Feasibility study of the *BrightBrainer*™ integrative cognitive rehabilitation system for elderly with dementia

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Abstract

Purpose—To describe the development of BrightBrainer™ integrative cognitive rehabilitation system and determine clinical feasibility with nursing home-bound dementia patients.

Method—BrightBrainer cognitive rehabilitation simulations were first played uni-manually, then bimanually. Participants sat in front of a laptop and interacted through a game controller that measured hand movements in 3D, as well as flexion of both index fingers. Interactive serious games were designed to improve basic and complex attention (concentration, short-term memory, dual tasking), memory recall, executive functioning and emotional well-being. Individual simulations adapted automatically to each participant's level of motor functioning. The system underwent feasibility trials spanning 16 sessions over 8 weeks. Participants were evaluated pre- and post-intervention, using standardized neuropsychological measures. Computerized measures of movement repetitions and task performance were stored on a remote server.

Results—Group analysis for 10 participants showed statistically significant improvement in decision making ($p<0.01$), with trend improvements in depression ($p<0.056$). Improvements were also seen in processing speed ($p<0.13$) and auditory attention ($p<0.17$); however, these were not statistically significant (partly attributable to the modest sample size). Eight of nine neuropsychological tests showed changes in the improvement direction indicating an effective rehabilitation ($p<0.01$). BrightBrainer technology was well tolerated with mean satisfaction ratings of 4.9/5.0 across participants.

Conclusions—Preliminary findings demonstrate utility within an advanced dementia population, suggesting that it will be beneficial to evaluate BrightBrainer through controlled clinical trials and to investigate its application in other clinical populations.

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Introduction

Alzheimer's disease (AD) is an insidious degenerative disorder marked by progressive memory loss and neurocognitive decline that leads to eventual social and occupational impairment. Population estimates suggest that approximately 5.2 million Americans have AD with about 200 000 below the age of 65 and the remaining above. Forecasting suggests an increase to about 10 million Americans with AD in the coming decades and eventually reaching 13.8 million by year 2050 [1]. AD is the sixth leading cause of death in the United States and the fifth leading cause of death for Americans over the age of 65; a projected 450 000 older Americans will die from AD-related complications in 2013. According to the American Alzheimer's Association, AD is the only cause of death among the top 10 in America without a way to prevent it, cure it or even slow its progression. The economic impact is no less harrowing with associated care costs of about $203 billion for a given year.

Recently proposed guidelines from the National Institute on Aging [2] for the diagnosis of dementia due to Alzheimer's disease describe three distinct stages of AD progression: (1) pre-clinical AD, which can begin 20 plus years before symptom expression; (2) mild cognitive impairment (MCI) due to AD; (3) eventually the third stage of dementia due to AD. This lengthy period of decline allows for opportunities to intervene and possibly disrupt the degenerative course.

To date, the primary form of AD symptom management is achieved via poly-pharmacy in the form of medications to address behavioral (e.g. agitation, depression) and cognitive symptoms (e.g. alertness, memory). Despite the alternative behavioral and psychological management techniques of aggression, agitation and psychosis, pharmacological approaches (involving atypical antipsychotic) are used as the first-line treatment [3,4]. Symptomatic treatment of cognitive dysfunction is typically achieved through the use of acetylcholinesterase inhibitor (e.g. Rivastigmine, Donepezil) and glutamate receptor antagonists (e.g. Memantine). Although there are no clinically approved AD interventions that can be classified as neuro-protective or disease modifying [5], early therapeutic interventions can be effective in improving cognitive function, treating depression, improving caregiver mood and delaying institutionalization. Since AD is a progressive disease, therapies change with the patient's disease stage, however after stage 2 AD patients are generally admitted in skilled nursing facilities (SNFs or nursing homes).

Virtual rehabilitation has been shown to increase aspects of attention and motivation [6], leading pioneering researchers to explore its use as a neurodiagnostic and cognitive rehabilitation tool. As noted by Rizzo and Bockwalter [7] in their early state-of-the-art review, an important question that needed to be answered first was whether persons with cognitive impairments can learn how to navigate and interact within virtual environments. By 2011, Cherniack [8] noted in his literature review that VR had become a promising

modality to diagnose and provide new rehabilitation interventions for neurologic and cognitive disorders in the elderly. Cushman et al. [9], for example, showed in a controlled study that a test of navigation in VR was capable of differentiating older normal controls from those with MCI and from those with early-stage AD. This exemplifies VR potential as a diagnostic tool of cognitive impairment. As far as therapy, a very recent control study used route finding training in a virtual city on patients with focal brain lesions, who showed deficits in spatial orientation, and on neurologic healthy controls [10]. Results showed that both groups improved in different aspects of spatial ability, including route finding. VR therapy has also been used to re-train activities of daily living in patients with dementia, such as shopping at a supermarket [11].

Prior research utilized VR for assessment and cognitive rehabilitation of individuals with MCI or with early-stage AD. By contrast, Burdea and his group performed a feasibility study of integrative VR (cognitive and motor rehabilitation) on patients with *advance-stage* AD who were residents of an SNF dementia ward [12]. Unlike other studies which utilized a keyboard or joystick as the patient's interface with the simulation, this feasibility study employed the novel BrightArm rehabilitation table [13]. While the system was rather complex (low-friction motorized tilting table, computerized forearm support with grasp sensing, vision tracking and TV display), the three participants were able to utilize the BrightArm system while assisted by an occupational therapist. They progressed in various custom simulations and the participant with advanced AD showed substantial improvement in her affective state.

