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Aging, training, and the brain: A review and future directions

Cindy Lustig,
Department of Psychology; University of Michigan.

Priti Shah,
Departments of Psychology and Combined Program in Education and Psychology; University of Michigan.

Rachael Seidler, and
Departments of Psychology and Kinesiology, University of Michigan.

Patricia A. Reuter-Lorenz
Department of Psychology. University of Michigan.

Abstract

As the population ages, the need for effective methods to maintain or even improve older adults' cognitive performance becomes increasingly pressing. Here we provide a brief review of the major intervention approaches that have been the focus of past research with healthy older adults (strategy training, multi-modal interventions, cardiovascular exercise, and process-based training), and new approaches that incorporate neuroimaging. As outcome measures, neuroimaging data on intervention-related changes in volume, structural integrity, and functional activation can provide important insights into the nature and duration of an intervention's effects. Perhaps even more intriguingly, several recent studies have used neuroimaging data as a guide to identify core cognitive processes that can be trained in one task with effective transfer to other tasks that share the same underlying processes. Although many open questions remain, this research has greatly increased our understanding of how to promote successful aging of cognition and the brain.

Introduction

Two inescapable facts will have major impact on individual lives and society in the next few decades. First, aging is associated with brain and cognitive changes that can limit functional capacity. Second, a large proportion of the population will be reaching the age at which those changes become a concern. Not surprisingly, there has been an upsurge of interest in cognitive training and other interventions that can slow or reverse those changes or ameliorate their detrimental effects. Some of these interventions show strong potential for benefitting older adults' cognition and performance, others make exaggerated claims that lack empirical support.

This paper reviews the literature on cognitive and behavioral interventions, with a particular focus on new approaches that incorporate neuroimaging data as a guide to program development and as an outcome measure. As we will outline, research in this area is promising, but there are many challenges yet to be overcome. We conclude with a discussion of whether training programs are worth the substantial investment they require of

Address correspondence to: Cindy Lustig Department of Psychology University of Michigan 530 Church Street Ann Arbor, MI 48109-1043 PH: 734 647 6925 clustig@umich.edu.

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participants, researchers, and funding agencies, and with recommendations for future research.

A brief history of cognitive interventions and healthy aging

Efforts to improve cognitive functioning in healthy, normally aging adults date back at least several decades. For an extensive review of the factors that may be related to successful aging, including observational studies and consideration of non-cognitive factors such as personality, stress, genetics, socioeconomic status, and alcohol consumption, we refer the reader to the recent review paper by Hertzog, Kramer, Wilson, and Lindenberger (2009), the commentary by King and Suzman (2009), and a related large-scale empirical study by Yaffe et al. (2009). Below we give a brief historical review of the behavioral-experimental approaches that laid the groundwork for the neuroimaging studies that are our main focus, in the approximate order of their development: strategy training, multimodal training, cardiovascular exercise, and process training.

Strategy training—Strategy training typically involves identifying tasks on which older adults do poorly and training them on strategies that may help increase performance. Many early training studies used this approach, for example, training in the method of loci in an attempt to improve memory performance (see Rebok, Carlson, & Lanbaurn, 2007 and Verhaeghen, Marcoen, & Goossens, 1992 for reviews). As we review below, these studies often found large and long-lasting effects on the trained task, but only limited evidence for transfer.

One of the main targets of strategy training has been memory; Rebok et al. (2007) report finding over 300 studies that evaluate effects of mnemonic training in older adults. They classify these studies into “single-mnemonic” approaches that provide training on a single strategy during one or a small number of sessions (e.g., method of loci, name-face mnemonic) and multiple strategy approaches across several sessions. Single strategy approaches tend to increase performance on near transfer tasks. Specifically, Verhaeghen et al. (1992) report memory improvements for different types of mnemonics taught including method of loci (d = .8), name-face (d = .83), peg-word (d=.62), imagery (d = .14), and organization (d = .85). Multiple strategy approaches (e.g., combining imagery and sentence generation mnemonics with self-testing) have also been shown to have substantial effects on near-transfer tasks (d = .73; Dunlosky, Kubat-Silman, & Hertzog, 2003). Rebok et al. point out that one major difference between single and multiple mnemonic approaches seem to be that multiple mnemonic approaches lead to more successful transfer to subjective everyday memory tasks. Individual differences also predict improvements from memory strategy training; relatively young older adults show greater effects of training than do those of more advanced age (Verhaeghen et al., 1992) and individuals who score higher on measures of cognitive plasticity (e.g., gains across multiple assessments of an unrelated, untrained test) also benefit more from memory training (Brehmer et al., 2008; Calero & Navarro, 2007).

Reasoning and problem solving have also been common training targets, including an early study by Labouvie & Gonda (1976). The Seattle Longitudinal Study incorporated strategy training in inductive reasoning and spatial orientation (Baltes & Willis, 1982; Boron, Turiano, Willis, & Schaie, 2007; Schaie and Willis, 1986; Willis & Schaie, 1985; Willis & Nesselroade, 1990). Individuals who received training improved on the targeted skills (d = .6 to .8 for reasoning, .4-.6 for spatial abilities; Schaie & Willis, 1986) and the effects lasted up to seven years post-training. Beneficial effects of training have also been found for the game “Twenty Questions”, which requires individuals to search a space of possible answers via strategic questions. Older adults are less likely to use optimal search strategies, but Denney et al. (1979) demonstrated that their performance improved after watching a model

use more strategic, constraining questions (that is, questions that divide the search space in about half).

Goal management, an important aspect of executive control relevant for everyday planning and problem solving, has been the target of recent studies. For example, a program of goal management training originally developed for brain-injured patients was recently used with older adults. Training consisted of 12 sessions that provided strategies for identifying high risk situations and stopping "automatic pilot" behavior in such situations, breaking down goals into sub goals, and so forth. Overall, individuals in the goal management intervention group improved on a variety of self-reported measures of functioning compared to the control group. Specifically, individuals in the training group reported reduction in annoyance at their own executive failures, increased ability to manage executive failures, and decreased anxiety (Levine et al., 2007; van Hooren et al., 2007).

A recent well-known intervention, the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study, is one of the first large-scale randomized control trials comparing different approaches to training (Ball et al., 2002). The ACTIVE study included four groups of participants: two types of strategy training (memory training and reasoning training), as well as a speed-of-processing training group (discussed below) and a no-contact control group. All three training groups received a 10-session intervention. The reasoning training consisted of strategies for inductive reasoning tasks such as finding the next item in a series. The memory-training group was provided instruction in mnemonic strategies for remembering verbal information such as word lists by organizing items in the list. Both the reasoning and mnemonics groups showed improvements on measures that targeted the skills learned that lasted five years after training ($d = .26$ for interaction of reasoning vs. control group improvement, $d = .23$ for the interaction of memory vs. control group improvement). Interestingly, the reasoning training group showed improvement not only on reasoning tasks, but five years post training showed less decline on self-reported Instrumental Activities of Daily Living ($d = .29$; Willis et al., 2006).

In summary, there are numerous studies of strategy training in older adults targeting memory, inductive and spatial reasoning, goal management, and verbal and non-verbal search processes. These studies find substantial improvements in trained and near transfer tasks, but show modest to no effects on far transfer tasks and everyday activities. In part, this lack of transfer may be due to the limited applicability of some strategies (e.g., method of loci) to most real-life tasks. Perhaps it is not surprising, then, that broader approaches that incorporate training on multiple strategies and/or focus on strategic processes applicable to a wide range of cognitive tasks (e.g., goal management) lead to the greatest levels of transfer.

Multimodal approaches—Multimodal approaches were developed in part as a response to the concern about the limited transfer effects of strategy-focused approaches discussed above. These are usually much more complex interventions or lifestyle changes, and may include a social component as well as a cognitive one. Examples include participation in classes that teach new skills (e.g., quilting, photography), engagement in cognitively-demanding activities such as bridge playing, or participation in volunteer work. These intervention programs are often designed to be enjoyable or socially meaningful for older adults, increasing the chances that they will maintain the activities and skills even after the formal training period has ended. The complexity of these programs is both a strength and a weakness – they often have broad benefits but these transfer effects are relatively small. From a scientific standpoint, it is often unclear as to which aspect(s) of the protocol are responsible for the transfer benefits that do occur.

