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Cognitive Training: Influence on Neuropsychological and Brain Function in Later Life

Professor George W. Rebok
Department of Mental Health, The Johns Hopkins University

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Summary

Recent success of cognitive training with normally functioning, older adults has engendered growing optimism about the modifiability of neuropsychological and brain function in later life and the potential to influence everyday behaviour, mental wellbeing, and quality of life. This paper reviews the latest scientific advances and results in this rapidly evolving area, factors that affect training responsiveness, and the challenges that researchers will face in trying to implement new training platforms in the future. Cognitive training is currently being conducted against a backdrop of increasing sophistication of methods, design, and analysis. At the same time, advances in emerging technologies, electrophysiology, biomarker assays, and genetics are moving the field forward at an accelerating pace. There is increasing evidence that training can affect multiple cognitive variables, including memory, reasoning, speed of processing, and spatial relations, that the effects can be long-lasting, and that training gains may transfer to more distal outcomes related to everyday cognitive functioning and behaviour. Large-scale cognitive training studies such as project ACTIVE (Advanced Cognitive Training for Independent and Vital Elderly) and other recent intervention studies are contributing significant new knowledge that validates the efficacy of training for members of the older population. However, important questions remain about the neural and psychological mechanisms underlying training and transfer effects, the dosage levels needed to produce these effects, who benefits most from training and why, how to cross-train and combine training modalities, and the best ways to embed training programmes within the broader context of everyday life and ageing. The contributions of cognitive training to the development of mental capital and mental wellbeing across the life course are discussed, along with the need for lifespan public health models and policies to deliver cost-effective training at a population-based level.

1. Introduction

There is growing optimism in both scientific and lay communities about the modifiability of neuropsychological and brain function in later life and the potential of cognitive training to influence everyday behaviour, mental wellbeing, and quality of life (Ball et al., 2007; Centers for Disease Control and Prevention and the Alzheimer's Association, 2007; Elias and Wagster, 2007; Fillit et al., 2002; Kramer and Willis, 2002; Park et al., 2007; Rebok et al., 2007; Shumaker et al., 2006; Studenski et al., 2006; Willis and Schaie, 1994). Recent research studies provide increasing evidence that: training can affect multiple cognitive variables, even when measured with different modalities, including working memory, abstract reasoning, attention and concentration, speed of information processing, and spatial relations; the effects can last months or, in some cases, even years;, and that training gains may transfer to more distal outcomes related to everyday cognitive functioning (Bherer et al., 2005, 2006; Bottiroli, et al., 2007; Cavallini et al., 2003; Craik et al., 2007; Erickson et al., 2007; Jennings and Jacoby, 2003; Jennings et al., 2005; Kramer et al., 1995; Mahncke, Connor et al., 2006; Stuss et al., 2007; West et al., 2003; Willis et al., 2006), everyday behaviour (Ball et al., 2007; Kramer and Willis, 2002; Studenski et al., 2006), and quality of life (Fabre et al., 1999; Wolinsky et al., 2006a; Wolinsky et al., 2006b).

This review aims to summarise the latest scientific advances and results on cognitive training with older adults, factors that affect transfer of training and training responsiveness, and challenges that researchers will face in trying to implement innovative training approaches in the future. The review will focus on cognitive training in normally functioning elderly, but the responsiveness of cognitively impaired elderly to training also will be briefly considered. In addition to cognitive training studies targeting specific domains of cognition such as working memory, attention, and speed of processing, the review will include cognitive stimulation approaches involving group activities that are designed to increase cognitive and social functioning in a nonspecific manner.

2. Early results of cognitive training research: 1980s and 1990s

Over two decades of research have established that older adults can improve their cognitive abilities (Ball and Sekuler, 1986; Ball et al., 1988; Hayslip et al., 1995; Kliegl et al., 1989; 1990; Rasmusson, et al., 1999; Rebok and Balcerak, 1989; Schaie and Willis, 1986; Willis et al., 1981) with training protocols targeting working memory, abstract reasoning, speed of processing, and spatial abilities, among other cognitive neuropsychological domains showing early age decline. These studies also involved teaching strategies or skills in order to optimise cognitive functioning (e.g. mnemonic strategies).

