Serious games for screening pre-dementia conditions: from virtuality to reality? A pilot project

Chiara Zucchella, PsyD^a Elena Sinforiani, MD^a Cristina Tassorelli, MD, PhD^b Elena Cavallini, PhD^c Daniela Tost-Pardell, MEng^d Sergi Grau, MEng^d Stefania Pazzi, MEng^e Stefano Puricelli, MEng^e Sara Bernini, PsyD^a Sara Bottiroli, PsyD, PhD^r Tomaso Vecchi, PsyD, PhD^{c.g} Giorgio Sandrini, MD^b Giuseppe Nappi, MD^r

^a Alzheimer's Assessment Unit, Laboratory of Neuropsychology, C. Mondino National Neurological Institute, Pavia, Italy
^b Neurorehabilitation Unit, C. Mondino National Neurological Institute, Pavia, Italy
^c Department of Brain and Behavioral Sciences, University of Pavia, Italy
^d Polytechnic University of Catalonia (UPC), Barcelona, Spain
^e Consorzio di Bioingegneria e Informatica Medica -CBIM, Pavia, Italy
^t C. Mondino National Neurological Institute, Pavia, Italy
^g Brain Connectivity Center, C. Mondino National Neurological Institute, Pavia, Italy

Correspondence to: Chiara Zucchella E-mail: chiara.zucchella@mondino.it

Summary

Conventional cognitive assessment is based on a pencil-and-paper neuropsychological evaluation, which is time consuming, expensive and requires the involvement of several professionals. Information and communication technology could be exploited to allow the development of tools that are easy to use, reduce the amount of data processing, and provide controllable test conditions. Serious games (SGs) have the potential to be new and effective tools in the management and treatment of cognitive impairments in the elderly. Moreover, by adopting SGs in 3D virtual reality settings, cognitive functions might be evaluated using tasks that simulate daily activities, increasing the "ecological validity" of the assessment. In this commentary we report our experience in the creation of the Smart Aging platform, a 3D SGand virtual environment-based platform for the early identification and characterization of mild cognitive impairment.

KEY WORDS: dementia, mild cognitive impairment, neuropsychological assessment, serious games, virtual reality

Introduction

Mild cognitive impairment (MCI) is an intermediate stage between normal aging and dementia (Petersen et al., 2001a,b; Petersen et al., 2009; Gauthier et al., 2006; Scott and Barrett, 2007). Current conceptualizations of MCI recognize different subtypes, based on the presence or absence of memory impairment, namely amnestic (aMCI) and non-amnestic (naMCI). These, in turn, may represent the prodromes of different dementia types: patients who present with single-domain naMCI can progress to non-AD dementing conditions such as frontotemporal dementia, whereas multipledomain naMCI can progress to Lewy body dementia or vascular dementia (Jak et al., 2009; Petersen et al., 2009). Patients with aMCI often progress to AD with an annual rate of conversion of approximately 10-15%, compared with a rate of about 1-2% in healthy controls (Schmidtke and Hermeneit, 2008).

Since there is not, as yet, a cure for dementia, strategies designed to modify its onset or progression could have a significant impact. Research is, indeed, now focusing on the identification of at-risk populations, as the early recognition of MCI opens up potential new targets for therapeutic interventions: early diagnosis offers the best opportunity to understand the disease progression, to begin long-term planning, and ultimately to implement a treatment regimen (Lopez et al., 2005; Weimer and Sager, 2009; Emery, 2011). Despite this, as the symptoms are often subtle and patients maintain their independence in activities of daily living, in many cases MCI goes unnoticed and patients are frequently not identified until significant loss of cognitive function has occurred (Magsi and Malloy, 2005; Weimer and Sager, 2009).