A recent approach to multimodal training was developed by Stuss, Winocur, Craik, and colleagues (Craik et al., 2007; Stuss et al., 2007; Winocur et al., 2007a, 2007b), who combined three 4-week training modules, two of which were highly strategic in nature: memory strategy training, goal management training. The third was a psychosocial intervention that focused on self-efficacy. Because of its emphasis on strategy, it might be considered a descendent of the approaches discussed above, but incorporating multiple domains. This intervention led to improvements in simulated real-life tasks, self-reported executive functioning, overall well-being, and memory. These results suggest that combined training of multiple strategies along with a psychosocial intervention may overcome limitations of prior strategy-based training approaches.

Several studies have used video games to train attention and perception in young adults with impressive effects (Green & Bavelier, 2006), and these methods have also been tried in older adults. Green and colleagues argue that video games may be especially effective for training because they provide many of the features of successful cognitive training paradigms: task variability, feedback, adaptivity, and motivation (Green & Bavelier, 2008; see also Basak et al., 2008). Such games are increasingly popular in older adults (especially the Nintendo Wii) and often relatively inexpensive. Early studies of video game training with older adults used either laboratory-developed games that target specific skills (Salthouse & Somberg, 1982) or simple off-the shelf games such as PacMan. In one classic study, for example, Salthouse and Somberg asked older adults to practice a video game called “Space Trek” that they developed and embedded with practice in memory scanning, speed of processing, visual discrimination, signal detection, and temporal anticipation. They found that individuals improved in these skills throughout 50 sessions of training, and benefits remained at a one-month follow up test. Studies of early relatively simple off-the-shelf video games, such as Pac Man & Donkey Kong (Clark, Lamphear, & Riddick, 1987) and Super Tetris (Goldstein et al., 1997) also showed improvements in training, but typically only on relatively simple reaction time tasks (d = .70 in Clark et al., 1987; see also Dustman, Emmerson, Steinhaus, Shearer, & Dustman, 1992; Goldstein et al., 1997).

Other studies that use more complex games have shown more extensive transfer effects. For example, Drew and Waters (1986) found that training on Atari's “Crystal Castle” game, which requires strategic thinking as well as sensorimotor skills led to improvements in manual dexterity and performance on the Wechsler adult intelligence scale (WAIS). However, because they used a very limited control group (n = 2) the degree to which improvements were training-related remains unclear. Recently, Basak and colleagues (2008) found that 23.5 hours of practice on a complex strategy game (Rise of Nations) led to improvements on a variety of tasks including mental rotation, visual change detection, and Raven's progressive matrices. The largest effect sizes were for measures of executive function (eta-squared = .4).

Other multimodal interventions focus on having older adults learn new activities that are cognitively, physically, and/or socially engaging. Tranter and Koutstaal (2008) provided seniors with choices of a variety of stimulating activities to do at home (e.g., logic puzzles, creative drawing) as well as in the laboratory (e.g., playing with marble runs, playing intellectual board games). They found significant gains in fluid intelligence as measured by the Cattell Culture Fair test (d = .56 compared to controls). As another example, Noice et al. (2004) randomly assigned older adults to a theater performance class, a visual arts class, or a no-contact control group. The theater class was expected to be most demanding, as it requires individuals to learn large amounts of meaningful information, juggle multiple tasks simultaneously, and so forth. Indeed, the theater-performance group improved on memory and problem solving compared to both of the other control groups (d = .3 for memory, 1.0 for problem solving compared to no contact control group). The Senior Odyssey program,

based on the Odyssey of the Mind program used with students of kindergarten through college-age, takes a similar approach (Stine-Morrow, Parisi, Morrow, & Park, 2008). Older adults were divided into teams to participate in creative problem-solving activities such as designing a strong balsa wood structure. This program had positive effects on speed of processing (d = .79), as well as need for cognition (d = .39), and mindfulness (d = .42; all effect sizes reported in comparison to the control group).

The ExperienceCorps program increases older adults' involvement in the wider community in addition to their social interactions with age peers. In this program, older adults volunteer as tutors in underserved elementary school communities. In a randomized trial older adults who participated in ExperienceCorps increased their participation in cognitive activities (e.g., reading books) outside of their volunteer experience, compared to a wait-list control group. Those in ExperienceCorps also increased their social networks and activities, and their physical activity (Fried, Carlson, Freedman, Frick, Glass, Hill, McGill, Rebok, Seeman, Tielsh, Wasik, & Zeger, 2004).

Cardiovascular training—Aerobic exercise training can be viewed as another "multimodal approach" to improving cognitive function in older adults. Animal research has demonstrated that aerobic exercise is associated with increased neurogenesis and angiogenesis in the brain (van Praag et al., 1999a, 1999b, 2005;Black et al., 1990;Swain et al., 2003). Here we review the behavioral and cognitive effects of exercise training. The effects of aerobic exercise on brain structure and function in older human adults are reviewed below in the section "Neuroimaging as an outcome".

Both cross sectional (Etnier et al., 1997a) and longitudinal data (Colcombe & Kramer, 2003) indicate that aerobic exercise training improves cognitive function in older adults in many domains, with the largest improvements occurring on tests of executive function. Many cross sectional studies have demonstrated that high-fit older adults show better performance than their low-fit peers in simple reaction time tasks, tests of motor learning, and cognitive assessments (Etnier et al., 1997b; Dustman et al., 1984; Spirduso & Clifford, 1978; Etnier et al., 2001).

Exercise intervention studies have shown that older adults improve on cognitive measures following participation in aerobic training programs (see reviews by Colcombe & Kramer, 2003; Erickson & Kramer, 2009). Meta-analyses have shown that the benefits of aerobic training in older adults are greatest for tasks measuring executive function (i.e. flanker task, etc., Hedges g = .68), followed by improvements in controlled (g = .46), spatial (g = .43), and speed (reaction time, g = .27) tasks (Colcombe & Kramer, 2003). More limited improvements are typically observed for sensorimotor tasks. For example, it has been shown that older adults who exercise regularly have better balance than their sedentary peers, but this benefit is only seen under single-task conditions (Melzer et al., 2009). Somewhat surprisingly given the usual correlation between fitness and executive functions, fitness did not convey a benefit for balance measures made under dual task conditions. Interestingly, in one study a large proportion (94%) of both older men and women independently continued with physical activity for one year following participation in the intervention (Emery et al., 1992). This suggests that exercise programs are a feasible way to improve quality of life in older adults.

Process training—A fourth popular approach to remediating age-related decline in cognitive function has been training specific cognitive processes, but without explicit strategy training. These programs typically train participants on a set of tasks thought to load heavily on a specific cognitive process, and measure transfer on a separate, untrained set of tasks also thought to load highly on the targeted process.

One of the first studies of this sort targeted speed of processing and attentional breadth (Ball et al., 1988). Young and older adults were trained on a task that required detection or discrimination (frowning versus smiling) of a cartoon face presented at a central fixation task and localizing faces that occurred at unpredictable locations on the periphery. Improvement in performance on the peripheral task lasted for at least six months. This task was later incorporated as the speed of processing training in the ACTIVE trial (Advanced Cognitive Training for Independent and Vital Elderly; Ball et al.), and a later study that used this speed of processing and attentional breadth training actually found transfer to driving performance (Willis et al., 2006). Consistent with the multimodal approaches described above, a related study (Cassavaugh &Kramer, 2009) found that driving performance was also improved after training on a number of cognitive processes (working memory, manual control, attention).

Several studies have examined executive processes such as dual-tasking and task-switching. Early studies of dual-task training in older adults found that training reduced dual-task costs, but did not examine transfer from one pair of tasks to another (McDowd, 1986; Greenwood & Parasuraman, 1991). A later study by Kramer and colleagues (Kramer, Larish, & Strayer, 1995) provided evidence that dual-tasking ability per se could transfer across tasks with very different surface features if training occurred under a variable priority procedure. Studies have shown that dual-task training in the motor domain also leads to transfer, with the magnitude of benefits depending on the specifics of the training protocol (cf. Silsupadol et al., 2009a, 2009b; effect sizes ranging from d = .27 - .72 across various transfer measures).