For reasons of experimental control, early training studies tended to be ability-specific, targeting single cognitive abilities rather than multiple ability domains. Typically, these studies showed significant training effects compared to no-treatment or social contact control groups, with training gains averaging 0.19-0.73 SD (Floyd and Scogin, 1997; Verghaeghen et al., 1992). This research also demonstrated that cognitive training is specific to the ability being trained with little transfer of training to untrained cognitive domains, and improvements are limited to tasks similar to the training itself (Kramer and Willis, 2002; Neely and Bäckman, 1995; Willis et al., 1981; Willis and Schaie, 1994). Early studies showed some evidence of the durability of training effects ranging from between one or two months and up to one year or more (Oswald et al., 1996; Sheikh et al., 1986; Stigsdotter and Bäckman, 1989; Stigsdotter et al., 1993; Willis and Nesselroade, 1990; Willis and Schaie, 1994), although not every study found evidence for maintenance effects (e.g. see Anschutz et al., 1987; Scogin and Bienias, 1988).

3. Recent training approaches: 2000 to the present

Ultimately, the goal of cognitive training is to enhance or sustain cognitive abilities at healthy levels for longer portions of the lifespan, in the hope that everyday functioning will benefit. Following the early studies, new questions arose for cognitive training research, including the long-term clinical outcomes of interventions and the transfer of training to measures of functioning on everyday tasks (Jobe et al., 2001). There were also questions about the representativeness of the samples, as most of these were regional, convenience samples that lacked diversity. Other concerns involved the lack of intent-to-treat designs, failure to control for attrition, replicability of the findings, and the clinical meaningfulness of the findings.

To address these questions, later research has turned to more sophisticated designs with larger and more representative samples and with everyday abilities as the primary target outcome. An example of this newer approach can be seen in the ACTIVE (Advanced Cognitive Training for Independent and Vital Elderly) intervention trial jointly funded by National Institute on Aging (NIA) and the National Institute of Nursing Research (NINR), which is the single, largest cognitive training study undertaken to date (Ball et al., 2002; Jobe et al., 2001; Willis et al., 2006). ACTIVE was a randomised controlled trial of three cognitive interventions (memory, reasoning, speed of information processing) designed to maintain functional independence in older adults aged 65 and above by improving basic mental abilities (Ball et al., 2002; Jobe et al., 2001). Several features made ACTIVE unique in the field of cognitive interventions: (a) use of a multi-site, randomised, controlled, single-blind design; (b) intervention on a large, diverse sample of older adults (N = 2,832, mean age = 73.6 years, range = 65-94 years; 26% African-Americans); (c) use of common multi-site intervention protocols; (d) primary outcomes focused on long-term, far-transfer effects as measured by performance-based tests of daily activities; and (e) an intent-to-treat analytical approach.

The trial phase consisted of baseline assessment followed by the cognitive interventions, immediate post-test, booster training for a subsample, and post-tests at one, two, three, and five years. The three interventions had equivalent intensity and duration across ten, 60-75 minute sessions and were conducted in small group settings. In all three conditions, Sessions 1-5 focused on strategy instruction and exercises to practice the strategy. Sessions 6-10 provided additional practice exercises, but no new strategies were introduced.

Memory training focused on verbal episodic memory. Participants were taught mnemonic strategies for remembering lists and sequences of items, text material, and main ideas and details of stories and other text-based information. Training exercises involved laboratory-like tasks as well as everyday tasks and activities such as recalling a shopping list. *Reasoning training* focused on the ability to solve problems that follow a serial pattern. Participants were taught how to identify, block, and mark patterns in abstract series. Training involved both laboratory-type tasks and reasoning in everyday activities, such as understanding the pattern in a bus schedule. *Speed training* focused on visual search and the ability to identify and locate visual information quickly in a divided attention format, with and without distractors. Participants practiced tasks on a computer and proceeded to more complex tasks and faster presentation speeds at their own pace.

Results of the ACTIVE trial showed immediate and significant task-specific effects for all three interventions (Ball et al., 2002) that were durable through five years (memory: effect size, 0.23; reasoning: effect size, 0.26; speed of processing: effect size, 0.76) (Willis et al., 2006). Some evidence also was found for transfer of intervention effects to everyday functional performance, as measured by IADL difficulty (reasoning: effect size, 0.29) and everyday speeded performance (speed of processing – booster only: effect size, 0.30) (Willis et al., 2006). Plans are currently under way to continue to follow the ACTIVE sample through 10 years post-training to determine the very long-range effects of cognitive training and transfer to everyday abilities, and to examine heath, genetic, and cognitive moderators (including cardiovascular disease, diabetes, depression, APOE genotype, and low cognition and engagement) in individual response to training.

