Curr Psychiatry Rep (2010) 12:20–27
DOI 10.1007/s11920-009-0085-y

Cognitive Exercise and Its Role in Cognitive Function in Older Adults

Nicola Gates · Michael Valenzuela

Published online: 8 January 2010

Abstract Converging lines of research indicate that complex mental activity is associated with reduced dementia risk. Thus, intense interest exists in whether different forms of cognitive exercise can help protect against cognitive decline and dementia. However, there is considerable confusion in terminology that is hindering progress in the field. We therefore introduce a concrete definition of cognitive training (CT) and make this the focus of our article. Clinical research that has evaluated CT in normal aging, mild cognitive impairment, and dementia is then critically reviewed. Despite many methodological shortcomings, the overall findings indicate that multidomain CT has the potential to improve cognitive function in healthy older adults and slow decline in affected individuals. Finally, practical issues, including the strengths and weaknesses of commercial products, are explored, and recommendations for further research and clinical implementation are made.

Keywords Cognitive training · Cognitive intervention · Cognitive exercise

Introduction

Complex mental activity can promote several neuroplastic mechanisms, a phenomenon that is conserved well into advanced age [1] and hence may be exploited for the mitigation of age-related changes in cognition. For example, meta-analyses have shown that individuals with higher levels of mental activity are at only about half the risk of developing dementia [2] and have a reduced rate of incident cognitive decline [3], and that late-life mental exercise exhibits a dose-dependent relationship with dementia risk reduction independent of early life experiences [2]. Interventions based on augmenting complex mental activity therefore represent a promising new approach to combating age-related cognitive decline and to dementia prevention. In this review, we discuss important definitions, summarize the results of recent clinical trials, and finally introduce some of the major commercial products in this burgeoning field.

Definitions

Mental activity, *cognitive exercise*, and *cognitive intervention* are commonly used nonspecific terms that encompass disparate interventions based on different theoretical constructs. Although the review of Clare and Woods [4] provided a taxonomy of cognitive interventions into "cognitive rehabilitation," "cognitive stimulation," or "cognitive training" (CT) and hence the basis for differentiation, significant confusion remains. Similar interventions have, for example, been labelled differently: computer-based repetitive training has been referred to as "cognitive intervention" [5] and "cognitive rehabilitation" [6-8]. Qualitatively different interventions have also been given the same label, with "cognitive stimulation" being used to refer to generic discussion topics [9], training in memory strategies [10], and CT exercises [11]. In our opinion, this ongoing confusion has hampered the development and validation of cognitive interventions in general and may have contributed to the mixed findings to date. Consequently, this article focuses on one form of cognitive intervention: CT.

Cognitive Training

CT, defined under the Cochrane protocol of Martin et al. [12], is "an intervention providing structured practice on tasks

N. Gates (✉) · M. Valenzuela
Neuropsychiatric Institute, Prince of Wales Hospital,
Randwick, Sydney, NSW 2031, Australia
e-mail: nicola.gates@student.unsw.edu.au

relevant to aspects of cognitive functioning, using standardized tasks" and "intended to address cognitive function and/or cognitive impairment directly." Based on this and similar definitions [13], we have developed an operational definition of CT that includes four components: 1) repeated practice, 2) on tasks with an inherent problem, 3) using standardized tasks, and 4) that target specific cognitive domains. CT programs adhering to this definition have been studied across the age and clinical spectrum, from healthy older adults [14-19] to those with preclinical dementia or mild cognitive impairment (MCI) [7•, 8, 20-23] to those diagnosed with Alzheimer's disease (AD) [5, 11, 24-30].

Clinical Evidence

Methodological Issues

Reviews across the population groups identified above agree that the field continues to face many challenges, primarily a lack of randomized clinical trials and methodological issues [4, 13, 22, 31-34••]. The most prominent design issues include small sample sizes, lack of randomization, absence of active or placebo controls, limiting of outcome measures due to combined treatment interventions, and lack of longitudinal follow-up. Despite these important limitations, there is promising evidence that CT may be an effective cognitive and functional intervention for the aged. A summary of results from randomized controlled trials of CT in this area is presented in Table 1 and in more detail subsequently.

