Clinical Interventions in Aging

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REVIEW

Aging brain: the effect of combined cognitive and physical training on cognition as compared to cognitive and physical training alone – a systematic review

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Abstract: This review presents a critical examination of current knowledge of the impact of combined cognitive and physical training on cognition in healthy elderly subjects. The objectives are to evaluate the contribution of cognitive and physical training to the enhancement of cognition, and to determine the interest of combining these two training types in one intervention in terms of the benefits for cognition (direct and transfer), long-term maintenance, and transfer to daily living. To do so, a systematic electronic search was conducted in PubMed and Google Scholar. Exclusion criteria were animal and pathological aging studies. We focused on the shared and different behavioral impacts of these two types of training on cognition, as well as their functional and structural impact on the brain. The review indicates that both cognitive and physical training have an impact on cognition and on the brain. However, each type of training seems to preferentially enhance different cognitive functions and specifically impact both brain structure and function. Even though some results argue in favor of a complementarity between cognitive and physical training and the superiority of combined cognitive and physical training, the current state of knowledge does not permit any definitive conclusion. Thus, the present review indicates the need for additional investigations.

Keywords: cognitive training, physical training, combined cognitive and physical training, healthy adults

Introduction

Western society is facing a significant increase of the elderly population. Individuals are living even longer and are confronted with disability and fragility.[1–3] Even though majority of the elderly have relatively well-preserved health, 20% of older adults aged 70 years or more experience difficulties in their everyday activities and lose their independence.[4,5] It is well established that normal aging induces anatomo-physiological changes in the brain that impact some aspects of cognition,[6] and particularly speed of processing, working memory, and executive functions.[7,8] This decline is mostly due to a dysfunction of the pre-frontal cortex, which is especially vulnerable and thus becomes prematurely atrophied in normal aging.[9] Some authors have shown that in the face of this atrophy, the aging brain reorganizes its functioning, for example, in terms of the hemispheric lateralization of the solicited regions. Indeed, the Hemispheric Asymmetry Reduction in Older Adults (HAROLD)[10] model holds that for any given cognitive task, older adults exhibit bilateral brain activation, whereas young adults exhibit unilateral activation to achieve the same performance. For instance, it has been

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found that when young and older adults had to perform an episodic memory task, although both groups succeeded in the task, the older adults exhibited a bilateral recruitment of pre-frontal regions, whereas the young adults exhibited unilateral recruitment of these same regions.[10] Two hypotheses can explain this phenomenon. The compensatory hypothesis postulates that older adults would compensate for the difficulties they face by additionally recruiting contralateral regions to contribute to the ongoing task.[10,11] The dedifferentiation hypothesis postulates that asymmetry reduction results from difficulties in recruiting specific cerebral regions that are required for a given task, thus leading to a more generalized recruitment.[12] Based on this idea, some authors proposed the Compensation Related Utilization of Neural Circuits Hypothesis (CRUNCH) model,[11] in which they explained that for a given task, older adults need more neuronal resources than young adults, thus resulting in this over-recruitment of brain regions in older adults.[13] The HAROLD and CRUNCH models provide relevant explanations about how the aging brain adapts and organizes its functioning in response to the age-related decline in cognition. However, the Scaffolding Theory of Aging and Cognition (revised-version – STAC-r)[7] proposes a more complete approach to aging cognition.

STAC-r not only takes into consideration age-related cognitive decline and its negative impact on the brain and cognition, but also positive aspects that can counteract and delay brain neurodegeneration in normal aging. In fact, many factors can influence cognition through life in both positive (high levels of education, social interaction, intellectual stimulation, physical activity) and negative (low level of education, lack of physical activity, health problems, alcohol or drug abuse) ways.[14] The STAC model suggests that as people age, there is an adaptation and a reorganization of brain functioning. More precisely, brain deterioration due to age-related decline results in a response in the form of a scaffolding of new compensatory networks, depending on the factors that positively and negatively influence cognition. STAC-r is the first model to explicitly include the concept of behavioral interventions, such as cognitive and physical training, while also modeling cognitive and cerebral aging, and to consider that training contributes to the scaffolding of new neuronal networks. In a more general way, this model proposes that having a rich cognitive and physical environment throughout life helps to preserve brain function.[7]

Behavioral interventions that aim to protect brain function against age-related decline are often described in terms of cognitive training (particularly oriented toward memory and executive functions)[15,16] and physical training (especially aerobics).[17] The question addressed by this review is whether it is relevant to combine cognitive training and physical training in one training intervention in order to improve the training outcomes as compared to each of these training modes administered alone.

Methods

Search strategy

A systematic electronic search was conducted in PubMed and Google Scholar with the following keywords: cognitive training, physical training, combined cognitive and physical training (CCPT), working memory, executive function, cognitive enhancement, endurance, aerobics, walking, everyday activities, elderly, and healthy older adults. The research was restricted to the period from January 2000 to November 2017 and to articles written in English. The search was also complemented by references to articles and "related articles".

Selection process

We only considered empirical studies that used a training intervention designed for healthy older adults. Animal studies, studies of persons with cognitive impairments, or studies that did not use a training design were excluded. A total of 52 studies are included in this review: 32 relating to single cognitive training, 10 relating to single physical training, and 11 relating both to cognitive and physical training. Among these 11 last studies, three are based on a direct comparison between cognitive and physical training alone and eight studies addressed CCPT.

Evaluation of methodological quality

We performed a qualitative evaluation of the 52 studies that were included in the review. We used the Physiotherapy Evidence Database (PEDro) scale.[18] This scale contains 11 criteria that evaluate the methodological quality of studies. Each fulfilled criterion is worth 1 point, and non-fulfilled criterion is worth 0 point. Total score between 9 and 11 points means a good methodological quality, total score between 6 and 8 means medium methodological quality, and total score of less than 6 points means low methodological quality. Tables 1–3 report levels of methodological quality of the studies that used, respectively, cognitive training alone, physical training alone, and cognitive and physical training together.

In the following sections, we will first present the impact of cognitive and physical training on cognition, and brain structure and function. Then, the differential

Table 1 Evaluation of methodological quality of the reviewed studies concerning cognitive training according to the PEDro scale[76]

References	Inclusion/ exclusion criteria[a]	Randomization of groups[b]	Concealment[c]	Similarity of baseline characteristics[d]	Blinded participants[e]	Blinded therapist[f]	Blinded assessor[g]	Key outcome[h]	Intention to treat[i]	Between groups statistics[j]	Mean/ standard deviation[k]	Final score
Ackerman et al[33]	Yes	NA	NA	NA	No	No	No	Yes	Yes	No	Yes	4
Anguera et al[32] Experiment 2	Yes	No	Yes	NA	Yes	No	No	Yes	Yes	Yes	No	6
Ball et al[44] ACTIVE study	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	9
Basak et al[28]	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Berry et al[38]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Borella et al[15]	Yes	Yes	NA	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Brehmer et al[42]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Buschkuehl et al[81]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Cao et al[16]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Cavallini et al[47]	No	No	No	No	No	No	No	Yes	Yes	Yes	No	3
Chapman et al[34]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Cheng et al[82]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Dahlin et al[37]	No	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Dahlin et al[90]	No	NA	No	Yes	No	No	No	Yes	Yes	Yes	Yes	5
Heinzel et al[39]	Yes	No	No	No	No	No	No	Yes	Yes	Yes	Yes	5
Heinzel et al[39]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Karbach and Kray[31]	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes	4
Li et al[41]	No	Yes	No	Yes	No	No	No	Yes	Yes	Yes	No	
Mahncke et al[83]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
McAvinue et al[48]	No	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Mozolic et al[36]	Yes	NA	No	Yes	Yes	No	No	Yes	Yes	Yes	No	6
Mozolic et al[91]	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8
Rebok et al[29] ACTIVE study	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	10
Richmond et al[84]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Schmiedek[30]	No	No	No	Yes	No	No	No	Yes	Yes	Yes	No	4
Smith et al[46]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9
Stepankova et al[85]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Strenziok et al[35]	Yes	NA	No	Yes	No	No	No	Yes	Yes	No	No	4

(*Continued*)

Table 1 (*Continued*)

References	Inclusion/ exclusion criteria[a]	Randomization of groups[b]	Concealment[c]	Similarity of baseline characteristics[d]	Blinded participants[e]	Blinded therapist[f]	Blinded assessor[g]	Key outcome[h]	Intention to treat[i]	Between groups statistics[j]	Mean/ standard deviation[k]	Final score
von Bastian et al[86]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Willis et al[45] ACTIVE study	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	10
Wolinsky et al[87]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	8
Zinke et al[88]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7

Notes: [a]Eligibility criteria were specified; [b]participants were randomly allocated to groups; [c]allocation to groups was concealed; [d]the groups were similar at baseline regarding the most important prognostic indicators; [e]participants were not aware of the group in which they were allocated (blinded); [f]staff that administered training was not aware (blind) of the group status (intervention or control); [g]assessors measuring at least one key outcome were not aware (blind) of the group status; [h]measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; [i]all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat"; [j]the results of between-group statistical comparisons are reported for at least one key outcome; [k]the study provides both point measures and measures of variability for at least one key outcome. Yes = 1 point, no = 0 points.

Abbreviations: NA, not applicable; PEDro, Physiotherapy Evidence Database.