Although effective, there are limits on the wide-scale dissemination of costly training platforms such as ACTIVE that involve participants meeting in small groups for paper-and-pencil training sessions led by a trained facilitator. Increasingly, researchers are exploring alternative training approaches to improve cognitive abilities in older adults (Park et al., 2007; Rebok et al., 2007). These include collaborative training (Margrett and Willis, 2006; Saczynski, Margrett and Willis, 2004), online and CDROM-based training (Baldi et al., 1996; Bond et al., 2001; Günther et al., 2003; Plude and Schwartz, 1996; Mahncke et al., 2006; Morrell et al., 2006; Saczynski, Rebok et al., 2004; 2007; Shapira et al., 2007), and videotaped and audiotaped training (Rebok et al., 1997; West and Crook, 1992). These novel, 'trainer-less' training platforms are designed to overcome limitations of the more traditional approaches, including problems related to accessibility and costs of training. Limiting training to small-group didactic sessions with a certified trainer may limit the number of older persons able to access the training, thereby reducing its public health impact.

4. Activity-based approaches to cognitive improvement

Much recent research in cognitive ageing has demonstrated the effectiveness of stimulating mental, social, and physical activity for retaining mental function in later life (Butler et al., 2004; Hultsch et al., 1999; Kramer et al., 2006; Noice and Noice, 2006; Noice et al., 2004; Stine-Morrow et al., 2007; Verghese et al., 2003; Wilson et al., 1999; Wilson et al., 2002). A growing number of observational epidemiologic studies have shown that leisure-time cognitive, physical, and social activities are each consistently associated with better cognitive and functional health (for review, see Studenski et al., 2006). Multiple large-scale studies have demonstrated that mid- and later-life cognitive activity is associated with better cognitive health (Stern et al., 1999; Wang et al., 2002; Wilson et al., 1999; Wilson et al., 2002). Observational studies, however, are limited in their capacity to draw causal inferences between lifestyle activity and amelioration of age-related cognitive decline and impairment (Christensen et al., 1999; Hultsch et al., 1999; Wilson et al., 1999). These studies may reflect bias in high-functioning individuals' predisposition toward cognitively and physically enriching activities, or prodromal changes in activity occurring prior to the clinical onset of incipient neuropathology, such as Alzheimer's disease (e.g., Saczynski et al., 2006; Salthouse, 2006; Small et al., 2001).

There have been a few recent attempts to experimentally manipulate the types and amount of activity in order to overcome the limitations of observational studies. Fried et al. (2004) evaluated the feasibility of recruiting, retaining, and increasing activity levels in older, at-risk individuals using the multi-modal, Experience Corps®: Baltimore (ECB), activity intervention. Core features of the ECB programme that led to unprecedented 'doses' of exposure included: placing a critical mass of trained, older volunteers in teams of 10 or more in schools; having them fulfil meaningful roles to meet school needs in literary development, library support, and behavioural conflict resolution; requiring a commitment of 15 hours/week over an academic year; and providing an incentive reimbursement to offset volunteer expenses. Seniors worked with children in Kindergarten through 3rd grade, an age-range where such support can be most beneficial to future academic success (Heckman, 2006). The multimodal ECB activity programme was designed to further bolster memory and components of executive functioning in the volunteers via programme activity in four ways: 1) exercise mental flexibility through the need to shift across ECB roles; 2) develop working memory skills via reading comprehension exercises with children; 3) apply library skills in learning and using the Dewey decimal system to help children locate and select age-appropriate books; and 4) cooperatively problem-solve with team members, students, and teachers. The cognitive activity embedded within this social health promotion programme and roles resulted in measurable gains in executive functioning and working memory, with the gains being greatest for older adults who showed executive functioning deficits at baseline (Carlson et al., in press).

