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Recommendations for the Use of Serious Games in Neurodegenerative Disorders: 2016 Delphi Panel

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The use of Serious Games (SG) in the health domain is expanding. In the field of neurodegenerative disorders (ND) such as Alzheimer's disease, SG are currently employed both to support and improve the assessment of different functional and cognitive abilities, and to provide alternative solutions for patients' treatment, stimulation, and rehabilitation. As the field is quite young, recommendations on the use of SG in people with ND are still rare. In 2014 we proposed some initial recommendations (Robert et al., 2014). The aim of the present work was to update them, thanks to opinions gathered by experts in the field during an expert Delphi panel. Results confirmed that SG are adapted to elderly people with mild cognitive impairment (MCI) and dementia, and can be employed for several purposes, including assessment, stimulation, and improving wellbeing, with some differences depending on the population (e.g., physical stimulation may be better suited for people with MCI). SG are more adapted for use with trained caregivers (both at home and in clinical settings), with a frequency ranging from 2 to 4 times a week. Importantly, the target of SG, their frequency of use and the context in which they are played depend on the SG typology (e.g., Exergame, cognitive game), and should be *personalized* with the help of a clinician.

Keywords: serious games, neurodegenerative disorders, recommendations, ICT, Delphi Technique

INTRODUCTION

The use of Information and Communication Technologies (ICT) in the health domain is progressively expanding. Recently, increasing attention is devoted to the field of neurodegenerative disorders (ND), such as Alzheimer's disease (AD), where ICT is employed both to support and improve the assessment of different functional and cognitive abilities (Aalbers et al., 2013; Robert et al., 2013; König et al., 2015), and to provide alternative solutions for patients' treatments, stimulation, and rehabilitation. A field which is rapidly growing is that of Serious Games (SG), which are mental and/or physical contests played with a computer in accordance with specific rules, which use entertainment to promote training, education, health, public policy, and strategic communication objectives (Zyda, 2005). Contrary to other ICT-based tools, such as computerized testing or cognitive training, SG embeds the playful and entertaining aspects typical of video-games into the 'serious' activity, by applying a pedagogic scenario to the game scenario (Alvarez, 2007). The features typical of SG, such as the presence of a game challenge and of long-term goals, have been proposed to make SG more adapted than classical computer-based training to sustain generalization of learnt activities to real life situations (Whyte et al., 2015). For this reason, recommendations for the *design* of SG targeting ND are starting to emerge (e.g., Bouchard et al., 2012; Fua et al., 2013; Mader, 2015; Ben-Sadoun, 2016). However, recommendations on the *use* of SG in these populations are still rare. In 2014, we proposed some initial recommendations for the use of SG in people with ND, gathered by experts in the field during a consensus group (Robert et al., 2014). Specifically, we systematically analyzed the Strengths, Weaknesses, Opportunities and Threats (SWOT) of employing SG with these patients, and reported practical guidelines on when, where, and with whom SG should be employed, and to specify which categories of patients and which abilities should be targeted. Since then, a few empirical studies were published on the use of SG in these populations, describing the feasibility of employing SG targeting improvements in social/emotional wellbeing (Beneviste et al., 2012), SG training cognitive abilities such as executive functions (Manera et al., 2015), and Serious Exergames including a combination of cognitive training and physical training (Ben-Sadoun et al., 2016). A few more SG were designed for these patients to train cognitive abilities such as memory (Kim et al., 2015) and several aspects of visual attention (Mader et al., 2012), but they have not been tested so far on patients with neurodegenerative diseases. Based on these new works and on the experience gained by different research centers involved in the use of SG in people with neurodegenerative diseases in the last years (e.g., the CoBTeK research laboratory of the University of Nice Sophia Antipolis, France; the Hopital Broca in Paris, France; the Radboud Alzheimer Center, Nijmegen, the Netherlands; the Gazzaley's lab in San Francisco, CA, United States) the aim of the present work is to update the recommendations published in 2014, thanks to a Delphi expert panel.

Neurodegenerative Disorders

Neurodegenerative disorders progress through several stages in several years, and ultimately lead to dementia, a decline in mental ability severe enough to interfere with activities of daily living. Dementia can result from different causes, the most common being AD. It is often preceded by a pre-dementia stage, known as mild cognitive impairment (MCI), characterized by a cognitive decline greater than expected for an individual's age, which, however, does not interfere notably with activities of daily living (Petersen et al., 1997). Depending on the etiology and the disease's stage, dementia can be characterized by cognitive, behavioral, motor, and/or functional symptoms. The biological processes involved in ND are very heterogeneous, and include neuroinflammation, gliosis, synaptic loss, neurodegeneration, cerebral atrophy, and alterations of the blood-brain barrier permeability (Raz et al., 2016). These molecular alterations are due, among others, to alterations in the bioenergy metabolism, to hypoperfusion/hypoxia, and to dysfunctions of the cerebrovascular hemodynamic. From a therapeutic point of view, much research aims to modify the course of the disease or to reduce the impact of the clinical symptoms. Social interaction, physical and cognitive activities, and motivation can have a major impact on the disease progression. Hence, non-pharmacological approaches targeting people's lifestyle are of particular interest.

