE face-to-face assessment; thereafter, after a 2-month interval from the videoconference administration, the TICSM-PT was applied by telephone. This allowed avoiding any learning effect (Mitsis et al., 2010). The MMSE ("gold standard", face-to-face administration) (Folstein et al., 1975) takes approximately 5 to 10

minutes to administer and has a maximum possible score of 30 points. The same psychologist conducted all assessments. Permission was obtained from the Psychological Assessment Resources, Inc. (PAR, Inc.) for the use of the TICS with a delayed recall item (TICSM) (Castanho et al., 2015).

3. Statistical analyses

Descriptive statistics (mean, standard error of the mean and range) were obtained for the socio-demographic and cognitive variables: gender, age, education, MMSE and TICSM-PT domains. The characteristics of the distribution of the data were analyzed with Skewness (Sk) and Kurtosis (K) values. Independent sample t-tests were calculated to compare the TICSM-PT and the MMSE scores between genders, level of education and age groups (young old: individuals less than 75 years; oldest old: individuals with 76 years and higher). A similar analytical procedure was used to compare healthy individuals and early Alzheimer's disease patients. Furthermore, these scores were also compared between settings (community and day care centers) for the healthy subsample/group.

Linear regression analyses were conducted to determine the most relevant predictors (age, education, gender and healthy or Alzheimer's disease group) of the results of the different administration methods. Confidence intervals (95% level) were calculated for each independent variable. Covariance matrix and R squared change statistics were obtained. Correlation analyses were conducted to assess the magnitude of association between administration procedures of the TICSM-PT and the MMSE, and other variables. Furthermore, measures of association were also obtained between the same domains assessed through different administration forms of the TICSM-PT, as a strategy to comprehensively explore the similarities between the results of videoconference and telephone. A receiver operating curve (ROC) analysis was conducted to evaluate the discriminative ability of the TICSM-PT VC to distinguish between normal and cognitively impaired individuals. For this purpose, the TICSM-PT telephone total score with a cutoff of 13.5 was used as the test variable. This follows the threshold recently validated in a previous paper of our group (Castanho et al., 2015). P-values equal or less than 0.05 were considered to be significant. SPSS v23 (IBM SPSS Statistics) was used to perform all descriptive and statistical analyses.

4. Results

The descriptive statistics for the TICSM-PT (videoconference and telephone) and the MMSE (in person) are presented on Table 2 (Mean \pm SE). The TICSM-PT (both administration methodologies) and the MMSE scores presented acceptable Sk (range: - 1.34 to -0.01) and K values (range: -0.66 to 0.16). There were no significant differences between male and female individuals in any of the tests. The older individuals exhibited significantly lower performance, and individuals with higher education levels presented significantly higher scores. Alzheimer's disease patients had decreased performance in all tests. Community dwellers had higher scores on both administration forms of the TICSM-PT.

Table II. Descriptive statistics for TICSM-PT (VC and telephone) and MMSE (face-to-face) total scores.

	TICSM-PT VC ^a		TICSM-PT Telephone ^a		MMSE ^a	
	Mean (SE)	N	Mean (SE)	N	Mean (SE)	N
Gender						
Male	15.5 (1.09)	27	14.6 (1.17)	25	24.1 (0.96)	28
Female	12.9 (0.95)	40	13.6 (1.19)	36	23.9 (0.94)	41
t(df), p	t (65) =1.8, p=.075		t (59) =0.6, p=.575		t (67) =0.1, p=.883	
Age						
Young Old	17.3 (0.83)	35	17.1 (1.08)	31	26.0 (0.71)	36
Oldest-Old	10.3 (0.85)	32	10.7 (1.03)	30	21.9 (1.07)	33
t(df), p	t (65) =5.8, p=.001		t (59) =4.3, p<=.001		t (67) =3.3, p<=.001	
Education						
Lower	11.2 (0.90)	28	11.5 (1.2)	26	22.6 (1.08)	29
Higher	15.9 (0.97)	39	15.8 (1.06)	35	25.0 (0.84)	40
t(df), p	t (65)=-3.4, p=.001		t (59) =-2.6, p=.012		t (67)=-1.8, p=.070	
Group						

Healthy	15.9 (0.69)	50	16.4 (0.86)	43	26.2 (0.50)	50
AD	8.1 (5.12)	17	8.1 (1.14)	18	18.1 (1.35)	19
t(df), p	t (65) =5.6, p<=.001		t (59) = -5.4 , p<=.001		t (67) = -7.0, p<=.001	
Setting						
C	18.8 (1.12)	20	19.7 (1.41)	16	27.2 (0.57)	20
DC	14.0 (0.69)	30	14.5 (0.93)	27	25.6 (0.73)	30
t(df), p	t (48) =3.8, p<=.001		t (41) = 3.2, p=.003		t (48) = 1.5, p=.129	

TICSM-PT = Telephone Interview for Cognitive Status Modified–Portuguese–Portuguese; MMSE = Mini Mental State Examination; AD = Alzheimer’s disease.

After exclusion/inclusion criteria, of the n = 69 recruited individuals, n = 8 were not able to participate in the telephone assessment due to changes in contact information, health problems, death or persistent difficulties to be reached within the time frame. The videoconference evaluation was stopped for one AD participant due to major difficulties in focusing attention and because the patient was unable to respond to the instrument questions.

Non-AD participants.

The analysis of the correlation matrix revealed that the different administration procedures presented positive and significant correlations between each other (Table 3). There was a significant association between performance on the TICSM-PT VC and the TICSM-PT telephone scores ($r=.885$, $p<.001$), the TICSM-PT VC and the MMSE ($r=.801$, $p<.001$), and the TICSM-PT telephone and the MMSE ($r=.808$, $p<.001$). As expected, age and education revealed to be significantly associated with each method. Setting showed a significant association with both administration methods of the TICSM-PT and with the MMSE. The magnitude and significance of these effects and the variance-covariance matrix are also presented in Table 3. Linear regression analyses indicated that the socio-demographic variables (gender, age, education and group) significantly predict scores in the distinct administration procedures, explaining 47.5% (R^2 adj=.475), 59.2% (R^2 adj =.592) and 45.6% (R^2 adj =.456) of the total variance of the TICSM-PT VC, TICSM-PT telephone and MMSE, respectively. On this, group was the most relevant contributor to these models, being a significant (positive) predictor in each of the different administration procedures. Education level was a significant predictor of total score on the TICSM-PT via videoconference. The coefficients of individual variables in each model are presented in Table 4. The magnitude of correlation between the same domains, assessed

through different modalities, revealed moderate to strong effects (range: .495 to .866), suggesting good convergent validity of TICSM-PT assessed through videoconference (Table 5).

Table III. Correlations and variance-covariance matrix between administration methods and socio-demographic variables.

	TICSM-PT VC	TICSM-PT Telephone	MMSE	Setting	Gender	Age	Education
TICSM-PT VC	1.05	.90	.84	-.52	-.08	-6.5	1.42
TICSM-PT Telephone	.885**	.98	.81	-.47	-.04	-6.12	1.19
MMSE	.808**	.801**	1.04	-.46	.00	-5.29	.77
Setting	-.678**	-.639**	-.610**	.55	.00	3.90	-.22
Gender	-.149	-.082	.008	.000	.25	.18	-.36
Age	-.727**	-.703**	-.591**	.596**	.042	77.56	-9.8
Education	.400**	.348**	.218*	-.087	-.209	-.325*	11.91

TICSM-PT = Telephone Interview for Cognitive Status Modified–Portuguese–Portuguese; MMSE = Mini Mental State Examination; VC = Videoconference

*p<.05; **p<.01. The top-half (in grey) of the table represents the variance-covariance matrix; the bottom-half represents correlations between variables.

Table IV. Prediction of TICSM-PT (VC and telephone) and MMSE scores, based on socio-demographic characteristics.

		B	SE	Beta	t	p
TICSM-PT VC	(Constant)	17.2	2.62		6.56	.000
	Gender	-1.64	1.01	-.136	-1.62	.111
	Age	-4.69	.99	-.396	-4.73	.000
	Education	2.761	1.02	.230	2.71	.009
	Group	6.32	1.12	.464	5.65	.000

F(4,62)=25.04, p<.001; R2=.617; R2adj=.592

TICSM-PT Telephone	(Constant)	14.99	3.34		4.48	.000
	Gender	-.58	1.33	-.043	-.43	.667
	Age	-4.6	1.29	-.332	-3.38	.001
	Education	2.51	1.34	.189	1.88	.066
	Group	7.06	1.43	.491	5.03	.000

F(4,56)=14.6, p<.001; R2=.510; R2adj=.475

MMSE	(Constant)	20.89	2.77		7.53	.000
	Gender	.06	1.09	.005	.06	.955
	Age	-2.18	1.07	-.196	-2.05	.045
	Education	1.51	1.10	.134	1.38	.174
	Group	7.38	1.16	.592	6.34	.000

F(4,64)=15.3, p<.001; R2=.477; R2adj=.456

TICSM-PT = Telephone Interview for Cognitive Status Modified-Portuguese-Portuguese; MMSE = Mini Mental State Examination; VC = Videoconference

Table V. Correlations and covariance matrix of TICSM-PT domains between VC and Telephone administration.