In another recent study using an activity-based intervention, Stine-Morrow and her colleagues (Parisi, Greene, Morrow and Stine-Morrow, 2007; Stine-Morrow, Parisi, Morrow et al., 2007) reported preliminary results from the Senior Odyssey programme, an ongoing team-based programme of creative and collaborative problem-solving. Participants in the first year of the programme showed improved speed of processing, marginally improved divergent thinking, and higher levels of mindfulness and need for cognition from pre- to post-training, compared with controls.

Larger scale, controlled trials of the Baltimore Experience Corps® programme and the Senior Odyssey programme are currently in progress.

5. Neural mechanisms of training-related change

A growing number of neuroimaging studies have examined the effects of training and practice on neural dynamics, or training-induced plasticity (Bor and Owen, 2007; Erickson et al., 2007; Imamizu et al., 2007; Jancke et al., 2001; Nyberg, 2005; Nyberg et al., 2003; Olesen et al., 2004; Valenzuela et al., 2003). Research using animal models (Briones et al., 2004; Kempermann et al., 1998; van Praag et al., 2005) has provided a basis for these studies by showing selective effects of experience on brain structure and function. There is also a growing literature on the effects of experience on *human* brain structure and function (Draganski et al., 2004; Kramer and Erickson, 2007; Maguire et al., 2003).

The neuroimaging studies cited above show several different patterns of results. Erickson et al. (2007) studied training-related changes in cortical activity as measured by functional magnetic resonance imaging (fMRI) in a sample of young adults during a dual task requiring executive control. They found that most regions involved in dual task processing before training showed reductions in activation following training. Olesen et al. (2004) investigated the effect of working memory training with young adults on brain activity measured with fMRI and found increased activity in prefrontal and parietal regions after training. Nyberg and colleagues (2003) trained younger and older adults in the use of the method of loci technique where one learns to associate words that are to be memorised with a particular spatial location. Patterns of brain activation were then assessed both pre- and post-training using positron emission tomography (PET). Only half of the older adults showed any benefit from training. Using neuroimaging data, the researchers found that younger adults showed increased activity in dorsal frontal regions of the brain associated with mental imagery and integration of information in working memory, but older adults showed no such difference. This may reflect a deficit in the reserve capacity of older adults. However both young and those older adults who showed improvement in memory performance after method of loci training had increased activity in the occipitoparietal and retreosplenial regions of the brain. These regions have been associated with spatial imagery and route-based learning, respectively. Thus, although not all older adults are able to benefit from training, those who did showed similar changes in neural activation patterns to the younger adults in the posterior regions of the brain.

In summary, the literature suggests that changes in neural activity following training are not accompanied by a simple monotonic increase or decrease in activity, and that changes are likely to be specific to certain brain regions (Erickson et al., 2007; Landau et al., 2004).

6. Individual differences affecting training responsiveness

It is often unclear what factors contribute to the success of cognitive training with older adults. What processes or strategies are being trained? Why do some individuals appear to benefit more than others? Recently, Bissig and Lustig (2007) examined the role of self-initiation of cognitive control in a training programme targeting recollection memory. Relative time spent on an open-ended, intentional encoding task that requires the self-initiation of cognitive control was highly predictive of improvement in the training task, and fully accounted for individual differences related to age and crystallised intelligence.

Studies to date have not systematically examined individual differences determining who benefits most from cognitive training (Park et al., 2007). As acknowledged by Salthouse (2006), it is possible that older adults with the poorest cognitive functioning or from the oldest age ranges stand to benefit the most from training. Longer-term longitudinal follow-up studies may be needed to evaluate the impact of training on less impaired individuals relative to untrained control participants, as in the ACTIVE study (Ball et al., 2007). Cognitive training studies demonstrate that diverse socioeconomic, ability level, and ethnic populations benefit from traditional forms of cognitive training. Training effects have been demonstrated for wide age ranges including the oldest-old (Kramer and Willis, 2002; McDougall, 2002; Singer et al., 2003; Yang et al., 2006), normal elderly (Ball et al., 2002; Baltes, 1987; Baltes and Willis, 1982; Rasmusson et al., 1999; Willis et al., 2006), and those with mild cognitive impairment (Belleville, 2008; Belleville et al., 2006; Haslam et al., 2006; Rapp et al., 2002; Troyer et al., 2008; Unverzagt et al. 2007; also see recent meta-analyses by Grandmaison and Simard, 2003 and Sitzer et al., 2006 on cognitive training effects in Alzheimer's disease), indicating that human brains continue to have substantial neural plasticity in later life.

