



Review

Cognitive and neural plasticity in old age: A systematic review of evidence from executive functions cognitive training

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ABSTRACT

Cognitive training is a popular intervention aimed at attenuating age-related cognitive decline, however, the effects of this intervention on brain structure and function have not been thoroughly explored. Core executive functions (working memory, inhibition, cognitive flexibility) are dependent upon prefrontal brain regions—one of the most vulnerable areas of age-related decline. They are also implicated in numerous cognitive processes and higher-order functions. Training executive functions should therefore promote cognitive and neural enhancements in old age. This systematic review examined the effects of executive functions training on brain and cognition amongst healthy older adults across 20 studies. Behavioral performance consistently improved on trained cognitive tasks, though mixed findings were reported for untrained tasks. Training-related structural changes were reported, evidenced through increases in grey matter and cortical volume. Functional changes were not consistent, though a general pattern of increased subcortical and decreased frontal and parietal activation emerged across studies, indicating that training may potentially reduce reliance on compensatory neural mechanisms. Training executive functions appears to promote cognitive and neural plasticity in old age, though further research is required to develop a more comprehensive framework which connects and elucidates the mechanisms underlying cognitive training, cognitive transfer, and cognitive aging.

1. Introduction

With ongoing advancements in medicine and technology, people across the world are living longer, bringing about a dramatic rise in the number of older adults within the population. As a result, the prevalence of age-related health problems is becoming a worldwide public concern.

The aging process is characterized by declines in physical, neurobiological, and cognitive capacities that can affect every day functional activities such as driving, paying bills, and remembering important dates or appointments. In particular, executive functions (EFs) play a fundamental role in everyday functioning but are vulnerable to the effects of age-related cognitive decline (Reuter-Lorenz et al., 2016). EFs refer to a group of top-down mental processes that form the foundations for higher-order functions (e.g., planning, reasoning, decision making, problem solving). Three core EFs are typically represented in the literature: *working memory* – the ability to simultaneously hold and actively manipulate stimuli in mind before recalling the required information; *inhibition* – the ability to suppress dominant responses or irrelevant information, and; *cognitive flexibility* – the ability to switch

between multiple tasks, mental sets, or perspectives (e.g., Diamond, 2013; Karr et al., 2018; Miyake et al., 2000). Performance on measures of these core EFs have been found to predict the ability to efficiently carry out numerous functional activities in older adulthood including instrumental activities of daily living, medication adherence, and complex aspects of financial decision making (e.g., Bangma et al., 2017; Bell-McGinty et al., 2002; Cahn-Weiner et al., 2002; Insel et al., 2006). Thus, as EFs are implicated in a range of different cognitive processes and are substantially afflicted with increasing age, improving these functions would likely promote global cognitive improvements in older adulthood. Such improvements may manifest through more efficient cognitive and neural processing which could, in turn, help ameliorate the effects of cognitive decline and enhance performance on everyday tasks (e.g., improve memory capacity, strengthen attention and focus).

Cognitive training has become one of the most prominent interventions aimed at combating age-related cognitive decline. Two main approaches to cognitive training have been investigated: strategy-based and process-based training. Strategy-based training targets the use of performance-enhancing strategies (e.g., mnemonics) which aims to compensate for age-related cognitive deficits (Brehmer et al., 2014;

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Willis and Belleville, 2016). On the other hand, process-based training aims to *restore* deficient cognitive processes through repeated practice on tasks targeting specific cognitive domains (without specific strategy instructions; Cameron et al., 2015; Karbach, 2014). Process-based training interventions have targeted a variety of cognitive domains including—but not limited to—speed of processing (e.g., Edwards et al., 2013; Nouchi et al., 2016; Takeuchi and Kawashima, 2012), attention (e.g., Chambon et al., 2014; Jiang et al., 2017), and working memory (e.g., Borella et al., 2010; Dahlin et al., 2008; Heinzel et al., 2014), among many other domains.

The essence of process-based training lies in the premise that constant practice on a task enhances performance on the same, and similar tasks (Jonides, 2004; Thorndike, 1906; Willis and Warner Schaie, 2009). As such, the majority of cognitive training studies have reported significant training-related improvements (e.g., faster reaction time, improved accuracy) on trained tasks (e.g., Heinzel et al., 2016; Rose et al., 2015; Sandberg et al., 2014). That is, trained participants demonstrated better performance on trained tasks at post-test than at pre-test compared to participants in a control group. What has been termed the ‘cognitive training controversy’ (Sala and Gobet, 2019), however, stems from contradictory findings regarding whether training improvements can generalize or ‘transfer’ to untrained tasks measuring the same construct as the trained task (*near-transfer*) as well as untrained tasks tapping a different cognitive construct and everyday activities (*far-transfer*; e.g., Könen et al., 2016; Shipstead et al., 2010). To address these equivocal findings, numerous reviews and meta-analyses have been conducted but have, ironically, also reported mixed conclusions regarding the generalizability of cognitive training (e.g., Au et al., 2015; Karbach and Verhaeghen, 2014; Melby-Lervåg and Hulme, 2013, 2016; Schwaighofer et al., 2015).

Despite the plethora of training studies that have been conducted, relatively few have investigated the effects of cognitive training and its implication on the structure and function of the aging brain. This is a critical avenue of research as numerous studies have documented the association between aging and neurobiological degeneration evidenced by global and regional loss in brain volume (atrophy), white matter hyperintensities (reflecting demyelination and axonal loss), and functional rearrangement (changes in neuronal recruitment when engaging in tasks; e.g., Cabeza, 2002; Fotenos et al., 2005; Raz et al., 2005; Reuter-Lorenz and Lustig, 2005; Yoshita et al., 2006). Such changes in neural structure and function—particularly within the prefrontal cortex (PFC)—have been linked to poorer performance on cognitive tasks involving executive functions (Grieve et al., 2007; Gunning-Dixon and Raz, 2003; Gunning-Dixon et al., 2009; Yuan and Raz, 2014). Training executive functions may therefore rehabilitate executive functioning and everyday performance, and potentially restore neural degeneration in older adults. Thus, investigating the effects of EF training on both brain and behavior have critical theoretical and practical implications for the understanding of the neural mechanisms underlying cognitive aging and training.

A landmark neuroimaging training study conducted by Dahlin et al. (2008) demonstrated that, in order for transfer to occur, the training and transfer tasks must share related information processing components and engage similar neural circuitry. After training working memory updating in both younger and older adults, the researchers found that trained younger adults exhibited transfer to an untrained updating task but not to an untrained inhibitory control task. The trained older adults, however, did not exhibit transfer to either untrained tasks. Their imaging data indicated that, in younger adults, both updating tasks (but not the inhibition task) activated the same striatal region at pre-test, and the same pattern of increased striatal activation was also observed for both updating tasks at post-test. In older adults, however, no overlapping striatal activation or change was observed. These findings may suggest that older adults require more extensive training to elicit neural changes and cognitive transfer compared to younger adults. Alternatively, it may suggest that the capacity to alter

behavioral and neural functioning in older adults may be more limited compared to that of younger adults. This interpretation aligns with the magnification account of cognitive training which posits that high-performing individuals (e.g., young adults) benefit more from training as they are able to build upon already efficient cognitive processes (e.g., Lövdén et al., 2012). In contrast, some studies have provided evidence for the compensation account which upholds the notion that high-performing individuals are already performing at an optimal level, and, as such, low-performing individuals (e.g., children, older adults) benefit more from training as they have more room for improvement (e.g., Karbach et al., 2017). Thus, as the neural mechanisms underlying cognitive training amongst older adults are not well understood, it is important to further investigate the effects of EF training on both cognitive plasticity (changed patterns of cognitive behavior such as reduced susceptibility to distractors) and neural plasticity (neuronal-level changes including neurogenesis, network reorganization, etc.; Greenwood and Parasuraman, 2010).

