Computerized Cognitive Intervention in Cognitively Normal Very Elderly Individuals

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Computerized Cognitive Intervention in Cognitively Normal Very Elderly Individuals

By

Rebecca West, M.A., M.Ph.

A Dissertation Submitted to the Faculty in Psychology In Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy,
The Graduate Center, The City University of New York

2016
Computerized Cognitive Intervention in Cognitively Normal Very Elderly Individuals

by

Rebecca K. West

This manuscript has been read and accepted for the Graduate Faculty in the department of Psychology: Cognition, Brain, & Behavior, to satisfy the dissertation requirement for the degree of Doctor of Philosophy.

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Abstract

**Background:** The elderly population, and especially the oldest-old (those aged 85 and older) and old-old (those aged 75 and older), are the fastest growing segments of the U.S. population, increasing the need for disease-modifying treatments for Alzheimer’s disease (AD) and other age-related forms of cognitive decline. There is significant evidence that modifiable, non-pharmaceutical factors and interventions like cognitive activity and cognitive training may slow the course of AD and cognitive decline. However, little is understood about how cognitive training may translate into improved cognitive functioning, as a potential strategy for preventing decline. To the best our knowledge, this has never been studied in the very elderly. This study examined the effectiveness of a computerized cognitive training program (CCT program) CogniFit Personal Coach, and an active control games program (games program), in cognitively healthy individuals aged 80 and older. Three hypotheses were examined (1) compared to the games participants, CogniFit Personal Coach participants are expected to demonstrate greater positive change in overall cognitive function (a global cognitive composite) immediately following training; (2) compared to the games participants, CogniFit Personal Coach participants are expected to demonstrate greater positive change in the specific cognitive functions of memory, executive functioning/attention, and language, immediately following training; and (3) those with less education (as determined by a median split) will benefit more from participating in cognitive training, especially those using the CogniFit Personal Coach, compared to those with more education.
**Methods:** Sixty-nine older adults were randomized to the CCT program (n=39) or an active control (games) program (n=30). Participants completed a baseline neuropsychological assessment, and were then asked to train for 20 minutes using their program every other day, for 24 total training sessions. After completion of training, participants again completed the neuropsychological assessment. The primary outcome measure consisted of a global cognitive composite, and the secondary outcomes were specific cognitive outcome measures (memory, executive functions/attention, and language), comprised of the means of Z-scores of their respective tests (follow-up scores use baseline coefficients to calculate Z-scores for the follow-up composite scores).

**Results:** Linear mixed models demonstrated no significant interaction of program and time (from baseline to follow-up) on the global and specific cognitive composite scores reflecting that the two groups did not differ in the change of cognition from before to after treatment. Further, no significant main effects of time on overall cognitive functioning (the global cognitive composite) or on the specific cognitive domains were found for the overall sample, though scores in each factor did improve non-significantly, and memory improved at a trend level. Additional analysis found that those with less education (no college degree) were found to improve significantly on the global cognitive measure and language functioning compared to those with more education (college degree) in both the CCT and games programs.

**Discussion:** This study demonstrates that there was no beneficial effect of the CCT program compared to the games program for overall cognition or specific cognitive domains in individuals aged 80 and older who are cognitively healthy. However, the findings do suggest that cognitive training of any kind, even at a less challenging level of an active control, may be
beneficial for those without college degrees. The findings may demonstrate that improvement in
cognition by an active cognitive training program for individuals who are cognitively normal
might not be an effective strategy, or alternatively, that in the oldest old, perhaps due to less
cognitive and brain reserve, CCT has no effect. A variety of personal, state, and training program
variables likely influence the efficacy of cognitive training, and future research will be crucial to
improve understanding of the relationships between cognitive training, cognitive functioning,
and modifier factors.
ACKNOWLEDGEMENTS

I cannot thank enough: Dr. Laura Rabin, Dr. Michal Schnaider-Beeri, my research assistants, my dissertation committee, Dr. Jeremy Silverman, the Alzheimer’s Disease Research Center at the Icahn School of Medicine at Mount Sinai, and finally, my family who have supported my long (and forever ongoing) educational journey.
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Introduction

Overview

By the year 2030, it is expected that one in five Americans will be elderly (age 65 and older), with the oldest-old (age 85 and older) representing the fastest-growing segment of the population (Mackun & Wilson, 2011). With the significant increase in the elderly population comes a serious escalation in healthcare concerns. In addition to physical ailments, aging brings declines (some considered part of “normal” aging and others as symptoms of pathological conditions) in aspects of cognition and motor control (Mahncke, Bronstone, & Merzenich, 2006). These declines are often the result of Alzheimer’s disease (AD), the most common form of dementia, along with other neurodegenerative conditions. While dementia occurs in only about 1% of those between the ages of 60 and 64, the prevalence doubles approximately every 5 years (Ferri et al., 2005). This places the prevalence at nearly 33% in those aged 85-89, and as high as 56% in those aged 95 and older (Corrada, Brookmeyer, Paganini-Hill, Berlau, & Kawas, 2010; Jellinger & Attems, 2010) leading to enormous healthcare costs and critical aging-related issues that must be addressed such as age of retirement, pension, and social security benefits; and individually, losses of independence and increased burdens for caregivers (Thompson & Foth, 2005). Though progress has been made in terms of understanding AD and cognitive decline risk factors, course, and neuropathology, there remains a dearth of preventative agents and disease-modifying treatments (La Rue, 2010). However, there is robust evidence suggesting that lifestyle factors, such as cognitive and physical activity, may delay the onset or slow the progression of age-related or pathologic cognitive decline. The increased interest in these lifestyle changes and their effects stems from observational studies suggesting that more active individuals, such as those who frequently read, play musical instruments, or complete puzzles, demonstrate a
reduced risk of developing dementia (Verghese et al., 2003; Verghese et al., 2006; Wilson et al., 2002). It is believed that the neuropathology of dementia emerge years before diagnostic criteria are met. If lifestyle interventions, such as puzzles or mental exercises, can be used to slow or halt neuropathology, the onset of dementia may delayed, thereby reducing the incidence of dementia. Cognitive decline and dementia are also related to declines in activities of daily living (Deary et al., 2009) such as the ability to manage finances, prepare meals, and complete housework; if lifestyle interventions are effective, more seniors will be able to continue living in their own homes without regular assistance and potentially delaying institutionalization, the most costly component of dementia care. Therefore, intervening during the earliest stages of cognitive decline in order to delay or reduce cognitive deterioration is an indispensable step in improving public health.

Many lifestyle factors are modifiable, and recent campaigns illustrate the growing interest in such interventions. For example, the Alzheimer’s Association and Centers for Disease Control and Prevention (CDC) have joined together to develop the “Healthy Brain Initiative,” which recommends prevention research to determine the impact of behavioral interventions for maintaining cognition and preventing cognitive decline (Alzheimer’s Association, 2013).

This forthcoming introduction will characterize cognitive decline, both pathologic and non-pathologic, in the elderly. It will then briefly review the pharmaceutical and non-pharmaceutical interventions for cognitive decline, with special attention to the newest category of non-pharmaceutical interventions, computerized cognitive training. Finally, the importance of age and education on the efficacy of cognitive training will be examined, and an approach to computerized cognitive training in the older elderly (those 80 years and above) will be outlined. Importantly, this paper will highlight the importance of understanding and utilizing non-
pharmaceutical, pre-onset interventions in the elderly. These interventions may delay or even prevent the onset of dementia, maintain healthy cognition and daily functioning through the lifespan, and slow the progression of cognitive symptoms, especially in older elderly, who are at an especially high risk due to their advanced age.

**Cognitive Decline**

Cognitive decline broadly refers to any number of changes in cognitive functioning, even within a single cognitive domain such as memory or language, and can range from expected age-related decline to non-normative, pathological decline (Plassman, Williams, Burke, Holsinger & Benjamin, 2010). Age-related decline is generally considered to be non-pathological and natural, a common (and often subtle) decline that occurs as part of normal aging. Pathological cognitive decline is often the clinical result of a neurodegenerative condition. Dementia refers to conditions characterized by significant cognitive decline in domains including learning, memory, language, and attention, and a notable decline in ability to perform everyday activities, when not better explained by delirium or another mental disorder (American Psychiatric Association, 2013).

Alzheimer’s Disease (AD) is the most common form of dementia, accounting for between 50% to 80% of all cases, with the risk for AD increasing dramatically with age (Daviglus et al. 2010). Table 1 details AD and several other classifications of cognitive decline; the current paper focuses on literature related to cognitive decline and AD.

**Age-related cognitive decline.** A certain degree of cognitive decline is to be expected as part of the normal aging process. Some cognitive functions peak quite early in life, including short term memory, visual searching, and visual manipulation and comprehension (for example, completing a puzzle, identifying missing pieces of pictures, and manipulating shapes to create...
patterns); these may begin to decline in early adulthood (Hartshorne & Germine, 2015). Other cognitive skills, such as vocabulary comprehension, ability to answer general knowledge questions, arithmetic ability, and ability to explain topics, concepts, and similarities between items, can improve well into mid-life (Hartshorne & Germine, 2015). Declines in speed of processing, aspects of executive functioning and reasoning, spatial orientation, and memory are observed in many older adults who do not manifest any clear pathology or clinical disorder (Salthouse, 2009; Deary et al., 2009). Age-related cognitive decline has been associated with a number of causes including genetic influences (Deary et al., 2009; Mortensen & Hogh, 2001), oxidative stress (Craft et al., 2012), cardiovascular disease, inflammation, and loss of brain mass. Additionally, unhealthy diet and exercise (Deary et al., 2009) have been associated with age-related cognitive decline, as these habits lead to cell damage and death. Education level is also strongly associated with late-life cognition; education may represent healthier habits, a larger exposure to lifetime cognitive stimulation, and a stronger ability to compensate for cognitive decline (Jefferson et al., 2011) through cognitive and brain reserve (Liberati, Raffone, & Belardinelli, 2012; Liu et al., 2012). There is also robust evidence that cognitive aging is closely related to childhood intelligence (Deary et al., 2009), with one study showing that at age 80, as much as 50% of the variance in cognitive ability can be determined from childhood intelligence (Deary et al., 2009), likely the effect of genetic influences on both intelligence and cognitive ability in old age. Age-related cognitive decline may also be related to physical declines in sensation, such as hearing loss (Mahncke et al., 2006), which limit information processing.

Still, this decline does not occur in everyone, with many elderly individuals experiencing little or no cognitive decline, and it does not occur across all cognitive processes. A recent evaluation of cognitive skills over the life span suggests that indeed, there is no age at which
individuals are at the peak performance on all, or even most, cognitive skills (Hartshorne & Germine, 2015). For example, verbal intelligence does not tend to decline with age (Mahncke et al., 2006), nor does general knowledge or semantic memory, sustained attention, implicit memory, and expressive or receptive language functioning (Drag & Bieliauskas, 2010). In fact, those cognitive functions and abilities related to experience and exposure tend to peak in later life (Hartshorne & Germine, 2015). There are also significant inter- and intra-individual differences in non-pathologic cognitive decline.

One major theory of non-pathologic decline is the ‘wear and tear’ theory, which suggests that over the years the brain is simply worn down, with deteriorations in the number and strength of neural connections and physical brain changes (such as mass loss) leading to cognitive decline (Fotenos, Snyder, Girton, Morris, & Buckner, 2005). This decrease in neuronal connections may lead to negative plasticity, a sort of negative learning where cognitive functioning is made less efficient by de-differentiating neural networks from specific cognitive function into weaker, less specific functioning. Sensory declines cause difficult, “noisy” processing of information, and reduced cognitive activity leads to weakened or un-reinforced synaptic connections, and the brain essentially learns to work less efficiently, with more work required for the brain to complete what were once easy tasks (Mahncke et al., 2006; Lustig, Shah, Seidler, & Reuter-Lorenz, 2009). If non-pathologic decline is actually a result of negative plasticity, it is possible that such learning can be avoided or counteracted with positive brain plasticity. In this way, “natural” cognitive decline may be attenuated. The introduction of a cognitive activity or regimen of cognitive activities in those at risk of cognitive decline, i.e. the elderly and especially the oldest-old, may be useful to maintain cognitive functioning and prevent decline.
**Alzheimer’s Disease.** Two broad types of AD, early onset and late onset (approximately 1-5% of the AD cases [Reitz & Mayeux, 2014]), have been identified; late-onset AD is the far more common type of AD occurring in individuals 65 years and older, with risk increasing significantly with every 5 years of life. The primary clinical symptom is episodic memory loss (van der Flier, Pijnenburg, Fox, & Scheltens, 2010) accompanied by declines in one or more other cognitive domains (e.g., executive functioning, language), in addition to daily functioning.

Late onset AD is progressive and irreversible, and by the time that cognitive symptoms appear, the changes in the brain that have likely caused the cognitive symptoms have been developing for years, if not decades. The brain changes most closely associated with AD, the so-called “hallmarks” of AD, are extracellular beta amyloid plaques, which accumulate at synaptic terminals, interfering with synaptic functioning, and eventually resulting in neuronal death, and intracellular tau protein tangles, which develop intracellularly (Tang & Kumar, 2008), destroying the skeleton of the neuron thus impairing its nutrient system and leading to neuronal death.

Further, several neurochemical changes are associated with AD, including reduced production of acetylcholine, a neurotransmitter of extreme importance for cognition (Proctor, 2005). Plaques and tangles are generally seen in extensive amounts in the brains of AD patients, and are thought to play the major role in causing degeneration and death of neurons, which manifests behaviorally as cognitive and functional decline (Mosconi, Brys, Glodzik, De Santi, Rusinek, & Mednes de Leon, 2007).

These structural and chemical brain changes present as cognitive and other functional alterations. Usually, mild memory problems are the first symptom to develop, followed by increased memory loss and declines in judgment, competency in everyday tasks, and even mood. Then, more serious memory loss and confusion emerge, with the patient having trouble
recognizing family members, significant declines in ability to complete daily activities, and behavioral/psychiatric changes such as paranoia. Finally, at the latest stage of AD, the patient is unable to care for him/herself on any level or communicate effectively, and physical decline occurs (e.g., losing weight or inability to eat, excessive sleeping, and even seizures) (National Institution on Aging [NIA], 2010). The serious impact of AD on the ever-growing population of older adults, and especially old-old and oldest-old, who are at the highest risk, requires an urgent focus on treatment and preventative measures.

**Risk and protective factors.** Risk factors for AD and other dementias are numerous. The unquestionably strongest risk factor is age accompanied by female gender; approximately two-thirds of AD patients are women (Carter, Resnick, Mallampalli, & Kalbarczyk, 2012; Herbert, Weuve, Scherr, & Evans, 2013; Van der Flier & Scheltens, 2005). The best-supported genetic factor associated with late onset AD is the APOE, or apolipoprotein E, gene. The E4 allele of this gene (E3 is the normal variant) increases the risk of late onset AD, and 40% of those with late onset AD have one or both APOE 4 alleles. Up to eighteen additional AD risk factor genetic susceptibility loci have been identified (Lambert, Ibrahim-Verbaas, Harold, et al., 2013). Cardiovascular disease, specifically the metabolic syndrome (defined by Eckel, Grundy, & Zimmet [2005] as abdominal obesity, hypertension, high tryglicerides, and hyperglycemia), and diabetes are also significant risk factors for AD, as is smoking. In addition, Major Depression appears to increase the risk for AD (NIA, 2010; Plassman et al., 2010). Numerous other possible risk factors continue to be investigated ranging from medical to nutritional and lifestyle variables.

The relationship between these risk factors and AD and other dementias is highly complicated, and by the time that cognitive symptoms appear, the brain changes that have likely
caused the cognitive symptoms have been developing for years. Some suggest the AD pathology begins as much as 20 years before clinically visible cognitive symptoms appear, with numerous studies finding brain changes, including neurodegeneration and development of plaques and tangles, to be predictive of AD (Hinrichs, Singh, Xu, Johnson, and the Alzheimers Disease Neuroimaging Initiative, 2011; Miller, 2009). The already advanced state of degeneration before any diagnosis is given makes treatment of AD difficult and limited, and suggests that interventions before clinical symptoms appear may be of beneficial use.

Several protective factors for late-onset AD have also been identified. The most robust protective factor is formal education, a finding that has been replicated in numerous populations, ethnicities, and races (Alley & Crimmins, 2009; Meng & D’Arcy, 2012). Lifestyle factors, including regular physical and cognitive exercise, seem to be related to a reduced risk of AD (NIA, 2010; Plassman et al., 2010). Specific dietary actions, like consuming a “Mediterranean diet” appear to reduce the risk of AD, with those adhering to such a diet having a 28% lower risk of being diagnosed with mild cognitive impairment (MCI) (a disorder where memory problems are greater than expected due to age, but generally do not interfere with functioning; for additional information see Table 1), compared to those who do not adhere (Scarmeas, Stern, Mayeux, Manly, Schupf, & Luchsinger, 2009). Physical activity may be beneficial; a review of randomized controlled trials of the effects of exercise on cognition found that exercise programs lasting at least 6 weeks, one hour, three times a week had a positive impact on cognition for both the cognitively healthy and individuals with cognitive impairment (Tseng, Gau, & Lou, 2011).

These studies, and earlier research describing significant correlational evidence linking cognitive, social, leisure, and physical activity with better cognitive functioning in old age (Christensen, Korten, Jorm., Henderson, Scott & Mackinnon, 1996; Singh-Manoux, Richards, &
Marmot, 2003), suggest that such factors may increase cognitive reserve [see Mechanisms for Cognitive Training, below] and decrease stress related to aging (Qiu, De Ronchi, & Fratiglioni, 2007). Overall, the numerous modifiable factors that appear to be related to AD and other dementias suggest that early interventions may be especially useful, and implementing interventions like cognitive activity prior to dementia diagnosis, including in those at high risk, may be important for reducing or delaying cognitive decline (NIA, 2010; Rosen, Sugiura, Kramer, & Whitfield-Gabrieli, 2011).

**Treatments and Interventions for Cognitive Decline**

**Pharmacological treatments.** Treatment for dementia currently focuses on managing the cognitive and behavioral symptoms. There are currently several FDA-approved drugs for AD (National Institutes of Health [NIH], 2015), which temporarily treat symptoms but do not appear to impact the actual disease progression (Mahncke et al., 2006; NIH, 2015; Rafi & Aisen, 2015), see Table 2 for additional details. For example, depression of activity in cholinergic neurons is well documented in AD, leading to reduced levels of brain acetylcholine, important for attention and possibly memory. The most common medications used to treat AD are acetylcholinesterase (AChE) inhibitors, which increase brain levels of acetylcholine. AChE inhibitors modestly benefit individuals with mild or moderate AD but, like other AD medications, do not slow the progression of the disease (Deardorff, Feen, & Grossberg, 2015). These drugs may maintain or improve cognition, but only for a brief period, after which decline continues at the same rate as for unmedicated individuals (Beier, 2003; Mangialasche, Solomon, Winblad, Mecocci, Kivipelto, 2010). In addition to AChE inhibitors, AD is also treated with NMDA antagonists like memantine (Namenda®) which regulate glutamate activation and block the negative effects of excess glutamate (Mangialasche et al., 2010). Other approaches are being considered, including
treatments to reduce the production of amyloid-beta and tau, and increasing nerve growth factors to improve neuronal health and reduce neuronal death (Mangialasche et al., 2010; Rafi & Aisen, 2015).

Medications tend to be prescribed once cognitive symptoms have begun, meaning that the neural degeneration has been occurring for years before the agent is introduced (Miller, 2009). Additionally, medication tends to be costly, a concern for individuals who may already be dealing with expensive medical care in their later years, and they may produce side effects like decline in liver functions, nausea, loss of appetite, diarrhea, dizziness, confusion, and headaches (NIA, 2015). Finally, no pharmacological approaches are available for age-related cognitive change; the medications are approved only for individuals who already developed clinical signs of dementia.

**Non-pharmacological approaches.** Because the current research has found pharmacological approaches to provide only limited benefits against cognitive decline in AD, the interest in nonpharmacological approaches has grown. Non-medical interventions offer a new approach to disrupting the onset of cognitive decline and dementia, most of which can be implemented prior to any cognitive decline, in all ages including older elderly, without major concerns of side effects. Growing and consistent evidence for a relationship of cognitive, social, and physical activity with cognitive performance suggests the need for non-pharmacological interventions to diminish cognitive decline.

**Physical, social, and leisure activity.**

**Physical activity.** An association between physical activity and cognitive function in older adults has been consistently reported (Ahlskog, Geda, Graff-Fadford, & Petersen 2011; Bherer, 2015; Kelly, Loughrey, Lawlor, Robertson, Walsh, & Brennan, 2014; Kirk-Sanchez &
McGough, 2013; Lovden, Xu, & Wang, 2013; Tseng, Gau, & Lou, 2011). Further, there is evidence showing that those with higher cardiorespiratory fitness were less likely to show significant longitudinal decline on cognitive tasks, including visual and verbal memory tasks (Wendell, Gunstad, Waldstein, Wright, Ferrucci, & Zonderman, 2014). Intervention studies have demonstrated strong evidence for these relationships as well. For example, individuals with MCI tasked to train on and play handball showed improvements on the Mini Mental State Examination (MMSE) cognitive tasks over a control group who maintained their everyday activities (Wei & Ji, 2014). It is difficult to determine whether physical activity improves cognition and lowers the risk of dementia, whether those with better cognition tend to participate in physical activity, or whether a third factor, such as genetics, is related to both (Jedrziewski, Lee, & Trojanowski, 2007). Further, reducing cardiovascular disease and systemic inflammation through exercise may lower the risk of dementia, as both cardiovascular disease and inflammation have been linked to dementia (Jedrziewski et al., 2007). Physical activity may also influence neurogenesis and increase neurotrophic growth factors, thereby reducing the risk for dementia by increasing synaptic connections and brain mass (Jedrziewski et al., 2007). The overall benefits of increasing physical activity in older adults, in comparison to minimal risks, are great, and further research to identify the cognitive benefits of such interventions will elucidate this connection and inform the future development and implementation of such interventions.

**Social interaction.** Social interactions may also be effective at improving or maintaining cognition. A vast amount of correlational evidence suggests that individuals who regularly engage in social activity, especially activity that includes a strongly stimulating cognitive component, are less likely to be diagnosed with AD or to experience cognitive decline (Barnes,
Mendes de Leon, Wilson, Bienias, & Evans, 2004; Ballesteros, Kraft, Santana, & Tziraki, 2015; Crowe, Andel, Pedersen, Johansson, & Gatz, 2003). Further, social activity can increase the likelihood that an individual will utilize resources, such as programs to maintain cognitive health, as well as regular healthcare, and intellectual activities, by enhancing self-efficacy and providing regular opportunities to discuss concerns and interests with others (Stine-Morrow, Shake, Miles, & Noh, 2006). Still, controlled clinical trials of purely social interventions are uncommon. Haslam, Haslam, Jetten, Bevins, Ravenscroft, & Tonks (2010) examined 73 elderly individuals in residential care, some of whom took part in reminiscing activities once per week, for four weeks, either individually or in a group. At the end of intervention, the intervention group showed greater improvement in general cognitive ability and in subjective well-being. Mortimer et al. (2012) found that cognitively healthy elderly randomized to a social interaction group demonstrated increases in brain volume and on some neuropsychological tasks.

The social component of other types of interventions (e.g., physical, cognitive) may be an important variable in their effectiveness (Noack, Lövdén, Schmiedek, & Lindenberger., 2009). Social interaction may enhance or maintain cognitive health as a result of reduction of stress, and social interaction itself has a strong, challenging cognitive component (Depp, Vahia, & Jeste, 2010). Additional randomized, controlled trials of social interventions are required to better understand the effect of social interaction on cognition, but the correlational evidence clearly suggests that social activity is of significant importance to healthy cognitive aging.