CT in Healthy Older Adults

Whether older cognitively intact individuals can benefit from CT remains controversial, as two recent meta-analyses yielded different conclusions [33, 34••]. However, different clinical trials were identified within each review. Examination of longitudinal randomized controlled trials of training adhering to our definition demonstrated that CT can help slow the rate of age-related cognitive decline on a range of cognitive tasks, with on average a moderate effect size (ES) of 0.6 [34••].

The largest randomized trial to date, the ACTIVE (Advanced Cognitive Training for Independent and Vital Elderly) study, which involved 2802 older Americans, compared three training programs (memory strategy, reasoning, and speed of processing) and a no-contact control and measured performance immediately after training and at 1- and 2-year follow-up. Results indicated that domain-specific training led to improvement in the targeted cognitive functions, with computer-based speed training resulting in the greatest gains compared with pen-and-paper reasoning and memory strategy training [15]. Although the transfer of gains to functional measures was not evident at 2 years, subsequent investigation revealed that the positive functional benefits were manifest at 5-year follow-up [17].

Training relying specifically on computer delivery was investigated in the randomized trial of Mahncke et al. [35] using the commercially available Posit Science (San Francisco, CA) program. Training exercises designed to improve aural language processing resulted in improvements in both targeted cognitive function and nontrained cognitive function in the experimental group compared with control participants. In addition, memory performance remained enhanced at 3-month follow-up.

Although the limited number of well-designed randomized trials of training in healthy older adults limits the extent to which conclusions can be drawn, both these studies indicate that CT can result in the generalization of benefit to nontrained functions, and that such benefits persist. Furthermore, there are indications that computer-delivered training is efficacious and potentially associated with better outcomes (Gates, unpublished data).

CT in MCI and At-Risk Groups

The opportunity to intervene at the preclinical dementia stage with nonpharmacologic strategies that are safe and engaging carries enormous potential for helping prevent dementia. However, to date, few studies have been conducted. Trials of memory strategy training have resulted in limited improvement on objective memory and cognitive function [20, 23], suggesting that impaired memory function may be resistant to the benefits of a unimodal memory intervention. For example, a randomized trial of memory strategy training within a larger memory intervention, including cueing, categorization, chunking, and method of loci, found no difference between trained and wait-list control participants on objective measures of memory at the end of training or at 3-month follow-up [23].

In contrast, trials of multidomain CT in MCI have shown positive effects [6-8, 21]. The Rozzini et al. [7•] randomized study of 59 independently living individuals diagnosed with MCI used TNP computer software [36] to train multiple cognitive functions with modulated complexity. At 3-month follow-up, episodic memory was significantly improved in the combined CT and medication treatment group compared with the medication-only and no treatment control groups. Furthermore, the CT and medication treatment group had a greater reduction in depressive symptoms and behavioral and neuropsychiatric disturbance than the group receiving pharmacologic treatment alone. This single trial suggests that in the context of MCI, multidomain CT can potentially lead to enduring positive effects on memory as well as generalized benefit in neuropsychiatric symptoms. However, the paucity of randomized controlled trials makes it difficult to make

Table 1 Cognitive training characteristics and cognitive outcomes in randomized controlled trials of healthy older adults and those with mild cognitive impairment and Alzheimer's disease