Within the field of cognitive aging, the application of structural and functional brain imaging and recording techniques are particularly important as brain changes typically precede behavioral changes (e.g., Burggren and Brown, 2014; Lampit et al., 2015; Reuter-Lorenz et al., 2016). Additionally, overt behavioral changes (such as reaction time and accuracy) might not always be observable amongst individuals within the older population. For instance, older adults possessing high cognitive reserve (i.e., neural resources accumulated through genetic and/or environmental factors such as longer education and participation in physical or cognitively demanding activities; Cabeza et al., 2018; Tucker and Stern, 2011) may be better equipped to employ alternative behaviors or mechanisms to compensate for deficient cognitive processes (e.g., setting reminders, utilizing additional neural resources; Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Lustig, 2005). Changes in such actions and mechanisms may not be sufficiently measured using behavioral tasks alone. Furthermore, given that reduced mobility is typically experienced in older age, behavioral indices such as reaction time might not be suitable to measure changes in cognitive ability within this population (e.g., Daley and Spinks, 2000; Fraser and Bherer, 2013). Therefore, it is important to employ both behavioral and neural measures when evaluating training-related changes in an aging population.

As most training studies targeting older adults have mainly focused on behavioral or cognitive changes, it is plausible that confounding factors, such as those mentioned above, may, in part, contribute to some of the null findings reported within the literature. For instance, it is possible that some training programs elicited enhancements in brain structure or functioning, but the study did not last long enough to observe overt behavioral improvements. When neural measures are not included, potential training-related changes may be overlooked. Thus, the application of functional and/or structural brain measures reduces the probability of underestimating intervention effects and provides deeper insight into the mechanisms underlying cognitive training and aging.

The substantial focus placed on cognitive training interventions has inspired numerous reviews examining its effects on cognition (measured using behavioral indices from cognitive tasks). However, very few studies have systematically reviewed the effects of cognitive training at the neural level. The aim of the current study was to therefore provide a systematic review to piece together and elucidate the effects of EF training on both cognitive and neural plasticity amongst healthy older adults. This study also sought to explore training characteristics (e.g., training adaptiveness, length of training) that potentially promote improvements in the brain and behavior. Further, by examining both behavioral and neural outcomes, this review aimed to explicate the link between training-related cognitive and neural change, and provide further insight into the mechanisms underlying cognitive training.

2. Method

This systematic review was conducted and reported in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2011).

2.1. Eligibility criteria

2.1.1. Type of studies

To examine whether EF training elicited cognitive and neural plasticity, eligible studies included those which incorporated a pre-test–intervention–post-test design. Cross-sectional studies were therefore excluded. Cognitive training interventions must have included at least three training sessions. Interventions comprising less than three training sessions were not considered ‘training,’ but rather, once-off practice sessions and were therefore excluded from the review. Studies were not restricted to randomized controlled trials as many cognitive training studies employ pseudo-randomization methods to ensure that factors such as age, intelligence, education level, and cognitive status are equivalent across training and control groups. Studies must have also included a control group (active or passive) to control for test-retest effects.

2.1.2. Types of training

Cognitive training interventions must have targeted at least one core EF (cognitive flexibility, inhibition, working memory). Additionally, the cognitive intervention must have constituted process-based training—that is, participants needed to have engaged in repeated practice of tasks or games that exercise specific cognitive functions (as opposed to strategy-based training in which strategies are trained to compensate for, rather than restore, deficient cognitive functions). Studies were also excluded if the cognitive training program included components other than cognitive practice (e.g., physical activity, pharmacological supplements, brain stimulation). These types of studies were excluded to avoid potential confounding effects as physical activity training and brain stimulation, for example, have been found to enhance cognitive performance (e.g., Bherer et al., 2013; Rahe et al., 2015).

2.1.3. Types of participants

Eligible studies included healthy older adults ($M_{age} \geq 60$ years old) with no neurological, psychiatric, or medical illnesses or impairments. Studies comprising samples of older adults with clinical health issues (e.g., stroke, MCI, dementia, depression, insomnia, hearing impairment, balance impairment) were excluded unless a group of healthy older adults was also examined.

2.1.4. Types of outcome measures

Studies must have included at least one neural outcome measure. In particular, eligible studies must have examined structural or functional brain changes in response to EF training. Studies that only examined baseline neural structure or function, for example, were excluded. Structural outcome measures must have focused on changes in brain structure, assessed using magnetic resonance imaging, diffusion tensor imaging, or similar methods. Functional outcome measures must have focused on changes in neural activity, assessed using methods such as functional magnetic resonance imaging and electroencephalography.

2.2. Search methods and selection of studies

Database searching was completed on 2nd June 2018, and included searches within Embase, Ovid, PubMed, and Scopus, in addition to ‘grey literature’ databases including ProQuest Conference Papers Index and ProQuest Dissertations and Theses Database. Searches were not limited in terms of publication dates or language, though no articles

within the search results were reported in a language other than English.

The following keywords were entered into each database: (older adult* OR elder* OR aging OR ageing) AND (cog* training OR brain training OR comp* training OR game training OR multi* training OR working memory training OR dual task training OR n-back training OR updating training OR inhib* training OR switching training OR shifting training OR flexibility training) OR (cog* intervention OR brain intervention OR comp* intervention OR game intervention OR multi* intervention OR working memory intervention OR dual task intervention OR n-back intervention OR updating intervention OR inhib* intervention OR switching intervention OR shifting intervention OR flexibility intervention) AND (brain imag* OR imaging OR neuroimag* OR neural OR magnetic resonance imaging OR MRI OR fMRI OR DTI OR diffus* OR voxel OR grey matter OR gray matter OR white matter OR brain vol* OR brain struct* OR brain func* OR electrophys* OR EEG OR ERP OR event-related potential OR connectivity OR network OR neuroplast* OR plast*).

To locate additional studies, reference books related to cognitive aging, cognition, and aging were searched, in addition to reference lists of relevant research and review articles. Additionally, relevant psychology, cognition, neuropsychology, and neuroscience journals were also searched. To search for potential grey literature, conference papers, dissertations, reports, and documents were examined by conducting an additional database search and by contacting relevant authors within the field. Conference papers and proceedings were located using the ProQuest Conference Papers Index. For papers that appeared to be relevant, original authors were contacted to obtain additional information where required. Additionally, the ProQuest Dissertations and Theses Database was searched. Despite this comprehensive search for grey literature, no relevant articles or unpublished studies were retrieved.

The screening process was undertaken by two independent reviewers. There was excellent inter-rater reliability between the two reviewers (Cohen’s $\kappa = 0.80$). All disagreements were resolved after a discussion of the basis for inclusion or exclusion for each study. Both independent reviewers agreed upon the eligibility and inclusion of the final set of studies included in the review.