**Leisure activities.** Leisure-time activity in the form of crossword puzzles, drawing, painting, or reading, may confer protection against dementia and MCI. Some studies have found that leisure activities reduce the risk of dementia and MCI, even after controlling for initial health and education (Park, Gutchess, Meade, & Stine-Morrow, 2007; Verghese, et al., 2006).
Additional studies have suggested that leisure activities are only protective when they are cognitively challenging, with activities such as reading being protective (Leung et al., 2010), while activities like television watching are not—and may even increase the risk of cognitive impairment (Rundek & Bennett, 2006; Wang et al., 2006).

The relationship between leisure activity and cognitive health has been reported in several large aging projects. The Bronx Aging Study, a well-regarded study of aging and cognition, reported that mentally stimulating leisure activities, including working on crossword puzzles, drawing and painting, and playing cards, was related to a delay in memory decline (Hall, Lipton, Sliwinski, Katz, Derby, & Verghese, 2009). The Three-City Study, with over 5000 participants, found that cognitively active leisure activities were related to a reduced risk of dementia (Akbaral, et al., 2009). Cheng, Chan, and Yu (2006) found that elderly persons with dementia who were assigned to play mahjong demonstrated improvements in memory and MMSE scores, even up to a month after the mahjong play intervention ended. Lifetime leisure activity is a difficult variable to measure and quantify; as such, designing clinical trials to measure its true role in prevention of cognitive decline and AD is challenging. However, similar to social activities, many leisure activities have a component of cognitive effort; this cognitive effort may be the mechanism behind the benefits of leisure activity to cognitive functioning.

Cognitive interventions

**Overview.** Interventions that train one or more cognitive abilities have been shown to improve general cognition and specific cognitive functions for healthy elderly as well as for the cognitively impaired (see Table 3). Cognitive training methods started with traditional, non-computerized methods like “method of loci training” (Thompson & Foth, 2005) and have evolved with technology to computerized, multi-media programs. The popularity of cognitive
training programs has increased immensely in recent years (Kueider, Parisi, Gross, & Rebok, 2012) but true evidence based, well designed clinical trials are relatively few. Some major cognitive domains found to improve with the use of traditional (non-computerized) cognitive interventions include attention, executive functioning, explicit memory, reasoning, speed of processing, and spatial orientation (Thompson & Foth, 2005). Newer computerized cognitive training programs have been found to improve numerous cognitive skills as well, including attention, memory, speed of processing, visuospatial skills, and subjective functioning (Kueider et al., 2012; Lampit, Hallock, & Valenzuela, 2014; Reijnders, van Heugten, & van Boxtel, 2013). Cognitive training may thus be a good strategy for maintaining cognitive health and preventing dementia.

**Mechanisms underlying the potential beneficial effects of cognitive training.** The theory of “use it or lose it” often is invoked to describe the utility of cognitive interventions, which suggests that if aging individuals continue to “practice” their cognitive functions, then these functions can be maintained. In other words, using cognitive training may strengthen synaptic connections that might otherwise fail or degrade due to lack of stimulation. As such, cognitive stimulation will serve a protective role, which suggests that cognitive interventions may be most effective in preventing or delaying dementia in those who have not experienced significant pathologic cognitive decline. Still, studies of cognitive interventions in AD and MCI are promising (Barnes et al., 2009; Cipriani, Bianchette, & Trabucchi, 2006; Kanaan, McDowd, Colgrove, Burns, Gajewski, & Pohl, 2014; Kinsella et al., 2009; Troyer, Murphy, Anderson, Moscovitch, & Craik, 2008), and hopes for improving cognition via intervention should not be limited to cognitively healthy individuals.
Plasticity. Neural plasticity, the mechanism that serves as the foundation for the “use it or lose it” theory, suggests that cognitive interventions may promote neurogenesis. Humans (if not all animals) sustain the ability for brain change, or plasticity throughout their lives even though some deterioration in brain structure and/or function can be observed in nearly all elderly individuals (Aldwin & Gilmer, 2004). That is, elderly individuals appear to maintain some plasticity and ability for brain change (Kramer & Willis, 2002), including those with AD (Tarraga, et al., 2006). This positive plasticity (Mahncke et al., 2006) may be one way that cognitive training improves cognition.

Neural plasticity has been described as the capacity to acquire cognitive skills (Mercado, 2008), and each individual appears to have a range of potential plasticity (Baltes & Lindenberger, 1988). The brain appears to be highly plastic and capable of generating new synaptic connections and neurons throughout the lifespan (Eriksson, et al., 1998), particularly when activated by enriched environments. Cognitive training programs attempt to activate neural plasticity by introducing novel and complex stimuli that may promote neuronal changes, including the development of new neuronal networks and functional synapses (Burke, Hickie, Breakspear, & Gotz, 2007; Greenwood & Parasuraman, 2010).

As new or challenging activities are introduced, neural structures reorganize and grow, allowing for cognitive processing to be more effective and efficient (Park & Bischof, 2013; Wilson & Bennett, 2003). Additionally, neural changes beyond synaptic strengthening may explain plasticity. Physical changes to neurons and alterations in neurochemistry, including changes in the production, modulation, and release of neurotransmitters, may also be important for neural plasticity (Daffner, 2010; La Rue, 2010; Sawaski, Werhahn, Barco, Kopyley, & Cohen, 2003). Similarly, stimulation of the neurotrophins necessary to promote the growth of
and maintain neurons seems to be prompted by cognitive training and novel stimulation (Valenzuela & Sachdev, 2009). Cognitive stimulation even appears to promote neurogenesis and synaptic strengthening in areas specifically important to memory. The hippocampus demonstrates neurogenesis in response to cognitive enrichment, and mental exercise in cognitively healthy elderly increases those neurotrophic and nerve growth factors important for protection of the hippocampus (Valenzuela & Sachdev, 2009). Cognitive training programs may provide the novel cognitive stimulation that promotes synaptic development and neurogenesis, important in maintaining cognitive functioning during aging, regardless of pathogenic progression or current level of cognitive functioning.

**Cognitive reserve.** The lack of a clear, direct relationship between brain pathology and dementia symptomatology, and the ability of certain individuals to cope with greater degrees of brain damage and pathology, provides important evidence for the theory of cognitive reserve, which states that existing cognitive networks and ability are able to buffer against brain damage to a certain extent (Stern, 2006). Cognitive reserve may explain the disparities in cognitive symptoms of those with similar brain damage (Stern, 2006), including individuals who show AD pathology at autopsy, but who did not demonstrate significant cognitive dysfunction during life, and may explain why cognitive activity is associated with cognitive change independent of neuropathology (Wilson et al., 2013). There is no specific amount of brain pathology at which point cognitive decline must become apparent, and this is particularly true in the oldest old, for which the relationship between dementia severity and the extent of AD neuropathology is weak (Caselli et al., 2015; Haroutunian, et al., 2008; Stern, 2012; Wilson et al., 2013).

Cognitive reserve theories provide insight into how cognitive training may improve cognition or delay dementia. Cognitive reserve describes an ability to cope with neural damage,
and to recruit cognitive processes needed to compensate for damage (Depp et al. 2010). High education, challenging occupations, high IQ, and other cognitive activity appear to provide individuals with greater reserve (La Rue, 2010). Cognitive reserve is modifiable, through learning and experience, and may delay or reduce the impact of dementia; cognitive training may provide the necessary cognitive activity to strengthen and maintain neuronal connections, thereby strengthening cognitive reserve. Those with higher cognitive reserve might be able to cope with, and endure, greater amounts of damage to the brain from lesions, cardiovascular disease, and other risks for AD, and handle greater damage to the frontal lobes before AD symptoms develop (Papp et al., 2009), as compared to those with less reserve. Cognitive reserve as a mechanism for cognitive interventions appears to be a measure of prevention, not likely a measure that can reverse pathologic cognitive decline. Therefore, introducing cognitive training in those without cognitive decline may be the most beneficial way to boost reserve.

Cognitive reserve appears closely related to brain reserve, which suggests that more brain mass or neural count will provide greater coping and compensation (La Rue, 2010), simply because larger brains with more mass can cope with greater amounts of damage. A correlational study by Sole-Padulles et al. (2009) found that thicker cortices are related to greater executive functioning in healthy elderly, and those estimated to have greater reserve (those with high IQs, educational attainment, and intellectual activity) show greater brain volume and lower brain activity (assumed to be from more efficient processing) during tasks, and a number of neuroimaging studies evaluating brain changes in response to cognitive training have recently been published (see the section Neural changes, below). However, a criticism of brain reserve models is that they may ignore the importance of individual differences (Stern, 2009); greater
brain mass and neuronal count do not fully account for cognitive functioning, as there is variability in the capacity of individuals to compensate for neuronal loss.

Cognitive reserve may be enhanced by cognitive activity, by strengthening neural connections to reduce neuronal loss in cognitive and even sensory and motor areas (Mahncke et al., 2006). One of the major impacts of cognitive training may be through increasing cognitive reserve by simply using and training cognitive, sensory, and motor skills, thereby maintaining and improving cognitive skills that may otherwise be lost. Cognitive reserve may also be useful in explaining the effects of cognitive training; those who benefit most may rely on cognitive reserve, while those with less cognitive reserve may benefit more by increasing neural connections that may have been previously lost. It is important to empirically investigate whether cognitive training enhances cognitive reserve later in life; cognitive reserve is often thought of as developing early in life, and subsequently individuals with strong reserve benefit later in life.

Neural changes.

Until very recently, cognitive functioning was almost exclusively the outcome measure of cognitive training studies. Some recent studies are additionally assessing the neural correlates of and neural changes related to cognitive training, which may provide important evidence for plasticity and cognitive reserve in older adults as well as additional insight into the mechanisms supporting cognitive training gains. A recent review examining neural changes in response to cognitive training as they related to the neural networks affected by AD, in individuals with MCI, found a range of increased brain activity as well as increased grey matter volume; the authors suggested that cognitive training likely prompts compensatory mechanisms that are reflected in the increased activation (Hosseini, Kramer, & Kesler, 2014). Belleville & Bherer (2012) also recently reviewed the structural and functional impact of cognitive training on older
cognitively healthy and MCI participants, finding overall increased grey matter volume, white matter integrity, and cortical thickness, and a differential effect on task related activation: increased activation for those with MCI, and a pattern of increased and decreased activation for those with healthy cognition. A pilot study of individuals with MCI demonstrated an increase in left hippocampal activation after verbal memory training, compared to an active control group (Rosen et al., 2011), and hippocampal volume was increased in cognitively healthy individuals who completed episodic memory training (Engvig et al., 2014). Improvements in cerebral blood flow and neural connectivity have been found to be correlated with cognitive training gains in cognitively healthy older adults (Chapman et al., 2015). Generally, the neural changes associated with cognitive training appear task-relevant and supportive of the idea of neural plasticity even in advanced age; further there is a pattern of increased activation, which may suggest an increase in compensatory abilities due to cognitive training (Valkanova, Rodriguez, & Ebmeier, 2014).

**Amyloid deposition reduction.** Evidence supporting the impact of cognitive training on brain activation provides the impetus for examining the potential impact of cognitive training directly on AD neuropathology. The reduced deposition of amyloid, by inhibiting the development of new amyloid plaques, may be an additional possible mechanism for the utility of cognitive training. Toxic soluble amyloid is known to trigger oxidative stress and inflammation that leads to plaque buildup, and eventual neuronal death. Beta-amyloid deposits are one of the major neurological hallmarks of AD, and it has been shown that mice who live in enriched environments demonstrate a reduced deposition of beta-amyloid (Lazarov et al., 2005). This relationship has been identified in humans, as well; those in the highest tertile of cognitive activity (measured as frequency engaging in common cognitively demanding tasks: reading or playing games, for example) at early- and mid-life have been found to have less beta-amyloid
deposition, compared to those in the lowest tertile of cognitive activity (controlling for age, sex, and education), as measured using the recently developed Pittsburgh Compound B (Landau et al., 2012). Further, in those with the AD risk factor Apoe4, higher lifetime cognitive activity may moderate the deposition of beta-amyloid (Wirth, Villeneuve, La Joie, Marks, & Jagust, 2014). This is a new area of research, and there is not yet evidence for beta-amyloid reduction from cognitive training in humans, but the possibility of this direct association would suggest an even better advantage of utilizing training with MCI and AD patients.

Evidence for the benefits of cognitive training is still evolving, so it is not surprising that the mechanisms by which cognitive training improves functioning also require elucidation. Recent reviews of cognitive training studies are cautiously optimistic regarding cognitive training (Liberati, Raffone, and Belardinelli, 2012; Kueider et al., 2012; Lustig et al., 2009; Reijnders et al., 2013), suggesting that the evidence supporting the utility of cognitive training will continue to accumulate.

(Non-computerized) cognitive intervention trials. As support for the possibility that stimulating neural plasticity and enhancing cognitive reserve may protect against and delay onset of cognitive decline has increased, so have trials examining the utility of cognitive interventions. Studies of cognitively healthy and cognitively impaired persons who received specific memory training have shown gains on tests of global cognition, objective and subjective memory tasks and questionnaires, memory self-efficacy, and locus of control; some of these improvements were maintained at one month follow-up (Bailey, Dunlosky, & Hertzog, 2009; Buiza et al., 2008; Fairchild & Scogin, 2010; Hastings & West, 2009; Lustig & Flegal, 2008; McDougal, Becker, Pituch, Acee, Vaughan, & Delville, 2010; West, Bagwell, & Dark-Freudman, 2008). Troyer and colleagues (2008) found that individuals with MCI improved on memory strategy knowledge,
but not on actual memory tasks. In one study of non-computerized cognitive training (mnemonics and cognitive problem-solving training, conducted in person and with take-home assignments), individuals with cognitive decline or MCI demonstrated improvements on the MMSE and the Alzheimer’s Disease Assessment Scale (ADAS) (Tsai et al., 2008). In another study of a similar non-computerized cognitive training program, improvements on specific memory tasks, even at a four-month follow-up, were found for individuals with MCI (Kinsella et al., 2009). Other studies, however, found no improvement on primary memory measures (Bugos, Perlstein, McCrae, Brophy, & Bedenbaugh, 2008; Craik et al., 2007; Troyer et al., 2008).

Research on the outcome of programs that specifically train speed of processing have found improvements on trained tasks, as have programs that specifically trained reasoning ability; generally no improvement was found in non-trained activities (Margrett & Willis, 2006; Wadley, Benz, Ball, Roenker, Edwards, & Vance, 2006; Willis et al., 2006). The findings from non-computerized cognitive training demonstrates the effectiveness of training individual domains, however, benefits do not seem to transfer to other, untrained cognitive domains.

**Computerized Cognitive Training**

Due to recent advances in technology and the increasing interest in cognitive training, computerized cognitive training methods have gained popularity. Currently, there are numerous commercially available cognitive training programs, as well as programs under development, ranging from video games (e.g., Big Brain Academy for the Nintendo Wii) to scientifically developed and assessed programs (e.g., Lumosity [www.lumosity.com] and Posit Science’s Brain Fitness [www.positscience.com]). The rise in popularity of these programs has outpaced the research leading 69 scientists to draft a letter (“A Consensus on the Brain Training Industry from the Scientific Community,” Allaire et al., 2014), published by the Stanford Center for
Longevity, decrying claims made by companies producing the programs. These scientists explained that the research is still extremely limited and does not support statements made by such companies that the programs can make consumers “smarter, more alert, and able to learn faster and better.” Recommendations were made for more, and more rigorous and independent, studies of the programs, and the scientists encouraged the public to be skeptical of claims made by cognitive training companies.

Currently, computerized cognitive training is among the most commonly used form of cognitive intervention for the elderly. Although such training has been criticized for using technology unfamiliar to older adults, the number of older adults purchasing and using computers continues to increase. The United States Census estimates that, as of 2013, 65.1% of homes with a householder aged 65 or older have a computer, with 58.3% of homes with a householder aged 65 or older having internet access (File & Ryan, 2014). Comparatively, in 2003, 34.7% of homes with a householder aged 65 or older had a computer, with 29.4% of homes with a householder aged 65 or older having internet access (Day, Janus, & Davis, 2005).

Computerized cognitive training programs have the advantages of utilizing multimedia and being interactive. In addition, such programs can be performed at the residence of the participant, with flexible hours of use, and they are available for extended use. They also avoid the need for a live instructor, provide unique and variable tasks and stimuli, and some computerized cognitive training programs can adjust the content or difficulty level to the user and provide immediate feedback (Green & Bavelier, 2008; Kueider et al., 2012). In research contexts, computerized programs have the advantage of recording every participant response, saving a vast amount of information automatically, therefore maximizing opportunities for assessing change while minimizing mistakes of data entry.
Examination of computerized programs has included simple games, such as “Pac-Man,” “Tetris,” and “Donkey Kong,” (Lustig et al., 2009), which typically yield short-term improvements in the task performance and reaction time, but little else. Cognitively healthy elderly trained to play the “Rise of Nations” video game improved significantly on numerous cognitive tasks, including working and visual short term memory and task switching, as compared to a control group (Basak, Boot, Voss, & Kramer, 2008). However, an examination of the Nintendo Wii game “Big Brain Academy” in healthy older adults did not find that the video game training transferred to improvements on cognitive tasks (Ackerman, Kanfer, & Calderwood, 2010). Video games appear to be most effective at improving speed of processing and reaction time (Kueider et al., 2012), but may not be useful for other cognitive functions like memory or executive functioning. Further, video games may not provide generalization of cognitive skills beyond those directly trained by the games.

Computerized cognitive training programs have been, and continue to be, evaluated for efficacy in cognitively healthy and cognitively impaired elderly. There are dozens of available brain training software applications and websites (a sample can be found in Table 4), ranging in cost from free to several hundred dollars, only some of which have been scientifically tested. Table 5 lists a sample of randomized controlled trials from 2010-2015 examining computerized cognitive interventions, both commercially available and not. Recent randomized controlled studies have yielded mixed results in both participants with MCI and dementia and in those who are cognitively healthy. For example, Rosen and colleagues (2011) investigated the outcome of individuals with MCI who participated in intensive training for two months using Brain Fitness by Posit Science, a program with seven auditory exercises intended to train speed of processing and auditory memory. A control group listened to audio books, played visually stimulating
online games, and read online newspapers. The intervention group showed significant improvement in verbal memory as compared to the control group.

Gaitán, Garolera, Cerulla, Chico, Rodriguez-Querol, & Canela-Soler, (2012) evaluated the Spanish computerized cognitive training program FESKITS Estimulación Cognitiva, a commercially available online program that trains a number of abilities including attention, working memory, visual memory, and executive functioning. Participants included those with MCI and mild AD who were already receiving group-based, pen-and-paper cognitive training. On cognitive measures, the computer-based training did not benefit participants any more than the traditional cognitive training, though non-cognitive measures of anxiety and decision making did show improvements. Moreover, the Brain Fitness program by Dakim, which trains six cognitive domains with a vast number (over 400) of exercises, was found to improve delayed memory, though not immediate memory or language functioning, compared to a wait list, inactive control group (Miller et al., 2013).

There is a great deal of interest in utilizing computerized cognitive interventions in cognitively healthy and cognitively declining elderly, but there is still a great need for these programs to be tested in a rigorous scientific manner (Kueider et al., 2012). Although much of the current computerized cognitive training literature emphasizes the positive effects of training, negative results are equally as common, especially for secondary cognitive outcomes (Valenzuela & Sachdev, 2009). Recent reviews of the computerized cognitive training literature find gains vary greatly depending on cognitive domain (Ballesteros et al., 2015), with training often ineffective for improving attention (Kueider et al., 2012), executive functioning (Kueider et al., 2012, Lampit et al., 2014), or verbal memory (Lampit et al., 2014). Training often fails to improve individual test measures as well, such as the Controlled Oral Word Association test.
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performance (Wolinsky, Vander Weg, Howren, Jones, & Dotson, 2013), Digit Vigilance Test (Wolinsky, Vander Weg, Howren, Jones, & Dotson, 2013), MMSE (Herrera, Chambon, Michel, Paban, & Alexcio-Lautier, 2012; Nouchi et al., 2012; Zhuang et al., 2013), Digit Span tests (Herrera et al., 2012), tests of Immediate Memory (Miller et al., 2013), and quality of life measures (Lin, Chen, Vance, & Mapstone, 2013). Further, gains are often not maintained beyond training (Ballesteros et al., 2015) and are often relatively small (Gaitan, Garolera, Cerulla, Chico, Rodriguez-Querol, & Canela-Soler, 2013; Peretz, Korczyn, Shatil, Aharonson, Birnboim, & Giladi, 2011; Valenzuela & Sachdev, 2009; Zhuang et al., 2013).

Still, there is promising evidence that interventions could be useful for maintaining or improving cognition. Further, as evidence mounts that these programs may be beneficial, an interest in examining them in concert with other lifestyle interventions (diet, exercise) has grown. There is now a shift in the study of computerized cognitive training towards combining the training with such interventions (Schneider & Yvon, 2013). In light of the advantages of computerized cognitive training it is imperative that research into these technology-based interventions continues. Future research also needs to identify those who will benefit most from training, in terms of slowing or halting the onset of dementia, as well as identifying the characteristics of programs that are effective. Improved understanding of the utility of computerized cognitive training programs will guide the implementation of such programs as preventative measures for those at risk of dementia.

Moderating variables in computerized cognitive training. Certain sociodemographic, social, and lifestyle factors may impact the effectiveness of cognitive training. Motivation, personal theories of intelligence, age, education, health, baseline cognitive functioning, level of cognitive impairment, and additional cognitive stimulation have been suggested as influencing
the outcome of cognitive training (Bagwell & West, 2008; Borella, Carretti, Zanoni, Zavagnin, & De Beni, 2013; Brehmer et al., 2008; Jaeggi, Buschkuehl, Shah, & Jonides, 2014; Kwok et al., 2011; Lustig et al., 2009; Rebok et al., 2013; Verhaeghen, Marcoen, & Goossens, 1992). Here, we focus on two of these potentially influential variables, age and education.

**Age.** Examining age as a factor in cognitive interventions is especially important as within the elderly, the oldest old are the fastest growing segment of the population in the United States (Mackun & Wilson, 2011), and age is the most significant risk factor for dementia. It is apparent that older adults can demonstrate cognitive improvement after cognitive training, which may be maintained for months or years, but such research has mainly examined younger elderly (Borella et al., 2013; Rebok, Carlson, & Langbaum, 2007; Yang & Krampe, 2009). We are aware of no computerized cognitive training studies that exclusively enrolled oldest-old. In one study where the average participant age was above 80, computerized cognitive training did improve cognitive functioning (Miller et al., 2013). A second study examining retest learning in younger and older elderly found the oldest-old to show significant learning over time (Yang, Krampe, & Baltes, 2006). However, other studies have suggested that the rate of improvement may not be impacted by age, or may grow smaller with increasing age (Rebok et al., 2013; Singer, Lindenberger, & Baltes, 2003; Verhaeghen et al., 1992). With such a limited number of cognitive training studies examining the old-old and oldest-old, it is difficult to know how such programs fare with this segment of the population specifically.

Differences in cognitive training effectiveness between younger and older elderly could additionally be explained by age-related changes to the brain. A recent meta-analysis (Spreng, Wojtowicz, & Grady, 2010) examined brain differences between younger and older adults in the “task-positive network” (TPN). The TPN is described as areas of the brain active during
cognitive tasks, including the prefrontal cortex, superior parietal cortex, ventral occipital cortex, postcentral gyrus, and supplementary motor area. The meta-analysis concluded the current fMRI and PET literature demonstrates that older adults compensate for losses in functioning by utilizing their prefrontal cortices more during cognitive tasks, compared to younger adults (even when performance is equal across groups). The authors suggested that older adults might require additional use of their prefrontal region to compensate for loss in efficiency at performing cognitive tasks. This difference in how young and old brains work can likely be extended to how young-old and oldest-old brains work. For example, young-old and oldest-old, performing similarly on memory tasks, demonstrated different networks of neural activation (Beeri, Lee, Cheng, Wollman, Silverman, & Prohovnik, 2009). Oldest-old had less activation in the hippocampus, medial frontal gyrus, and parietal areas, compared to the young-old, which the authors suggested may be the result of brain atrophy in the oldest-old. Cabeza and Dennis (2012) posited several major changes with aging, including structure declines in the frontal lobes and greater activation in regions exhibiting deterioration (until a task becomes too difficult). These changes that occur as individuals age and brain atrophy increases are not fully understood, with decreased activation possibly indicating efficiency or, conversely, declines in ability due to neuronal loss. What does appear clear is that brain activation in response to cognitive tasks differs qualitatively across age groups.