Study	Sample size, *n*	Cognitive training	Control condition	Duration, *min/wk*	Total sessions, *n*	Follow-up, *mo*	Primary cognitive outcome measures	Generalization outcome measures
Scogin and Bienias [18]	27 healthy older adults	Memory strategy training by completion of a 92-page manual	No contact	NR	NR	36	Cognitive specific: immediate and delayed recall of 20 nouns, 15 names and faces, 15 shopping items; Benton Visual Retention Test; Digit Span Test	Metamemory Questionnaire, Self-Rating Depression Scale
Stigsdotter and Backman [19]	18 healthy older adults	Multifactorial memory strategy training and attention exercises, relaxation training, cognitive activation training with problem-solving and visuospatial tasks	No contact	NR	8	42	Buschke Selective Reminding Test	NR
Heiss et al. [24]	80 AD patients	Multidomain (memory, perceptual, and motor tasks); computer drill CT	Active	120	52	None	Global: MMSE; domain specific: Corsi Blocks, selective reminding test, fragmented pictures test, token test, supermarket test, orientation test, Praxis test, reaction time test, tapping task	NR
Davis et al. [25]	37 AD patients	Memory strategy and attention training	Active	60 (180 for homework)	5	–	Global: MMSE; domain specific: logical memory test, visual reproduction test, Digit Span Test, Verbal Series Attention Test, COWAT, category fluency test, finger-tapping test	Quality of Life Assessment (patient), GDS
Ball et al. [15]	2832 healthy older adults	3 training groups: memory strategy, reasoning, computerized speed of processing	No contact	120–150	10	24	Composite scores from domain-specific measures	ADL, IADL, driving habits questionnaire
Rapp et al. [20]	19 MCI patients	Memory strategy training (cueing, categorization, chunking, method of loci) within a larger, multifaceted intervention	No contact	6	96	6	Domain specific: Memory Functioning Questionnaire, Memory Controllability Questionnaire, word list (immediate and delayed recall), story paragraph (immediate and delayed recall), grocery list (immediate and delayed recall), names and faces (immediate and delayed recall)	Profile of Mood States
Cahn-Weiner et al. [26]	34 AD patients	Memory strategy training	Active	45	6	2	Domain specific: Hopkins Verbal Learning Test-revised, Brief Visuospatial Memory Test-revised, BNT, COWAT, Judgment of Line Orientation, TMT	ADL Questionnaire

Loewenstein et al. [27]	44 AD patients	Cognitive rehabilitation training	Active[a]	90	24	3	Domain specific: face-name association, orientation, object memory, change (for purchase), balancing checkbook, Continuous Performance Test	Basic ADL, depression
Olazaran et al. [28]	72 AD, 12 MCI patients	Multidomain training (pen and paper)	Active	60	103	12	ADAS-Cog, MMSE	Functional Activities Questionnaire, GDS
Derwinger et al. [48]	81 healthy older adults	Memory strategy training	No contact	120	10	8	Recall of number sequences	NR
Mahncke et al. [35]	182 healthy older adults	Posit Science (San Francisco, CA) computer-based training	Active contact and no contact	240	40	3	Global and specific: RBANS	NR
Oswald et al. [14]	375 healthy older adults	Multidomain training (memory, information processing, problem solving)	No contact	90	30	72	Composite cognitive score	NR
Requena et al. [30]	86 AD patients	Stimulation program, including computer exercise CT	Active	225	520	–	Global: MMSE, ADAS-Cog	GDS
Willis et al. [17]	2832 healthy older adults	Reasoning training	No contact	120	10	72	–	IADL
Galante et al. [5]	11 AD patients	Multidomain computer training, NPT [36, 49]	Active	180	12	9	Global: MMSE; domain specific: prose memory, word repetition test, Corsi Blocks, Raven's Coloured Progressive Matrices, digit cancelation, semantic and phonemic fluency, constructional and ideomotor apraxia	NPI, GDS, IADL, BADL
Rozzini et al. [7•]	59 MCI patients	ChEI and multidomain computerized CT (attention, abstract reasoning, visuospatial abilities with the NPT) [36, 49]	No contact and ChEI alone	12	72	3	Global: MMSE; domain specific: story paragraph, letter verbal fluency, semantic verbal fluency, Raven's Progressive Coloured Matrices, RCFT copy and recall	GDS (15 items), NPI, BADL
Tarraga et al. [11]	46 AD patients	Multidomain (attention, gnosis language, memory, orientation, calculation), Internet based program within a multifactorial intervention	Active	75	72	5.5	Global: ADAS-Cog, MMSE; domain specific: BNT, verbal fluency, story recall	Rapid Disability Rating Scale-2, GDS
Troyer et al. [23]	50 MCI patients	Memory strategy training (spaced retrieval, memory book, semantic association, logical location) within a larger mixed intervention	Wait list	25	10	3	Domain specific: word list of 2-syllable nouns, digit span, memory strategy knowledge, Multifactorial Memory Questionnaire	NR