In view of these considerations, there is a crucial need to develop efficient and reliable new screening tools; these should also be easy to administer in order to ensure their widespread dissemination. Conventional cognitive assessment is based on a pencil-and-paper neuropsychological evaluation, which is time consuming, expensive and requires the involvement of several professionals (Kang et al., 2008). Information and communication technology could be exploited to develop tools that are easy to use, reduce the amount of data processing, and provide controllable test conditions (Caltagirone and Zannino, 2008). Serious games (SGs) are computer games designed for purposes other than pure leisure and their application has recently been proposed in the health domain, in particular in the assessment and rehabilitation of psychiatric and neuropsychological conditions; they have the potential to be new and effective tools in the management and treatment of cognitive impairments in the elderly (Cherniack, 2011).

Moreover, by adopting SGs in 3D virtual reality (VR) settings, cognitive functions might be evaluated using tasks that simulate daily activities, thereby increasing the "ecological validity" of the assessment (Campbell et al., 2009). These tasks could then be implemented and used to "boost brain function", as recently suggested by Bavelier and Davidson (2013).

In this commentary we describe the process by which we created a 3D SG- and virtual environment-based platform (the Smart Aging platform) for the early identification and characterization of MCI. This project presented us with two main challenges: i) to achieve scientifically-driven transposition of tasks traditionally evaluated with pencil-and-paper tests into tasks to be performed in an ecologically valid virtual enrivonment, and ii) to create a navigation system sufficiently userfriendly to be satisfactorily used by subjects who are potentially cognitively impaired and may have limited experience of information technology (IT).

The Smart Aging platform

The roadmap

A multidisciplinary team was created, which included neurologists, psychologists, neuropsychologists, biomedical engineers, game designers and game developers.

On the basis of the published literature, the team of neurologists, neuropsychologists and psychologists (CZ, CT, ES, EC, SB, SB, TV, GS, GN) selected the battery of conventional tests to be used. These include two short screening tests: the Mini-Mental State Examination – MMSE (Folstein et al., 1975), which provides a global index of cognitive functioning, and the Montreal Cognitive Assessment – MoCA (Nasreddine et al., 2005). The MoCA is a cognitive screening test for detection of MCI, but it is more oriented to executive functions. To define more precisely the cognitive profile of subjects and to increase the degree of correlational validity and sensitivity, all subjects also performed the following tests: Free and Cued Selective Reminding

Test – FCSRT (Frasson et al., 2011) for episodic memory assessment, Trail Making Test Parts A and B – TMTA and TMTB (Giovagnoli et al., 1996) for the evaluation of divided attention and cognitive "shifting", the Wisconsin Card Sorting Test (WCST) (Laiacona et al., 2000) for the evaluation of problem solving, planning and cognitive flexibility, and phonological and semantic fluency (Novelli et al., 1986; Spinnler and Tognoni, 1987) for the assessment of executive functions. Subsequently they defined the setting and the tasks that were to be developed within the VR environment in order to be able to test the necessary cognitive functions: reasoning and planning, attention, memory and visuospatial orientation.

Following the definition of these scientifically-based clinical requisites, the next step, through interaction with the technical team, was to develop the software and hardware, as well as define the environment to be developed (a loft apartment) and the actions to be created. Particular attention was paid to the selection of the navigation modalities and tools, which represented the most critical aspect in the development of the system.

In the first instance, a mouse was used for navigation. However, this technical solution proved to be unsuitable for those unfamiliar with computers. Indeed, difficulty moving in the environment interfered with the execution of tasks, making cognitive scores unreliable. To overcome this issue, and taking into consideration data from the literature (Cernich et al., 2007), the platform was then modeled for use with a touch screen. In this way, movements within the environment are accomplished by clicking on red arrows positioned to the right, to the left, at the top and at the bottom of the screen and selections are made directly on the screen by physically touching the desired icons and objects. For users with minimal computer experience or some level of cognitive impairment this modality was found to be easier to learn and more intuitive than a mouse.

By means of a test-and-re-test approach, these IT solutions were progressively refined and evaluated in several subjects (see below), starting with healthy young subjects who were familiar with IT, then adults who were inexperienced IT users, and finally IT-naïve elderly people.

The exchanges between the different professionals in the multidisciplinary team allowed us to define the variables to be recorded and create a database of patient scores calculated using specific algorithms that take into account the time to perform each task, the attempts to accomplish the correct action, the number of wrong choices, and so on.

