Recommendations for ICT use in Alzheimer's Disease:

Monaco CTAD expert meeting

P.H.Robert, A.Konig, S.Andrieu, F.Bremond, I.Chemin, P.C.Chung, J.F.Dartigues , B.Dubois, G.Feutren, R.Guillemaud, P.A.Kenisberg, S.Nave, B.Vellas, F.Verhey, J.Yesavage, P.Mallea

Affiliations :

Abstract :

Alzheimer disease (AD) and other related dementia represent a major challenge for health care systems within the aging population. It is therefore important to have the better instrument in order to assess clinical characteristics of these disease.

In this area Information and communication technology (ICT), are of interest. Such techniques enable the patients' performances and actions in real time and real life situations to be captured and accurately evaluated.

The aim of this article is to provide basic recommendation concerning the development and the use of ICT for Alzheimer's disease and related disorders.

During he ICT and Mental Health workshop (CTAD meeting in Monaco on the 30th October 2012) an expert panel was set up to prepare the first recommendations for the use of ICT in dementia research. The expert panel included geriatrician, epidemiologist, neurologist, psychiatrist, psychologist, and representatives from the pharmaceutical industry and patient association.

The recommendations are divided into three sections corresponding to 1/ the clinical targets of interest for the use of ICT, 2/ the conditions, the type of sensors and the outputs (scores) that could be used and obtained, 3/ finally the last section concerns specifically the use of ICT within clinical trials.

Alzheimer disease (AD) and other related dementia represent a major challenge for health care systems within the aging population. In AD, “dementia” is diagnosed when the disease has reached the stage where cognitive or behavioral (neuropsychiatric) symptoms interfere with social functioning or instrumental activities of daily living [1]. It is also recommended that the core clinical criteria, based on “functional impairment”, should be used to diagnose all causes of dementia, including AD, in all clinical settings [2].

Finding an acceptable method to assess functional impairment is of high interest since other disease domains than cognition are increasingly recognized as important outcome measures in clinical practice as well as in clinical trials for anti-dementia drugs. The choice of outcome measures in these trials is often constrained by tradition and availability. Therefore, cognition-based psychometric measures are usually the preferred option. However, the clinical relevance and « meaningfulness » of such measures has been questioned as they may not adequately identify responders to therapy or address important aspects of outcome [3].

In this area Information and communication technology (ICT), are of interest. Such techniques enable the patients’ performances and actions in real time and real life situations to be captured and accurately evaluated.

ICT is a means to cope with the increasing number of patients with chronic diseases in our aging society. As indicated by Eghdam & al (2012) [4] for individuals with chronic illness affecting cognitive capacities either directly (eg, dementia) or indirectly (eg, diabetes), ICT has become a fundamental part in their daily lives by providing a wide range of useful services and tools to use at home, work, or anywhere else [5].

Over the last few years, research has focused on the development and use of various sensors to monitor activities of the elderly as well as of AD patients. These include cameras and microphones for activity recognition [6] embedded sensors [7] or sensors placed on the body [8].These techniques raise multiple challenges.

The aim of this article is to provide basic recommendation concerning the development and the use of ICT for Alzheimer's disease and related disorders.

METHOD

CoBTek (for Cognition – Behaviour – Technologies) is a Research Unit at Sophia-Antipolis University (UNS) in Nice, France. CoBTek missions are, using Information and Communication Technologies, and most particularly imaging and video analytic techniques: 1/ To improve diagnostic and treatment of behavioural and cognitive symptoms in Alzheimer disease and related disorders 2/ To develop new strategies in order to prevent, help and assist elderly people 3/ To improve autonomy in the elderly.

The ICT and Mental Health workshop took place during the CTAD meeting in Monaco on the 30th October 2012. The workshop was organized by the CoBTeK team. An expert panel was set up to prepare the first recommendations for the use of ICT in dementia research. The expert panel included geriatrician, epidemiologist, neurologist, psychiatrist, psychologist, and representatives from the pharmaceutical industry and patient association. The starting presentation was held by the CoBTeK team as well as the discussion which was audio recorded. A first draft of the recommendations regarding use of ICT in AD was circulated to experts in December 2012.The final version of the manuscript has been validated by all authors on …..

RECOMMENDATIONS

The recommendations are divided into three sections corresponding to 1/ the clinical targets of interest for the use of ICT, 2/ the conditions, the type of sensors and the outputs (scores) that could be used and obtained, 3/ finally the last section concerns specifically the use of ICT within clinical trials.

1/ What are the Clinical targets ?