Table 2 Evaluation of methodological quality of the reviewed studies concerning physical training according to the PEDro scale[76]

References	Inclusion/ exclusion criteria[a]	Randomization of groups[b]	Concealment[c]	Similarity of baseline characteristics[d]	Blinded participants[e]	Blinded therapist[f]	Blinded assessor[g]	Key outcome[h]	Intention to treat[i]	Between groups statistics[j]	Mean/ standard deviation[k]	Final score
Boyke et al[64]	Yes	No	NA	NA	No	NA	NA	Yes	Yes	Yes	Yes	5
Cassilhas et al[70]	Yes	Yes	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	7
Chapman et al[60]	Yes	Yes	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	7
Colcombe et al[17] Study 2	Yes	Yes	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	7
Liu-Ambrose et al[63]	Yes	Yes	NA	Yes	NA	No	Yes	Yes	Yes	Yes	Yes	8
Liu-Ambrose et al[61]	Yes	Yes	NA	NA	NA	NA	NA	Yes	Yes	Yes	Yes	6
Sink et al[58]	Yes	Yes	NA	Yes	NA	NA	Yes	Yes	Yes	Yes	Yes	8
Voelcker-Rehage et al[68]	Yes	Yes	NA	Yes	NA	NA	NA	No	Yes	Yes	Yes	6
Voss et al[53]	Yes	Yes	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	7
Voss et al[59]	Yes	Yes	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	7

Notes: [a]Eligibility criteria were specified; [b]participants were randomly allocated to groups; [c]allocation to groups was concealed; [d]the groups were similar at baseline regarding the most important prognostic indicators; [e]participants were not aware of the group in which they were allocated (blinded); [f]staff that administered training was not aware (blind) of the group status (intervention or control); [g]assessors measuring at least one key outcome were not aware (blind) of the group status; [h]measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; [i]all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat"; [j]the results of between-group statistical comparisons are reported for at least one key outcome; [k]the study provides both point measures and measures of variability for at least one key outcome. Yes = 1 point, no = 0 points.

Abbreviations: NA, not applicable; PEDro, Physiotherapy Evidence Database.

Table 3 Evaluation of methodological quality of the reviewed studies concerning combined cognitive and physical training according to the PEDro scale[76]

References	Inclusion/ exclusion criteria[a]	Randomization of groups[b]	Concealment[c]	Similarity of baseline characteristics[d]	Blinded participants[e]	Blinded therapist[f]	Blinded assessor[g]	Key outcome[h]	Intention to treat[i]	Between groups statistics[j]	Mean/ standard deviation[k]	Final score
Combined cognitive and physical training												
Frantzidis et al[79]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Linde and Alfermann[62]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Oswald et al[73]	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8
Pieramico et al[78]	Yes	Yes	No	NA	NA	NA	No	Yes	Yes	Yes	No	5
Rahe et al[74]	Yes	No	No	Yes	Yes	No	No	No	Yes	Yes	Yes	6
Shah et al[77]	Yes	No	No	No	Yes	No	No	Yes	Yes	Yes	No	5
Theill et al[75]	Yes	No	No	Yes	NA	No	No	Yes	Yes	Yes	Yes	6
Wenger et al[76]	Yes	Yes	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	7
Direct comparison of cognitive and physical training alone												
Chapman et al[66]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Chapman et al[67]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Håkansson et al[69]	Yes	Yes	No	NA	NA	No	Yes	Yes	Yes	Yes	No	6

Notes: [a]Eligibility criteria were specified; [b]participants were randomly allocated to groups; [c]allocation to groups was concealed; [d]the groups were similar at baseline regarding the most important prognostic indicators; [e]participants were not aware of the group in which they were allocated (blinded); [f]staff that administered training was not aware (blind) of the group status (intervention or control); [g]assessors measuring at least one key outcome were not aware (blind) of the group status; [h]measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; [i]all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat"; [j]the results of between-group statistical comparisons are reported for at least one key outcome; [k]the study provides both point measures and measures of variability for at least one key outcome. Yes = 1 point, no = 0 points.

Abbreviations: NA, not applicable; PEDro, Physiotherapy Evidence Database.

and complementary effects of CCPT will be addressed. Tables 4–6 present details concerning the procedure and results of each cited study in this review, respectively, for cognitive training alone, physical training alone, and cognitive and physical training together. In the tables, we only reported statistically significant (ie, $p < 0.05$) outcomes that are described as increase or decrease compared to baseline. Giving the irregularity in report of effect size in the selected studies, we did not include this data in the tables. However, globally, the effect sizes (reported as η^2) are in the range between 0.001 and 0.88 in studies concerning cognitive training alone, between 0.01 and 0.97 in studies concerning physical training alone, between 0.14 and 0.34 in studies concerning CCPT, and between 0.001 and 0.37 in studies that report direct comparison between cognitive and physical training alone.

Specific impact of cognitive and physical training on cognition, and brain structure and function

Several studies have shown the benefits of either cognitive (Table 4) or physical (Table 5) training on older adults' brain and cognition. Some models of aging consider that brain structure and function adapt and reorganize due to cognitive and physical training (STAC-R),[19] meaning that this non-pharmacological method induces plasticity in the aging brain. Cognitive and physical training are both said to improve and support cognitive functions and to delay neurodegenerative processes. Although both cognitive and physical training seem to have an impact on cognition and brain, each type of training has specific effects that are inherent to their respective natures. Below, we present the impact, first, of cognitive training and, second, of physical training on brain structure and function, and on cognition. Different meta-analysis and systematic reviews of these studies are available[20–25] and our purpose is not to exhaustively address all points that have been already discussed in these reviews. We focused especially on transfer to untrained tasks and to everyday life and on maintenance.

Cognitive training

In the present review, we focus on cognitive training, although other types of cognitive interventions[26] are used to improve cognition (eg, cognitive stimulation, cognitive rehabilitation). Cognitive training is based on the assumption that the aging brain and cognition can be improved through training (neuroplasticity) and uses repetitive exercises (laboratory made or commercial software such as Brain Aging, Big Brain Academy, and Brain Challenge) targeted at specific cognitive functions, such as memory, attention, or executive function. One or more functions can be targeted during one and the same training intervention[27] and the training can be performed individually or in small groups, although the work remains individual and there is no interaction with other people. The tasks are usually performed on a computer but pencil-and-paper exercises can also be proposed. On the behavioral level, exposure to cognitive training is supposed to improve performance of cognitive tasks and older adults' everyday life. On the brain level, it is thought to induce functional and structural changes that help to reduce cognitive decline. These training-related changes are measured by 1) cortical thickness and gray matter volume reflecting quantity and state of neurons, 2) integrity of the white matter reflecting structural connectivity, and 3) neuronal activity and functional connectivity in specific networks in the resting condition (default mode network or dorsal attention network) or in task-specific conditions.

All the studies of cognitive training cited in the present review are presented in Table 4. Globally, most of the studies that used appropriate, controlled intervention designs have shown beneficial effects (statistically significant differences between trained and control group, and pre-test and post-test) of cognitive training in older adults on performance in cognitive tasks (trained or untrained) and/or on brain function and structure. Improvements after training with laboratory tasks have, in particular, been found for working memory,[15,28] speed of processing,[29,30] and executive functions.[31,32] Some of the studies addressed the issue of using commercial brain training games,[33] and also showed a positive impact on older adults' cognition. Studies investigating changes on brain level are less frequent. Among the 32 studies listed in Table 4, only eight studies investigated the impact of cognitive training on brain structure and function. Four studies measured white matter integrity or connectivity,[16,25,34,39] two studies measured gray matter volume,[36,39] two studies measured cerebral blood flow (CBF),[34,36] and three studies measured functional activity.[32,37,38] The main positive structural changes have been reported after single or multi-domain training in white matter in frontal,[16] fronto-temporal,[34] occipitotemporal,[35] and occipital[16] regions. Functional changes, expressed by 1) changes in CBF,[34,36] 2) changes in functional connectivity,[16,35] 3) increase in task-related blood oxygen level dependent responses,[37] 4) increase of theta power,[32] and 5) decrease in N100 amplitude,[38] were reported. These functional changes occurred, in particular, in frontal, parietal, and occipital regions and in subcortical regions

Table 4 Detailed information of the cited studies concerning cognitive training

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
Ackerman et al[33]	78	60.7	NA	Nintendo Wii Big Brain Academy Software, verbal and visual working memory, executive functions and speed processing, reading sessions	NA	1 group cognitive training and reading sessions training	1 hour per day, 5 days per week during 8 weeks for each training (40 hours)	Wii performance, knowledge tests, cognitive abilities test battery (Gc, Gf, PS)	CT Increase of Wii task-specific improvements and of domain knowledge	No transfer to cognitive and perceptual speed abilities	2 months – no benefits due to training
Anguera et al,[32] Experiment 2	46	66.83	16.9	Video game training (NeuroRacer game – sign and drive tasks)	C	3 groups Multitasking (MTT) Single task (STT) Control no-contact (CNC)	1 hour per day, 3 days per week during 4 weeks (12 hours)	Sustained attention, UFoV, visual working memory, working memory, dual tasking, basic motor and speed of processing, EEG (event-related spectral perturbation, focused on middle frontal theta)	MTT Increase of reduction of multitasking cost in NeuroRacer game STT and MTT Increase of component task skills	MTT group: Increase of sustained attention Increase of working Memory EEG Increase of middle frontal theta power and long-range coherence	6 months maintenance of reduction of multitasking cost in NeuroRacer game for MTT group
Ball et al,[44] ACTIVE study	2,832	73.6	13	Memory, reasoning, or speed processing training	RC	4 groups Memory (MEM) Reasoning (REA) Speed (SPE) vs control group (CG)	10 sessions 2 times per week (12 hours 30 minutes)	Episodic verbal memory (RAVLT, HVLT, RBPR), reasoning (letter series, letter sets, words series), speed of processing (UFoV),	NA	REA Increase of reasoning performance SPE Increase of speed processing MEM Increase of memory performance	2 years Maintenance of: REA Reasoning performance enhancement SPE Speed processing enhancement MEM Memory

(*Continued*)

