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## Computer Brain Gym: A Rehabilitation Program for Individuals with Alzheimer's Disease

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# Computer Brain Gym: A Rehabilitation Program for Individuals with Alzheimer's Disease

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**Background:** Alzheimer's disease (AD) is the most common form of dementia. This randomized control trial investigated the effects of the newly developed computer brain gym (BG) system on the cognitive function and mental health of patients with Alzheimer's disease.

**Materials and Methods:** Twenty-three participants with AD who were exhibiting mild to moderate cognitive impairment were recruited and randomly divided into two groups. Group 1 received computer BG training, whereas Group 2 received conventional occupational therapy (OT). The patients underwent treatment for 12 weeks, with treatment sessions occurring twice per week for 45 minutes per session; additionally, they received assessments at pretest and posttest the treatment.

**Results:** No statistically significant differences were evident in the Mini-Mental State Examination (MMSE) or Cornell Scale for Depression in Dementia (CSDD) after the intervention. After cognitive training, the global rating scale of the BEHAVE-AD score improved in the BG group (from  $1.55 \pm 1.04$  to  $0.82 \pm 0.75$ ,  $p=0.046$ ). When regarding the aggressiveness score after training, the difference between the BG group and the OT group reached statistical significance (BG group:  $-0.82 \pm 1.94$ , OT group:  $1.00 \pm 1.86$ ,  $p=0.030$ ).

**Conclusion:** BG can improve mental health, preserve cognitive function, and represents a suitable rehabilitation program for patients with mild to moderate AD. Therefore, exergame has the potential to serve as an alternative to OT as a rehabilitation program for patients with AD. (Rehabil Pract Sci 2023; 2023(1): 1 - 10)

**Key Words:** dementia, exergame, mental health, occupational therapy

## INTRODUCTION

According to the definition of the World Health Organization (WHO), Taiwan is an aging society and may consequently face serious social problems. The percent-

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age of elderly individuals ( $\geq 65$  years of age) in Taiwan was 16.85% as of December 2021.<sup>[1]</sup> The incidence of dementia has been shown to increase with age, with dementia rates of 5-8% of elderly people being reported in the United States and rates of 2-4% of elderly people being reported in Taiwan.<sup>[2]</sup>

Alzheimer's disease (AD) is the most common form of dementia. Alzheimer's disease is a slowly progressive neurodegenerative disease, caused by the accumulation of beta-amyloid and overproduction of amyloid precursor protein.<sup>[3]</sup> Patients with early AD exhibit degradation of the temporal lobe and hippocampus, which results in the deterioration of cognitive function.<sup>[3]</sup> There are four clinical stages of Alzheimer's disease:<sup>[4]</sup> (1) the pre-clinical stage, which is characterized by mild memory loss without impaired activities of daily living; (2) the early stage, where several symptoms begin to appear in patients, such as disorientation of place and time, loss of memory and concentration, change in the mood, and anxiety;<sup>[5,6]</sup> (3) the moderate stage, in which the patients show increased memory loss, trouble in reading, and writing, an inability to recognize family, and poor impulse control; and (4) the late stage, in which the patient becomes bedridden and has difficulty in swallowing and urination.

Occupational therapy (OT) programs can improve short-term physical performance and psychological well-being among elderly people with dementia.<sup>[7]</sup> An occupational therapist can design a program to help a patient with AD in performing daily tasks by using modified methods. An occupational therapist can also adapt a patient's environment to maximize the skills that are necessary to enhance quality of life and may provide step-by-step directions for basic and instrumental activities of daily living (ADL).<sup>[8]</sup> Occupational-based interventions have been shown to improve ADL and improve performance in leisure activity.<sup>[9]</sup> However, OT programs are usually provided in rehabilitation centers or related clinics; thus, attending therapy sessions can be inconvenient for patients with dementia.