The benefit from cognitive training does not appear to depend primarily upon demographic variables such as age or education (Ball et al., 2007). However, poor cardiovascular health, use of anticoagulants and other medications (e.g. antihistamines, antilipemic agents), mild neuropsychological deficits, and lack of physical activity/fitness all may serve to reduce responsiveness to training (Boron, Turiano et al., 2007; Hill et al., 1989; Kramer and Willis, 2002; Rasmusson et al., 1999; Unverzagt et al., 2007). There is some evidence that better health status is associated with maintaining and improving cognitive status and independent living following a combined memory and psychomotor training programme (Oswald et al., 2002).

One additional factor that might affect training responsiveness is the extent to which the individual invests in the training programme and complies with instructions. In a recent study, Bagwell and West (2008) showed that older trainees in a memory intervention programme who were compliant with the training regimen (using trainer ratings based on attendance, homework completion, and class participation), made significantly greater training-related gains compared to an inactive training group and a control group.

7. Transfer of cognitive training

Transfer of training-induced cognitive changes across time, to broader measures of functional abilities, and across different modalities of measurement, is imperative if training is to have value beyond the procedural specifics of individual exercises (Barnett and Ceci, 2002; Mahncke et al., 2006; Salomon and Perkins, 1989). Prior cognitive training research has shown that the training outcomes are highly specific to the cognitive ability being trained (Brooks et al., 1993; Hill et al., 1988; Kliegl et al., 1990; Mohs et al., 1998; Neely and Bäckman, 1995; Oswald et al., 1996; Rebok and Balcerak, 1989; Yesavage, 1985) and are limited to tasks that are very similar to the training itself (Jennings et al., 2005; van Hooren et al., 2007). That is, there is frequently little transfer to other laboratory cognitive tasks or to analogues of the training tasks encountered in everyday situations. However, techniques for improving processing speed have shown evidence of transfer to laboratory-based everyday activities such as Timed Instrumental Activities of Daily Living (Edwards et al., 2002; 2005) and faster complex reaction time on a Road Sign Test (Roenker et al., 2003). In addition, people trained using speed-of-processing interventions make fewer dangerous manoeuvres on subsequent on-road driving evaluations (Roenker et al., 2003).

With regard to optimising transfer effects, one approach would be to train at the level of complex activities reflecting real-world tasks, not at the level of basic abilities (Salomon and Perkins, 1989). For example, in a memory training programme, we might integrate value-based processing with the need for accuracy and completeness in memory performance (Castel, 2008; Goldsmith and Koriat, 2008). Through deliberate exercise of complex tasks, we may simultaneously exercise the underlying constituent abilities on which those tasks depend, *and* their coordination. Transfer may be more likely to occur under these conditions because individuals practice component skills in varying and relevant contexts which provide continuous opportunities to meet tractable challenges (Stine-Morrow et al., 2007; Swezy and Llaneras, 1997). This is the implied mechanism from correlational data suggesting that complex activity is a protective mechanism for late-life cognition (e.g., Wilson et al., 2002; but see Hultsch et al., 1999).

One major problem of intervening at the level of complex activity is that we do not yet have a good understanding of which activities, at which intensity, exercise particular cognitive abilities. What we need is the equivalent of understanding which 'muscle groups' are moved by particular physical exercises. Another problem lies in how to measure improvement in complex activities. Careful experimental work needs to be done to link particular abilities to particular training-related activities and experiences.

8. Multimodal training

An important limitation of many traditional cognitive training approaches is that they do not incorporate multiple training modalities. Approaches that combine cognitive training with pharmacotherapy (Rozzini et al., 2007; Yesavage et al., 2007), exercise (Colcombe and Kramer, 2003; Fabre et al., 2002; Larson et al., 2006), nutrition (Gillette et al., 2007; González-Gross et al., 2001), life style change (Gomez-Pinilla, 2008; Small et al., 2006), self-efficacy enhancement (Cervone et al., 2006; West et al., 2008), and other modes of intervention may potentially produce additive, or even synergistic benefits.