Table 4 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
								daily functioning (IADL, EPS, EPT, OTDL, ES, CRT, timed IADL)			performance enhancement
Basak et al[28]	40	69.39	15.9	Video game (rise of nations) training	C	2 groups Rise of nations (RON) vs CG – no training, no contact	4–5 weeks (23 hours 30 minutes)	Operation span, task switching, n-back task, visual short-term memory, Raven's Advanced Matrices, stopping task, functional field of view, attentional blink task, enumeration, mental rotation	Increase of scores on RON (time spent on the game, number of wonders built, speed of playing)	Better performance in RON group than in CG: Increase of mental rotation Increase of task switching Increase of n-back Increase of visual short-term memory Increase of Raven's Advanced Matrices	NA
Berry et al[38]	30	71.93	17.24	Perceptual training (Sweep Seeker program)	RC	2 groups Perceptual training (PT) vs CG	40 minutes per day, 3–5 days per week during 3–5 weeks (10 hours)	Trained perceptual task Untrained perceptual task, working memory task, EEG (event related potential focused on N100)	PT Increase of perceptual discrimination abilities (accuracy and speed) on trained task	PT group better performance in than CG group Increase of untrained perceptual task Increase of working memory EEG decrease in N1 amplitude after training correlated with WM improvement	NA

Borella et al[15]	40	69.08	9.3	Working memory training (CWMS)	RC	2 groups WMT vs CG	1 session every 2 days during 2 weeks (8 hours)	CWMS, vocabulary, digit span forward and backward, pattern comparison (speed processing), Stroop, Dot Matrix (visuo-spatial WM), Cattell (fluid intelligence)	WMT Increase of verbal working memory	WMT group better performance than CG group: Nearest increase of visuo-spatial WM Near Increase of short-term WM Far Increase of fluid intelligence Increase of processing speed	8 months Maintenance of fluid intelligence and processing speed benefits for WMT group
Brehmer et al[42]	45	63.8	15.3	Spatial and verbal working memory training (Cogmed)	RC	2 groups WMT vs active control (AC)	26 minutes per day, 4–5 days a week during 5 weeks (10 hours)	Digit spans, PASAT, Stroop, RAVLT, Raven, Questionnaire – CFQ	WMT Increase of Cogmed	WMT group better performance than CG group Near Increase of spans Far Increase of PASAT Far Decrease of memory complain in everyday life	3 months Maintenance of short-term and working memory benefits, and decrease of memory complain for WMT group and of PASAT improvements for AC group
Buschkuehl et al[81]	39	80	NA	Working memory training	RC	2 groups WMT vs AC	45 minutes per day, 2 days a week during 3 months (18 hours)	Trained working memory tasks, digit spans, block spans, verbal free recall (WAIS), visual free recall (computerized memory function test)	WMT Increase of trained working memory tasks	WMT Near Increase of block span Far Increase of visual episodic memory	12 months No significant group differences between pre-test and follow-up
Cao et al[16]	48	70.1	10.2	Memory, reasoning, processing speed, attention, strategy, and/or problem-solving training	RC	3 groups Multi-domain cognitive training (MCT) vs single-domain cognitive training (SCT) vs CG	24 sessions over 12 weeks (24 hours)	CMMSE, RBANS, Stroop, CWST Word interference,	NA	NA	12 months MCT Increase of RBANS total score, language index score,

(*Continued*)

Table 4 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
								VRT, CTT 1 and 2, ADL, MRI (DTI) (only follow-up) – white matter integrity			attention index score, delayed memory index score, visual reasoning, ADL SCT Increase of RBANS total score, visuospatial/
Cao et al[16]	48	70.1	10.2	Memory, reasoning, processing speed, attention, strategy, and/or problem-solving training	RC	3 groups Multi-domain cognitive training (MCT) vs single-domain cognitive training (SCT) vs CG	24 sessions over 12 weeks (24 hours)	CMMSE, RBANS, Stroop, CWST Word interference, VRT, CTT 1 and 2, ADL, MRI (DTI) (only follow-up) – white matter integrity	NA	NA	12 months MCT Increase of RBANS total score, language index score, attention index score, delayed memory index score, visual reasoning, ADL SCT Increase of RBANS total score, visuospatial/constructional index score, attention index score, visual reasoning DTI Decrease of axial diffusivity in posterior

											parietal white matter in MCT group, fractional anisotropy downgrading, mean and radial diffusivity augmentation in SCT group
Cavallini et al[47]	60	Young adults (YA) = 24.1 Younger elderly (YE) = 64.2 Older elderly (OE) = 74.4	NA	Loci mnemonics training (LMT) and strategic training (ST)	C	6 groups Young adults LMT (YA LMT) vs Young adults ST (YA ST) vs Younger elderly LMT (YE LMT) vs Younger elderly ST (YE ST) vs Older elderly LMT (OE LMT) vs Older elderly ST (OE ST)	9 sessions over 3 months (13 hours 30 minutes)	Ecological memory tasks (story recall, shopping list recall, memory for activities planned for the week, memory for faces/names, memory for places), digit spans, memory for lists of figures, memory for word-lists, metamemory questionnaire, everyday memory questionnaire, self-efficacy questionnaire	NA	No differences due to training type (except memory for places) Improvement due to trainings (LMT and ST) in all memory tasks but more important in ecological memory tasks YA and OA estimate higher level of memory performance after training	NA
Chapman et al[34]	37	62.5	NA	Strategic attention, integrated reasoning, innovation	RC	Cognitive training (CT) vs CG	1 session per week in groups, 2 individual sessions per week during 12 weeks (36 hours)	Trained function measure (test of strategic learning), non-trained function measures (TMT, CVLTII, similarities, backward digit span, color word interference, working memory, DKEFS) MRI (CBF, DTI)	NA	CT relative to CG Increase of test of strategic reasoning, similarities Increased CBF and functional connectivity in default mode network and central executive network, increased white matter integrity in left uncinated fasciculus	NA

(*Continued*)

Table 4 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
Cheng et al, 2012	270	70.25	9.56	Memory, reasoning, problem solving, visuospatial abilities, health and physical exercise (multi-domain cognitive training) – different types of reasoning training (single cognitive training)	RC	3 groups MCT and SCT vs CG	2 sessions a week over 12 weeks (24 hours)	MMSE RBANS, Stroop, VRT, TMT	NA	MCT Increase of RBANS total, immediate and delayed memory, visual reasoning, SCT Increase of RBANS total, visuo-spatial abilities, visual reasoning, word interference, language	6-months SCT Increase of RBANS language 12-months MCT Increase of RBANS total and immediate and delayed memory, visual reasoning, language SCT Increase of word interference
Dahlin et al[37]	64	YA = 23.88 OA = 68.32	YA = 13.61 OA = 13.27	Updating in working memory training (numbers, letters, colors, spatial locations) keep-track task	PR	4 groups Young adults trained (YAT) vs young adults control (YAC) vs older adults trained (OAT) vs older adults control (OAC)	3 sessions per week during 5 weeks (11 hours 15 minutes)	Letters memory task (criterion updating task), perceptual speed (digit symbol substitution), working memory tasks (computation span, digit spans, n-back task), episodic memory (recall of concrete nouns, pair-association learning), verbal fluency, reasoning	YAT and OAT Increase of all trained tasks	YA and OA Increase of letters memory task (criterion task) YA Increase of 3-back task, recall of concrete nouns	18 months YA and OA Maintenance of letters memory enhancement (criterion task) YA Maintenance of 3-back effect

Dahlin et al[90]	NA	YA OA	NA	Updating in working memory training (numbers, letters, colors, spatial locations) keep-track task	NA	4 groups YAT vs YAC vs OAT vs OAC	3 sessions per week during 5 weeks (11 hours 15 minutes)	Letter memory task (criterion up-dating task), working memory tasks (n-back task), Stroop, fMRI	YAT and OAT Increase of updating in working memory	YAT Increase of letter memory, 3-back fMRI greater activity after training in left striatum for 3-back and letter memory task OAT Increase of letter memory fMRI greater activity after training in left striatum for letter memory task	NA
Heinzel et al[39]	38	YA = 24.1 OA = 66.00	YA = 16.36 OA = 15.61	Working memory training (n-back task)	C	2 groups YAT vs OAT	12 training sessions over 4 weeks (9 hours)	Digit spans, D2, digit symbols substitution, verbal fluency, Stroop interference, Raven's SPM, figural relations fcMRI (GMV)	YA and OA Increase of working memory	OA Increase of digit spans forward, D2, digit symbols substitution, Stroop interference, figural relations, MRI no changes in gray matter volume and functional connectivity in WM network, no changes in blood oxygen level dependent response in WM network	NA
Heinzel et al[39]	62	YA : 25.9 OA : 66.07	YA : 17.9 OA : 16.07	Working memory training (n-back task)	PR	4 groups YAT vs YAC vs OAT vs OAC	3 sessions per week during 4 weeks (9 hours)	Digit spans (short-term memory), CERAD immediate and delayed	YA and OA Increase of working memory (n-back task) YA > OA	YAT better performance than YAC in digit symbol substitution, verbal fluency	NA

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Table 4 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
								recall (episodic memory), digit symbols substitution (processing speed), verbal fluency (executive functions), Raven's Progressive Matrices (fluid intelligence), figural relations test		OAT better performance than OAC in digit span forward, delayed recall, digit symbol substitution	
Karbach and Kray[31]	56 each age group	Children = 9.2, YA = 22.4, OA = 68.7	NA	Task switching training, task switching plus verbal self-instruction training, task switching plus verbal self-instruction training plus training variability, single task training	C	3 groups OA vs children vs YA	4 sessions (2 hours 40 minutes)	Stroop, verbal working memory, spatial working memory, fluid intelligence	All age groups: Decrease of switching cost, but reduction less pronounced in variability group during training	Near (switching task) All age groups: Decrease of mixing and switching cost greater after task switching trainings than single task training, and greater in children and OA than YA Far All age groups after task switching training Decrease of reduction of interference (Stroop task) Increase of verbal and spatial WM, and of fluid intelligence	NA