Cognitive stimulation, such as puzzles and games, is effective for improving quality of life and social interaction.<sup>[9]</sup> Exergames, which utilize advances in technology to promote user well-being, have recently emerged as a new exercise interface. Exergames enable users to exer-

cise in their own homes or in community settings. In light of the characteristics of elderly individuals, many researchers have begun to investigate the potential for using exergames to improve older adults' attitudes toward cognitive training, as well as their willingness to engage in cognitive training. Cohen et al. performed the first study to conduct a therapeutic game for patients with AD.<sup>[10]</sup> Moreover, Gao and Mandryk found that casual exergame play yields acute cognitive benefits, as evidenced by improved cognitive performance on tests requiring focus and attention.<sup>[11]</sup> Therefore, exergaming exhibits significant potential as a cognitive intervention for patients with AD.<sup>[12,13]</sup>

In this study, we used a computerized brain gym (BG) system developed by our team to investigate the effects of exergames on the cognitive function and mental health of patients with AD. The system's games included a series of games related to Chinese idioms, calculations, lenovo pairings, and lyrics of traditional Chinese songs.<sup>[14]</sup> We hypothesized that the BG system could improve the cognitive function and mental health of patients with AD.

## MATERIALS AND METHODS

### 1. Participants

The protocol that was used in this study was reviewed and approved by the Institutional Review Board of Chang Gung Memorial Hospital (IRB No. 103-5846C). The clinical trial registry number was NCT02978768. Twenty-three participants with AD exhibiting mild to moderate cognitive impairment were recruited from the Dementia Center of Chang Gung Memorial Hospital in Taoyuan, Taiwan.

#### 1-1 Inclusion criteria

Elderly individuals (hereafter referring to those aged 60 years and over) with mild to moderate AD were recruited based on their Mini-Mental State Examination (MMSE) and Clinical Dementia Rating Scale (CDR) scores (mild: MMSE 20–23, CDR 1; moderate: MMSE 10–19, CDR 2). Participating patients needed to be able to follow verbal commands in Chinese.

#### 1-2 Exclusion criteria

Patients with a history of stroke or other brain disorders, amputations or other limb defects, intolerance to

moderate-intensity exercise, or other non-AD forms of dementia (such as vascular dementia) were excluded from this experiment.

## 2. Assessment tools

The following mental, psychological, and behavioral domains were assessed.

### 2-1 Dementia scale

The MMSE, which is scored on a range from 0 to 30, was used to assess the mental status of each participant. Mild AD is expressed as 0.5–1 on the CDR and 20–23 on the MMSE, whereas moderate AD is expressed as 2 on the CDR and 10–19 on the MMSE.

### 2-2 Psychological domain

The Cornell scale for depression in dementia (CSDD; scored on a range from 0 to 38) was used to assess the mood of each participant for any depressive tendency relating to symptoms, behavioral problems, physical signs of distress, and ideas on a periodic function (score >10: probable major depression; score >18: definite major depression).

### 2-3 Behavioral domain

The Behavioral Symptoms in Alzheimer's Disease (BEHAVE-AD) rating scale (symptomatology score of 0-75 and global rating of 0-3) was used to assess whether each participant experienced paranoid or delusional ideations, hallucinations, activity disturbances, aggressiveness, diurnal rhythm disturbances, affective disturbances, anxiety, or phobias. The higher symptomatology and global rating score indicate more severe condition.

## 3. Study design

The experimental design included participants who were diagnosed with mild to moderate AD and who attended a hospital-based daycare center for dementia at the Taoyuan Chang Gung Memorial Hospital. The participants were randomly divided into the following two groups; Group 1, which was the experimental group, received computer BG training, whereas Group 2, which was the control group, received conventional OT for cognitive training.