Serious Games for People with Neurodegenerative Disorders

Boosted by the publication of a Nature letter showing that video game training can enhance cognitive control in older adults (Anguera et al., 2013), there is now a growing interest in developing SG specifically adapted to people with ND. Evidence is accumulating showing that video-games and VR-applications can successfully be employed for early detection and monitoring of physical and cognitive impairment (e.g., Tarnanas et al., 2013; Aalbers et al., 2016; Negut et al., 2016; Zygouris et al., 2017), but also to train physical and cognitive abilities in people with AD, MCI, and related disorders. In the field of training, most of the research work so far has been conducted employing commercial video-games and cognitive games (such as Wii Fit and Wii Sport, Lumosity) designed for an entertaining purpose, and with a 'typical' healthy user in mind. In their review on the use of video-games in people with dementia-related disorders, McCallum and Boletis (2013) showed that: (a) Exergames, i.e., games that promote physical condition and/or aerobic fitness can positively affect several areas of mobility in participants with mild AD and MCI, such as balance and gait (Padala et al., 2012), and voluntary motor control (Legouverneur et al., 2011); (b) cognitive games can improve cognitive functions, such as attention and memory (Stavros et al., 2010; Weybright et al., 2010) and visuo-spatial abilities (Yamaguchi et al., 2011); (c) physical and cognitive games can have a positive impact on social and emotional functions, for instance they can improve the mood and increase positive affect and sociability (Weybright et al., 2010; Boulay et al., 2011) and reduce depression (Férez-Calvo et al., 2011). As

the field is young, less evidence is available on the efficacy of SG specifically designed for the training of people with ND. However, evidence collected in three studies suggests that SG and Serious Exergames are acceptable and motivating even for people with dementia. Beneviste et al. (2012) designed a SG based on musico-therapy targeting patients with AD and mild to moderate dementia aiming at improving patients' self-image to reduce their behavioral symptoms. Players use Wiimotes with WiiPistol to improvise or play predefined songs on a virtual keyboard. Results of a 2-month usability study conducted on seven AD patients confirmed that the SG was usable by AD patients despite their motor and cognitive impairments, and that patients were overall very satisfied with the game and expressed a desire to repeat the experience. Manera et al. (2015) found similar results with 'Kitchen and cooking,' a SG designed to train executive functions and praxis in people with MCI and early AD. The results of a 4-week feasibility study conducted on 21 participants (with MCI or early to moderate AD) confirmed that the game was acceptable and usable both at home and in a nursing home setting, and that patients were able to improve their game performance over the training, as confirmed by the fact that they became faster in the game activities. Finally, Ben-Sadoun et al. (2016) showed that X-Torp, a Serious Exergame designed to train physical, cognitive and social functions, was well accepted by people with dementia and MCI ($N = 10$) and healthy elderly controls ($N = 8$), and that during a 1-month trial participants experienced mainly positive emotions, improved their cardio-respiratory fitness, and were able to progress in the cognitive games scenarios. A summary of the training

features of these three feasibility/pilot studies is reported in **Table 1**.

Data on the frequency of use employed in the three feasibility studies is converging with the recommendations reported by Robert et al. (2014). A consensus group including expert of ND (health domain) and of VG/SG design (ICT domain) and commercialization (business domain) met in a standalone meeting, and were asked to respond to questions concerning the ideal clinical population and target of SG, their frequency of use, and their context of use (with whom and where). Results (reported in **Figure 1**) suggested that: (a) SG were considered between 'adapted' and 'very adapted' to people with MCI, and between 'not very adapted' and 'adapted' to people with AD and related disorders; (b) SG was rated between 'adapted' and 'very adapted' for assessment, stimulation and rehabilitation of people with AD and related disorders, to train family caregivers and healthcare professionals, with the best rated target being stimulation; clinical targets rated between 'adapted' and 'very adapted' included physical, cognitive and social stimulation, as well as apathy (while agitation and improvements in activities of daily living were considered between 'not very adapted' and 'adapted'); (c) SG should be employed regularly ('everyday' and 'once a week' were both rated between 'adapted' and 'very adapted,' while 'on request' was rated between 'not very adapted' and 'adapted'); (d) SG were rated between 'adapted' and 'very adapted' to be employed at home, in day centers and nursing homes, and between 'not very adapted' and 'adapted' to be employed in the hospital; (e) SG were rated between 'adapted' and 'very adapted' to be employed with someone (being either

TABLE 1 | Summary of the existing studies on SG tested on participants with MCI and/or dementia.