Li et al[41]	87	YA = 25.85 OA = 73.9	NA	Spatial working memory training (2-back)	PR	4 groups YAT vs YAC vs OAT vs OAC	1 time per day during 45 days (11 hours 15 minutes)	3-Back spatial WM task, 2- and 3-back numerical WM tasks, complex span, simple decision speed	YA and OA Increase of 2-back spatial WM task	YAT and OAT Near Increase of 3-back spatial WM task Far Increase of 2- and 3-back numerical WM tasks	3 months Maintenance of benefits for YAT and OAT for: 2-and 3-back spatial WM, and 2-and 3-back numerical WM
Mahncke et al[83]	182	70.9	16.3	Auditory-language training	RC	3 groups CT vs AC vs no contact control group (NCC)	5 days per week during 8–10 weeks (40 hours)	RBANS (6 auditory cognition tests) + for CT group only speed of processing, forward aural speech recognition span	CT Increase of all trained tasks	CT Increase of auditory memory	3 months Maintenance of memory enhancement
McAvinue et al[48]	36	70.5	NA	Auditory and visuospatial short-term and working memory	RC	2 groups Adaptive cognitive training (ACT) vs non-adaptive training control group (NATCG)	5 sessions per week during 5 weeks (12 hours 30 minutes)	Digit spans, Letter-number sequencing (short-term and WM) Word and story recall immediate and delayed (episodic memory) Goals questionnaire, ARCES and MFS	NA	ACT larger improvement than NATCG in digit span forward, delayed word recall ACT and NATCG improvement of scores on all questionnaires	3 and 6 months Maintenance of training effects on digit span forward ACT and NATCG Maintenance of improvement of scores on all questionnaires
Mozolic et al[36]	48	69.3	15.5	Visual and auditory selective attention (suppression of distracting background noise)	NA	2 groups CT vs AC	1 session per week during 8 weeks (8 hours)	MRI (CBF, GMV)	NA	CT Increase of CBF in right inferior frontal cortex linked to decrease of distractibility	NA
Mozolic et al[91]	66	69.4	15.8	Visual and auditory selective attention (suppression of distracting background noise)	RC	2 groups CT vs AC	A session per week during 8 weeks (8 hours)	2 Tasks of visual selective attention (cross-modal or within modal distractors) Audiovisual multisensory	NA	CT Decrease of cross-modal interference Decrease of multisensory integration during auditory and visual selective attention,	NA

(*Continued*)

Table 4 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
								integration task Symbol digit modalities Test, Walk and talk paradigm, n-back task, Stroop, TMT, HVLT, POMS, HSQ-12,		Increase of processing speed (Symbol Digit Modalities Test) Increase of dual-task performance, n-back task, TMT	
Rebok et al,[29] ACTIVE study	2,832	73.6	13	Memory, reasoning, or speed processing training	RC	4 groups MEM REA SPE vs CG	10 sessions 2 times per week (12 hours 30 minutes)	Episodic verbal memory (RAVLT, HVLT, RBPR), reasoning (letter series, letter sets, words series), speed of processing (UFoV), daily functioning (IADL, EPS, EPT, OTDL, ES, CRT, timed IADL)	NA	REA Increase of reasoning performance SPE Increase of speed processing MEM Increase of memory performance	1, 2, 3, 5, 10 years Maintenance of REA reasoning performance enhancement SPE speed processing enhancement 1, 2, 3, 5 years MEM Maintenance of memory performance enhancement 5, 10 years All trained groups as compared to CG – estimation of better quality of life

Richmond et al[84]	40	66	17	Working memory training	RC	2 groups CT vs AC	5 days per week during 5 weeks (12 hours 30 minutes)	Complex, digit, and reading spans (short and working memory) TEA (attention), CVLT (verbal memory), Raven's Progressive Matrices (fluid intelligence) Questionnaire of general cognitive change	CT Increase of working memory trained task	CT Near Increase of reading span Far Increase of memory (reduction of repetition in CVLT) Increase of self-reported improvement in everyday memory	NA
Schmiedek et al[30]	204	YA = 25.4 OA = 71	YA = 15.9 OA = 13.3	Perceptual speed, working memory, and episodic memory training	PR	4 groups YAT vs OAT vs YAC vs OAC	1 session per day during 100 days (100 hours)	Working memory – updating (animal span, 3-back numerical, memory updating span), Working memory complex spans (reading span, counting span, rotation span), episodic memory (word pairs), Raven's Matrices, paper-and-pencil BIS test	Both age groups Increase of trained task (except word list in older adults)	Near Working memory YA: Increase of 3-back numerical OA: Increase of animal span Far Working memory OA: Increase of rotation span Reasoning YA: Increase of BIS numerical and figural-spatial OA Increase of Raven Episodic memory YA: Increase of BIS verbal, numerical, figural-spatial, OA Increase of word pairs	NA

(*Continued*)

Table 4 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
Smith et al[46]	487	75.3	15.7	Speed and accuracy of auditory information processing,	NA	2 groups CT vs AC	5 days per week during 8 weeks (40 hours)	RBANS (auditory memory/attention), RAVLT, RBMT (immediate and delayed recall), WMS-III (letter-number sequencing, digit span backwards), CSRQ-25, LSS, CFQ, GDS	NA	**CT** greater improvement than AC: RBANS RAVALT, digit span backward, processing speed, CRSQ-25	NA
Stepankova et al[85]	68	68	15	Working memory (verbal version of n-back task)	RC	3 groups Cognitive training low-frequency (CTL) vs cognitive training high-frequency (CTH) vs CG	2–4 days per week during 5 weeks (20–40 hours)	Working memory (digit spans, letter-number sequencing), visuospatial skills (block design, matric reasoning), verbal version of n-back task	CTL and CTH Increase of n-back trained task	CTL and CTH Increase of visuospatial skills Increase of working memory CG group Increase of visuospatial skills	NA
Strenziok et al[35]	42	69.21	16.4	Video game training: brain fitness (auditory perception), space fortress (visuomotor/working memory), rise of nations (strategic reasoning)	NA	3 groups Brain fitness (BF) vs Space fortress (SF) vs RON	6 days (6 hours)	Reasoning (WAIS III matrix reasoning, EPT), episodic memory (WMS logical memory subset), working memory (visuospatial delayed matching-to-sample task, letter number sequencing, spatial working memory task)	Increase of scores in BF, SF, RON games	BF Increase of everyday problem solving Increase of reasoning (matrix reasoning, ETP) SF Increase of working memory Increase of reasoning	NA

								MRI (DTI)		(EPT) MRI BF Strongest changes in axial diffusivity in temporo-occipital junction, reduced functional connectivity between SPC and ITL SF reduced functional connectivity between SPC and ITL	
von Bastian et al[86]	123	YA = 23.27 OA = 68.42	NA	Working memory storage and processing (numerical complex span), relational integration tower of fame), supervision (figural task switching)	PR	4 groups YAT vs OAT vs young adults active control (YAAC) vs older adults active control (OAAC)	20 sessions over 4 weeks (10 hours)	Different version of trained tasks (near transfer), working memory (intermediate transfer: binding, N-back), reasoning (far transfer: Raven's Matrices, BOMAT) Quiz on general knowledge	YAT and OAT Increase of trained task performance except figural task switching, with larger improvement in YAT	Near YAT and OAT Increase of verbal complex span Intermediate YAT Increase of word-position binding in working memory	NA
Willis et al,[45] ACTIVE study	2,832	73.6	13	Memory, reasoning or speed processing training	RC	4 groups MEM REA SPE vs CG	10 sessions 2 times per week (12 hours 30 minutes)	Episodic verbal memory (RAVLT, HVLT, RBPR), reasoning (letter series, letter sets, words series), speed of processing (UFoV), daily functioning (IADL,	NA	REA Increase of reasoning performance SPE Increase of speed processing MEM Increase of memory performance	1, 2, 3, 5 years Maintenance of REA reasoning performance enhancement SPE speed processing enhancement 1, 2, 3, 5 years MEM

(*Continued*)

Table 4 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (groups)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Transfer to cognitive tasks or changes in brain structure and/or function (post-training immediate measures)*	Follow-up
								EPS, EPT, OTDL, ES, CRT, timed IADL)			Maintenance of memory performance enhancement 5 years All trained groups as compared to CG – estimation of better quality of life
Wolinsky et al[87]	1,534	73.6	13	Memory, reasoning or speed processing training	RC	4 groups MEM REA SPE vs CG	10 sessions 2 times per week (12 hours 30 minutes)	Internal locus of control (12-item cognitive-specific scales of Lachman et al[89])	NA	REA and SPE Increase of internal locus of control	5 years Maintenance of internal locus of control for: REA and SPE
Zinke et al, 2013	80	77.2	14	Visuospatial and verbal working memory training, executive control	RC	2 groups CT vs CG	9 sessions over 3 weeks (4 hours 30 minutes)	Corsi bloc span, letter span plus task Tower of Hanoi (near transfer), Raven's Matrices, Stroop (far transfer)	CT increase of trained task performance	CT Near Increase of letter-span plus task (verbal working memory) Far Increase of Raven's Matrices (fluid intelligence)	9 months Maintenance of benefits of training in trained task and transfer to verbal working memory

Note: *Data in this column may show both items or just one of the items shown in the heading.