The BG utilizes computer 'Mental Wii' dual-mode control, which was created by our own team with the use of Microsoft Visual Studio C++. The game designs of modes one and two were based on the Montreal Cognitive

Assessment (Mo CA). Mode one uses a touch screen to operate games, including flash cards, 20 take 3, phonic card discrimination, zookeeper, and phrase identification (Figure 1). Mode two uses fun cube-operated games, including sequence matching, picture selection by songs, animal identification, numerical orders/reverse orders, color orders/reverse orders, pictorial orders/reverse orders, picture selection by songs, shape selection, finding errors, antonyms, time challenges, and connection tests (Figure2). The cognitive games are composed of six types of games (Table 1). The players are requested to complete the game as soon and as accurately as possible. Additionally, they will provide feedback with time to complete the game, and they will earn points. The BG was developed by a team consisting of a neurologist, physiatrist, and professor of computer science of Chang Gung Memorial Hospital and Chang Gung University.<sup>[14]</sup>

The conventional OTset, which is a common functional training set applied to elderly individuals with dementia, includes a bean-string activity, coloration, paper cutting/folding, eye-hand coordination, and artistic creation (Figure3).

Baseline assessments were conducted upon entry into this study. Participants completed the training course over a 12-week period, wherein they attended two sessions per week for 45 minutes per session.

## 4. Statistical analyses

The independent variable was the multimodal intervention. Dependent variables included (1) cognitive functioning, which was determined based on the MMSE scores, and (2) behavioral outcomes, which were determined based on the CSDD and BEHAVE-AD.

Mann-Whitney U test was used to compare differences in age, body weight, body height, MMSE scores, and CDR scores because of the small sample size. The Fisher's exact test was conducted to compare the sex distribution and level of education in the two groups. The Wilcoxon signed-rank test was used to analyze the effect of the intervention on MMSE, CSDD and BEHAVE-AD scores. Furthermore, for the comparison of the intervention after each intervention between the two groups, the Mann-Whitney U test was applied. Statistical significance was set at  $p < 0.05$ . SPSS version 22.0 (IBM Corporation, Armonk, NY, USA) was used to process the data.

## RESULTS

The demographic data of all subjects are presented in Table 2. The results demonstrated no significant differences in age, body height, MMSE, CDR score, or level of education between the two groups (Table 2).

No statistically significant differences were evident in the MMSE or CSDD after intervention in either group (Table 3). For the behavior domain, the BG group demonstrated improvement in their BEHAVE-AD global

rating scores (pretest:  $1.55 \pm 1.04$ , posttest:  $0.82 \pm 0.75$ ;  $p=0.046$ ) after 12 weeks of training, but the improvement did not reach statistical significance in the OT group. In the BEHAVE-AD symptomatology scores, no statistically significant differences were found in either group (Table 3). Examination of the details of the BEHAVE-AD symptomatology scores revealed that there was a significant difference after training in aggressiveness between the BG and OT group (Table 4).

Table 1. Design of the cognitive game

Memory games	Short-term delay recall
	Animal naming
	Forward/backward digit span
Attention games	Number arranging
	Counting game
	Calculating game
	Color search
	Change blindness
Abstract games	Classification game
	Antonyms
Orientation games	Time and place
Naming games	Matching game
Execution games	Trail making test

Table 2. Demographic data for the participants before intervention

	BG (n=11)	OT (n = 12)	p-value
Age (Year)	$78.27 \pm 11.62$	$76.50 \pm 5.92$	0.324
Body Height (cm)	$156.78 \pm 11.79$	$150.40 \pm 6.91$	0.186
Body Weight (kg)	$64.12 \pm 9.50$	$57.09 \pm 6.90$	0.036*
MMSE (Score)	$15.36 \pm 7.75$	$16.50 \pm 4.17$	0.666
CDR (Score)	$1.09 \pm 0.49$	$0.83 \pm 0.25$	0.187
Sex			
Male	6	3	0.214
Female	5	9	
Level of education			
Uneducated	3	3	0.549
Elementary school	0	5	
Junior high school	3	2	
Senior high school	1	2	
College	2	0	

\* $p < 0.05$

Abbreviations: MMSE: Mini-Mental State Examination; CDR: Clinical Dementia Rating Scale scores.