Bright Cloud International (a spinoff of Rutgers University, Highland Park, NJ) has been developing the *BrightBrainer* as a compact and portable follow-up to the BrightArm. This article presents the design characteristics of the BrightBrainer, as well as its evaluation protocol and first feasibility study on a group of 10 older adults. These were residents of Roosevelt Care Center, a 420-bed SNF located in Edison, NJ.

Methods

The BrightBrainer integrative cognitive therapy system

The BrightBrainer system, shown in Figure 1a, consisted of a computer, a bimanual game controller, a remote clinical server and a library of custom-designed integrative cognitive simulations.

The bimanual game controller—The BrightBrainer utilised the Razer Hydra bimanual controller [14] consisting of a source, two-wired pendants and USB communication with the computer rendering the simulations. The source was stationary on the table, while the pendants were held by the participants. Each pendant (see detail in Figure 1b) was a lightweight plastic ergonomic enclosure with antenae and wires to the source, as well as several buttons and switches. BrightBrainer utilised an analog trigger-like switch on which study participants placed their index finger. This allowed the system to detect the degree of flexion/extension of the index in each hand. This was utilized in the games as part of avatar control or for dual-tasking settings. The source created a low-intensity magnetic field that induced voltages in the pendant antenae proportional with their

distance and orientation versus the source. In order to measure them correctly, the pendants had to be first placed on the source support base as a calibration method. Each pendant was sampled at 125 readings/second, a frequency sufficient to allow real-time control of the game avatars.

The table supporting the BrightBrainer had to be selected to minimize metal content that would have otherwise interfered with the pendant readings. Participants sat in a chair facing the computer, or in a wheelchair for those who were using it for mobility.

The computer was an HP Pavilion dv7t-7000 Quad Edition Entertainment Notebook, running Windows 7 (64 bit) operating system. It processed the game controller data to track the participant's arm and index movement, rendered real-time game graphics and interactive sound, and automatically stored game data during each therapy session. In order to achieve real-time processing of the controller data, game rendering, file management and internet communication, the laptop used a quad-core 2.3 GHz Intel Core i7 CPU. While the i7 had its own embedded graphics hardware, this hardware was considered insufficient for the quality of graphics to be provided by BrightBrainer. Instead real-time graphics were rendered by a mid-range NVIDIA GeForce GT 650 M graphics card with 2 GB of graphics memory (embedded with the laptop). Graphics were presented on the laptop 17.3 inches display with 1920×1080 pixel resolution. This high resolution gave participants good detail of the virtual scene and contributed to their sense of immersion in the therapeutic games.

Remote clinical server—After the completion of each rehabilitation session, game data were uploaded via a dedicated Internet connection to a remote clinical server for storage and subsequent analysis. Data were stored in an MySQL database [15] via a custom-designed Python application which read and parsed the output files of the games.

Custom rehabilitation games—Unlike off-the-shelf games, BrightBrainer had the ability to adapt to each participant's motor capabilities each day. This adaptation was based on arm reach and index excursion baselines performed at the start of each therapy session. The therapy games could be played either in unimanual or bimanual modes.

Arm reach baseline was done one-arm-at-a-time, by asking the participant to draw a circle either on a horizontal sheet of virtual paper (for reaching horizontally), or on a virtual black board (for reach in the vertical plane) (Figure 2). Baseline software then placed rectangles that were maximally enclosed in the circles, and the rectangles mapped to the full dimensions of the game scenes. Instead of one-to-one mapping between physical arm and avatar movements, the system used mapping that was arm specific. This method was initially used by precursor technology developed at Rutgers University for patients with arm and hand spasticity [16].

Arm reach baselines were immediately followed by index baselines. Unlike arm baselines, both index finger ranges were baselined at the same time. As seen in Figure 2c, the participants saw two spheres that moved vertically between target blocks, in proportion with the index physical movement on each pendant trigger. First, the participants were instructed to flex, and the two balls moved up a certain percentage of full range. Subsequently, the

participants were asked to extend the index of each hand and the balls moved down, again a certain percentage of full range. The resulting range for the index fingers were then mapped to the hand avatars that would flex when the trigger buttons had been pressed, and extend when the participants had extended their index fingers.

Games to train focusing—Three games were developed to train patient's ability to focus.

Breakout 3D game was an adaptation of the game developed earlier by this group for unimanual training of stroke survivors on the BrightArm system [13]. The scene (Figure 3a) depicted an island with an array of crates placed in a forest clearing. The crates could be located on the side of the clearing furthest away from the participant or in the center of the island. Two paddle avatars of different colors were each controlled by one of the participant's hands. Depending on the location of the crates on the island, the predominant arm movements were left–right (crates away from the participant), or in–out movements (crates in the center of the island). The participant needed to bounce a ball with either paddle, so to keep it in play, and attempt to destroy all the crates. The sound of waves was added to help the participants relax. The difficulty of the game was modulated by the speed of the ball, the size of the paddles and the number of crates to be destroyed in the allowed time. The difficulty was further increased by adding a dual-tasking condition, namely the requirement to press the trigger at the moment of bounce. If the pendant trigger had not been pressed in time, the ball passed through the virtual paddle avatar and became lost. The game score was calculated as

$$Score = (if\ bimanual: 1.25,\ else: 1) \times Hits \times \left(\frac{Ball\ Speed}{Paddel\ Length} \right) \times \left(\frac{1}{log\ (Misses+2)} \right)$$

where *Hits* represented the number of crates destroyed, *Ball Speed* was the speed of the ball, *Paddle Length* was the length of the paddle avatars. The games became more difficult and thus the score increased with more crates to be destroyed, faster balls and smaller paddle avatars. The score decreased logarithmically with more balls lost, and a 2 was added to prevent artifacts when no balls had been lost (division by 0). Logarithm is used to lessen the impact of a game with an unusual number of mistakes has on the overall game averages. Furthermore, it was estimated that bimanual play tends to increase the difficulty for participants somewhere between 0 and 50%. Consequently, a 25% bonus was given for games that had been played in bimanual mode.

