The use of information and communication technologies (ICT) for the assessment of patients with Alzheimer's disease and related disorders

SUMMARY

The occurrence of neurodegenerative disorders such as dementia has risen by unprecedented levels in part due to increases in average lifespan, thus engendering high socio-economic costs. Alzheimer's Disease (AD) is the most common type of dementia and represents a central health problem in Western society, recognized mainly as a cognitive disorder where memory functions are primarily affected in the early stages of the disease. Diagnosis of AD has to be made mainly by the assessment of clinical features. Lately, emphasis is placed more and more on early diagnosis and detection of cognitive decline and related symptoms so that patients can benefit sufficiently from effective treatment and access to information, advice and support. At the same time, clinical assessments of cognitive and functional changes in AD have traditionally relied on cognitive neuropsychological screening tests, which can be biased by the clinician's subjectivity and are not always sensitive to the earliest disease-related changes. In addition, the role of biomarkers has received increasing interest as early markers for AD, but involve invasive (eg, lumbar puncture), time-consuming (neuropsychological assessment) or expensive (PET) hospital-based procedures. Detecting early changes before clinical AD symptoms develop is crucial for the development and eventual success of therapeutic interventions. Better measures for cognitive, functional and behavioral changes are therefore needed in the early stages of the disease. Assessment methods involving simple, non-invasive and more accessible cost-effective tools are greatly required. For these reasons, information and communication technology (ICT), such as movement sensors and imaging and video processing, could be of interest because they enable the patients' performances and actions to be captured objectively, in real time, and in real life situations. The use of these types of ICT may allow early identification of subjects in preclinical stages of AD as well as monitoring of the disease's progression and treatment effects over time.

The general aim of this thesis was to investigate the potential contribution of ICT use for clinical assessment of cognitive, behavioral and functional changes in patients with AD and related disorders. In particular, focus was on the early stages of cognitive decline in order to allow earlier access to preventative intervention such as tailored cognitive and physical training through serious games. For this purpose, the use of different sensors including actigraphy, video analyses and speech analyses, were investigated in clinical practice.

The thesis consists of three parts: first a review of ICT use for the specific case of apathy assessment and recommendations for ICT use for clinical assessment. In part II, different sensor-based studies are presented followed by part III, addressing the conclusion to consider the use of ICT within clinical trials for endpoint measures and follow-up. Finally, proposed recommendations are presented for the use of ICT-based Serious Games as a potential early intervention tool for patients.

In **Chapter 2**, an overview was given of current assessment tools for apathy in clinical practice and new approaches to assessment methods with the help ICT for which with a narrative literature review was conducted. The results suggest that there is evidence that apart from the currently used assessment methods for apathy, new ICT approaches could provide clinicians with valuable additional information for an earlier detection and therefore more accurate diagnosis of apathy. However, there are no ICT techniques specifically designed for the assessment of apathy, but nevertheless several techniques seem to be promising and deserve more study.

In **Chapter 3,** basic recommendations have been provided concerning the development and the use of ICT for AD and related disorders. During an ICT and Mental Health workshop an expert panel consisting of clinicians (geriatrician, neurologist, psychiatrist,

psychologist), ICT engineers, representatives from the industry and patient association, was set up to prepare the first recommendations for the use of ICT in dementia research. The recommendations were divided into three sections corresponding to 1) 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.

In **Chapter 4,** we assessed motor activity in Mild Cognitive Impairment (MCI) and healthy control subjects (HC) carrying out short functional activity tasks using ambulatory actigraphy. Secondly, the influence of depressive symptoms on motor activity was investigated. We found that MCI subjects had significantly reduced mean motor activity while carrying out directed and semi-directed activities, compared to healthy control subjects. However, no difference was found in motor activity between MCI subjects with or without depression. Together, these results indicate that actigraphic measurement of motor activity during the evaluation of instrumental activities of daily living (IADL) and motor tasks is a potential objective tool in detecting early changes in MCI. Depressive symptoms seem not to be associated with motor activity in MCI subjects.