The platform

The final VR system consists of a desktop personal computer equipped with a sound card. Subjects navigate through and interact with the environment using a touch screen monitor.

The application is based on a first-person paradigm, so there is no user 3D avatar. The environment and the vir-

tual position of the user within the environment appear as though they were being filmed front-on and the navigation model allows users to move within the environment at a constant height in relation to the floor and to rotate the "head" within a limited range of angles.

The virtual scenario

The 3D environment consists of a loft containing, in a limited space, the basic elements, within a house, with which one interacts: a kitchen area, a bedroom area, a living room area and a bathroom (Fig. 1).

The virtual environment is equipped with the following elements:

 fixed elements that do not allow any interaction: walls, floor, ceiling, windows and decorative elements such as paintings, curtains and carpets;

 fixed elements that cannot be moved but can be used as surfaces for putting down and picking up movable objects: bed, table, couch, kitchen worktop, shelves;

 container elements with doors that can be opened and closed to allow things to be put in or taken out: kitchen cupboards, fridge and wardrobe;

interactive elements with specific functions: burners, sink;

– movable elements such as clothes, books and food. A 2D frame able to show 2D information such as instructions, scoring feedback and miniatures is superimposed on the environment. The 2D frame also allows 2D user interaction.

The serious game tasks

The SG tasks to be implemented in the Smart Aging platform (SASG tasks) have been designed to engage subjects in task-specific scenarios where they are asked to perform tasks simulating daily activities. Five Smart Aging tasks have been developed in order to evaluate different cognitive functions: executive functions (reasoning and planning), attention (selected



Figure 1 - An example of the virtual environment used in the Smart Aging platform.

and divided), memory (short- and long-term, prospective) and visuospatial orientation.

Table I provides brief descriptions of these tasks and also indicates the cognitive functions that are tested by each of them.

For each task the subject is provided with written instructions explaining what he/she is requested to do; these are visible on the screen for up to 30 seconds and the subjects can start the task when they are ready.

Before beginning the first task, the subjects perform a 10-minute familiarization task in order to familiarize themselves with the environment and learn how to move around and interact with the objects. No other feedback is provided while the subjects are performing the tasks.

The execution of all the SASG tasks, including the familiarization task, can take up to 30 minutes.

While the participant experiences the virtual environment and performs the tasks, the system records various measures (positions, times and actions). For each task, a performance-based *evaluation index* has been created. This index takes into account the following parameters: the number of correct actions, the number of errors, the number of false recognitions, the number of omissions, the time needed to complete the task, and the distance covered.

The recording system

Before starting the tasks, each user must register in the *demographics* section of the application, which is where clinical and demographic information is collected; the subject is also asked to indicate how frequently he/she uses a computer (never, daily, weekly), how frequently he/she uses a touch screen (never, sometimes, often), and his/her ease in using a touch screen (poor, medium, good).

After registering, each user is assigned a personal identification number which he/she has to enter in order to start the tasks. This procedure ensures correct matching of the user with his/her recorded performances on the paper-and-pencil tests and on the SASG tasks.

For pencil-and-paper tests, age-, gender- and education-corrected scores are calculated from the raw performance scores according to Italian population-based norms. These scores provide a picture of the subject's cognitive profile. The score on each SASG task is instead a composite score derived from constituent variables, i.e. the number of successfully accomplished tasks, the time needed to accomplish them, the number of errors, omissions and attempts, the modality of navigation and the distance covered in the loft during the performance of the tasks.

Pilot test of usability

The platform was tested in terms of usability in a group of 50 healthy subjects with an age range of 24-78 years.

Table I - The Smart Aging tasks.

