Published in final edited form as:

Int J Gaming Comput Mediat Simul. 2013 ; 5(3): 72–82. doi:10.4018/jgcms.2013070105.

How Interventions Might Improve Cognition in Healthy Older Adults

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Abstract

Many of the cognitive declines in healthy aging are moderated by experience, suggesting that interventions may be beneficial. Goals for aging outcomes include improving performance on untrained tasks, remediating observed cognitive declines, and ensuring preservation of functional ability. This selective review evaluates current progress towards these goals. Most research focuses on untrained tasks. Interventions associated with this outcome include games and exercises practicing specific cognitive skills, as well as aerobic exercise, and modestly benefit a relatively narrow range of cognitive tasks. Few studies have directly tested improvements in tasks on which individuals have been shown to experience longitudinal decline, so this goal has not been realized, though remediation can be examined rather easily. Little work has been done to develop psychometrically strong functional outcomes that could be used to test preservation of independence in everyday activities. Virtual reality approaches to functional assessment show promise for achieving the third goal.

Keywords

aging; cognition; cognitive decline; interventions; cognitive interventions; games; exercise; functional outcomes; independence

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A very wide range of cognitive processes, including speed, working memory, executive functions, memory, linguistic abilities, and knowledge are affected in old age. However, longitudinal age declines in cognition tend to be gradual but typically not statistically significant until about age 60 (see Schaie, 2005). The relative amount of decline varies by cognitive domain, with a correlation of about −.33 for age and episodic memory, and −.50 for age and speed (e.g., Verhaeghen & Salthouse, 1997). A few domains like language, remain stable until after the 70s (McGinnis & Zelinski, 2000), though declines in sensory and perceptual processes may create functional impairments such as difficulties in communication (e.g., Schneider & Pichora-Fuller, 2000).

Although many of the declines associated with age may be due to degenerative physiological processes, recent evidence also points to the effects of certain moderators of performance that affect the extent to which age changes may be observed. These inform the basis of

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interventions to enhance cognitive processes in healthy older adults, that is, the majority of older persons, who do not develop dementing diseases or cognitive impairment, but who experience “normal” aging declines.

Cohort differences

Substantial increases in reasoning and related abilities in people of different generations when compared at the same ages (e.g., Schaie, 2005), suggest that changes in the cognitive environment may affect some abilities that have been observed to decline with age. Zelinski & Kennison (2007) evaluated two birth cohorts of people aged 56–82, one born on average in 1908 and the other born on average in 1924 on reasoning, spatial ability, list recall, text recall, and vocabulary. The more recently born cohort had better scores at age 74 on all tests except for vocabulary, even though that group did show declines on all tests with age. The explanation for the observed cohort differences was that the skills associated with better performance are reinforced by the broader social culture and these affect scores into old age (Zelinski & Kennison, 2007).

Education

In samples representing the population of older American adults, education is a better predictor of performance on cognitive tasks than either health or depression, even though these are both important covariates of performance (Zelinski & Gilewski, 2003). Education is used as an index of cognitive reserve, the capacity for maintaining high levels of cognitive performance in the face of negative brain changes associated with medical conditions or normal aging, due to compensatory processes. Cognitive reserve is protective of decline even in dementia, whereby highly educated individuals reach the threshold of functional deficit for diagnosis with much more brain damage than those with low levels of education (Stern, 2006). Nevertheless, there is little current evidence that the benefits of cohort or education do much more in healthy older individuals than to raise the baseline of performance. Both cohort and education provide their benefits early in life; age declines still occur for both those born more recently and with high levels of education (Kennison, Petway, & Zelinski, under review). This is where the potential to further reduce effects of decline in aging through interventions comes into play.

Malleability of Cognitive Functions

The findings of cohort differences and education in explaining individual differences in older adults’ cognitive performance suggest that it is possible to protect brain function in older adults through targeted experiences. The processes affected by cognitive aging are strongly related to each other (e.g., Zelinski & Lewis, 2003), and are observed in basic processes of perception, speed, working memory, and executive control, as well as in more complex cognitive domains. This suggests that improvement of cognitive skills in older adults can be supported by training programs that reflect this complexity.