TICSM-PT VC		TICSM-PT Telephone					
		Orientation	Registration	Attention Calculation	Comprehension	Language Repetition	Delayed Recall
Orientation	r	.866**					
	Covariance	.902					
Registration	r		.668**				
	Covariance		.685				
Attention Calculation	r			.851**			
	Covariance			.858			
Comprehension	r				.670**		
	Covariance				.673		
Language Repetition	r					.605**	
	Covariance					.599	
Delayed Recall	r						.495**
	Covariance						.498
M± SE TC		5.4 ± .23	2.1 ± .17	3.1 ± .29	1.6 ± .13	0.8 ± .05	0.9 ± .15
M± SE Telephone		4.9 ± .27	2.4 ± .20	2.8 ± .27	2.2 ± .7	0.9 ± .05	1.2 ± .17
Paired t-test		t(58)=4.0, p<.001	t(58)=-2.1, p=.038	t(58)=1.8, p=.081	t(58)=-4.1, p<.001	t(58)=-1.1, p=.260	t(58)=-1.92, p=.060

TICSM-PT = Telephone Interview for Cognitive Status Modified-Portuguese-Portuguese

VC = Videoconference

**p<.01

The area under the curve (AUC) statistic (Figure 2), obtained from the receiver operating curve (ROC) analysis, was 91.7% (95% confidence intervals: 84.5–98.8%). This result evidences the high level of accuracy for cognitive impairment and outstanding discriminative power of TICSM-PT VC. The calculated optimal TICSM-PT VC cutoff score for cognitive impairment was 11.5. Using this threshold, the sensitivity and specificity are 87.8% and 84.6%, respectively.

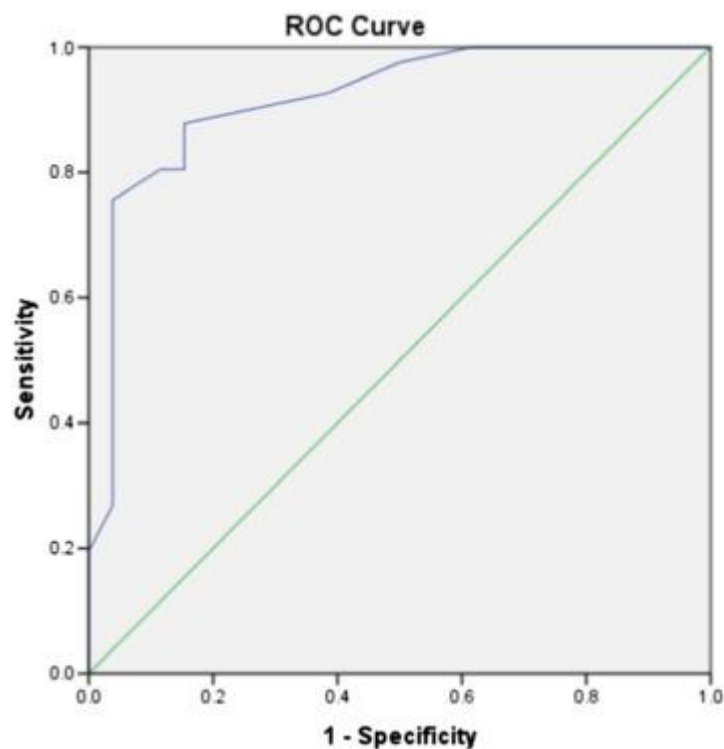


Figure 2. Receiver operating curve (ROC) analysis of the TICSM-PT Videoconference. The area under the curve (AUC) statistic is 91.7% (95% confidence intervals: 84.5 – 98.8%).

An informal discussion followed each VC assessment. Feedback concerning the videoconference testing modality is presented in Table 6. None of the participants requested to “not be evaluated again” and all showed interest in potential follow-up studies using the same methodology. All individuals who reported that had previously ‘chatted (online)’ using a computer (14.5%), indicated being “fully at ease” throughout the videoconference test administration. Most participants did not indicate any preference between the videoconference and the telephone approach, if a computer was to be available, but most indicated that “enjoyed seeing the evaluator face-to-face”. Only 3% of participants admitted that they “felt anxious/nervous” during the videoconference evaluation, but were able to resume after a brief reassurance by the test administrator/psychologist. Eighty-four percent reported that testing

instructions were “easy to understand” and 75% found it “easier to communicate” with the psychologist during videoconference evaluation compared to telephone. Despite feeling comfortable with the equipment (88.0%), 11.5% of participants indicated that videoconference had poor sound and visual quality.

Table VI. Feedback from individuals concerning TICSM-PT VC assessment.

		N of participants who took part in the discussion	% of total sample
Interpersonal communication.	Ease in communication between psychologist and participant	52	75
	Being anxious or nervous during examination	2	2.8
	Ease in understanding test instructions during VC assessment	58	84
Satisfaction with the equipment	Comfort with the equipment used	61	88
	Poor audio or visual quality	8	11.5
	Ease in manipulating the computer	10	14.5

VC = Videoconference

5. Discussion

Here, we demonstrate that cognitive assessment conducted via videoconference, using the TICSM(-PT) as the base instrument, is a valid and useful method. A strong association was found between the TICSM-PT applied by videoconference and by telephone, and between these and the MMSE face-to-face, encouraging the use of the approach as reliable. Across the TICSM-PT domains, correlations were considered from adequate to good evidence of convergent validity between the two approaches (videoconference and telephone). As expected, socio-demographic characteristics, such as age and education, affected the TICSM-PT total score (decrease), both when applied by videoconference and by telephone, which is expected due to the age related cognitive decline. Using the ROC curve, TICSM-PT VC showed a high accuracy for cognitive impairment discrimination, albeit the optimal cutoff of the TICSM-PT VC for dementia in this study being lower than the one reported in the previous TICSM PT by

telephone validation study of our group (Castanho et al., 2015). The cutoff score may be influenced by the inner characteristics of the study population, which was here comprised by a more heterogeneous sample. The findings indicate that a videoconference approach may be, at least as valid as the telephone method of administration, suggesting that cognitive assessments of individuals with suspected or diagnosed dementia using videoconference merits further development and may significantly aid in diagnosis and/or patient follow-up.

The potential uses of technology in providing access to care are wide, including in older populations (Ball and Puffett, 1998) as here addressed. In fact, overall, eHealth is becoming an everyday term and is, to various degrees, permeating the lives of many. For instance, in a recent study, Salisbury et al (2016) conducted a trial test of the effectiveness of integrating a (multicomponent) telehealth intervention into general practice for the treatment and management of depression. The need of telemedicine is, however, not confined to mental disease. In cognitive assessment it can be of use as a pre-step, or as a follow-up, to more in-depth/in-office consultations. The allying of technology and neuropsychological assessment, for those in multiple contexts, should become a readily available reality and it requires continued studies. For example, in older adults, the intra- and inter-individual heterogeneity in cognitive ageing, and the need to reach diverse populations, challenges the adaptability of the available instruments currently used to assess and/or screen for (in general) cognitive status. More so, older people represent a significant portion of the population in remote areas, where specialized care is a challenge (Ramos-Rios et al., 2012). More so, with advancing years, many individuals, due to functional, health or other limitations, make the transition from community dwelling to partial- or full-time care to assisted-living facilities. Thus, health services via technologies can provide to those in need substantial monitoring/support (Tyrrell et al., 2001), across health groups and residential settings.

Further highlighting the promising uses of the technology, videoconference has been used in clinical areas of patient diagnosis/assessment. For instance, Ciemins and colleagues examined the reliability of the MMSE administration via remote administration in a sample of 72 patients with diabetes (Ciemins et al., 2009). Findings revealed that 80% of individual test items demonstrated an agreement of $\geq 95\%$ between 'remote' to 'face-to-face' methods. Barton et al. described a videoconference neuropsychological assessment in a clinical setting

(Barton et al., 2011). Using videoconference, a comprehensive battery of tests comprising clinical and neurologic assessments was performed in 15 veterans. Results indicated that videoconference is a feasible method to provide consultation and care to people who could otherwise not have access to it. It was also possible to reach a working diagnosis and recommend relevant treatments for each patient. A more recent study investigated the feasibility of administering a measure of global cognitive function, the Montreal Cognitive Assessment test, face-to-face and then remotely via videoconference in 11 participants with Parkinson's disease (Stillerova et al., 2016). The authors reported that the higher scores in the test were not favored by either method of administration (i.e. videoconference via Skype or face-to-face) and concluded that videoconference evaluation may be a viable option to screen for cognition in patients with the disease.

The use of the technology may expand to randomized clinical trials. When managing clinical trials two of the most significant challenges are recruiting the right participants and retaining them for the duration of the trial. Burden of travel, and time and distance from the study site, may render it difficult to recruit participants. This can contribute to dropout rates, potentially causing long delays and increasing the risk of the study to fail. Videoconference may provide solutions in order to overcome these limitations in studies of this nature. De Las Cuevas and colleagues (2006) carried out a randomized clinical trial with 140 psychiatric patients that were randomized to receive treatment either face-to-face or via videoconference. Results indicated that treatment via the latter had equivalent efficacy to the in-person conventional treatment (De Las Cuevas et al., 2006). Additionally, Dorsey and colleagues evaluated in a randomized clinical trial the feasibility, effectiveness and economic benefits of videoconference care for 20 individuals with Parkinson disease in their home (Dorsey et al., 2013). They reported that videoconference offered similar clinical control, and saved participants 100 miles of traveling and 3 hours of time.