Because the ability to shift from one task to another has been identified as a primary marker of executive control, a number of recent studies have attempted to train task-switching in older adults. Minear, Shah, and Park (2002) followed an approach similar to that used in dual-task training, and asked individuals to practice switching between a variety of task-pairs, and then measured improvement in the ability to switch between unpracticed pairs of tasks. They found that two hours of training improved older adults' switching performance (d =.95) relative to a control group who practiced the identical tasks in pure, non-switch blocks. A more recent study (Karbach & Kray, in press) found that practice on task-switching led to improvements not only on measures of switching, which might be considered near transfer, but also on measures of interference control, working memory, and fluid intelligence (d = .4 for older adults across these tasks).

In addition to the dual-task training described above, several other procedures have been used in the motor-training literature such as strength training, balance training, visual feedback training, and hand steadiness training, (cf. Kornatz et al., 2005; Seidler & Martin, 1997; Hatzitaki et al., 2009). In general, the findings are that while transfer effects are modest, older adults exhibit similar magnitudes of learning and transfer as do young adults (Seidler, 2004; Seidler, 2007a). This finding is especially important given the impairments in motor learning by older adults (Seidler, 2006). This preservation of learning and transfer appears to be consistent across a broad range of motor tasks (Seidler, 2007b), indicating that important aspects of sensorimotor plasticity are not detrimentally affected by the aging process. However, while initial learning and transfer may be relatively spared with age, long-term retention appears to be reduced. For example, Rodrigue, Kennedy, and Raz (2005) found that the acquisition of a mirror-writing skill did not differ across age, but that at a five-year followup, older adults showed less retention of the skill (and took longer to re-learn it) than did young or middle-aged adults.

Finally, data from a set of memory-training studies highlights the importance of careful task analysis and the value of individual differences data in considering which processes are actually being trained. Jennings and Jacoby (2003) developed a repetition-lag procedure

designed to target recollective processes at retrieval: Lure items were repeated during a recognition task, and participants were required to reject them as unstudied items both on their first presentation and upon their repetition. As participants gained proficiency in the task, the distance between lure items was increased, increasing demands on source memory and presumably on recollective processes at retrieval. However, using a slightly modified version of this procedure, Bissig and Lustig (2007) found that individual differences at encoding, rather than retrieval, were highly predictive of success in the training task. A later study showed that manipulations at encoding affected both performance on the training task and transfer to other tasks, including measures of everyday memory (Lustig & Flegal, 2008).

Summary of behaviorally-based approaches—Each of the methods described above has its strengths and weaknesses. Strategy-based training often results in large benefits to the trained task, but limited transfer. Multimodal approaches have the inverse set of pros and cons: Transfer effects can be widespread, but are often small. The complex nature of multimodal programs makes it hard to know which aspect(s) of the protocol leads to transfer and should be further emphasized, although their immersive and often social nature may encourage continued practice and maintenance of whatever benefits do accrue. Cardiovascular training has had relatively large and widespread effects, but the underlying mechanisms of these effects are still unclear, and these methods may not be accessible to older adults with physical limitations. Process-based methods have shown good promise for transfer as well, but require careful task analysis to determine what processes are being trained and to pick the appropriate transfer tasks. As we will describe below, neuroimaging data may be a powerful tool for facilitating this task analysis and thus improving transfer.

Across these different methods, some general themes emerge. On a promising note, it is evident that older adults can show plasticity and training-related changes, albeit at lower levels than those seen in young adults. The basic principles derived from the literature on skill learning in young adults also appear to apply to cognitive training in older adults. As the most prominent example, a consistent finding is that, varied training leads to greater generalization. The well-established literature on learning and the development of expertise has important lessons for designing effective interventions for older adults. In the next section, we discuss new approaches that use neuroimaging data to guide and assess cognitive interventions.

Neuroscience as a guide to process-based training

The process-based approaches described above use task analysis in their attempts to derive which component processes may be shared between the trained task and a target transfer task. However, it is often difficult to “look inside the black box” and know exactly how a subject is approaching a task. Further complicating the issue, different individuals and different age groups may use different strategies, making transfer even more unlikely.

Recently, several investigators have used neuroimaging to guide their selection of trained and outcome tasks. The underlying assumption here is that if two different tasks show robust recruitment of a particular brain region, it is likely that they both engage the cognitive process(es) subserved by that brain region. Therefore, improving the function of that brain region (and presumably that process) in Task A should have beneficial effects for its use in Task B.

A precursor of this approach is the training program originally developed by Merzenich and colleagues to remediate developmental language disorders and more recently applied to older adults (Mahnke et al, 2006; Merzenich et al., 1996). Although not directly based on neuroimaging data, it incorporates exercises designed to reverse purported “negative” plasticity—detrimental brain changes that are thought to result from decreased brain

engagement and declining sensory systems, which may increase neural noise. The training program is designed to increase the engagement of down-regulated neuromodulatory structures and intensively exercise language reception. Participants complete sensorily- and cognitively- demanding exercises that require the discrimination and identification of acoustic stimuli that range from frequency-modulated signal sweeps to nonsense syllables to aurally presented stories. The generalization of benefits was measured using a battery of auditory-based neuropsychological tests that yielded a global auditory memory score.

Following the training period, the global memory score showed significant improvement that was only evident in the training group. The effect size associated with this improvement was a modest d = 0.25. The benefits were more robust (effect size of d= 0.61) if individuals who had relatively high auditory memory scores to start with (greater than 85% accuracy) were eliminated from the analysis. At a three-month follow-up test, the training group retained some gains on digit span. Unfortunately global memory was not measured at this time point, limiting conclusions about long-term gains. The success of this training procedure is thought to result from its “retuning” or recalibration of the auditory system so that the signals it feeds forward to medial temporal and cortical regions are less noisy and can therefore be processed more effectively. However, this explanation has not yet been directly tested using neuroimaging methods with older adults.

Persson and Reuter-Lorenz (2008) took a different approach to improving executive function, selecting training and transfer tasks based on their known reliance on a specific region of the brain. A substantial body of brain imaging evidence from PET and fMRI has established that the left inferior frontal gyrus (IFG) in the region of the pars triangularis (Brodmann's Area 45) is activated in working memory tasks that place demands on interference control (Jonides & Nee, 2006). Importantly, tests of episodic and semantic memory that include a high interference component also activate this brain region. Indeed, Nelson et al. (2009) documented that overlapping regions of left IFG are activated when controlling interference in different working memory and semantic memory tasks. Overlap was evident in both group and individual level analyses. Motivated by these observations, Persson & Reuter-Lorenz (2008) hypothesized that if neural overlap implicates functional (process) overlap, there is the potential for transfer of training between these different memory domains.

In a recent study with young adults (Persson and Reuter-Lorenz, 2008) found that eight 50-minute sessions of training on working memory tasks with high levels of interference produced a marked reduction in interference on unpracticed episodic and semantic memory tasks (Cohen's d= 0.80 and 0.70, respectively). Control groups who completed 8 sessions of practice on similar working memory tasks that omitted the interference component, or on a perceptual matching task using the same stimulus sets, showed no performance change on the transfer measures. Pilot work with a group of ten older adults has demonstrated successful transfer of training benefits to the semantic (d= .60) and episodic task (d= .40). This promising result awaits verification in a larger population of subjects and proper control groups. Nevertheless, the principle behind the work, namely that neural overlap predicts functional overlap is a critical one that may be key to effective transfer and the development of other successful interventions.

An important new study by Dahlin and colleagues (2008) provides the first direct support for the overlap principle, while also indicating some potential boundary conditions for its operation. This group focused on the process of memory updating. Updating is required, for example, when an individual is listening to a running stream of letters and has to remember the most recent three letters. Because the stream is constantly changing, the listener must continually discard and retain new letters from the stream. Participants were trained on a

series of 5 different updating tasks over the course of several weeks. One of the transfer tasks, N-back, also required updating but differed from the training tasks in their stimulus materials and response requirements. An additional task, Stroop, which relies on a number of executive functions, but not on updating, was also included to assess the specificity of the training effects.