Task	Cognitive functions tested
TASK 1 - OBJECT SEARCH The subject is shown the contents of the kitchen and then required to identify the location of a list of objects.	Memory, spatial orientation and attention
TASK 2 - WATER THE FLOWERS WHILE LISTENING TO THE RADIO The subject is asked to turn on the radio and press the spacebar every time the word "sun" is aired, while at the same time watering the flowers on the windowsill in the dining area.	Executive functions (planning), divided attention (dual task)
TASK 3 - MAKE A PHONE CALL The person is asked to make a phone call using the phone book and the phone on the bedside table. The subject is asked to remember to turn the TV on after making the phone call.	Executive functions, selective attention, working memory, prospective memory
TASK 4 - CHOOSE THE RIGHT OBJECT A 2D screen with 24 images of objects is shown. The subject has to identify the 12 objects that he had to look for in Task 1.	Memory (recognition)
TASK 5 - FIND THE OBJECTS The subject is asked to find all the objects that he looked for in Task 1.	Long-term memory (recall), spatial orientation and attention

One of the major problems encountered was the difficulty navigating with the mouse within the 2D and 3D environments. To overcome this it was decided to switch to a touch screen, which proved adequate for the performance of the tasks in all the subjects.

Another issue was the unexpected greater complexity of some tasks when performed in the virtual scenario. For example task 2 (Water the flowers while listening to the radio), which assesses executive functions, requires sequential planning of actions and proved too difficult even for healthy adult subjects. For this reason the sequence of actions had to be simplified. Finally, although the game tasks were originally devised for self-administration, elderly people who were inexperienced IT users were found to need some minimal assistance in the familiarization phase.

The planning of the screening phase

In order to define the reliability of SASG tasks as a tool for screening pre-dementia conditions, a test on a general population sample is mandatory. The study population will consist of 1200 volunteers who will be stratified by gender (female/male), age (50-60, 61-70, 71-80 years) and education (primary, middle, high, university). These subjects are currently being recruited through public entities, universities for the elderly, social clubs, etc.

Among these subjects, "healthy" people will be defined as those who have a negative history for neurological and psychiatric disease and a performance within normative ranges on all the neuropsychological tests (MMSE, MoCA, FCSRT, TMTA and TMTB, WCST, verbal fluency). Subjects who fail in at least one of these tests will be considered "at risk" of developing cognitive disorders and will be referred to their general practitioner.

All the enrolled subjects will undergo pencil-and-paper tests and SASG tasks. To ensure that the provision of instructions, the test administration and the scoring

are as homogeneous as possible, the neuropsychological tests and the SASG tasks will be administered by psychologists who have received specific training. Once the collection of data from the normative sample has been completed, the next step will be to evaluate the validity (specificity and sensitivity) of the SASG tasks as a screening test for cognitive impairment by comparing the scores recorded on the traditional tests with the scores obtained on the SASG tasks. Furthermore, we will evaluate the validity of the SASG tasks for the mnestic domain by comparing the scores on tasks 1, 4 and 5 with the scores recorded on the FCSRT and on semantic fluency. Finally, the validity of the SASG tasks for assessing executive functions will be evaluated by comparing the scores on tasks 2 and 3 with the scores recorded on TMTA, TMTB, WCST and phonological fluency.

Discussion

Since the introduction of personal computers, neuropsychology as a field has recognized the advantage of computerization of various assessment measures. By the mid-1980s, neuropsychologists had transferred paper-and-pencil measures to computerized platforms and started to explore the equivalence of these measures to traditional tests (Eckerman et al., 1985). Computers offer several advantages over traditional testing, including more rigorous standardization of administration, more accurate timing of presentation and response latencies, ease of administration and potentially reduced assessment times. In addition, computerized testing platforms yield easily accessible data, particularly because scoring and data display can be incorporated into the software program, allowing automated data exporting for research purposes. As a further development, VR gaming and interactive video gaming are new and promising tools for assessing and training people with cognitive impairments