In this background, it can be foreseen that individuals could do a diagnostic neuropsychological evaluation via the use of a videoconference approach. However, a few considerations and challenges on the use of technology must be addressed. Foremost, the privacy, security and confidentiality of (free) videoconferencing software must always be taken into account; each country's ethical/security standards must be followed. More so, women, older and less

educated individuals may be less receptive to technology. For example, Kerschner and Hart (Zimmer and Chappell, 1999, Tun and Lachman, 2010) indicated that men, younger individuals, and those with higher education, are more receptive and report less anxiety. The link found between education and technology acceptability is of consideration. Studies have revealed that higher levels of education are associated to higher levels of both computer knowledge and computer interest and lower levels of computer anxiety (Ellis and Allaire, 1999). Here, importantly, the guided-informal discussion (on satisfaction and how difficult and stressful the participants considered the videoconference and telephone evaluations) indicated that the participants' acceptability of videoconference administration was satisfactory and on par with the acceptability of the telephone assessment. This is critical because the VC administration has several advantages, including the possibility to capture the participants' non-verbal cues, such as facial expressions and attentiveness, as well as to detect for the use of external cues/test aids. This helps not only the interviewer-participant communication, but also the overall assessment. Also, when applying videoconference (and telephone) methodologies surrounding distractions are of concern (e.g. ambient noises that make harder to hear/follow the instructions and test questions). These can potentiate sensory deficits, which can decrease the capacity to interact over a videoconference/telephone connection. Individuals with impairment can have difficulties in maintaining and sustaining attention. We speculate that in the present study the participants (particularly those with impairment) were able to maintain attention due to the brevity of the telephone/videoconference evaluation. Moreover, health professionals should primarily focus on the development of a therapeutic relationship and on patients' motivation. A recommendation is to start the evaluations with a brief conversation, or with a few questions that should not invalidate or conflict with the questions of the instrument, but would put the participant more at ease. In the present study, in some occasions, some instructions or questions had to be repeated. It could not be easily determined if because these could not be understood due to audio problems or because the participant could not, in fact, "cognitively" comprehend the question. Thus, instruments should be adapted or developed to include two or three "easy to answer" non-interfering questions, dispersed throughout the assessment, so to internally assess and/or control for this. Finally, it would be of great relevance the design/development and validation of an instrument that could be used in all settings here considered (in-person and non in-person) across ageing groups.

In sum, used with care and due considerations, technology can be used to improve the capacity to reach a great number of individuals, located at multiple stations, in a short period of time, offering timely responses, avoiding time and money loss due to travel and time missed at work, and aiding in clinical studies and epidemiological data collection. Beyond its use to carry out cognitive assessments, improving the assistance to (older) individuals, with cognitive impairment or not (and still professionally active or not), it can be speculated to help in the management of clinical conditions. Videoconference can be effective in direct patient interventions and psychotherapy in providing, for instance, greater continuity of care and access to isolated individuals. It can also potentially allow to enhance the structure of an intervention program, the possibility of relapse prevention and the exchange of nonverbal communication between the therapist and patient.

Currently, a limitation of computerized cognitive testing in older people is the lack of psychometric data (for example, normative, reliability and validity data) compared with traditional “paper and pencil” measures (Fazeli et al., 2013). Available studies are limited because of the small sample sizes used and with cohorts composed of mainly psychogeriatric inpatients or medical geriatric hospitalized patients. Here, we add to the present body of work, with results supporting the hypothesis of good acceptability of cognitive assessment via a videoconference method, comparable to the traditional face-to-face administration, in both community dwellers and those resorting to partial or full care in care centers. Results from the study are promising and demonstrate the suitability of using *eHealth* approaches in older individuals and may be a very useful and needed alternative to assess cognitive progression.

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CHAPTER VI

Cognitive decline assessment based on informants' report: state of the art

Abstract

Improving how we assess people who may have cognitive impairment is a health and social priority; thus, initiatives that accurately increase cognitive diagnosis rates have attracted attention. Most screening tests involve questions to directly evaluate cognitive functioning, but it is overall considered that if properly used informant-based questionnaires can also be extremely useful to health professionals, in an effort to assess the impact of cognitive decline on an individual's functionality. Here, it is aimed to summarize research results regarding the role and clinical utility of using existing informant-based instruments, informants' characteristics and their influence, paying a special focus to the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). To date, extensive research supports that informant reports can be seen as a complementary method to standard cognitive evaluations, especially when it is not possible to assess a patient with severe cognitive impairment. However, one needs to be aware of methodological issues, biases and limitations when using informant ratings, as well as the characteristics of the populations to which they are applied.

1. Introduction

Both in clinical and epidemiological research, a diagnosis of cognitive impairment and dementia must ideally result from several sources of information, including clinical and medical history, sociodemographic characteristics, and cognitive and functional evaluations. Direct cognitive assessments by a trained professional using established tests are one of the core tools for diagnosis (Knafelc et al., 2003; Potter et al., 2009). However, the progressive deterioration of cognitive and functional abilities, particularly in individuals with cognitive impairment, raises some practical issues when using direct cognitive evaluations (Marosszeczy & Sansoni, 2008). Many frequently used instruments comprise also an important limitation - the ceiling effect - given their sensitivity to educational level and culture. For instance, the Mini Mental State Evaluation (MMSE), the gold standard instrument for the evaluation of cognitive impairment, displays ceiling effects that make it insensitive to early signs of dementia, particularly in individuals with higher educational levels. Longer neuropsychological measures are less likely to present ceiling effects but they involve an extensive training to administer and are usually time consuming to be used in general practice (Galvin et al., 2006).

Considering the limitations of the cognitive instruments, and the fact that patients do not always report accurately the information needed to establish a diagnosis of cognitive decline, informant reports have been used as sources of historical information. According to Jorm (2004), tests based on informant's reports provide an alternative and complementary approach, allowing the performance of longitudinal assessments. Such instruments are easily applicable to individuals with high or low educational background and premorbid cognitive levels. Moreover, they are not thought to be directly influenced by patient's compliance, and are less threatening to the self-esteem of the person being assessed (Isella et al., 2002). Nevertheless, the assessment based on informants' reports do not replace conventional cognitive assessments, instead it allows the identification of changes in cognitive abilities that may or not be related to impairment or dementia in a specific period of time.

2. Informant's characteristics and their influence

Relatives of geriatric patients can provide the health professional with valuable diagnostic information. For instance, a family member or caregiver may make the initial contact to

express their concerns about a person, whom they care for, who either, for instance, refuses to see a psychologist or is not capable to answer questions. Moreover, relatively small changes can be noticed more easily by relatives than by the patient, especially in individuals with high education. Quantifying these observations can be useful, especially when other screening procedures are not available. As relatives usually report on changes in cognitive functioning, their information is possibly not confounded by the patient's age or level of education (de Jonghe, 1997). As patients with cognitive impairment present an increasing lack of self-awareness of cognitive and functional loss as the disease evolves, informants are often the most critical source to obtain information concerning cognitive and instrumental status in routine activities of daily living (Schinka, 2010).

Regardless of the advantages of informants' reports, the main limitation of this type of data collection is the possible absence of a qualified informant, or a person who can answer accurately. Some studies have shown that assessments can be influenced by the informant's characteristics, such as affective state, personality, depression or burden. These studies reinforce that informants with these characteristics tend to have a biased perception of the individual's behavior. It is not uncommon for the relative to fail in recognizing a memory problem that occurs in an older person with dementia, and regard this problem as a normal part of aging (Senanarong et al., 2001). For instance, in the Honolulu-Asia Aging Study, family informants failed to recognize cognitive problems in 21% of community dwelling individuals diagnosed with dementia years later (Ross et al., 1997). Accuracy of the informant's reports might also be influenced by the frequency of contact and the type of relationship between patient-informant (McLoughlin et al., 1996; Tierney et al., 1996).

Despite the advantages of an informants' report, structured informant-based information has not been incorporated systematically into quantitative instruments (Flicker et al., 1997), being mostly used only in clinical practice. Several tools have been created based on data collected from informants concerning cognition and basic and instrumental activities of daily living, so that the information could be standardized. Since then, cognitive tests and informant reports have been used as complementary aspects in research, enhancing the potential of cognitive screening.

3. Informant-assessment instruments

The existing literature regarding instruments based on informant's reports is immense. Here we consider only the tools with the purpose of screening and diagnosis of cognitive decline based on the exclusive use of informant reports.

Blessed Dementia Rating Scale (BDRS; Blessed et al., 1968)

The BDRS appears to be the first scale based on informants' report. It is a 22-item clinical rating scale that assesses difficulties in performance of various activities of daily living and behavior, personality and emotional changes in the preceding 6 months. The BDRS scores range from 0 to 17, and the informant indicates whether the individual had no loss, some loss or severe loss of functionality. The maximum score is 28 points, with higher scores indicating greater functional difficulty. BDRS takes 11 to 15 minutes to administer and has good validity, test-retest reliability and internal consistency.

Geriatric Evaluation by Relatives Rating Instruments (GERRI; Schwartz, 1983)

The GERRI scale evaluates the frequency of alterations in behavior and functional capacity over a two-week period prior to assessment, depending on the relative or caregiver observations of the patient. It comprises 49 items encompassed in three categories: cognitive functioning, social functioning and mood. It shows a good correlation between the areas that proposes to evaluate, but has a moderate validity when compared to other instruments.

Dementia Questionnaire (DQ; Silverman et al., 1986)

The DQ was designed to detect the presence or absence of dementia, to ascertain the type of dementia and to estimate the age of its onset. It consists of 50 questions that can be administered face-to-face or telephone to the informant and takes 15 minutes to complete. DQ was further validated in a sample of 74 individuals and the authors found a sensitivity of 100% and specificity of 90%, concluding then it can be used in research studies to screen dementia (Kawas et al., 1994).

Cognitive Behavior Rating Scale (CBRS; Williams et al., 1986)

CBRS is a rating scale to be used by relatives or significant others to assess patient's function. It consists of nine subscales or dimensions: language deficits, apraxia, disorientation, agitation,

need for routine, depression, higher cognitive deficits, memory disorder and dementia. These subscales can be plotted out on a profile sheet with t-scores and percentile norms available to compare with individuals without dementia. This instrument includes 116 questions and its greatest utility is on evaluating the cognitive consequences of dementia, since many demented individuals may refuse to be evaluated or be unable to complete demanding neuropsychological assessments.