2.3. Assessment of methodological quality

The Cochrane Risk of Bias Tool (Higgins and Green, 2011) was used to assess the methodological quality in each study in terms of selection, performance, detection, attrition, and reporting biases. The sources of bias were adapted to assess the methodology and design of a typical cognitive training study, including: a) random sequence generation (selection), b) blinding of participants (performance), c) blinding of outcome assessment/assessor (detection), d) incomplete outcome data (attrition), e) selective reporting (reporting), and f) other bias. ‘Allocation concealment’ was omitted as this source of bias was not described in any of the included studies. A rating of low, unclear, or high risk was appraised for each source of bias within each included study. Two independent reviewers assessed risk of bias for each study. All evaluations were congruent between the two reviewers.

3. Results

From 1839 search results, a total of 20 studies were included in this review. See Fig. 1 for the PRISMA flow diagram.

3.1. Overview of studies

The majority of studies were conducted in Europe (55%), followed by North America (20%), Asia (20%), then Australia (5%). See Table 1 for a summary of intervention and design characteristics for each study included in the review.

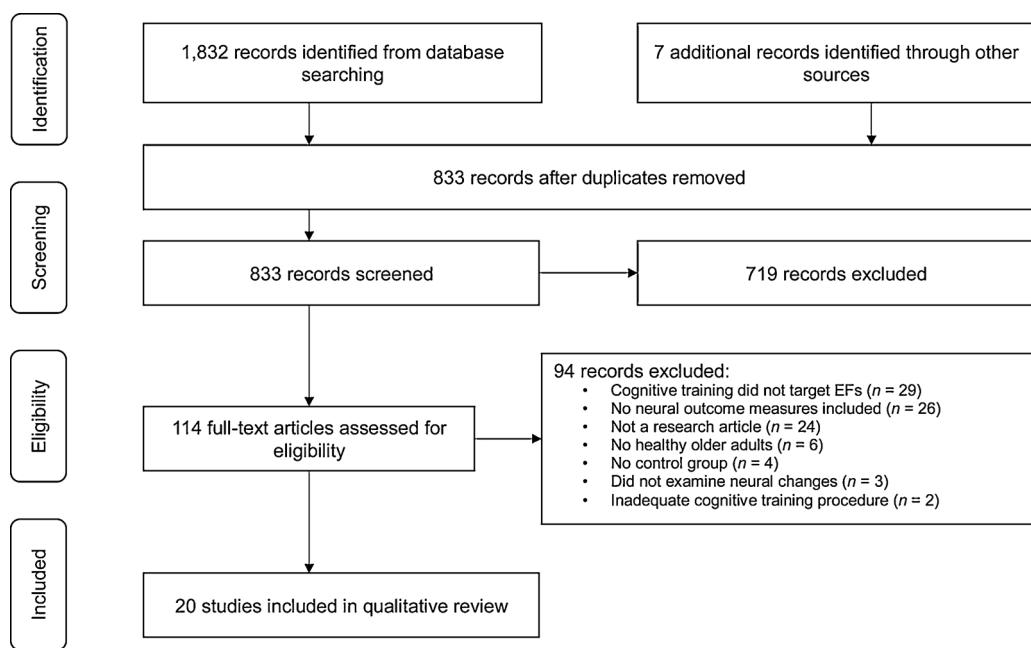


Fig. 1. PRISMA flow diagram summarizing study screening and selection for review.

3.1.1. Participants

Across the included studies, the cumulative number of participants totaled 635 healthy older adults (37% males, 63% females). Participants' age ranged from 60 to 88 years ($M_{age} = 69.44$, $SD = 2.59$). The majority of studies administered the Mini-Mental Status Examination (MMSE; Folstein et al., 1975) as a cognitive screening measure, applying a cut-off score of 24–27 (out of 30). Five studies did not report the use of any cognitive screening measures.

3.1.2. Training interventions

Four different types of EF interventions were implemented: working memory training (20%), inhibitory control training (15%), cognitive flexibility training (5%), and multidomain training (interventions training multiple cognitive domains including at least one EF; 60%). These training programs were mostly adaptive in difficulty (80%) rather than non-adaptive (20%). Most interventions took place in a laboratory (85%), though some were completed at the participants' own home (15%). All training programs were completed on a digital device such as a computer or tablet.

The duration of training sessions across interventions ranged from 15 to 90 min ($M = 50.63$, $SD = 16.74$). On average, 24 sessions were administered ($SD = 19$, range = 8–100) across 4–24 weeks ($M = 8.06$, $SD = 5.03$). Overall, total time spent training ranged from 8 to 100 h across the studies ($M = 21.80$, $SD = 21.45$).

3.1.3. Study design

The mean sample size was comparable for training and control groups ($M_{training} = 21.40$, $SD = 5.72$; $M_{control} = 17.10$, $SD = 9.46$). Across the studies, 50% included a passive control group, 25% included an active control group, and 25% included both types of control groups. To assign participants to groups, most studies employed randomization methods (75%), though some studies did not randomly assign participants (25%). On average, the attrition rate across included studies was approximately 16.25%.

3.1.4. Methodological quality

Fig. 2 summarizes the methodological quality of all included studies, illustrating the potential risk for each source of bias. Appraisals for each source of bias for each study are presented in Table 2. Overall, risk was low or unclear for each source of bias. The majority of studies

(65%) were appraised as unclear for selection bias as many authors reported 'randomly' allocating participants to different intervention groups but did not specify the method of randomization. Without explicitly asking participants at the end of the study, it is impossible to accurately determine whether participants were completely blinded to group allocation. As participant knowledge of group allocation was not reported by any of the included studies, participation bias was evaluated as low risk where studies included an active control group (50%) as this would have reduced the likelihood of participants learning which group they were assigned to. Risk of detection bias was mostly unclear as the authors in 20% of studies specified that they employed an outcome assessor who was blinded to participant group assignment.

The majority of studies reported some degree of participant attrition, and most studies provided a comparison of demographic characteristics between participants who dropped out and those who remained in the study. Bias concerning incomplete outcome data was deemed 'unclear' where studies did not provide this comparison, and 'high' where higher drop-out rates were related to lower cognitive performance (e.g., older participants, lower intelligence). Thirty percent of studies were deemed to have a high risk of bias concerning selective reporting where statistics or findings were not reported for all outcome measures, or an intervention group was excluded from overall analyses. High risk of 'other bias' included studies that comprised a very small sample size, a sample of participants all or mostly from the same gender, or studies that comprised no set training program (i.e., there was large variability in the amount of time participants spent training within the study).

3.2. Neural outcomes

Table 3 summarizes structural and functional neural outcomes for included studies. Note that training-related changes indicate that the trained group demonstrated statistically significant changes relative to the control group.

3.2.1. Structural outcome measures

3.2.1.1. Brain volume. Five studies employed structural magnetic resonance imaging (MRI) methods to explore training-related changes in structural brain volume. Of these studies, three reported a training-related increase of brain volume within areas including the midsagittal

Table 1
Summary of Study Design and Intervention Characteristics for Each Study Included in Review.