The *Kites* game presented two kites flying over water, while the sound of wind was played (Figure 3b). One kite was green and the other was red, and they had to be piloted through like-colored target circles. The circles alternated randomly in their color and their position on the screen, while remaining in one horizontal plane. The difficulty of the game was modulated by the speed of the circles, the duration of the game, the visibility (a foggy sky gave participants less time to react) and the presence of air turbulence (as a disturbance). The game determined the percentage of targets entered versus those available, and displayed

it at the end of the game as summative feedback on performance. Furthermore, the game software determined an overall performance score, given by the formula:

$$Score = (if \ bimanual: 1.25, else: 1) \times Ring \ Frequency \times 100 \times \frac{(Rings - 1.2 \times Errors - Misses)}{Rings}$$

where *Ring Frequency* was the number of targets rings per second, which was multiplied by a weighted percentage of rings successfully flown through. This weight was the result of the total target rings (*Rings*) minus 1.2, the number of rings that had been flown through with the wrong kite (*Errors*) and further subtracted by the number of target rings missed. The above weight was then divided by the total number of rings. Note, the weighting for errors is greater than that of misses to penalize for the strategy of flying two kites together in unison, which greatly simplifies the complexity of playing the game in bimanual mode. A 25% score bonus was given if the game had been played in the bimanual mode, similar to the scoring of *Breakout 3D*.

Musical Drums was the third game to train focusing. It presented a scene with a number of drums, two mallets controlled by the participant's arms and notes which scrolled across the screen (Figure 3c). The musical notes changed color from red to green the moment they overlapped the drums, indicating the time to hit them with the mallets had come. If the notes were not hit in time, and passed the drums, an error was recorded. The difficulty of the game increased with the beat of the song (faster scrolling notes), and the number of drums was 1 or 2 drums per arm (more locations to watch). At the end of the *Musical Drums* game, BrightBrainer displayed the percentage of notes hit as a summative feedback of performance. The game score was computed as

$$Score = (if \ bimanual: 1.25, else: 1) \times (0.4 + 0.6 \times Number \ of \ Drums) \times Percent \ Notes \ Hit$$

The number of drums factor is scaled down by 0.6 and added to a bias of 0.4 so that the increased weight from a second drum (0.6) is a little more than half the weight from a single drum (1.0). This estimate for increased difficulty is used to scale the percentage of notes correctly hit. Finally, the score was increased by the same 25% bonus when the game was played in the bimanual mode (as above).

Games to train memory—The participants played two such games, one for short-term memory and the other for delayed recall (long-term memory).

Card Island trained short-term visual memory and focusing using an array of cards arranged face down on the sand of an island (Figure 3d). The participants were asked to pair them by turning cards face up by overlapping their hand avatars over cards and simultaneously pressing the pendant trigger. Each hand avatar was allowed to move over half of the island, corresponding to half of the initial card array. Card pairs were randomly placed, such that they could be on one side of the divide or across it. Once a card had been seen by the patient, when it turned face down again, its back pattern color changed to provide a memory cue. If two subsequent cards matched they disappeared from the island, otherwise the cards turned

face down, and had to be paired again. The game ended when all cards were paired (no cards left on the island), or the allowed time elapsed. Game difficulty was increased with the number of cards to be paired and variety was created by a number of card arrays made up of different sets (pets, fruits or food items). The *Card Island* game was scored with the formula:

$$Score = (if\ bimanual:1.25,\ else:1) \times 10 \times \left(Matches - \frac{Mistakes}{6}\right) \times \left(\frac{1}{log\ (Duration)}\right)$$

As above, the bonus is 25% for bimanual play and the scalar multiplier of 10 was heuristically set so that scores typically have double-digit values. The penalty for *Mistakes* was set to 1/6 of the benefit for correct *Matches* based on empirical evidence, which suggests 17% accuracy tends to be a lower performance bound. By design, scores are kept positive to limit the effect a single game poor performance has on the overall game averages. Similarly, the logarithm of *Duration* time was employed to limit the impact of a particularly fast or slow solution time (due to chance) had on the overall game averages.

Participants' long-term visual and auditory memory (delayed recall) was trained by *Remember that Card* (Figure 3e). The game consisted of two parts interspaced by other games the participants had to play. During the first part of the game, the participants had to inspect a number of cards arrayed in a forest clearing face down. They used the pendants to turn the cards face up in a manner similar to that used in *Card Island* game. This time however once a card had been turned face up, a corresponding sound was played. For example, if a card depicted a cow, then a "Moooo" sound was played, if the card showed a cat, then the sound played was "Meow" and so on. Once a card had been turned face up, it remained so, and it played the corresponding sound every time the hand avatar overlapped it. The participants were instructed to select one of the cards by placing the hand avatar over it and squeezing the pendant trigger. After a number of other games had been played, the participants were presented with the second part of the *Remember that Card* game. During this phase, they saw the array of cards, this time arranged face up, and had to remember and select the card originally selected. The difficulty of the game increased with the number of cards (choices) as well as the number of other games to be played before the card selection occurred. The game scored participant's performance with the formula:

$$Score = (if\ bimanual:1.25,\ else:1) \times \frac{\{Deck\ Size \times (Correct\ Pick + 1) \times Intermission\ Duration\}}{60}$$

The *Deck Size* represented the number of card choices, and *Intermission Duration* is the length of time (in seconds) separating the two parts of the game. This was converted to minutes by division by 60. *Correct Pick* was a binary number, 0 when the participant did not remember the card that had been selected in the first part of the game and 1 when the selection was correct. A 1 was added to *Correct Pick* to prevent 0 scores. Otherwise, all incorrect picks will be assigned the same 0 score independent of the level of difficulty (i.e. *Deck Size* and *Intermission Duration*). Finally, the participants were awarded a 25% bonus if they played in bimanual mode.