Table 1 (continued)

Study	Sample size, *n*	Cognitive training	Control condition	Duration, *min/wk*	Total sessions, *n*	Follow-up, *mo*	Primary cognitive outcome measures	Generalization outcome measures
Barnes et al. [39]	47 MCI patients	Computerized CT (single domain)	Active	500	30	–	Global: RBANS; domain specific: BNT, California Verbal Learning Test, COWAT	GDS

[a] Control of multidomain computer exercises, termed *mental stimulation training*

AD Alzheimer's disease, *ADAS-Cog* Alzheimer's Disease Assessment Scale, cognitive subscale, *ADL* activities of daily living, *BADL* basic activities of daily living, *BNT* Boston Naming Test, *ChEI* cholinesterase inhibitor, *COWAT* Controlled Oral Word Association Test, *CT* cognitive training, *GDS* Geriatric Depression Scale, *IADL* instrumental activities of daily living, *MCI* mild cognitive impairment, *MMSE* Mini-Mental State Examination, *NPI* Neuropsychiatry Inventory, *NPT* neuropsychological training, *NR* not reported, *RBANS* Repeatable Battery of Assessment of Neuropsychological Status, *RCFT* Rey-Osterrieth Complex Figure Test, *TMT* Trail Making Test

conclusive statements in this area; further research of this type must be a top international priority.

CT in Dementia

Although the number of published studies investigating CT in dementia exceeds those with normative and preclinical groups, findings have been mixed. A 2003 Cochrane review concluded that there were no significant positive benefits from CT in this population [13]. However, the nature of the training programs included in the review were highly variable, ranging from multidomain computerized exercises to memory strategy training and training in compensatory devices. As mentioned, this confusion of intervention type creates significant issues when attempting to interpret and integrate results across trials. A subsequent review and meta-analysis separated training in compensation strategies from CT, and CT was found to have a greater benefit (ES, 0.54) compared with restorative techniques (ES, 0.36) [32].

The separation of memory strategy training from CT as defined here can also provide further insights. Studies of memory strategy training have demonstrated no effect on general cognitive measures [25, 26, 37]. In contrast, randomized trials of multidomain CT in AD have demonstrated positive effects on global cognitive measures [5, 11] and functional measures [38]. Tarraga et al. [11] randomly assigned individuals with mild AD to computer-based CT in combination with an integrated psycho-stimulation program or to one of two control groups (integrated psycho-stimulation program alone or no intervention). Following high-volume training, the CT group demonstrated better performance on the primary global cognitive measure (AD Assessment Scale, cognitive subscale) and on secondary neuropsychological tests at 24-week follow-up compared with both control groups. Another randomized investigation of multidomain CT demonstrated delay of clinical progression by the end of training and at 3-month follow-up compared with a control group [5]. Consequently, some evidence suggests that multidomain CT may benefit those with AD by slowing the disease's progression.

Practical Issues

Computer-Based CT

Traditional pen-and-pencil CT exercises are being increasingly replaced by computer-based programs. This trend seems to be driven by several factors, including greater community access to computers, commercialization of computerized products, and research interest. Computer-based CT has been successfully delivered to healthy older adult [15, 35], MCI [6-8, 21, 39] and AD populations [5, 11], and as an implementation strategy, it is likely superior for several reasons. First, computer delivery facilitates multimodal and multidomain training, which seems to be a key factor for functional efficacy. The magnitude of the ES may be stronger when exercises are implemented via computer. Within the ACTIVE study, for example, 5-year post ES were 0.76 for computer-based information speed training, compared with 0.23 to 0.26 for traditional memory and reasoning training [17], although this result may also be due to a domain-specific effect.