(Christiansen et al., 1998; Davies et al., 1999; Riva et al., 1999; Rizzo et al., 1998; Rose et al., 1999; Zhang et al., 2001; Jack et al., 2001; Kang et al., 2008). These tools involve the use of computer-based programs that are designed to simulate real-life objects and events. VR and interactive video gaming may have some advantages over traditional therapeutic approaches as they may give people an opportunity to practice, on a daily basis, activities that are not or cannot be practiced within the hospital environment. The stimulating challenge will be to develop tools that, while exploiting the latest technological solutions, are fairly easy to use, even for those who have little familiarity with computers, such as older people. In fact, significant inter-individual differences exist in computer use and familiarity (Iverson et al., 2009), and literature data suggest that results from computerized versus examiner-administered testing may be different in computer-experienced versus computer-naïve populations (Feldstein et al., 1999). To address this issue, in the Smart Aging platform a touch screen is used to accomplish movements in the environment: this choice is supported by the data gathered in our pilot testing and by literature data showing that individuals with minimal computer experience or some level of cognitive impairment find it easier to learn to use a touch screen than a mouse, and that touch screens are more intuitive (Chernick et al., 2007).

Indeed, in clinical practice, it is essential to ensure that individuals with less computer familiarity are not misdiagnosed as having frank cognitive impairment; for this reason it is very important to understand the relationship between computer familiarity and test performance in order to improve diagnostic accuracy when using computerized neurocognitive testing. In the *demographics* section of the application participants provided ratings based on their own assessment of their computer familiarity; even though these appraisals are subjective, it will be interesting to perform subgroup analyses in order to correlate computer familiarity with performance on the SASG tasks.

Once validated, the Smart Aging platform will constitute a powerful screening tool for the early detection of cognitive impairments on a wide scale. Indeed, this approach offers several advantages over the available screening tools for MCI: it is more user-friendly, ecological and motivating for end-users, while on a healthcare level it is less time and resource consuming. Furthermore, unlike other tools that investigate a single cognitive function, this platform will allow the evaluation of multiple cognitive domains (memory, executive functions, divided and selective attention) in order to characterize the different MCI subtypes.

Finally, to further develop the platform, parallel forms of the scenarios and tasks with different levels of complexity will be defined so that the system may also be used as a rehabilitation tool.

Acknowledgments

The Smart Aging project is funded by the Italian

Functional Neurology 2014; 29(3): 153-158

Ministry of Education, University and Research (Id Number PON04a3_00372).

References

- Bavelier D, Davidson RJ (2013). Brain training: Games to do you good. Nature 494: 425-426.
- Caltagirone C, Zannino GD (2008). Telecommunications technology in cognitive rehabilitation. Funct Neurol 23:195-199.
- Campbell Z, Zakzanis KK, Jovanovski D, et al (2009). Utilizing virtual reality to improve the ecological validity of clinical neuropsychology: an FMRI case study elucidating the neural basis of planning by comparing the Tower of London with a three-dimensional navigation task. Appl Neuropsychol 16: 295-306.
- Cernich AN, Brennana DM, Barker LM, et al (2007). Sources of error in computerized neuropsychological assessment. Arch Clin Neuropsychol 22 Suppl 1: S39-S48.
- Cherniack EP (2011). Not just fun and games: applications of virtual reality in the identification and rehabilitation of cognitive disorders of the elderly. Disabil Rehabil Assist Technol 6: 283-289.
- Christiansen C, Abreu B, Ottenbacher K, et al (1998). Task performance in virtual environments used for cognitive rehabilitation after traumatic brain injury. Arch Phys Med Rehabil 79: 888-892.
- Davies RC, Hohansson G, Boschian K, et al (1999). A practical example using VR in the assessment of brain injury. Int J Virtual Reality 4: 3-10.
- Eckerman DA, Carroll JB, Foree D, et al (1985). An approach to brief field testing for neurotoxicity. Neurobehav Toxicol Teratol 7: 387-393.
- 9. Emery VO (2011). Alzheimer disease: are we intervening too late? Pro. J Neural Transm 118: 1361-1378.
- Feldstein SN, Keller FR, Portman RE, et al (1999). A comparison of computerized and standard versions of the Wisconsin Card Sorting Test. Clin Neuropsychol 13: 303-313.
- Folstein MF, Folstein SE, McHugh PR (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatry Res 12: 189-198.
- Frasson P, Ghiretti R, Catricalà E, et al (2011). Free and Cued Selective Reminding Test: an Italian normative study. Neurol Sci 32: 1057-1062.
- 13. Gauthier S, Reisberg B, Zaudig M, et al (2006). Mild cognitive impairment. Lancet 367: 1262-1270.
- Giovagnoli AR, Del Pesce M, Mascheroni S, et al (1996). Trail making test: normative values from 287 normal adult controls. Ital J Neurol Sci 17: 305-309.
- Iverson GL, Brooks BL, Ashton VL, et al (2009). Does familiarity with computers affect computerized neuropsychological test performance? J Clin Exp Neuropsychol 31: 594-604.
- Jack D, Boian R, Merians AS, et al (2001). Virtual realityenhanced stroke rehabilitation. IEEE Trans Neural Syst Rehabil Eng 9: 303-318.
- Jak AJ, Bangen KJ, Wierenga CE, et al (2009). Contributions of neuropsychology and neuroimaging to understanding clinical subtypes of mild cognitive impairment. Int Rev Neurobiol 84: 81-103.
- Kang YJ, Ku J, Han K, et al (2008). Development and clinical trial of virtual reality-based cognitive assessment in people with stroke: preliminary study. Cyberpsychol Behav 11: 329-339.