Table 3. Effects of intervention on MMSE, CSDD and BEHAVE-AD scores

	BG				OT				between-group p-value
	pretest	posttest	difference	within-group p-value	pretest	posttest	difference	within-group p-value	
MMSE	15.36±7.75	17.09±7.34	1.73±5.04	0.384	16.50±4.17	16.08±3.70	-0.42±2.94	0.607	0.353
CSDD	8.18±6.15	6.64±4.20	-1.55±3.83	0.239	10.50±4.06	10.83±8.76	0.33±8.57	0.894	0.975
BEHAVE-AD									
Symptomatology scores	6.09±8.03	4.36±3.01	-1.73±8.56	0.766	12.00±9.18	16.25±18.09	4.25±15.23	0.609	0.805
Global rating	1.55±1.04	0.82±0.75	-0.73±1.01	0.046*	1.42±1.08	1.00±0.95	-0.42±0.79	0.096	0.433

\*p &lt; 0.05

Abbreviations: MMSE: Mini-Mental State Examination; CSDD: Cornell Scale for Depression in Dementia; BEHAVE-AD: Behavioral Symptoms in Alzheimer's Disease rating scale.



Figure 1. Training details of the BG group, mode one

Mode one uses a touch screen to operate the game: (A) flashcard, (B) 20 take 3, (C) phonic card discrimination, and (D) zookeeper.

Table 4. Effects of intervention on BEHAVE-AD symptom category scores

	BG				OT				between-group pvalue
	pretest	posttest	difference	within-group pvalue	pretest	posttest	difference	within-group pvalue	
Paranoid and delusional ideation	1.36±2.62	0.91±1.58	-0.45±2.21	0.684	3.50±4.60	4.50±5.99	1.00± 3.95	0.679	0.825
Hallucinations	0.18±0.60	0.27±0.65	0.09±0.94	0.785	1.25±1.76	1.67±3.42	0.42±3.15	0.893	0.587
Activity disturbances	0.55±1.81	0.82±1.25	0.27±1.49	0.581	0.83±1.75	1.33±2.23	0.50±2.58	0.598	0.708
Aggressiveness	1.18±1.99	0.36±0.92	-0.82±1.94	0.180	1.50±1.31	2.50±2.65	1.00±1.86	0.056	0.030*
Diurnal rhythm disturbances	0.55±1.04	0.45±0.82	-0.09±0.54	0.564	0.75±0.87	0.67±0.98	-0.08±1.00	0.763	0.735
Affective disturbances	0.55±0.93	0.27±0.47	-0.27±1.01	0.414	1.75±1.42	1.75±1.96	0.00±2.09	0.719	0.600
Anxieties and phobias	1.73±1.90	1.27±1.01	-0.45±2.25	0.723	2.42±1.56	3.83±3.97	1.42±3.58	0.280	0.399