Relative's Assessment of Global Symptomatology (RAGS; Raskin & Crook, 1988)

The RAGS provides a brief survey of psychiatric and behavioral symptoms noted by a caregiver or a close friend of the patient. It contains 21 items and each item has sub-items with five answering options ranging from "never" to "too much". Slightly different from the other questionnaires, each item includes sample descriptors. For instance, the item "Appears forgetful?" is followed by this descriptor: "Forgets names; misplaces objects; forgets appointments; needs to be reminded of routine".

Informant Questionnaire on Cognitive Decline in Elderly (IQCODE; Jorm & Korten, 1989)

The IQCODE consists of 26 items in its full version and 16 items for short version. It requires usually a relative who lives with the subject to compare the current patient's cognitive and functional behavior concerning to his or her level of functioning 10 years earlier. This instrument has been found to be equivalent to the use of brief screening instruments such as the MMSE and has well-defined psychometric properties (Cherbuin & Jorm, 2013). The IQCODE has been used and assessed in different languages including English, Chinese, Dutch, French, German, Italian, Spanish, Korean, Japanese, Thai, Finnish, Norwegian and Persian.

Present functioning Questionnaire (PFQ; Crockett et al., 1989)

The PFQ is a measure that consists of 60 items developed to form five scales: personality, everyday functioning, language, memory and self-care. The scores represent the caregivers' impressions of the subject's deficits, as well as they reflect the number of problems endorsed by them. Psychometric analyses of this measure revealed high levels of reliability and validity.

Détérioration Cognitive Observée (DECO; Ritchie & Fuhrer, 1992)

DECO is a 19-item Likert scale that encompasses changes in behavior (activity level, semantic and visual memory, memory of places, events and procedures, visuospatial performance and new skills learning) as observed by an informant. It has to be performed by a person who has had at least monthly contact with the patient during the last three years. In previous studies, this tool has been shown highly sensitive to early changes in cognitive functioning and when compared to MMSE, it showed a better performance in evaluating initial signs of dementia (Lenger et al., 1996).

Short Memory Questionnaire (Short MQ; Koss et al., 1993)

The Short MQ is composed of 14 questions and is intended to support in the diagnosis of dementia and depression. Although it has shown excellent psychometric properties, the initial work possibly had a bias, since the questionnaire was answered by the caregivers of patients with dementia, while those without dementia responded to their own questionnaires.

Informant Interview for the diagnosis of Dementia and Depression in older adults (IDD-GMS; Lewis et al., 1998)

The IDD-GMS uses information from relatives to detect dementia and depression in older individuals. It consists of 36 questions and with a cut-off inferior than 13 for dementia and less than 16 for depression, IDD-GMS presents a sensitivity of 84% and specificity of 80%.

Concord Informant Dementia Scale (CIDS; Waite et al., 1998)

The CIDS is a standardized 31-item scale designed to evaluate changes over the previous five years. The questions were chosen to cover a range of domains affected by dementia: memory, orientation, judgment and problem solving, involvement in community affairs, involvement in home and hobbies and personal care. A further four items were added to cover language.

Brief Cognitive Scale (BCS; Krishnan et al., 2001)

This scale consists of 18 questions designed to assess cognitive functions (memory, executive function, language) that affect everyday activities. BCS exhibited good sensitivity, specificity and reliability, however, according to the authors other studies have to be done before its use in clinical practice.

Alzheimer's Disease Caregiver Questionnaire (ADCQ; Solomon et al., 2003)

The ADCQ is an 18-item yes/no questionnaire that can be completed by a relative in 5-10 minutes. It includes questions concerning several aspects of cognition, including memory, language, executive function, visuospatial abilities and praxis. ADCQ also comprises items regarding functional abilities, mood and behavior as well as progression of symptoms. Published studies suggest a sensitivity of 90% and specificity of 85%.

Alzheimer's Disease (AD8; Galvin et al., 2005)

The AD8 is an 8-question tool completed by the relative/caregiver and takes less than 5 minutes to complete. It detects changes in individuals compared to a previous level of function and patients serve as their own control. This instrument also distinguishes individuals with very mild dementia from those without dementia. A score of 0 or 1 suggests normal cognition and a score of 2 or greater suggests that cognitive impairment is likely to be present. Its sensitivity is greater than 84% and the specificity greater than 80%.

4. Informant Questionnaire on Cognitive Decline in Elderly (IQCODE; Jorm & Korten, 1989)

Among the reviewed instruments, the IQCODE differs from the other functional measures in several important ways. First, although it evaluates some of the more characteristic instrumental activities of daily living, it focuses on discrete everyday behaviors dependent on specific cognitive abilities often affected by dementia (Farias et al., 2004). Another unique aspect of the IQCODE is its ease to be administered. Furthermore, allows longitudinal studies to evaluate cognitive decline, unlike the other tools that, in general, assess the current status of the individual.

First described in 1989, the use of the 26-item IQCODE is prevalent in both clinical practice and scientific studies. The IQCODE was initially conceived as an interview of 39 items: 26 of memory and 13 on intelligence. With preliminary analysis, 12 items were eliminated due to the lack of understandability by the informants and an item was eliminated for not presenting a good correlation with the other items. For each item, the informant scores change on a five-point ordinal hierarchical scale, with responses ranging from 1 "has become much better" to 5 "has become much worse". A reduced version of the IQCODE consisting of 16 items was validated by Jorm (1994) and, subsequently, other studies were performed using this version.

Summarily, the instrument was designed as a brief assessment, usually administered to a relative, or a close friend, living with the older individual for at least 10 years. The purpose is to compare changes in the subject's memory, cognition and language ability during the period of coexistence. Thus, the IQCODE instead of measuring cognition at a single point in time, it measures cognitive decline over a 10 year period. Although most studies use the instrument in a self-administration format, it can also be applied by telephone or letter, or face-to-face interview (Jorm et al., 1989; Law & Wolfson, 1995; Fuh et al., 1995; Hénon et al., 1997; Louis et al., 1999; Lim et al., 2002; Tang et al., 2003).

Psychometric properties

The greater part of research provides information on the psychometric characteristics of the IQCODE, as well as validation against measures of cognitive change: neuropathology, neuroimaging and neuropsychological assessment (Cordoliani-mackowiak, 2003; Jorm et al., 2000; Rockwood, 1998). Test-retest reliability has shown the instrument to be very good over short or long periods with correlations of 0.96 over 3 days and 0.75 over 1 year. Several other studies evaluated the internal consistency of the full version of IQCODE, measured by Cronbach's alpha coefficient, and found that is uniformly high, ranging from 0.93 to 0.97 (Jorm & Korten, 1988; Jorm et al., 1989; Jorm and Jacomb, 1989; Fuh et al., 1995; De Jongue et al., 1997; Morales et al., 1997; Tang et al., 2003). Concerning the IQCODE cut-offs, there is no consensus on the optimal threshold once it varies with the demographics of the population and the testing purpose. Researchers have generally chosen to use an absolute cut-off ranging from 3.3-3.6 in community samples to 3.4-4.0 in patient samples.

The IQCODE has also been shown potentially encouraging properties when compared to standard assessments of neuropsychological functioning. Most data is on the MMSE, with correlations from 0.37 to 0.72. Still, the IQCODE's scores were found to be significantly related with cognitive domains in particular tests, such as executive function (visual verbal test, trail making test B), language (Boston Naming test, verbal conceptual thinking), memory (CERAD word list, WMS-R Logical Memory) and attention (Trail Making test A, forward digit span) (Gavett et al., 2011; Farias et al., 2004). The validity of the IQCODE against clinical diagnosis has also been shown in a number of investigations. Although a diagnosis of dementia cannot be made using the IQCODE by itself, the instrument can be used to 'flag up' the need for further evaluation or to help with a diagnosis along with other cognitive tests or research. Some

authors have demonstrated that the IQCODE features are comparable with those of the MMSE, even suggesting that, in some occasions, it may be a more sensitive test and valid method to screen for dementia. Moreover, the IQCODE has performed equally well or better in combination with other cognitive tests at identifying individuals with a diagnosis of dementia, depending on the cut-offs selected (Jorm, 1997; Harwood et al., 1997; Flicker et al., 1997). Besides being considered a screening tool for dementia, a number of investigators have evaluated the IQCODE as a potential predictor of Mild Cognitive Impairment (MCI) (Isella et al., 2002; Ayalon, 2011). However, the results in this regard have been conflicting. According to Isella et al. (2006) and Ehrensperger et al. (2009), the IQCODE was as sensitive as the MMSE in distinguishing between MCI and healthy individuals; whereas, Dutra de Abreu et al. (2008) and Sikkes et al. (2010) could not confirm these results. An explanation for that is the IQCODE consists of items of low complexity that might not be sufficient to discriminate between MCI and healthy groups.

Influence of the informant's characteristics

There are few reports in the literature on the influence of informant's characteristics on informant reports' scores. In a research by Jorm and colleagues (1996), which included the participation of 144 subjects, the results were not influenced by informant socio-demographic characteristics (such as age and educational level). Regarding the quality the relationship between the informant and the patient, Fuh et al. (1995), in a sample of 416 individuals, using IQCODE as a screening instrument for dementia, emphasized that the coexistence period, as well as the frequency of contacts did not influence the findings. On the other hand, studies with a more qualitative approach indicate that some informants, due to emotional problems, influenced significantly the results. For instance, Del-Ser et al. (1997) observed that the informants, due to a state of anxiety, gave greater emphasis to cognitive problems. Additionally, in the Chinese validation of the IQCODE, the authors noted that some informants, in certain situations, seemed uncertain about changes in the mental status or were reluctant to talk about changes in their relatives. Also to be kept in mind is that in a situation of cognitive impairment, where changes may be subtle and may go unnoticed, more often to informants who do not spend much time with the participants are more prone to actually better note changes.