Even if plasticity is limited in the oldest-old, cognitive training could draw upon such compensatory processes, and strengthen those new networks. In addition to developing new networks to compensate for disruption, older individuals may be more likely to maintain their strongest networks, which are used often and may even require less activation due to their efficiency (Stern, 2006). The oldest-old may also have begun experiencing some cognitive
deficits, and therefore may be able to experience greater gains, compared to younger-old who have not experienced such deficits.

Further, oldest-old show smaller associations between their cognitive abilities (i.e. having strong memory functioning does not necessarily suggest equivalent language or executive functioning), as compared to younger elderly (Ram, Rabbitt, Stollery, & Nesselroade, 2005; Schretlen, Munro, Anthony, & Pearlson, 2003). Therefore, cognitive interventions that specifically train individual, weak functions may be most useful in the oldest-old. The physical brain differences and cognitive functioning differences between cognitively healthy oldest-old and young-old elderly indicate that cognitive training might produce different results in these two groups. Therefore, it is important that future studies specifically examine age-related differences in training outcomes and determine the impact of cognitive training on the oldest-old.

Education. Higher education, as well as regular participation in cognitively stimulating activities, may reflect a brain that is more prepared to change and improve with training. Though most cognitive training studies control for education as a covariate, few examine education as a potential modifier of training or training gain. For studies that have investigated this issue, results are mixed. Education may be associated with strategy use during cognitive training (Saczyński, Willis, & Schaie, 2002), and may also be associated with willingness or motivation during cognitive training (Bagwell & West, 2008). Conversely, lower education predicts greater cognitive gains after cognitive training in individuals with MCI and mild to moderate AD (Olazarán et al., 2004), and in individuals with subjective memory complaints (Kwok, Bai, Li, Ho, & Lee, 2013a). However, not all studies examining education as a potential predictor of cognitive training gains found education to have a role (Ball, Edwards, & Ross, 2007; Ball, Ross, Roth, & Edwards, 2013). Further several studies of the effect of education on training gains are
more than a decade old at this point (Rebok et al., 2013), and do not account for advances in
cognitive training in recent past decades. Higher educational attainment also has consistently
been found to associate with higher cognitive functioning (Drag & Bieliauskas, 2010), though
ceiling effects can be a limitation in cognitive training studies such that those with lower
education have more opportunity to demonstrate cognitive gains (Kwok et al., 2013a; Kwok, et
al., 2013b).

Though education has not been closely studied as a predictor of cognitive training
performance and gain, the relationship between education and numerous factors associated with
successful aging makes it a factor of particular interest. Education is considered a proxy for
cognitive reserve, a potential mechanism for the effect of cognitive training. Education does not
merely reflect years spent in school, but also possibly (for some individuals) the ability to
develop learning strategies, the ability to enter into mentally challenging occupations, higher
intelligence, and a cognitively engaging lifestyle (Liberati et al., 2012). Thus, individuals with
greater education attainment may have more motivation and ability to demonstrate cognitive
gains after cognitive training.

The relationship between cognitive reserve and education may also suggest that those
with lower education can expect greater cognitive gains from cognitive training. In one study in
which lower educational attainment was found to be associated with greater cognitive training
gains (Olazarán et al., 2004), it was suggested that the relationship between cognitive reserve,
cognitive training, and pathology may be the reason. Individuals with greater cognitive reserve
may demonstrate better cognitive functioning even with greater AD pathology; therefore
individuals with higher education may have greater AD pathology that impedes cognitive
training gains and/or learning (Olazarán et al., 2004; Scarmeas & Stern, 2003). Olazarán et al.
(2004) only found an improvement in cognition in those with lower education in the training group, but not in the control group (which received only psychosocial support). Likewise, Kwok et al., (2013) found subjects with lower education to respond best to cognitive training, while the low education subjects in the control group (who participated in common community center activities) did not cognitively improve. These findings suggest that significant cognitive challenge, beyond everyday activities, may be necessary for cognitive improvement in low education populations. The lack of clear understanding of the relationship between education and cognitive training gains appoints to the need for research to identify how varying educational levels may affect cognitive training results.

**Future Directions for Cognitive Training**

Research into cognitive training is still in its infancy, and numerous questions and issues remain. Critiques of cognitive training have one major issue in common, the need to improve the transfer of skills from trained tasks to real world settings. It remains unclear whether improvements made in cognitive training programs generalize to cognitive functions and tasks that were not directly trained. In general, it appears that cognitive training programs that focus on a variety of cognitive skills (La Rue, 2010) are preferable, and more likely to transfer beyond the trained tasks. The duration of any effects is also a major question for cognitive training programs. Because cognitive training is relatively new, few longitudinal examinations have been made, and it is unclear whether improvements can be maintained beyond the time period of training. Future studies should attempt to follow participants for as long as possible to assess cognitive stability and change along with decline to MCI or dementia. Further, it is unclear whether training actually delays the onset of dementia, or whether general cognitive engagement and participation in cognitive training are markers of strong cognitive reserve or ability. Thus, at
present there is disagreement over whether cognitive exercise, and specific cognitive training, truly impacts cognitive decline (Park, et al., 2007; Salthouse, 2006).

Individual differences may further complicate matters (Park, et al., 2007). Compliance with cognitive training may be related to self-efficacy or higher education. General physical health may also lead to differences in training outcomes, along with broader self-rated health variables such as energy level. Research on cognitive training has recently expanded to include studies of multi-domain interventions (for example, cognitive training in combination with physical exercise), as well as studies examining brain changes that occur during and after cognitive training. The support for cognitive training and its role in improving or maintaining cognitive functioning in cognitively healthy and cognitively impaired elderly continues to grow, but research is still limited.

**Targeting skills in need of training.** While it will be extremely important to develop and identify cognitive training programs that allow for a transfer of skills, it is equally important to develop programs that target the weakest skills of a given individual (Stuss et al., 2007). Cognitive decline is not consistent across aging, inter-individually or intra-individually, with studies showing that the within-subject variability in cognitive function increases with age (MacDonald, Li, & Backman, 2009). Cognitive training programs that assess the weaknesses and strengths of an individual’s cognitive functioning, and tailor the intervention accordingly, would seem to provide the best opportunity for cognitive change.

**Standardized outcome measures.** It is suggested that outcome measures should include tasks of working memory, episodic memory, executive control, speed of processing, and an overall composite score (Papp, Walsh, & Snyder, 2009). The rationale is that assessing a wide variety of cognitive functions, over time, may provide important information about transfer of
trained skills. Additionally, using a composite score as a primary outcome measure could be useful in identifying small but consistent changes across cognitive domains; in cognitively healthy elderly, these small changes may not be easily identified within domains, but when compiled into a composite score, may be more easily detectable. Further, such an approach could reduce problems caused by ceiling effects and the increase of error rates due to numerous statistical tests. When possible, standardized measures should be used (La Rue, 2010) as well as subjective measures of memory and well-being (Papp et al., 2009). The use of standardized individual neuropsychological measures or more extensive neuropsychological batteries would allow for more consistent interpretation of results, and would also allow for more accurate meta-analyses and reviews of cognitive training.

**Identifying those who would benefit the most.** Commercial cognitive training programs are advertised to individuals of all ages. As aging population grows, however, it is important to understand what kinds of training most benefit older adults. Most studies of cognitive training have been carried out in the younger elderly; the few studies that examined the old-old and oldest-old yielded ambiguous results (Singer et al., 2003; Verhaeghen et al., 1992; Yang et al., 2006). Future research should consider how cognitive training affects younger vs. older elderly, and examine why there might be differences in the results of cognitive training in these populations. For example, the younger elderly tend to show more consistency in ability level across cognitive functions than the oldest-old, who are more likely to show decline in one function while maintaining high ability in others (Ram et al., 2005; Schretlen, et al., 2003). Thus, programs that specifically train participants’ weak cognitive functions may be the most effective for the old-old and oldest-old. Research has yet to explore this possibility.
Further research into how cognitively healthy and impaired persons are affected by cognitive training is also essential. It is likely that these two groups will have different levels of competency with training programs, different levels and patterns of improvement, and different longitudinal results. Identifying how healthy and impaired individuals improve using cognitive training will allow for the development of programs to reduce or delay dementia and improve functioning in the elderly. As more randomized controlled trials are reported, assessments can be made regarding the optimal duration and format of training and which cognitive functions are most improved by training. In addition, researchers can determine how cognitive training can be best utilized at various points during the course of cognitive aging and eventual decline.

Research of cognitive aging and decline is crucial since it may yield improvements in the quality of individual and their families’ lives in addition to impacting healthcare policy and public health. With Americans living increasingly longer, it is critical that all opportunities for improving their cognition be taken. While pharmaceutical options are likely to improve over time, there is also great potential in simple, risk-free, and non-invasive changes in lifestyle factors. By developing effective, convenient, and broadly useful cognitive training programs, the impact of dementia may be diminished and a larger percentage of the oldest of old may be able to maintain cognitive health and better quality of life.

Methods

Specific Aims and Hypotheses

The effects of a computerized cognitive training program, CogniFit Personal Coach, were compared to those of an active control games program (hereby referred to as the games program), in cognitively healthy old-old and oldest-old participants (all above the age of 80).
Composite and single cognitive function scores, from a neuropsychological battery, were used to compare effectiveness of the programs.

**Aim 1.** To compare the effectiveness of the CogniFit Personal Coach and games programs on improving cognitive functioning, as assessed immediately following training.

**Hypothesis 1.** Compared to the games participants, CogniFit Personal Coach participants are expected to demonstrate greater positive change in overall cognitive function (a global cognitive composite) immediately following training.

**Hypothesis 1b.** Compared to the games participants, CogniFit Personal Coach participants are expected to demonstrate greater positive change in the specific cognitive functions of memory, executive functioning/attention, and language, immediately following training.

**Aim 2.** To compare effectiveness of cognitive training on those with differing levels of education.

**Hypothesis 2a.** Those with less education (as determined by a median split) will benefit more from participating in cognitive training, especially those using the CogniFit Personal Coach, compared to those with more education.

**Participants**

**Recruitment.** Community dwelling and assisted living nondemented old old (80+ years of age) individuals were recruited to participate in a study of computerized cognitive training. Participants were recruited from a previous longitudinal study conducted by Dr. Michal Schnaider-Beeri and Dr. Jeremy Silverman at the Icahn School of Medicine at Mount Sinai (ISMMS) in New York, NY and the James J. Peters Veteran Affairs Medical Center (JJP-VAMC) in the Bronx, NY. Participants were also recruited via local flyers, newspapers, and
talks. Flyers (see Appendix 1) were sent to New York City area senior centers, independent living centers, YMCAs, computer centers, colleges and universities, and posted to ISMMS broadcast notifications (weekly emails sent to all ISMMS and Mount Sinai Hospital employees). In addition, the project was advertised in SeniorPlanet, an online senior technology website. Two additional advertisements were placed in the Riverdale Press (see Appendix 2). Talks were given at senior centers in Brooklyn and Manhattan. Finally, participants were recruited from ongoing research studies at the Alzheimer’s Disease Research Center (ADRC) at the ISMMS, using flyers sent to eligible individuals who had agreed to be contacted regarding additional research opportunities.

From the previous longitudinal study, the research staff attempted to contact 79 individuals identified as potentially eligible (meeting the age requirement, agreed to be contacted again, and active in the previous study until its conclusion). There were 32 who research staff were unable to contact (moved or disconnected telephone number), 11 were eligible but did not express interest, 21 did not have a computer or internet compatible with the program, 9 were enrolled, 3 were identified as no longer eligible (cognitive decline) and 3 were no longer living. From the ongoing ADRC studies at the ISMMS, research staff attempted to contact 110 participants. Of these 110, 21 replied, and 18 enrolled (the remaining 3 did not enroll due to not meeting criteria (no computer) or disinterest.

**Inclusion Criteria.** All potential participants were required to have a Mini Mental State Examination (MMSE; Folstein, Robins, & Helzer, 1983) score that was not below the 25th percentile for their age, access to a computer with Internet capability, and time and desire to participate. Potential participants were considered not eligible if they were currently enrolled in a study utilizing cognitive intervention, or if they had a medical disease that would preclude
consistent participation, might affect cognitive functioning, or that might interfere with the
capacity to manage a computer screen, mouse, or keyboard. All participants completed a brief
survey prior to beginning the study, which asked about computer and Internet use (“Do you have
home access to a computer and the Internet? What are the days per week, and hours per day of
use?”), and willingness to participate (“Would you participate in an Internet based program that
may train your mental capabilities? What if it had 20-minute sessions on three days per week for
8 weeks?”). Potential participants were asked if they were participating in any other cognitive
interventions, if they were able to see and hear information on a computer screen, and if they had
any diagnoses of cognitive impairment.

Sample. Sixty-nine individuals met eligibility criteria, were enrolled, and completed the
informed consent and baseline neuropsychological training. Sample characteristics and details
regarding drop-out are presented in Table 6.

Measures

Pre-training Assessment. The first two sessions of the CogniFit Personal Coach and the
games program comprise the CogniFit Neuropsychological Examination– NEM, which
specifically assesses the cognitive weaknesses of each participant. The NEM is a two-session, 17
task assessment (nine tasks at first session, eight tasks at second session) of 14 cognitive domains
(Shatil, Korczyn, Peretz, Breznitz, Aharonson, & Giladi, 2008): working memory, contextual
memory, visual short-term memory, visual scanning, inhibition, auditory short-term memory,
response time, updating, planning, eye-hand coordination, naming, spatial perception, divided
attention, and shifting (see Table 7). The NEM is used to create an individualized training
program for those randomized to the CogniFit Personal Coach program. As an example, a person
who demonstrated weakness in naming, but scored high in time estimation in the pre-training
NEM, would be provided with training sessions including more tasks intended to improve naming and fewer tasks intended to improve time estimation. Thus, CogniFit determines the composition of cognitive tasks to be presented during the training sessions based on participants’ relative performance on the NEM. All participants complete the NEM, but only those randomized to the CogniFit Personal Coach are presented with training that is individualized to their performance on the NEM.

The NEM was validated against the Cambridge Neuropsychological Test Automated Battery (CANTAB) and other tests, and demonstrated high reliability and validity, internal consistency of 0.70 (Cronbach's alpha), and test-retest reliability was 0.80 (intraclass correlation coefficient; Haimov, Hanuka, & Horowitz, 2008).

Table 8 presents a list of NEM tasks. The NEM is presented to participants at the start of the program and at the end of the 24-session training cycle. The NEM is not included as one of the outcome measures of the current study.

**Computerized Cognitive Training Programs.** Participants are randomized to one of two training programs, CogniFit Personal Coach, or the CogniFit games active control program, both described below.

*Choice of cognitive training program.*

Several commercially available programs have been utilized in randomized controlled trials (see Table 5). Of these, CogniFit Personal Coach was chosen as it met several important criteria. Cognifit Personal Coach addresses a wide range of cognitive domains (see Table 7); older elderly are more likely than younger elderly to show variability in their abilities across cognitive domains (Ram et al., 2005; Schretlen, et al., 2003), and within-subject cognitive variability increases with age (MacDonald, Li, & Backman, 2009), so training that incorporates a
range of cognitive domains is especially important for this population. Further, Cognifit Personal Coach is adaptive, such that it customizes training to address the cognitive weaknesses of the user; training weaker skills may be important for an effective cognitive training program (Stuss et al., 2007).

**CogniFit Personal Coach.** CogniFit Personal Coach is an adaptive-interactive system that utilizes 19 tasks (described in Table 9), designed to train 14 cognitive functions (described in Table 7). Each training session includes tasks reflecting a range of cognitive abilities but emphasizes tasks with poorest NEM performance. A patented application, ITS (Individualized Training System), uses algorithms on data provided by the NEM and the ongoing training to adjust the challenge level of training tasks (CogniFit Science Book, 2010). The tasks are intended to encompass a broad range of cognitive functions and serve to keep participants interested and engaged. Participants in the current study used a research version of the commercially available product. Participants completed 20-minute training sessions, three times per week, with one day rest between training sessions, for a total of 24 sessions. Feedback and encouragement are provided by the CogniFit Personal Coach program at each session. Each training session has a combination of three tasks. CogniFit Personal Coach can be used on PC or Mac computers; Internet access is required. Importantly, CogniFit is easy to use regardless of level of computer expertise. Adherence and compliance with the program protocol is monitored by automated electronic data upload when logging out of the program.

**Games (active control) program.** The games (active control) program, also provided by CogniFit, consists of 12 simple games. Games have been found to be useful for improving cognitive functioning (Achtman, Green, & Bavelier, 2008; Drew & Waters, 1986). The games in this control program conform to recommendations for mental stimulation often made by
healthcare providers, offering potential performance improvements on the outcome measures. This active control program, unlike a passive comparison or paper and pencil games, was chosen so the procedures of the two groups would be as similar as possible, and to facilitate double-blindness. In both the CogniFit Personal Coach and the games program, participants receive identical pre-training instruction. Additionally, they are assessed with the NEM at the beginning and end of the program and they complete 20-minute cognitive training sessions, three times per week, with 1 day of rest between the sessions for a total of 24 training sessions. The length of time spent training is identical to CogniFit Personal Coach. The computer games included in this program are presented in a predefined order for all participants and are described in Table 10. Participants complete four games per session, compared to three tasks for the CogniFit Personal Coach.

**Neuropsychological Assessment.** Details of the neuropsychological assessment can be found below.

**Mini Mental State Examination (MMSE).** The MMSE (Folstein et al., 1983) is a 30-item test of global cognition that assesses aspects of basic orientation, concentration, memory, and language. The MMSE is the most widely used instrument for identifying individuals with cognitive dysfunction. The elderly exhibit a high prevalence of cognitive dysfunction that may influence their test performance, and therefore their normative data may differ from those in younger subjects. Thus, norms for the MMSE have been primarily presented for the elderly population (Crum, Anthony, Bassett, & Folstein, 1993). The MMSE has been translated into numerous languages and is widely used in studies of dementia, as well as in clinical practice (Brayne, 1998). A score below the 25th percentile (corresponding to a score of 25; Bravo &
Hebert, 1997) is an exclusion criterion for the current study. The MMSE is not an outcome measure for this study.

**Neuropsychological evaluation.** Cognitive performance was assessed with tests from the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) neuropsychological battery used by the Alzheimer’s Disease Research Center (ADRC- Dr. Sano, PI; Beeri et al., 2006) and the Unified Data Set (UDS) (Morris et al., 2006). Table 11 lists the tests and cognitive domains they comprise, and the details of each test can be found below. This evaluation has detailed administration and scoring procedures and was carefully designed to serve a variety of purposes directly relevant to this project. It was chosen based on the following criteria: (a) standardized published tests, (b) sensitivity to age-related cognitive decline, (c) minimal test-retest effects (Ivnik et al., 1999; Benedict & Zgaljardic, 1998) through use of multiple forms or stimuli that are not remembered across assessment visits, and (d) characterizes a breadth of cognitive functions sensitive to neurodegenerative cognitive change. Importantly, this battery was designed independently of the CogniFit Personal Coach program and thus the outcome measures derived from it will assess generalization of performance gains beyond the specific tasks of the CogniFit Personal Coach or games programs. The neuropsychological evaluation takes approximately 60 minutes to complete. The tests, and their scoring in terms of raw scores, divided into cognitive domains, are described below:

**Memory.** There are two types of verbal memory tasks; word list and paragraph recall.

1. Word List Memory: Three word list memory tasks assess learning and memory for verbal information. These tasks are included in the CERAD and UDS batteries, and derive from the Alzheimer’s Disease Assessment Scale (ADAS, Rosen, Mohs, & Davis, 1984). (a) Immediate recall: This is a free recall memory test that assesses learning ability for new verbal information.
Participants are presented 10 items on printed cards to read aloud. Immediately following presentation of all 10 words, participants are asked to recall as many words as possible. On each of the three learning trials, the 10 words are presented in a different order. The maximum score on each trial is 10. The maximum total score for immediate recall is 30. (b) Delayed recall: This task tests the ability to recall, after 15 minutes, the 10 words presented in the word list memory test. Participants are asked to recall the 10 words they had seen earlier on the printed cards. The maximum total score is 10. (c) Recognition. This task tests the ability to recognize, also 15 minutes after immediate recall, the 10 words from the word list memory task. These words are presented on cards among 10 distracter words. The number of distracter words correctly identified is also counted. The maximum score for each is 10, for a total recognition score of up to 20.

2. Logical Memory Story A: Three paragraph memory tests assess learning and memory for verbal information. (a) Immediate recall: Story A from the Logical Memory subtest of the Wechsler Memory Scale-III (Wechsler, 1997b). Participants are read aloud a brief story by the examiner. Immediately following the story, participants are asked to recall as much of the story, in the exact words of the story, as they can. The maximum score for immediate recall is 25 details from the story. (b) Delayed recall: Recall for Story A is tested 15 minutes later; participants are asked if they remember the story they were read and to recall as much of that story as possible. The maximum score for delayed recall is 25 details from the story. (c) Recognition: Immediately following the delayed recall test, participants are asked 15 yes/no questions to evaluate recognition for the story. The maximum score of the recognition task is 15.

Attention/Executive Functions. There are four tests used to assess attention and executive functioning.
1. Target Cancellation Tests, Diamond and TMX: These tests are used to assess vigilance and speeded attention (Byrd, Touradji, Tang, & Manly, 2004). Participants must identify target stimuli randomly interspersed among distracter stimuli on a sheet of 8.5-x11 paper. One task requires the identification of diamonds among other geometric figures, and another is to identify a specific triple group of letters (TMX) among other triple groups of letters. The time taken to identify targets is the score for this test. The number of correct targets identified is also recorded.

2. Trail Making Test, Parts A and B: Trail Making Tests measure timed attention, mental flexibility and sequencing (Reitan & Wolfson, 1993). In Part A, participants connect unsystematically ordered numbers on an 8.5 x 11 inch page by drawing a line in sequence. In Part B, participants connect unsystematically ordered numbers and letters on an 8.5 x 11 page, in alternating order (i.e. 1, A, 2, B, etc.). The time taken to complete each test is the score for this test. The number of errors in each part is also recorded.

3. Digit Symbol Substitution Test: This is a written test of visuoperceptual processing in which participants are given a key of numbers and matching symbols and a symbol matching each number (Wechsler, 1997a). Below the key is a test section with numbers and empty boxes. Participants are tasked to fill as many empty boxes as possible with a symbol matching each number within 90 seconds. The score is the number of correct number-symbol matches, with a maximum score of 93.

4. Digit span, Forward and Backward: This is a subtest of the Wechsler Adult Intelligence Scale (WAIS)-III (Wechsler, 1997a). The examiner reads a list of digits and the participant is asked to immediately repeat them back. In the Digit Span Forward task, the participant repeats the digits in the same order as they were read, and in the Digit Span Backward task, the participant repeats the digits in reverse order. The number of correct answers in the forward and backward sections
and the number of successfully repeated digits are recorded. There is a maximum score of 12 correct answers for both tests. Additionally, the number of correctly repeated digits (eight repeated digits for Digits Forward, and seven repeated digits for Digits Backward) is also recorded.

Language. Three tests are used to evaluate language.

1. Similarities: Similarities is a subtest from the WAIS-III (Wechsler, 1997a). The test measures abstract thinking by asking participants to state how pairs of words are alike, for example, how an "orange" and "banana" are alike. The score is the sum of scores of correctly answered pairs (rated on a 0-, 1-, and 2- point scale), with a maximum of 33.