	MinWii	Kitchen and cooking	X-Torp
Feasibility study	Beneviste et al., 2012	Manera et al., 2015	Ben-Sadoun et al., 2016
SG for whom?	Older adults with AD and mild to severe dementia	Older adults with MCI and mild to moderate dementia	Older adults with MCI and mild to moderate dementia
What is the clinical target?	Increase self-esteem; reduce behavioral symptoms	Train executive functions (e.g., planning) and praxis	Train physical and cognitive activity in a positive emotional context
Where was it used?	Clinical setting	Clinical setting, home, nursing home	Clinical setting
With whom was it used?	Clinician and by groups of 3–4 participants	Clinician and alone	Clinician
When (how frequently) was it used?	Once a week	Once a week in a clinical setting; As much as they wanted at home/nursing home	3 times/week
Training duration	4–8 weeks	4 weeks	5 weeks
Session duration	Mean of 10-20 min	As much as wanted	Mean 35–40 min
Number of participants	7	21 (MCI and ND)	18 (10 ND, 8 controls)
Participants' clinical baseline data	MMSE between 10 and 25	For AD, MMSE between 15 and 24; for MCI, MMSE between 24 and 30	For ND, MMSE between 16 and 27, CDR > 0

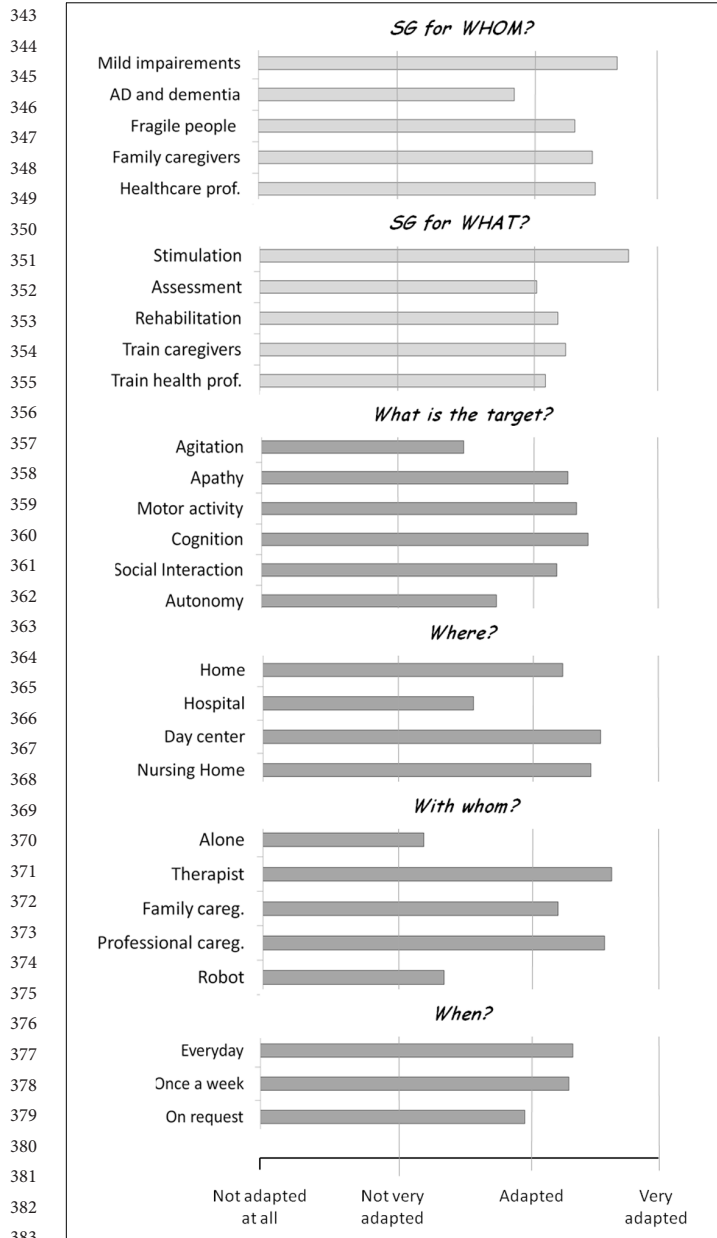


FIGURE 1 | Results of the recommendations for the use of SG drafted in the 2013 IA workshop. Adapted from Robert et al. (2014). In a Delphi panel, participants were provided with questions concerning the ideal clinical population and target of SG (light gray bars). Next they were asked to focus on older adults with cognitive impairment, and were asked questions about the clinical target, the frequency of use, and their context of use (with whom and where) of SG in these population (dark gray bars). For each question, participants were provided with a number of response alternatives, and asked to rate each item on a 4-point scale, from 'not adapted at all' to 'completely adapted.'

a therapist, a family caregiver or a professional caregivers), and between 'not very adapted' and 'adapted' to be employed alone (or with a robot).