Abbreviations: ADL, activities of daily living; ARCES, Attention-Related Cognitive Errors Scale; BIS, Berlin Intelligence Structure test; BOMAT, Bochumer Matrizentest; C, controlled study; CBF, cerebral blood flow; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; CFQ, Cognitive Failures Questionnaire; CMMSE, Chinese version of Mini Mental State Examination; CRT, complex reaction time; CSRQ-25, 25-item Cognitive Self-Report Questionnaire; CTT, Colour Trials Test; CVLT, California Verbal Learning Test; CWMS, Categorization Working Memory Span Task; CWST, Colour-Word Stroop Test; D2, test of attention; DKEFS, Delis Kaplan Executive Function System; DTI, diffusion tensor imaging; EEG, electroencephalogram; EPS, everyday problem solving; EPT, everyday problem test; ES, everyday speed of processing; fMRI, functional magnetic resonance imaging; Gc, crystallized intellectual abilities; GDS, Geriatric Depression Scale; Gf, fluid intellectual abilities; GMV, gray matter volume; HSQ-12, 12-Item Health Status Questionnaire; HVLT, Hopkins Verbal Learning Test; IADL, Instrumental Activities of Daily Living; LSS, Life Satisfaction Scale; MEM, memory training group; MFS, Memory Failures Score; MMSE, Mini Mental State Examination; MRI, magnetic resonance imaging; NA, not applicable.; OTDL, observed tasks of daily living; PASAT, Paced Auditory Serial Addition Test; POMS, profile of mood states; PR, pseudo-randomized study; PS, perceptual speed; RAVLT, Rey Auditory Verbal Learning Test; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; RBMT, Rivermead Behavioral Memory Test; RBPR, Rivermead Behavioural Paragraph Recall; RC, randomized controlled study; REA, reasoning training group; SPE, speed processing training group; SPM, Standard Progressive Matrices; TEA, Test of Everyday Attention; TMT, trail making test; U, uncontrolled pre–post study; UFoV, useful field of view; VRT, visual reasoning test; WAIS, Wechsler Adult Intelligence Scale; WM, working memory; WMS, Wechsler Memory Scale; WS, within subject study.

Table 5 Detailed information of the cited studies concerning physical training

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (group)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Impact on brain structure or function, or cognition, or physical health*	Follow-up
Boyke et al, 2008	69	60	NA	Juggling training	RC	2 groups Jugglers vs controls	12 weeks	MRI (VBM)	10 of 44 individuals accomplished 60 seconds of endurance juggling 15 individuals accomplished between 40 and 60 seconds of endurance juggling	Jugglers Increase of gray matter in the hMT/V5 area, right hippocampus and nucleus accumbens bilaterally	3 months No maintenance of benefits
Cassilhas et al[70]	62	68.15	NA	Resistance training	RC	3 groups Moderate physical training (MPT) vs high physical training (HPT) vs active control group (AC)	3 sessions per week during 24 weeks (72 hours)	Resistance measures (chest press, leg press, vertical traction, abdominal crunch, leg curl, lower back) Neuropsychological tests: WSM-R, digit spans, similarities, Corsi blocks, RCF, Toulouse-Pieron's attention test Questionnaires: POMS, GDS, SF-36 Hemodynamic measures, body measures, 1-RM test – intensity measure	MPT and HPT Increase of all resistance measures, higher improvement than AC in 1-RM test scores	MPT and HPT higher improvement than AC in digit span forward, Corsi's block backward, similarities, Rey's figure immediate recall, POMS, SF-36 MPT higher improvement than AC Toulouse-Pieron test	NA
Chapman et al[60]	37	64	NA	Aerobic training (bike and treadmill)	RC	2 groups Physical training (PT) vs control group (CG)	3 sessions per week during 12 weeks (36 hours)	Physiological measures (weight, heart rate, VO_2 max, RPE) Neuropsychological measures (TMT, CVLT-II, WMS-II, DKEFS-color word, backward digit spans) MRI (CBF)	PT Increase of VO_2 max, RPE	PT relative to CG Increase of immediate and delayed text memory MRI Increase of relative cerebral blood flow in anterior cingulate bilaterally	NA
Colcombe et al[17] (Study 2)	29	65.60	15.1	Aerobic or stretching and toning	RC	2 groups Aerobic training (AT) vs stretching and toning group vs AC	3 times per week during 24 weeks (54 hours)	Physiological measures (VO_2 max), Flanker task, fMRI	AT relative to AC Increase of VO_2 max Resistance to interference	AT relative to AC Decrease of reduction in conflict (flanker task) fMRI Increase of task-related activity in attentional control	NA

(*Continued*)

Table 5 (*Continued*)

References	N	Mean age (years)	Mean education (years)	Intervention	Study design	Trained functions (group)	Frequency and duration of training (total hours)	Measures	Results (trained task)	Impact on brain structure or function, or cognition, or physical health*	Follow-up
										areas (middle frontal gyrus, superior frontal gyrus, and superior parietal lobule)	
Liu-Ambrose et al[63]	74	82.25	NA	Home-based resistance and balance training	RC	2 groups Resistance and balance training (RBT) vs CG	3 sessions (30 minutes) per week 6 months	TUG (functional mobility), Physiological Profile Assessment (physiological falls risk) Executive functioning (shifting – TMTB, updating – verbal digit backward, span, inhibition – Stroop), Physiological falls risk PASE questionnaire	NA	RBT as compared to CG Improvement of response inhibition (Stroop) Reduction of falls	12 months Reduction of falls
Liu-Ambrose et al[61]	155	69.6	NA	Resistance training (RT) or stretching (AC – balance and tones exercises)	RC	3 groups High-frequency resistance training (HRT) vs low-frequency resistance training (LRT) vs AC (stretching)	1–2 sessions per week during 12 months (48–96 hours)	TUG (functional mobility), gait speed, 1-RM, peak muscle power Executive functions (Stroop, TMT, verbal digit spans) MRI (whole brain volume)	NA	HRT and LRT Increase of selective attention and conflict resolution (Stroop) Increase of gait speed HRT Increase of peak muscle power MRI Decrease of whole brain volume in HRT and LRT	NA
Sink et al[58]	1,635	70–89 (range)	>9	Walking, resistance, and flexibility training or health education program	RC	2 groups PT vs AC (health education)	3–4 sessions per week during 24 months (320 hours)	Cognitive functions: Digit symbol coding (WAIS), HVLT-R, TMT, category fluency, speed of processing and executive function (flanker task, n-back, switching task) FAQ	NA	No effects of training	NA
Voelcker-Rehage et al[68]	91	69.6	12.8	Cardiovascular or coordination training –		3 groups Cardiovascular training (CT)	3 sessions per week during 12 months (144 hours)	Cognitive functions: Flanker – executive		Increase of cardiovascular fitness after 12 months in CT group	NA

				relaxation and stretching	RC	vs coordination training (COT) vs AC		control, visual search – perceptual speed, cardiovascular fitness – oxygen consumption (calculation of heart rate), motor fitness – action speed and reaction speed, fMRI – during Flanker test	NA	Increase in CT and COT groups of action speed fMRI Decrease of activation in several superior, middle and medial frontal areas in CT group Increase of activation in some frontal, parietal areas, and subcortical structure in COT group	
Voss et al[53]	70	64.87	16.1	Aerobics (walking) or flexibility, toning and balance exercises (active control group)	RC	2 groups AT vs AC	48 weeks (32 hours)	VO_2 max, digit spans, spatial working memory task, task switching, Wisconsin card sorting task MRI (DTI – cerebral white matter integrity)	NA	AT relative to AC: Increase of VO_2 max Increased VO_2 max associated with increased backward digit span MRI: Increased VO_2 max associated with increase fractional anisotropy in prefrontal, parietal, and temporal lobes and greater improvement in short-term memory in AT group	NA
Voss et al[59]	65	66.34	YA = 15.87 OA = 15.9	Aerobics (walking) or non-aerobic fitness (stretching and toning)	RC	2 groups AT vs AC	48 weeks	VO_2 max, BMI Digit spans, spatial working memory task, task switching, Wisconsin card sorting task MRI (DTI), fMRI	NA	VO_2 max – not provided Increase in digit span performance associated to increase of aerobic fitness in AT group AT and AC Increase in functional connectivity in default mode network and frontal parietal network After 12 months, larger increase in connectivity in default mode network and frontal executive network in AT group	NA

Note: *Data in this column may show just 1, 2, or all 3 items shown in the heading.

Abbreviations: BMI, body mass index; C, controlled study; CBF, cerebral blood flow; CVLT, California Verbal Learning Test; DKEFS, Delis Kaplan Executive Function System; DTI, diffusion tensor imaging; FAQ, Functional Assessment Questionnaire; fMRI, functional magnetic resonance imagery; GDS, Geriatric Depression Scale; HVLT, Hopkins Verbal Learning Test; MRI, magnetic resonance imagery; NA, not applicable.; PASE, Physical Activities Scale for the Elderly; POMS, profile of mood states; PR, pseudo-randomized study;RC, randomized controlled study; RCF, Rey complex figure; RPE, rating of perceived exertion; SF-36, Short Form 36; 1-RM, single-repetition maximum lift; TMT, Trail Making Test; TMTB, Trail Making Test version B; TUG, timed-up and go; U, uncontrolled pre–post study; VBM (voxel-based morphometry); VO2 max, maximal oxygen consumption; WAIS, Wechsler Adult Intelligence Scale; WMS, Wechsler Memory Scale; WS, within subject study.