5. Concluding remarks

Dementia care and assessment will still remain a challenge for many years. There are many ways of assessing individuals for possible dementia and there is no clear agreement about the best way to do it. Nevertheless, one aspect is shared, the overall concern that the instruments used may be influenced by factors unrelated to the instrument itself, such as socio-demographic, ethnic, language, gender, clinical or cultural characteristics of the individual under evaluation. Thus, one approach that has been used to evaluate the individual's cognitive functioning, and that has been found to be minimally related to education and other factors, is to ask someone who knows him/her about changes they have been observed. Data collected from informants has, therefore, been increasingly appreciated both on clinical practice and scientific studies, but it is not free of bias or relevant concerns.

Among the informant reports, the IQCODE has been a widely used instrument in different countries and cultural backgrounds, suffering across populations only slightly cultural and language changes. The IQCODE has the advantage of being independent of the patient's premorbid intelligence and requires minimal training in application and scoring (Lim et al., 2003). Additionally, it can assess people in studies who would normally be excluded due to acute illness, lack of cooperation, low education or death. All these factors make IQCODE an attractive initial assessment tool for aiding in the diagnosis of dementia. However, the relative minor changes across settings raise a "red flag" concerning if it fully and aptly considers that populations do differ in basic cultural and socio-demographic characteristics of care in addressing cognitive trajectories/evolution. In fact, the IQCODE may work better for prediction of future dementia in combination with collateral sources (Isella et al., 2006), with studies noting that the main drawback of using the IQCODE is that its score might reflect or be biased by informant's own characteristics. For instance, informants with anxiety and/or depression tend to report greater cognitive decline than indicated by the standard cognitive assessment (Gavett et al., 2011). The validity of this questionnaire undoubtedly requires objectiveness and honesty on the part of the informant. It is recommended though to consider the emotional states of the informant when interpreting the IQCODE results and whether different types of informants provide reliable information.

In conclusion, informant reports are seen as complementary to standard cognitive assessments, especially when it is not possible or feasible to evaluate a patient with dementia. Nevertheless, there is a need to be aware of methodological issues (e.g. informant's cognitive and healthy status) and the biases and limitations when using informant ratings (e.g. socially desirable responses, negative information over positive information or otherwise). As a result, future work should focus on the continuous process of examining the informant reports validity and discrepancies with direct cognitive tests and find a way to deal with lowered validity in research, either by the exclusion of certain informants or the adjustment of scores.

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CHAPTER VII

Teresa Costa Castanho, Liliana Amorim, Pedro Silva Moreira, Carlos Portugal-Nunes, Joana Almeida Palha, Nuno Sousa, Nadine Correia Santos

Screening cognitive decline using informant's reports: an exploratory study on the use of the Informant Questionnaire on Cognitive Decline in Elderly (IQCODE) in community dwelling older individuals

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Screening cognitive decline using informant reports: an exploratory study on the use of the Informant Questionnaire on Cognitive Decline in Elderly (IQCODE) in community dwelling older individuals

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Abstract

Background: The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) was developed as a screening tool for cognitive alterations in an older person's everyday life, as indicated by a proxy. The present study explored the applicability of the Portuguese version of the IQCODE as a screening instrument for cognitive impairment in older community-dwellers without dementia and with low educational background.

Methods: 125 community-dwelling individuals aged 52 and more (mean = 66.06, SD = 7.554) were recruited from the general population; 123 proxies acted as informants. Cronbach's alpha coefficient was used to assess for IQCODE reliability and convergent validity was evaluated through the correlation between IQCODE and the Mini-Mental State Examination (MMSE).

Findings: No associations were found between the IQCODE and the informants and participants' socio-demographic characteristics. Pearson's correlation coefficient showed no association between the IQCODE and the MMSE ($r = -.071$, $p = .434$). IQCODE presented a good internal consistency (Cronbach's alpha = 0.85). Regarding cognitive trajectory as perceived by the informants, most participants were rated as a "bit worse" (49.6%) and as experiencing "not much change" (41.6%) compared to 10 years ago.

Interpretation: The lack of variability in the responses of informants may indicate that the IQCODE is not an informative tool when applied in community-dwelling older individuals with characteristics similar to those explored in this study.

Keywords: IQCODE; Informant; cognitive screening; everyday function; aging

1. Introduction

Cognitive decline is a common trait associated with ageing. The vulnerability of older individuals to cognitive impairment and dementia places them at increased risk for loss of function and decreased independence in everyday life, also increasing the burden on family and/or caregivers. Under these circumstances, one of the most important aspects is to provide an early diagnosis that may lead to better treatment and care of the individual, as well as a better support of his/her family or caregiver. A proper diagnosis and assessment gives to patients, and their families, a realistic opportunity to plan and implement necessary measures (Kirkvold & Selbaek, 2015).

The assessment of cognitive impairment and dementia has traditionally been carried out by using neuropsychological batteries of tests. These represent an important way to assist in the identification of clinical cases (or suspect ones), and can be used both in clinical and research contexts. The inclusion of an informant's report in clinical practice can be a complement to the neuropsychological testing (Sampaio et al., 2008) by providing a historical insight into the cognitive trajectory of the individual. On this, much of what we know about the value of these informant ratings, in evaluating cognitive impairment and functional change, is based on an extensive empirical support on the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). The informant should be someone who knows the current performance of the individual/patient in comparison to his/her previous status. This insight can be useful in assessing changes and possibly indicating cognitive impairment in early stages. Informants are often able to provide a more objective assessment of a patient's cognitive and functional status since patients themselves may attribute their deficits to age, lifestyle changes, stress and other factors. Small changes may be noticed more easily by relatives than by the patient or the assessing clinician/researcher, especially in people with higher education (Carr et al. 2000), or when a patient's underlying cognitive pathology affects his/her own self-perception (Sampaio et al., 2008). Additionally, informant's reports can also be used without requiring the physical presence of the individuals and when there is a lack of cooperation and/or low levels of education or literacy. More so, an advantage of informant-based assessment is the fact that may comprise less threat to the self-esteem of the individual being examined (Waite et al., 1998).

Given the potential benefits of such approach, there is a growing interest in developing and improving instruments based on informant's reports. Here, considering that the low educational status of the present older adults in Portugal compromises the usage of some cognitive instruments in the screening of cognitive impairment, informant-based information may be highly valued in clinical practice and research contexts. Therefore, a study was conducted to explore the applicability of the Portuguese version of the IQCODE as a screening test for cognitive impairment in older people, without dementia, with low educational background living in the community.

2. Materials and Methods

Description of the instrument

The most commonly used measure based on informant's reports is the IQCODE (Jorm & Jacomb, 1989). It provides complementary information to other cognitive tests, and it rates changes that may occurred in the patients' cognitive and functional performance. The IQCODE has been found to increase slightly the level of accuracy of diagnostic screening when used in combination with cognitive screening instruments, such as the Mini Mental State Examination (MMSE) (Schinka, 2010). Although the IQCODE evaluates some of the most characteristic instrumental activities of daily living, it mainly focuses on discrete everyday behaviors that rely on specific cognitive abilities frequently affected by decline/dementia (Farias et al., 2004). The instrument consists of 26-items regarding memory function and instrumental activities of daily living, and it can be self-administered or used by a trained-individual and/or professional. As proposed by the authors in the original study, the IQCODE should be applied to a relative, a close friend or formal caregivers in institutions, that has had a continuous contact with the older/elderly individuals for at least the previous ten years, with the purpose of comparing the present performance of the individual with his/her performance ten years ago (Jorm, 1994).

The IQCODE scores can range from a minimum of 1.0 (much improved) to a maximum of 5.0 (much worse), with 3.0 indicating no change. In general, scores ranging between 3.3 - 3.6 in community samples and 3.4 – 4.0 in clinical samples are used as proposed cut-offs for dementia (Cherbuin & Jorm, 2013 in Lerner, 2013). Using these cut-offs commonly employed in clinical practice, the sensitivity and specificity of IQCODE for dementia diagnosis across

studies are usually above 75% (Quinn et al., 2014). Furthermore, validation studies show that the IQCODE has a good internal consistency and reliability on test-retest at intervals of days ($r = 0.96$) or years ($r = 0.75$) (Jorm, 1991). Its administration and scoring takes 5 to 7 minutes and it has been translated into several languages, and validated in different countries, presenting well-defined psychometric properties.

Translation and back translation procedures

The original 26-items version questionnaire (Jorm & Jacomb, 1989) was translated from English to Portuguese (Portugal) by two psychologists with excellent acquisition of English and a biochemist with expertise in neurosciences. Backward translation of the Portuguese version was performed by another psychologist and a linguist. Modifications were done in the adapted version, and minimal changes and tips suggested by the participants were considered in the process. Specifically, the item 26 (“Using his/her intelligence to understand what’s going on and to reason things through”) was subjected to a variety of changes to the final translation “Be aware of what is happening around you and think about the situation itself”. The structure of the questionnaire and its instructions were maintained as in its original format: “much improved/ *‘muito melhor’* =1; “a bit improved/ *‘um pouco melhor’* =2; “no change/ *‘sem alterações’* =3; “a bit worse/ *‘um pouco pior’* =4; and, “much worse/ *‘muito pior’* =5. After the pilot testing two other options were added to the questionnaire: “Not applicable/ *‘Não se aplica’*” and “Doesn’t know/ *‘Não sabe’*”. No changes were made to the scoring and the rating criteria from the original instrument. The final version, to verify ease of understanding and interpretations of all items, was checked by administering the IQCODE-Portuguese version to 11 informants. Finally, the IQCODE was administered in the study sample.