Prior to training the participants were scanned using fMRI to obtain baseline measures of the transfer tasks, along with one of the training tasks, letter memory, referred to as the criterion task. After the training period, scanning was repeated. In young adults, both tasks posited to require updating (the letter-memory criterion task and the n-back transfer task) activated an overlapping region of striatum, in addition to some fronto-parietal sites. The criterion task and the Stroop task shared fronto-parietal activation, but did not overlap in the striatum. Older adults did not show striatal activity during the pre-training assessment on any task, although they did show activation of fronto-parietal sites.

This pattern of overlap and dissociation in the brain activation data turned out to align impressively well with the patterns of behavioral transfer. For young adults, performance on the criterion task (letter memory) showed marked improvement over the 5-week training period (d= 3.0). Moreover, these benefits transferred to the N-back task with significant (d = 1.20) post-training improvement. In contrast, training did not improve Stroop performance. This suggests that the shared striatal activations for letter-memory and n-back seen at pretraining provided an important substrate for transfer effects. Consistent with this interpretation, young adults increased activations in striatum for both the letter-memory and n-back tasks after the training period, even though the n-back task had not been practiced. There were no training related activation changes associated with Stroop performance.

The data from older adults confirmed the importance of this shared striatal substrate. They showed dramatic post-training improvements (d = 3.75) on the letter-memory criterion task but no transfer of benefits to N-back performance. It is worth noting that although older adults showed large improvements in the letter-memory updating task, their performance both pre- and post-training was substantially below that of young adults. Further, although training increased older adults' striatal activity during the letter-memory task to significant levels, they still showed no activation in this region during the n-back task. Taken together, these data suggest that the shared striatal component seen at pre-training for young adults was an important factor in the transfer effects seen from letter-memory training to the n-back task, and that the lack of this component limited both overall performance and transfer benefits for older adults. Put another way, it is perhaps not surprising that boosting striatal updating processes via letter-memory training had no benefit to the n-back task for older adults, given there was no evidence that these two tasks engaged overlapping striatal processes before training.

In sum, very few training programs with older adults to date have harnessed cognitive neuroscience and brain imaging to guide the development of process-specific interventions. However, the few that have are promising and suggest the potential fruitfulness of this approach.

Neuroimaging data as an outcome measure

The above section deals with neuroimaging data as a guide to designing training protocols and predicting patterns of transfer. Brain data can also be used as an important outcome measure. As such, it has the potential to reveal insights about cognitive processes that are not easily obtained by behavior alone. Even when young and older adults (or even individuals within the same age group) show similar behavioral patterns, they may have engaged different processes to perform the task. On the other hand, if older adults engage

the same processes as young adults but do so less efficiently, the result may be age differences in performance. The results of Cabeza, Anderson, Locantore, and MacIntosh (2002) provide an instructive example: Older adults whose performance matched young adults' on a memory task had more bilateral patterns of activation in prefrontal cortex than did young adults. In contrast, older adults with lateralized patterns of activation that resembled young adults' had much lower memory performance.

Below we attempt to organize the existing literature on training-related brain changes (both structural and functional) using the following framework: Increases in size or activation levels are hypothesized to represent increased use of the processes mediated by a region; decreases in size or activation indicate decreased use (or increased efficiency). Both increases and decreases contribute to shifts – the activation of a somewhat different network related to task performance after training than before training (cf. Kelly and Garavan, 2005). These shifts are hypothesized to represent more global changes in strategy or emphasis as opposed to simpler increases/decreases in component processes. As described below, this framework is likely oversimplified in some respects, but it provides a starting point for organizing the data on training-related changes in older brains.

Structural changes—Consistent with the findings that experts tend to have enlarged brain structures related to their type of expertise (e.g., Gaser & Schlaug, 2003; Maguire et al., 2003), cognitive, cardiovascular, and sensorimotor interventions are generally associated with brain structural increases. These training-related changes appear to be of similar size in young and older adults.

In a naturalistic study using adult participants ranging from earlier adulthood through middle age (age 25-50 yrs), Pagnoni and Cekic (2007) found that a group of participants who had been meditating for at least three years did not show the same age-related declines in putamen volume as did a comparison group of age-matched controls. A similar trend was found for whole-brain gray matter volume. Furthermore, although performance on a sustained attention task had a strong negative relationship with age in the control group ($r = -.72$), it remained constant across age in the meditators, and correlated with putamen volume when the two groups were collapsed.

However, some notes of caution are needed here: Given that Pagnoni and Cekic (2007) used a naturalistic sample, one cannot make any causal judgments about the relation between meditation, brain structure, and performance or rule out a "third-variable" explanation for the correlation results. Furthermore, although several studies have found increases in gray matter volume associated with meditation, the regions affected vary considerably across studies, raising concerns about the reliability of these effects (see Luders et al., 2009 for a brief discussion).

Using a more experimental approach, Boyke et al. (2008) randomly assigned older adults (M age = 60) to either a three-month juggling training program or a control condition. Structural scans were taken at three timepoints: before training, at the end of the three-month training period, and three months after training had ceased. Not all of the older adults in the training group were able to master the juggling skill, but those who did showed a significant increase in gray matter volume in area MT/V5, a middle temporal region usually associated with visual motion processing. This increase reversed after training was stopped. Similar trends were seen when the older adult group was analyzed as a whole (including both those who did and did not master the juggling skill).

Boyke et al. (2008) described the training-related MT changes in this older adult sample as "slightly smaller" than those seen in a previous study using young adults (Draganski et al.,

2004), but did not report whether those age differences were significant. In addition, the older adults showed training related changes in hippocampus and nucleus accumbens, two regions that had not shown changes in young adults. The authors suggest that the hippocampal changes might be related either to generalized benefits of the physical activity involved in juggling for neurogenesis, or to its role in spatial representations. The nucleus accumbens changes were thought to be linked to its involvement in reward and motivation.

Cardiovascular training also appears to have beneficial effects on brain function. Most studies on this topic are naturalistic, examining the correlations between pre-existing fitness status and cognitive measures. One exception is Colcombe et al. (2006), who randomly assigned young (age 18-30) and older adults (age 60-79) to a cardiovascular training program or a stretching and toning program for six months. Young adults did not show any change over the training period regardless of condition, but older adults in the cardiovascular training program showed significant increases in anterior white matter volume and in gray matter volume in inferior frontal gyrus, anterior cingulate, and superior temporal gyrus. No cognitive measures were taken in this study, but the heavy involvement of prefrontal regions is consistent with the previously-described benefits of cardiovascular training for executive functions. Importantly, the positive effects appear to be restricted to training that improves cardiovascular fitness – stretching and weight training do not appear to have substantial benefits to cognition.

All of these studies have their limitations. Most studies of training and structural change use of voxel-based morphometry, which has been criticized for potentially distorting estimates of atrophy, errors in classification of white and grey matter, and image registration problems (Ashburner & Friston, 2001; Bookstein, 2001; Karas et al., 2003; Kennedy et al., 2009; Tisserand et al., 2002). As noted above, in naturalistic studies it is difficult to establish what the causal relationship is between the behavior and brain structures of interest, or to determine whether some other unknown factor may be influencing both variables. In experimental studies, there are concerns about whether the images taken at different timepoints in the study (e.g., pre- and post-training) have been properly co-registered, and other sources of variability in image acquisition and processing that can distort results (see Littman, Jens, Christian, & Stiehl, 2006 for discussion). Studies in which structural change is correlated with behavioral change, or behaviors for which naturalistic and experimental studies yield converging results, may be interpreted with more confidence.

In summary, the few studies of structural changes consistently link changes to *increases* in size. This pattern differs somewhat from training effects on activation levels, which as described below show both increases and decreases as a result of training. The Boyke et al. (2008) study suggests that training must be maintained in order for these structural increases to be maintained.