In **Chapter 5,** we investigated the use of a video monitoring system for automatic event recognition for the assessment of IADL in 19 healthy subjects and 19 MCI patients who had to carry out a standardized scenario consisting of several IADLs such as making a phone call while they were recorded by 2D video cameras. After the recording session, data was processed by a platform of video signal analysis in order to extract kinematic parameters detecting activities undertaken by the participant. We compared our automated activity quality prediction as well as cognitive health prediction with direct observation annotation and neuropsychological assessment scores. With a sensitivity of 85.31% and a precision of 75.90%, the overall

activities were correctly automatically detected. Activity frequency differed significantly between MCI and HC participants ($p < 0.05$). In all activities, differences in the execution time could be identified in the manually and automatically extracted data. We obtained statistically significant correlations between manually as automatically extracted parameters and neuropsychological test scores ($p < 0.05$). However, no significant differences were found between the groups according to the IADL scale. The results suggest that it is possible to assess IADL functioning with the help of an automatic video monitoring system and that even based on the extracted data, significant group differences can be obtained.

In **Chapter 6**, we investigated the quantitative assessment of autonomy in dementia patients based not only on gait analysis but also on the participant performance on IADL automatically recognized by a video event monitoring system (EMS). Three groups of participants (healthy controls, MCI, and AD patients) had to carry out a standardized scenario consisting of physical tasks (single and dual task) and several IADL such as preparing a pillbox or making a phone call while being recorded. Video sensor data were processed by an EMS that automatically extracts kinematic parameters of the participants' gait and recognizes their carried out activities. These parameters were then used for the assessment of the participants' performance levels, here referred as autonomy. Autonomy assessment was approached as classification task using artificial intelligence methods that takes as input the parameters extracted by the EMS, here referred as behavioral profile. Activities were accurately recognized by the EMS with high precision. The most accurately recognized activities were "prepare medication" with 93% and "using phone" with 89% precision. The diagnostic group classifier obtained a precision of 73.46% when combining the analyses of physical tasks with IADL.

In a further analysis, the created autonomy group classifier obtained a precision of 83.67% when combining physical tasks and IADL. Results suggest that it is possible to quantitatively assess IADL functioning supported by an EMS and that even based on the extracted data the groups could be classified with high accuracy.

In **Chapter 7,** we evaluated the interest of using automatic speech analyses for the assessment of MCI and early-stage AD. For this, HC subjects and patients with MCI or AD were recorded while performing several short cognitive vocal tasks. The voice recordings were processed, and the first vocal markers were extracted using speech signal processing techniques. Second, the vocal markers were tested to assess their "power" to distinguish among HC, MCI, and AD. The second step included training automatic classifiers for detecting MCI and AD, using machine learning methods and testing the detection accuracy. We obtained classification accuracy of automatic audio analyses as follows: between HCs and those with MCI, 79%, between HCs and those with AD, 87% and between those with MCI and those with AD, 80%, demonstrating its assessment utility. Thus, automatic speech analyses could be an additional objective assessment tool for elderly with cognitive decline.

In **Chapter 8,** an opinion paper was presented suggesting that new ICT - such as automated speech and video analysis techniques and wearable accelerometers – may be successfully employed in clinical trials to improve the functional and cognitive assessment of these patients, thus contributing to an earlier AD diagnosis and providing additional ecological and objective end-point measurements.

In **Chapter 9**, we systematically analyzed the Strengths, Weaknesses, Opportunities, and Threats (SWOT) of employing Serious Games (SG) with patients with Alzheimer's disease and other related disorders (ADRD) in order to provide practical

recommendations for the development and use of SG in these populations. These analyses and recommendations were gathered, commented on and validated during a 2-round workshop in the context of the 2013 Clinical Trial of Alzheimer's Disease (CTAD) conference, and endorsed by stakeholders in the field. The results revealed that SG may offer very useful tools for professionals involved in the care of patients suffering from ADRD. However, more interdisciplinary work should be done in order to create SG specifically targeting these populations. Furthermore, in order to acquire more academic and professional credibility and acceptance, it will be necessary to invest more in research targeting efficacy and feasibility. Finally, the emerging ethical challenges should be considered a priority.

In **Chapter 10,** we provided a general discussion of our findings; its implications for clinical practice and AD trials, recommendations for future use of ICT, methodological considerations and recommendations for future research. Furthermore, the last chapter includes a summary of the findings, a description of knowledge valorisation, a list of author affiliations, list of publications, information about the author and acknowledgements.