Sample and data collection

Potential participants were directly approached at local health care centers of Póvoa de Varzim, Braga and Guimarães (Portugal). A total of $n=125$ community-dwellers and their informants agreed to participate. The study was conducted in accordance with the Declaration of Helsinki (59th Amendment) and approval was obtained from the national and local ethics committees. Written consent was provided from all participants prior to participation. The exclusion criteria

for participation included inability to understand informed consent, participant choice to withdraw from the study, incapacity and/or inability to attend the cognitive assessment session, dementia and/or diagnosed neuropsychiatric and/or neurodegenerative disorder. Written consent was provided from all participants prior to participation. The evaluations were conducted between May 2013 and June 2014.

Procedures and instruments

Two psychologists carried out the administration of the IQCODE with an informant nominated by the participant. The only selection criterion was being a close relative of the subject who had been living with him/her for the last 10 years. Considering that IQCODE alone may not be suitable for cognitive impairment screening and has been recommended for use in combination with screening measures, the informant report was applied together with the Portuguese version of the Mini-Mental State Examination (MMSE). The MMSE is an assessment scale measuring cognition that taps different cognitive functions such as memory, orientation, attention, calculation and visuospatial performance. The scores of the MMSE range from 0 to 30, where lower values indicate poorer cognitive function. Therefore, it was used as an indicator of cognitive functioning.

3. Statistical analyses

Descriptive statistics (mean, standard error of the mean and range) were obtained for the socio-demographic and cognitive variables: gender, age, education, IQCODE scores and MMSE scores. An independent samples t-test was conducted to compare the IQCODE scores between the informant genders. A one-way between subjects ANOVA was performed to compare the effect of the type of informants in the IQCODE scores. To study IQCODE reliability, Cronbach's alpha coefficient was calculated. Item-total correlation was used to evaluate the internal consistency of the IQCODE. Concerning convergent validity, Pearson correlations were determined between IQCODE and MMSE. It was also explored the association between socio-demographic variables and the cognitive tests. SPSS v23 (IBM SPSS Statistics) was used to perform all descriptive and statistical analyses

4. Results

The non-informant sample consisted of 125 older subjects, with 59 men (47.2%) and 66 women (52.8%). 62.3% of the participants have between 4 and 9 years of education. The average age of the total sample was 66.06 years ($\pm 7,554$) and it ranged 52 to 85 years (Table 1). A final sample of 123 corresponding informants completed the IQCODE. The average age of the total group of informants was 56.01 years ($\pm 14,989$), most were female (66.4%), 52% had between 4 and 9 years of education, and the majority were relatives of the non-informant (88%). Specifically, informants were most often spouses (35.2%) or daughters (24.8%). The sociodemographic variables of the study participants/non-informants and their informants are shown in Table 2. Two informants were excluded due to missing information.

Table 1. Participants and informants sample characterization

Participants (n=125)			Informants (n=123)	
Gender	Male	n=59 (47.2%) ^a	Male	n=39 (31.2%) ^a
	Female	n=66 (52.8%) ^a	Female	n=84 (67.2%) ^a
Age (yrs), range		66.06 (7.55), [52-85] ^b		56.0 (14.98), [20-83] ^b
Education level	< 4 yrs	n=31 (25.4%) ^b	< 4 yrs	n=14 (11.2%) ^b
	4– 9 yrs	n=76 (62.3%) ^b	4– 9 yrs	n=65 (52.0%) ^b
	> 9 yrs	N=15 (12.3%) ^b	> 9 yrs	n=38 (30.4%) ^b
Informant's relationship with the participant	—	—	Wife	n=44 (35.2%) ^b
	—	—	Daughter	n=31 (24.8%) ^b
	—	—	Husband	n=22 (17.6%) ^b
	—	—	Son	n=7 (5.6%) ^b
	—	—	Friend	n=7 (5.6%) ^b
	—	—	Sister	n=4 (3.2%) ^b
	—	—	Nephews	n=2 (1.6%) ^b
	—	—	Others	n=2 (1.6%) ^b
	—	—	Brother	n=1 (0.8%) ^b

Data presented as: ^aMean (SD), range; ^bn (%)

Table 2 shows the mean scores of IQCODE and MMSE instruments. One sample t-test showed that the IQCODE mean is significantly different ($t = -10.58, p < .000$) from the 3.38 cutoff

established by Jorm (1994) for community samples. No associations were found between the IQCODE and the informants' characteristics. Specifically, there was no significant correlation between the IQCODE score and informants' age ($r = -.033$, $p = .724$), no significant association between the IQCODE score and their education ($r = .068$, $p = .464$) and no statistically significant differences between this instrument and female informants ($M = 3.171$, $SD = .260$) and males ($M = 3.121$, $SD = .197$); $t(123) = -1.132$, $p = .260$. Moreover, there was no statistically effect of the type of informant on the IQCODE scores ($F[33, 89] = .976$, $p = .528$). Concerning the participants' sample, there was also no correlation between the IQCODE results and their age ($r = -.009$, $p = .918$) and education ($r = -.123$, $p = .177$). Furthermore, there was no significant difference between sexes ($t = -1.13$, $p = .260$). The Pearson's correlation coefficient showed no significant association between the IQCODE and the MMSE, that is, the convergent validity of IQCODE is not guaranteed by MMSE ($r = -.071$, $p = .434$). A correlation test between the IQCODE and a split sample of participants with scores on the MMSE below and above 23 (threshold for cognitive impairment for the Portuguese population (Guerreiro et al., 1994)) further indicated no association. Regarding cognitive trajectory as perceived by the informant, 3.2% participants were rated as a "bit better", 41.6% were rated as experiencing "not much change", 49.6% as a "bit worse" category and 6.4% as "much worse", compared to 10 years ago.

Table 2. Descriptive statistics for the cognitive tests.

	Mean (SD)	Min	Max
IQCODE	3.15 (0.25)	2.88	4.42
MMSE	25.88 (3.19)	11	30

IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MMSE, Mini Mental State Examination

Regarding the internal consistency of the IQCODE, the Cronbach's alpha was 0.85, considered a good value, ensuring the reliability of the instrument. However, as noted in Table 4, there are some item-total correlations that were not superior to 0.30. Item 14 (Learning new things in general/ *'Aprender coisas novas em geral'*) has the best item-total correlation ($r = .606$). The items with the lowest item-total correlation were items 7 (Remembering his/her address and telephone number/ *'Lembrar a morada e o número de telefone'*), 12 (Knowing how to work

familiar machines around the house/ *'Saber como utilizar electrodomésticos em casa'*) and 24 (Handling financial matters/ *'Lidar com assuntos financeiros'*).

Table 3. Psychometric characteristics of the IQCODE

	Corrected item-total correlation	Mean \pm SD	Cronbach's Alpha if item deleted
1. Recognizing the faces of family and friends (Reconhecer a cara de familiares e amigos)	.480	3.02 \pm 0.36	.849
2. Remembering the names of family and friends (Lembrar o nome de familiares e amigos)	.463	3.08 \pm 0.37	.849
3. Remembering things about family and friends e.g. occupations, birthdays, addresses (Lembrar coisas acerca da família e amigos (por ex.: profissões, datas de aniversário, moradas))	.428	3.15 \pm 0.52	.848
4. Remembering things that have happened recently (Lembrar coisas que aconteceram há pouco tempo)	.554	3.14 \pm 0.48	.846
5. Recalling conversations a few days later (Lembrar de conversas alguns dias mais tarde)	.457	3.25 \pm 0.62	.847
6. Forgetting what he/she wanted to say in the middle of a conversation (Esquecer o que queria dizer a meio de uma conversa)	.473	3.23 \pm 0.58	.847
7. Remembering his/her address and telephone number (Lembrar a morada e o número de telefone)	.242	3.15 \pm 0.68	.853
8. Remembering what day and month it is (Lembrar o dia e o mês em que está)	.468	3.07 \pm 0.45	.848
9. Remembering where things are usually kept (Lembrar onde as coisas estão guardadas habitualmente)	.400	3.35 \pm 0.79	.848
10. Remembering where to find things which have been put in a different place from usual (Lembrar onde encontrar as coisas que foram colocadas num sítio diferente do habitual)	.470	3.42 \pm 0.80	.846
11. Adjusting to any change in his/her day-to-day routine (Adaptar-se a mudanças na rotina diária)	.490	3.30 \pm 0.87	.845

12. Knowing how to work familiar machines around the house (Saber como utilizar electrodomésticos em casa)	.212	3.21 ± 0.88	.855
13. Learning to use a new gadget or machine around the house (Aprender a usar um novo electrodoméstico ou máquina em casa)	.463	3.30 ± 0.92	.846
14. Learning new things in general (Aprender coisas novas em geral)	.606	3.29 ± 0.74	.842
15. Remembering things that happened to him/her when he/she was young (Lembrar coisas que lhe aconteceram quando era jovem)	.445	3.17 ± 0.87	.846
16. Remembering things he/she learned when he/she was young (Lembrar coisas que aprendeu quando era jovem)	.447	3.18 ± 0.85	.846
17. Understanding the meaning of unusual words (Compreender o significado de palavras pouco utilizadas)	.409	3.25 ± 0.87	.848
18. Understanding magazine or newspaper articles (Compreender artigos de revistas ou de jornais)	.367	3.35 ± 1.07	.850
19. Following a story in a book or on TV (Seguir uma história de um livro ou na televisão)	.363	3.11 ± 0.80	.849
20. Composing a letter to friends or for business purposes (Escrever uma carta para amigos, familiares ou para fins de negócios)	.377	3.70 ± 1.31	.852
21. Knowing about important historical events of the past (Lembrar acontecimentos históricos importantes do passado)	.429	3.36 ± 1.11	.848
22. Making decisions on everyday matters (Tomar decisões no dia-a-dia)	.540	3.13 ± 0.64	.845
23. Handling money for shopping (Lidar com dinheiro para fazer as compras)	.335	3.18 ± 0.85	.850
24. Handling financial matters, e.g. the pension, dealing with the bank (Lidar com assuntos financeiros (por ex.: reforma, coisas do banco))	.224	3.35 ± 1.03	.856