COGNITION :

Cognitive tests are assessments of human cognitive capacities. The administered tests include various forms.The earliest cognitive tests were developed over 100 years ago, and some of these are still in use today. Throughout the 20th century, "paper and pencil" cognitive tests were commonly used to measure intelligence, assist with the diagnosis of brain disorders such as Alzheimer's disease, and measure recovery from brain disease or injury.

The first computerized cognitive tests were developed in the 1970s [9]. Computerized testing offers accurate recording of reaction times, electronic capture and processing of data (minimizing human error) and standardization of test administration and automatic scoring (minimizing sources of response bias). Today, they can be used, according to the clinician experience, as an alternative to « paper and pencil tests » in clinical research and practice. The advantage is a better usability but they do not improve ecological validity of the assessment. In fact, for a research study, ecological validity means that methods,, material and settings of the study approximate a real-world context that is being examined. Experience sampling methodology (ESM) is a potential way to achieve this goal. ESM refers to a set of empirical methods that are designed to allow respondents to document their thoughts, feelings and actions outside the walls of a laboratory and within the context

of everyday life [10]. ICT and most particularly wearable smart phones can be of interest for the assessment of cognition. This has been already done for working memory evaluations [11] and could be applied as well to episodic memory tasks. For instance, as part of the cohort study AMI (Agrica-MSA-ISPED) of 1002 retired farmers, an ancillary project has been developed in which 60 subjects received an MRI with the use of the mobile phone PALM. This phone allowed to collect four times a day during a week (Computerized Ambulatory Monitoring) information regarding the activities of daily living of the subjects as well as their performances in neuropsychological tests of semantic memory and episodic memory. The obtained results of these tests are better associated with the brain imaging data (size of the hippocampus in particular) as with the test results conducted by neuropsychologists

Following these examples the expert panel underlined the interest to develop simple devices with easy and understandable scores, with as added value, in comparison to the present tools, ecological validity, reliability and limitation of the interjudge variability.

BEHAVIOURS AND ACTIVITIES OF DAILY LIVING :

Behavioural symptoms also called Neuropsychiatric symptoms (NPS) are frequently associated with cognitive deficits during the progression of Alzheimer disease (AD) and other dementia. NPS assessment is usually based on a structured interview, using subjective input from either the caregiver and/or the patient. For instance apathy which is the most frequent NPS [12] is usually assessed in clinical practice and research with the NPI apathy domain. It has also been proposed that ICT such as actigraphy could provide an objective assessment (Box 1).

This demonstrate that ICT use could be a source of additional information for the assessment of NPS.

Other ICT tools can also be used for the assessment and the understanding of motor disturbances. Recently, Robinovitch [13] demonstrated that Digital video cameras installed in common living areas (dining rooms, lounges, hallways) may provide insight into the sequences of events that most commonly lead to falls and, further to more valid and effective approaches for balance assessment and fall prevention in long-term care.

Behavior is not only NPS but also the ability of a subject to be involved in activities of daily living [14]. One of the key clinical features of Alzheimer's disease (AD) is impairment in daily living functioning [15].

The inability to perform Instrumental Activities of Daily Living [16] is present from the early stages of cognitive decline (Tuoko, 2005). As indicated in the recommendations from the NIA-AA [17] persons with Mild Cognitive Impairment (MCI) commonly have mild problems performing complex tasks [18]. Methods to assess IADL comprise self-reported questionnaires, performance-based assessment and informant-based questionnaires. These measurements have some limitations because they do not offer accurate, reproducible, objective and ecological perspectives. Moreover, these assessment batteries and standardized tools rely on quantitative scales, which are often lacking sensitivity. For this reason, information and communication technology (ICT), in particular, techniques involving imaging and video processing are of interest, and may overcome these limitations by reducing the inter/intra rater variability due to human interpretation biaises.

Goal directed behavior (GDB) is another definition presented during the discussion. GDB is a construct used to operationalize a broad spectrum of purposeful actions

and their determinants from the simplest single movement to the most complex patterns behaviors. GDB is a set of related processes (including cognition, emotion, motivation) by which an internal state is translated through action into the attainment of a goal [19].It is important to differentiate the semi directed (prespecified) activities from self initiated GDB activities.

The first one can be directly assessed by proposing a patient to carry out a series of prespecified tasks[20] and using this strategy it is possible to assess activities in real life time using ICT (Box 2).

The second one can also be tested by giving the patient a complex order (follow a recipe) and assess how he/she deals with the general recommendation in order to test initiation as well as execution. This type of assessment is very difficult to organize and time consuming.