In the present paper we aimed to update and refine these initial recommendations thanks to a Delphi expert panel. A number of

methodological changes were performed compared to the 2014 consensus panel. First of all, the 2014 recommendations were collected in a single round, without following the classical Delphi methodology. Indeed in the standard Delphi method (Linstone and Turoff, 1975) experts are asked to answer questions in two (or more) rounds. After each round, a facilitator provides a summary of the experts' responses, and encourages the experts to analyze, comment and (eventually) revise their earlier answers in light of the commentaries of other members of the panel. The recommendations reported in the present paper followed the classical Delphi method (see below). Second, in 2014 we asked participants to rate each question on a 4-point scale ('not adapted at all,' 'not very adapted,' 'adapted' and 'very adapted'). Here, we selected instead a 5-point scale ('not adapted at all,' 'not very adapted,' 'adapted,' 'very adapted' and 'completely adapted') to improve the symmetry of this Likert-type scale. Third, in the 2014 study several questions collapsed persons with MCI and more advanced stages of AD ('people with AD and related disorders'). As recommendations for these two groups may be quite different, in the present study we kept them as separated categories for all the questions. Forth, we collapsed in a single questions the 'Where' and 'With whom' questions (see below), in order to better explore the exact contributions of (and interactions between) these two factors. Finally, we added a number of response alternatives to several questions, in order to obtain more precise information (e.g., in the 'When' question, we employed 6 response alternatives instead of 3).

METHODS

The recommendations reported in the present paper were collected and discussed during the workshop "Innovation Alzheimer 2016," organized by the CoBTeK (Cognition – Behaviour – Technology) Research Unit of the Université Côte d'Azur, in Nice (France) on September 28th, 2016, in occasion of the 10th World Conference of Gerontechnology (ISG2016).

Participants

The expert panel ($N = 23$) included researchers and health care professionals working on autism and other neurological and developmental disorders ($n = 6$), neurodegenerative disorders ($n = 10$), or both neurodevelopmental and neurodegenerative disorders ($n = 2$); ICT engineers ($n = 2$); and game developers ($n = 3$).

Procedure

Following the DELPHI method, a list of questions was sent to all participants a week before the meeting via web-survey. Who, Where, When, and What questions were used as guidelines to structure the survey. Specifically, participants were asked to respond to the following questions:

- (a) SG for *whom*? Are SG adapted (i.e., appropriate) to the following populations?
 - Mild Cognitive Impairment (MCI);

- 457 ● Early to moderate dementia due neurodegenerative
458 disorders such as AD (dementia)
- 459 (b) *What is the clinical target (in each condition)?*
460
- 461 ● Assess (Physical, cognitive functions, IADL, . . .)
 - 462 ● Train physical activity (Muscles, cardio-resp. fitness)
 - 463 ● Train cognitive functions (Attention, memory,
464 executive functions, . . .)
 - 465 ● Improve autonomy (IADL)
 - 466 ● Improve wellbeing (Increase positive emotions, self-
467 esteem; reduce negative emotions, stress)
 - 468 ● Favor social exchanges (Improve sociability and favor
469 relations)
 - 470 ● Teach contents
- 471 (c) *Where should SG be used, and with whom (in each
472 condition)?*
473
- 474 ● At home, alone
 - 475 ● In a clinical facility (e.g., hospital, long-term residence,
476 at the doctor's office), alone
 - 477 ● At home, with a trained (professional or family)
478 caregiver
 - 479 ● In a clinical facility, with a trained (professional or
480 family) caregiver
- 481 (d) *When (how frequently) should SG be used (in each
482 condition)?*
483
- 484 ● Once a week
 - 485 ● Twice a week
 - 486 ● 3 times a week
 - 487 ● 4 times a week
 - 488 ● 5 times a week
 - 489 ● Everyday

490 Participants were asked to rate each item on a 1–5 scale
491 (1 = not adapted at all; 2 = not very adapted; 3 = adapted;
492 4 = very adapted; 5 = completely adapted).
493

494 Data Analysis

495 Results were collected, and analyzed. During the workshop, a
496 discussion session was organized with the objective to comment
497 on the survey results, and to generate practical recommendations
498 for the use of SG in MCI and dementia. Ratings from one
499 participant were not considered for data analysis because more
500 than 50% of responses were missing. Thus, reported data
501 refer to 22 participants. For descriptive analysis purposes, we
502 reported mean ratings. In order to compare ratings obtained
503 for people with MCI and people with dementia in the first
504 (“SG for whom?”) and second (“What is the clinical target?”)
505 question, we performed separate repeated-measures ANOVAs on
506 each response item with Group (MCI vs. dementia) as within
507 subject factor. For the second question, in order to account
508 for multiple comparisons ($N = 7$), Bonferroni corrections were
509 applied ($\alpha = 0.05/7 = 0.007$). The third question (“Where
510 should SG be used, and with whom”) was analyzed by means of a
511 repeated-measures ANOVA with Group (MCI vs. dementia),
512 Where (home vs. clinical facility) and with Whom (alone vs. with

a trained caregiver) as within-subject factors, in order to analyze
514 the effect of the three factors and their interactions. Finally, the
515 fourth question (“When should SG be used?”) was analyzed by
516 means of a repeated-measures ANOVA with Group (MCI vs.
517 dementia) and Frequency (1, 2, 3, 4, 5 and 7 days per week)
518 as within-subject factors. As the methodology employed in the
519 present study is not completely comparable to that employed in
520 the 2014 recommendations paper, we compared the results of the
521 two studies only at a descriptive level.
522