Study	Study Characteristics				Intervention				Control					
	Location	Total N	TG N	CG N	Age Mean (SD)	% Male	Name	Domains Trained	Session Length (min)	Total Trained (h)	Adaptive	Location	Type	
Akinoto et al. (2016)	Asia	21	P: 9 V: 5	7	67.92 (5.33)	66%	Cognitive control training (driving simulation)	Multidomain: inhibition, WM, task-switching, speed, visuospatial	20	24s/8w	8	Yes	Lab	AC
Anguera et al. (2013)	North America	46	16	AC: 15 PC: 15	67.10 (4.20)	35%	NeuroRacer	Multidomain: WM, speed, multitasking, switching, attention, visuospatial	60	12s/4w	12	Yes	Home	Both
Brehmer et al. (2011)	Europe	23	12	11	63.60	52%	In-house WM training	WM	25	25s/5w	10.42	Yes	Home	AC
Dahllin et al. (2008)	Europe	19	11	8	68.32 (1.79)	32%	Letter Memory Updating task	WM	45	15s/5	11.25	No	Lab	PC
Gaál & Czágler (2018)	Europe	40	20	20	65.70 (3.19)	0%	In-house task	Cognitive flexibility	60	8s/4w	8	Yes	Lab	PC
Gajewski and Falkenstein (2012) ^a	Europe	141	32	i: 35 ii: 34 iii: 40	70.90 (5.20)	40%	MAT, Sudoku, Mental-Aktiv, Ahano	Multidomain: WM, inhibition, flexibility, speed, memory, reasoning, dual-tasking, attention, visuospatial	90	32s/16w	48	Yes	Lab	Both
Gajewski and Falkenstein (2018) ^a	Europe	141	32	i: 35 ii: 34 iii: 37	70.90 (5.20)	40%	Training from Gajewski and Falkenstein (2012)	Multidomain: WM, inhibition, flexibility, speed, memory, reasoning, dual-tasking, attention, visuospatial	90	32s/16w	48	Yes	Lab	Both
Küper et al. (2017) ^a	Europe	103	32	i: 34 ii: 37	70.33 (4.40)	40%	Training from Gajewski and Falkenstein (2012)	Multidomain: WM, inhibition, flexibility, speed, memory, reasoning, dual-tasking, attention, visuospatial	90	32s/16w	48	Yes	Lab	Both
Wild-Wall et al. (2012) ^a	Europe	103	32	i: 34 ii: 37	70.33 (4.40)	40%	Training from Gajewski and Falkenstein (2012)	Multidomain: WM, inhibition, flexibility, speed, memory, reasoning, dual-tasking, attention, visuospatial	90	32s/16w	48	Yes	Lab	Both
Heinzel et al. (2016)	Europe	29	15	14	66.04 (4.35)	38%	n-back training	Multidomain: WM, inhibition, flexibility, speed, memory, reasoning, dual-tasking, attention, visuospatial	45	12s/4w	9	Yes	Lab	Both
Ji et al. (2016)	Asia	34	18	16	70.06 (5.53)	42%	In-house inhibitory control training	Inhibition	60	12s/4w	12	Yes	Lab	PC
Kim et al. (2017)	Asia	27	14	13	71.44 (3.55)	4%	In-house cognitive control training	Multidomain: Updating, shifting, inhibition, dual-tasking	60	24s/8w	24	Yes	Lab	PC
Kühn et al. (2017)	Europe	48	ini: 18 multi: 15	15	69.00 (4.20)	49%	ini: Schiff Ahoi multi: in-house cognitive training COGPACK	ini: inhibition multidomain: inhibition, memory, visuospatial, arithmetic	15	varied/ 8w	M _{inh} = 12.60 M _{multi} = 10.1	Yes	Lab	PC
Lampit et al. (2015)	Australia	12	7	5	71.43 (7.24)	33%		Multidomain: Memory, attention, speed, updating, switching, inhibition, language	60	36s/12w	36	No	Lab	AC
Lövdén et al. (2010) ^b	Europe	25	12	13	69.32 (3.10)	56%	Cognitive training from COGITO study	Multidomain: Perceptual speed, episodic memory, WM	60	100s/ 24w	100	No	Lab	PC
Raz et al. (2013) ^b	Europe	37	24	13	70.88 (7.95)	—	Cognitive training from COGITO study	Multidomain: Perceptual speed, episodic memory, WM	60	100s/ 24w	100	No	Lab	PC
Mozolic et al. (2010)	North America	48	23	25	69.50 (2.82)	47%	In-house inhibitory control training	Inhibition	60	8s/8w	8	Yes	Lab	AC

(continued on next page)

Table 1 (continued)

Study	Study Characteristics	Intervention						Control							
		Location	Total N	TG N	CG N	Age Mean (SD)	% Male	Name	Domains Trained	Session Length (min)	Session /Week	Total Trained (h)	Adaptive	Location	Type
Niu et al. (2016)	Asia	26	16	10	69.37 (4.12)	42%	In-house cognitive control and memory training	Multidomain: Updating, switching, memory strategy	50	18s/6w	15	Yes	Lab	PC	None
O'Brien et al. (2017)	North America	24	9	15	70.88 (7.95)	29%	Brain Fitness (Positive Science)	Multidomain: WM, auditory memory and processing	60	18s/10w	18	Yes	Lab	PC	None
Tusch et al. (2016)	North America	35	17	18	75.69 (6.13)	23%	CogMed	WM	40	25s/5w	16.67	Yes	Home	AC	Nonadaptive WM training

Note. ^a Denotes studies comprising the same sample of participants from the Dortmund training study. ^b Denotes studies comprising the same sample of participants within the training group from the COGITO study (control group comprises different participants). TG = training group, CG = control group, AC = active control, PC = passive control, WM = working memory. Multi = multidomain, referring to training targeting multiple cognitive domains including at least one core EF.

segment of the genu (anterior part) of the corpus callosum (Lövdén et al., 2010b), post-central gyrus (Lampit et al., 2015), and right inferior frontal gyrus triangularis (Kühn et al., 2017). One study reported that, over a period of six months, all participants (trained and controls) exhibited shrinkage of the hippocampus, lateral PFC, caudate, and cerebellum, however, trained participants demonstrated less shrinkage of cerebellar volume than the passive controls (Raz et al., 2013). Similarly, Lampit et al. (2015) observed a reduction in grey matter volume in their active control group (compared to an increase in the training group). One study found no training-related changes in grey matter volume (Mozolic et al., 2010).

3.2.1.2. Connectivity of neural pathways. Two multidomain training studies examined changes in structural connectivity using diffusion tensor imaging (DTI). The primary parameters typically measured include fractional anisotropy and mean diffusivity. Two additional subcomponents of diffusivity are also often explored: axial diffusivity and radial diffusivity. Reductions in fractional anisotropy and axial diffusivity indicate degradation of axonal structural integrity, whereas increases in mean diffusivity and radial diffusivity index degradation of myelin integrity (Madden et al., 2009). One study reported a training-related increase in fractional anisotropy and decrease in mean diffusivity (driven by decreased radial but not axial diffusivity) (Lövdén et al., 2010b). However, a different study did not observe any training-related changes in fractional anisotropy (Lampit et al., 2015).