Table 6 Detailed information of the cited studies concerning cognitive and physical training

References	N	Age (years)	Education (years)	Intervention	Study design	Trained functions (group)	Frequency and duration of training (total hours)	Measures	Results (trained tasks)	Impact on brain structure or function, or cognition, or physical health*	Follow-up
Combined cognitive and physical training											
Frantzidis et al[79]	103	68.9	NA	Brain fitness (auditory perception – cognitive training) and Nintendo Wii – Balance Board (physical training)	RC	2 groups Cognitive and physical training (CPT) vs active control group (AC)	1 hour 3 to 5 days per week during 8 weeks (cognitive training)	EEG	NA	CPT relative to AC: Increase of synchronization at rest	NA
Linde and Alfermann[62]	70	67.5	NA	Processing speed, attention, sensory, short- and long-term memory, visuospatial skills, logical reasoning, concentration and/or aerobic endurance and strength training	RC	4 groups Cognitive training (CT), physical training (PT), combined cognitive plus physical training (CCP), control group (CG)	2 sessions per week during 16 weeks (32 hours)	Cognitive measures (reasoning – LPS50+, concentration – 2D, processing speed – TMTA, short-term memory – word list test, cognitive speed – digit-symbol substitution) Physiological measure (VO_2 max)	NA	CT, PT, and CCP as compared to CG Increase of concentration CPP Increase of cognitive speed VO_2 max – no changes	3-months follow-up PT Maintenance of concentration gains CPP Maintenance of cognitive speed gain CP as compared to CG Increase of cognitive speed
Oswald et al[73]	375	79.5	NA	Fluid abilities, attention, memory, balance, perceptual and motor coordination, flexibility, psychoeducation	RC	6 groups CT, PT, CCP, psychoeducational training (PE), combined psychoeducational plus physical training (CPP), CG	A session per week during 30 weeks (45 hours)	Cognitive measures (NC-G, MT-G, DS-G, NAI, ACT, CWT-G, MS-G, ST, PT, FT, WL, WP, WAIS-info, word fluency, WAIS-sim, SCAG), physical measures (KTK, bending, arm-lifting test, KT, TTAC, TTJC, walking and running tests, HT), emotional status (SDS), independent living (scale of independence), health status (clinical assessment of organ functions, self-rating of perceived health),	NA	CT Increase of cognitive function CCP Increase of cognitive function, emotional status, physical function, and independent living CPP Increase of independence living Increase of everyday competence	5 years follow-up CCP Increase of cognitive function, emotional status, and independent living

							subjective aging (NSL-S), quality of life (NLQ-S), general well-being (NSW-S)			
Pieramico et al[78]	30	60–75	8–18	Multimodal training (cognitive, aerobic training and sensorial stimuli, fun-recreational activities)	RC	2 groups Multimodal training (MCT) vs CG	6 days per week during 6 months	MMSE (prose memory), TMT, executive functions (FAB, FAS), prose memory (Babcock story), motor and process skills (OT-E motor skills and process skills) MRI, fcMRI (cortical thickness) Dopamine-related gene polymorphisms	NA	MT Increase of long-term prose memory, process skills MT Changes in strength of functional connectivity in default mode network and dorsal attentional network Carriers of DRD3 ser9gly and COMT Val158Met polymorphisms – greater benefits from MCT	NA
Rahe et al[74]	30	66.73	15.6	Cognitive training (memory, attention, executive functions), physical training (strength, flexibility, coordination)	C	2 groups Single cognitive training (SCT) vs CPT	6.5 weeks (19 hours 30 minutes)	DemTect test, figural memory (CFT, RCF, MTF tests), auditory divided attention (BTA) executive functions (TMT, semantic and letter fluency), working memory, self-reported physical activity (IPAQ, MET-score)	NA	SCT and CPT Increase of divided attention, immediate memory CPT Increase of general cognitive state, delayed memory, verbal fluency, MET-score, IPAQ	12 months follow-up CPT Increase of divided attention, general cognitive state, delayed memory, verbal fluency SCT Increase of immediate memory, verbal fluency
Shah et al[77]	191	67.6	NA	Cognitive training (brain fitness and visual-based programs), physical training (walking, resistance)	C	4 groups PT vs cognitive stimulation (CS) vs CPT vs CG	16 weeks (PT: 69 hours CS: 40 hours CPT: 160 hours)	Cognitive measures CAMCOG-R, RAVLT, COWAT, CogState battery, Detection, N-back, Groton maze learning, visual memory, questionnaires (HADS, MFQ, SF-36)	NA	CPT as compared to CG Increase of long-term delayed verbal memory CG Better memory functioning (MFQ) CPT and PT	NA

(*Continued*)

Table 6 (*Continued*)

References	N	Age (years)	Education (years)	Intervention	Study design	Trained functions (group)	Frequency and duration of training (total hours)	Measures	Results (trained tasks)	Impact on brain structure or function, or cognition, or physical health*	Follow-up
								Physical fitness (total sum of strength, distance, Borg's scale) PET (cerebral glucose metabolism)		Increase of walking distance CPT Increase of glucose metabolism in left sensorimotor cortex	
Theill et al[75]	63	71.8	13.9	Walking, verbal working memory training (n-back task, serial position training)	C	3 groups Simultaneous training (ST) vs single working memory training (SWMT) vs CG	2 sessions per week during 10 weeks (10 hours)	Motor-cognitive dual task, executive control, reasoning, memory span, processing speed, selective attention, paired-associate learning	ST and SWMT Linear progress in n-back and serial position tasks performance during training	ST and SWMT Increase of cognitive control ST Increase of motor-cognitive dual task performance Larger improvement in ST group than SWMT for paired-associates learning	NA
Wenger et al[76]	118	YA = 26.05 OA = 64.95	NA	Spatial navigation in virtual reality + walking on treadmill or walking on treadmill training alone	RC	4 groups Young adults navigation + walking (YNW) vs young adults walking (YW) vs older adults navigation + walking (ONW) vs older adults walking (OW)	42 training sessions (50 minutes each) during around 118 days (35 hours)	Digit symbols, Raven's Matrices Navigation performance MRI (cortical thickness)	Not provided	YNW and ONW Increase of navigation performance (nearest transfer) YNW Increase of cortical thickness (left precuneus, left paracentral lobule)	4 months Maintenance of navigation performance gain
Direct comparison of cognitive and physical training alone											
Chapman et al[66]	36	63.5	NA	Memory advanced reasoning training – SMAR (metacognitive strategies – strategic attention, integrative reasoning,	RC	2 groups CT vs PT	3 hours per week during 12 weeks (36 hours)	Physiological measures (weight, heart rate, VO_2 max, RPE) Cognitive measures (test of strategic learning, similarities – WAIS-III,	NA	CT as compared to PT Increase of CBF (orbital, medial, and middle frontal cortices) CT as compared to PT	NA

				innovation) – Aerobics (walking on treadmill, stationary cycling)				working memory, DKEFS, COWAT, category and letter fluency, TMT B, CVLT, WMS-II MRI (CBF)		Increase of strategic learning, working memory PT as compared to CT Increase of immediate and delayed text memory PT as compared to CT Decrease of RPE	
Chapman et al[67]	58	63.3	NA	Memory advanced reasoning training – SMAR (metacognitive strategies – strategic attention, integrative reasoning, innovation) Aerobics (walking on treadmill, stationary cycling)	RC	3 groups CT vs PT vs CG	3 hours per week during 12 weeks (36 hours)	Cognitive measures (test of strategic learning – MIM subtest) MRI (CBF, VBA), fcMRI	NA	CT as compared to PT and CG Increase of CBF (medial orbitofrontal cortex, PCC), correlation between innovative performance and increased functional connectivity in central executive network and default mode network CT Increase of innovation performance	NA
Håkansson et al[69]	23	70.8	8	Working memory training (CogMed), physical aerobic exercise (Xbox Kinect), or mindfulness practice (Mindfulness App)	RC	3 groups Cognitive (COG) vs physical (PHY) vs mindfulness (MIN)	1 session (1 hour)	Physiological measure (RPE) BDNF in serum WM performance	NA	PHY Increase of BDNF level Positive correlation between working memory performance and BDNF	NA

Note: *Data in this column may show just 1, 2, or all 3 items shown in the heading.

Abbreviations: ACT, aging concentration test; BDNF, brain-derived neurotrophic factor; BTA, Brief Test of Attention; C, controlled study; CAMCOG, Cambridge cognitive assessment; CBF, cerebral blood flow; CFT, complex figure test; COWAT, Controlled Oral Word Association Test; CVLT, California Verbal Learning Test; CWT-G, color word test; D2, test of attention; DKEFS, Delis Kaplan Executive Function System; DS-G, digit symbol substitution test; EEG, electroencephalogram; FAB, Frontal Assessment Battery; FAS, phonemic verbal fluency; fcMRI, functional connectivity magnetic resonance imagery; FT, figure test; HADS, Hospital Anxiety and Depression Scale; HT, handgrip test; IPAQ, International Physical Activity Questionnaire; KT, Knocking Test; KTK, physical coordination test; LPS50+, Leistungs-Prüf-System 50+; MET, metabolic equivalent; MFQ, Memory Functioning Questionnaire; MIM, Multiple Interpretations Measure; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imagery; MS-G, memory span; MTF, Modified Taylor Figure; MT-G, Maze Test; NA, not applicable; NAI, neuropsychological aging inventory; NC-G, number connection test; NLQ-S, self-rating questionnaire: neuropsychological assessment of life quality; NSL-S, self-rating questionnaire: neuropsychological symptom list; NSW-S, self-rating questionnaire, neuropsychological assessment of subjective well-being; OT-E, occupational therapy evaluation; PCC, posterior cingulate cortex; PET, positron emission tomography; PR, pseudo-randomized study; PT, picture test; RAVLT, Rey Auditory Verbal Learning Test; RC, randomized controlled study; RCF, Rey Complex Figure; RPE, rating of perceived exertion; SCAG, Sandoz clinical assessment geriatrics; SDS, Zung Self-Rating Depression Scale; SF-36, Short Form 36; ST, sentence test; TMT, Trail Making Test; TMTA, Trail Making Test version A; TTAC, Table-Tennis-Accuracy-Test; TTJC, Table-Tennis Juggle Test; U, uncontrolled pre–post study; VBA, Voxel-Based Analyses; VO2 max, maximal oxygen consumption; WAIS, Wechsler Adult Intelligence Scale; WL, word list; WM, working memory; WMS, Wechsler Memory Scale; WP, word pairs; WS, within subject study.

(thalamus, striatum). However, some studies did not report changes on brain level due to cognitive training.[16,36,39]

Transfer to untrained tasks and maintenance

Two critical issues making it possible to judge the efficiency of cognitive training are transfer and maintenance. If training is transferred to untrained tasks, then this provides evidence that the training improves cognition in a more general way. Several studies mention transfer to nearest, near, and far abilities relative to the trained tasks. However, it is not clear as to what exactly these transfers refer. Although some authors have attempted to define these concepts,[40] not all studies use these informal definitions. Maintenance corresponds to the period after the end of the training after which positive outcomes of the training are still present. Several studies have focused on these two points, although not always with the same distinction concerning transfer and not always with the same post-training period in order to determine maintenance. This makes the comparison of these studies complicated and general conclusions difficult to draw. Among the 32 studies we listed in Table 4, only one study did not report data concerning transfer and one study did not find a transfer effect. In some studies, near,[41] far,[31] or both transfer effects were found depending on the authors' classification.[42] However, many of these studies do not explicitly state what kind of transfer was examined. The situation is at its worst regarding the long-term maintenance of training benefits. Sixteen of the studies presented in Table 4 did not examine this issue. In the remaining studies, the interval between immediate post-training evaluation and follow-up varies from 2 months[33] to 10 years,[29] with periods of 3, 6, and 12 months being the most frequently studied. Globally, these studies provide some evidence in favor of long-term maintenance, at least for some of the benefits of cognitive training at behavioral and brain level. However, to reach better understanding of transfer and maintenance of cognitive training outcomes, more systematic investigations are need.