523 RESULTS

524 SG for Whom?

525 Results are reported in **Figure 2A**. SG were rated between ‘very
526 adapted’ and ‘completely adapted’ for people with MCI, and
527 between ‘adapted’ and ‘very adapted’ to people with dementia.
528 Repeated-measures ANOVA confirmed that SG were rated as
529 more adapted to people with MCI compared to people with
530 dementia [$F_{(1,21)} = 16.87, p = 0.001$], suggesting that SG are
531 considered as more adapted to people with initial cognitive
532 decline than to people which are already losing autonomy
533 in activities of daily living. However, SG are considered to be
534 adaptable also to people with dementia.
535

536 What Is the Clinical Target?

537 Results are reported in **Figure 2B**. Participants reported that
538 SG are between ‘very adapted’ and ‘completely adapted’ for
539 assessment, to train physical and cognitive functions, improve
540 wellbeing, and teach contents. Improving autonomy and favoring
541 social exchanges were considered from ‘adapted’ to ‘very adapted.’
542 For people with dementia, SG were rated between ‘adapted’ and
543 ‘very adapted’ for all the specified targets. This is in line with
544 responses to the question ‘SG for whom,’ and it suggests that
545 all these domains do represent useful targets for SG in this
546 population. Repeated-measures ANOVAs (Bonferroni corrected)
547 conducted to compare people with MCI and dementia for
548 each category suggested that SG were considered as more
549 adapted to people with MCI compared to people with dementia
550 to train cognitive functions [$F_{(1,20)} = 17.44, p < 0.001$], to
551 improve autonomy [$F_{(1,20)} = 10.80, p = 0.004$] and wellbeing
552 [$F_{(1,21)} = 9.32, p = 0.006$] and to teach contents [$F_{(1,20)} = 15.42,$
553 $p = 0.001$]. All the other contrasts did not reach statistical
554 significance ($p > 0.007$).
555

556 Where Should SG Be Used, and with Whom?

557 Results for all these patient populations (**Figure 2C**) suggest that
558 SG are mostly adapted (between ‘very adapted’ and ‘completely
559 adapted’) to be employed with a trained caregiver, both in
560 a home and in a clinical setting. The use of SG by patients
561 alone was rated between ‘adapted’ and ‘very adapted’ for people
562 with MCI, and between ‘not very adapted’ and ‘adapted’ for
563 people with dementia. Repeated-measures ANOVA with Group
564 (MCI vs. dementia), Where (home vs. clinical facility) and
565 With whom (alone vs. with a trained caregiver) as within-
566 subject factors confirmed a significant effect of With whom factor
567
568
569
570