Following these examples the expert panel underlines:

- For the assessment of NPS objective data covering day and night behavior are needed

- NPS real time assessment must be validated in comparision to the NPI domains.

- ICT devices enable the patients' performances and actions to be captured in real time and real life situations and to be accurately evaluated. This is particularly important for activities of daily living and the semi directed activities

- the potential interest of serious game for assessing self initiated goal directed behaviour should be explored

2/ Which sensors, which conditions of assessment and scoring system?

Table 1 summarize studies done in elderly subjects wirh AD and related disorders. The general recommendations concerning the use of ICT are listed in table 2. The different types of sensors need to be simple and easy to use to avoid a population selection based on their ability to understand device utilization. Various potential sensors exist, and therefore, the choice should be done accordingly to study conditions (in a clinical consultation setting, in Nursing home, at home) and to population groups (patients, family caregiver, professional career). Technical progress may allow the implementation of one device with multiple sensors (eg actigraphy, body temperature, audio recording). The choice of devices depends on available budget and agreements between clinicians, ICT engineers and final end users. In addition the quality of sensor processing often depends on a correct installation / calibration and some sensors have practical issues such as battery for wearable sensors or data storage/transmission.

Concerning the audio and video recording devices it is particularly important to employ automatic recording and analysis of the data. This is crucial when long term monitoring is required, such as for the assessment of behavioural disturbances. In order to develop this type of automatic recording, clinicians must describe in full details to the ICT engineers the characteristics of the behavioural sequences that need to be captured.

Use of ICT devices in everyday life raises several issues that must be discussed in each specific situation. However, ICT tools utilisation is not only problematic, it may has even some positive effects, at least for a short term period. For example

involving more actively the patient or empower the couple patient/ caregiver in the assessment procedure.

The use of video recording devices (wearable or fixed) is particularly often discussed: *"Is there any change in the way of life of the people when there is a camera in the room?"*. This is mostly depending on the person. However, long term use of such devices seems to indicate a good acceptance. Usually, the person only notices the presence of the video sensor at the beginning of the experimentation but this awareness disappears rapidly [21]. A very important factor to increase acceptance is the understanding of the reason for installing the sensor.

Furthermore, it is important to provide the subject with systematic feedback about the data that are collected.

As these technologies rely on the acquisition of a large number of data collected in the context of the daily life of individuals, there is a need to consider first the respect of privacy and the protection of individual data. It is important to conduct this ethical reflection on a case-by-case basis for each project, as these innovative technologies may elicit specific ethical questions.

Concerning the output coming from the devices used for assessments, the following points have been underlined:

- In everyday clinical practice the output (the clinical score) needs to be simple as possible and easily understandable. The score needs to be obtained automatically or at least be understandable to users without high technical competences.

(patient, caregiver, clinician, researcher).

- Correlation should be established between ICT scores and classical tools scores.

- ICT devices allow the capture and correlation of several clinical indicators at the same time (eg ADL and NPS) . In addition, it could be of interest to develop an assessment of multi processing skills.

- ICT characteristics allow to combine different scores (Box 3) coming from one single domain (cognition) or from different domains (e.g. cognition, motricity, emotion, nutrition). However, this type of combination needs to be defined and described in a preliminary step between the clinician and the engineers after taking into account the end user point of view.

4 / ICT in clinical trials for Alzheimer's disease

Most of the information indicated in the previous sections can be applied as well to the particular case of clinical research.

It is possible to separate expert suggestions into two parts: the wishes and the requirements.

Wishes;

- In clinical studies, including therapeutic pharmacological and non pharmacological trials, and most particularly cohort follow up studies, one of the major cause for drop outs is that patient are reluctant to return to the center. With the use of ICT, it may be possible to assess cognition, behaviour and/or activities of daily living directly in the patient's home environment and by therefore decrease the number of visit in the center.

- ICT use may be able to help to keep blinding about the evolution of the patient

- ICT may help to have a more objective and homogeneous assessment of behavioural disturbances and by reducing variability.

- The use of serious games can be of interest to train the investigator and/or staff members on how to rate or manage certain behavioural problems

- The association of ICT and biological data may help to foster new ideas and solve common medical problems (falls, sleep disorders). For example the ICT device can provide researchers with some information on sleep parameters (e.g. apnea, Co2 Level). Having a biological component being part of the discussion process could only aid to the hypothesis generation as well as to the hypothesis testing

Requirements

Before using ICT devices in clinical trials, several steps need to be achieved:

- ICT needs to be accepted by regulatory administration. In fact, it seems hard to shift from a well establish end point into a surrogate marker. Unless we get this new endpoint to be approved, technologies are interesting but only as investigational technologies for clinical trial. This explains the importance of introducing ICT into clinical practice in a first step before getting it accepted as a validated clinical endpoint by drug regulators.