2. Boston Naming Test: Participants are asked to name 30 black and white line drawings representing a range of high to low frequency words. The Boston Naming Test (Mack, Freed, Williams, & Henderson, 1992) has 60 total drawings, and the last 30 are used. The score is the number of correctly identified drawings (either spontaneously identified or identified after a semantic clue) with a maximum score of 30.

3. Category Fluency and Letter Fluency: For Category Fluency, which evaluates semantic verbal fluency, participants are asked to generate words within three categories: animals, clothing, and food, in 60 second trials. The score is the sum of the numbers of words in the three categories. For Letter Fluency, which assesses phonemic fluency, participants name as many words as possible beginning with the letters F, A, and S. The test is given in three 60 second trials. The single measure is the sum of words in all three trials. Repeated and incorrect words are noted, but these data do not contribute to the total score (Borkowski, Benton, & Spreen, 1967).
Procedure

**Research staff training.** Eight different examiners conducted the cognitive/neuropsychological evaluations. These examiners were upper level undergraduate students, individuals who had recently completed their B.A. degrees, and master’s level graduate students, from the City University of New York. All examiners completed human subjects research training and were trained by Dr. Elizabeth Guerrero-Berroa, whose expertise is neuropsychology of the elderly. The accuracy of the neuropsychological data was ensured by a well-established set of standardized procedures. All examiners were trained by reviewing training materials with Dr. Guerrero-Berroa for four to six hours, over two days, after which they observed an experienced tester. Finally, examiners administered all tests to Dr. Guerrero-Berroa. As an examiner began to conduct tests with research participants, he or she was regularly observed and any issues are identified at the time of testing. The examiner completed scoring of the tasks, and upon entry of the neuropsychological evaluation data, scoring and range checking was completed.

Prior to the start of the project, Adi Ben-Nun of CogniFit trained the PI to set up the program, register participants, and use the program. The PI also received access to the program to learn and explore the tasks and the NEM, to be fully informed before beginning the current study. Subsequently, the PI set up the computerized cognitive training and instructed participants on the details. The PI kept in regular contact with CogniFit staff during execution of the project.

**Blinding.** Participants were blinded to training program (CCT or control). Cognifit produced both the Personal Coach and active control programs, and graphics, pre-training
instructions, and the two-session Neuropsychological Examination were identical for the two programs. Further, to eliminate potential examiner bias, the neuropsychological examiners were also blinded to program assignment. Thus the set-up, instruction, and technical support on the intervention was performed by the PI, but the neuropsychological examination was completed by a trained examiner who was blinded to program assignment (training is described in the Research Staff Training section above).

**Study procedure.** A flowchart of study procedures can be found in Figure 1. Participants were assigned an individual identification number upon expressing interest confirming eligibility, at which time a research visit was scheduled. Participants were then randomly assigned to the CogniFit Personal Coach (hereby referred to as the computerized cognitive training, or CCT, group) or games active control group (hereby referred to as the games group) through use of a computerized random number generator.

Participants and staff conducting the neuropsychological assessments were blinded to program assignment. The procedures of the two groups were as similar as possible to facilitate double-blindness: identical pre-training instruction; the two-session Neuropsychological Examination-CogniFit (NEM) at the beginning and end of the program; and 20-minute training sessions, every other day, with one day of rest between sessions, for a total of 24 sessions. All graphics, fonts, opening screens, and pre-and post training evaluations, were identical for the CCT program and the control program. Participants were informed during the consent process that they would be randomized to one of two interventions, but that they would not be told during the course of the study which program they received.

At initial visit, all participants provided informed consent approved by the ISMMS or Jewish Home and Healthcare Institutional Review Boards. In most cases, the full baseline
neuropsychological assessment was completed during this visit; however, some participants completed a baseline assessment during the weeks prior to beginning the computer program. These individuals were also participating in an ADRC longitudinal healthy aging study, which employs a neuropsychological assessment that includes most of the same evaluations; remaining evaluations were then completed at this baseline visit. During this initial visit, the computer program was set up and instruction on use of the program was provided. During this visit, the instructor determined whether participants were capable users of the mouse and keyboard, could read the screen effectively, could hear the auditory signals of the programs, and could perform all procedures relevant to the correct functioning of the programs. Participants then completed the first session (session one of the NEM) with an examiner.

Research staff contacted participants weekly to identify and resolve technical problems and record any adverse events. Further, CogniFit provided technical support 24 hours per day, seven days per week, and the PI was available by telephone to assist with any technical issues or questions at any time. Participants were asked to complete one session every other day. After the baseline visit (during which the first session of the NEM was completed), participants self-administered the remainder of the sessions of the CCT or the games programs. Once participants had completed the training sessions, a visit was scheduled to complete the follow-up neuropsychological assessment.

**Power analysis**

Table 12 displays the effect sizes (differences in Z-scores between the two groups) that are detectable with 80% power, using a two-sided alpha of 5%, with n=30 participants in each of the two groups (Oakes & Feldman, 2001). Effect sizes are a function of $R^2$, the proportion of variance in the follow-up score that is explained by the baseline score. $R^2$ was expected to be
high, as baseline scores will strongly predict follow-up scores (high $R^2$), hence it is easier to
detect smaller effects of treatment.

Effect sizes between $d = 0.19$ and 7.14 have been calculated for computerized cognitive
training interventions (Keuider et al., 2012); there is wide variability in effect sizes in studies of
computerized cognitive training. With $R^2$ expected to be high, moderate effect sizes can be
expected; for example, if $R^2$ is .5, there is 80% power to identify an effect size of .52.

The current study has 39 subjects randomized to the training program and 30 subjects
randomized to the control program, and therefore may not have adequate power to detect the
small effect sizes observed in some studies, but there is power to detect moderate effect sizes.
Further, data from the current study can be used to estimate effect sizes to use in sample size
calculations for future larger-scales studies of computerized cognitive training in the old-old and
oldest-old.

**Outcome Measures**

**Primary outcome: global cognitive composite.** A recent review of the effects of cognitive
interventions in healthy elderly (Papp et al., 2009) recommended that the primary outcome
should assess several key domains and “lead to an omnibus composite score.” Composite
cognitive scores have been noted as most appropriate for identifying treatment-related cognitive
improvements in the cognitively normal oldest-old (Papp et al., 2009). Composite scores reduce
ceiling and floor effects, a major challenge for cognitive training outcome assessment, as well as
other measurement problems such as extreme scores. Additionally, composite scores avoid Type
I error introduced by multiple outcomes. It was expected that cognitive changes from baseline to
follow-up could be subtle, but would occur in numerous cognitive domains since CogniFit
attempts to train multiple cognitive domains. Based on these various considerations, the primary
outcome measure is a global cognition composite of the 17 neuropsychological scores in Table 11, which cover a broad range of functions.

The global composite score was calculated at baseline as the mean of Z-scores, each directed so a positive score refers to good cognition. The coefficients used to calculate the Z-scores at baseline were used for the follow up composite score.

**Secondary outcomes.**

**Specific cognitive domains.** Since CogniFit Personal Coach trains a variety of cognitive functions, it is of interest to assess its efficacy in specific domains in addition to a global cognitive composite. Three secondary outcome scores, memory, executive functions/attention, and language, were calculated. At baseline, these scores were the means of the baseline Z-scores of their respective tests. As with the composite cognition score, at follow up, the coefficients used to calculate the Z-scores at baseline are used for the follow up composite score. The Memory function score is the sum of Z-scores on the following tests: Word List Memory, Immediate recall; Word List Memory, Delayed recall; Word List Memory, Recognition; Logical Memory Story A, Immediate recall; Logical Memory Story A, Delayed recall; and Logical Memory Story A, Recognition. The Attention/Executive function score is the mean of the Z-scores on the following tests: Target Cancellation Tests (diamond and TMX); Trail Making Test (Parts A and B); Digit Symbol Substitution Test; and Digit Span tests (Forward and Backward). The Language function score is the mean of the Z-scores on the following tests: Similarities; Boston Naming Test; and Category Fluency and Letter Fluency tests; see Table 11. Both the primary and secondary outcome measures are independent of the NEM assessment and cognitive training.
**Potential covariates.** Positive effects of cognitive training have been found in various age groups but less attention has been paid to the old-old and oldest-old, possibly because these groups are thought to possess less neural plasticity suggesting that they may benefit less from cognitive training (Rebok et al., 2013). Age as a continuous variable was included in the data analysis models as a covariate.

The literature on sex differences in cognitive function is extensive and suggests that males and females may demonstrate different strengths and weaknesses with regards to cognitive functioning (Rahe et al., 2015). Further, there is evidence of sex differences in cognitive training effects, with females demonstrating stronger training improvements (in individuals with MCI, Rahe et al., 2015). To control for the potential of a sex difference in cognitive change due to training over time, sex has been included as a covariate.

Evidence on the effects of education on cognitive training gains is mixed. In one study, highly educated individuals benefited more from memory training (Rebok et al., 2013). Olazarán et al. (2004) and McDougall et al. (2010) found that individuals with less education benefited more from cognitive-motor training than those with more education. Other studies examining this relationship have not found a significant effect of education (Gagnon & Belleville, 2012; Rasmusson, Rebok, Bylsma, & Brandt, 1999). Individuals with higher education often perform better on baseline cognitive testing prior to training (Rebok et al., 2013). This suggests that those with less education have more opportunity to improve on cognitive tests, making education a potentially interesting covariate. In the current study, years of education was collected as a categorical variable, 12 years, 13-15 years, and more than 15 years. Overall, 29% of the entire sample had 12 years (7%) or 13-15 years of education (22%) (no college degree), while 71% had more than 15 years (college degree).
Finally, number of training sessions was used as a covariate because the analysis is intent-to-treat, with all participants included in the analysis regardless of completion of training.

Statistical and Analytic Plan

Overview. Although all hypotheses were directional, conservatively, two-sided hypothesis tests were used to compare the CCT group to the games group, to accommodate unexpected results. Linear mixed model analyses were performed to identify the interaction of group assignment with time (from baseline to follow-up), to determine whether the groups changed at different rates from baseline to follow-up neuropsychological tests. The linear mixed models were run with training group and time as fixed factors, subjects as a random factor, and the training group by time interaction. The interaction term was used to assess whether the rate of change from baseline to follow-up neuropsychological tests differs between the training groups. No participants were excluded due to the lack of training adherence or missing data, and participants who did not complete training but were seen for a follow-up neuropsychological assessment, as well as those who did not complete a follow-up neuropsychological assessment, were included in the study analyses (intent-to-treat [ITT] analysis, which reflects the usefulness of the intervention in real life [Chakraborty, 2009]).

Detailed analytic plan. Statistical analyses were conducted using SPSS (version 20.0). Since there was only one primary outcome measure, the significance level was set at 5%. No corrections for multiple comparisons were made for secondary outcome measures. Data were cleaned and range checked for irregular values. The data were reviewed for outliers, by identifying values more than 1.5 interquartile ranges about the 3rd and below the 1st quartiles. Outlying observations were not excluded but were reviewed to determine if they were possible
values. Next, participant characteristics were reviewed and analyses conducted to assess differences between groups on age, sex distribution, and education.

Descriptive analyses of the baseline raw data were carried out, identifying means and standard deviations (see Table 13). Group differences over time on normal continuous variables were evaluated using t-tests and group differences over time on skewed variables were evaluated using Wilcoxon tests to compare group medians.

Baseline neuropsychological tests were Z transformed using the mean and SD of the entire sample at baseline (Rexroth et al., 2013). The cognitive domains of overall cognition, memory, executive function/attention, and language were calculated as the average of those Z-scores (see Table 11 for tests used in each cognitive factor). Follow-up Z scores were then calculated, using the means and standard deviations of the baseline raw data (Rexroth et al., 2013). Again, the Z-scores corresponding to the tests for each factor were averaged to create the follow-up cognitive domains. Normality of the Z-scores, and of the cognitive domains (averaged from Z-scores), was assessed at baseline and follow-up (details are presented in the Results section). For the first set of outcome measure analyses, we conducted unadjusted t-tests comparing the means of outcome measures within cognitive training groups over time.

Linear mixed models were conducted with the fixed effects of time, treatment group, and the interaction between time and treatment group (to assess whether the rate of change in outcome over time differs between the training groups), and the random effect of subject. The covariates of sex, education, age, and number of sessions completed were included. The linear mixed model approach allowed for the analysis to include all participants, including those who are missing data at baseline or follow-up, eliminating the loss of data and allowing for an intent-
to-treat approach to data analysis. Such measures to account for missing data are considered superior to simpler imputations of data (Beunckens, Molenberghs, & Kenward, 2005).

Additionally, we conducted analyses examining the impact of education on the effect of cognitive training on cognition. The sample was highly educated (see Table 6), so education level groups were based on education levels of college degree and no college degree (though most in the no college degree group had at least some college, and all had graduated high school). We conducted linear mixed models with the fixed effects of time, education level, and the interaction between time and education level (to assess whether the rate of change in outcome over time differs between the education level groups), and the random effect of subject, for age, sex, program, and sessions completed. Additionally, t-tests within groups of education were conducted for descriptive purposes. Finally, the impact of the interaction of time and treatment group on the NEM was examined. Linear mixed models were conducted with the fixed effects of time, treatment group, and the interaction between time and treatment group (to assess whether the rate of change in outcome over time differs between the training groups), and the random effect of subject. The covariates of sex, education, age were included.

Results

Study Sample

Sample demographics can be found in Table 6. A total of 69 individuals were enrolled. Participants were randomly assigned to the CCT group (n=39) or the games group (n=30). The mean age of participants was 85.81 years, 65.2% of the participants were female, and 71% of the participants had more than 15 years of education. Participants in the CCT and games groups did
not differ on age or sex. They did differ significantly on education, ($\chi^2=6.317, p=.042$), with higher than expected numbers of participants with 12 years of education, and higher than expected numbers of participants with more than 15 years of education, in the games group; there was a higher than expected number of participants with 13-15 years of education in the CCT group.

**Attrition and Training Completion**

Fifty-one participants completed at least 75% of the training (31 in the CCT group, 20 in the games group). The CCT group completed 19.20 sessions on average (SD=8.99), while the games group completed 16.88 sessions on average (SD=9.93); this is not a significant difference ($t(67)=1.005, p=.319$).

Additional information regarding completion of training can be found in Table 6. There was no significant difference in drop-outs between the CCT and games groups ($\chi^2=2.27, p=.518$).

**Data Analysis**

Data cleaning and range checking identified several outlying observations at baseline and follow-up. Outlying observations were not excluded, but reviewed to determine that they are possible values, which was indeed the case for all of them.

Participants were cognitively normal as determined by the MMSE (mean 29.06, range 25-30; a score below the 25th percentile, corresponding to a score of 25 (Bravo & Hebert, 1997), was an exclusion criterion. Further, a comparison of means of the participants with age norms on several of the neuropsychological tests shows that these participants are in the middle and upper percentiles on the tests. For example, mean scores at baseline on Word List Memory: Immediate recall (22.09), Trail Making Test: Trail A (49.06) and Trail Making Test: Trail B (112.91) were
all between the 50th and 75th percentiles for individuals age 80-89 (Beeri et al., 2006). For Category Fluency, the mean score of 46.57 at baseline was equivalent to an 82nd to 89th percentile score for 84-86 year olds (Lucas et al., 1998).

Descriptive characteristics for all cognitive tests at baseline and follow-up for the entire sample can be found in Table 13. At baseline, there was a significant difference between the games group and the CCT group on one of the neuropsychological tests; the games group scored significantly higher on the Logical Memory Story Recall-Immediate test at baseline (16.21), compared to the CCT group (14.24), t(63)=-2.04, p=.046. There were no other differences in baseline scores between the two intervention groups; see Table 14. For the three most skewed variables, Word List Memory: Recognition, Trail Making Test: Trail A, and Trail Making Test: Trail B, Wilcoxon tests were also used to compare group medians. No significant differences were found between the games and CCT groups (Word List Memory: Recognition [p=.936]; Trail Making Test: Trail A [ p=.491]; and Trail Making Test: Trail B [ p=.947]).

Baseline neuropsychological tests were converted into Z-scores. The cognitive domains of overall cognition, memory, executive functions/attention, and language were calculated as the average of the relevant Z-scores. The means and standard deviations of the baseline neuropsychological tests were then used to calculate Z-scores for the follow-up neuropsychological tests. See Outcome Measures and Table 11 for the descriptions of the tests included in each cognitive domain.

Linear mixed models were used to identify an overall effect of time, an increase or decrease in cognitive functioning from baseline to follow-up regardless of program, with time as the fixed factor, subjects as a random factor, and no interaction term. Covariates for the linear mixed models included treatment group, age, education level, sex, and number of training
sessions completed. No significant effect of time on the overall cognitive functioning (the global cognitive composite) \(F(1, 53.232)=2.177, p=.146\), was found. Additionally, no significant effects of time on the specific cognitive domains were found; language \(F(1, 51.114)=.000, p=.984\), attention/executive functioning \(F(1, 50.718)=.007, p=.934\), or memory functioning \(F(1, 53.370)=3.761, p=.058\), though the change for memory functioning was trend level.

Overall, results suggest that participants did not significantly improve or decline as a function of time between baseline and follow-up.

**Comparison of CCT vs. games on Overall Cognitive Functioning (Global Cognitive Composite)**

To identify whether the groups demonstrated significant between-group differences over time on overall cognitive functioning (based on the global cognitive composite), linear mixed models were run, with fixed effects of time and treatment group, interaction between time and treatment group, and the random effect of subject, with covariates age, education level, sex, and number of training sessions completed. No significant interaction of treatment group with time on the overall cognitive functioning \(F(1, 55.991)=.198, p=.658\), was found, see Table 15. When the linear mixed model was again run on individuals who completed training (defined as having completed at least 75% of the training sessions, \(n=31\) on CCT and \(n=20\) on games), no significant interaction of treatment group with time was found on the overall cognitive functioning \(F(1, 48.957)=.057, p=.813\) was found, see Table 16. There were no significant between-group differences over time on overall cognitive functioning.

**Specific Cognitive Domains**

To determine whether the groups demonstrated significant between-group differences over time on the specific cognitive domains, linear mixed models were run with fixed effects of
time and treatment group, interaction between time and treatment group, and the random effect of subject, with covariates age, education level, sex, and number of training sessions complete. No significant interaction of treatment group with time was found for the cognitive domains of attention/executive (F(1, 53.739)=.730, p=.397), language (F(1, 52.862)=.251, p=.618), or memory (F(1, 55.851)=.092, p=.763), see Table 15. Linear mixed models were then run for completers only and once again no significant effects of treatment group over time on attention/executive (F(1, 48.649)=.372, p=.545), language (F(1, 48.430)=.647, p=.425), or memory (F(1, 48.843)=.282, p=.598) functioning were found. See Table 16. No significant between-group differences over time were found on the specific cognitive domains.

Unadjusted t-tests were used to determine within-group changes on the neuropsychological tests, for descriptive purposes. In the CCT group, participants significantly improved on Logical Memory Story A: Immediate recall (from 14.34 (4.45) to 16.48 (4.05) correctly identified items, t(28)=-3.581, p=.001), Logical Memory Story A: Delayed recall (from 13.44(4.57) to 15.33(3.89) correctly identified items, t(26)=-3.416, p=.002), and Digit Span Backward (from 7.54(2.56) to 8.25(2.52) correct items, t(27)=-2.097, p=.045). In the games group, participants significantly improved on the Boston Naming Test (from 25.11(3.07) to 26.68(2.47) correct items, t(18)=-2.535, p=.021). See Table 17 for complete list of within group t-tests. The CCT and games groups did not significantly improve on any other individual cognitive tests, and they did not significantly decline on any tests.

**Education**

Analyses examining the impact of education on the effect of cognitive training were also conducted. Participants reported education as either 12 years, 13-15 years, or more than 15 years. A majority of participants had more than 15 years, so participants were split into two groups:
those with a college degree (equivalence of more than 15 years) and without a college degree (equivalence of 15 or fewer years of education; 12 years or 13-15 years). These two groups did not differ in age ("high" education mean age 85.93, "low" education mean age 85.5, t(67)=-.374, p=.709), MMSE (high education mean 29.04, low education mean 29.11 t(64)=.199, p=.843), or number of training sessions completed (college degree group mean 18.32, no college degree group mean 17.87, t(67)=-.180, p=.858). Further, they did not differ in proportion assigned to CCT and games programs (χ²=.824, p=.429), or sex (χ²=1.296, p=.278). Linear mixed models were run, with fixed effects of time and education group, interaction between time and education group, the random effect of subject, with covariates age, training program, sex, and sessions completed. A significant interaction of education with time was found for the overall cognitive composite (based on the global cognitive composite) (F(1, 55.080)=4.755, p=.034). A significant interaction of education and time was also found for the cognitive domain of language (F(1, 52.688)=5.298, p=.025). No significant effects were found for memory (F(1, 56.013)=.692, p=.409) or attention/executive functioning (F(1, 52.709)=1.585, p=.214), see Table 18 for details.

To clarify these interactions, t-tests within groups of education were run for descriptive purposes. Those without a college degree significantly improved on the overall cognitive functioning (t(13)=2.59, p=.023), and showed trend level improvements for language (t(13)=-2.01, p=.066), and memory functioning (t(13)=1.98, p=.069), however, they did not significantly improve (or decline) on attention/executive functioning. The group with college degrees did not significantly improve (or decline) on overall cognitive functioning or on any of the specific cognitive domains. The t-tests and linear mixed models results suggest that cognitive activity, regardless of training group, was effective at improving overall cognitive functioning and
language in those without a college degree, but training was not effective at improving global or specific cognitive functioning in those with a college degree. See Table 19 for details.

**NEM**

Analyses examining the interaction of training group and time on 13 of the NEM tasks (see Table 8 for full list of NEM tasks) were also conducted. A significant interaction of training group with time, demonstrating a significant improvement for the CCT participants compared to the games participants, was found for three tasks: “The Flowers” (interaction for two accuracy measures: longest correct sequence in level 1, $F(1, 52.975)=4.85, p=.032$; and longest correct sequence in level 2, $F(1,41.384)=4.86, p=.033$), “Pictures Trio” (interaction for accuracy percentage, $F(1,48.947)=5.51, p=.023$), and “Pictures and Words” (interaction for total correct answers, $F(1,52.772)=6.18, p=.016$).

**Discussion**

**Summary of results**

This study examined the effect of a computerized cognitive training program, CogniFit Personal Coach, with an active control games program also produced by CogniFit, in cognitively healthy individuals aged 80 and older. Participants completed a comprehensive neuropsychological test battery, then trained on the program in 20-minute sessions, every other day, for 24 sessions (7-8 weeks), and lastly completed a follow-up neuropsychological test battery. The two groups were comparable at baseline, suggesting that randomization into the two groups was successful, even if the number of participants in each group was unequal. The two groups did not differ in age, sex, or on any but 1 of the 17 neuropsychological tests at baseline (the games group scored higher on the Logical Memory Story-A Immediate recall test). The games group was significantly more educated. Overall, participants on the whole did not
significantly improve or decline on overall cognitive functioning (based on the global cognitive composite), or the specific cognitive domains, over time.

Cognitive domain scores were computed as the average of z-scores, so that participants had an overall cognitive functioning score (global cognitive composite), a memory score, an attention/executive functioning score, and a language score. The study had three hypotheses: (1) compared to the games participants, CCT participants were expected to demonstrate greater positive change in overall cognitive functioning (according to the global cognitive composite score) immediately following training; (2) compared to the games participants, CCT participants were expected to demonstrate greater positive change in the specific cognitive functions of memory, attention/executive functioning, and language, immediately following training; and (3) those with fewer years of education were expected to benefit more from participating in cognitive training, with CCT participants expected to demonstrate greater positive change compared to games participants, compared to those with more years of education.