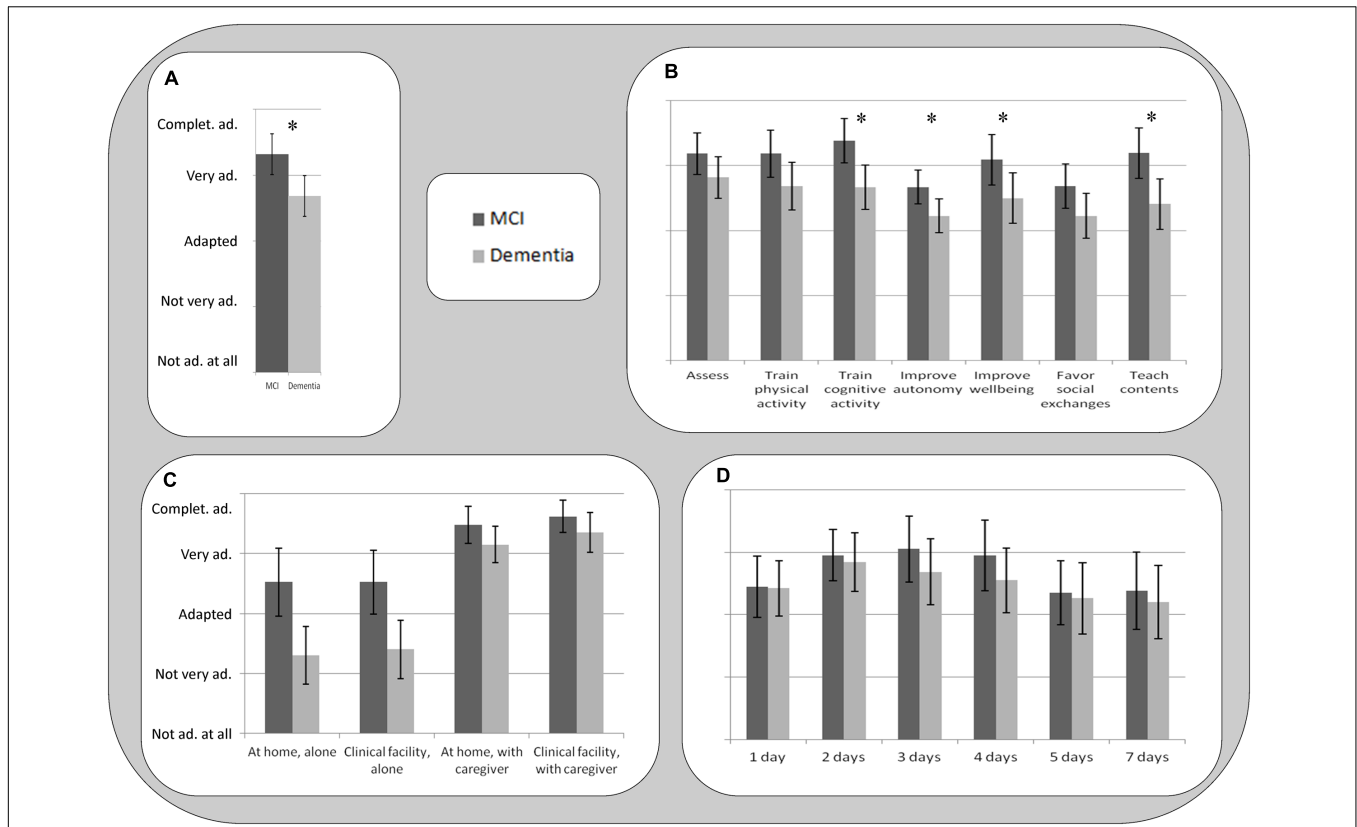


FIGURE 2 | Results of the rating questions. Error bars represents 95% Confidence Intervals for the ANOVAs. *Reported in (A,B) show significant paired contrasts in the repeated-measures ANOVA with Group (MCI vs. Dementia) as within-subject factor. (A) SG for whom? Are SG adapted to: older people with MCI; and early to moderate dementia due neurodegenerative disorders (dementia); (B) What is the clinical target? Assess; train physical activity; train cognitive functions; improve autonomy; Improve wellbeing; favor social exchanges; teach contents. (C) Where should SG be used, and with whom? At home, alone; in a clinical facility, alone; at home, with a trained caregiver; in a clinical facility, with a trained caregiver. (D) When (how frequently) should SG be used? 1, 2, 3, 4, 5, and 7 days per week.

[$F_{(1,19)} = 54.82, p < 0.001$], with SG use with a caregiver as more adapted compared to SG use alone. The Where factor was not statistically significant [$F_{(1,19)} = 1.30, p = 0.269$], thus suggesting that SG are considered as equally adapted to be employed at home and in a clinical facility. A significant effect of Group was also found, with SG rated as more adapted to be employed with people with MCI compared to people with dementia in all the settings [$F_{(1,19)} = 22.03, p < 0.001$]. Interestingly, a significant interaction between Group and With whom factor was also found [$F_{(1,19)} = 12.67, p = 0.002$], suggesting that employing SG with a trained caregiver is especially important for people with dementia. No other 2-way or 3-way interaction reached statistical significance (all $ps > 0.360$).

When (How Frequently) Should SG Be Used?

Results (Figure 2D) suggest that all the game frequencies were rated between ‘adapted’ and ‘completely adapted’ for all conditions, and the mean ratings of the different game frequencies can be visually described as skewed Gaussian distributions. Repeated-measures ANOVA with Group (MCI vs. dementia) and Frequency (1, 2, 3, 4, 5 and 7 days

per week) as within-subject factors revealed no significant main effect of Group [$F_{(1,18)} = 3.45, p = 0.008$], and Frequency [$F_{(5,90)} = 1.72, p = 0.139$], and no significant interaction between Group and Frequency [$F_{(5,90)} = 0.60, p = 0.704$]. Converging with descriptive data, the ANOVA’s contrast tests revealed an almost-significant quadratic contrast [$F_{(1,18)} = 4.27, p = 0.053$], suggesting that categories in the middle of the curve were rated as more adapted compared to extreme values (1 and 7 days per week). For participants with MCI and dementia, the highest scores were obtained for game frequencies from 2 to 4 days a week.

DISCUSSION

Since the publication of our previous recommendations on the use of SG (Robert et al., 2014), a number of SG were developed and tested with older people with MCI and dementia to train physical and cognitive abilities and to improve emotional wellbeing (Beneviste et al., 2012; Manera et al., 2015; Ben-Sadoun et al., 2016). These studies showed promising results, but also a number of usability challenges. Reported difficulties included, for instance, a higher fatigability of people with MCI and dementia

in physically stimulating SG compared to healthy older adults (Ben-Sadoun et al., 2016), and, for several participants with cognitive impairment, low motivation to play SG when not accompanied by a family or professional caregiver (Manera et al., 2015). These difficulties were reported despite these SG were specifically designed for people in these populations. This suggests that the feasibility of employing SG with people with ND does not depend only on the game design features: an important component is the training format and structure. This confirms the importance of providing recommendations not only for the *design*, but also on the *use* of SG, that should be tested in clinical trials. Starting from the recommendations published in 2014 (Robert et al., 2014), the aim of the present paper was to draft guidelines for the use of SG in people with ND, thanks to a review of recently published studies employing SG in these populations, and gathering the opinion of experts in the field in a Delphi expert panel. A summary of the main recommendations is reported in **Table 2**.