Second, computer-based interventions enable algorithms to set the initial level of task difficulty with reference to the individual's baseline competency and then gradually increase task difficulty in a customized fashion, in effect providing an individualized intervention. These features also allow effective control of ceiling and floor effects, which theoretically may be a key ingredient for successful cognitive exercise regimes, as individuals are continually cognitively challenged. In addition, computer-based interventions enable the unobtrusive real time monitoring of cognitive performance, the standardization of intervention, and potentially the reduction of personnel and implementation costs, making this an attractive research option.

Commercial Products

Our definition of CT is compatible with the form of training provided by several commercial products, some of which are listed in Table 2. Despite the current limited empiric or independent research, commercial claims abound regarding the enhancement of cognitive function through training [40]. These claims and the proliferation of commercial products seem to be outpacing clinical research, although many companies are increasingly undertaking direct research [35, 41] or sponsoring academic research [39, 42]. In general, investigation of commercial products should be of the same standard as that of pharmacologic studies [33, 40] and hence should inform widespread community implementation. The main risks of irresponsible marketing of CT products are that users may develop unrealistic expectations and that an exciting new research option may be prematurely discredited.

Role of CT in the Cognitive Function of Older Adults

Current research suggests that the clinical role and type of CT intervention may differ depending on the older adult population and AD prevention stage. Three stages of AD prevention have been identified: primary prevention to reduce disease incidence in cognitively healthy individuals; secondary prevention to slow progression of preclinical disease to clinical disease (often translating to reduction of MCI "conversion" to dementia); and tertiary prevention, the reduction of disability due to cognitive symptoms in diagnosed patients [43].

Exercise drills in healthy older adults produce positive effects [34••] and are commensurate with the definition of primary prevention. Similarly, CT has been shown to help maintain and enhance function in MCI [6-8, 21]—consistent with secondary prevention—and may therefore slow disease progression in at-risk individuals. Two studies demonstrated that multidomain CT is beneficial in AD groups, with training leading to improved global cognitive function [5, 11], suggesting that CT can provide secondary prevention in the diagnosed population. Although memory strategy training to date has demonstrated limited benefit on cognitive function—and therefore has no impact at primary and secondary stages—it may be beneficial at tertiary prevention when aimed at improving impaired memory

Table 2 Summary of commercially available cognitive training products

Product	Manufacturer	Product description	Published research	Multiple cognitive domain
Brain age	Nintendo DS (Redmond, WA)	Palm device	No	Yes
http://www.brainbuilder.com	Advanced Brain Technologies (Ogden, UT)	Software	No	Yes
http://www.lumosity.com	Lumos Labs (San Francisco, CA)	Website	Yes	Yes
Brain fitness program 2.0	Posit Science (San Francisco, CA)	CD, requires Internet	Yes	No
Insight	Posit Science	CD, requires Internet	Yes	Yes
http://www.happyneuron.com	Scientific Brain Training (Palo Alto, CA)	Website	Yes	Yes
http://www.cognifit.com	CogniFit (Yoqneam, Israel)	CD or downloads, requires Internet	No	Yes
http://www.mybraintrainer.com	MyBrainTrainer (Los Angeles, CA)	Website	No	Yes
http://www.mpowerbrainfitness.com	Dakim (Santa Monica, CA)	Software and touch screen	No	Yes

CD compact disc

function and reducing disability. Several clinical trials have also investigated the benefit of combining CT with medication [7•, 27, 44], with results indicating that combination CT treatment provided greater benefit than medication alone. These findings suggest that CT may play an important adjunctive and synergistic role with traditional pharmacologic treatment at different disease stages.