Combining training modalities, however, also has the potential for producing interference effects: 'more' may not always be better. Researchers need to carefully plan and sequence multimodal interventions, taking into account participants' limited capacity for processing multiple modalities. Some forms of training may work better in isolation, and some may work better when combined with other modalities. We recommend that researchers investigate the relative contributions of individual interventions before advocating a combined approach.

Although multimodal approaches to cognitive training show considerable promise, they have seldom been implemented. Yesavage and his colleagues are currently studying the use of donepezil as a augmentation strategy to enhance the effects of cognitive training in normal, older adults and those diagnosed with mild cognitive impairment (MCI) (Yesavage et al., 2007). In a study by Rozzini et al (2007), an MCI group receiving cholinesterase inhibitors (ChEIs) and cognitive training showed significantly improved memory and abstract reasoning and reduced depressive mood at a three-month follow-up compared with a ChEIs-only-treated group. However, the study did not include a cognitive-training alone group so the effects of combining treatment strategies remains unknown.

The cognitive benefits of physical exercise have been noted for both aerobic and anaerobic activity (Colcombe and Kramer, 2003). Fabre and colleagues (2002) combined cognitive and physical training using a full factorial design. They reported that combined aerobic and cognitive training led to greater effects on memory performance than aerobic training or cognitive training alone. However, their study was limited to a small convenience sample (N=32) of unimpaired older adults aged 60-76. Small and his colleagues (2006) studied the effects of a short-term healthy lifestyle programme combining mental and physical exercise, stress reduction, and healthy diet on cognition and brain metabolism in 17 non-demented middle-aged and older adults (mean age = 53 years, range = 35-69 years) with mild age-related memory complaints. They reported improved measures of verbal fluency and reduced dorsolateral prefrontal cortical metabolism, suggesting that such a programme may result in greater cognitive efficiency of a brain region involved in working memory functions.

To date, though, no studies have examined the combined effects of physical training and structured cognitive training on cognitive function in a large, representative sample of community elderly. There also have been few combined intervention studies systematically examining the different types of training using multiple comparison groups.

9. Statistical modeling of training effects

Researchers are developing new designs and statistical models for analysing training effects (Elias and Wagster, 2007). One approach for the assessment of intervention effects that has attracted considerable attention is growth mixture modelling (McArdle, 2006; McArdle and Nesselroade, 2002; Muthén et al., 2002). These models allow for the inclusion of both categorical and continuous latent variables in the same model. With regard to training, the models allow for the identification of subsamples that respond differentially to the training, based on variable response patterns. Investigators can study this, based on who best responds to the intervention and individual difference variables that contribute to growth (improvement) or lack of improvement (Elias and Wagster, 2007; Langbaum et al., in press). There is also interest in documenting test-retest effects (Salthouse et al., 2004) and the cost-effectiveness of cognitive training and cognitive stimulation programmes for older adults (Becker et al., 2008; Frick et al., 2004; McCrory, 2007).

10. Designing a public health framework for training delivery

These are exciting times for cognitive training research. The possibilities of increasing cognitive abilities in later life that transfer to everyday function and confer lasting benefit are rapidly increasing. New approaches that combine cognitive training with exercise, pharmacotherapy, nutritional interventions, and lifestyle modification are propelling the field forward at an accelerating pace. Interest in developing more effective cognitive training that can be used to promote healthy cognitive ageing at a population level is rapidly growing in both scientific and lay communities.

At the same time, there is growing concern about the current use of cognitive training with older adults, and its widespread application. As stated in a recent editorial in *Nature Neuroscience,* 'Mental exercise games are being claimed to slow brain ageing, but the evidence for this idea is not yet conclusive' (Editorial, 2007). Salthouse (2006) systematically reviewed the literature on the 'mental-exercise hypothesis' and concluded that there is little evidence to suggest that mental training alters the rate of cognitive ageing. Although training alone may not be sufficient to alter the life course with respect to decline, it may compress the point of cognitive decline and disability into a smaller window at the end of life. Training gains may also be a useful predictor of future mental status (Boron, Willis and Schaie, 2007).