Game to train decision making and problem solving (executive function)—
Participants played the *Pick-and-Place* game which was asking them to pick up a virtual ball
and follow a prescribed ideal path to a target, while the actual arm movement was traced in
real time (Figure 3f). Dual tasking was implemented at increased levels of difficulty by
requiring the maintenance of grasp on the pendant trigger en route to the target, lest the ball
fell from the hand avatar and had to be picked up again. Difficulty was further increased by
requiring that the participants pick the ball matching the color of the target from among two
or three balls available. Finally, the ideal path guide to the target was removed in the last
weeks of therapy. The score of the game was calculated to reflect these multiple game
settings as:

$$
\begin{aligned}
Score = &((if\ bimanual{:}1.25,\ else{:}1) \\
&+ (if\ Multiple\ Pickup\ Possibilities{:}0.2,\ else{:}0) + (if\ Guide\ Shown{:}0,\ else{:}0.2) + (if\ Grasp\ Required{:}0.2,\ else{:}0)) \\
&\times \frac{15}{log\,(Averge\ Pick\ Time + Averge\ Drop\ Time)}
\end{aligned}
$$

The score increased by 25% if the game had been played in bimanual mode (which allowed
both hands to pick up and transport balls simultaneously). There are incremental offsets to
the bimanual weighting to account for increased difficulty: selecting from multiple balls
(0.2), the lack of visual cues to direct ball movement (0.2) and whether grasp is required to
pick up a ball (0.2). The scalar multiplier of 15 was heuristically set so that scores typically
have double-digit values. Scores are inversely proportional to the logarithm of the sum of
time to select and pick the ball, then transport it to the target. Thus, participants who took
longer time to pick up the ball and/or transport it to the target received smaller scores.
Similar to *Card Island*, logarithm is employed to limit the effect of unusual performance
times (good or bad) on the overall average scores.

Each of the games included a summary of performance feedback once completed, and
rewards if the game had been won. These rewards were visual (fireworks, congratulatory
text) and auditory (applause, cheering), provided positive reinforcement and were meant as
morale boosters.

Feasibility study design—A feasibility evaluation was conducted in order to gauge
the clinical effect and the participants' acceptance of the BrightBrainer system and therapy in
a sample of institutionalized dementia patients. The inclusion criteria for this study specified
residency in an SNF, cognitive deficits subsequent to dementia, traumatic brain injury, or
stroke, absence of severe visual deficits and absence of severe upper extremity motor deficits
so as to be able to hold and move the BrightBrainer pendants.

Exclusion criteria were total lack of active movement in either arms, blindness, or severe
cognitive delay. All participants were residents of Roosevelt Care Center and received
medical clearance from their treating physicians for participation. All potential subjects had
the opportunity to review and discuss the study with an investigator on the research team.
Subsequently, eight residents were recruited and subsequently self-consented using a form
approved by the Western Institutional Review Board (an independent board overseeing

research involving human subjects) which reviewed and approved this feasibility study in accordance with Federal Guidelines. Two additional residents gave assent, and they were consented by their legally authorized representatives. The BrightBrainer system was subsequently installed at the Center in a dedicated room and then pre-tested for usability by three healthy volunteers (age 64–68). Subsequently, the 10 residents underwent integrative cognitive rehabilitation on the BrightBrainer in Summer 2013. None dropped from study and all completed the experimental therapy.

Participants characteristics

The vital statistics, depression level, cognitive state, co-morbidities, ambulation, education and language primarily spoken by the 10 participants are summarized in Table 1 (parts 1 and 2). Participant pool was comprised of three females and seven males between the ages of 55 and 73 (M/SD = 63.4/6.04 years). Ethnically, there were two African-American participants (all male) and eight Caucasians (among them 3 female). Seven participants were diagnosed with dementia in the community while two of the remaining three sustained cerebral vascular accidents and the last was admitted secondary to failure to thrive. Depression levels varied among participants, with one expressing moderate levels of depression (initial score 20), one expressing mild levels of depression (initial score 16), six endorsing minimal depression (initial scores 13, 11, 3, 2, 7 and 8), and two denied depression altogether (initial score 0). The participants' education levels varied and ranged from eight grade to completing university (M/SD=12.4/3.37 years in school). One participant had completed grade school, five completed high school, two attended some college and two had graduated college. Nine were native English speakers and one was not (bilingual in Spanish and English). Testing procedure integrity was maintained through the use of a research assistant fluent in Spanish. All participants had multiple medical problems, their co-morbidities are listed in Table 1 (part 2). Three participants ambulated via wheelchairs, one with a rolling walker and the rest independently.

Data collection instruments—The feasibility study used an ABA protocol, data being collected pre- (A), during training (B) and post-trials (A). Therapy consisted of 16 sessions over eight weeks, with each participant attending two rehabilitation sessions per week. Rehabilitation session data consisted of arm reach and index range baselines, heart rate and blood pressure, number of repetitions for each arm, as well as game performance data collected during play. At the end of the eight weeks of training, participants rated their experience on a subjective evaluation paper questionnaire with nine questions and free form comments. Ratings ranged from 1 (least desirable outcome) to 5 (most desirable one).

The pre- and post-intervention evaluation sessions involved data collection of neuropsychological measures of attention/concentration, processing speed, learning, memory and executive functioning by a neuropsychologist consultant. He was blinded to the therapy methodology, scope and any pre-diagnosis of dementia the participants might have received.