Clinical Recommendations

Research suggests that CT may have therapeutic benefit, and there have been no reports of adverse outcomes [4]. Clinicians therefore may wish to consider CT as a treatment option. Our reviews of the area suggest that computerized multidomain brain training, or cross-training, is most likely to lead to meaningful benefits, and several products are available. There are, however, issues that should be considered in consultation with patients. The straightforward issues of access and feasibility should be reviewed initially. Economic resources and computer access need to be taken into account, as do prerequisite skills such as literacy and numeracy levels, sensory acuity, and motor dexterity and coordination. We recommend that clinicians become familiar with using a range of products themselves and develop specific knowledge about level of supporting scientific research, nature of instruction and structure with the program, and whether training is domain specific or multidomain. In addition to the content of the exercises, their adaptability, feedback of results, and support systems also vary considerably between products. Matching patients to training programs may require exploration of several options. Fortunately, several programs offer free initial trials to facilitate this process. Clinicians interested in accessing a consumer information sheet about CT developed by the authors can find it at http://www.brainage.med.unsw.edu.au.

Finally, it is important to emphasize to patients and to cognitively intact individuals interested in embarking on CT that there is no guarantee that any such training will eliminate the risk for dementia or cognitive impairment. CT is therefore best viewed as only part of a wider strategy of maximal risk reduction and maintenance of optimal brain health. CT complements and should be combined with other risk reduction strategies, including participation in cognitive, social, and physical leisure activities [45, 46], as well as careful control of vascular risk factors [47].

Conclusions

CT is a specific form of cognitive intervention that aims to stimulate residual neuroplastic pathways in the aged brain. Research suggests that CT can be beneficial across the aged spectrum, including in healthy adults and those at risk with MCI and AD. Training exercises seem to have greater efficacy than memory strategy training, and training in multiple cognitive domains seems to have greater benefit than unimodal training. In addition, increasingly popular computer-based programs may produce more effective outcomes on global and domain-specific cognitive measures. More rigorous research is required to adequately determine "dose," frequency, and duration of optimal intervention. CT is therefore a promising new intervention that can contribute to maintaining optimal cognition in older adults and potentially help prevent dementia as part of a comprehensive risk reduction strategy.

Acknowledgment Dr. Valenzuela is supported by a University of New South Wales Vice Chancellor's Fellowship.

Disclosure Miss Gates is a former director of HeadStrong Cognitive Fitness, Australia, a commercial, Internet-based CT enterprise, and maintains a financial interest. No other potential conflicts of interest relevant to this article were reported.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Brehmer Y, Li SC, Straube B, et al.: Comparing memory skill maintenance across the life span: preservation in adults, increase in children. Psychol Aging 2008, 23:227–238.
2. Valenzuela MJ, Sachdev P: Brain reserve and dementia: a systematic review. Psychol Med 2006, 36:441–454.
3. Valenzuela MJ, Sachdev P: Brain reserve and cognitive decline: a non parametric systematic review. Psychol Med 2006, 36:1065–1073.
4. Clare L, Woods RT: Cognitive training and cognitive rehabilitation for people with early-stage Alzheimer's disease: a review. Neuropsychol Rehabil 2004, 14:385–401.
5. Galante E, Venturini G, Fiaccadori C: Computer-based cognitive intervention for dementia: preliminary results of a randomized clinical trial [in Italian]. G Ital Med Lav Ergon 2007, 29(3 Suppl B):B26–B32.
6. Cipriani G, Bianchette A, Trabucchi M: Outcomes of a computer-based cognitive rehabilitation program on Alzheimer's disease patients compared with those on patients affected by mild cognitive impairment. Arch Gerontol Geriatr 2006, 43:327–335.
7. • Rozzini L, Costardi D, Chilovi V, et al.: Efficacy of cognitive rehabilitation in patients with mild cognitive impairment treated with cholinesterase inhibitors. Int J Geriatr Psychiatry 2007, 22:356–360. *This was the first randomized, longitudinal trial of CT in patients with MCI with domain-specific, global cognitive, and psychiatric outcome measures. Significant improvements were found in memory and executive function, as was a reduction in neuropsychiatry symptoms following training intervention.*
8. Talassi E, Guerreschi M, Feriani M, et al.: Effectiveness of a cognitive rehabilitation program in mild dementia (MD) and mild