Borella et al, for example, addressed the issues of transfer and maintenance in a systematic way.[15] They examined nearest (visuo-spatial working memory), near (ie, short-term memory), and far transfer (ie, fluid intelligence, inhibition, speed processing) of working memory training at post-test, on the one hand, and long-term maintenance (8-month follow-up), on the other. Nearest, near, and far transfers were observed at post-test and follow-up, although at follow-up the effects of transfer were in general significantly lower than at post-test. These results suggest that benefits from working memory training may transfer to several cognitive functions, some of them, such as intelligence, being loosely related to trained task, and that this transfer may persist through time. Transfer of cognitive training outcomes to fluid intelligence in older adults was frequently observed[28,31,43] but not always.[33]

Transfer to everyday activities

Because the crucial goal of cognitive training is to improve people's lives and preserve their autonomy, some authors have looked at the transfer of cognitive training benefits to everyday activities. Ten of the 32 reported studies addressed this issue, and only one did not report any effect of cognitive training on everyday living. Although the question is extremely important, it is not a straightforward task to draw conclusions about the transfer of training benefits to everyday life. This is partly due to the difficulty of objectively evaluating this transfer. In fact, everyday life abilities are most frequently evaluated with subjective measures, such as self-reported questionnaires (eg, Instrumental Activities of Daily Living). For example, Ball et al investigated the short and long-term impact of cognitive training in independence-related activities on everyday life.[44] These authors were involved in the ACTIVE study, which is the largest study to have investigated cognitive training and included 2,832 older adults who were followed up for over a period of 10 years.[29] They examined if training one specific cognitive function – memory, reasoning, or speed processing – would have benefits on cognition and everyday life. The transfer of acquired abilities to daily living was assessed via the everyday problem solving task (ie, reasoning abilities), everyday speed task (ie, rapidity of interactions in everyday life), and self-rated questionnaires such as activities of daily living, instrumental activities of daily living (IADL), and driving habits (ie, difficulties encountered in driving). Contrary to the short-term benefits of the trained abilities, Ball et al failed to show any generalization to everyday life after a 2-year follow-up.[44] However, the authors suggested that the functional decline of the participants after the 2-year follow-up was not great enough to make it possible to observe the long-term transfer of the training. In fact, Willis et al and Rebok et al reported that in the ACTIVE study, the autonomy of the participants in the training groups, as estimated by the self-reported IADL questionnaire, declined less than that of those in the control group both 5 and 10 years after the end of the training.[29,45] The IMPACT (Improvement in Memory with Plasticity-based Adaptive Cognitive Training)[46] study also examined the participants' self-perception of cognitive functioning and mood in everyday life with the Cognitive Self-Report

Questionnaire. Results showed that the participants noticed the improvement in their cognition and mood after training. Other authors have also reported an improvement in everyday life due to training, manifested in terms of reduced memory disorders,[42] better estimated self-efficacy,[47] better achievement of goals, and satisfaction with the achieved goal.[48] One study showed correlation between increased white matter integrity in the occipito-temporal region (ventral attention network) after auditory perception training and improvement in everyday problem solving.[35]

Physical training

Physical training has been shown to induce health benefits and general well-being. Indeed, maintaining a good physical condition through life lowers the prevalence of some diseases like cancer, diabetes, and cardiovascular diseases;[49,50] increases life comfort and autonomy; and delays dependence.[51] Beyond the beneficial effects of physical training on body health, some authors have taken an interest in the impact of physical training on brain health, which in turn positively impacts cognition, without necessarily targeting one specific cognitive function (eg, memory, attention, reasoning, speed). The literature suggests that the neural mechanisms responsible for the impact of physical training on cognition are due to neurogenesis (ie, production of new neurons), angiogenesis (ie, growth of new blood vessels from preexisting ones), synaptogenesis (ie, formation of synapses between neurons), and the action of neurotrophins (proteins that support the survival, development, and functions of neurons).[52] In the present review (all studies are presented in Table 5), we focused only on physical training, especially on aerobic training, which has been shown to bring about the greatest impact on the aging brain and cognition[17,53] and delaying dependence in the healthy elderly,[54] although other types of intervention are also used to improve cognition (physical activity, physical exercise).[55] Physical training consists of targeted exercises as classified by the World Health Organization guidelines[56] that involve muscle strength and/or endurance[57] and usually includes aerobics (ie, capacity to perform large-muscle activity over a long period of time), balance (ie, backward walking, walking and turning around, one-leg stand), muscle-strengthening, resistance (ie, ability to produce force to overcome inertia or a load), and flexibility (ie, practice in the range of movements necessary in daily life).

Interestingly, some authors have suggested that physical training may improve cognition in the same way as cognitive training and that they can therefore be used interchangeably.[6] Among the 10 studies listed in Table 5 (seven using structural and/or functional MRI), only one study did not report any significant improvement in cognition.[58] However, the fact that this study was conducted with sedentary older adults aged more than 70 years may at least partly explain this result. All the other studies report effects on cognitive function, on brain structure/function, or on both. In addition, in seven studies listed in Table 6 (four using MRI,[66,67,78,79] one using positron emission tomography,[77] one using electroencephalogram,[79] and one examining serum brain-derived neurotrophic factor [BDNF][69]) that included groups undergoing single physical training (not combined with other kinds of training), positive effects of physical training on cognition and on brain structure or function were reported. Concerning cognition, improvements were especially observed for short-term[59,60] and working memory,[53] long-term immediate and delayed memory,[60] attention,[61,62] and executive functions.[63] On the brain level: 1) structural changes have been found in both white[53,59] and gray matter,[64,65] and 2) functional changes have been observed at the level of functional connectivity,[53,59] CBF,[60,66,67] and task-related pattern of blood oxygen level dependent response.[17,68] Some authors[61] suggested that the thickening of the gray matter might be due to an increase in the level of BDNF. This suggestion is in line with the observation that only physical training, as compared to cognitive and mindfulness training, produced an immediate increase in serum BDNF, which, in addition, was correlated with improved working memory performance.[69]

Differences in outcomes of physical training as function of exercise type

When two or more physical exercises were used and compared, authors have reported some differences in training outcomes. On the brain level, Voss et al showed that walking training induced greater white matter integrity in pre-frontal, parietal, and temporal regions than stretching training.[53] These authors also observed a greater increase in functional connectivity in the default network and frontal executive network after aerobic training than after stretching and toning training after 12 months of training. Voss et al also reported a greater increase in white matter integrity in the default mode network and frontal executive network after walking training than after stretching training.[59] An increase in the hippocampal volume after walking training, but not stretching, was also observed.[65] Colcombe et al showed increased Flanker task-related activity in the attentional network (superior and medial frontal gyrus and superior parietal gyrus) after aerobic training but not after stretching training.[17] Surprisingly, for the same task, Voelcker-Rahage et al reported a decrease in activity after aerobic training in several cortical areas, especially in the superior and medial frontal gyrus.[68] On the contrary, they reported increased Flanker task-related activity in the inferior frontal gyrus, thalamus, caudate, and superior parietal lobule after coordination training. These findings provide evidence that not every type of aerobic training induces neuroplasticity to the same extent.

On the cognitive level, although no given form of physical training (ie, aerobics, running, muscle building) is thought to specifically improve any particular cognitive function, some studies have pointed out that the outcomes of physical training for cognition may depend on the type of physical activity used in the training. For example, Colcombe et al and Liu-Ambrose et al showed improvements in resistance to interference after aerobic training,[17,63] and Voss et al found an improvement in working memory.[59] However, working memory improvement has also been observed after resistance training.[70] These results suggest that combining different types of activity in physical training sessions may well be a better way to train because these combined activities act on more than one aspect of cognitive function while, at the same time, different types of training may act on one and the same function and potentially reinforce the benefits. Combining different types of physical training would therefore be more efficient than using only a single type. However, Voss et al investigated the impact of aerobic versus stretching training on short-term memory, working memory, and executive control and showed that working memory was enhanced only in the walking training group.[53] Stretching training did not lead to any working memory improvement, suggesting that not all types of physical training have the same impact on the same cognitive function. Some authors consider that aerobic training is the most efficient in terms of cognitive enhancement and its impact is thought to be mediated by cardiovascular fitness.[53]

Equivalence between physical training and physical activity through life

One interesting question related to physical training is whether the training outcomes on cognition are equivalent to or different from those produced by a high level of physical activity through life. This point was addressed by Colcombe et al.[17] These authors observed that, after 6 months, older adults who took part in aerobic training (study 2) achieved a high level of resistance to interference that was associated with reduced activity in the anterior cingulate cortex. Interestingly, the same pattern of results was observed in non-trained older adults with a high level of aerobic fitness (study 1). These results suggest that the neurocognitive benefits of cardiovascular fitness may come both from a physically active life that leads to physical fitness and from physical training. This is an important argument in favor of physical training in older adults.