\*p &lt; 0.05

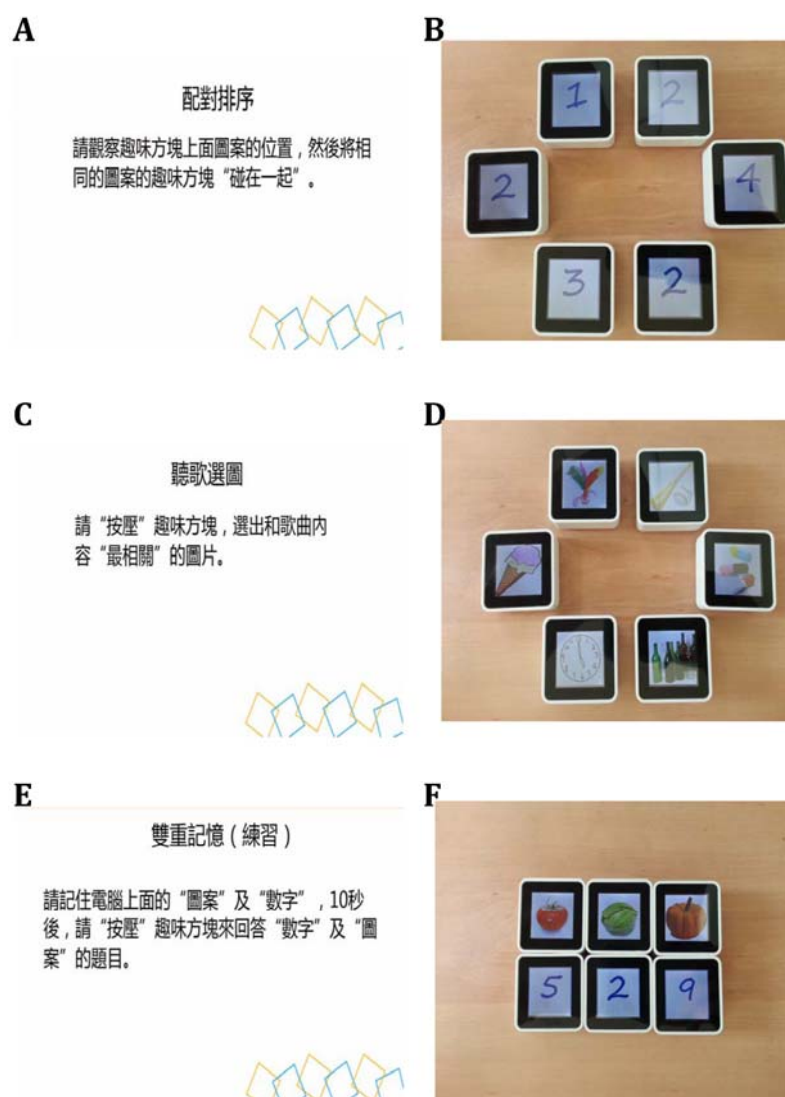


Figure 2. Example of training details in the BG group, mode two

Mode two uses fun cube to operate the game: (A) and (B) sequence match, (C) and (D) picture selection by songs, (E) and (F) picture and digital memory.





Figure 3. Example for conventional OT training program

(A) Bean-string activity, (B) eye-hand coordination, (C) puzzle, (D) coloration, and (E) paper cutting/folding.

## DISCUSSION

This study compared the effect of a traditional OT program and exergame in patients with Alzheimer's disease. Our results did not indicate statistically significant improvement or deterioration based on the MMSE or CSDD after 12 weeks of training. However, the global rating score improved after training in both the BG and OT groups but reached statistical significance only in the BG group.

Moreover, the BG group showed a trend in improvement in aggressiveness after 12 weeks of training than the OT group. To our knowledge, studies discussing the effects of exergames in the behavior domain are scarce. We may infer that both OT and BG had a mainte-

nance effect on the mental health of patients with AD. Furthermore, BG seemed to exert beneficial effects on the mental health of the participants.

### Treatment options for AD

AD is a progressive neurodegenerative disease. The current treatment paradigm is multifaceted for the treatment of the symptoms and to reduce the long-term clinical decline. There are two types of medications that are approved to treat AD, including cholinesterase inhibitors and N-methyl D-aspartate (NMDA) antagonists. However, these medications are effective in treating the symptoms without changing the progression of AD. Moreover, side effects of gastrointestinal and nervous systems have been reported.<sup>[4]</sup> Therefore, nonpharmacologic interventions and behavioral interventions are the first-line options for