Neuroplasticity

In parallel with the work on factors associated with cognitive outcomes in older adults, research over the past 40 years suggests that experiences constantly remodel the adult brain. Michael Merzenich and colleagues, for example, found that changes in stimulation as well as the effects of top-down processes such as attentional focus affect neuroplastic responses.

Changes in enervation of sensory inputs affect cortical responses so that they reorganize according to the available stimulation; for example, transection of nerves in the fingers of monkeys resulted in changes over time to somatosensory cortex response patterns so that representations of tactile stimulation reflected enervation from areas surrounding the lesion rather than the lesioned area (see, e.g., Buonomano and Merzenich, 1998). Polley, et al. (2006) showed that rats trained to respond to specific stimulus features, such as the frequency or intensity of sound, produced cortical responses based on the training focus, even though their experimental stimuli included both feature sets. This suggests that attentional/reward system plays an important roles in cortical reorganization. This leads to the observation that neuroplasticity is both positive and negative; practice in discrimination produces gains in the quality of representations that underlie neural responses, whereas disuse produces reductions in differentiation of representations (e.g., Draganski & May, 2008).

Merzenich and colleagues (e.g. Mahncke et al., 2006) suggested that cognitive aging effects represent negative plasticity. Cognitive declines arise from reductions in the schedules of brain activity associated with less cognitively demanding activities in old age, from declines in the brain's ability to detect signals against spontaneous neural network noise, from reduced neuromodulation of attention, and from negative learning. Reversing these processes by introducing intense, frequent, and extensive adaptive practice in perceptual discrimination, attention, and memory should, according to their model, improve cognitive performance in older people. They argued that engagement in reward systems is a critical feature of the model, which we will allude to in discussion of the relevance of games to cognitive training later.

It is important to note that it is not only the cognitive skills that are trained that should benefit from increasing the experiences that produce positive plasticity; these skills should extend to tasks that are not trained but share functions with the trained tasks arising from similar brain substrates (e.g., Dahlin, et al., 2008). Thus, the point of interventions for cognitive training of older adults involves a set of hierarchical goals: to produce transfer to untrained tasks, to rehabilitate and improve declining skills, and to ensure preservation of functional ability so that older adults may remain independent longer (see, e.g., Jobe, et al., 2001). The purpose of this article is to report on the relative success of current interventions to improve cognition in older adults with respect to the goals suggested here.

Improvement of Untrained Tasks

Cognitive intervention studies demonstrate that, with training, older and younger adults can improve performance relative to control groups (Zelinski, 2009). Studies training general cognitive strategies such as mnemonics show benefits that are often quite narrow and specific, with positive effects typically confined to the particular task that was trained (Ball et al., 2002; Park et al., 2007). Studies that use the principles of positive plasticity suggested by Mahncke et al. (2006) : adaptive, extensive practice of basic cognitive tasks involving perceptual discrimination and speed and executive control processes, and modulation of attention and reward systems have successfully demonstrated transfer to untrained activities (Zelinski, 2009; see Zelinski, Dalton, and Smith, 2011, for details). The types of training examined include working memory updating, multimodal training through real time strategy video games, attentional switch tasks and speeded perceptual discrimination (see Hindin & Zelinski, 2012 for details).

Physical fitness is associated with better cognitive performance (see Etnier et al., 1997). Randomized controlled aerobic exercise interventions with sedentary older adults have demonstrated cognitive enhancement in older adults for executive abilities, controlled processes such as choice RT, spatial, and simple RT tasks (e.g., Colcombe & Kramer, 2003). Animal models indicate that aerobic exercise produces neurogenesis, whereas studies with middle aged and older adults show that it increases hippocampal volume (Pereira, et al., 2007). Neuroimaging of older adults who engage in aerobic exercise has also established increased neural activity in the brain regions associated with executive control, as well as increases in the plasticity of brain networks as a result of cardiovascular training (see Hertzog, Kramer, Wilson, & Lindenberger, 2009).