For hypotheses 1 and 2, no significant interactions of program with time were found on overall cognitive functioning (global cognitive composite) or the three specific cognitive function domains. This was true both for the entire sample and for those who fully completed the training. Notably, there were some within-group improvements over time on individual cognitive tests. Specifically, the CCT group improved on Logical Memory-Story A- Immediate Recall, Logical Memory Story B-Delayed Recall, and Digit Span Backwards, and the games group improved significantly on the Boston Naming test.

These results demonstrate that the CCT group did not gain greater improvement over time on overall cognitive functioning, or the specific cognitive domain scores, compared to the games group (nor did the games group demonstrate greater improvement over the CCT group).
The within-group improvements suggest that the use of a cognitive training program improved performance on some of the individual cognitive tests, but the linear mixed models suggest that those effects did not differentiate the two groups from each other on overall cognitive functioning or specific cognitive functions (neither the CCT group nor the games group improved or declined more than the other).

For hypothesis 3, results indicated that those with less education (no college degree) improved significantly on overall cognitive functioning (the global cognitive composite) and language functioning compared to those with more education (college degree), regardless of program assignment.

**Overall Cognitive Functioning (Global Cognitive Composite) and Specific Cognitive Domains**

**Interaction of training group with time.** The lack of an interaction between training group and time for the overall cognitive functioning and specific cognitive domains suggests that neither the CCT nor the games program was superior to the other in generating positive cognitive change. Though there is significant support for the potential utility of cognitive training programs, there remains a serious lack of understanding about the conditions under which cognitive training is effective, the impact of individual differences on cognitive training efficacy, and the possibility of significant improvement on skills and functions not specifically trained (“transfer”). Further, while the literature tends to emphasize the positive effects of cognitive training, there may well be substantial “publication bias”, i.e. that the studies where no significant results were found were not published (Dwan et al., 2008).

As in any field, studies of cognitive training reveal both positive and negative findings, and studies of cognitively healthy individuals have not found any specific test or function that
consistently improves. For example, recent studies of computerized cognitive training in healthy elderly have shown the training to be ineffective, or no more effective than the control condition, at improving immediate memory and language [Miller et al., 2013], attention and global cognition [Nouchi et al., 2012], Stroop and Controlled Oral Word Association test performance [Wolinsky et al., 2013], and some measures of attention, executive function, and mental flexibility [Peretz et al., 2011]).

Factors affecting cognitive training effectiveness. It is unclear why the CCT group did not demonstrate an advantage over the games group on the overall cognitive functioning and specific cognitive functions, but current literature provides clues regarding a number of potential factors involved in effective and non-effective computerized cognitive training. These include training program characteristics like training session length, frequency, location (home-based versus group- or clinic- based); difficulty of the program and control. They also include participant characteristics such as baseline cognitive performance, education, motivation, and belief in the malleability of cognition, these characteristics may predispose individuals to, or protect them from, decline (La Rue, 2010). For example, higher education, as well as regular participation in cognitively stimulating activities, may equip individuals with a brain that is functionally and structurally more able to cope with or compensate for damage (La Rue, 2010). These factors also may be associated with an aged brain that is more prepared to change and improve with training. Further, compliance with cognitive training is important to monitor, but it is necessary to recognize that compliant participants may have higher levels of self-efficacy or higher education, and may have more energy to take part in the programs. These variables are considered below in terms of their potential to impact cognitive training.
Training program characteristics. The characteristics that are important to an effective cognitive training program continue to be assessed by current cognitive training studies. In the current study, the length of the training sessions may have been problematic. Lampit et al., (2014), for example, found that sessions that last less than 30 minutes may not be as effective as those that last longer. The CogniFit programs (Personal Coach [CCT] and the games program) have sessions that last about 20 minutes each. It has also been suggested that at-home training without assistance, and frequent (more than three times per week) training may be ineffectual (Lampit et al., 2014). Notably, the CogniFit programs are completed 3-4 times per week (once every other day). Short but frequent sessions may lead to boredom, cognitive overload, or fatigue. Additionally, that the program is conducted at home, unsupervised, may lead to compliance and adherence issues. Participants may be completing the sessions more or less often than every other day, for example. External factors may also impact the effectiveness of training; studies examining unsupervised, at home use of assessment and evaluation software have noted issues like distraction or interruption of training by other software (for example, antivirus software pop-ups) on the computer (Woodard & Rahman, 2012), issues with speaker use (headphone use may be more immersive and reduce outside noise [Woodard & Rahman, 2012]), or distractions in the environment (family members or others in the room or telephone calls, for example [Luxton, Pruitt, & Osenbach, 2014]). These distractions may impact performance, motivation, or focus.

The meta-analysis by Lampit and colleagues (2014, p.13) even suggested that “the popular model of purely home-based training is unlikely to result in cognitive benefits in unimpaired older adults.” As of now, some of the most effective cognitive training programs have been those that were group-based (Ballesteros et al., 2015; Lampit et al., 2014), compared
to those that were home-based and self-administered (Ballesteros et al., 2015; Lampit et al., 2014). Lampit et al. (2014) noted that group-based programs likely benefit from social aspects including motivation and encouragement from a trainer and social interaction with the group. Social contact and interaction in a psycho-educational component of cognitive training examined by Jean et al. (2009) potentially provided a reduction in anxiety, which the authors suggest likely strengthened the impact of the training. Balleseros et al. (2015) describe the possible additive benefits of social interaction when addressing the benefits of activities like dance, and posit that interventions combining social, cognitive, and physical activity are promising. The home-based cognitive training program of the current study included very limited social interaction, thus it likely lacked an advantage that is found in group-based training programs or training programs with a greater social component.

The current study also utilized an active control (games program) that was likely less challenging than the cognitive training program, but for a variety of reasons may have been similarly useful. Individuals in both conditions participated in the social aspect of the research study (meeting with research staff), were given a novel cognitive task, and were made aware of their cognitive functioning, and these variables may have been more important than the actual difference between the CCT and games programs. Effect sizes for computerized cognitive training are often small, and active controls are likely to limit the effects of such programs (Papp et al., 2009). Active controls may sometimes be similarly effective—for example, reviews by Martin, Clare, Altgassen, Cameron, and Zehnder (2011) and Ballesteros et al. (2015) found that improvements in memory and global cognitive functioning demonstrated by individuals using a cognitive training program were no greater than improvements found in those using an active control. In such situations, Jacoby & Ahissar (2013) suggest, personal factors like motivation and
arousal (discussed below) may be more impactful on training efficacy and transfer of skills than the differences between cognitive training and active control programs.

**Participant characteristics.** The current sample was well educated and cognitively strong, performing well at baseline. Therefore there may have not been much opportunity for improvement, especially on tasks like Word List Memory- Recognition where a ceiling effect was found (See Table 13). This is a common problem in studies of computerized cognitive training where participants are cognitively intact (for example, Bozoki, Radovanovic, Winn, Heeter, & Anthony, 2013) and may be engaged in a number of other cognitively and physically challenging activities (Ackerman et al., 2010). Individuals already engaged in challenging activities may not benefit significantly from additional cognitive training (Kwok et al., 2011). Further, individuals who participate in research to enact lifestyle changes are generally in better cognitive and physical health and may not show dramatic change (Schneider & Yvon, 2013).

The current study examined old-old and oldest-old participants specifically, and age may have been a factor in the efficacy of the programs. It has been reported that plasticity may be more limited in older age (Greenwood & Parasuraman, 2010; Park & Reuter-Lorenz, 2009; Singer et al., 2003). Older age has been found to be associated with smaller training gains, potentially due to reduced plasticity (Zinke, Aeintl, Rose, Putzmann, Pydde, & Kleigel, 2013) and reduced training transfer (Borella et al., 2013; Zinke et al., 2013), though not all studies support these findings. Calero, López Pérez-Díaz, Navarro González, and Calero-García (2013) found significant variability in the plasticity of the old-old, with greater plasticity in those with higher levels of cognitive functioning.

There are also a variety of state factors that could impact training efficacy (Jacoby & Ahissar, 2013) but were not addressed in this study: motivation (Boquete, Rodríguez-Ascariz,
Amo-Usanos, Martínez-Arríbas, Amo-Usanos, & Otón, 2011; Thompson et al., 2013) and affect (Konen & Karback, 2015) may impact cognitive training performance and gains as well as performance on the outcome measures, especially in a relatively small sample. Additionally, opinions and beliefs regarding the malleability of cognition were not collected from the participants and these beliefs may be integral to the utility of cognitive training (Jaeggi et al., 2014). If personal factors are relevant to the impact of cognitive training, such factors may obscure potential differences between a computerized cognitive training program and an active control, by providing a placebo effect that allows any cognitive challenge to be effective.

**Transfer of skills.** In the current study there were few direct similarities between the program tasks and neuropsychological tests that served as the outcome measure. Transfer of skills from trained tasks to tasks and tests that were not directly trained is one of the major issues of cognitive training research. There is inadequate evidence for “far transfer,” or transfer of training to unrelated skills and tasks, in cognitive training programs (Ballesteros et al., 2015; Lustig et al., 2009; Papp et al., 2009). It is common for studies to demonstrate improvements on directly trained skills and skills that are very similar to trained tasks (“near transfer”), while improvements in skills that are not related (“far transfer”) are not as common and primarily observed in young adults (Park & Bischof, 2013). Additionally, transfer effects in the old-old and oldest-old are often weaker (Borella et al., 2013). Thus, improvements on the tasks trained may have not been translated to improvements on the outcome measures.

In addition to the dissimilarities between the CogniFit programs tasks and the outcome tasks, which may limit transfer, the programs do not specifically teach cognitive strategies. While the CogniFit programs do provide training on a wide variety of cognitive functions, instruction in specific strategies for processing and utilizing cognitive information training is a
program characteristic that is considered important to the possibility of transfer. Strategy training may be the most effective type of cognitive training for eliciting transfer of skills (Lustig et al., 2009), allowing participants to employ strategies outside of the training program. The absence of strategy training may be one reason that improvements on the trained cognitive tasks did not translate into broad improvements on the outcome measures.

Analysis of the NEM data, in which CCT program users improved significantly more than control users on three tests, further supports the possibility that the CCT program produced near, but not far, transfer. Participants who used the CCT program trained on tasks very similar to the NEM tasks. For example, the “Pattern Memory” task in the CCT program is very similar to the “The Flowers” task in the NEM, see Tables 8 and 9. Games participants did not train on tasks with many similarities to the NEM tasks, so this likely explains why CCT participants, but not control participants, showed improvement on those NEM tasks. Therefore, because CCT participants improved on tasks very similar to the ones they trained on, near transfer appears to have occurred, but this did not translate into far transfer improvement on the outcome measures of the study.

**Within group change.** Unadjusted t-tests revealed significant within-group changes for both groups. The CCT group improved on two of the memory measures (Logical Memory Story A-Immediate recall, and Logical Memory Story A-Delayed recall) and one of the attention/executive functioning measures (Digit Span Backward). The games group improved significantly on the one of the language functioning measures (Boston Naming Test). The test-retest time differences was short (approximately two months apart), which could suggest practice effects. Indeed, analysis of practice effects (based on a common method described by Duff et al., [2005] and Dikmen, Heaton, Grant, & Temkin [1999]) finds practice effects on these tests,
though they are generally small effect sizes (.28 or smaller, though as noted below, Logical Memory test has been found to have a large practice effect [Lo, Humphreys, Byrne, & Pachana, 2012]).

Logical Memory tests have been found to improve after cognitive interventions in individuals with Parkinson’s disease (Eckroth-Bucher & Siberski, 2009) and late-life depression (Naismith, Diamond, Carters, Norrie, Redoblado-Hodge, Lewis, & Hickie, 2013), and other story recall tests have been found to improve after memory or cognitive training (Buschert et al., 2011; Hohaus, 2007; Huckans, Hutson, Twamley, Jak, Kaye, & Storzbach, 2013; Klusmann et al., 2010; Sisco, Marsiske, Gross, & Rebok, 2013). However, other intervention studies have not found cognitive interventions to improve Logical Memory tests (Gates & Baker, 2014, Kanaan et al., 2014; Strenziok, Parasuraman, Clarke, Cisler, Thompson, & Greenwood, 2014) or other story recall tests (Tarraga et al., 2006). Most cognitive interventions include a memory-training component or even teach memory strategies. Thus, for CogniFit, transfer to the Logical Memory tests may be an outcome of relatively near transfer or improvement on a trained skill. CogniFit Personal Coach includes several memory tasks, though none specifically story recall, and claims to train cognitive functions such as auditory short-term memory and contextual memory (see Table 7 for details), both relevant to story recall. The importance of the type of training in improvement of a cognitive skill is clearly demonstrated by Sisco and colleagues (2013), who evaluated the effectiveness of memory, reasoning, and speed of processing training on improving story recall. Not surprisingly, those who completed memory training improved the most at recalling story details verbatim. Thus, improvements on the Logical Memory tests may be due to near transfer effects of memory training in the CogniFit cognitive training program. However, the Logical Memory test has been found to have a large practice effect (Lo, Humphreys, Byrne,
& Pachana, 2012), so it is possible that improvements were simply due to practice and a short test-retest time period.

CCT participants also significantly improved on the Digit Span Backward task, though the p value (.045) was small. Again, this may be a result of near transfer (or even directly trained tasks), as the CogniFit Personal Coach program (CCT program) includes a task called “Memory Drills,” in which items (including numbers) are presented and must be remembered in forward and backwards order (See Table 9 for details). The program also claims to train auditory short-term memory and working memory (See Table 7), so it is likely that participants were able to transfer their training from the cognitive training program to Digit Span Backward. Digit Span improvement has been noted in some studies of cognitive training (mnemonic training in cognitively healthy older adults [Brehmer, Rieckmann, Bellander, Westerberg, Finscher, & Backman, 2011]; computerized cognitive training in older adults with MCI [Herrera, et al., 2012]; video game – based brain training in cognitively healthy older adults [McDougall & House, 2012]), but these results are not universal (non-computerized cognitive training in healthy and AD participants [Cavallo, Cavanna, Harciarek, Johnston, Ostacoli, & Angilletta, 2013]; video game – based brain training in cognitively healthy older adults [Nouchi et al., 2012]). As above, the studies in which improvements were found in Digit Span included interventions that directly trained memory for items, including numbers, pictures, and words, so improvements on digit recall tasks are likely due to the tasks being directly, or nearly directly, trained. For this test, the possibility of practice effects is much less likely (Dong, Thompson, Tan, Lim, Pang, & Chen, 2013).

Surprisingly, those using the games program showed a significant improvement on the Boston Naming test. The Boston Naming test has been found to improve after cognitive training
(Rojas et al., 2013), though not in all cases (Barnes et al., 2009; Miller et al., 2013). The games program does not directly train any naming skills, or even language skills, so the mechanism behind this improvement is unclear. As above, a practice effect is possible. A small practice effect on the Boston Naming test has been found (Zec, Markwell, Burkett, & Larsen, 2005), when tests were separated by 9 to 15 months; here with a much shorter amount of time between tests, the likelihood of a practice effect is increased.

Overall, the improvements on the tests by the CCT and games groups are likely due to a combination of direct training and practice effects. Without additional information or the inclusion of covariates, it is difficult to evaluate based on these within group t-tests whether the training programs are fully responsible for improvements on the cognitive tests.

**Education and Cognitive Training**

In the current study we found an interaction of level of education with time on overall cognitive functioning (global cognitive composite) and language functioning. Participants were split into two groups: those with a college degree (equivalence of 16 years of education or more) and without a college degree (equivalence of 15 or fewer years of education). Linear mixed models demonstrated that those with less education improved significantly more than those with more education, and t-tests for descriptive purposes demonstrated that those with no college degree improved significantly on overall cognitive functioning, while those with a college degree did not improve (or decline) significantly on any cognitive domain (See Tables 18 and 19). These analyses controlled for age, sex, sessions completed, and also training group. Further, the education groups did not differ in number of participants randomized to CCT program versus games program. The impact on these two outcome measures is surprising—global cognition and
language have not been closely evaluated in the cognitive training literature (Lampit et al., 2014).

**Education and overall cognitive functioning (global cognitive composite).** Education is associated with cognition, including better cognitive functioning (Lachman, Agrigoroaei, Murphy, & Tun, 2010; Parisi et al., 2012) and lower risk of dementia (Ngandu et al., 2007; Valenzuela & Sachev, 2009), and is considered a highly significant proxy for cognitive reserve (Drag & Bieliauskas, 2010; Premi et al., 2013). Despite this important relationship between education and cognitive aging, studies have not found a clear pattern with regard to the relevance of education to cognitive training. Some evaluations of this relationship have found that education does not impact the effectiveness of cognitive training (Gagnon & Belleville, 2012; Rasmusson et al., 1999; Verhaeghen et al., 1992). Other studies have found that less educated participants improve more (McDougall et al., 2010; Olazaran et al., 2004) or less than highly educated participants (Belleville, 2008; Gross & Rebok, 2011; Rebok et al., 2013) from cognitive training. Generally, studies of computerized cognitive training control or match for education, rather than evaluating it as a potential moderator (for example: Berry et al., 2010; Buschert et al., 2011; Engvig et al, 2012, Optale et al., 2009; Wolinsky et al., 2006). Consistent with this study’s results, participation in cognitive activity has been shown to moderate the relationship between lower levels of education and cognitive functioning, such that those with lower levels of education who participated in frequent cognitive activity demonstrated episodic memory performance that was similar to those with higher levels of education (Lachman et al., 2010). This finding suggests that cognitive activity is especially important to those with lower levels of education.
Because the literature on cognitive training is relatively recent, we can only speculate on the mechanisms underlying a greater cognitive improvement from cognitive training in participants with less education. Individuals with lower education may find cognitive training more challenging, more difficult (Kwok et al., 2013b), or more novel, compared to those with more education; challenge is likely an important component of an effective cognitive training program (Vidovich, Lautenschlager, Flicker, Clare, & Almeida, 2009). It may be that those with more education in this sample actually have more neuropathology but perform equally to those with less education due to increased cognitive reserve; such greater amount of neuropathology may hinder neural plasticity and cognitive improvement. Individuals with less education are less likely to use cognitive strategies. Perhaps the cognitive training or even simply participation in a cognitive study increased awareness of or interest in using cognitive strategies, while those with more education may have been using such strategies already. Therefore those with less education, but not those with more education, developed methods to improve their cognitive performance during the course of the study. Those with less education may have engaged less in other challenging cognitive activities during the time of cognitive training compared to those with more education (those with higher education engage in more cognitively stimulating activities on a daily basis compared to those with lower education [La Rue, 2010]); therefore a challenging cognitive activity may have been novel and thus more impactful to those with less education.

Individuals with less education have been found to perform worse on cognitive tests compared to those with more education (Meguro et al, 2001; Backman et al., 2004; Parisi et al., 2012), including on baseline measures in cognitive training studies (Rexroth et al., 2013). If participants with less education performed worse at baseline, they would have more room for
improvement, and indeed, those with lower education did perform worse at baseline on four of the neuropsychological tasks (Similarities, Letter Fluency, Category Fluency, and Digit Span Backward). Similarities, Letter Fluency, and Category Fluency are three of the four tests included in the language function; participants with less education improved significantly compared to those with more education on the language function in addition to overall cognitive functioning. Still, two of those tasks (Letter Fluency and Category Fluency) have no upper score limit, so there was the opportunity for both groups to improve significantly. Further, there is the threat of a ceiling effect on some of the tests—i.e., the recognition tasks (Word List-Recognition was found to have a median score at baseline equal to the maximum possible score and Logical Memory Story A-Recognition mean score at baseline was 13 of 15). However, for Similarities and Digit Span Backward, the group means were well below the maximum possible score, again allowing for room for improvement for both groups; additionally, the linear mixed models utilized for this study adjusted for baseline levels. Thus, it is not clear that ceiling effects are the primary mechanism for the relationship between education and cognitive improvement in our study.

Finally, cognitive training via a computer and the internet may be frustrating for older adults (Rute-Perez, Santiago-ramajo, Hurtado, Rodriguez-fortiz, & Caracuel, 2014; Wild, Mattek, Maxwell, Dodge, Jimison, & Kaye, 2012); there was a non-significant but trend level (p=.09) difference in computer use between those with more and less education, such that those with less education were less likely to use the computer daily. The additional challenge of using the computer, which in itself may be beneficial in terms of social interaction, feelings of well-being, and even cognitive functioning [Ordonez, Yassuda, & Cachioni, 2011; Shapira, Barak, & Gal, 2007]), may have additionally augmented the efficacy of the training programs.
Participants with more education may have greater levels of AD neuropathology, compared to those with less education, and the neuropathology may hinder learning. Higher levels of education have been suggested to delay clinical signs of dementia (Stern, Alexander, Prohovnik, & Mayeux, 1992), therefore those in this study with more education may have more neuropathology while demonstrating no clinical signs of dementia. It is very common for neuropathology related to AD to be found in older individuals without cognitive decline or impairment (Bennett et al., 2012), and greater neuropathology may reduce plasticity and/or the ability to learn (Jellinger & Attems, 2010). Therefore, if the participants in this study with lower levels of education also have lower levels of AD neuropathology, they may have a greater potential for learning and improvement. These possibilities are speculative given that we do not have an index of neuropathology for participants in the current study.

It is possible that those with lower education increased use of cognitive strategies during the course of the training. Although strategy training was not explicitly taught by these programs, those with less education may have self-initiated new strategy use during the course of the training, while those with more education may have already been using cognitive strategies before the start of training. It has been shown that those with more education use more cognitive strategies (Gross & Rebok, 2011), and that cognitive training can improve strategy use (Gross & Rebok, 2011). Self-initiated strategy use appears to be important for cognitive functioning (Drag & Bieliauskas, 2010), and cognitive training programs that do not explicitly teach strategies may still implicitly encourage strategy use. It may be possible that the novel use of cognitive strategies, self-initiated during training, benefited those with less education, while those with more education did not increase their use of self-initiated cognitive strategies. Further, Zinke et al. (2013) found that individuals with worse baseline scores (as was the case for those with less
education) improved more after training, and suggested a situation of “latent potential” in which these individuals had unused cognitive capabilities drawn out by cognitive training. Participants with less education may have discovered or uncovered (consciously or unconsciously) cognitive strategy and ability that may have allowed them to show greater improvement than those with more education.

Individuals with more education are generally found to engage in regular challenging cognitive activity (and may also engage in more social and physical activities [Ajrouch, Blandon, & Antonucci, 2005; Browning, Sims, Kendig, & Techuva, 2009; Cornwell, Laumann, & Schumm, 2008; Kaplan, Newsom, McFarland, & Lu, 2001]), with more opportunities and resources to become involved in such activities (Lachman et al., 2010). It is possible that those with less education were less likely to be involved in other cognitively challenging activities during the course of training, therefore the training was a new and potentially more impactful stimulation to their cognitive functioning. Indeed, individuals already engaged in cognitively challenging activities may not show benefit from the addition of a cognitive training program (Kwok et al., 2011). However, more educated individuals may also be more motivated or effortful in cognitive challenges (Parisi, 2010), which is in opposition to our findings. External cognitive (and social and physical) activities, however, were not evaluated or controlled for in this study.

Those with less education (no college degree) improved on a number and variety of cognitive tasks. In fact, on 16 of the 17 cognitive tasks, the scores improved, though most often non-significantly, for those with lower education. These individuals therefore demonstrated improved overall cognitive functioning, regardless of program assignment. This is surprising, as it was expected that those with less education and assigned to the CCT program would
demonstrate greater improvements than those with less education and assigned to the games program. In previous studies finding a moderating effect of education on training gains, improvements in cognition occurred only in those in the training groups, but not in the control group (Kwok et al., 2013b; Olazaran et al., 2004). The findings of this study may suggest either that there was not a considerable difference in the cognitive challenge provided by the CCT program compared to the games programs, or that even a limited amount of cognitive challenge may be advantageous for those with less education. Lachman et al. (2010) demonstrated that cognitive activity (reading, completing crossword puzzles, writing, or attending lectures) at the frequency of as little as once a week, could compensate for lower levels of education. In this study, it seems that the addition of thrice weekly cognitive activity, even at the hypothetically less challenging level of the games program, was enough to improve cognitive functioning in those with lower levels of education.