Transfer to everyday activities

Generally, the transfer of physical training outcomes to everyday life was not evaluated in the studies we included in the present review. Only Liu-Ambrose et al reported that physical training reduced falls in everyday life and that this reduction was linked to improvement of executive function.[63]

Summary of findings for cognitive and physical training

To summarize, both cognitive and physical training seem to induce changes in brain and cognition of healthy older adults. However, studies exploring physical training outcomes have seldom examined long-term maintenance and transfer to everyday life. Thus, it seems important for future studies to address this shortcoming. Concerning short-term changes at brain level, both trainings seem to have some positive outcomes for the structure and function of older adults' brains, although these changes have more frequently been examined in studies focusing on physical training. Both types of training seem to impact frontal lobe functioning and increase white matter integrity in frontal and parietal regions, with physical training being more frequently reported to confer such benefits. By contrast, as far as the hippocampus is concerned, structural and functional changes have been examined and reported almost exclusively by studies involving physical training. Concerning short-term changes in cognition, both training programs have been reported to impact positively on, in particular, executive functions (ie, planning, inhibition, and coordination) and memory (ie, short, long-term, and working memory). Beyond these convergent benefits, cognitive and physical training also have a differential impact on cognition. Cognitive training tends to improve problem solving and fluid intelligence, and reduce the cost of multitasking, whereas physical training tends to improve spatial memory, speed, and resistance to interference. There is no strong evidence of a systematic transfer of the benefits of training to untrained tasks and even less to everyday life activities, ie, the main aims of cognitive training. In addition, when transfer occurs, it does not seem to systematically persist through time.

Combined cognitive and physical training

Both cognitive and physical training are used in clinical interventions, because they have been proved to have a certain effectiveness. Given that there is some evidence that they influence brain structure and function, on the one hand, and cognition, on the other, in different ways, one may hypothesize that they should bring about greater benefits for cognition when they are combined in one intervention than when either form of training is used alone.

Two systematic reviews of literature investigated this question.[71,72] The authors showed that CCPT, whether simultaneous or subsequent, would produce better benefits on cognition as compared to cognitive and physical training alone. However, these reviews point out two issues: the impact of cognitive training seems to be limited to trained functions[71] and the benefits of CCPT seem to be difficult to evaluate in populations with cognitive impairment.[72] In fact, these two reviews put the emphasis on the impact of CCPT on healthy versus cognitively impaired populations, whereas the present review is entirely focused on the comparison of impact of single versus combined training on healthy older adult's brain and cognition.

Only a few empirical studies have systematically investigated this question. To our knowledge, only four behavioral studies[62,73–75] and two neuroimaging studies[76,77] have directly compared single versus combined training and their impact on cognition in healthy older adults (all cited studies concerning CCPT are shown in Table 6). In addition, two studies have compared combined training with a control group only,[78,79] and three studies have compared single physical training with single cognitive training and a control group.[66,67,69]

Methodological issues for combined cognitive and physical training

Before we address the effectiveness and potential advantage of CCPT over single physical and single cognitive training, it is necessary to point out an important methodological question. Indeed, the organization of protocols in which physical and cognitive training are combined raises the question of whether the training modes should be sequential or simultaneous. In the studies listed in Table 6, two studies used simultaneous training,[75,76] performing a cognitive task while walking on a treadmill. Both sequential and simultaneous CCPT may have their advantages and drawbacks. The advantage of sequential training is that individuals can be entirely focused on the current training. However, in the sense that cognitive and physical parts of the training are not performed at the same time, there is no direct possible interaction between the mechanisms underpinning each training session. Conversely, although simultaneous training permits an interaction between these mechanisms, the fact that individuals are confronted with a dual task might mean that they do not focus fully on all aspects of each training session. Is it possible to run and simultaneously perform cognitive training efficiently? This point is a matter of debate in the literature. Indeed, it has been shown that dual tasks are particularly difficult for older adults. Consequently, multitasking is very sensitive to aging, and the cost of performing a dual task increases as people age.[80] However, Theill et al showed that older adults do not find it any more difficult to follow CCPT (ie, performing cognitive tasks while walking on a treadmill) than to undertake single cognitive training. They argued that the mobilization of multiple resources and abilities corresponds to the way that people act during their everyday activities.[75] The question of sequential or simultaneous training also raises the issue of the duration of the training. Indeed, in the case of sequential training, the difficulty lies in deciding whether it is better to keep the same training duration as for single training (eg, 1 hour per week), but to dedicate only half this time to each component (eg, 30 minutes per week of cognitive training and 30 minutes per week of physical training), or to double the overall training time in order to keep the same training time for each type of training (eg, 1 hour per week of cognitive training and 1 hour per week of physical training) as compared to their respective single training session times. In the latter case, it is not clear whether any advantage observed for combined training is due to the combination of the training types or simply to the fact that training lasts for twice as long. It is therefore possible that the design of the training may influence its outcomes, although, as far as we know, no studies have directly compared sequential training with simultaneous training.

Advantage of combined cognitive and physical training

Short-term outcomes on cognition and brain

Among the five studies that directly compared CCPT with single physical or cognitive training on short-term outcomes, all observed an advantage of combined training. Oswald et al showed positive specific outcomes after cognitive training alone, combined physical and psychoeducational training, and CCPT but not after physical training alone.[73] However, as compared to control group, CCPT brought the largest gains in cognitive functioning, emotional status, and physical functioning. Theill et al compared groups receiving CCPT (ie, simultaneous working memory and cardiovascular training) or single training (ie, working memory) with a control group. They reported an improvement in executive control after both types of training, whereas only the CCPT group exhibited improved performance in a motor-cognitive dual task and also achieved greater gains in paired-associates learning. These results suggest that CCPT may produce both similar and specific outcomes to single physical and cognitive training.[75] Two other studies confirm this suggestion. Linde and Alfermann reported that, compared to a control group, sequential CCPT and single cognitive and physical training increased concentration, but that only CCPT improved cognitive speed.[62] Rahe et al found that CCPT and single cognitive training improved divided attention and immediate memory, whereas CCPT additionally improved general cognitive state, delayed memory, and verbal fluency. However, there was no control group in this study.[74] This was also the case in the study by Wenger et al where simultaneous CCPT training was reported to produce greater improvement in spatial navigation performance than single physical training, but neither of these training types resulted in cortical thickening.[76] Finally, Shah et al reported a greater improvement in long-term verbal memory after sequential CCPT than in a control group. In addition, the CCPT group presented increased glucose metabolism in the left sensorimotor cortex, and this was correlated with better performance in the memory task. There was no advantage of single physical or cognitive training on cognition.[77]

Globally, the CCPT training seems to result in greater short-term benefits than single training, whether cognitive or physical. However, the results have to be treated with caution because in the reported studies, the sequential CCPT took twice the amount of time as the single training program. Thus, the greater benefits at both the behavioral and brain level observed after this training could be due to reasons other than the simple combination of cognitive and physical training, such as a superior training time.

In addition, positive outcomes of CCPT were shown in two studies that compared CCPT to a control group only. Frantzidis et al reported increased frontoparietal synchronization at rest after CCPT as compared to a physically active control group. Unfortunately, they did not report behavioral outcomes.[79] Pieramico et al observed an improvement in long-term memory and processing skills due to CCPT as compared to a passive control group.[78] Changes in the strength of the functional connectivity of the default mode and dorsal attentional networks were also observed. In addition, carriers of DRD3 ser9gly and COMT Val158Met polymorphism of dopamine-related genes benefited more from CCPT.

Long-term maintenance

The question of the long-term maintenance of benefits due to CCPT was addressed by four studies. All of these have shown the persistence of benefits: at 5-year follow-up,[73] at 1-year follow-up,[74] at 4-month follow-up,[76] and at 3-month follow-up.[62] Oswald et al observed, 4 years after the end of the training, improvement of cognitive functioning after both cognitive training alone and CCPT, with the largest improvement after CCPT. Importantly, the participants from CCPT group expressed higher degree of independent living, and the symptoms of cognitive impairment were less pronounced among the members of the CCPT group than control group.[73] In the Linde and Alfermann's study, the benefits due to single training were also found to be maintained, suggesting that there is probably no specific mechanism responsible for maintaining the benefits of CCPT.[62] In Rahe et al's study, an improvement in divided attention was observed immediately after the end of single cognitive training and CCPT, but only the CCPT group showed further improvement at 1-year follow-up.[74] The authors suggested that physical training might enhance brain metabolism and plasticity, whereas cognitive training, by increasing mental demand, might use and reinforce the enhanced brain metabolism and guide brain plasticity. In other words, physical and cognitive training play a different but complementary role in brain plasticity. Physical training can be seen as an initiator of brain plasticity, while cognitive training would then subsequently reinforce the direction introduced by physical training. These results suggest that CCPT makes a robust contribution to slowing down attentional deficit in aging over the long term.

Transfer to everyday activities

Generally, the transfer of CCPT outcomes to everyday life was not evaluated in the studies we included in the present review. Only Oswald et al reported that this training has a positive impact on independent living and every day competence at short term and only on independent living at long term (5 years).

Conclusion and recommendations

The main aim of this review was to examine the potential advantage of combining cognitive and physical training into one intervention in older adults in terms of both immediate and long-term benefits on cognition and everyday life. It seems very clear that cognitive and physical training both have positive outcomes for brain structure and function, as well as in terms of improved cognition. In addition, some studies are beginning to show a positive impact of training on the autonomy and quality of everyday life of elderly people. However, too little studies examined this point and clearly future studies should seriously investigate weather and to what extent cognitive and physical training improves older people's everyday life. Especially, there is a cruel lack of data concerning physical training. Importantly, some evidence suggests that cognitive and physical training may complement one another and help improve both brain structure and function, and cognition. Unfortunately, here again too little studies compared in a systematic way CCPT with each of these training sessions administered alone. Thus, although the conclusions of these few studies indicate an advantage for combined training, further studies are necessary to be able to draw more robust conclusion in favor of this training. However, at the level of clinical application, although the experimental data are too few and not always unequivocal, it seems preferable to consider these two training types when planning interventions designed to improve cognitive capacities in older people. The role of future studies will be to provide more evidence in favor of advantage of combined training and to investigate methodological issues inherent to the design of CCPT in order to determine the most efficient protocols.

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Disclosure

The authors report no conflicts of interest in this work.

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