- Laiacona M, Inzaghi MG, De Tanti A, et al (2000). Wisconsin card sorting test: a new global score, with Italian norms, and its relationship with the Weigl sorting test. Neurol Sci 21: 279-291.
- Lopez OL, Becker JT, Saxton J, et al (2005). Alteration of a clinically meaningful outcome in the natural history of Alzheimer's disease by cholinesterase inhibition. J Am Geriatr Soc 53: 83-87.
- Magsi H, Malloy T (2005). Underrecognition of cognitive impairment in assisted living facilities. J Am Geriatr Soc 53: 295-298.
- Nasreddine ZS, Phillips NA, Bédirian V, et al (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 53: 695-699.
- Novelli G, Papagno C, Capitani E, et al (1986). Tre test clinici di ricerca e produzione lessicale: taratura su soggetti normali. Archivio di Psicologia, Neurologia e Psichiatria 47: 477-486.
- Petersen RC, Doody R, Kurz A, et al (2001a). Current concepts in mild cognitive impairment. Arch Neurol 58: 1985-1992.
- Petersen RC, Roberts RO, Knopman DS, et al (2009). Mild cognitive impairment: ten years later. Arch Neurol 66: 1447-1455.
- Petersen RC, Stevens JC, Ganguli M, et al (2001b). Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of

the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 56: 1133-1142.

- Riva G, Rizzo A, Alpini D, et al (1999). Virtual environments in the diagnosis, prevention and intervention of agerelated diseases: a review of VR scenarios proposed in the EC VETERAN Project. Cyberpsychol Behav 2: 577-591.
- Rizzo AA, Buckwalter G, Neumann U (1998). Basic issues in the application of virtual reality for the assessment and rehabilitation of cognitive impairments and functional disability. Cyberpsychol Behav 1: 59-78.
- Rose FD, Brooks BM, Attree EA, et al (1999). A preliminary investigation into the use of virtual environments in memory retraining after vascular brain injury: indications for future strategy? Disabil Rehabili 21: 548-554.
- Schmidtke K, Hermeneit S (2008). High rate of conversion to Alzheimer's disease in a cohort of amnestic MCI patients. Int Psychogeriatr 20: 96-108.
- Scott KR, Barrett AM (2007). Dementia syndromes: evaluation and treatment. Expert Rev Neurother 7: 407-422.
- Spinnler H, Tognoni G (1987). Standardizzazione e taratura italiana di test neuropsicologici. Ital J Neurol Sci 6 (Suppl 8)
- Weimer DL, Sager MA (2009). Early identification and treatment of Alzheimer's disease: social and fiscal outcomes. Alzheimers Dement 5: 215-226.
- Zhang L, Abreu B, Masel B, et al (2001). Virtual reality in the assessment of selected cognitive function after brain injury. Am J Phys Med Rehabil 80: 597-604.