reducing neuropsychiatric symptoms in AD.<sup>[15]</sup> Previous research has demonstrated that compared with only taking medications, patients who received an occupation-centered activity program composed of 60-minute sessions occurring 5 times per week for 12 weeks had better improvement of MMSE, fall-related factors, and quality of life.<sup>[8]</sup> Moreover, one study demonstrated that OT was effective in slowing cognitive decline; specifically, its effectiveness seemed to be proportional to the number of hours of OT that were received.<sup>[16]</sup> In contrast, a meta-analysis demonstrated conflicting results, and the overall effect of OT intervention did not reach statistical significance in improving quality of life for patients with dementia.<sup>[17]</sup> In our study, no significant improvement in the MMSE score was noted after 12 weeks of training in the OT group. A possible explanation may be the lower frequency and intensity (twice a week and 45 minutes per session) of our OT program compared to a previous study.<sup>[8]</sup>

### Exergame for AD

With the advancement of technology, exergames may offer a novel strategy for improving cognitive function. Previous research has shown that a cognitive training program of 5 days a week at 15 to 20 minutes a day for six months, which included reading and arithmetic tasks, could improve the MMSE in AD patients.<sup>[18]</sup> Hwang et al. found that a daily program of using a “computer-assisted cognitive rehabilitation” could delay memory deterioration in patients with AD.<sup>[19]</sup> Moreover, Savulich et al. found that memory games on an iPad produced high levels of enjoyment and motivation that were maintained throughout all hours of game play and improved episodic memory (memories of locations and events) compared with patients who attended the clinic as usual.<sup>[20]</sup>

Several exergames are available on the market, such as Super Mario Bros (SMB) and the Xbox Kinect. Research has demonstrated that the benefits of the action videogame, Super Mario Bros seem broader than those from the Kawashima Brain Training program. The variability, task difficulty, and elicited motivation and arousal of SMB may partly explain the cognitive improvement.<sup>[21]</sup> Furthermore, six weeks of Xbox 360 Kinect cognitive game training could also improve the slowness and

complexity of electroencephalography and cognitive functions in older subjects with mild cognitive impairment.<sup>[22]</sup>

### Community- or hospital-based setting

A systemic review found that half of the exergame interventions were performed in the community, and the remaining interventions were conducted in hospitals, rehabilitation wards, or nursing homes, thus indicating that exergaming interventions could be implemented in both environments, and may be more suitable in a community setting.<sup>[13]</sup> In the present study, although we provided free daycare programs at our hospital-based dementia center in a suburban area, most of the participants could only be brought to our center 2 days per week by their caregivers. Therefore, the availability of the exergames seemed to be a challenge of the daycare program for patients with AD. Thus, after proper education of the family or caregiver, the exergame may be a good candidate for community-based cognitive training.

### Limitation

The following limitations were present in our study: (1) participants were limited to small numbers of elderly people with mild to moderate AD in both groups; (2) the participants were randomly assigned to groups, rather than case-matched; and (3) recruitment of participants with AD is very difficult, and the small number of cases in this study may have been insufficient to demonstrate significance. Therefore, the results may not be generalizable to all patients with AD or elderly individuals with minimal cognitive impairment. Future research should undertake a case-matched study of elderly individuals with various levels of cognitive impairment.

## CONCLUSION

BG can improve mental health and preserve cognitive function; additionally, it is a suitable rehabilitation program for patients with mild to moderate AD. Therefore, we propose exergames has a potential to serve as a rehabilitation program for patients with AD.

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## CONFLICT OF INTERESTS STATEMENT

The authors declare that there are no conflicts of interest.