cognitive impairment (MCI): a case control study. Arch Gerontol Geriatr 2007, 44(Suppl 1):391–399.
9. Spector A, Woods B, Orrell M: Cognitive stimulation for the treatment of Alzheimer's disease. Expert Rev Neurother 2008, 8:751–757.
10. Wenisch E, Cantegreil-Kallen I, De Rotrou J, et al.: Cognitive stimulation intervention for elders with mild cognitive impairment compared with normal aged subjects: preliminary results. Aging Clin Exp Res 2007, 19:316–322.
11. Tarraga L, Boada M, Modinos G: A randomized pilot study to assess the efficacy of an interactive, multimedia tool of cognitive stimulation in Alzheimer's disease. J Neurol Neurosurg Psychiatry 2006, 77:1116–1121.
12. Martin M, Clare L, Altgassen M, et al.: Cognition-based interventions for older people and people with mild cognitive impairment. Cochrane Database Syst Rev 2006, 4:006220.
13. Clare L, Woods B: Cognitive rehabilitation and cognitive training for early-stage Alzheimer's disease and vascular dementia. Cochrane Database Syst Rev 2003, 4:CD003260.
14. Oswald W, Gunzelmann T, Rupprecht R: Differential effects of single versus combined cognitive and physical training with older adults: the SimA study in a 5-year perspective. Eur J Ageing 2006, 3:179–192.
15. Ball K, Berch D, Helmers K: Effect of cognitive training interventions with older adults—a randomized control trial. JAMA 2002, 288:2271–2281.
16. Brenes GA: Cognitive training may improve targeted cognitive functions in older adults. Evid Based Ment Health 2003, 6:54.
17. Willis S, Tennstedt SL, Marsiske M: Long term effects of cognitive training on everyday functional outcomes in older adults. JAMA 2006, 296:2805–2814.
18. Scogin F, Bienias JL:A three-year follow-up of older adult participants in a memory-skills training program. Psychol Aging 1988, 3:334–337.
19. Stigsdotter N, Backman A: Long -term maintenance of gains from memory training in older adults: two 3 1/2-year follow-up studies. J Gerontol Psychol Sci 1993, 48:P233–P237.
20. Rapp S, Brenes G, Marsh AP: Memory enhancement training for older adults with mild cognitive impairment: a preliminary study. Aging Ment Health 2002, 6:5–11.
21. Gunther VK, Schafer P, Holzner BJ, et al.: Long-term improvements in cognitive performance through computer-assisted cognitive training: a pilot study in a residential home for older people. Aging Ment Health 2003, 7:200–206.
22. Belleville S: Cognitive training for persons with mild cognitive impairment. Int Psychogeriatr 2008, 20:57–66.
23. Troyer A, Murphy K, Anderson N, et al.: Changing everyday memory behaviour in amnestic mild cognitive impairment: a randomised controlled trial. Neuropsychol Rehabil 2008, 18:65–88.
24. Heiss WD, Kessler J, Mielke R, et al.: Long-term effects of phosphatidylserine, pyritinol, and cognitive training in Alzheimer's disease. A neuropsychological, EEG, and PET investigation. Dementia 1994, 5:88–98.
25. Davis RN, Massman PJ, Doody RS: Cognitive intervention in Alzheimer disease: a randomized placebo-controlled study. Alzheimer Dis Assoc Disord 2001, 15:1–9.
26. Cahn-Weiner DA, Malloy PF, Rebok GW, Ott OR: Results of a randomized placebo-controlled study of memory training for mildly impaired Alzheimer's disease patients. Appl Neuropsychol 2003, 10:215–223.
27. Loewenstein D, Acevedo A, Czaja S, Duara R: Cognitive rehabilitation of mildly impaired Alzheimer disease patients on cholinesterase inhibitors. Am J Geriatr Psychiatry 2004, 12:395–402.