Those with more education (college degree and above) did not demonstrate improved overall cognitive functioning and improved (again, most often non-significantly), on only 9 of the tasks. It is likely that some combination of mechanisms and variables, including performance at baseline, level of challenge and novelty, neuropathology, and use of self-initiated strategy, certainly in addition to other unknown variables, benefited participants with less education.

**Education and language.** It is notable that participants with lower education showed improvements in language functioning compared to those with more education. In the current study, the language domain is a composite of language fluency, ability to describe the similarities between items, and ability to name items in pictures.

As noted earlier, individuals with less education may have had more room for improvement, scoring lower on some of the baseline measures, compared to those with more
education. Indeed, three of the four measures on which those with less education had lower baseline scores were components of the language function, the only specific cognitive function that significantly improved for those with less education. Still, again as noted above, two of those tasks (Letter Fluency and Category Fluency) have no upper score limit, so there was room for both groups to improve significantly. Additionally, on the Similarities task, the group means for both the less education and more education groups were well below the maximum possible score, allowing for improvement from both groups. Further, using t-tests to examine within group change on each of these tests individually, the lower education group did not demonstrate significant change over time for the single tests of Letter Fluency, Category Fluency, Boston Naming, or Similarities. However, the lower education group did show non-significant positive change for each of these tests, while participants with more education showed non-significant negative change on three of these tests. Again, it is not clear that potential for improvement, based on baseline performance, is a primary mechanism for the relationship between education and improvement on language functioning.

Far transfer effects have been found on language-related tasks (Carretti, Borella, Zavagnin, & De Beni, 2012), and in the current study, those with less education improved on language functioning regardless of program. Active control programs have been documented as being similarly, or more effective, than cognitive training programs at improving language functioning. For example, Barnes et al. (2009) found that their control condition participants, who, among other tasks, listened to books and read, improved more than the cognitive training group on language functioning. Similarly, Miller et al. (2013) found that individuals in both the training and control groups improved on language functioning as long as they completed at least 40 training sessions.
Though the four tasks are grouped together as a factor called language (due to factor analysis; this is a factor also described in other papers, for example, Brickman et al., 2011), the tasks may also represent functions like semantic memory (Boston Naming test [Morris et al., 2006; Jefferson et al., 2011], Letter and Category Fluency [Jefferson et al., 2011]), and reasoning/conceptualization (Similarities [Rute-perez et al., 2014; Oswald, Gunzelmann, Rupprecht, & Hagen, 2006; Uchida & Kawashima, 2008]). Language functioning is believed to peak very late in life (Hartshorne & Germine, 2015), and to be relatively stable (Drag & Bieliauskas, 2010), so it may be informative to evaluate changes in language more specifically, as changes in semantic memory and reasoning/conceptualization. Semantic memory has been identified as being strongly related to late-life cognitive activities (Jefferson et al., 2011), and may not show age-related decline (Drag & Bieliauskas, 2010), suggesting that cognitive function may be open to positive change, even in late life. Conversely, abstract reasoning may show age-related decline relatively early (Deary et al., 2009), and the two training programs did not claim to improve abstract reasoning or conceptualization, so it is surprising to see change in this domain (the Similarities test on its own did not show significant improvement, but did show a potential trend of improvement with a p value of .171). Still, it is possible that individuals with less education were made self-aware of their cognition (increased meta-cognition) through use of a cognitive training program. Meta-cognition is considered a potential outcome of and mediator of success in cognitive training (Belleville, 2008; Clare, Wilson, Carter, Roth, & Hodges, 2004), and it may encourage deeper thinking (Rojas et al., 2013), and thereby reasoning/conceptualization. Still, the exact relationship of education, cognitive training, and language is unclear, but it is encouraging to discover that cognitive activity, even an active control, may be beneficial for language functioning in individuals with lower levels of education.
**Overall Findings**

The current study did not find the computerized cognitive training program to be more effective at improving cognitive functioning than the games program. Though this study did have limitations (discussed below), there is an inadequate understanding of the utility of computerized cognitive training programs for improving cognition in cognitively healthy elderly, and the current findings suggest that computerized cognitive training may not be effective for every population. The current literature has identified effect sizes that generally are not large (Lampit et al., 2014; Papp et al., 2009), suggesting that while these programs may induce small improvements in cognition, these improvements may not be relevant to everyday or clinical situations, and there is not enough evidence to suggest that these programs may delay onset of cognitive impairment (Papp et al., 2009) or reduce dementia incidence (Lovden, Xu, & Want, 2013). Recent research has incorporated cognitive training with other methods considered potential mediators of cognitive decline, such as physical exercise and healthy diet (Ahlskog, Geda, Graff-Radford, & Petersen, 2011; Alles, Samieri, Feart, Jutand, Laurin, & Barberger-Gateau, 2012; Bherer, 2015; Feart, Samieri, & Barberger-Gateau, 2015; Kirk-Sanchez & McGough, 2014). Such combined efforts may be more effective and ongoing research into these combined interventions may shed light on the benefits of computerized cognitive training in the context of a more comprehensive intervention (Bamidis et al., 2014; Bherer, 2015; Ngandu et al., 2015).

The finding of an effect of education is especially significant, as the relevance of education to the effectiveness of cognitive training is not only unknown, but not well studied (see Education and overall cognitive functioning [global cognitive functioning], above). In the current study, participants without college degrees showed significant improvement on overall cognitive
functioning and language scores, regardless of program, compared to participants with college degrees.

**Study Strengths**

The present study was a double-blind controlled, randomized clinical trial with objective cognitive outcome measures unrelated to the cognitive training programs utilized. The neuropsychological battery we used is well validated, and included tests assessing a variety of cognitive skills. The study was conducted at the Icahn School of Medicine at Mount Sinai, which provided the necessary resources, and was bolstered by the guidance and advice of investigators who are leaders in the field of cognitive aging.

Moreover, we utilized an intent-to-treat analysis, believed to be the best analytical approach for randomized, controlled intervention trials. Covariate data including demographic information as well as computer and internet use was collected to develop an analytic model that best identified the true effects of cognitive training. Participants and neuropsychological evaluators were blind to program assignment; at this time additional data regarding the effectiveness of blinding, whether participants suspected that they were enrolled in the training program or the games program, is being collected.

The use of an active control allows researchers to identify whether individuals may be able to improve cognitive functioning with the use of simple, free cognitive activity. New cognitive learning and activity on their own may be effective at maintaining cognition, so it may be the case that use of the computer and internet, including a novel set of tasks, was beneficial. Use of computers is associated with greater cognitive functioning (Tun & Lachman, 2010), and Ordonez et al. (2011) demonstrated that older adults who trained in computer lessons not only improved their computer skills but also improved on memory, visuospatial, and language skills.
Though overall there was not an effect of time on cognitive functioning (participants in both groups did not generally improve from baseline to follow-up on overall cognitive functioning or specific cognitive functions), participants with less education, who may also be less computer-literate or computer-savvy, improved significantly over time regardless of training program. These participants may have benefitted from using the computer and internet, which in itself may have been a cognitively-challenging task.

Finally, we enrolled individuals aged 80 and older, an age group generally understudied and even less so in the context of computerized cognitive training. Clear differences exist in brain functioning, cognitive ability, and computer use of different older age groups (Beeri, et al., 2009; Cabeza & Dennis, 2012; Ram et al., 2005; Rebok et al., 2013; Schretlen et al., 2003; File & Ryan, 2014). Therefore, it is important to assess the effectiveness of cognitive training specifically within different age groups to best understand its utility and tailor its use to those who can most benefit.

**Study Limitations**

Although the sample size is believed to have been sufficient to identify modest improvements in cognitive function, it may have been too limited to identify smaller effect sizes (common in cognitive training studies) and there is a possibility that with a larger sample size, some additional significant findings may have resulted. This is even more likely to be an issue with cognitively healthy, computer literate, old-old and oldest-old participants. Such a population has survived to at least the age of 80, and thus is likely to have experienced unusually successful and stable cognitive aging and may not show significant gains or declines in cognition over a brief period of time, even with the use of a cognitive training intervention.
Some significant changes from pre- to post-assessment did occur within each group. Therefore, there may have been a limitation of the control program being effective or challenging enough to render any improvements indistinguishable from improvements gained from use of the CCT.

The design and implementation of this study was challenging in a number of ways. Though increasing numbers of older adults are using computers and the internet, such technologies are not yet widely embraced by older adults (Fischer, David, Crotty, Dierks, & Safran, 2014) and so recruitment from such a population was difficult. Recruitment from the pool of individuals enrolled in ongoing longitudinal aging studies in the Alzheimer’s Disease Research Center at the Icahn School of Medicine at Mount Sinai was especially fruitful, however, these individuals often comprise highly successful cognitive agers, with high scores on the neuropsychological assessments and strong, stable cognitive functioning; therefore, inclusion of these individuals may have limited the possibility of finding significant improvements on neuropsychological tests.

Compliance with the program varied. Though participants were given instructions to complete the program one session at a time, every other day, some rushed through the program, and others took considerably longer to complete the program than the expected 7-8 weeks. The CogniFit company believes the program is most effective if completed one session at a time, every other day, so non-compliance may have reduced the impact of the training. Compliance may also have depended on participants’ familiarity with computers and the program they received. Though participants were blinded to program assignment, reports from participants suggested that some found the CCT program to be extremely challenging, though participants with greater computer literacy tended not to have this issue. Further, based on personal reports
from some participants, the control program may have been boring or underwhelming, and it may have been that those with greater computer literacy who experienced boredom may have dropped out due to disinterest in the control program.

As with many computerized cognitive training studies, there was significant attrition, reducing statistical power. This was generally due to lack of interest and lack of time. Participants were generally retired, but were also often involved in numerous social, political, and physical activities. Again, this speaks to the overall strong physical and cognitive health of this sample, reducing the likelihood of producing cognitive improvements with a cognitive training program.

The current sample is not representative of all old-old and oldest-old. Our participants were generally well-educated individuals, with computer and internet access and strong cognitive health, and the vast majority were Caucasian. Therefore, results cannot be generalized to all old-old and oldest-old individuals.

Analysis did not exclude participants who did not fully comply with the protocol; such analysis was utilized to generate results more representative of the effectiveness of the program in a real-world setting, however, this may have underestimated the efficacy of the program in those who did complete the protocol. According to Armijo-Olivo et al. (2009), such analysis ("intent-to-treat") may not provide a full assessment of the treatment effect of those who do comply when non-adherence in the program is high. Analysis including only those who completed the program was conducted, in order to better assess the efficacy of the program, with similar results.

Finally, a number of variables that may modify the relationship between cognitive training and cognitive gains were not explored including state variables such as motivation and
affect, levels of neuropathology, health variables such as self-rated health and cardiovascular disease, and current levels of physical, social, and cognitive activity. These variables may be relevant to the efficacy of cognitive training and should be included in future research.

**Additional Future Directions**

There is still a great need to evaluate computerized cognitive training more closely, to assess its effectiveness on non-trained tasks and cognitive functions, and to evaluate which variables impact its effectiveness. Randomized, controlled trials (RCTs) will continue to be, as in any other field of study, the gold-standard for best identifying the effect of computerized cognitive training, and though the number of RCTs continues to grow, the literature on computerized cognitive training remains mixed and so it is imperative that more and larger-scale RCTs are developed and conducted. When possible, RCTs should continue to assess participants for as long as possible to address the role that computerized cognitive training could potentially have in delaying or slowing cognitive decline. A second major direction for the evaluation of computerized cognitive training is the examination of how such programs may improve cognitive functions and skills not directly trained by the program. If such transfer of cognitive skills is possible, programs that train the weakest cognitive functions and skills of the user will be especially practical.

There remains a need to assess and improve the usability of cognitive training programs (Boquete et al., 2011; Callari, Ciairano, & Re, 2012; Fisher et al., 2014). If a program is difficult to use for an older individual, it has little chance of being effective. Large font, clear audio, straightforward directions, uncomplicated interfaces, technical support, and demonstrations are important basic components that are not well addressed by the literature. For unsupervised at-home programs, it may be beneficial for users to complete more than one session with an
instructor or researcher; this may reduce drop-out and give the user an opportunity to identify technical issues and questions about use (Rute-Perez et al., 2014).

The addition of long-term follow-up cognitive assessments after training is complete would allow for a greater understanding of the extended benefits of cognitive training, and the addition of a booster session or sessions would provide additional insight to the effectiveness of cognitive training over a long period of time. Finally, the interaction of education with cognitive activity found in this study suggests a need for additional, larger scale studies that recruit a larger group of individuals with lower levels of education.

Conclusions

The current study examined the effectiveness of a computerized cognitive training program, CogniFit Personal Coach, and an active control games program, in cognitively healthy old-old and oldest-old. Participants using CogniFit Personal Coach were not found to improve significantly more than the games group on overall cognitive functioning, or specific cognitive domains, though they did improve on three individual cognitive tests (compared to one test for the games group). Further, those with less education (no college degree) improved significantly on the overall cognitive functioning while those with more education (college degree) did not improve on overall cognitive functioning or specific cognitive domains. Overall, this study demonstrates that though cognitive training may be beneficial, it is not necessarily beneficial to all individuals aged 80 and older, who are cognitively healthy. The current study further highlights the important role of education in the efficacy of cognitive training.
### Dementias and cognitive decline

<table>
<thead>
<tr>
<th>Type</th>
<th>Alzheimer’s disease</th>
<th>Vascular dementia</th>
<th>Mild cognitive impairment (MCI)</th>
<th>Age related cognitive decline</th>
</tr>
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<td>Prevalence</td>
<td>Most common cause of dementia among people aged 65 and older</td>
<td>Second most common cause of dementia, accounting for about 20 percent of all dementias</td>
<td>Variation in estimated prevalence, from 8-26 per 1000 person-years</td>
<td>Likely to occur in all elderly, prevalence difficult to determine</td>
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<td>Neurological hallmarks/ Major features</td>
<td>Three major hallmarks: Amyloid plaques</td>
<td>General loss of gray matter, tissue death in thalamus, basal ganglia, amygdale, hippocampus, and angular gyrus. Enlargement of the ventricles, shrinkage of the corpus callosum</td>
<td>Not clear as to the underlying pathology of MCI. Neuropathology may resemble very early AD</td>
<td>Brain volume generally decreases, neurons and connections are lost</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Non-reversible, develops over years, and leads to severe loss of mental functioning</td>
<td>May coexist with AD. Symptoms often begin after a stroke, suddenly. Vascular dementia may not progress- but further strokes will likely cause progression. With no further cardiovascular incidents, symptoms may improve</td>
<td>Many patients with this condition later develop dementia, some do not. Numerous markers are being developed to identify those most likely to convert to AD</td>
<td>These changes are generally considered normal, not signs of dementia, and not an indication of progression to dementia</td>
</tr>
</tbody>
</table>

### Table 1

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<thead>
<tr>
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</tr>
<tr>
<td>Symptoms</td>
<td>Limited changes in personality and emotion until late stages. Language, memory likely to be impacted. Wandering, depression, functional declines (may be temporary). Symptoms may also depend on the type of vascular dementia.</td>
<td>Cognitive and memory problems are not so severe as to be considered dementia, but are greater than “normal” cognitive aging.</td>
<td>Usually slower cognitive processing and some declines in memory with age.</td>
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<tr>
<td>Treatment</td>
<td>No treatment slows progression. Several medications treat symptoms, especially cholinesterase inhibitors. Treat mild / moderate symptoms, for months to few years. Medications maintain cognitive skills, limit changes in behavior, personality. Behavioral treatment, anti-depressants, cognitive exercises may be useful.</td>
<td>Treatment and medication generally address symptoms. Medication and behavioral treatments may be used to improve cardiovascular problems and prevent additional brain injury from cardiovascular disease. Cholinesterase inhibitors may be effective at temporarily reducing cognitive symptoms.</td>
<td>No FDA –approved treatments for MCI. Treatments for AD can be used and show an effect on the rate of progression from MCI to AD. Not generally treated with medications. Cognitive exercises and behavioral modifications may improve symptoms.</td>
<td></td>
</tr>
<tr>
<td>Causes</td>
<td>Environmental, genetic, and lifestyle variables are believed to cause AD. Early onset, or familial AD, is inherited, and late onset AD is more common in individuals with the apolipoprotein E 4 allele. Other genes have also been implicated.</td>
<td>Brain damage from cerebro- or cardio-vascular problems, often strokes. Other causes: genetic disease, other brain damage, endocarditis, hypotension, accumulation of amyloid protein. Even one stroke can cause</td>
<td>Causes are unclear. MCI is hypothesized by some to be an early stage of AD, suggesting that the causes of AD are the causes of MCI. Often attributed to normal (non-pathologic) biological changes that cause neural death and damage. Age, environmental influences, medical influences, all generally are believed to impact age related cognitive</td>
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</table>
in AD. Poor physical and mental health may increase the risk of AD. It is likely a combination of these factors that cause AD. dementia (single-infarct dementia). Strokes on left side of the brain or affecting the hippocampus are more likely to cause dementia. Multi-infarct dementia (MID), is caused by several small strokes, damaging multiple areas, lesioning white matter.
Table 2

*Current pharmaceutical treatments for AD, and several directions for future pharmaceutical treatments*

<table>
<thead>
<tr>
<th>Drug types</th>
<th>Disease stage</th>
<th>Activity</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholinesterase inhibitors</td>
<td>All stages</td>
<td>Increasing levels of acetylcholine by preventing breakdown, may increase acetylcholine release in the brain</td>
<td>Donepezil, rivastigmine, galantamine</td>
</tr>
<tr>
<td>NMDA receptor antagonists</td>
<td>Moderate and severe</td>
<td>Decreasing glutamate excitotoxicity and regulating glutamate activation</td>
<td>Memantine</td>
</tr>
<tr>
<td>Anti-amyloid therapies</td>
<td>Mild and moderate</td>
<td>Decreasing β-amyloid production and aggregation, or clearing β-amyloid</td>
<td>Those in Phase III clinical trials include solanezumab, gantenerumab, MK-8931. Additional β-amyloid are in Phase I and Phase II trials, and newer trials are evaluating β-amyloid therapies for prevention</td>
</tr>
<tr>
<td>Anti-tau therapy</td>
<td>Mild and moderate</td>
<td>Decreasing tau aggregation and activation</td>
<td>Numerous treatments to inhibit tau aggregation and stabilize microtubules are in Phase I and Phase II clinical trials</td>
</tr>
<tr>
<td>Nerve growth factors</td>
<td>Mild and moderate</td>
<td>Reducing cell death by increasing nerve growth factors</td>
<td>CERE-110 is in a Phase II clinical trial</td>
</tr>
</tbody>
</table>

*Note. Adapted from Avand & Sabbah, 2015; Rafi & Asien, 2015; NIH Alzheimer’s Disease Medications Fact Sheet, 2015*
### Table 3

*Randomized, controlled trials: Non-computerized cognitive training*

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcome measures</th>
<th>Effects</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDougal et al., 2010</td>
<td>285 cognitively healthy</td>
<td>Memory training vs. health promotion training</td>
<td>Memory self-efficacy, metamemory, memory performance, IADL</td>
<td>Memory group made greater gains on global cognition, had fewer memory complaints. Both groups maintained performance on other cognitive measures, IADLs at 24 months. Minority participants made greater gains on some memory tasks</td>
<td>12 sessions</td>
</tr>
<tr>
<td>Fairchild &amp; Scogin, 2010</td>
<td>53 cognitively healthy</td>
<td>Memory training vs. social support</td>
<td>Positive Affect and Negative Affect Schedule (PANAS), Multifactorial Memory Questionnaire (MMQ), objective and subjective memory tasks</td>
<td>Memory group showed significant improvement in objective and subjective memory tasks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Bailey, Dunlosky, &amp; Hertzog, 2009</td>
<td>77 cognitively healthy</td>
<td>At home self memory training vs. control</td>
<td>Word list recall</td>
<td>Memory training group showed gains in word list memory</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Park et al., 2009</td>
<td>129, various cognitive functioning</td>
<td>Cognitive training program vs. observational control</td>
<td>Geriatric Depression Scale (GDS-SF), MMSE</td>
<td>Those with cognitive dysfunction showed improvements after the cognitive training program</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Description</td>
<td>Outcome &amp; Length</td>
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<tr>
<td>Hastings &amp; West, 2009</td>
<td>185 cognitively healthy</td>
<td>Individual memory training vs. group memory training vs. control</td>
<td>Both memory training groups showed improvements, which were maintained for 1 month after training. 6 weeks</td>
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<tr>
<td>Kinsella et al., 2009</td>
<td>52 MCI</td>
<td>Cognitive rehabilitation with caregivers vs. control</td>
<td>Memory group performed significantly better at memory tasks, strategy knowledge, after training and at 2 week and 4 month follow-up. 5 weeks</td>
<td></td>
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<tr>
<td>West, Bagwell, &amp; Dark-Freudeman, 2008</td>
<td>84 cognitively healthy</td>
<td>Group cognitive rehabilitation vs. control</td>
<td>Significant improvements for the training group for memory self-efficacy, locus of control, and word/story recall. 6 weeks</td>
<td></td>
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<tr>
<td>Troyer, Murphy, Anderson, Moscovitch, &amp; Craik, 2008</td>
<td>68 MCI</td>
<td>Classroom memory training vs. control</td>
<td>Memory group showed significantly better strategy knowledge after intervention and at 3 month follow-up, but no improvement in objective memory task performance. 10 weeks</td>
<td></td>
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<tr>
<td>Bugos et al., 2008</td>
<td>39 cognitively healthy</td>
<td>Piano instruction vs. control</td>
<td>Piano group significantly improved on the Trail Making Test and Digit Symbol measures. 6 months</td>
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<tr>
<td>Buiza et al., 2008</td>
<td>238 Cognitively healthy and memory impairment</td>
<td>Cognitive training group 1- structured training. Group 2- unstructured training. Control</td>
<td>Group 1 showed gains in immediate memory, short-term memory, and working memory. 2 years</td>
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<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Intervention Details</td>
<td>Outcome Description</td>
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<tr>
<td>Willis et al., 2006</td>
<td>2832</td>
<td>Memory, speed of processing, or reasoning training, or control</td>
<td>Reasoning group better IADLs compared to control group, booster training for speed of processing group showed a significant effect on speed of processing. Intervention groups maintained targeted cognitive ability through 5 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Craik et al., 2007</td>
<td>49</td>
<td>Memory training, either with immediate entry into the study or 3 month delay</td>
<td>No obvious training related improvements, but some evidence for improvement in Logical stories secondary measures and strategy use, primarily in group that was immediately entered into study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Margrett &amp; Willis, 2006</td>
<td>98</td>
<td>Reasoning training individually, or with a spouse, or control group</td>
<td>Both training groups performed better than control group on several reasoning measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wadley et al., 2006</td>
<td>181</td>
<td>Lab-, or home-based speed of processing training, controls- social contact and no contact</td>
<td>Home- and laboratory-based processing speed gains did not differ significantly. Both training groups improved on processing speed significantly more than control groups.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lustig &amp; Flegel., 2008</td>
<td>32</td>
<td>Integrated Sentences training vs. Strategy Choice training</td>
<td>Both conditions improved on self-reports of everyday memory errors. The strategy-choice group performed better on recognition memory.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Tsai, Yang, Lan, & Chen, 2008

25 with subjective cognitive complaints

Cognitive training vs cognitive stimulation

ADAS-cog, MMSE, selective reminding task (SRT) and clock-drawing task (CDT)

CT group improved on cognitive performance (ADAS-cog, MMSE), and SRT, CS group improved on cognitive performance (ADAS-cog, MMSE) and CDT. All improvements remained at follow-up, and CS group had additional gains on the ADAS-cog score, the CT group had additional gains in SRT. No significant differences between the groups.