Standardized neuropsychological measures used were the Beck Depression Inventory, Revised [17], the Neuropsychological Assessment Battery, Attention Module (Orientation,

Digit Span and Dots) and Executive Functioning Module (Generation subtest) [18], the Hopkins Verbal Learning Test, Revised [19], the Brief Visuospatial Memory Test, Revised [20] and the Trail Making Test [21]. Alternate test forms were used whenever possible to minimize test-taking practice effect. Raw scores were utilized in all data analysis.

Experimental protocol—At the start of each session, the participants underwent baseline measurements, which included the reach of each arm, index fingers extension/ flexion and blood pressure and pulse rate. The duration of the BrightBrainer therapy increased from 20 min of actual play per session in weeks 1 and 2, to 25 min in week 3 and 4, to 30 min (weeks 4 and 6) and 40 min in the last two weeks of rehabilitation.

Session training intensity was similarly increased, primarily by switching from unimanual interaction (first 4 weeks) to bimanual play (last 4 weeks). During each session, the participants played a sequence of the games described earlier, which was repeated as needed to achieve the prescribed session duration for that week. The difficulty of each exercise was progressively increased from easier games with no required pushing of the pendant trigger in weeks 1 and 2, to most difficult ones requiring sustained grasping in weeks 7 and 8. Each game difficulty was progressively increased by adjusting game parameters, for example the speed of balls in *Breakout 3D* or the number of cards to be paired in *Card Island*.

Statistical methods—Comparisons of continuous variables pre-to-post were done by paired t-tests. For emotive outcomes, a negative difference means a lower degree of depression. Reduction in depression is a positive outcome. With the exception of depression scores, results were transformed so that the larger the mean difference the more positive the finding. p Values less than 0.05 were deemed statistically significant; no multiple-testing adjustment was done. Results are expressed as 95% confidence intervals to document the precision of all statistical estimates. In addition to test individual variables for the significance of the magnitude of improvement over time, a non-parametric sign test was employed to determine if the number of tests which showed improvement yielded a statistically significant result. Although low power makes negative statement less reliable, any positive statistically significant findings imply the findings are robust and not obscured by the small sample size. All analyses were conducted using SAS 9.3 (SAS Institute, Inc., Cary, NC) [22].

Results

Participants' emotive and cognitive outcomes

Demographic characteristics of the total sample are presented in Table 2. Paired t-tests were used in the comparison across testing sessions (pre-intervention versus post-intervention). Testing variables included emotive assessment and neuropsychological measures of attention, processing speed, memory and executive functioning (as measured by the aforementioned neuropsychological instruments). Statistically significant improvement was seen on one measure of executive functioning (Word Generation) ($t(9)=-3.29$, $p=0.009$). The Beck Depression Inventory, 2nd Ed. ($t(9)=2.20$, $p=0.056$), The Trail Making Test A ($t(9)=-1.68$, $p=0.125$) and the NAB Digits Forward test ($t(9)=-1.48$, $p=0.17$) did not reach statistical significance; however, the sign of the score changes was in the hypothesized

direction. The Trail Making Test B (t(9)=−1.03, p=0.331), Dots (t(9)=−0.77, p=0.462), NAB Digits Backwards (t(9)=0.63, p=0.541), BVMT-R Trials 1–3 (t(9)=−0.26, p=0.799), and HVLT-R Trials 1–3 (t(9)=−0.07, p=0.943) were not statistically significant. Eight out of nine individual tests demonstrated mean gains in the direction of improvement (p=0.01).

Arm repetitions

The tracking capability of the BrightBrainer pendants was used in BCI proprietary software that measured, as a secondary outcome, the number of repetitions induced with each simulation. These repetitions were added to determine the total number of repetitions for each arm and therapy session. Subsequently, participant-specific data were averaged to obtain the group movement repetitions for a given session, and plotted over the 16 therapy sessions (Figure 4). Participants started in unimanual mode using their dominant arm (right arm for 9 participants and left arm for the remaining one). Thus, the graph is flat at 0 repetitions for the recessive arm until session 9, while for the dominant arm there is a steady increase in average number of repetitions from about 50 at the start of training to about 230 at midpoint through the intervention. This is explained by the progressive increase in session time as well as game difficulty (with corresponding higher scores). With increased difficulty came an increase in the standard deviation of repetitions, indicating that the group performed less uniformly. For the second half of training, interaction mode switched to bimanual and there was a steady increase in the number of repetitions in the non-dominant arm. This corresponded to a momentary reduction in the repetitions of the dominant arm, possibly because now both arms contributed to the interaction. Eventually, the dominant arm increased its repetition to an average of 300 per session, similar to the number for the recessive arm. This is indicative of equal contributions by both arms in the simulated tasks, coupled with an even larger standard deviation for the last 2 weeks of training.

A survey has been done on the number of repetitions during outpatient physical therapy and occupational therapy for stroke survivors [23]. Researchers observed an average of upper extremity repetitions per session of 39 for active-exercise movements, 34 for passive-exercise movements and 12 for purposeful movements (total 85 arm repetitions). In a subsequent, larger observational study (312 PT or OT sessions observed, versus 38 in the first study) [24], the same team counted 32 repetitions for the upper extremity. The number of repetitions induced in BrightBrainer was substantially larger than the number of repetitions observed in the above studies. With 300 repetitions for *each arm* (600 total upper extremity repetitions), BrightBrainer induced 1875% more active repetitions than in a conventional physical or occupational therapy session.

Blood pressure and pulse were taken just before and at the end of each session. Despite the increase in physical exertion, and longer immersion in the synthetic world, participants did not exhibit a substantial increase in either blood pressure or pulse rate as a consequence of their play.