<p>25. Handling other everyday arithmetic problems, e.g. knowing how much food to buy, knowing how long between visits from family or friends (Lidar com outros problemas concretos do dia-a-dia (por ex.: saber a quantidade de comida a comprar, saber quanto tempo decorreu entre visitas de familia ou amigos))</p>	<p>.457 3.11 ± 0.54 .847</p>
<p>26. Using his/her intelligence to understand what's going on and to reason things through (Ter noção do que se passa à sua volta e pensar sobre a situação em si.)</p>	<p>.488 3.09 ± 0.46 .848</p>

5. Discussion

In this study, the lack of variability in the responses of informants may indicate that the IQCODE is not an informative tool when applied in community dwelling older individuals in samples with characteristics similar to the present one. Most of the informants rated the participants as having no changes (41.6%), or just a slight decline (49.6%), on cognition, when compared to 10 years ago. The study follows results by others indicating that relatives may find it difficult to accurately remember the individuals' performance 10 years ago and, thus, are less successful in identifying individuals with cognitive impairment (Jorm et al., 1991). For instance, informants from the study of Razavi and coworkers (2014) characterized 34 participants with mild cognitive impairment or dementia as having no impairment. In the Areza-Fegyveres and colleagues (2008) study sample, neither the elderly nor the informant were ideal respondents, the participants perceived alterations in their cognition with more accuracy and earlier than the informant. In a Singaporean community survey, Lim et al. (2003) observed that "there were a few instances when the informant appeared reluctant to 'mark down' their elderly relative".

Here, no significant correlation was found between IQCODE total scores and the MMSE, which may possibly be explained by the fact that the older participants were independent in their daily life and, presumably, cognitively healthy. Despite measuring the same construct, the MMSE is

a cognitive assessment directly performed with the participant/patient, whereas the IQCODE is based in information from a proxy (Kirkvold & Selbaek, 2015). In the current work, no associations were found between the IQCODE scores and the participants and informants socio-demographic variables (gender, age, educational level). The same results, that the educational level and age of the informant, and the type of relationship maintained between the informant and the individual under evaluation, do not influence the questionnaire scores are also supported by the original studies of this instrument (Jorm and Korten, 1988; Jorm and Jacomb, 1989), as well as by other authors (Fuh et al., 1995; Morales et al., 1995). Besides this, the IQCODE has found to have near-zero correlations with an individual's level of education or with their cognitive ability earlier in life. This contrasts with the conventional cognitive impairment screening tools, which are usually affected by education and premorbid intelligence as well as the presence of cognitive impairment (Jorm, 2004). Concerning the IQCODE reliability, the current results demonstrate that the instrument has a Cronbach's alpha of 0.85, which was found to be slightly lower compared to the original (0.95) presented by Jorm and Korten (1998), as well as with other studies (Fuh et al., 2005; Tang et al., 2003). It is also of note that the items 7, 12 and 24 met the conditions to be removed from the scale in order to increase internal consistency, since they might not be measuring the same thing as the rest of the items. Furthermore, most of the remaining items were greater than the respective alpha factor, so that all items may not be included, overall indicating for the non-suitability of the scale for the considered sample population.

In this context, the use of informant's reports in community-dwellers, without any suspicion of cognitive decline, can raise many questions. For instance, an informant may lack familiarity with the individual's situation because they may not observe him/her with sufficient frequency (Neumann, 2000). It may also happen that older people may be less active or take part in activities that are less cognitively challenging, making a decline in cognition and functionality less clear to the informants. Or even, they may present mild difficulties, but do not meet criteria for dementia because they are still able to function independently. Informants' reports can also be influenced by other factors such as the affective state of the individual and the informant, the personality of the subject and the quality of the relationship between them. Sometimes, there is a strong denial in family members: they can underreport symptoms or impairment in order to protect the older relative from embarrassment in certain circumstances

or answer questions in a manner that will be viewed favorably by others (i.e., social desirability bias). Specifically, wives or children may minimize or deny the presence of memory and cognitive deficits out of respect for their husbands or fathers (McLoughlin, 1996; Ross, 1997). Considering what was previously demonstrated, the absence of an evaluation of the influence of informant's cognitive abilities and emotional state on the accuracy of IQCODE in the present study was a major drawback. Among the limitations of this study, one possible caveat is also the fact that the necessary number to verify the IQCODE validation was not reached. So, due to the small sample size, the findings cannot be considered conclusive. Ideally, the study needs to be continued in a larger sample, adding a clinical sample as well. The current study also lacked on other measures of cognitive decline and this should be included in future research. Furthermore, due to the cross sectional design of this study, no follow-up data is available. Taking into account the preliminary results of this study and its limitations, other statistical analysis that can add up on ensuring that the instrument has the necessary properties or is able for use were not possible to be performed.

Considering these limitations, there is extensive literature with several recommendations on IQCODE that can be followed. Some authors suggest that IQCODE should consist of complex cognitive and instrumental activities of daily life items that could be able to indicate those patients more prone to cognitive impairment (Sikkes, 2010). For instance, it should be used more complex cognitive behaviors (e.g., cooking a complete meal) frequently involving micro-competencies in several domains, such as memory and executive function, that may show a decline in qualitative aspects of performance rather than a vulgar inability to complete tasks (Schinka, 2010). Also of consideration, Quinn and colleagues (2014), in an extensive review about the diagnostic accuracy of IQCODE on community dwelling older adults, showed that although the instrument has reasonable psychometric properties, the test as a complement may not be suited for dementia screening. Specifically, when the IQCODE is used to assess broad populations of older subjects, the instrument may 'label' individuals with dementia who do not have it and miss the diagnosis in a considerable proportion of individuals (Quinn et al., 2014). Finally, in another study, with a sample of psychogeriatric daycare attendants, the IQCODE tended to underestimate the patient's cognitive scores. Diesfeldt (2007) concluded that, in order to understand deficits, direct evaluations of cognitive abilities with the patients may be used rather than informant-based measures.

Finally, some changes in the ICQODE format should be considered. The use of a dichotomously scored ICQODE may be easier for informants to rate an individual as stable or worsened than a graded rating. It would be interesting to restructure the five-category as two-category to establish clinical cut scores important for clinical diagnosis and/or other criteria (Butt, 2008). Furthermore, the IQCODE could be abbreviated. Fuh and colleagues (2005) concluded that the IQCODE should be shortened from 26 to 17 items. Also of interest is to know whether certain items gather greater informant congruence than others, maybe leading us to a theory of how the individual's perception of reality can be understood by others. Of final consideration, given that relatives may find difficulties in remembering individuals' performance 10 years ago, perhaps it should be a focus on ratings of more recent time frames than changes over long time frames.

Adapting an informant questionnaire for use in a cultural context different from its place of origin requires a rigorous process of validation. It is important to know the peculiarities of the sample to be investigated, taking into consideration that almost always an instrument is designed for a specific type of population. Canino and Alegria (2008, pg. 10) warn that "the adequacy of a diagnostic instrument in a given culture does not guarantee its reliability or validity in another, even given a faithful translation". In summary, although family members or close companions will remain important sentinels, the results of this study raise contrasting strengths and weaknesses and some doubts on whether health professionals should depend on their older patients' informants to recognize and report memory problems.

6. References

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CHAPTER VIII

General discussion and future perspectives

1. Discussion and conclusions

Similar to the worldwide trend, demographic changes in Portugal in the last decades have been characterized by a gradual increase in the proportion of the aged population (Governo de Portugal, 2012). This significant population phenomenon carries with it the need for appropriate gerontological-focused research on how to maintain, delay and/or even optimize health, cognition and well-being related aspects throughout aging (Tesch-Roemer, 2010). Aging is associated with a gradual decline in cognitive function that may translate into compromising everyday functioning. In fact, cognitive decline across the life span is overall characterized by increasing difficulties in memory, information processing speed and other executive functions (Buschke et al., 1995). Nevertheless, it has also been noted that cognitive trajectories vary inter-individually, and/or intra-individually, across aging, suggesting that it may not be due just to biological or brain structure function processes, but it can be associated with other factors, such as psychological and social aspects and educational background (Riddle, 2007; Paulo et al., 2011; Santos et al., 2012). Therefore, reliable and practical standardized methods to assess and/or screen for cognitive and neuropsychological measures are needed to assist health care professionals in clinical practice and to provide for more inclusive population studies on aging. More so, instruments of rapid-application, that adapt to a normal consultation, are also of need. Such strategy would grant insights into the cognitive performance of the individual and of the population, reaching all, potentially allowing for efficient and practical screenings tool for early diagnosis of mild cognitive impairment or dementia. In this sense, and considering that despite Portugal being one of the most rapidly ageing European countries, to date no telephone screening had been validated for Portuguese population (Santana et al., 2015). The main scope of the present thesis was to investigate the viability of rapid screening instruments in the evaluation of cognitive heterogeneity and cognitive impairment screening in older individuals. Within the scope of this thesis, three cross-sectional studies were performed. They are briefly summarized and their implications discussed below.