SG for Whom?

Serious Games were rated as more adapted to people with MCI compared to people with dementia. The results are converging with those reported in our previous recommendations (SG were considered between 'adapted' and 'very adapted' to people with MCI, and between 'not very adapted' and 'adapted' to people with AD and related disorders; Robert et al., 2014), and suggest that SG may be more useful for people with initial cognitive decline than to people which are already losing autonomy in activities of daily living. This can be explained, on one hand, by the recognition that the cognitive decline associated to dementia (working memory, attention, etc.) makes it more challenging to design and employ SG in this population; and on the other hand, by the recognition that early interventions targeting initial cognitive decline are

supposed to be more effective compared to late interventions (Barnett et al., 2014). Anyway, SG are considered as adaptable also to people with dementia. This is confirmed by recent studies showing that SG are usable in people with dementia both when played alone (e.g., Manera et al., 2015) and with a clinician (Ben-Sadoun et al., 2016). Ongoing studies are also exploring the efficacy of ICT-based devices (e.g., avatars, contextual helps) in supporting older adults with SG use, showing initial promising results.

What Should Be the Target?

Assessment, training and promoting wellbeing were all rated as good targets for SG in people with MCI and dementia. Similarly, in the 2014 recommendations, assessment, stimulation and rehabilitation were all rated as good targets for people with AD and related disorders. Favoring social exchanges was not considered as the best target because most of the existing SG for older adults are not social (i.e., they are designed for a single player). However, emerging SG are also targeting the social domain. Some of these SG are showing promising results (Ben-Sadoun et al., in preparation). Trainings targeting the cognitive domain and teaching contents may be more suitable to people with MCI compared to people with dementia, as they require some intact learning abilities to be optimized. However, beyond the selection of a clinical target for each patient's category, an important aspect to take into account is that the selection of a SG should be *personalized*, and based on extensive clinical assessments aiming at identifying primary and secondary targets in the cognitive, motivational and emotional domains for each patient (Mishra et al., 2016). The assessment can also help to define the main follow up parameters, and the kind of feedback needed by each patient based on his/her challenges. For all conditions, SG should ultimately aim at targeting improvements in daily activities (autonomy). In other words, improvements in game activities should generalize to untrained abilities (Anguera et al., 2013), and demonstrate an impact on real life. SG design principles, such as inclusion of long-term goals embedded in a cohesive narrative instruction, and of specific generalization activities (e.g., instructional supports), may be important for encouraging transfer of knowledge from the computer to in-person settings. However, even improving autonomy in the SG activity alone could have a positive impact on motivation and quality of life: indeed the need of autonomy is one of the main drivers of the intrinsic motivation to play videogames in younger people (Deci and Ryan, 2000; Przybylski et al., 2010). This does not necessarily extend to people with ND. Is the need of autonomy the main motivational driver also for older adults with cognitive impairment, or are there other needs (e.g., social satisfaction/recognition)? To advance the work in this area, more research should be devoted to the design of SG in these target populations (De Schutter and Vanden Abele, 2015).

TABLE 2 | Recommendations for the use of SG in people with neurodegenerative disorders in a nutshell.

Are SG adapted to whom?

- SG are completely adapted to older people with MCI;
- Designing SG for people with dementia is challenging, but important.

What should be the SG target?

- Assessment, training and promoting wellbeing are good targets for people with MCI and dementia
- For MCI, SG for physical and cognitive stimulation are particularly suitable;
- SG choice should be personalized based on clinical assessment aiming at identifying training targets in different domains.

Where should SG be used, and with whom?

- SG can be employed both at home and in clinical facilities;
- SG are more effective when the patient is accompanied by a caregiver/clinician;
- some SG can be used alone;
- Home-based training is still challenging due to technical issues.

How often should SG be used?

- Training frequency between two and four times a week were rated as the most adapted; But
- Frequency of use for SG should be personalized based on the game features and the patient's clinical profile and motivation;
- Clinician follow up is crucial to keep the SG motivating (no loss of interest, no addiction).

Q15

Where Should SG Be Used, and with Whom?

The experts suggested that most of the SG are more effective when the patient is accompanied by a trained caregiver (similarly,

799 in the 2014 paper, SG were rated as more adapted for use with
 800 a family/professional caregiver, or a healthcare professional).
 801 This is consistent with the general recommendations on SG
 802 usability drafted by Alvarez et al. (2012) who suggested the
 803 importance of assisting the player to improve his/her game
 804 understanding (how to play?) and motivation (why to play)?
 805 The presence of a caregiver is considered as more important
 806 for people with dementia compared to people with MCI, due
 807 to their lower degree of autonomy. The presence of a trained
 808 person is important for different reasons, including: to motivate
 809 people to use the game; to help progressing in the game
 810 scenario (in case people get stuck), reminding them about game
 811 rules and commands; to make sure the SG are played safely,
 812 especially for physical SG; and to embed the SG in a positive
 813 social and emotional context. The fact that the presence of a
 814 caregiver represents a key element in SG adoption raises potential
 815 ecological and economical barriers to the use of SG outside the
 816 research and clinical context. Possible solutions include involving
 817 a family caregiver, organizing SG group sessions, or providing
 818 remote assistance. Avatars and other game assistance solutions
 819 may also be useful to promote independent SG use in people with
 820 cognitive impairment (Phan Tran et al., in preparation).