Note. Pubmed "cognitive training" or "cognitive intervention" or "memory training" or "memory intervention"
Table 4

*Sample of the commercially available English language “brain training” software and internet programs*

<table>
<thead>
<tr>
<th>Program</th>
<th>Program objective</th>
<th>Publisher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain age</td>
<td>“Designed to help stimulate your brain and give it the workout it needs like solving simple math problems, counting currency, drawing pictures on the Nintendo DS touch screen, and unscrambling letters.” For all ages.</td>
<td>Nintendo, <a href="http://www.brainage.com">www.brainage.com</a></td>
</tr>
<tr>
<td>Nintendo DS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain Builder</td>
<td>“BrainBuilder is a scientifically designed, computer-based Brain Fitness program that can improve memory, attention and BrainSpeed.” For all ages.</td>
<td>Advanced Brain Technologies, <a href="http://www.brainbuilder.com">www.brainbuilder.com</a></td>
</tr>
<tr>
<td>Lumosity</td>
<td>“Drawing on the newest developments in neuroscience, Lumosity.com offers brain training exercises that work. Regardless of your age, Lumosity can make you smarter and more mentally fit.” For all ages.</td>
<td>Lumos labs, <a href="http://www.lumosity.com">www.lumosity.com</a></td>
</tr>
<tr>
<td>Posit Science</td>
<td>“The Brain Fitness Program speeds up and sharpens auditory processing—the listening system of the brain. By improving the quantity and quality of what your brain takes in through sound, it drives an overall improvement in thinking, focus, and memory.” For all ages, but designed for those 65+.</td>
<td>Posit Science, <a href="http://www.positscience.com">www.positscience.com</a></td>
</tr>
<tr>
<td>Brain fitness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posit Science</td>
<td>“The InSight brain fitness software targets visual processing—how efficiently your brain takes in and reacts to what you see. InSight speeds up and sharpens visual processing so you can focus better, notice more, and react quicker.” For all ages, but designed for those 65+.</td>
<td>Posit Science, <a href="http://www.positscience.com">www.positscience.com</a></td>
</tr>
<tr>
<td>Insight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NeuroNation</td>
<td>“NeuroNation brain training exercises aim to improve your working memory, which is your ability to process information quickly, make rational decisions and ignore distractions. What's more, working memory is directly related to intelligence - the more you train, the smarter you can be.” For all ages.</td>
<td>Neuronation <a href="http://www.neuronation.com">www.neuronation.com</a></td>
</tr>
<tr>
<td>Fit Brains</td>
<td>“The Fit Brains program offers balanced cognitive stimulation across 6 major brain areas, including: Focus, Memory, Speed, Logic, Visual and Language. The system</td>
<td>Rosetta Stone <a href="http://www.fitbrains.com">www.fitbrains.com</a></td>
</tr>
</tbody>
</table>
automatically adapts to each user to offer personalized training at appropriate levels for each area of the brain, and is based on strong foundation of cognitive data from more than 300 million brain training sessions completed.”

Happy Neuron “Entertaining brain games that are fun and scientifically developed and validated to challenge your mind and keep it in top gear at all times. The comprehensive cognitive program stimulates your attention, language, memory, visual-spatial and executive function skills. Incorporate brain fitness into your lifestyle and start building your cognitive reserve today. Minimizes the natural effects of brain aging by maximizing the brain's natural capacity to learn and its ability to adapt to new information.” For all ages.

Happy Neuron, Inc. www.happy-neuron.com

Cognifit Personal Coach “CogniFit Personal Coach starts by providing you a scientific assessment of your individual strengths and weaknesses before you begin your training. This allows the program to be personalized and deliver optimal cognitive training to maintain and improve those skills essential for an active and healthy life.” For adults.

Cognifit, www.cognifit.com

My Brain Trainer “Contains short, fun individual exercises designed to stimulate different parts of your brain. Just as regular workouts in a gym improve your physical fitness, regular mental workouts of only 10 - 20 minutes daily can improve your cognitive function and brain processing speed. The exercises provide you with immediate feedback with respect to your performance (speed, accuracy, consistency, perceptual threshold), so you can see just how much you're improving. “ For all ages.

MyBrainTrainer, LLC, www.mybraintrainer.com

Focus Fitness “Focus Fitness is designed to help individuals, ages 13 and up, achieve greater life success by working to improve their attention to detail, listening skills, and concentration. For adults with cognitive impairments or who want to avoid age-related cognitive decline, the exercises range from simple tasks to activities that are quite challenging.” For ages 13 and up.

BrainTrain www.braintrain.com/focus-fitness

Cogmed QM “Cogmed QM … is clinically proven to strengthen and increase working memory capacity with rigorous and engaging exercises. Cogmed QM is a comprehensive, computer-based training you can do at home. The software guides you through multiple rotating exercises each day. These exercises are designed to train working memory.” For adults.

Cogmed www.cogmed.com/qm
| Brain Fitness | “You can also cross-train your brain to achieve peak mental functioning. The challenges in the Dakim BrainFitness program are designed to stimulate six essential cognitive domains. Dakim’s scientifically based brain exercises are developed in conjunction with leading physicians and neuroscientists and enhanced with high entertainment value to keep the program interesting and fun.” For ages 60+. Dakim, Inc. www.dakim.com |
| BrainTrain | MindPower Builder | “The MindPower Builder provides the flexible options, controls and ease of use you need to create a cognitive rehabilitation or cognitive enhancement program for individuals with a wide variety of different cognitive deficits, including learning, memory, or neurologically based disorders.” For children and adults. BrainTrain. www.braintrain.com |

Table 5

*Trials of computerized cognitive interventions from 2010 to 2015*

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Intervention</th>
<th>Cognitive outcome measures</th>
<th>Effects</th>
<th>Training time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peretz et al., 2011</td>
<td>155 cognitively healthy elderly</td>
<td>Personalized cognitive training program (Cognifit Personal Coach) vs. games control</td>
<td>Neuropsychological Exam (NexAde), evaluating cognitive skills including attention, memory, and executive functioning</td>
<td>Intervention group improved significantly more in tests of visuo-spatial working memory and learning, and focused attention</td>
<td>3 months</td>
</tr>
<tr>
<td>Garcia-Campuzano et al., 2013</td>
<td>24 cognitively healthy elderly</td>
<td>Complex matching task program vs. passive control</td>
<td>Wechsler Memory Scale</td>
<td>Training group increased their memory performance on the WMS</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Strenziok et al., 2014</td>
<td>42 cognitively healthy elderly</td>
<td>Auditory perception training, visuomotor/working memory training, and strategic training</td>
<td>WAIS III Matrix Reasoning subtest, Everyday Problems test, Word Series and Letter Series tests, Wechsler Memory Scale Logical Memory subtest, Letter Number Sequencing subtest of WAIS III</td>
<td>Strongest effects for the Auditory perception training; participants improved on everyday problem solving and reasoning</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Study</td>
<td>Sample Characteristics</td>
<td>Intervention Description</td>
<td>Outcome Description</td>
<td>Duration</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------------------------------------</td>
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</tr>
<tr>
<td>Wolinsky et al., 2013</td>
<td>681 cognitively healthy older adults</td>
<td>Computerized visual speed of processing training (3 arms-10 hours on site, 14 hours on site, 10 hours at home) vs. active control (10 hours crossword puzzles)</td>
<td>All intervention groups improved on UFOV, Trails A and B, Symbol Digit Modalities, and Stroop</td>
<td>5-8 weeks, some participants received booster session at 11 months post-randomization</td>
<td></td>
</tr>
<tr>
<td>Zhuang et al., 2013</td>
<td>33 cognitively impaired elderly</td>
<td>Computer based cognitive training program with five tasks vs. inactive control</td>
<td>No significant change for either group, though trend for improvement for intervention group on memory, visuospatial, and language skills, compared to control group</td>
<td>24 weeks</td>
<td></td>
</tr>
<tr>
<td>Herrera et al., 2012</td>
<td>22 cognitively impaired elderly (amnestic MCI)</td>
<td>Computer based cognitive training program with 6 memory and attention tasks vs. active control (stimulating cognitive activities)</td>
<td>Intervention group improved on episodic memory and recognition, compared to control group</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td>Gaitán et al., 2013</td>
<td>60 cognitive impaired elderly (MCI or mild AD), already using cognitive training</td>
<td>Computer based cognitive training (FESKITS, Estimulación Cognitiva) vs. Pen-paper based cognitive training</td>
<td>No significant effects on cognitive functions for either group</td>
<td>3 months</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Intervention</td>
<td>Outcome Measures</td>
<td>Intervention Duration</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>-----------------------</td>
<td></td>
</tr>
<tr>
<td>Rosen et al., 2011</td>
<td>12 cognitively impaired elderly (MCI)</td>
<td>Computer based cognitive training (Posit Science program) with 7 processing speed tasks vs. active control (computer based tasks – reading, game playing)</td>
<td>Repeatable Battery for the Assessment of Neuropsychological status (RBANS) neuropsychological battery</td>
<td>2 months</td>
<td></td>
</tr>
<tr>
<td>Miller et al., 2013</td>
<td>69 cognitively healthy elderly</td>
<td>Computer based cognitive training (Brain Fitness, Dakim) vs. wait list</td>
<td>Neuropsychological exam including tests of immediate memory, delayed memory, and language</td>
<td>2 months</td>
<td></td>
</tr>
<tr>
<td>Nouchi et al., 2012</td>
<td>32 cognitively healthy elderly</td>
<td>Computer based cognitive training program “Brain Age” vs. active control (computer game “Tetris”)</td>
<td>Extensive neuropsychological exam including Mini-Mental State Examination and tests of executive functioning, attention, and processing speed</td>
<td>4 weeks</td>
<td></td>
</tr>
</tbody>
</table>

Note: Pubmed search “cognitive training”, age 65 and older, clinical trial. Limited to English-language papers that include cognitive outcome measures and are not multidomain trials.
Table 6  
*Participant characteristics*

<table>
<thead>
<tr>
<th></th>
<th>Entire sample</th>
<th>CCT group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>69</td>
<td>39</td>
<td>30</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>85.81 (3.64)</td>
<td>85.38 (3.858)</td>
<td>86.37 (4.902)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.2% 12 years</td>
<td></td>
<td>2% (1 participant) 12 years</td>
<td>13.33% 12 years</td>
</tr>
<tr>
<td>21.7% 13-15 years</td>
<td></td>
<td>30.1% 13-15 years</td>
<td>10% 13-15 years</td>
</tr>
<tr>
<td>71.0% more than 15 years</td>
<td></td>
<td>66.67% more than 15 years</td>
<td>76.67% more than 15 years</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>24 males, 45 females</td>
<td>12 males, 27 females</td>
<td>12 males, 18 females</td>
</tr>
<tr>
<td><strong>Completion of training</strong></td>
<td>51 completed at least 75% of the training</td>
<td>31 completed at least 75% of the training</td>
<td>20 completed at least 75% of the training</td>
</tr>
<tr>
<td></td>
<td>49 completed follow-up visit</td>
<td>29 completed follow-up visit</td>
<td>20 completed follow-up visit</td>
</tr>
<tr>
<td><strong>Attrition</strong></td>
<td>18 did not complete at least 75% of the training</td>
<td>7 did not complete at least 75% of the training</td>
<td>11 did not complete at least 75% of the training</td>
</tr>
<tr>
<td>Dropout due to:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of time: 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of interest: 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health: 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Computer or program issues: 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of contact: 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death in family: 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive Ability</td>
<td>Definition</td>
<td>Example</td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Divided Attention</td>
<td>The ability to execute more than one task at a time</td>
<td>Cooking dinner and talking on the telephone</td>
<td></td>
</tr>
<tr>
<td>Eye-hand Coordination</td>
<td>The degree to which the hand and eye are synchronized</td>
<td>Threading a needle</td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>The ability to ignore irrelevant information while performing a task</td>
<td>Inhibit pressing the gas pedal when you see the green light turning yellow</td>
<td></td>
</tr>
<tr>
<td>Naming</td>
<td>The ability to recall and retrieve a word</td>
<td>Meeting an acquaintance and recalling his name</td>
<td></td>
</tr>
<tr>
<td>Planning</td>
<td>The ability to anticipate and develop the best way to execute a task</td>
<td>Planning the order in which you will run your errands on a busy day</td>
<td></td>
</tr>
<tr>
<td>Shifting</td>
<td>The ability to redirect your attention from one channel of information to another</td>
<td>Stop reading and taking care of the baby when she starts to cry</td>
<td></td>
</tr>
<tr>
<td>Spatial Perception</td>
<td>The ability to evaluate how things are arranged in a given space and perceive their relation to the surroundings</td>
<td>Navigating through a crowd without bumping into anyone</td>
<td></td>
</tr>
<tr>
<td>Response Time</td>
<td>The ability to perceive a simple stimulus and respond to it</td>
<td>Scanning a video and hitting the “Play” button at the right point in the film.</td>
<td></td>
</tr>
<tr>
<td>Visual Scanning</td>
<td>The ability to find relevant information in your surroundings</td>
<td>Locate your friend in a crowded restaurant</td>
<td></td>
</tr>
<tr>
<td>Type of Memory</td>
<td>Description</td>
<td>Example</td>
<td>Note</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>Visual Short-Term Memory</td>
<td>The ability to temporarily retain a small amount of visual information – shapes, colors, relative locations, or movement directions – active and available for a short period of time.</td>
<td>While driving on a new road, you pass a sign showing the 4 next closest destinations. After a few seconds you try to remember how many miles appeared next to your destination on that sign.</td>
<td></td>
</tr>
<tr>
<td>Auditory Short-Term Memory</td>
<td>The ability to remember auditory information over a brief period of time – about three to four seconds.</td>
<td>You attend an event and are presented to some new colleagues. A few seconds later you turn to one of them trying to recall his name and start a conversation.</td>
<td></td>
</tr>
<tr>
<td>Updating</td>
<td>The ability to respond in a flexible and adaptive manner in order to keep up with the changes in the environment.</td>
<td>During the period of road repairs you need to change your permanent route and use the new route until the repairs are finished.</td>
<td></td>
</tr>
<tr>
<td>Contextual Memory</td>
<td>The ability to memorize and discriminate the actual source of a specific memory including time, place, people, or any other source related to a memory event. You hear a song and try to remember when and where you heard it before.</td>
<td>You hear a song and try to remember when and where you heard it before.</td>
<td></td>
</tr>
<tr>
<td>Working Memory</td>
<td>The span of information that can be manipulated while performing a task</td>
<td>Remember the whole structure of a story to get its meaning</td>
<td></td>
</tr>
</tbody>
</table>

*Note: Ref: Cognifit “Science Book” CogniFit Research The Basis for Cognitive Vitality*
<table>
<thead>
<tr>
<th>Name of task</th>
<th>Cognitive function assessed</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>The numbers</td>
<td>Eye-hand coordination, response time</td>
<td>The task is to click on 10 numbers according to their order; the numbers in this task are stationary throughout the task.</td>
</tr>
<tr>
<td>Blue square</td>
<td>Response time</td>
<td>The task is to click on a blue square six times as fast as possible.</td>
</tr>
<tr>
<td>Blue bulb</td>
<td>Eye-hand coordination, response time</td>
<td>The task is to click on a light bulb each time it lights up.</td>
</tr>
<tr>
<td>Blue Circle</td>
<td>Eye-hand coordination, spatial perception</td>
<td>The task is to click on a blue circle, which moves after each click, avoiding distractor stimuli.</td>
</tr>
<tr>
<td>Pictures and words</td>
<td>Naming, working memory, visual short-term memory</td>
<td>A sequence of four pictures is presented, followed by written words. For each word the task is to decide whether its picture was or was not displayed before. This task is then repeated with spoken instead of written words.</td>
</tr>
<tr>
<td>The Ball track</td>
<td>Eye-hand coordination, spatial perception</td>
<td>The task is to track a moving ball with the computer mouse cursor.</td>
</tr>
<tr>
<td>Higher numbers, bigger shapes</td>
<td>Inhibition</td>
<td>A pair of rectangles is presented, each enclosing a number. The task is to choose the larger shape regardless of number, and later, the higher number regardless of the size of the shape.</td>
</tr>
<tr>
<td>Letters</td>
<td>Naming</td>
<td>Pictures of objects are presented, each one for a very short time, followed by 2x2 grids containing letters. The task is to choose the first letter of the name of the object out of the four letters.</td>
</tr>
<tr>
<td>Activity</td>
<td>Relevance</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>----------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Objects seen or heard before</td>
<td>Naming, working memory, visual short-term memory, auditory short-term memory, contextual memory</td>
<td>A sequence of pictures and spoken words presented words is presented. As each item is presented, the task is to decide whether each was seen before, heard before, or neither.</td>
</tr>
<tr>
<td>The moving square</td>
<td>Eye-hand coordination, spatial perception</td>
<td>A square shaped route and a blue square are presented, and the task is to track the square as it moves along the route, changing direction and speed.</td>
</tr>
<tr>
<td>The flowers</td>
<td>Spatial perception, visual short-term memory</td>
<td>A sequence of flowers, which light up, is presented on the screen. The task is to repeat the sequence in order.</td>
</tr>
<tr>
<td>The numbers</td>
<td>Working memory, visual short-term memory</td>
<td>A sequence of numbers is presented, and the task is to repeat the sequence in order.</td>
</tr>
<tr>
<td>The maze</td>
<td>Planning</td>
<td>Three mazes, of increasing complexity, are presented. The task is to navigate through the puzzles.</td>
</tr>
<tr>
<td>Pictures trio</td>
<td>Visual scanning, working memory, visual short-term memory</td>
<td>Three objects on cards are presented at a time. The task is to choose the set of cards displaying the three objects that were previously presented.</td>
</tr>
<tr>
<td>A purple circle</td>
<td>Eye-hand coordination, spatial perception</td>
<td>The task is to track a purple ball which moves around the screen, bouncing off of the walls and off of a rectangle in the center of the screen.</td>
</tr>
<tr>
<td>Stroop</td>
<td>Inhibition</td>
<td>This is a Stroop-like task. The task is to press the computer “space bar” only when the word and color match.</td>
</tr>
<tr>
<td>A purple circle + Stroop</td>
<td>Divided attention, shifting</td>
<td>This task combines the purple circle and Stroop tasks.</td>
</tr>
<tr>
<td>Task</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Filing cabinet</td>
<td>One or more objects are presented on the screen. The tasks is to select the appropriate category for each object among several optional categories, or choose “Does not belong” if the object does not belong to any of the available categories. Objects can be presented either as pictures, written words or spoken words.</td>
<td></td>
</tr>
<tr>
<td>Keeping track</td>
<td>A route is displayed, with a ball at the starting point. The ball starts moving, and the task is to track it with the mouse cursor, always moving at the same speed as the ball. Occasionally the ball and also the route disappear. The task is to continue moving the cursor at the same speed/direction as the ball would be moving had it not disappeared.</td>
<td></td>
</tr>
<tr>
<td>Two in One</td>
<td>Two rooms with differently colored walls are displayed. In each room, a colored ball is moving on a collision course with a wall. The task is to identify whether the color of the wall where the ball will hit matches the color of the balls, and if not, click the wall to change the color before the balls collide with the walls, while working simultaneously on the two rooms.</td>
<td></td>
</tr>
</tbody>
</table>
| Attention Alert   | There are two tasks,  
1. Following a ball in a track (the "Keeping track" task), in which the ball moves inside a track. The task is to follow it with the mouse cursor, while keeping it inside the ball.  
2. Ball moving inside a square with 8 colored walls (the "Two in One" walls task). The task is to click a wall when the ball is moving towards it and has different color than that of the wall.  
The screen is divided into panels (two or four). The task is to shift between panels (which become active and inactive) and complete the tasks. |
| Jigsaw 9          | A picture is shown for a short period of time (3 sec.). Then it is divided into pieces and jumbled up. The task is to rearrange the pieces into their proper places, while doing the lowest possible number of steps (this number is stated as the recommended number for each puzzle). |
| Flags             | A flag is presented for short period of time. The task is to then identify the flag that was presented among an array of flags.                                                                                                                                 |
| Simon Says        | Visual or auditory directions (targets) are provided, and a set of arrows is displayed. The task is to follow the directions to click or not click arrows, and ignore distracters. There are three types of distracters: irrelevant (colors), partially relevant (3, 6, 9, 12, 15, or 18 colors), fully relevant (all colors). |
East, West, North, South) and directly relevant (up, down, left and right).

**Memory Drills**
A series of items: numbers, cards, objects, sounds, through visual and/or auditory modes, are presented. The task is to memorize the items and their order, and to repeat the series. In some cases the repetition is in the order that the series was presented, in some cases in the backwards order, and in some cases in any order the examinee prefers.

**Pattern Memory**
In this task, an object moves across a network of nodes. The task is to remember the route and repeat it by clicking on the nodes through which the object passed. The length of the route, as well as its complexity (going in diagonal direction, or repeating intersections) varies during the task.

**Crossroads**
The task is to prevent moving objects from colliding, by clicking on an intersection they are heading towards. Simultaneously, pictures are displayed on the corners of the screen, the task here is to press the spacebar if they are identical.

**Word Quest**
A collection of letters is arranged randomly in a square-shaped grid. Within this letter-filled grid words are hidden. The objective of the game is to find and mark all of the hidden words within the grid. These words can be found in a vertical, horizontal or diagonal position. Some are spelled backwards. The words to search for are given as pictures (all at once, one by one). Number of words in each matrix is 8.

**Name Me**
A picture is presented, and then a grid of four letters appears. The task is to recall the name of the object in the picture and select the first letter of that word. The task continues to include two pictures, with a set of instructions, such as “Select the first letter of the object that was presented first” or "Select the first letter of the object that was presented second" or "Select the first letter for each of the objects that were presented"

**Mix and Match**
A large circle surrounded with 8 smaller circles (periphery) is presented. The task is to detect and click as fast as possible all the objects in the peripheral circles which are identical to the central circle. The duration of the small objects presence on the screen will get shorter, the similarity of the graphical objects will get higher, number of available objects and number of the correct once will also vary.

**Water Lillies**
Flowers are highlighted one after the other. The task is to remember the order of the flowers, and then click them according to the instruction given, either in the order they opened or in the reverse order. The sequence length (number of the flowers to memorize) increases. Difficulty manipulation is done by increasing the number of flowers on the screen and the delay between the presentation and the turn.