## REFERENCE

1. R. O. C. Demographic Indicators: Percentage of Population for Age 65 and Over. Taiwan's Ministry of the Interior. 2020 Available at: <https://www.moi.gov.tw/cp.aspx?n=602>
2. Prince M, Bryce R, Albanese E, et al. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement* 2013;9:63-75.e2.
3. Sturm VE, Yokoyama JS, Seeley WW, et al. Heightened emotional contagion in mild cognitive impairment and Alzheimer's disease is associated with temporal lobe degeneration. *Proc Natl Acad Sci USA* 2013;110:9944-9.
4. Breijyeh Z, Karaman R. Comprehensive Review on Alzheimer's Disease: Causes and Treatment. *Molecules* 2020;25:5789.
5. Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: a review of an emerging area of research. *Gait and posture* 2002;16:1-14.
6. Pettersson AF, Olsson E, Wahlund LO. Motor function in subjects with mild cognitive impairment and early Alzheimer's disease. *Dement Geriatr Cogn Disord* 2005;19:299-304.
7. Kumar P, Tiwari SC, Dey AB, et al. Occupational therapy improve the quality of life for older people with mild to moderate dementia in a memory clinic. *J Am Geriatr Soc* 2012;60:S-69.
8. Kim KU, Kim SH, Oh HW. The effects of occupation-centered activity program on fall-related factors and quality of life in patients with dementia. *J Phys Ther Sci* 2017;29:1188-91.
9. Small field S, Heckenlaible C. Effectiveness of Occupational Therapy Interventions to Enhance Occupational Performance for Adults With Alzheimer's Disease and Related Major Neurocognitive Disorders: A Systematic Review. *Am J Occup Ther* 2017;71:7105180010p1-9.
10. Cohen GD, Firth KM, Biddle S, et al. The first therapeutic game specifically designed and evaluated for Alzheimer's disease. *Am J Alzheimers Dis Other Dement* 2008;23:540-51.
11. Gao Y, Mandryk RL. The acute cognitive benefits of casual exergame play. *Proc SIGCHI Conf Hum Factor Comput Syst (CHI '12)*. Association for Computing Machinery, NY USA 2012;1863-72.
12. Stanmore E, Stubbs B, Vancampfort D, et al. The effect of active video games on cognitive functioning in clinical and non-clinical populations: A meta-analysis of randomized controlled trials. *Neurosci Biobehav Rev* 2017;78:34-43.
13. Zhao Y, Feng H, Wu X, et al. Effectiveness of Exergaming in Improving Cognitive and Physical Function in People With Mild Cognitive Impairment or Dementia: Systematic Review. *JMIR Serious Games*. 2020;8:e16841.
14. Zhang T, Lin CC, Yu TC, et al. Fun cube based brain gym cognitive function assessment system. *Comput Biol Med* 2017;84:1-8.
15. Atri A. The Alzheimer's Disease Clinical Spectrum: Diagnosis and Management. *Med Clin North Am* 2019;103:263-93.
16. Peralta P, Gascón A, Latorre E. Occupational Therapy Prevents Cognitive Impairment on Long-Term Care Residents. *Phys Occup Ther Geriatr* 2017;35:119-31.
17. Ojagbemi A, Owolabi M. Do occupational therapy interventions improve quality of life in persons with dementia? A meta-analysis with implications for future directions. *Psycho geriatrics* 2017;17:133-41.
18. Kawashima R. Mental exercises for cognitive function: clinical evidence. *J Prev Med Public Health* 2013;46:S22-7.
19. Hwang JH, Cha HG, Cho YS, et al. The effects of computer-assisted cognitive rehabilitation on Alzheimer's dementia patients memories. *J Phys Ther Sci* 2015;27:2921-23.
20. Savulich G, Piercy T, Fox C, et al. Cognitive Training Using a Novel Memory Game on an iPad in Patients with Amnesic Mild Cognitive Impairment (aMCI). *Int J Neuropsychopharmacol* 2017;20:624-33.

21. Perrot A, Maillot P, Hartley A. Cognitive Training Game Versus Action Videogame: Effects on Cognitive Functions in Older Adults. *Games Health J* 2019;8:35-40.
22. Amjad I, Toor H, Niazi IK, et al. Xbox 360 Kinect

Cognitive Games Improve Slowness, Complexity of EEG, and Cognitive Functions in Subjects with Mild Cognitive Impairment: A Randomized Control Trial. *Games Health J* 2019;8:144-52.