Activation ups and downs—Within the motor training field, Doyon and colleagues (Doyon et al., 2003; Doyon and Benali, 2005) have recently proposed a theoretical framework to describe the dynamic cerebral changes that occur during different phases of training. These include a fast early learning stage, a slow later stage, consolidation, automaticity, and retention. The model suggests that, in the fast learning phase, both the corticostriatal and the cortico-cerebellar systems are recruited, along with prefrontal and parietal regions that contribute to the more cognitively demanding aspects of early learning. Once the skill becomes well learned (slow, later stage of learning), however, the two systems dissociate; the cortico-cerebellar system underlies sensorimotor adaptation and the cortico-striatal system uniquely contributes to the formation of motor sequence representations. Thus, the automaticity and retention phases of learning are associated with a reduced, more efficient and focal pattern of brain activity.

Cognitive intervention studies rarely have the multiple assessments of brain activity needed to fully test whether the stages suggested by Doyon apply to non-motor functions, although the most parsimonious assumption is that they do. However, the particular brain regions involved are likely to be slightly different, especially in the later stages of training. When training first begins, prefrontal and parietal regions related to cognitive control are predicted to become more active, especially if the training program serves to increase engagement of controlled processing that older adults may not have self-initiated prior to training. To the degree that training leads to more efficient processing, activation in these regions may decrease, and both increases and decreases may be seen in the networks more specifically involved in task performance. Below we review the existing literature to examine the degree to which these predictions hold true, and whether training-related activation changes are the same for young and older adults.

Unless otherwise noted, the studies described below used BOLD fMRI. Questions often arise about the validity of such results because of age-related atrophy, changes in the hemodynamic response and its coupling to neural activity, performance differences, and other potential confounds (see the June 2007 special issue of this journal edited by G.G. Brown for more extensive discussion). Several different methods have been proposed to help control for these potential confounds (e.g., Aguirre, Zarahn, & D'Esposito, 1998; Buckner, Snyder, Sanders, Raichle, & Morris, 2000; Huettel, Singerman, & McCarthy, 2001), but they are not applied consistently across studies. These issues may be of particular concern for cardiovascular-training studies. For other types of training, they are less problematic to the extent that interpretation focuses on training-related changes within an age group or interactions with age (where any main effects of age on the BOLD response would presumably be constant across conditions; see discussion by Buckner et al. (2000)) rather than overall differences between young and old adults. Other methods such as arterial spin-labelling fMRI may reduce some vascular concerns and have other advantages such as increased stability (Detre, Wang, Wang, & Rao, 2009), but have not yet been regularly applied in studies of cognitive intervention in older adults.

Repetition priming—Repetition priming (faster and/or more accurate responses to stimuli after repeated exposures that does not require the conscious memory of those previous exposures) might be thought of as a very basic and specific form of training. It is different from most of the training protocols discussed above in that the training or practice effects occur for items, rather than for skills or processes. However, the aging and neuroimaging literature on repetition priming is fairly well-established, compared to that on other forms of training, and may provide important proof-of-principle demonstrations of plasticity in the aging brain.

Simple repetition priming for repeated semantic judgments is generally preserved or only very slightly decreased for older adults or even Alzheimer's patients compared to young adults (see Fleischman & Gabrieli (1998) for a review of age and Alzheimer's effects on different measures of priming). Repetition-related decreases in activation generally follow a similar pattern (e.g., Bergerbest et al., 2009; Lustig & Buckner, 2004). Likewise, Soldan et al. (2008) found similar repetition-priming performance and priming-related increases and decreases in activation for a possible/impossible objects task. In summary, basic repetition effects on both behavior and brain activation appear to be largely preserved with age, although these effects may be numerically smaller or not as long lasting (Wiggs et al. 2006). For example, Kennedy, Rodrigue, and Raz (2007) found that both young and old adults showed priming effects for fragmented pictures on an immediate test, but only young adults retained these benefits at a five-year followup test (see the section on motor learning for similar findings in a mirror-writing task (Rodrigue et al., 2005)).

Bergerbest et al. (2009) suggest that priming procedures may provide an important window into the question of whether or how the "extra" activations often seen in older adults as compared to young adults may be related to dysfunction or compensation. For example, in verbal tasks, young adult brain activation is typically left-lateralized, whereas older adults show a more bilateral pattern (see e.g., reviews by Cabeza, 2002; Reuter-Lorenz & Lustig, 2005). Using a voxelwise approach, Bergerbest et al. (2009) found that older but not younger adults showed repetition-related decreases in activation in right prefrontal cortex, in addition to the left prefrontal reductions seen in both groups. In addition, the activity reductions in right middle frontal cortex correlated with priming-related reaction time reductions for both age groups. The authors suggest that initial activation of right prefrontal regions by older adults might serve as a form of compensation for somewhat reduced activations in left-hemisphere regions, and that repetition and priming reduced the need for these compensatory processes. As will be described later, a similar pattern has been seen for skill- or process-based training (Erickson et al., 2007).

While simple repetition priming is largely preserved, there are small age-related declines in word stem completion priming (Fleischman and Gabrieli, 1998). An early PET study (Backman et al., 1997) found repetition-related reductions in right visual cortex (BA 19) that were if anything greater for older adults than for young subjects. However, a later event-related fMRI study (Daselaar et al., 2005) found that older adults had smaller priming-related reductions in left temporal gyrus, cerebelleum, and right occipital (BA 17/18) regions. Foreshadowing the results of the Bergerbest et al. (2009) study, reductions in right prefrontal cortex activity were found for the older adults but were not significant in young adults.

In summary, the literature on repetition priming suggests that older adults' brains and behavior still show plasticity and experience-related change, but that such plasticity is reduced by age. nIn addition, repetition appears to reduce additional (right prefrontal) activations that have been associated with compensatory processing, suggesting that training on these items reduces the need for the processes associated with those regions (Bergerbest et al., 2009; Daselaar et al. 2005). Do similar patterns hold when training is focused not on items, but on skills and processes?

Cognitive and cardiovascular interventions—One of the very first studies to combine behavioral and neuroimaging assessments of training effects in older adults used very short-term training on the method of loci (Nyberg et al., 2003). Within one PET scanning session, participants completed a serial recall pretest (18 words), were taught the method of loci and a list of locations to use, and then completed a post-training serial recall test. Young and older adults showed similar activation changes in frontal, parietal, and medial temporal regions during the training period and acquisition of the loci. However, the successful use of the mnemonic strategy varied by age and individual: While all of the young adults showed an increase in memory performance between pre- and post-test, only half of the older adults did. Even those older adults who did show significant change improved less than did the young adults. Both young and older adults who showed post-training improvements also showed greater pre-to-post-test increases in occipotemporal cortex than did the older adults who did not increase performance. Only young adults showed significant increases in left prefrontal cortex. The authors suggested that the lack of occipitotemporal activation in the non-improved older adults likely represented a failure to use the strategy, whereas the overall age deficit in frontal activation represented a more general decrease in processing resources.

A valuable aspect of the Nyberg et al (2003) study is its use of neuroimaging to constrain interpretations about the source of age or individual differences in training benefits. They

replicated previous individual and age differences in the size of strategy-based training effects, but the brain data invited more specific explanations of those differences in terms of failures to use the strategy by some individuals versus a general age deficit in speed or executive processing. A more recent event-related fMRI study (Braver et al., 2009) that also used very short-term training focused on activation dynamics rather than magnitudes. They found that a single session of training on a working memory task (the AX-CPT, a modified continuous performance task that requires rule maintenance and updating) was able to (at least temporarily) shift older adults' processing to a more proactive mode. Before training, older adults showed less prefrontal activation than did young adults at the cue phase of the trial, and more activation at the probe. Training specifically increased the cue-related prefrontal activation pattern in the older adults, and this increase correlated with an increase in a behavioral index of proactive control.