**Supermind**
The computer chooses a secret code, consisting of sets of 2, 3 or 4 digits and/or symbols. The task is to reveal the combination by making educated guesses, and adjusting the next guesses according to feedback received.
<table>
<thead>
<tr>
<th>Task</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ship Shape</td>
<td>An abstract pattern is displayed for a short time, and then disappears. The task is to use shapes on the left side of the screen in order to re-create the pattern. There is an option to briefly see the original pattern by using the &quot;show pattern&quot; button located at the bottom of the screen.</td>
</tr>
<tr>
<td>Match the Time</td>
<td>An event will be presented (visual or auditory). The task is to produce another event by clicking on an object for the same duration of time.</td>
</tr>
<tr>
<td>Mouse Challenge</td>
<td>The task is to bring the mouse cursor to target locations on the screen, while the mouse cursor changes its behavior. The cursor becomes more sensitive, up-down sides reversed, left-right reversed. The number of clicks that have to be performed, the size of the target to be clicked and their distances are manipulated.</td>
</tr>
<tr>
<td>Time Estimation</td>
<td>The task is to select the event that occurred for the longest time period among two (levels 1-4) or three stimuli (levels 5, 6), presented one after the other.</td>
</tr>
<tr>
<td>Task</td>
<td>Description</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Puzzles</td>
<td>The task is to construct pictures from scattered parts.</td>
</tr>
<tr>
<td>Fowl Play</td>
<td>The task is to “shoot” the flying ducks using the mouse.</td>
</tr>
<tr>
<td>Crazy Cartoon</td>
<td>The task is to color and animate a drawing.</td>
</tr>
<tr>
<td>Matryoshka Bang</td>
<td>The task is to click on the animated Matryoska dolls, which disappear and reappear.</td>
</tr>
<tr>
<td>Bursting Your Bubbles</td>
<td>The task is to aim to shoot bubbles at the top of screen to burst rows of bubbles. Hitting a group of two or more of the same color will cause all to burst. The lines of bubbles descend occasionally.</td>
</tr>
<tr>
<td>Basket-balls</td>
<td>The task is to use the mouse to move a paddle at the bottom of the screen to “bounce” a ball into a basket.</td>
</tr>
<tr>
<td>Eating Plus</td>
<td>The task is to “eat” the target with using the arrow keys to guide a black square, without hitting the sides of the screen. The target moves after each round.</td>
</tr>
<tr>
<td>The Bouncing Ball</td>
<td>The task is to use a black rectangle at the bottom of the screen to bounce a ball upwards and explode 20 small rectangles at the top of the screen.</td>
</tr>
<tr>
<td>Bull’s Eye</td>
<td>The task is to hit the moving target with by clicking with the mouse.</td>
</tr>
<tr>
<td>Free Draw</td>
<td>The task is to draw, freely; colors and line widths can be changed.</td>
</tr>
<tr>
<td>Tearing Down the Wall</td>
<td>The task is to click on clusters of bricks of the same color to tear down a brick wall.</td>
</tr>
<tr>
<td>The Orange Touch</td>
<td>The task is to touch the orange square by moving the black circle using the arrow keys.</td>
</tr>
<tr>
<td>Wild Strawberries</td>
<td>The task is to guide the moth through the maze of strawberries, eating berries and avoiding the monster, using the arrow keys.</td>
</tr>
<tr>
<td>-------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>The Bottom Line</td>
<td>The task is to connect the numbers in ascending order using the mouse.</td>
</tr>
</tbody>
</table>
### Secondary outcome measures: Cognitive functions and their corresponding tests

<table>
<thead>
<tr>
<th>Secondary Outcome Measures: Cognitive Functions</th>
<th>Corresponding Tests</th>
</tr>
</thead>
</table>
| **Attention/Executive Functions**              | (1) Target Cancellation Tests, Diamond and TMX  
|                                                | (2) Trail Making Test, Parts A and B  
|                                                | (3) Digit Symbol Substitution Test  
|                                                | (4) Digit Span, Forward and Backward  |
| **Language**                                   | (1) Similarities  
|                                                | (2) Boston Naming Test  
|                                                | (3) Category Fluency and Letter Fluency |
Table 12

*Power analysis- Detectable differences for power =80%, alpha=5%, n=30 per group*

<table>
<thead>
<tr>
<th>R²</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.80</td>
<td>0.33</td>
</tr>
<tr>
<td>0.50</td>
<td>0.52</td>
</tr>
<tr>
<td>0.20</td>
<td>0.65</td>
</tr>
</tbody>
</table>
Table 13

*Test characteristics at baseline and follow-up*

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Possible range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>Word List Memory: Immediate recall</td>
<td>66</td>
<td>13</td>
<td>30</td>
</tr>
<tr>
<td>Word List Memory: Delayed recall</td>
<td>66</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Word List Memory: Recognition</td>
<td>65</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Logical Memory Story A: Immediate recall</td>
<td>65</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>Logical Memory Story A: Delayed recall</td>
<td>62</td>
<td>2</td>
<td>22</td>
</tr>
<tr>
<td>Logical Memory Story A: Recognition</td>
<td>61</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Boston Naming Test</td>
<td>65</td>
<td>19</td>
<td>30</td>
</tr>
<tr>
<td>Target Cancellation Tests: Diamonds (time)</td>
<td>65</td>
<td>26</td>
<td>110</td>
</tr>
<tr>
<td>Target Cancellation Tests: TMX (time)</td>
<td>65</td>
<td>45</td>
<td>136</td>
</tr>
<tr>
<td>Test</td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>Similarities</td>
<td>66</td>
<td>12</td>
<td>33</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>65</td>
<td>11</td>
<td>72</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>65</td>
<td>27</td>
<td>90</td>
</tr>
<tr>
<td>Trail Making Test : Trail A</td>
<td>65</td>
<td>23</td>
<td>150</td>
</tr>
<tr>
<td>(time)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making Test : Trail B</td>
<td>65</td>
<td>60</td>
<td>300</td>
</tr>
<tr>
<td>(time)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Span Forward</td>
<td>65</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Digit Span Backwards</td>
<td>65</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Digit Symbol Substitution Test</td>
<td>63</td>
<td>21</td>
<td>68</td>
</tr>
</tbody>
</table>
Table 14

*T-tests comparing CCT and games groups on individual cognitive tests at baseline*

<table>
<thead>
<tr>
<th>Test</th>
<th>Games Mean</th>
<th>Games SD</th>
<th>CCT Mean</th>
<th>CCT SD</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word List Memory: Immediate recall</td>
<td>21.31</td>
<td>4.91</td>
<td>22.70</td>
<td>4.85</td>
<td>1.15</td>
<td>.254</td>
</tr>
<tr>
<td>Word List Memory: Delayed recall</td>
<td>5.76</td>
<td>2.66</td>
<td>6.00</td>
<td>2.79</td>
<td>.36</td>
<td>.723</td>
</tr>
<tr>
<td>Word List Memory: Recognition</td>
<td>19.06</td>
<td>1.43</td>
<td>19.14</td>
<td>1.33</td>
<td>.30</td>
<td>.762</td>
</tr>
<tr>
<td>Logical Memory Story A: Immediate recall</td>
<td>16.21</td>
<td>3.51</td>
<td>14.24</td>
<td>4.10</td>
<td>-2.04</td>
<td>.046*</td>
</tr>
<tr>
<td>Logical Memory Story A: Delayed recall</td>
<td>14.54</td>
<td>4.70</td>
<td>13.19</td>
<td>4.29</td>
<td>-1.17</td>
<td>.247</td>
</tr>
<tr>
<td>Logical Memory Story A: Recognition</td>
<td>13.00</td>
<td>1.47</td>
<td>12.49</td>
<td>1.65</td>
<td>-1.26</td>
<td>.213</td>
</tr>
<tr>
<td>Boston Naming Test</td>
<td>25.76</td>
<td>2.80</td>
<td>26.69</td>
<td>2.58</td>
<td>1.40</td>
<td>.167</td>
</tr>
<tr>
<td>Target Cancellation Tests: Diamonds (time)</td>
<td>62.36</td>
<td>16.76</td>
<td>59.27</td>
<td>20.35</td>
<td>-.65</td>
<td>.517</td>
</tr>
<tr>
<td>Target Cancellation Tests: TMX (time)</td>
<td>77.29</td>
<td>20.61</td>
<td>74.11</td>
<td>19.29</td>
<td>-.64</td>
<td>.525</td>
</tr>
<tr>
<td>Similarities</td>
<td>26.41</td>
<td>4.26</td>
<td>24.76</td>
<td>4.87</td>
<td>-1.45</td>
<td>.153</td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>46.76</td>
<td>14.86</td>
<td>46.42</td>
<td>11.45</td>
<td>-.11</td>
<td>.917</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>56.03</td>
<td>12.23</td>
<td>57.81</td>
<td>14.54</td>
<td>.52</td>
<td>.603</td>
</tr>
<tr>
<td>Trail Making Test: Trail A (time)</td>
<td>47.64</td>
<td>13.33</td>
<td>50.14</td>
<td>27.54</td>
<td>.44</td>
<td>.661</td>
</tr>
<tr>
<td>Trail Making Test: Trail B (time)</td>
<td>107.25</td>
<td>36.84</td>
<td>117.19</td>
<td>62.43</td>
<td>.75</td>
<td>.457</td>
</tr>
<tr>
<td>Test</td>
<td>Score 1</td>
<td>Score 2</td>
<td>Score 3</td>
<td>Score 4</td>
<td>Score 5</td>
<td>Score 6</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>Digit Span Forward</td>
<td>9.10</td>
<td>2.14</td>
<td>9.33</td>
<td>2.00</td>
<td>.45</td>
<td>.657</td>
</tr>
<tr>
<td>Digit Span Backwards</td>
<td>7.34</td>
<td>2.33</td>
<td>7.44</td>
<td>2.43</td>
<td>.17</td>
<td>.868</td>
</tr>
<tr>
<td>Digit Symbol Substitution Test</td>
<td>41.11</td>
<td>7.79</td>
<td>44.36</td>
<td>10.68</td>
<td>1.34</td>
<td>.187</td>
</tr>
</tbody>
</table>
Table 15

Linear mixed models examining the interaction between cognitive training program and time on cognitive functioning, controlling for age, sex, education, and number of training sessions completed

<table>
<thead>
<tr>
<th></th>
<th>Games program</th>
<th></th>
<th></th>
<th>CCT program</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
<td>Baseline</td>
<td>Follow-up</td>
<td>F</td>
<td>df</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Language</td>
<td>-.013</td>
<td>.72</td>
<td>-.006</td>
<td>.53</td>
<td>.004</td>
<td>.71</td>
</tr>
<tr>
<td>Attention/Executive</td>
<td>-.041</td>
<td>.47</td>
<td>-.034</td>
<td>.49</td>
<td>.038</td>
<td>.69</td>
</tr>
<tr>
<td>Memory</td>
<td>.030</td>
<td>.76</td>
<td>.114</td>
<td>.78</td>
<td>-.043</td>
<td>.77</td>
</tr>
<tr>
<td>Global cognitive composite</td>
<td>-.018</td>
<td>.44</td>
<td>.024</td>
<td>.38</td>
<td>.008</td>
<td>.50</td>
</tr>
</tbody>
</table>
Table 16

Linear mixed models examining the interaction between cognitive training program and time on cognitive functioning, controlling for age, sex, education, and number of training sessions completed for “completers” only.

<table>
<thead>
<tr>
<th></th>
<th>Games program</th>
<th></th>
<th>CCT program</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Language</td>
<td>-.049</td>
<td>.76</td>
<td>.006</td>
<td>.54</td>
</tr>
<tr>
<td>Attention/Executive</td>
<td>-.007</td>
<td>.42</td>
<td>-.069</td>
<td>.48</td>
</tr>
<tr>
<td>Memory</td>
<td>.048</td>
<td>.76</td>
<td>.160</td>
<td>.77</td>
</tr>
<tr>
<td>Global cognitive composite</td>
<td>-.029</td>
<td>.48</td>
<td>.028</td>
<td>.39</td>
</tr>
</tbody>
</table>

*Note. “Completers” are those who completed at least 75% of the cognitive training sessions.*
Table 17

*T-tests comparing pre- and post- training scores on individual tests, split by training group*

<table>
<thead>
<tr>
<th>Test</th>
<th>CCT group</th>
<th></th>
<th>Games group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td>t</td>
<td>df</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Word List Memory: Immediate recall</td>
<td>22.10</td>
<td>4.87</td>
<td>23.03</td>
<td>3.94</td>
</tr>
<tr>
<td>Logical Memory Story A: Immediate recall</td>
<td>14.34</td>
<td>4.45</td>
<td>16.48</td>
<td>4.05</td>
</tr>
<tr>
<td>Target Cancellation Tests: Diamonds</td>
<td>58.17</td>
<td>18.72</td>
<td>57.59</td>
<td>15.22</td>
</tr>
<tr>
<td>Target Cancellation Tests: TMX</td>
<td>73.03</td>
<td>17.47</td>
<td>76.62</td>
<td>26.25</td>
</tr>
<tr>
<td>Boston Naming Test</td>
<td>27.04</td>
<td>2.13</td>
<td>27.36</td>
<td>2.28</td>
</tr>
<tr>
<td>Word List Memory: Delayed recall</td>
<td>5.93</td>
<td>2.93</td>
<td>6.31</td>
<td>2.77</td>
</tr>
<tr>
<td>Word List Memory: Recognition</td>
<td>19.00</td>
<td>1.47</td>
<td>19.04</td>
<td>1.80</td>
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<tr>
<td>Logical Memory Story A: Delayed recall</td>
<td>13.44</td>
<td>4.57</td>
<td>15.33</td>
<td>3.89</td>
</tr>
<tr>
<td>Logical Memory Story A: Recognition</td>
<td>12.58</td>
<td>1.62</td>
<td>13.00</td>
<td>1.79</td>
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</tbody>
</table>

*p < .05*
<table>
<thead>
<tr>
<th>Test</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Max</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Max</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Similarities</td>
<td>25.59</td>
<td>4.72</td>
<td>26.50</td>
<td>3.36</td>
<td>-1.76</td>
<td>27.090</td>
<td>26.71</td>
<td>4.17</td>
<td>25.67</td>
<td>4.48</td>
<td>1.78</td>
<td>20.090</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>46.14</td>
<td>12.24</td>
<td>45.04</td>
<td>11.21</td>
<td>.61</td>
<td>27.546</td>
<td>45.43</td>
<td>14.31</td>
<td>45.71</td>
<td>13.19</td>
<td>-.22</td>
<td>20.829</td>
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<td></td>
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<tr>
<td>Category Fluency</td>
<td>59.07</td>
<td>15.25</td>
<td>59.11</td>
<td>15.72</td>
<td>-.02</td>
<td>26.986</td>
<td>56.71</td>
<td>12.43</td>
<td>56.57</td>
<td>11.08</td>
<td>.07</td>
<td>20.943</td>
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<td></td>
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<tr>
<td>Trail Making Test: Trail A</td>
<td>48.10</td>
<td>24.09</td>
<td>43.45</td>
<td>17.02</td>
<td>1.20</td>
<td>28.239</td>
<td>46.72</td>
<td>14.34</td>
<td>46.61</td>
<td>10.47</td>
<td>.04</td>
<td>17.970</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making Test: Trail B</td>
<td>113.00</td>
<td>62.17</td>
<td>114.38</td>
<td>63.07</td>
<td>-.24</td>
<td>28.815</td>
<td>106.78</td>
<td>36.40</td>
<td>118.83</td>
<td>57.90</td>
<td>-1.09</td>
<td>17.290</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Span Forward</td>
<td>9.21</td>
<td>1.97</td>
<td>9.64</td>
<td>1.62</td>
<td>-1.10</td>
<td>27.281</td>
<td>9.05</td>
<td>2.20</td>
<td>9.24</td>
<td>2.23</td>
<td>-.41</td>
<td>20.684</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Span Backwards</td>
<td>7.54</td>
<td>2.56</td>
<td>8.25</td>
<td>2.52</td>
<td>-2.10</td>
<td>27.045*</td>
<td>7.00</td>
<td>2.41</td>
<td>7.24</td>
<td>1.87</td>
<td>-.61</td>
<td>20.548</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Symbol Substitution Test</td>
<td>45.50</td>
<td>9.95</td>
<td>44.11</td>
<td>10.64</td>
<td>.73</td>
<td>27.472</td>
<td>42.06</td>
<td>7.52</td>
<td>41.41</td>
<td>6.71</td>
<td>.67</td>
<td>16.513</td>
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</tbody>
</table>

*significant at the .05 level. Target Cancellation Tests: TMX, Target Cancellation Tests: Diamonds, Trail Making Test: Trails A and Trail Making Test: Trails B are measured in time- seconds.
**Table 18**

*Linear mixed models examining the interaction between education and time on cognitive functioning, controlling for age, sex, sessions complete*

<table>
<thead>
<tr>
<th></th>
<th>No college degree</th>
<th></th>
<th>College degree</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Language</td>
<td>-.51</td>
<td>.75</td>
<td>-.38</td>
<td>.72</td>
</tr>
<tr>
<td>Attention/Executive</td>
<td>-.22</td>
<td>.67</td>
<td>-.17</td>
<td>.84</td>
</tr>
<tr>
<td>Memory</td>
<td>-.11</td>
<td>.81</td>
<td>.09</td>
<td>.90</td>
</tr>
<tr>
<td>Global cognitive composite</td>
<td>-.29</td>
<td>.55</td>
<td>-.14</td>
<td>.70</td>
</tr>
</tbody>
</table>

*Note.* *significant at the .05 level*
Table 19

*T-tests comparing pre- and post- training scores on domains, split by education*

<table>
<thead>
<tr>
<th>Domain</th>
<th>No college degree</th>
<th></th>
<th>College degree</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Language</td>
<td>-.57</td>
<td>.85</td>
<td>-.38</td>
<td>.72</td>
</tr>
<tr>
<td>Attention/Executive</td>
<td>-.36</td>
<td>.75</td>
<td>-.17</td>
<td>.84</td>
</tr>
<tr>
<td>Memory</td>
<td>-.15</td>
<td>.86</td>
<td>.09</td>
<td>.90</td>
</tr>
<tr>
<td>Global cognitive composite</td>
<td>-.36</td>
<td>.62</td>
<td>-.15</td>
<td>.70</td>
</tr>
</tbody>
</table>

*Note.* *significant at the .05 level*
Recruitment
Potential participants recruited via talks, flyers, newspapers, advertisements, and through ongoing research studies with the Alzheimer's Disease Research Center (ADRC)

Screening
Potential participants called the researchers to discuss project
Potential participants completed a survey to confirm eligibility
A baseline visit was scheduled

Pre-enrollment
Potential participants were assigned an individual identification number
Potential participants were randomly assigned to the training group

Initial visit
Informed consent
Baseline neuropsychological exam (if not recently assessed by ADRC)
Registration and first session of cognitive training program

Training
Self-administered training, one session every other day, for 24 training sessions

Follow-up visit (approximately 2 months after initial visit)
Follow-up neuropsychological exam

Figure 1. Flowchart of project procedures
APPENDIX 1
The Family Studies Research Center at The Mount Sinai School of Medicine

Testing a Computerized Cognitive Training Program

The Family Studies Research Center at the Mount Sinai School of Medicine is conducting a research study of healthy cognition in aging. We plan to examine the use of computers and internet in individuals age 80 and older, and compare the effects of a computerized cognitive training program with a computerized games program.

We are currently seeking individuals to participate as to help us learn more about how these cognitive training programs affect cognitive functioning.

Who can participate?
• Individuals age 80 and older
• You must have no, or minimal, problems with your memory
• You must have, or have regular access to, a home computer with internet access

What does participation involve?
• You will receive 3 visits:
  ○ In visit 1, you will complete memory and thinking tasks, and a staff member will set up the computer program (internet-based) and help you use it for the first time. This visit will last 2-3 hours.
  ○ In visit 2, which will happen about 2 months after the first visit, you will again complete the memory and thinking tasks. This visit will last about 1 hour.
  ○ In visit 3, which will happen about 4 months after visit 2, you will again complete the memory and thinking tasks. This visit will last about 1 hour.
• The computerized training program will be provided free of charge.

If you have any questions, or are interested in participating, please contact Rebecca West at 212-659-5603. You can also contact Mrs. West at Rebecca.west@mssm.edu.

We look forward to hearing from you!

GCO#09-2339  MSSM IRB Approved through 1/4/2014
The Mount Sinai Icahn School of Medicine

Computerized Cognitive Training Program

We are seeking individuals age 80 and older to participate as to help us learn more about how cognitive training programs affect cognitive functioning.

Participants must have no or minimal problems with memory and regular access to a computer with internet.

Participation involves 3 visits over 7 months.
At the first visit, you will complete memory and thinking tasks, and you will receive the computer program and use it for the first time. You will then use the program for 20 minutes every other day, for 7 weeks.
In the second and third visits, you will again complete the memory and thinking tasks.

If you have any questions, or are interested in participating, please contact Rebecca West at 212-659-5603 or 917-657-4954.

You can also contact Ms. West at rebecca.west@mssm.edu

This research is taking place at the Mount Sinai Icahn School of Medicine. 50 E. 98th Street, Suite 1 B.

Participants may be seen in these offices, or in their homes, according to their preference.

We look forward to hearing from you!
GCO#09-2339 MSSM IRB Approved through 1/4/2014
APPENDIX 2
RESEARCH VOLUNTEERS:

Cognitively healthy seniors aged 80 and older needed to examine the effectiveness of two computerized cognitive training programs on improving memory and attention. Must have access to a computer with internet.

Participants will receive 3 visits from the research staff over 6 months, and will complete memory and thinking tasks at each visit. Participants will also use an internet-based computer program for 6 weeks, for no more than 1 hour per week.

The computerized training program will be provided free of charge. Participants do not need to travel.

Please contact Rebecca West at 212-659-5603 or Rebecca.west@mssm.edu
References


Alzheimer’s Association. (2013). *The Healthy Brain Initiative : A National Public Health Road*
http://www.cdc.gov/aging/healthybrain/roadmap.htm

Consensus on the Brain Training Industry from the Scientific Community. Max Planck
stanford.edu/blog/2014/10/15/the-consensus-on-the-brain-training-industry-from-the-

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental

Armijo-Olivo, S., Warren, S., & Magee, D. (2009). Intention to treat analysis, compliance, drop-
outs and how to deal with missing data in clinical research: a review. Physical Therapy

Cognitive functioning in aging and dementia: the Kungsholmen Project. Aging
Neuropsychology and Cognition, 11(2-3), 212-244.

memory intervention. Clinical Interventions in Aging, 3(2), 371-382.


Ball, K. K., Ross, L. A., Roth, D. L., & Edwards, J. D. (2013). Speed of processing training in
the ACTIVE study: how much is needed and who benefits? Journal of Aging and Health,
25(8 Suppl), 65S–84S. http://doi.org/10.1177/0898264312470167

Ball, K., Edwards, J. D., & Ross, L.. (2007). The impact of speed of processing training on

http://doi.org/10.1093/geronb/62.special_issue_1.19


http://doi.org/10.1016/j.neubiorev.2015.06.008


http://doi.org/10.1016/j.neubiorev.2014.03.019


http://doi.org/10.1016/j.neurobiolaging.2009.02.022


http://doi.org/10.1212/01.wnl.0000219668.47116.e6

Berry, A. S., Zanto, T. P., Clapp, W. C., Hardy, J. L., Delahunt, P. B., Mahncke, H. W., &


Mini-Mental and Modified Mini-Mental State Examinations derived from a non-demented elderly population. *International Journal of Geriatric Psychiatry, 12*(10), 1008-1018.


Buschert, V. C., Friese, U., Teipel, S. J., Schneider, P., Merensky, W., Rujescu, D., …


http://doi.org/10.1016/j.biotechadv.2011.08.021


http://doi.org/10.1093/gerona/gls112

Craik, F.I., Winocur, G., Palmer, H., Binns, M.A., Edwards, M., Bridges, K., ... & Stuss, D. T.


http://doi.org/10.1037/a0022687


http://doi.org/10.1212/WNL.0b013e31828726f5

http://doi.org/10.1016/j.neuropsychologia.2012.04.012


http://doi.org/10.1017/S1041610206003760


Jefferson, A. L., Gibbons, L. E., Rentz, D. M., Carvalho, J. O., Manly, J., Bennett, D. a., &


http://doi.org/10.1097/JGP.0b013e3181ab8b62

http://doi.org/10.1038/ng.2802

http://doi.org/10.1371/journal.pmed.1001756


Ngandu, T., Von Strauss, E., Helkala, E. L., Winblad, B., Nissinen, a., Tuomilehto, J., …


Oswald, W. D., Gunzelmann, T., Rupprecht, R., & Hagen, B. (2006). Differential effects of
http://doi.org/10.1007/s10433-006-0035-z
http://doi.org/10.1007/s11065-009-9119-9


http://doi.org/10.1016/j.bbr.2013.01.030


http://doi.org/10.1080/13825585.2015.1028883


http://doi.org/10.1007/s12603-012-0402-8


http://doi.org/10.1080/13607860601086546


http://doi.org/10.1037/0882-7974.18.2.306


Strenziok, M., Parasuraman, R., Clarke, E., Cisler, D. S., Thompson, J. C., & Greenwood, P. M.


http://doi.org/10.1371/journal.pone.0063614


programs for the community-dwelling elderly with subjective memory complaints.


http://doi.org/10.1016/j.neulet.2014.02.035

http://doi.org/10.1093/gerona/glt144


*Current Directions in Psychological Science, 12*(3), 87-91.


http://doi.org/10.1037/a0032982