3.2.1.3. Qualitative examination of characteristics moderating structural plasticity. In terms of training dose, no training-related changes in grey matter were found after 8 h of inhibitory control training (Mozolic et al., 2010), however increased cortical thickness was observed after 12 h of the same type of training (Kühn et al., 2017). Similarly, strengthened structural connectivity was reported after 100 h of multidomain training (Lövdén et al., 2010b) but not 36 h of multidomain training (Lampit et al., 2015).

Regardless of the type of control group being compared to (active or passive), studies reported training-related increases or maintenance of grey matter (Kühn et al., 2017; Lampit et al., 2015; Raz et al., 2013). In terms of connectivity, training-related changes were reported when findings were compared to a passive control group (Lövdén et al., 2010b), but not when compared to an active control group (Lampit et al., 2015). No distinct patterns were observed across training domain (single- versus multi-domain) or training adaptiveness (adaptive versus nonadaptive). Refer to Table 3 for a summary of neural changes across studies.

3.2.2. Functional outcome measures

3.2.2.1. Resting-state activation. Two studies examined changes in resting-state activation, reporting training-related increases between the right hippocampus and left superior temporal gyrus (Lampit et al., 2015) and increases in resting-state perfusion (cerebral blood flow) within the right inferior frontal cortex (Mozolic et al., 2010). Both studies also reported activation decreases in these same regions within their control groups. Additionally, Lampit et al. (2015) observed training-related decreases in functional connectivity between the posterior cingulate and right superior frontal gyrus compared to controls who exhibited increases in these regions.

3.2.2.2. Task-based activation

3.2.2.2.1. fMRI studies. Six studies utilized fMRI to examine task-based neural activation. Of these studies, two reported training-related decreases in neural activation within areas including the right inferior frontal gyrus and anterior insula (Kühn et al., 2017), as well as medial and lateral clusters within frontal and parietal regions (Heinzel et al., 2016). One study observed both training-related decreases and increases in activation, reporting decreased activity within frontal

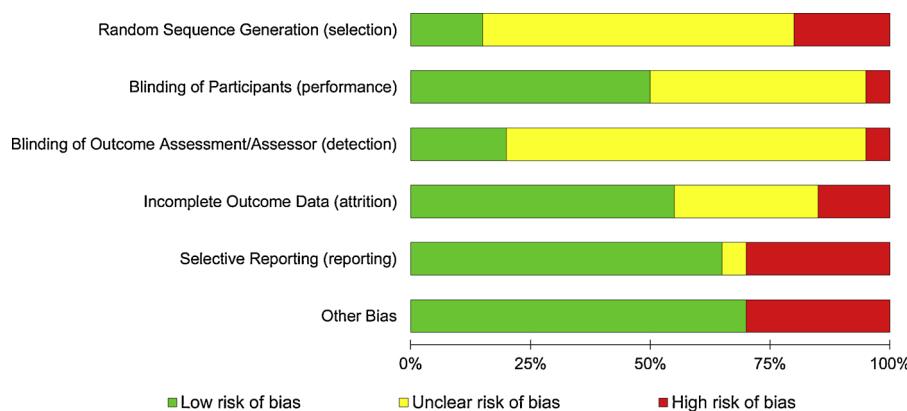


Fig. 2. Bar graph summarizing methodological quality in terms of potential risk for sources of bias across all included studies. Green segments represent low risk, yellow segments represent unclear risk, and red segments represent high risk.

and temporal regions including the anterior cingulate, DLPFC, and lingual gyrus, in addition to increased activity within subcortical regions including the thalamus and caudate (Brehmer et al., 2011). Two studies reported training-related increases in activation within both cortical and subcortical areas including the cerebellum and striatum (Dahlin et al., 2008) as well as posterior regions and the insula (Kim et al., 2017). One study was unable to report functional findings due to technical complications (Mozolic et al., 2010).

3.2.2.2.2. MEG studies. One study utilized magnetoencephalography (MEG), reporting training-related increases in high-gamma power within the left medial frontal gyrus (target condition) and left thalamus (non-target condition) compared to an active control group (Akimoto et al., 2016).

3.2.2.2.3. EEG studies. Ten studies utilized electroencephalography (EEG) techniques to examine training-related changes in functional activation. One study examined event-related spectral perturbations, reporting training-related increases in midline frontal theta activity and long-range theta coherence between frontal and posterior brain regions compared to both active and passive control groups (Anguera et al., 2013). All other studies examined event-related potentials (ERPs)—averaged EEG signals time-locked to certain events (e.g., stimulus presentation). Seven ERP studies reported training-related

increases in neural activation, evidenced by larger amplitudes for the occipital N1 (indexing sustained attention), central P2 (detection of stimulus features; Wild-Wall et al., 2012), occipital N2 (response selection; Gaál and Czigler, 2018; Gajewski and Falkenstein, 2012; Küper et al., 2017), frontocentral Ne (error monitoring; Gajewski and Falkenstein, 2012), frontal P3a (attention and novelty processing; Gajewski and Falkenstein, 2018), parietal P3b (allocation of cognitive resources; Gajewski and Falkenstein, 2012, 2018), fronto-cenroparietal P3 (Gaál and Czigler, 2018; Tusch et al., 2016), central readiness potential, centroparietal contingent negative variation (CNV, action preparation; Niu et al., 2016), and frontocentral switch positivity components (task-set reconfiguration; Küper et al., 2017). In contrast, three studies reported decreased amplitudes after training for the P3 at fronto-central sites (Küper et al., 2017), P3 at both frontocentral and parietal sites (O'Brien et al., 2017), and the parietal contralateral delay activity component (visual working memory load; Ji et al., 2016). Additionally, three studies observed a more anteriorly-distributed P3 component as task difficulty increased (Tusch et al., 2016), during target conditions, that is, when a target was present during a Visual Search task (Wild-Wall et al., 2012), and compared to a sample of young adults who exhibited a more centro-parieto-occipital P3 distribution (Gaál and Czigler, 2018).

Table 2
Assessment of Methodological Quality for Each Included Study Using the Cochrane Risk of Bias Tool.

Study	Random Sequence Generation	Blinding of Participants	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Akimoto et al. (2016)	Low	Low	Low	Unclear	Low	Low
Anguera et al. (2013)	Unclear	Low	High	High	Low	Low
Brehmer et al. (2011)	Unclear	Low	Unclear	Low	Low	High
Dahlin et al. (2008)	Unclear	Unclear	Unclear	High	High	Low
Gaál and Czigler (2018)	Unclear	Unclear	Unclear	Low	High	High
Gajewski and Falkenstein (2012)	Unclear	Low	Unclear	Low	High	Low
Gajewski and Falkenstein (2018)	Unclear	Low	Unclear	Low	High	Low
Heinzel et al. (2016)	High	Unclear	Unclear	Low	Low	Low
Ji et al. (2016)	Unclear	Unclear	Unclear	Unclear	Low	Low
Kim et al. (2017)	High	High	Unclear	Low	Low	High
Kühn et al. (2017)	Unclear	Unclear	Unclear	Unclear	Unclear	High
Küper et al. (2017)	Unclear	Low	Unclear	Low	High	Low
Lampit et al. (2015)	Low	Low	Low	High	Low	Low
Lövdén et al. (2010b)	Unclear	Unclear	Unclear	Unclear	Low	High
Mozolic et al. (2010)	Low	Low	Low	Low	Low	Low
Niu et al. (2016)	High	Unclear	Low	Low	Low	Low
O'Brien et al. (2017)	Unclear	Unclear	Unclear	Unclear	Low	Low
Raz et al. (2013)	High	Unclear	Unclear	Unclear	Low	High
Tusch et al. (2016)	Unclear	Low	Unclear	Low	Low	Low
Wild-Wall et al. (2012)	Unclear	Low	Unclear	Low	High	Low

Table 3
Summary of Structural and Functional Neural Findings for Each Study Included in Review.