28. Olazaran J, Muniz R, Reisberg B, et al.: Benefits of cognitive-motor intervention in MCI and mild to moderate Alzheimer disease. Neurology 2004, 2:2348–2353.
29. Kawashima R, Okita K, Yamazaki R, et al.: Reading aloud and arithmetic calculation improve frontal function of people with dementia. J Gerontol Med Sci 2005, 60A:380–384.
30. Requena C, Maestu F, Campo P, et al.: Effects of cholinergic drugs and cognitive training on dementia: 2 year follow-up. Dement Geriatr Cogn Disord 2006, 22:339–345.
31. Clare L: Cognitive training and cognitive rehabilitation for people with early-stage dementia. Rev Clin Gerontol 2003, 13:75–83.
32. Sitzer DI, Twamley EW, Jeste DV: Cognitive training in Alzheimer's disease: a meta-analysis of the literature. Acta Psychiatr Scand 2006, 114:75–90.
33. Papp KV, Walsh SJ, Snyder PJ: Immediate and delayed effects of cognitive interventions in healthy elderly: a review of current literature and future directions. Alzheimers Dement 2009, 5:50–60.
34. •• Valenzuela MJ, Sachdev P: Can cognitive exercise prevent the onset of dementia? Systematic review of randomized clinical trials with longitudinal follow-up. Am J Geriatr Psychiatry 2009, 17:179–187. *This was the first meta-analysis of the effect of CT on longitudinal performance in healthy adults*.
35. Mahncke HW, Connor B, Appelmann J, et al.: Memory enhancement in healthy older adults using a brain plasticity-based training program: a randomized controlled study. Proc Natl Acad Sci U S A 2006, 103:12523–12528.
36. Tonetta M: TNP—Training Neuropsiclogico di Mario Tonette [software, in Italian]. Stradella, Italy: BEAC-Biomedical; 1998.
37. Beck C, Heacock P, Mercer S, et al.: The impact of cognitive skills remediation training on persons with Alzheimer's disease or mixed dementia. J Geriatr Psychiatry 1998, 21:73–88.
38. Farina E, Fioravanti R, Chiavari L, et al.: Comparing two programs of cognitive training in Alzheimer's disease: a pilot study. Acta Neurol Scand 2002, 105:365–371.
39. Barnes D, Yaffe K, Belfor N, et al.: Computer-based cognitive training for mild cognitive impairment. Results from a pilot randomised, controlled trial. Alzheimer Dis Assoc Disord 2009, 23:205–210.
40. Soloman P, Murphy C: Early diagnosis and treatment of Alzheimer's disease. Expert Rev Neurother 2008, 8:769–780.
41. Merzenich M: Neuroscience via computer: brain exercise for older adults. Interactions 2007, 14:42–45.
42. Lumos Labs: Ongoing research using Lumosity. Available at http://lumosity.com/knowledge-centre. Accessed September 16, 2009.
43. Thal LJ: Prevention of Alzheimer disease. Alzheimer Dis Assoc Disord 2006, 20(Suppl 2):S97–S99.
44. Yesavage JA, Friedman L, Ashford W, et al.: Acetylcholinesterase inhibitor in combination with cognitive training in older adults. J Gerontol 2008, 63:288–294.
45. Valenzuela MJ: Brain reserve and the prevention of dementia. Curr Opin Psychiatry 2008, 21:296–302.
46. Verghese J, Lipton R, Katz M, et al.: Leisure activities and the risk of dementia in the elderly. N Engl J Med 2003, 348:2508–2524.
47. Hanon DE: Vascular risk factors, cognitive decline and dementia. Vasc Health Risk Manag 2008, 4:363–381.
48. Derwinger A, Stigsdotter N, Backman L: Design your own memory strategies! Self-generated strategy training versus mnemonic training in old age: an 8-month follow-up. Neuropsychol Rehabil 2005, 15:37–54.
49. Sinforiani E, Banchieri L, Zucchella C, et al.: Cognitive rehabilitation in Parkinson's disease. Arch Gerontol Geriatr 2004, 38(Suppl):387–391.