- It is important to understand the correlation between ICT data and results obtained by classical assessment tools.

- For NPS long term data need to be collected (24h during one month. It is particularly important to assess whether the frequency of the behaviour described by the caregiver (using the NPI) ris the same as the one recorded by the ICT device.

CONCLUSION

To summarize, special attention should be given to ICT solutions that provide personalized information; compensate for disabilities such as memory problems; help people with AD and their caregivers to cope with the NPS associated with the dementia; and provide help with their daily living activities [22].

One of the obvious results of this ICT and Mental Health workshop is to allow the interaction between ICT engineers and health professionals. For clinicians it is important to establish the exact type of indicators that are clinically relevant and that can provide useful information in daily practice. Secondly, for ICT engineers, the challenge is to adapt the constraints of the technology to the needs of the clinician.

The adopted approach tries to emphasize the clinician's user needs. In the next step, more attention should be paid to the user needs from patient / caregiver and to tool designs considering end user perspectives. It is of great importance that patients and caregivers be engaged in the assessment process and be able to give feedback on the feasibility and tolerability of the ICT sensors.

List of abbreviations

Tables 2 : Sensors characteristics and types:

Characteristics

- Sensitive to change
- Sensor easy to install / wear
- Immediate output for the clinician
- self explanatory (easy) explanation for the user
- Understandable feed back information
- Easy maintenance of the material

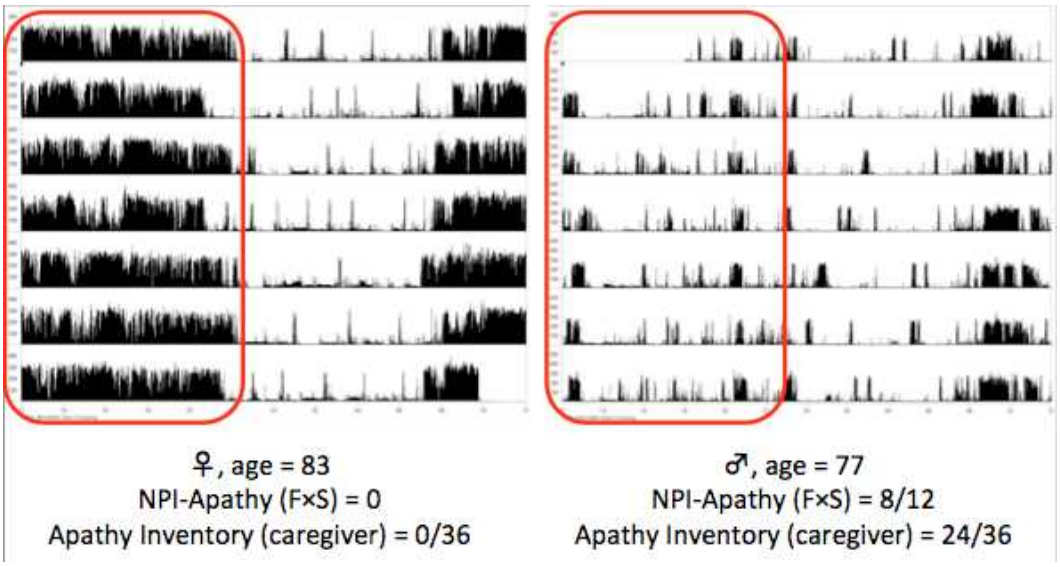
Sensors types:

- Actigraphy
- Video 2&3D – ambient
- Video 2&3D – wereable
- Speech tracking
- Multi modal sensors
- serious game

Box 1 : interest of actigraphy for the assessment of NPS

Box 1 : interest of actigraphy for the assessment of NPS

Ambulatory actigraphy, consisting of a piezoelectric accelerometer designed to record movements in three dimensions, allows for continuous, unobtrusive data acquisition of motor activity in the home environment. It has been initially used as a method for objectively evaluating sleep/wake disorders [23, 24]. In neurodegenerative and/or psychiatric disorders, actigraphy has been used to evaluate agitated behaviors [25] or depressive states [26]. More recent studies have shown that actigraphic locomotor activity assessment may be a useful, objective method to evaluate the severity of apathy in patients with Mild Cognitive Impairment [27] or AD [28, 29]. Recently, disrupted actigraphy assessed-circadian activity rhythms have been prospectively associated with an increased risk of developing MCI and dementia among healthy older women [30]. It could therefore be of interest to monitor the possible effects of the studied drug on both behavioral and circadian parameters using objective assessment methods such as actigraphy. This is illustrated here on 2 AD patients (with and without apathy) on a 7 day actigraphy monitoring