Participants' game performance

Performance as measured by game scores was another secondary outcome. Similar to arm repetitions, the participants' scores for a particular game and session were averaged and the

standard deviation calculated for the group. This was done for all sessions except the first two ones, where game data were not stored. Authors were concerned that the first two sessions may be more affected by learning effects (learning the system), thus they choose not to take the first two sessions into consideration. The graphs in Figure 5 show participants' progress over the rest of the intervention. *Pick-and-Place* was a game introduced later in the training, so its graph is only for sessions 7 to 16.

It can be seen that progress was different for each game, but that there was a general upward trend indicating better game abilities for the participants. Another common trend seems to be an increase in the score standard deviation toward the end of the intervention. Again this is indicative of a less-uniform group performance, with some participants being able to cope with the corresponding increase in game difficulty and others not. A further observation is that the increase in game scores was not linear, and that there were momentary reductions in scores. This corresponded with a modification of game parameters when the difficulty was set to the next (higher) level. For example, in *Pick-and-Place*, which trains executive function, once the game switched from unimanual to bimanual interaction in session 9, there was a reduction in performance due to increased cognitive load. Subsequently, after participants adapted to the need for split attention, their performance improved, even when cognitive aides (lines between balls and matching color targets) were removed in the last two weeks of therapy.

Participants' subjective evaluation of the BrightBrainer system

Participants were given the opportunity to rate the BrightBrainer prototype at the end of the intervention. All participants filled the numerical portion of the subjective evaluation form and 8 wrote free-form comments. They gave the BrightBrainer prototype an overall score of 4.52 out of 5. The statements "I would encourage another patient to use it", and "I liked the system overall". received almost perfect scores (4.95). This reflects a high degree of technology acceptance by the participants, which was one of the aims of the feasibility study. Even though the therapy sessions were intensive, and lasted up to 40 min, the participants practiced without complaining, or leaving the room. Participants scored lowest (3.11) the statement "There were few technical problems", followed by the length of exercising in a day (4.05).

Nurses felt that the participants were excited about the trials and were disappointed when the intervention ended. This is also reflected in the comments participants wrote, such as: "The games are something exciting I get to do" (Participant 7–60 yr. old male), "I look forward to these games and would like to play them again" (Participant 9–66 yr. old female), "I would like more days/time on the system" (Participant 3 – 57 yr. old female).

Discussion

Emotive and cognitive gains

The study presented here was non-pharmaceutical in nature, utilizing exclusively targeted virtual reality simulations. Mood improved post-training in 7 of the 10 participants, as seen in Table 2. Notably, Participant 2 showed a substantially reduced score (11 to 2) within the

"minimal" range, Participant 3's depression level dropped from "mild" to "minimal", Participant 5's mood improved from "minimal" to "normal", and Participant 9 went from "moderate" depression pre-intervention to "mild" depression post. Three participants showed a slight increase in depression of 1 to 3 points compared to their pre-intervention levels. The improvement in the participants' emotive state following the BrightBrainer therapy is in line with the earlier BrightArm studies [12,13] using integrative (motor + cognitive) training. Reduction in depressive symptoms by up to 50% in geriatric participants was previously induced by playing Wii games half an hour, three times/week [25]. This general decline in negative affect likely reflects the sense of empowerment the participants felt when playing games, as well as increased activity/social interaction.

Cognitive improvement was noted for word generation, which is commonly subsumed under the broader construct of executive functioning. Furthermore, two separate measures, one of verbal attention and the other of attention and processing speed almost reached significance. Indeed, of the 9 tests reported here 8 showed pre-post score changes in the improvement direction (Table 2). If the BrightBrainer treatment were not effective, one would expect about half of the score changes to go in one direction and half in the other. But since 8 out of 9 test scores (averaged for the group) moved in the "positive" direction, this is suggestive of an effective intervention. The p value for this sign test is $p<0.01$. The effect size for even the non-statistically significant changes on individual tests was such that even a modestly larger sample size would have demonstrated statistical significance. Given the generally advanced state of dementia observed among the participants, these results suggest a rather robust change in baseline functioning following relatively modest exposure to game-based cognitive training. Given the bimanual nature of the BrightBrainer interactions, one could speculate that improvements in aspects of attention, speed and fluency implicate greater engagement of frontal lobe structures. Previous research with cognitively impaired geriatric chronic post stroke patients yielded similar results with improvements in aspects of attention and executive functioning, although these results did not reach statistical significance [16].

Other studies have obtained results similar to the outcomes of the BrightBrainer system. A review of non-pharmacological cognitive training of patients with AD and dementia was undertaken by Yu et al. [26]. Studies have shown interactive computer training to be beneficial for such patients. Hofmann et al. [11] did an early pilot on ($n = 9$) AD patients (similar in size with the study described here) in which AD participants underwent interactive computer-based cognitive training of activities of daily living. They used a touch screen to navigate to a shopping center, purchase three items and respond to 10 multiple-choice questions. Following a 4-week training, task performance of AD participants improved substantially and they liked the technology. This warm response of dementia participants to the computer-based cognitive training technology is in line with the BrightBrainer study, albeit its training was through targeted games rather than simulated ADLs.

A randomized pilot study targeted higher functioning AD participants from an adult day care program [27]. The experimental group consisted of 15 participants who undertook 3 weekly 20-min sessions of Interactive Multimedia Internet-based System training, in addition to medication and an Integrated Psycho-stimulation Program (IPP) offered by the adult day

care. A control group had IPP and medication, and a second control group had only medication. After 12 weeks of training, the experimental group had improved outcome scores on their Alzheimer's disease Assessment Scale-Cognitive [28] and their Mini-Mental State Examination (MMSE) [29]. These gains were maintained at 24-week follow-up. By comparison, the control group receiving IPP had better outcomes than the controls receiving only medication; however, those gains were lost at follow-up. Thus, computer-based interactive tasks produced lasting cognitive improvements while the standard IPP within an adult day care program did not.