Study	Name	Training Program	Imaging Technique	Measures	Neuroimaging Findings	
					Structural	Functional
Mozolic et al. (2010)	Inhibition (adaptive, 8 h)	Resting-state perfusion; Structural MRI	Grey matter volume; Resting cerebral blood flow	- No change in grey matter volume (TG and AC)	TG ↑ cerebral blood flow in R inferior frontal cortex AC no change	
Raz et al. (2013)	Multidomain (non-adaptive, 100 h)	Structural MRI	Regional brain volume	- ↓ volume of hippocampus, lateral prefrontal cortex, caudate nucleus, cerebellum (TG and PC) - TG showed less shrinkage than PC in cerebellum	-	
Kühn et al. (2017)	Inhibition; Multidomain (adaptive, 10–12 h)	Structural MRI; Task-based fMRI	Cortical thickness; Functional activation during Stop-Signal task (untrained)	R inferior frontal gyrus: - TG _{inh} ↑ cortical thickness - TG _{multi} no change - PC ↓ cortical thickness	TG _{inh} ↓ activation R inferior frontal gyrus TG _{multi} and PC no change	
Lampit et al. (2015)	Multidomain (non-adaptive, 36 h)	Structural MRI; Resting-state fMRI; DTI	Grey matter volume; Functional connectivity; Metabolite signals; Fractional Anisotropy	- TG ↑ grey matter volume in R post-central gyrus (↓ AC) - No change in fractional anisotropy	TG ↓ connectivity between posterior cingulate and R superior frontal gyrus (↑ AC) TG ↑ connectivity between R hippocampus and L superior temporal gyrus (↓ AC) No change in metabolite signals	
Lövdén et al. (2010b)	Multidomain (non-adaptive, 100 h)	Structural MRI; DTI	Fractional Anisotropy, Mean Diffusivity, Voxels	Gen of corpus callosum: - TG ↑ fractional anisotropy, ↓ mean diffusivity, ↑ subcortical area - PC no change	-	
Brehmer et al. (2011)	Working memory (adaptive, 10.42 h)	Task-based fMRI	Functional activation during working memory task (untrained)	-	Low working memory load condition: TG and AC ↓ activation R inferior frontal gyrus, anterior cingulate, lingual gyrus TG ↑ thalamus (bilateral), L middle frontal region High working memory load condition: TG and AC ↓ anterior cingulate, hippocampus, parietal region TG ↓ DLPFC, lingual gyrus, insula, R inferior frontal and parietal cortex; ↑ caudate (bilateral)	
Dahlin et al. (2008)	Working memory (non-adaptive, 11.25 h)	Task-based fMRI	Functional activation during Letter (trained) and n-back (transfer) task	-	Baseline activation in bilateral parietal cortex, lateral and medial frontal cortex (letter memory) Baseline activation L supramarginal gyrus (n-back) TG ↑ activation in L frontal lobe, R temporal lobe, parietal lobe (bilateral), L cerebellum, L striatum	
Heinzel et al. (2016)	Working memory (adaptive, 9 h)	Task-based fMRI	Functional activation during Letter (trained) task and Sternberg (transfer) task	-	Overlapping baseline activation in frontoparietal regions between trained and transfer task TG ↓ medial frontal and anterior cingulate gyrus, mid-cingulate gyrus, supplementary motor area (bilateral), R middle and superior frontal gyrus, DLPFC, premotor cortex, R supramarginal gyrus, inferior parietal lobe, angular gyrus (n-back) TG ↓ R middle frontal gyrus extending to caudal superior frontal sulcus (Sternberg updating) PC no change for any task Overlapping ↓ in R medial frontal gyrus and caudal superior frontal sulcus during trained and transfer task after training	
Kim et al. (2017)	Multidomain (adaptive, 24 h)	Task-based fMRI	Functional activation during Multi-Source Interference Task (untrained)	-	Baseline activation in frontoparietal regions: bilateral middle frontal gyrus, superior parietal lobe, R medial frontal gyrus, striatum (bilateral) TG ↑ R frontal and parietal region, L anterior insula PC ↓ R supramarginal gyrus, L anterior insula	
Akimoto et al. (2016)	Multidomain (adaptive, 8 h)	MEG	High-Gamma Power during Oddball task (untrained)	-	Target condition: TG ↑ high-gamma power L medial frontal gyrus (100–200 ms) Non-target condition: TG ↑ L medial frontal gyrus (300–400 ms), L thalamus (0–100 ms, 200–300 ms) AC ↑ L thalamus (0–100, 200–300 ms), ↑ L medial frontal gyrus (300–400 ms)	

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Table 3 (continued)

Study	Name	Training Program	Imaging Technique	Measures	Structural	Neuroimaging Findings
Anguera et al. (2013)	Multidomain (adaptive, 12 h)	EEG	Event-Related Spectral Perturbations (ERSP) during Sign & Drive task (trained)	–	TG ↑ midline frontal theta power TG ↑ long-range theta coherence frontal and posterior regions TG ↓ medial prefrontal activation AC and PC no change	
Gaál and Czigler (2018)	Cognitive flexibility (adaptive, 8 h)	EEG	ERPs; N2, P3b during task-switching tasks (trained and untrained)	–	TG ↑ P3b and N2 amplitudes PC no change fronto-cen- parietal P3b distribution (older adults) centro-parieto- occipital P3b distribution (young adults)	
Gajewski and Falkenstein (2012)	Multidomain (adaptive, 48 h)	EEG	ERPs; N2, P3b, Ne, Nc during task-switching paradigm (untrained)	–	TG ↑ central N2, centroparietal P3b, frontocentral Ne amplitudes No change in frontocentral Nc (correct response monitoring)	
Gajewski and Falkenstein (2018)	Multidomain (adaptive, 48 h)	EEG	ERPs; P3a, P3b during <i>n</i> -back task (untrained)	–	TG ↑ frontal P3a (only in trial preceding target trial), parietal P3b (target and nontarget trials) amplitudes	
Ji et al. (2016)	Inhibition (adaptive, 12 h)	EEG	ERPs; contralateral delay activity (CDA) during Change Detection task (untrained)	–	TG ↓ parietal CDA amplitude (in 3-target condition, not 1 target or distractor conditions)	
Küper et al. (2017)	Multidomain (adaptive, 48 h)	EEG	ERPs; switch positivity, N2, P2, P3 during Stroop Switch paradigm (untrained)	–	TG ↑ frontocentral switch positivity and central N2 amplitudes; ↓ frontal and central P3 amplitude	
Niu et al. (2016)	Multidomain (adaptive, 15 h)	EEG	ERPs; readiness potential, P3, CNV during cognitive-motor task (untrained)	–	TG ↑ central readiness potential and centroparietal CNV amplitudes No change in centroparietal P3 amplitude PC no change	
O'Brien et al. (2017)	Multidomain (adaptive, 18 h)	EEG	ERPs; P3b, P1-N1-P2 during Oddball task (untrained)	–	TG ↓ frontocentral and parietal P3b amplitude TG and PC ↓ P3b latency No change in P1-N1-P2 amplitude or latency	
Tusch et al. (2016)	Working memory (adaptive, 16.67 h)	EEG	ERP; P3 during <i>n</i> -back (untrained)	–	↑ P3 latency with increasing task difficulty (TG and AC) P3 more anteriorly-distributed with increasing task difficulty TG ↑ P3 amplitude (frontal, central, and parietal regions) AC ↓ P3 amplitude	
Wild-Wall et al. (2012)	Multidomain (adaptive, 48 h)	EEG	ERPs; N1, N2, P2, P3b during Visual Search (untrained)	–	TG ↑ occipital N1 and central P2 amplitudes P3b distribution at post-test for TG, AC, and PC; nontargets (posteriorly-located), targets (anteriorly-located) No change in frontocentral N2 amplitude, or P2 and P3b latency	