Overall, based on the present review and previous reviews of this area (McDougall, 1999; Verhaeghen et al., 1992; Willis and Schaie, 1994), the bulk of the cognitive training literature appears to support the ability of older adults to benefit from cognitive training. This has far-reaching public health implications in terms of improving the mental capital and wellbeing of the older population. As Brookmeyer and his colleagues (2007) have demonstrated, even modest delays in the onset and progression of cognitive decline in Alzheimer's disease (AD) would produce widespread benefit at the population level. In 2006, the worldwide prevalence of AD was 26.6 million. By 2050, this will quadruple, such that one in 85 persons worldwide will be living with the disease. If interventions could delay both its onset and progression by a modest one year, there would be nearly 9.2 million fewer cases in 2050, with nearly all the decline attributable to decreases in persons needing high level of care (Brookmeyer et al., 2007). In other words, modest advances in therapeutic and preventive strategies that lead to even small delays in Alzheimer's onset and progression can significantly reduce the global burden of the disease.

At present, there is little direct evidence that cognitive training can delay the onset of AD, but it may increase the cognitive resources available to compensate for the impact of increasing cognitive deficits. This may delay the outward presentation of symptoms and have positive benefit for patients, their families, and society.

In their review of the accumulated longitudinal evidence supporting the cognitive reserve hypothesis, Frataglioni et al., (2004, p343) concluded that there is little doubt that "an active and socially integrated lifestyle in late life protects against dementia [and Alzheimer's disease]". However, training research has not adequately studied the effects of maintained cognitive abilities on the everyday functioning of older adults and their quality of life (Ball et al., 2002). Consistent with current conceptualisations of the disablement process (Wolinsky and Miller, 2006), the presumed etiological mechanism is that the age-related decline of cognitive abilities increases the likelihood of difficulty of performing activities of daily living (ADLs) and instrumental activities of daily living (IADLs), that in turn, leads to deterioration in health-related quality of life (HRQoL) (Ball et al., 2002; Jobe et al., 2001).

The ACTIVE study has reported evidence on the ability of speed-of-processing training to delay clinically relevant declines in HRQoL two years (Wolinsky et al., 2006a) and five years (Wolinsky et al., 2006b) post-training. The ACTIVE memory and reasoning training interventions did not have similarly protective effects. One plausible explanation for these findings is that speed-of-processing training is more clearly procedural, operating through sensory-motor elaboration and repetition, whereas the memory and reasoning interventions emphasise or require the explicit learning of new concepts (Wolinsky et al., 2006a; Wolinsky et al., 2006b). Procedural tasks exhibit a broader pattern of regional brain activation (i.e. neostriatum and cerebellum in addition to neocortex) than do explicit memory tasks (Cabeza and Nyberg, 2000), which may account for a greater sense of wellbeing reflected in the HRQoL ratings. It remains to be seen whether the speed-of-processing training will translate into more appropriate and reduced levels of health services utilisation and increased longevity. Attempts are currently under way to examine these more objective outcomes in the ACTIVE study, 10 years post-training.

Rapid growth in the population of older adults coupled with the findings reporting links between cognitive decline and institutionalisation (Langa et al., 2001; Strain et al., 2003), hospitalisation (Chodosh et al., 2004), chronic health conditions (Di-Carlo et al., 2000; Izquierdo-Porrera and Waldstein, 2002), and mortality (Schupf et al., 2005; Shipley et al., 2006) have resulted in an increased need for population-level alternatives to formal group-based cognitive interventions such as ACTIVE. The increasing demand for such intervention alternatives necessitates the development of cost-effective, self-administered, and flexible training platforms that can be easily distributed to the public.

11. Proposed next steps

There are a number of unanswered questions with regard to the efficacy of cognitive training with older adults and the underlying mechanisms of training-related improvements. In addition to the question of whether training can prevent cognitive decline in later life, we need to know: what constitutes 'successful training'; who are the best candidates for successful training; when to intervene; and how we can enhance training to broaden its transfer effects and durability. We also need to know more about optimal dosage and sequencing for delivering cognitive training, the best way to extend it to the cognitively impaired, and how to match interventions to individual risk profiles. From a public health perspective, we need to know how we can make training accessible and worthwhile to the entire older population, particularly those at highest risk for pathologic cognitive decline, and how to increase its cost-effectiveness. In future efforts, it will be important to draw on current cognitive ageing theory to inform cognitive training and *vice versa*.