In another study, 11 patients with AD diagnosis were randomly assigned to a computer-based cognitive training group ($n = 7$) and a control group ($n = 4$) [30]. The experimental group trained for 4 weeks, 3 sessions per week playing for 60 min a sequence of games targeted at different cognition domains (attention, memory, language, decision making). The control group had a similar number and duration of conversational sessions with a neuropsychologist. Results showed that the experimental group had a delay in the progression of their disease, while the control group had a substantial increase in cognitive impairment as reflected in MMSE scores at 9 months follow-up.

The results in the BrightBrainer pilot study done with SNF dementia participants do not include follow-up measures. This was due in part to the fact that many of the residents who participated in the study had been moved to other facilities due to internal reorganization. Thus, it remains unknown whether the improvements measured at the end of the intervention would have had a lasting effect.

Integrative cognitive and motor training with multi-sensory feedback

Providing multi-modal interaction with real-time feedback from VR simulations was the reason participants in this study felt immersed in virtual environments, similar to [31]. While multi-modality of VR-mediated training has been known, what is different in this study is the integrative nature of training. Other computerized cognitive therapy, such as Lumosity [32], requires minimum motor effort (2D micro-movements such as those involved in using a mouse, or touching a smart phone with one finger). By contrast, BrightBrainer rehabilitation involved unimanual or bimanual whole arm movements. The high number of task-oriented movement repetitions (300 per arm and session at the end of the intervention) provided light upper body physical training in the process of exercising the brain. This approach has been pioneered with the BrightArm rehabilitation robotic table on participants chronic post-stroke [13].

Another way to increase physical exertion while using BrightBrainer was to add wrist weights. After the formal intervention was competed by all participants, a test was done on playing the same games, this time with small weights at the wrist. Participant 9 volunteered to do so and was able to complete 40 min of training without experiencing discomfort, or reduction in game enjoyment. Several such sessions were then repeated with similar encouraging results. This gives an indication of the potential of BrightBrainer to be used by healthy populations who may want to remain physically and mentally fit. The bimanual nature of BrightBrainer training will represent a plus in this case.

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Conclusions

To the authors' knowledge, this is the first study of integrative bimanual cognitive training of dementia patients interacting with virtual reality simulations. Participants were institutionalized in an SNF, thus they were lower functioning. Nonetheless, they improved in aspects of executive functioning with additional (but statistical non-significant) improvements in depression, processing speed and auditory attention, following 8 weeks of training.

Some limitations of this study include the relatively small sample size, lack of control participants and the general severity of dementia. Since this was the first study of its kind, future research may consider utilizing the BrightBrainer in an Adult Day Care program, with possibly higher functioning participants. The addition of normal controls and of follow-up measures should provide further insight in the applicability of the BrightBrainer for use in clinical populations or healthy ones.
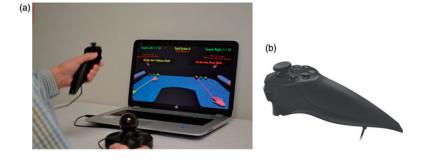
Acknowledgments

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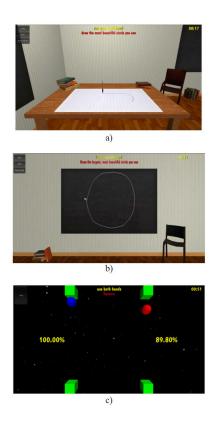
Implications for Rehabilitation

- It is possible to improve cognitive function in older low-functioning patients. Integrative rehabilitation through games combining cognitive (memory, focusing, executive function) and physical (bimanual whole arm movement, grasping, task sequencing) elements is enjoyable for this population.

- The severity of depression in these elderly can be reduced through virtual reality bimanual games.

- The number of upper extremity active repetitions performed in the process of solving cognitive problems with the BrightBrainer™ system is 600. This number is 18 times (1875%) larger than those observed by other researchers in conventional physical or occupational rehabilitation sessions.
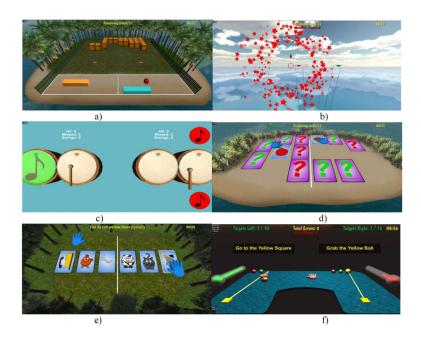
Figure 1.
The BrightBrainer integrative cognitive therapy system: (A) general view; (B) detail of the game controller pendant. Copyright Bright Cloud International Corp. Reprinted by permission.
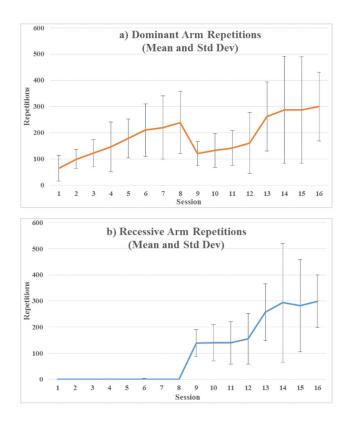
Figure 2.
Game baselines: (a) arm horizontal reach; (b) arm vertical reach; (c) index flexion/extension range [15]. Copyright Bright Cloud International Corp. Reprinted by permission.
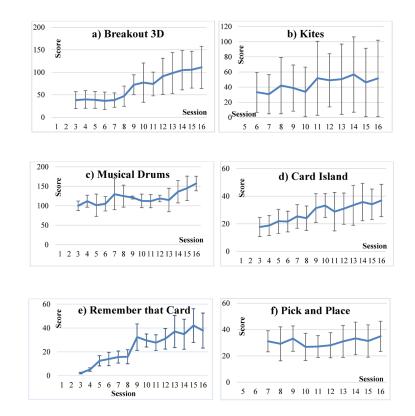
Figure 3.
Game scenes: (a) *Breakout 3D*; (b) *Kites*; (c) *Drums*; (d) *Card Island*; (e) *Remember that Card*; (f) *Pick and Place*. Copyright Bright Cloud International Corp. Reprinted by permission.