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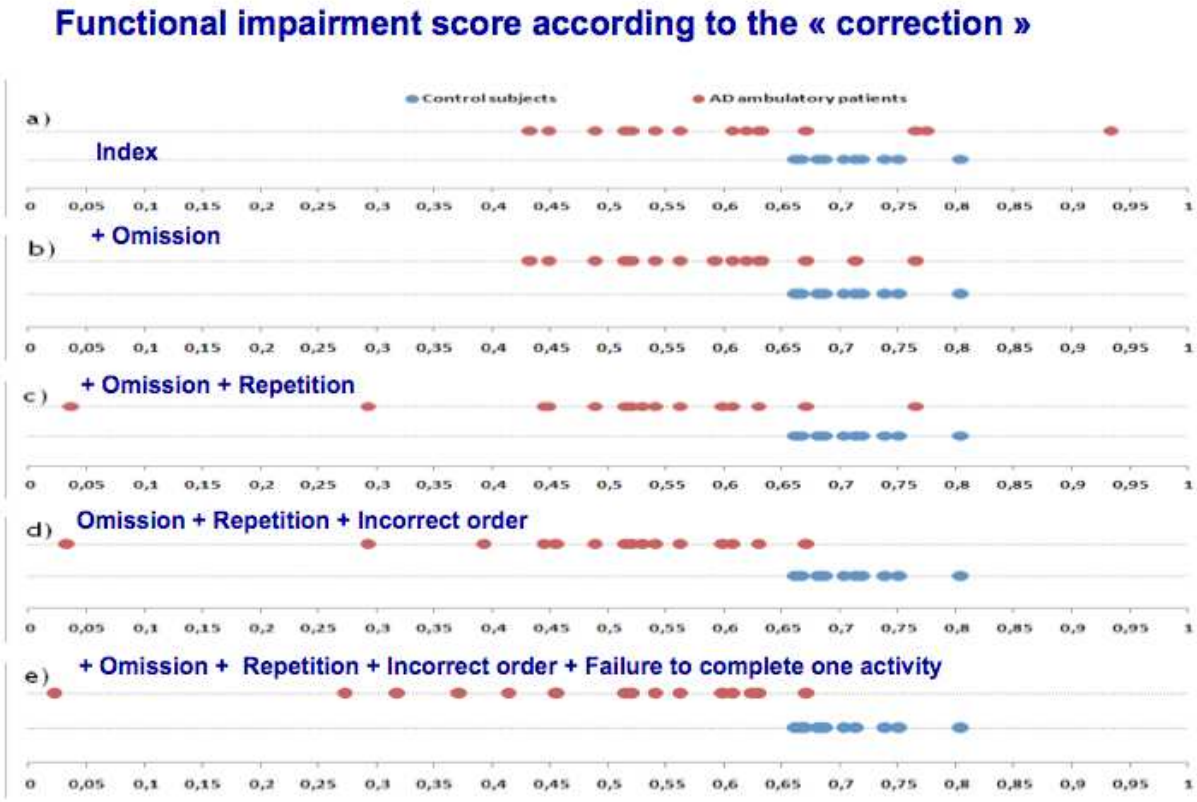
Box 2 : example of a scenario in order to test activities of daily living

SCENARIO INITIAL REQUIREMENT

- Relevant for patient and caregiver
- Close to real life
- Using motor functions
- Using cognitive processing
- Not too long scenario

"Your task is to perform this list of 10 activities in a logical manner within 15 min. These 15 minutes represent a typical morning period of everyday life" • Read the newspaper • Water the plant • Answer the phone • Call the taxi • Prepare the medication for today • Make the check for the Electricity Company • Leave the room when you are finished with all activities • Watch the TV • Prepare a hot tea • Write the shopping list for the lunch
(1) watch the TV before the phone call (2) water the flower just before leaving the room (3) call the taxi, which will arrived in 10 minutes and ask the driver to drive you to the market

Box 3 : example of scoring system for the assesment of daily activity using video sensors [31]



This composite score include: (Time spent doing activities / total time in the room adjusted by coefficient K (omission, repetition, incorrect order, failure to complete one activity) (ref)

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