In the first study, we translated/retro-translated, validated and explored the applicability of the most widely used telephone-based cognitive screening instrument, the Telephone Interview for Cognitive Status(-Modified) (TICSM), against a broader and more detailed face-to-face

assessment of cognitive function. We demonstrated that a telephone administration format, using the TICS_M-Portuguese (PT), captures cognitive test scores just as reliably and precisely as the traditional in-person method. The TICS_M-PT revealed positive associations with the global cognition measures Montreal Cognitive Assessment (MOCA) and Mini Mental State Examination (MMSE). The study has several implications. The TICS_M-PT format besides allowing for its administration both in person and over de telephone, can also be considered of use with individuals with visual or motor impairments, unlike the MMSE and MOCA. Also, it exhibited correlations with tests that assess for specific cognitive domains (e.g. executive function and working memory) that are particularly vulnerable to decline with ageing and dementia, indicating that it is an instrument that overall successfully evaluates multiple cognitive functions (Salthouse, 2010). Besides this, the TICS_M-PT presented satisfactory validity properties, indicating that it is a good screening tool for cognitive impairment among older individuals with low education levels.

Novel for telephone-based instruments in exploring psychological dimensions, we demonstrated that higher levels of trait anxiety and depressive symptoms were associated with lower performance on the test. Both depression and anxiety have been documented to be related to cognitive deficits and changes in brain structure and functioning. The literature has, in fact, demonstrated a linear relationship between depressive symptoms and lower cognitive functioning (Bierman et al., 2005; Dotson et al., 2008; Weisenbach et al., 2012). Deficits are most consistently seen on tasks involving episodic memory, working memory, attention and executive functioning. On the other hand, findings on the association between anxiety and cognitive performance are somewhat mixed. Although some studies have reported that anxiety is associated with cognition in older adults, many others show an inverted U-shaped function, meaning that an intermediate level of anxiety symptoms is related with an optimal cognitive performance, while low and high severity are related to a worse functioning (Beaudreau & O'Hara, 2009; Bierman et al., 2012; Stillman et al., 2012).

The maintenance of a cohort of aged individuals for in-person evaluations throughout time is a challenge, and that is the reason that makes telephone assessment an attractive alternative. This study, thus, provided evidence that the TICS_M-PT can be a means to reach people in their homes. This instrument proved to be relevant on cognitive impairment screening and its potential for both clinical practice and in epidemiological studies. In a world where the majority

of the population carries a mobile phone, the potential is even higher and something to consider in the near future.

In the study presented in Chapter V we addressed whether cognitive tests performed using videoconferencing could provide comparable information as an in-clinic evaluation. In order to perform this study, a sample of individuals from different settings (from community to non-community dwellers), with a diagnostic cognitive spectrum from normal to dementia, was evaluated. To validate the videoconferencing procedure, each participant was evaluated using the TICSMT-PT over the telephone, subsequently the same instrument was used via videoconference and, finally, cognitive evaluation was conducted face-to-face using the MMSE. We sought to determine if the use of the videoconference approach in different settings provided comparable information to an in-clinic assessment. A high correlation was found between the telephone and the videoconference versions of the TICSMT-PT assessments and also between these and the in-person MMSE. We also demonstrated that the videoconferencing approach had a high level of accuracy for detecting cognitive impairment and that the test findings acquired from the videoconferencing approach demonstrated good sensitivity and specificity. The participants also demonstrated to be “at ease” throughout the videoconference test administration and that there was no significant difference in approaches between locales. The findings of this study indicate that cognitive test assessment via videoconferencing is a tool for consideration by the health professionals to reliably follow-up their patients who live in different settings.

From a clinical and research point of view, the implementation of home-based technologies for cognitive test administration both enables a cut with the burden of travelling to the hospital and, also, a close patient follow-up of individuals living anywhere. Moreover, a follow-up period conducted at the home can possibly allow the detection of subtle changes that indicate cognitive decline. In the same line, the ease of a “at a distance” cognitive test assessment can also have advantages for clinical trials by allowing more frequent assessments of cognitive change in the individual’s natural environment. The results of this research highlight the importance of validating new technologies for clinical contexts.

Cognitive impairment and dementia are complex situations with clinical expression, including symptomatic dimensions with a high impact on the family; hence, the feedback of the relative

and/or caregiver should not be neglected. The accuracy of informant reports on individuals with cognitive impairment or with dementia has been addressed in the context of research. In the study presented in Chapter VII, in order to determine cognitive status in proxy-participants, the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) was used to capture participants change in memory over the past 10 years. The results revealed that there was a lack of variability in the responses of the informants suggesting that the IQCODE may not be an informative instrument when administered in community-dwelling older people. It was observed that there were no significant associations between the IQCODE total scores and the MMSE, as well as between the instrument and the participants or informants socio-demographic variables. It was also demonstrated that most of the informants rated the participants as having no changes, or just a slight decline, on cognition, when compared to 10 years ago. Regarding the IQCODE reliability, the analysis presented an adequate Cronbach's alpha, although slightly lower compared to the original validation study of this instrument and other research. Moreover, the results suggest that IQCODE perhaps should include fewer items, given that some items fail the statistical conditions to be removed from the questionnaire

Some researchers have raised concerns about the reliability of informant reports in research studies involving participants with cognitive impairment or dementia (Magaziner, 1997; Nelson et al., 1990). Although informant input is crucial to help in the diagnosis and management of cognitive impairment, families may not be consistent in recognizing the onset of memory loss and subtle changes in everyday functioning (Watson et al., 2005). Most likely, a routine and structured assessment, reinforced with family awareness concerning normal versus abnormal aging, may help overcome the complex barriers in understanding and identifying cognitive impairment and even more important, dementia (Watson et al., 2005). The wake-up call for health professionals is that they should undoubtedly take seriously family members who go to an appointment or spontaneously report memory problems that patients can disclose. Moreover, to strengthen informants' reports there is an ongoing need to compare them with cognitive performance measures and information from medical records and health care utilization (Neuman et al., 2000).

In conclusion, after evaluating about 300 people on this doctoral path, much more needs to be explored in this particular segment of the population. Cognitive decline does not affect all individuals in the same way, and it has been shown that some of the differences between and

within individuals can be attributed to medical history, lifestyle, mood and social support. The psychological and cognitive assessments represent one of the most effective methods of differential diagnosis in the discrimination between normal and pathological. . Within this thesis we demonstrated that measuring cognitive functioning is essential not only because it helps to characterize what normal cognitive aging may be, but also because it shows the role of demographic variations, such as education and and setting, in cognitive functioning.

Telephone assessments can enable the evaluation of a wider range of people, including those who live in rural areas or at great distances from medical centers. In fact, by using telephone instruments, such as the TICSM-PT, as an alternative to the traditional face-to-face assessments, cognitive deficits can be “catch” at early stages, allowing the monitoring of changes in a broad and diverse number of subjects. Whereas, the informant questionnaire IQCODE would probably be more useful in clinical situations, rather than in community-dwelling populations, where cognitive decline is more prevalent.

Although emerging in Portugal in the 90s, telemedicine has kept a low profile, especially in the context of neuropsychological assessment for research purposes. In this line, the present work not only contributed to the body of literature with new validated technologies to measure cognition, but also demonstrated the feasibility of these measurements to be performed continuous and discreetly from the context in which the person is.

2. Future perspectives

With this thesis, we not only added a new rapid cognitive screening instrument to the Portuguese context, using a completely different and feasible approach, but also emphasized the importance of developing tests that are able to detect the specific nature of cognitive deficits. Following the TICSM-PT validation study, future work should be focus on longitudinal studies as well as for continuous administrations in clinical and institutional-based settings.

Moreover, Skype allowed us to see in real time the performance of older people on cognitive tests. Usable and affordable technologies can provide multiple ideas to complement cognitive assessments. With the emergent and recent advances in technologies, it is now feasible to develop systems that monitor in an automatic way not only observable behaviors, but also internal physiological states of older individuals, which can also provide a physiological marker

of their decline status. Such technologies can not only support the characterization of older individuals' functional ability but also can help in the early detection and quantification of dementia signals and symptoms.

Several physiological indicators, including galvanic skin response, heart beat and respiration activity and corresponding assessment devices are being used (Alam et al., 2016), and can be an interesting complement to cognitive measures. There are also many physical changes that can be used to evaluate the older person's physiological reactions to cognitive tests such as increased heart rate, quick reflexes and facial changes. Furthermore, new technology is now able to "read" emotions based on facial cues. In telemedicine, where older people can be, as we demonstrated, evaluated over online, or using mobile platforms, the ability for a health professional to discern what the individual is feeling or their reactions when they do not know or have doubts in answering a particular question can be very useful particularly in advanced cases of dementia. Thus, following the work presented in this thesis, a next step would include some devices together with the evaluation by Skype, to give us the physiological information during the performance of cognitive tests.

Ultimately, also concerning other sources of information, here the findings regarding the informant questionnaire IQCODE encourage the verification of its validity properties in a larger, clinical sample or different groups of patients. Moreover, and *ad hoc* study is needed to investigate the informant's features that might influence their ratings, thus helping in the identification of the most reliable collateral sources. It would also be of interest to administer the IQCODE as a self-report instrument to the participant/patient concomitantly with the informant. Previous studies show that although instruments of self-reported decline cannot be used as a proxy for cognitive evaluation, since that neurodegenerative diseases are associated with a progressive loss of insight, they can be sensitive to dementia diagnosis after taking into account significant predictors of self-reported decline, such as depression, personality and instrumental activities of daily life.

3. References

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