821 Concerning the Where question, most of the SG are
 822 considered as useful to be delivered both at home and in
 823 clinical facilities. Clinical facilities have the advantage to allow
 824 a complete standardization of the training, and to provide a
 825 secure, controlled environment. The main problem, however, is
 826 represented by the travel time and costs. In order to improve
 827 study adherence, Ben-Sadoun et al. (2016) used a taxi to transport
 828 patients at clinical facility, resulting in a 100% adherence to the
 829 training. This strategy was also used by Maillot et al. (2012) for
 830 some of elderly subjects which came to the clinical facility during
 831 their Exergame training study. Although this is feasible in the
 832 context of a clinical study, it would be important, in the long term,
 833 to bring SG in the patient's home for the classical care. At present
 834 home-based training is still challenging due to technical issues
 835 (e.g., hardware setup, availability of an internet connection for
 836 data transfer), and to difficulties to monitor the training remotely,
 837 raising possible security problems. As technologies improve every
 838 day, well-designed feasibility studies in home-based setting are
 839 urgently needed to verify if home-based stimulation is safe and
 840 feasible, and for which patient populations. This is particularly
 841 relevant because new generations of older adults will be more
 842 and more used to employ ICT at home, thus potentially reducing
 843 usability problems.

844 How Often Should SG Be Used?

845 Training frequencies between two and four times a week
 846 were rated as the most adapted for people with MCI
 847 and dementia. Evidence collected in recent studies on both
 848 cognitive and cognitive-physical trainings converges with this
 849 recommendation (e.g., Anguera et al., 2013; Ben-Sadoun et al.,
 850 2016). However, these frequencies should be interpreted with
 851 caution. The frequency of use for specific SG should vary
 852 depending on a number of variables, including the presence of
 853 physical activity (and its intensity), the duration of each game
 854 session, the time that patient (and eventually the caregiver)

855 can devote to the activity, and the motivation to play. To
 856 maximize the training efficacy, it is important to establish
 857 the session frequency and duration (as well as the total
 858 training duration) based on the goals that the training is
 859 willing to achieve, and on the person's features. For instance,
 860 if the target for a patient is to improve the general physical
 861 fitness, a short intense Exergame training is probably less
 862 adapted compared to a long training with regular sessions,
 863 in which physical activity is progressively increased based on
 864 performance improvements. But the session duration and goals
 865 need to be adapted to the person's baseline physical fitness
 866 level, keeping into account eventual physical constraints and
 867 concurrent pathologies (for instance, the training designed for
 868 an ex-marathon runner should be radically different from the
 869 training for a smoker who never did active physical activity
 870 before).

871 Another crucial aspect to take into account when designing
 872 trainings is the motivation aspect. In general, the longer and more
 873 intense the training, the better. However, 'forcing' employing
 874 the SG too often may result in lowered motivation, or even
 875 in addiction, as there is a thin line between motivational
 876 and addictive aspects (Smith et al., 2011). Ideally, the features
 877 of the training should be adapted in order to increase the
 878 patient's motivation to play, thus optimizing the training results.
 879 Strategies to improve motivation include, for instance, the
 880 presence of a clinician motivating the person, helping to set
 881 the training pace, and modifying its frequency in a timely
 882 manner based on the patient's changes; the design of an
 883 adaptive game challenge, that keeps the player in the 'flow zone'
 884 (the feeling of complete and energized focus in an activity,
 885 with a high level of enjoyment and fulfillment) and improve
 886 the feeling of self-efficacy; for instance, the game becomes
 887 more difficult as the player progresses, but steps back to an
 888 easier level when the player is tired or show a decline in
 889 performance; or the presence of a well-designed game reward
 890 system.

891 LIMITATIONS

892 The present recommendations were gathered from a relatively
 893 small group of experts working in the domain of SG for health.
 894 In further work, it would be interesting to verify if these results
 895 hold for a wider expert population (e.g., through web-survey).
 896 Furthermore, it would be interesting to collect the opinion of
 897 healthcare professionals who do not work with SG and ICT
 898 in their practice, to verify the barriers for SG adoption in the
 899 healthcare domain. For instance, if clinicians non-expert in ICT
 900 consider SG as not adapted and not useful for people with ND,
 901 they will hardly suggest their use for training purposes. This
 902 means that more effort should be done to share the promising
 903 results of SG in these populations among the clinical community.

904 AUTHOR CONTRIBUTIONS

905 VM analyzed the data. All the authors contributed to draft the
 906 paper.

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1032 **Conflict of Interest Statement:** The authors declare that the research was
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