The Nyberg et al. (2003) and Braver et al. (2009) studies provide examples of using either the magnitude or timecourse of regional activations as an outcome measure in training interventions. They provide information about how older adults' approach to a task may change as a result of training – increased engagement of visuo-spatial processes related to the method of loci in Nyberg et al. (2003), a shift towards more proactive processing in Braver et al., (2009). In both cases, more successful training was associated with increases in activation in the critical regions or at the critical timepoints. However, both of these studies used very short-term training with immediate post-test assessments. Does longer-term training also lead to decreases in activation, which might be interpreted as more efficient processing according to the Doyon et al. (2005) framework?

The answer seems to vary across studies, and may depend in part on whether or not older adults activate the same regions as young adults prior to training. As previously described, Dahlin et al. (2008) found that increases in striatal activation were specifically related to updating processes in a letter memory task and improvements on the trained task after practice. They did not report any training-related decreases in activation. Likewise, Scalf et al. (2007) found that practice on a useful field of view task increased right prefrontal activations in older adults and that these activations correlated with improved performance, but did not report any practice-related decreases. In both of these studies, pre-training activations by older adults were generally the same or smaller than those seen in young adults; neither study reported any regions in which older adults showed more activation prior to training than did young adults.

Somewhat different results were found in a dual-task training study where before training, older adults showed greater activation in bilateral dorsal prefrontal cortex than did young adults, less activation in left ventral prefrontal cortex, and *proportionally* (relative to their left hemisphere activation) greater activation in right prefrontal cortex (Erickson et al., 2007). Young and older adults showed roughly equal benefits from training, and several important changes in activation were seen as well. Left ventral prefrontal cortex, which had been underactivated in older adults prior to training, increased activation after training to a level nearly equivalent to that seen in the young. Both young and older adults decreased activation in right ventral prefrontal cortex, suggesting either a decrease in the processes subserved by this region or an increased efficiency in those processes that was age-invariant. A crossover interaction occurred for the dorsal regions, such that young adults increased and older adults decreased activation after training. The authors speculated that this crossover might reflect more efficient cognitive control and task coordination by older adults after training, and an increased use of such processes by young adults after training.

Conceptually similar results were found for another executive task (flanker) after cardiovascular training (Colcombe et al., 2004). A six-month cardiovascular training

program that increased maximal oxygen uptake (VO2 max) also reduced behavioral conflict, reduced anterior cingulate activation, and increased activation in superior parietal regions associated with attention and portions of the right middle frontal gyrus associated with cognitive control. These benefits were specific to the cardiovascular training program; a stretching and toning program did not result in changes in either performance or activation. Reminiscent of the post-training shifts to more proactive control mechanisms reported by Braver et al. (2009) after strategy training, Colcombe et al. (2004) suggested that the increased prefrontal activations may have supported greater cognitive control in the form of biasing attention towards task-relevant features, thus reducing the conflict imposed by the task (and thus the anterior cingulate's response to such conflict).

Summary

At this point relatively few neuroimaging studies have investigated the effects of well-controlled cognitive or cardiovascular interventions, especially in comparison to the large number of behavioral studies or the more well-developed motor skills literature. A few tentative conclusions can be drawn from the findings so far: Structurally, training has consistently been associated with volumetric increases in the brain structures thought to be critical for performance of the trained task; there is no apparent evidence for volumetric reductions that might be expected from increased tuning, or refinement of the task circuitry. Simple repetition priming generally leads to similar decreases in activation for young and older adults, although they appear to be slightly smaller and/or of less duration for older adults. Both cardiovascular training and cognitive training and practice regimens that are focused on skills or processes as opposed to items consistently produce increased activation in task-relevant regions, although these increases may be less pronounced for older adults than for young adults undergoing the same training. Training of both sorts (cognitive and cardiovascular) also appears to reduce activation in at least some regions that older adults or poor performers activated more prior to training.

This pattern of increases and decreases may be related to the results of several studies examining the effects of Age X Load interactions on brain activations in working memory tasks. As working memory load increases, both young and older adults shift from a left-lateralized pattern to an increasing recruitment of right prefrontal regions (Cappell et al., under review; Mattay et al., 2006; Rypma, et al. 2001; Schneider-Garcas et al., in press; see Reuter-Lorenz & Cappell, 2008 for a review). Once load reaches a certain point, both performance and activation show a sudden sharp decrease, possibly reflecting disengagement with the task. Both young and older adults show this pattern, but the function relating load and activation is shifted left for older adults (or other inefficient processors), such that they show both the initial increase and the dropoff at smaller loads (Figure 1).

Training may serve to increase the engagement and/or efficiency of task-relevant (and in this case, left-hemisphere) regions, reducing the need for these presumably compensatory right-hemisphere activations. This framework could explain, for example, the results of Erickson et al. (2007): As older adults increased activation in the initially under-activated left ventral prefrontal cortex, activation in right ventral prefrontal cortex decreased. Likewise, in Colcombe et al. (2004), increased activation in cognitive-control regions reduced the conflict-detection demands on anterior cingulate and thus reduced its activations. Note that this framework predicts that left-hemisphere regions (or more generally, those regions that are initially activated by young adults or other efficient performers) will often show increased activation after training, but that this is not a necessary part of the pattern. Increased *efficiency* in the processes subserved by these regions would lead to reduced activations.

The above framework can explain the training-related reductions in age-related overactivations seen in some studies. However, it may seem surprising that there have been no reports of training leading to increased activations in regions recruited only by older adults, given that such activations are so often associated with good performance in non-training studies (see reviews by Cabeza, 2002; Reuter-Lorenz & Lustig, 2005; Park & Reuter-Lorenz, 2009). An absence of reported training-induced overactivation is even more surprising given that several structural imaging studies have reported that older adults show increases in volume in regions where young adults do not (Boyke et al., 2008; Colcombe et al., 2006). Notably, the association of extra activations with good performance occurs in single-session studies, before the task is well-practiced. By contrast, post-training neuroimaging assessments occur after several sessions of training, when performance has been relatively optimized.

Therefore, we predict that for tasks in which activation of additional regions by older adults is associated with better performance in single-session studies, the pattern of activation in these regions will change over the course of training. In such single-session studies, older adults' activation of regions (especially prefrontal regions) not seen in young adults likely reflects engagement with the task and the recruitment of compensatory processes. We would expect that early in training, compensatory overactivation would increase especially if training encouraged older adults to engage additional strategies or processes not used by young adults. However, following the framework described above, as training progresses, we would expect older adults' processing to become more young-adult-like, such that reliance on additional processes and their associated regions of activation – which may serve a scaffolding purpose (c.f., Park & Reuter-Lorenz, 2009) – would decrease. Effectively then, training would produce a rightward shift of the function relating task demand to activation.

Although this hypothesis would reconcile the positive association between the recruitment of additional regions and good performance in single-session studies with the reduction in such recruitment that follows training, it remains to be tested. As we describe below, this is one of many open questions regarding the efficacy of cognitive interventions and their effects on the brain.

Open questions and future directions

Training studies often require a substantial commitment on the part of the participant, the researcher, and the funding agency. Therefore it seems appropriate to ask, "Is it worth it?"

Our perspective is admittedly biased, but we believe the answer is an emphatic "Yes". There are important obstacles to overcome, especially with regards to clear, large, and durable effects on everyday cognitive tasks and quality of life. However, the studies reviewed above already show considerable progress towards these goals. In particular, the advances made in improving transfer from the trained task to other laboratory tasks are promising indicators for taking the next step, transfer to everyday-life activities. Training-related changes in brain activity and in brain structure also provide persuasive evidence that training does not just result in a subtle, task-specific shift – these are fundamental changes in the biological mechanisms underlying cognitive performance.

The question of whether training programs are successful depends in part on how "success" is defined. For example, Salthouse (2006) has offered a thorough critique of claims that cognitive engagement, training or other forms of "mental exercise" can reduce the *rate* of age-related cognitive decline. If this hypothesis is framed as an age X engagement interaction, with older adults showing more benefits from training or other activities, then there is very little evidence to support the idea that training is successful. Numerous studies have shown that young adults benefit more from training programs than do older adults

(e.g., Boyke et al., 2008; Dahlin et al., 2008; Kliegl, Smith & Baltes, 1989; Nyberg et al., 2003; Verhaeghen et al., 1992). Given that the capacity for plasticity seems to decline with age (Brehmer et al., 2008; Calero & Navarro, 2007; Dahlin et al., 2008; Nyberg et al., 2003), it is not surprising that young adults would be the ones to show greater benefits from training.