The level of improvement with training interventions for older adults was investigated in a meta-analysis of the relative untrained cognitive task improvements in older adults from 25 cognitive and 17 aerobic exercise interventions (Hindin & Zelinski, 2012). It compared the effect sizes associated with improvements in performance after accounting for practice effects; previous work for aerobic interventions (Colcombe & Kramer, 2003) had only assessed effects in those in the training group. Results indicated that estiumated average effect sizes were modest but roughly equivalent for aerobic and for cognitive training studies (with $d = .33$ or an equivalent $r = .16$ for both kinds of interventions). To compare the effect sizes from the meta-analyzed studies with that of a pharmacological intervention, Hindin and Zelinski (2012) estimated the effect size over 28 cognitive outcomes for young adult male volunteers in a study (Turner, et al., 2003) evaluating modafinil, a narcolepsy drug used off-label for cognitive enhancement compared to placebo. Using the same multilevel analysis methodology as for the meta-analysis of the aerobic and cognitive training studies, they found that benefits of modafinil with an estimated average $d = .23$, equivalent to an $r = .11$, compared to placebo, were rather similar to those of the nonpharmacological interventions.

Despite the similarity of the effect sizes for the untrained outcomes of both cognitive and aerobic interventions, it is likely that they may involve different mechanisms for the training benefit. Nevertheless, the goal of determining whether cognitive training is associated with improvements in untrained outcomes has, in a preliminary way, been met. Yet many questions remain. For example, it is not clear whether the cognitive improvements are due to the specific training methods used or to other confounding factors, such as possible benefits of interacting with project staff (Lövdén, et al., 2010). The long-term benefits to performance of either type of training in are unknown. That is, few studies have followed participants for more than a year after training ends; discontinuing either aerobic or cognitive training programs may be associated with fading of the effectiveness of their cognitive benefits. There is evidence that the neuroplasticity training tested in the study by Smith and colleagues (2009) effects were reduced three months after the training ended (Zelinski, et al., 2011).

Rehabilitation and improvement of declining cognitive skills

There is very little work at the current time on interventions conducted on populations of older adults where it can be established that abilities that have declined in those individuals have been improved. Although the aerobic and cognitive training studies clearly improve performance on untrained tasks, all of the studies are essentially cross-sectional in nature. No longitudinal study of healthy cognitive aging has used aerobic or brain plasticity interventions to improve performance in individuals showing declines from previously measured levels of ability that we are aware of.

However, there may be a dynamic relationship between changes in cognitive and physical activities thought to improve cognitive performance and objective cognitive performance changes. As already indicated, cognitive reserve has been thought to be protective of functional performance so that individuals who develop dementia in the face of high levels of reserve experience a later onset and steeper declines after onset (Stern, 2009). Most individuals do not develop dementia, however, so it is has been proposed that healthy older adults could experience smaller longitudinal declines in cognition assuming that reserve builds during adulthood because of beneficial lifestyle factors (Stern, 2009).

A series of harmonized analyses of four longitudinal datasets of people aged 55 and over from the US, Canada, and Sweden, with 9 – 21 years of follow-up, examined the relationships between engagement in positive lifestyle activities and cognitive change. Mitchell et al. (2012) examined the association between changes in everyday cognitively stimulating activities and in performance on semantic knowledge, memory, fluency, and reasoning. Positive relationships, controlling for education and baseline activity and test performance were observed for all measures except for reasoning. Lindwall, et al., (2012) investigated the relationship of changes in physical activity engagement with cognitive change and found a positive relationship for changes in reasoning but not the other tests. Brown et al., (2012) found no relationship between social activity engagement changes and cognitive changes. However, in other work, James, Wilson, Barnes, and Bennett (2011) did find that those who engaged in more social activities longitudinally declined less on episodic memory, semantic memory, working memory, speed, and visuospatial ability over five years.

These studies may suggest that the dynamics of cognitive and physical engagement with cognitive outcomes from the observational studies cited here can be harnessed to reverse previous decline patterns, but until interventions have been done on individuals with longitudinally observed decline patterns in otherwise healthy old age, the goal of rehabilitating and reversing declining skills has not yet been met.

Critically, there is no current evidence that *any* intervention can delay or prevent Alzheimer's disease or dementia (US Department of Health and Human Services, 2010). At best, aerobic exercise and cognitive engagement interventions have modest effects on relatively narrow outcomes. Exploratory work into the cognitive benefit of interventions in group cognitive activities, and civic engagement in several laboratories in the US is ongoing. Other pathways to cognitive improvement that involve combining approaches, for example aerobic and cognitive training, are also being tested. However, none of these studies are evaluating rehabilitation of observed declines in healthy older adults.