Figure 4.
Group average and standard deviation for BrightBrainer induced repetitions: (a) dominant arm; (b) recessive arm. Copyright Bright Cloud International Corp. Reprinted by permission.

Figure 5.
Game performance (group score mean and STD): games to train focusing (a, b, c); games to train memory (d, e); game to train executive function (f). Copyright Bright Cloud International Corp. Reprinted by permission.

Table 1

Participants characteristics pre-intervention. © Bright Cloud International Corp. Reprinted by permission.

Participant	1	2	3	4	5	6	7	8	9	10
Age (years)	62	55	57	64	58	73	60	69	66	70
Gender	Male	Female	Female	Male	Male	Male	Male	Male	Female	Male
Race	Black	White	White	White	White	White	Black	White	White	White
Depression Level	Minimal	Minimal	Mild	Normal	Minimal	Minimal	Minimal	Minimal	Moderate	Minimal
Cognitive state	Dementia Sev. Impaired visual and verbal attention Sev. impaired visual Memory and exec function	High average attention Avg. memory Avg. exec function	Low avg attention Sev. impaired memory Avg. exec function	Dementia Sev. impaired orientation Low avg attention Sev. impaired memory Sev. impaired exec function	Very superior orientation Sev. impaired attention Sev. impaired memory Low average exec function	Dementia Sev. impaired attention Mildly impaired memory Sev. impaired exec function	Dementia Moderately impaired orientation Moderately impaired attention Sev. impaired memory Sev. impaired exec function	Dementia Low average orientation Avg. attention Sev. impaired memory Sev. impaired exec function	Dementia Low to avg attention Avg. to high avg memory Low to avg. exec function	Dementia Sev impaired orientation Sev impaired attention Sev Impaired memory Sev Impaired exec function
Co-morbidities	Diabetes II Wo Comp Obesity Infarct Ostheoporosys Coronary Artery Gout Nos Hypertension Chronic kidney dis	Debility/fatigue Dehydratation Arthritis Hypothyroidism Anxiety Gastritis Nausea/vomiting	Right eye non functional Abnormal gait Angina Hypertension Hypothyroidism stroke Arterial disease Diabetes II Kidney failure Ischemia Obesity	Atherosclerosis Hypertension Stroke Anemia Ischemia Airway obstruct	Intracranial injury Hypertension Cerebral ischemia anemia	Cellulitis Debility	Ventricular stunt Hypothiroidism Alcohol Cirrosis liver Convulsions Diabetes I Hepatitis B, C	Adjustment disorder Obstructive Hydrocephalus Brain injury Trauma subdural Alcohol abuse Hyposmolality Disorder of Meninges	Schizophrenia Affective Psychoses Malignant Neoplasma Amputation stump Insomnia	Mental disorder Artheriosclerot Dementia Infarct Encelopathy Ischemic heart disorder Paranoid state Nos
Ambulation	Wheelchair	Walker	Wheelchair	Ambulatory	Ambulatory	Ambulatory	Ambulatory	Ambulatory	Wheelchair	Ambulatory
Language	English	English	English	English	English	English	English	English	English	Non- English
Education (years)	12	12	12	12	4	16	16	12	14	14

Table 2

Group statistical analysis of cognitive outcomes for the 10 participants following 8 week integrative training on the BB system. Copyright Bright Cloud International Corp. Reprinted by permission.

Variable	T_1	T_2	T_2-T_1	95% CI: T_2-T_1	p
BDI-II (depression)	8.0 (6.9)	5.5 (6.2)	−2.5*	(−5.1, 0.1)	**0.056**
NAB Digits Forward (auditory attention)	5.4 (1.8)	6.1 (2.1)	0.7*	(−0.4, 1.8)	0.17
NAB Digits Backwards (verbal attention/working memory)	3.1 (2.0)	3.3 (1.4)	0.2*	(−0.9, 1.3)	0.54
NAB Dots (visual attention)	1.7 (1.8)	2.1 (1.4)	0.4*	(−0.8, 1.6)	0.46
TMT-A (attention/processing)	94.7 (35.6)	99.8 (31.3)	5.1*	(−1.7, 11.9)	0.13
HVLT-R Trials 1–3 (memory)	16.3 (8.0)	16.2 (8.0)	−0.1	(−3.0, 3.2)	0.94
BVMT-R Trials 1–3 (memory)	8.9 (7.9)	9.2 (9.6)	0.3*	(−2.3, 2.9)	0.80
TMT-B (set shifting)	237.9 (101.0)	242.4(96.0)	4.5*	(−5.4, 14.4)	0.33
NAB Word Generation (executive function)	2.7 (2.5)	5.0 (3.7)	2.3*	(0.7. 3.9)	**0.01**

Bold p values indicate statistical significance or trend statistical significance.

*
is used to indicate improvement over time.