However, in practical terms, the more important question is whether older adults show benefits from training, not whether those benefits are larger for young adults. As Salthouse notes, training that changes the *level* of function may be of great practical significance even if the *rate* of decline per se is not affected. That is, an individual whose abilities can be improved by training may take longer to reach clinically-significant levels of dysfunction even if their unit of change on that ability from year to year is the same as someone who did not receive training. (Figure 2; see Hertzog et al. (2009) for similar arguments). Furthermore, the recent data from Yaffe et al. (2009) suggest that a number of factors including education and cardiovascular exercise can influence the rate of decline, not just the level of function; more long-term longitudinal studies are needed to see whether regular engagement in cognitive training has similar effects.

One of the most important problems for current and future research is how to improve transfer effects, which are often limited in both breadth and effect size. Both the process-based and cardiovascular training programs designed for the elderly show some promise in this regard, as do some recent multi-modal interventions. There is some indication that protocols that encourage the development of processes that support task performance but do not dictate specific strategies have greater likelihood of transfer (e.g., Lustig & Flegal, 2008). This may occur if participants are more likely to use and generalize trained processes that they generated themselves and thus are presumably comfortable using. An interesting new direction for improving the likelihood of transfer effects is the incorporation of neuroimaging data to identify core mental processes that operate in multiple task domains, which can then be targeted by cognitive interventions in one task context and assessed for improvement in another (Dahlin, et al., 2008; Klingberg et al., 2002; Persson & Reuter-Lorenz, 2008).

Related to the transfer issue, an important methodological problem is the need for better measures to assess everyday cognitive function in generally healthy older adults. Many current standardized measures were originally designed for clinical populations and often do not produce a sufficient range of performance in healthy adults to allow an adequate assessment of training effects. Others are self-report measures, which can raise concerns about placebo effects or participants lacking insight into beneficial changes that do occur. There have been some recent attempts to develop measures that better bridge between the lab and the work or home environments and that target the cognitive complaints of healthy older adults (e.g., Stuss et al., 2007); further development and standardization of such measures could be very beneficial to the field.

Meanwhile, neuroimaging measures may offer indices of intervention effects that are more sensitive and/or reliable than performance on laboratory tests. As the most obvious example, measures of brain volume or integrity (e.g., diffusion tensor imaging) can be assessed at multiple timepoints (before training, early stages, late stages, after training has ceased) without concerns about practice effects or other forms of cross-assessment contamination. Functional imaging studies often reveal age differences in activation even in the presence of similar behavior. This may be in part because behavioral assessments are generally limited to accuracy and reaction time, whereas activation data can be assessed along multiple dimensions including their magnitude, extent, location, and temporal properties. Just as the multi-dimensional nature of activation data make them more sensitive to age differences in

single-assessment studies, they may also be more sensitive to intervention effects. They may also provide a window into how an intervention is having its effects: increases in activation likely indicate new processes brought online, decreases in activation would indicate an increased efficiency of processing. Patterns that become more similar to young adults' after training would suggest improvements in a similar processing stream; patterns that become less similar would more likely be associated with an increased engagement of compensatory processes. As noted above, neuroimaging data are already being used to guide the selection of training and transfer tasks, and to understand why some training effects transfer for young but not older adults (e.g., Dahlin et al., 2008; Persson & Reuter-Lorenz, 2008).

Besides the breadth and size of transfer effects, there is the question of their efficiency (how much training is needed for significant benefits) and durability (how long those benefits last). As shown in Table 1, the length and spacing of the training period varies widely across studies, and the majority of studies do not include long-term follow-ups to assess durability. To our knowledge, there has been no systematic investigation of the time needed for a specific intervention or type of intervention (e.g., strategy vs. cardiovascular training) to take effect, or plotting of long-term retention curves over multiple intervals. However, those investigations that have included long-term follow-ups generally find positive results, especially if they include booster sessions.

Several studies have noted performance improvements that persist months or years after training (e.g., Ball et al., 1988; Emery et al., 1992; Salthouse & Somberg, 1982; Schaie & Willis, 1986). This is somewhat surprising – to use the physical-training analogy, one would not expect that a few weeks of weight training would have any noticeable benefits to one's muscular strength months or years later. A possible explanation is that participants continue to exercise, and thus maintain, the trained processes in their everyday lives. Booster sessions seem to have even more positive effects on the durability of training advances. On a practical level, intensive training for short periods followed by periodic reassessments and booster sessions – analogous to the periodical checks and re-training one undergoes for a driver's license or CPR certification - may be a useful method for preserving training benefits with minimal burden to the participant. From a research perspective, more data are needed to understand how activations and structures are affected by early versus late stages of training, and how they may change during maintenance periods. Structural data (both volume and integrity measures) may be of particular interest with regards to the duration effects, both because of their stability and because correlational studies have linked greater volume and integrity to reduced risk of cognitive decline and dementia – does a similar benefit hold when increases in volume and integrity are experimentally induced?

Ultimately, the ideal training program may build on the strengths of each of the methods described above. Strategy-based and process-based approaches can be optimized in part by neuroimaging to achieve the most efficient training regimens and broadest cognitive impact. These can then serve as optimized components to be included in a multi-modal program that is implemented in a setting that increases social interactions and that uses materials with obvious relation to everyday life (e.g., the essential components of task-switching training might be incorporated into a cooking or driving game), factors that will likely increase engagement and transfer. Finally, cardiovascular training components can promote a healthy and plastic brain that is best able to respond to training.

While significant hurdles reside on the path to optimal program design, considerable advances and new research tools are bringing us closer to identifying efficient, powerful training methods that produce real benefits to everyday life. Older brains can indeed learn "new tricks", and we are getting better at finding methods that will help them do so.

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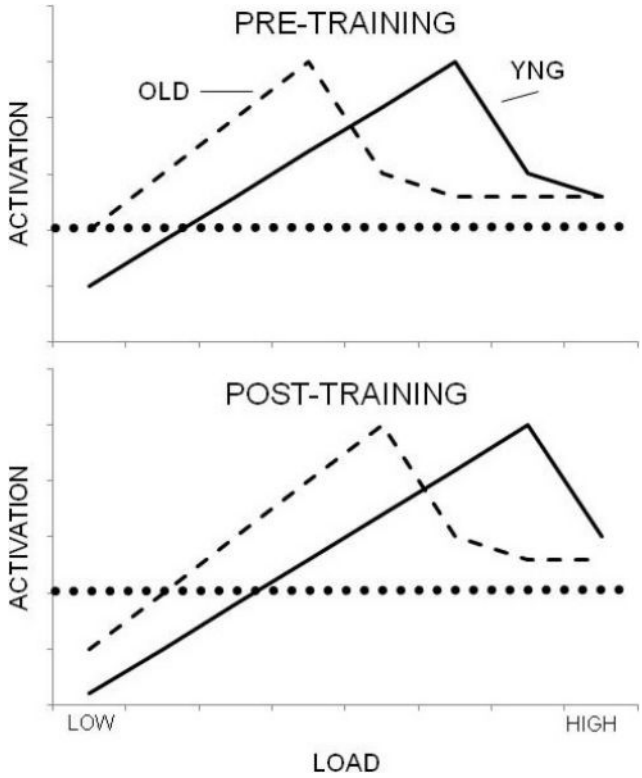

Figure 1. Hypothetical functions relating activation of additional regions (e.g., right prefrontal cortex during a verbal working memory task) to load

This figure shows the simplest case, in which activation/load slopes, maximal activation levels, and training benefits are assumed to be equivalent for both age groups. The horizontal line indicates the statistical threshold at which activation is detected. Both age groups show the same basic function in which increasing load is associated with increasing recruitment up to a critical point, after which it declines. (See text.) Older adults reach significant activation levels and the deflection point at smaller load levels than do young adults. Training shifts functions along the load axis for both age groups.