Note. ↑ symbolizes an increase in, or enhancement of, a structure or activity; ↓ symbolizes a decrease in, or reduction of, a structure or activity; TG = training group, AC = active control, PC = passive control, ERP = event-related potential, R = right, L = left.

Table 4
Summary of Cognitive Findings for Each Study Included in Review.

Study	Training Type	Control Type	Cognitive Findings			Association between Cognitive and Neural Outcomes	
			Cognitive Task (domain)	Sig.*	Cognitive Outcome	Correl-tion	Neural Outcome
Brehmer et al. (2011)	Working memory	AC	Span Board Forward (WM)	ns	Improvement on working memory training task	+	Activity decrease in R inferior frontal and parietal cortex, L fusiform gyrus, insula
			Span Board Backward (WM)	p = 0.04	ns		Activity increase in L thalamus
			Digit Span Forward (WM)	ns			
			Digit Span Backward (WM)	ns			Activity increase in R thalamus
			PASAT (attention)	p = 0.01	Improvement on working memory training task	+	Activity increase in L caudate
			Stroop (inhibition)	ns			Activity increase in R caudate
			RAVLT (memory)	p = 0.06	ns		
Dahlén et al. (2008)	Working memory	PC	Raven's (reasoning)	ns		—	—
			Letter Memory (WM)	p < 0.001	—	—	—
			n-back (WM)	ns			
Heinzel et al. (2016)	Working memory	PC	n-back (WM)	p < 0.001	Performance gain on 2-back task	—	Activation in medial and superior frontal gyrus (during 2-back)
			Sternberg paradigm (WM)	p = 0.035	ns		
			Digit Span Forward (WM)	ns	Performance gain on D2 test		Activation in medial and superior frontal gyrus (during 2-back)
			Digit Span Backward (WM)	ns			
			D2 (speed)	p = 0.003	Performance gain on Figural Relations test	—	Activation in medial and superior frontal gyrus (during 2-back)
			Digit Symbol (speed)	ns			
			Stroop (inhibition)	ns			
			Verbal Fluency (flexibility)	ns			
Tusch et al. (2016)	Working memory	AC	Raven's (reasoning)	p = 0.043	ns		
			Figural Relations (reasoning)	ns	n-back performance	+	P3 amplitude
			n-back (WM)	ns	Improvement on n-back	+	Increase in P3 amplitude
Gaál and Czágler (2018)	Cognitive flexibility	PC	Informative Cue (flexibility)	p < 0.001	ns		
			Noninformative Cue (flexibility)	n/a			
			Color Task (flexibility)	n/a			
			Attention Network Test – altering, orienting (attention)	p < 0.05			
			Digit Span (WM)	ns			
			Matrix Reasoning (reasoning)	ns			
Ji et al. (2016)	Inhibition	PC	Cancellation (speed)	ns		—	—
			Access composite (inhibition)	ns			
			Deletion composite (inhibition)	ns			
			Restraint composite (inhibition)	ns			
			WM composite (WM)	ns			
			Reasoning composite (reasoning)	p = 0.003			
			Visuospatial composite (spatial)	ns			
			Speed composite (speed)	ns			
			Memory composite (memory)	ns			
			Cross-modal interference (inhibition)	p < 0.05	Improvement on Cross-modal Interference Task	+	Perfusion in right inferior frontal cortex
Možolic et al. (2010)	Inhibition	AC	Visual attention (attention)	p = 0.003			
			Auditory attention (attention)	p = 0.007			
Kühn et al. (2017)	Inhibition, Multidomain	PC	Stop-Signal (inhibition)	p = 0.037	Stop-Signal performance at post-test (TG _{inh} only)	+	Cortical thickness in R inferior frontal gyrus

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Table 4 (continued)

Study	Training Type	Control Type	Cognitive Task (domain)	Cognitive Findings		Cognitive Outcome	Correlation	Association between Cognitive and Neural Outcomes	
				Sig.*	r			Neural Outcome	r
Akimoto et al. (2016)	Multidomain	AC	Three-Stimulus Oddball Task (attention)	ns	Reaction time	—	High-gamma power in L medial frontal gyrus	—	r = -0.65
Anguera et al. (2013)	Multidomain	Both	Test of Variables of Attention (attention)	p = 0.04	Reaction time	—	High-gamma power in L intraparietal sulcus	—	r = -0.62
			Useful Field of View (attention)	ns	Improvement on Sign & Drive task (TG only)	+	Midline frontal theta power increase	—	r = 0.76
					Improvement on Test of Variables of Attention task (TG only)	+	Midline frontal theta power increase	—	r = 0.56
Gajewski and Falkenstein (2012)	Multidomain	Both	Delayed Recognition (WM)	p = 0.03	RT at pre-test	—	—	—	—
			Dual-Task (dual-tasking)	ns	RT at post-test	+	N2 latency	—	r = 0.27
			Sign & Drive (multitasking)	p < 0.001	Error rates at pre-test	+	N2 latency	—	r = 0.33
			Task-switching (flexibility)	ns	Error rates at post-test	+	N2 latency	—	r = 0.25
			- reaction time	p < 0.01	Error rates at pre-test	+	N2 latency	—	r = 0.28
			- error rates	ns	Error rates at post-test	+	Ne amplitude	—	r = 0.17
					Error rates at post-test	+	Ne amplitude	—	r = 0.20
Gajewski and Falkenstein (2018)	Multidomain	Both	n-back (WM)	—	—	—	—	—	—
			- reaction time	ns	ns	—	—	—	—
			- working memory capacity	p < 0.001	Improvement in Stroop task	+	Activation increase within R supramarginal gyrus	—	r = .49
			Stroop (inhibition)	p < 0.05	Improvement in Stroop task	+	Activation increase within R superior postcentral gyrus	—	r = 0.42
Kim et al. (2017)	Multidomain	Both	Color Trails (flexibility)	p < 0.05	Improvement in Stroop task	+	Activation increase within R postcentral gyrus	—	r = 0.42
			Digit Span Forward (WM)	ns	Improvement in Verbal Paired Associates (recognition)	+	Activation increase within R supramarginal gyrus	—	—
			Digit Span Backward (WM)	ns	—	—	—	—	—
			Symbol Span (WM)	ns	—	—	—	—	—
			Verbal Paired Associates – recognition (memory)	p < 0.05	—	—	—	—	—
Kuiper et al. (2017)	Multidomain	Both	Stroop-Switch (executive control)	ns	—	—	—	—	—
			- reaction time	p < 0.05	—	—	—	—	—
			- accuracy	p = 0.05	Improvement in global cognition	+	Grey matter density in R post-central gyrus	—	r = 0.58
Lampit et al. (2015)	Multidomain	AC	Global Cognition (composite of memory, processing speed, and executive control measures)	p = 0.003	Improvement in global cognition	—	Connectivity: posterior cingulate – superior frontal gyrus	—	r = -0.77
					Improvement in global cognition	—	Connectivity: hippocampus – superior temporal gyrus	—	r = 0.59
Niu et al. (2016)	Multidomain	PC	EF composite; Memory composite	p = 0.032	Improvement in global cognition	+	Increase in centroparietal CNV amplitude	—	r = 0.74
O'Brien et al. (2017)	Multidomain	PC	Auditory Oddball task (attention)	ns	Change in self-reported perceptions of cognition	+	Change in parietal P3b amplitudes	—	r = 0.53
Wild-Wall et al. (2012)	Multidomain	Both	Visual Search (attention) - miss rate	p = 0.05	—	—	—	—	—