Ensure preservation of functional ability

The point of most interventions for cognition is that interventions should help older adults to remain independent. However, there has been very little movement towards that lofty and increasingly urgent goal. Only a few attempts have been made to develop outcome measures that readily simulate the cognitive demands of everyday activities. Those few measures that currently exist, however, do not appear to either actually or validly reflect either psychometric function or everyday functional abilities. Measures of subjective performance, for example, of whether users think that they have difficulties in everyday remembering tend to be very modestly to poorly correlated with actual performance on psychometric tests (see, e.g. Zelinski & Gilewski, 2004). Subjective improvement in everyday functioning was associated in one study with participation in a neuroplasticity-based intervention (Smith, et al., 2009) but effects were not significant three months after the intervention was discontinued (Zelinski, et al., 2011). Measures of how long it takes older adults to complete tasks that they can do accurately such as making change and reading instructions on a can of food are uncorrelated with cognitive tests such as reasoning or even other measures of everyday problem solving (Owsley, Sloane, McGwin, & Ball, 2002), so that they cannot be validated against current measurement approaches.

Studies that focus on measures of independence for older adults use very blunt and relatively rare outcomes such as the inability to engage in activities of daily living, for example, being able to cook or manage a checkbook (see, e.g., Ball et al., 2002). A review of functional living skills assessment instruments for healthy and impaired adults (Moore et al., 2007) suggested that, although some existing instruments have clinical utility, no instrument met the criteria that they argue are important in everyday function assessment. These criteria included development of test items based on participants' or caregivers' priorities rather than on experts' opinions, selection of items based on empirical analysis, efficiency and portability of testing procedures, and parallel measures of performance under both ideal and real-world conditions.

Many of the measures of behavioral performance for independence do address instrumental activities of daily living such as shopping, cooking, and medication management (Moore, et al., 2007). However, there is little assessment of other important activities associated with independence such as driving. Yet driving safely is an example of a behavior that is malleable and potentially can benefit from interventions. The overall rates for both fatal and nonfatal crashes for drivers age 70 and over declined substantially between 1995 and 2008, despite increases in the population of older drivers. Declines in crash rates have been significantly larger for drivers over age 70, and even greater for drivers over age 80, compared to the declines for drivers aged 35–54 (Cheung & McCartt, 2010). Although some of the change is attributed to safer cars and increasingly stringent rules for older adults' driver licensing in many states, improved general health, including better vision and cognition in the older population, is a critical factor (Cheung & McCartt, 2010). A pilot study of an intervention of computerized training of different aspects of attention in older drivers used driving performance on a simulator as an outcome. Results indicated suggested that the training reduced errors (Cassavaugh & Kramer, 2009). Simulator performance is not precisely the same as that of actual driving, so these results are suggestive, though encouraging.

Self-regulation of driving in older adults is another source of reduced crash risk. Adults over the age of 65 are more likely to use seat belts, to drive when conditions are safest, and are less likely to drive impaired, for example, to drink and drive, than other age groups (Centers for Disease Control, 2011). A substantial percentage of older adults self-regulate their driving because of concerns about visual and cognitive impairments (Braitman & McCartt, 2008). People whose processing speed is very slow have a relatively high rate of driving cessation. An intervention involving speeded visual perception training did not show improvements on untrained cognitive tasks, but, paradoxically, those individuals deficient in speeded visual perception who received the training were less likely to report cessation of driving 3 years after the intervention than those not receiving the training (Edwards, Delahunt, & Mahncke, 2009). The intervention, however, does not benefit individuals with normal processing speed for their age, (Edwards, et al., 2009) so it has limited benefit for the larger population of older adults.

There is clearly a need for more real life functional outcome assessment to test whether interventions do help healthy older adults maintain independence. Relatively little is known about how normal age declines in cognition contribute to daily functioning problems, and whether interventions will reverse such declines. Recent innovations in virtual reality approaches to assessment of everyday functioning, and the development of computer driven health games to improve daily functioning can play an important role in meeting this goal. Much remains to be done, but continued work in developing everyday outcome measures that can be used to evaluate the role of cognitive interventions in old age is critical for the future.