With regard to proposed next steps, the field needs more well-controlled studies of multi-faceted interventions that combine multiple cognitive skill-based training and other behavioural and non-behavioural intervention techniques. If these studies demonstrate interactive effects, combining cognitive training techniques with exercise, nutritional supplements, or drug therapy could magnify the benefits of existing training programmes for older adults. There is also a need for hybrid approaches that target both cognitive and functional abilities.

Many of the cognitive training interventions have been low-dose. We need more intensive, high-exposure interventions (e.g. activity-based, life style management, web-based, computerised, in-home, self-administered).

We also need to direct more attention to individual difference variables (health status, depression, self-efficacy) that may affect training responsiveness, transfer, and maintenance.

We need more studies focusing on the neural mechanisms of training, such as fMRI studies showing changes in brain activation levels during, and after, cognitive training, along with more studies of strategy usage and the strategy maintenance over time, and their role in training gains. Greater effort is now being focused on monitoring strategy usage, both during cognitive training and during the follow-up period, in order to determine whether those who improved did so because of increased strategy utilisation (Carretti et al., 2007; Dunlosky et al., 2007; Dunlosky et al., 2003; Lachman and Andreoletti, 2006; O'Hara et al., 2007; Saczynski, Rebok et al., 2007). The importance of understanding the mechanisms underlying training effects cannot be overstated, given that it is only through an understanding of mechanisms that interventions can be effectively targeted.

More attention also needs to be paid to cognitive plasticity across the lifespan (Brehmer et al., 2007; Brehmer et al., 2008). This includes studies of adults past age 80, since most training studies have involved younger-old cohorts (Verhaeghen et al., 1992) and since the prevalence of cognitive impairments increases steeply with age (Evans et al., 1989). Although the evidence seems clear that plasticity of cognitive functions declines with advancing age (e.g. Singer et al., 2003; Verhaeghen and Marcoen, 1996), it is also clear that the ageing brain does retain a considerable amount of reserve capacity (Reuter-Lorenz, 2002). Studies further developing cognitive training techniques with older adults who are just beginning to experience preclinical cognitive decline, but who do not yet have mild cognitive impairment (MCI) or dementia, will be an important direction for future cognitive training research (Acevedo and Loewenstein, 2007). Such interventions may provide a window of opportunity in which to delay, and possibly reverse, the further progression of impairment (Rebok et al., 2007).

Future research also needs to focus more attention on a frequently-overlooked factor in training – the nature of the social engagement experience, given that most training programmes (e.g. ACTIVE) are group-based. Social engagement, defined as the maintenance of many social connections and a high level of participation in social activities, is associated with cognitive functioning in older adults (Bassuk et al., 1999; Seeman et al., 2001; Holtzman et al., 2004). For instance, Barnes et al. (2004) found that regular participation in structured social activities may reduce cognitive impairment by 91% among those with higher levels (*versus* lowest levels) of social engagement. Other studies have found that greater social engagement is protective of the onset of dementia (Fratiglioni et al., 2000), and even longevity (Bennett, 2002). A possible explanation for these findings is that a social network could provide a sense of purpose, community, and opportunities for increased self-efficacy (Holtzman et al, 2004). Additionally, social engagement challenges people to communicate effectively and participate in complex personal exchanges (Bassuk et al., 1999), which may enhance cognitive performance. To the extent that cognition in adulthood is motivated by social and emotional goals (Carstensen, 1995, 2006), a socially collaborative context may be particularly effective for older adults (Dixon and Gould, 1996; 1998) and contribute to overall satisfaction with an intervention (e.g. Paggi and Hayslip, 1999; Parisi et al., 2007).

Finally, there is scope for more animal studies designed to elucidate the underlying biological mechanisms that may help inform the development of cognitive training interventions. Studies have shown that factors such as social stress can exacerbate the pathology and worsen cognitive performance in animal models of Alzheimer's disease (Dong et al., 2004; Jeong et al., 2006). A stimulatory environment, on the other hand, has been shown to slow development of pathology and improve cognitive performance in similar transgenic mouse models (Adlard et al., 2005; Lazarov et al., 2005). If the biological mechanisms that underlie these effects in animal models can be elucidated, then not only appropriate physical interventions might be developed for humans, but also there may be pharmacological interventions based upon the biological mechanisms.

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