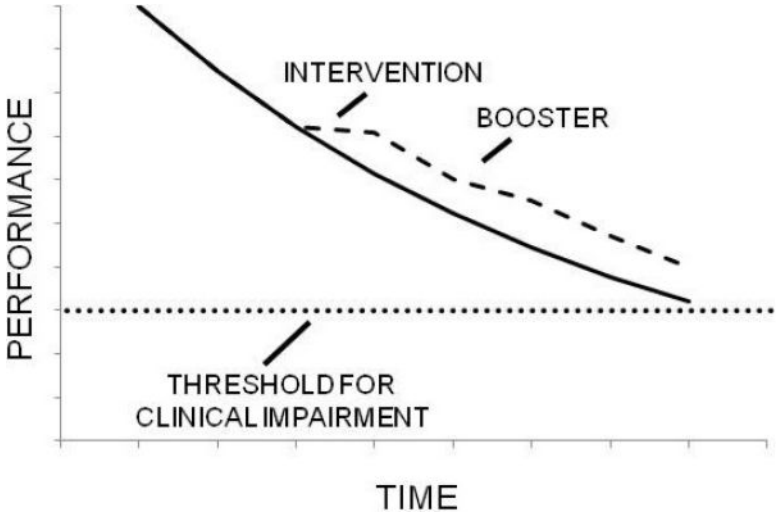

Figure 2. Interventions may have practical benefits even if they do not change the *rate* of decline

The solid line is an idealized function of general cognitive decline over age; the dashed line indicates the same but with a cognitive intervention (cognitive or cardiovascular training) and booster session. The horizontal dotted line indicates the threshold for clinical or functional impairment (e.g., giving up driving or control of finances, moving from independent to assisted living). Even if the rate of decline returns to normal after temporary shifts in the level of function due to the intervention and booster session, it may delay the point at which an individual reaches sufficient degrees of impairment to impact daily life.

Table 1

Training type, duration, and durability

The duration of training for each study is indicated at the level of detail available in the published paper; note that many do not specify the session duration.

Authors	Type of Training	Duration of Training	Longitudinal followup
Ball et al., 1988; Willis et al., 2002 (ACTIVE)	Strategy & Process	Ten 60-75-minute sessions	Yes, effects reduced but statistically significant 5 years later
Backman et al. (1997)	Repetition priming	One session immediately before test	No
Basak et al. (2008)	Multimodal	Fifteen 1.5 hour sessions	no
Bergerbest et al. (2009)	Repetition priming	One session immediately before test	no
Bissig & Lustig (2007)	Process Training	Four sessions/day for 7 days	no
Black et al. (1990)	Cardiovascular Training	Five and one-half to eight and one-half hours of training within 30 days	no
Boyke et al. (2008)	Cardiovascular Training	No report	yes. 3 months after training had ceased. Increases in brain volume reversed after 3 months with no practice
Boyke et al. (2008)	Strategy/practice	Three months	reversal of effects after 3-month followup
Braver et al. (2009)	Strategy	One session	no
Brehmer et al. (2008)	Strategy	Five to eight sessions	yes, effects remained 11 months following training
Calero & Navarro (2007)	Strategy	Two 1-hr sessions	no
Cassavaugh & Kramer (2009)	Multimodal	Eight sessions	no
Clark et al. (1987)	Multimodal	Two or more hours per week for 7 weeks	no
Colcombe et al. (2006)	Cardiovascular Training	Three 1-hour sessions per week for 6 months	no
Craik et al.; Stuss et al.; Winocur et al. (2007)	Multimodal	Twelve 3 hour training sessions	yes, 6 months after training
Dahlin et al. (2008)	Process Training Specific	Three 45 minute sessions for 5 weeks	no
Daselaar et al. (2005)	Repetition priming	One session immediately before test	no
Denney, Jones, & Krigel (1979)	Strategy	One session	no
Draganski et al. (2004)	Cardiovascular Training	No report	yes. 3 months after training had ceased. Increases in brain volume reversed after 3 months with no practice
Drew & Waters (1986)	Multimodal	Two sessions per week for 2 months	no
Dunlosky et al. (2003)	Strategy	Two 1-hr training sessions, 3 homework sessions	no
Dustman et al. (1984)	Cardiovascular Training	Three 1-hour sessions per week for 4 weeks	no
Dustman et al. (1992)	Multimodal	One session per week for 11 weeks	no
Emery et al. (1992)	Cardiovascular Training	Three sessions per week for 4 months (10 minutes stretching + 45 min cardio)	1 year follow-up, showed that participants continued physical activity during the year following their training-associated with lower anxiety,

Authors	Type of Training	Duration of Training	Longitudinal followup
			increase of cardiorespiratory endurance
Erickson et al. (2007)	Process Training	Five 1-hour sessions over 2-3 wk interval	no
Etnier & Landers (1997)	Cardiovascular Training	Three days	no
Etnier et al. (2001)	Cardiovascular Training	Three days	no.
Fried et al. (ExperienceCorps)	Multimodal	Fifteen hours per week, 2 weeks	no
Goldstein et al. (1997)	Multimodal	Five or more hours per week, 5 weeks	no
Greenwood & Parasuraman (1991)	Process Training	Two sessions	no
Hatzitaki et al. (2009)	Process Training	Twelve 25 minute training sessions	no
Jennings & Jacoby (2003)	Process Training	Seven 40-50 minute sessions	no
Karbach & Kray (2009)	Process Training	One 60-70 minute sessions per week, 6-8 weeks	no
Kornatz et al. (2005)	Process Training	Six weeks	no
Kramer et al. (1995)	Process Training	Eight 1.5 hour sessions	no
Labouvie & Gonda (1976)	Strategy	Single session immediately preceding transfer test.	yes, effects remained 2 weeks after training
Levine et al. (2007)	Strategy	Twelve sessions	no
Luders et al. (2009)	Multimodal	N/A: naturalistic study comparing meditators (5+ years experience) and age-matched controls	no
Lustig & Buckner (2004)	Repetition priming	One session immediately before test	no
Lustig & Flegal (2008)	Process Training	One session per day for 8 days	no
Mahnke et al. (2008)	Training Process specific, signal/noise discrimination	Five 1 hour sessions per week for 8 weeks	yes, sustained over 3 months
McDowd (1986)	Process Training	One session per week for 6 weeks	no
Minear et al. (2002)	Process Training	Two 1-hour sessions	no
Noice et al. (2004)	Multimodal	Nine 1.5 hour sessions in 4 weeks	no
Nyberg et al. (2003)	Strategy	Single session	Continued post-testing up to 4 months after post-test 1 neither problem solving/memory span declined, recall increased
Pagnoni & Cekic (2007)	Multimodal	N/A: naturalistic study comparing meditators (3+ years experience) and age-matched controls	no
Persson & Reuter-Lorenz (2008)	Process Training	Eight sessions/ 45 minutes 2 weeks	no
Salthouse & Somberg (1982)	Multimodal	Fifty sessions	no
Scalf et al. (2007)	Process Training	Five sessions	Yes, effects lasted after one month
Seattle Longitudinal Study (1982-2007)	Strategy	Varies, 5 or more sessions	no
Seidler (2004)	Process Training	One or two 1.5 hour sessions	yes, some effects lasted up to 7 years
Seidler (2006)	Process Training	One or two 1.5 hour sessions	no
Seidler (2007a)	Process Training	One or two 1.5 hour sessions	no
Seidler (2007b)	Process Training	One or two 1.5 hour sessions	no

Authors	Type of Training	Duration of Training	Longitudinal followup
Seidler & Martin (1997)	Process Training	Three 1 hour sessions per week for 5 weeks	no
Silsupadol et al. (2009)	Process Training	Three 45 minute sessions per week for 4 weeks	no
Soldan et al. (2008)	Repetition priming	Comparison over repeated exposures within session	no
Stine-Morrow et al. (Senior Odyssey; 2008))	Multimodal	Twenty weekly sessions	no
Swain et al. (2003)	Cardiovascular Training	Thirty days	no
Tranter & Koutstaal (2008)	Multimodal	Ten to twelve weeks	no
van Hooren et al. (2007)	Strategy	Twelve sessions	no