The Role of Games in Meeting the Goals of Interventions

Very few of the cognitive intervention studies, including the ones cited here, that have been successful in improving performance on untrained tasks, use a complex game approach to cognitive training. Yet games may be an important platform for encouraging sustained practice of cognitive skills. There has been no systematic evaluation of the role of long-term practice of cognitive interventions in outcomes; in the Hindin and Zelinski (2012) meta-analysis, the duration of cognitive training was approximately 6 weeks, with a range of 2 to 12 weeks during which there were an average of 17 sessions with a range of 3 – 45 sessions. In addition, it is likely that the discontinuation of direct cognitive training is associated with declines over time in the relative effect of the training on untrained outcomes (Hindin &

Zelinski, 2012), though this has not been carefully evaluated. One large trial of interventions to improve memory, reasoning, and processing speed indicated that booster sessions 12 months after the primary intervention was helpful in maintaining training gains (Ball et al., 2002). It is not known how long older adults would continue to participate in a typical intervention; however, even after engaging in a physical fitness intervention, such as a walking program, older adults are likely to be less active several years after the intervention has ended (McAuley, et al., 2007). This, of course, does not bode well for continued performance of repetitive and presumably, boring, cognitive exercises. We have elsewhere suggested that digital games that implicitly encourage practice of cognitive skills might be an avenue to sustained commitment to practice because games are fun (Zelinski & Reyes, 2009). Though this has not been tested in older adults to our knowledge, it was reported that five months after an action game play intervention that involved young men with no prior game experience, many of those participants spontaneously continued to play such games (Feng, Spence, & Pratt, 2007).

One model of why people enjoy games is the Presence-Involvement-Flow Framework (Takatalo, Nyman, & Laaksonen, 2008). It suggests that presence, which includes perceptual-attentive and spatial-cognitive processes that create the space of game play, involvement as the user's roles and attitudes towards the game space, and flow as the experience of the ability-challenge tension that motivates continuation of play. It has been suggested that motivation deepens attention and this is crucial to neuroplastic processes (e.g., Mahncke et al., 2006), and games may therefore provide an important platform for older adults to sustain practice of neurocognitive skills while being enjoyable. In addition, digital action games follow many of the principles of neuroplasticity; they involve extended practice of certain skills and actions, they require sensory discrimination, are adaptive to the player's level of competence and therefore maintain an appropriate level of challenge (Zelinski & Reyes, 2009).

Interest in developing commercial games to engage older adults as well as others in cognitive training has been burgeoning. Posit Science (positscience.com, San Francisco, CA) was the first company to test an intervention, its Brain Fitness program, in a large randomized controlled multisite clinical trial of people aged 65–93 (Smith et al., 2009; Zelinski et al., 2011), and showed successful improvement on untrained tasks . Posit Science has expanded its programs from the original auditory training program to visual training and executive function training in an online package called Brain HQ with testing extended to a wide range of users, including those with mild traumatic brain injury and cancer survivors. Another company, Lumos Labs (lumosity.com, San Francisco, CA), has created a substantial database of 600,000 users and is involved in supporting research on its online training program's efficacy. More broadly, SharpBrains (sharpbrains.com, San Francisco, CA) provides independent marketing and product information to companies, clinicians, and consumers about advances in applied neuroscience products, including games, to improve cognitive and emotional functioning across the life span. A professional society, the Entertainment Software and Cognitive Neurotherapeutics Society (ESCONS, escons.org), was recently organized to create collaborations and develop scientific guidance for the development of digital games to assist in diagnosis and treatment of mental health problems and to support cognitive functioning. It now holds annual meetings to showcase recent research in this area. Other organizations such as the Games for Health (gamesforhealth.org) society, supported by the Robert Wood Johnson Foundation, encourage research in a number of health related applications such as digital games to enhance cognition.

At this point in time, these developments are clearly exciting. Yet the evaluation of the progress towards the goals of cognitive interventions for aging remains similar for both the research-based and commercially-based arenas. Both standard interventions and some games have been shown to improve performance on untrained tasks. Limited work thus far has been done to improve performance in those with measurable previous declines, or on functional outcomes related to maintaining independence. There is much work ahead; the field is in its infancy, but there is reason to be optimistic about the role of games to improve cognition in older adults.

Acknowledgments

This research was supported in part by the Digital Aging Center of the Andrus Gerontology Center and grants R01AG10569, P50AG005142 from the National Institute on Aging and H133E080024 from the National Institute on Disability and Rehabilitation Research to the University of Southern California.

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