Note: * Significance of Group(training vs control) x Time (pre- vs post-test) interaction, indicating whether training group performed significantly better than control group; TG = training group, AC = active control, PG = passive control, WM = working memory, R = right, L = left, ns = nonsignificant.

3.2.2.3. Qualitative examination of characteristics moderating functional plasticity. Although Mozolic et al. (2010) did not observe any structural changes after 8 h of training, training-related functional increases in cerebral blood flow were found. Similarly, significant increases in frontal activation were observed in two other studies after 8 h of cognitive training (Akimoto et al., 2016; Gaál and Czígler, 2018). Decreased frontal and parietal activation was observed after 9–12 h training (Brehmer et al., 2011; Heinzel et al., 2016; Kühn et al., 2017), and increased activation in subcortical regions after 10 h training (Brehmer et al., 2011). Changes in resting-state connectivity between cortical and subcortical areas were reported after 36 h of training (Lampit et al., 2015). Similar increases and decreases in activation were observed across studies comprising different training domains, control groups, and training adaptiveness (see Table 3 for a summary).

3.3. Cognitive outcomes

Table 4 summarizes the cognitive findings from each included study.

3.3.1. Working memory training

Within the included working memory training studies, improvements were reported for trained tasks, namely, the letter memory (Dahlin et al., 2008) and *n*-back task (Heinzel et al., 2016). Mixed findings were reported for near-transfer to untrained working memory tasks, whereby improvements were observed on some tasks including the Sternberg and Span Board task, but not others, such as the Digit Span (Brehmer et al., 2011; Heinzel et al., 2016). Additionally, two studies reported no improvements on an untrained *n*-back (working memory updating) task (Dahlin et al., 2008; Tusch et al., 2016). Mixed findings were also reported regarding far-transfer to untrained cognitive domains beyond working memory. Evidence for transfer of training gains were reported for measures of attention, episodic memory, and processing speed, but not reasoning or flexibility (Brehmer et al., 2011; Heinzel et al., 2016).

3.3.2. Cognitive flexibility training

One task-switching training study (Gaál and Czígler, 2018) reported training-related improvements in accuracy, reaction time, and mixing-costs on the trained task but limited near-transfer to two similar untrained task-switching tasks and an attention task. No improvements were reported for any other untrained domain including working memory, reasoning, and processing speed.

3.3.3. Inhibition training

Two inhibition training studies reported improvements on trained inhibitory control tasks (Ji et al., 2016; Mozolic et al., 2010). Near-transfer to untrained inhibition tasks were inconsistent, with one study finding improvements on the Stop-Signal task (Kühn et al., 2017) and another reporting improvements on some inhibition tasks but not others (Ji et al., 2016). Far-transfer to domains beyond inhibition were limited to a composite measure of reasoning tasks, with no improvements in working memory, visuospatial, speed of processing, or memory composites (Ji et al., 2016).

3.3.4. Multidomain training

Mixed findings were reported regarding near-transfer. One study reported no transfer to an untrained inhibition (Stop-Signal) task (Kühn et al., 2017), however, another study observed improvements on a different inhibition measure (Stroop) as well as flexibility, but not working memory (Kim et al., 2017). In contrast, a different study reported improvements on a composite measure of EF tasks, though, this finding was driven by improvements on untrained working memory tasks and not on flexibility or inhibition tasks (Niu et al., 2016).

Far-transfer to untrained cognitive domains were also inconsistent across multidomain training studies. One study demonstrated training-

related gains on a composite measure of global cognition which included a combination of memory, speed, and EF measures (Lampit et al., 2015). For the attention domain, training-related improvements were only reported for the Test of Variables of Attention, but not for the Useful Field of View task (Anguera et al., 2013), or the Oddball task (Akimoto et al., 2016; O'Brien et al., 2017). Improvements were observed for untrained working memory tasks (Anguera et al., 2013; Gajewski and Falkenstein, 2018), as well as episodic memory assessed using the Verbal Paired Associates (recognition) task (Kim et al., 2017). Limited training-related improvements were reported on the Visual Search task (Wild-Wall et al., 2012). Two studies demonstrated transfer to task-switching paradigms (Gajewski and Falkenstein, 2012; Küper et al., 2017).

3.3.5. Qualitative examination of characteristics moderating cognitive plasticity

Exploration of training dose indicated that 8 h of multidomain training did not promote transfer (Akimoto et al., 2016). However, studies employing 8 h of single-domain training demonstrated cognitive transfer, though improvements were limited and generally restricted to trained and near-transfer tasks (Gaál and Czígler, 2018; Mozolic et al., 2010). Similarly, both single- and multi-domain training interventions lasting 9–15 h promoted limited transfer, generally to near-transfer tasks (e.g., Heinzel et al., 2016; Kühn et al., 2017; Anguera et al., 2013). However, two single-domain training studies targeting working memory did not report any transfer (O'Brien et al., 2017; Tusch et al., 2016). Multidomain training studies lasting at least 36 h reported far transfer to global cognition and executive control (e.g., Gajewski and Falkenstein, 2012, 2018; Lampit et al., 2015).

Two studies employed cognitive training that did not adapt task difficulty to participant performance (nonadaptive training). Of these studies, a working memory training intervention demonstrated improvements on the trained task but no near- or far-transfer tasks (Dahlin et al., 2008), whereas a nonadaptive multidomain training intervention promoted significant improvements to global cognition (Lampit et al., 2015). Studies employing adaptive training generally reported transfer to trained and near-transfer tasks, and limited transfer to far-transfer tasks (see Table 4 for a summary of cognitive findings). Similar patterns of cognitive changes were observed across studies employing different control groups; however, when comparing against an active control group, a working memory training study reported no far-transfer to inhibitory control or reasoning (Brehmer et al., 2011), whereas a different working memory intervention reported transfer to these measures when comparing against a passive control group (Heinzel et al., 2016).

3.4. Correlation between cognitive and neural outcomes

Refer to Table 4 for a summary of cognitive and neural associations in each study.

3.4.1. Association between cognitive and structural brain changes

Two studies explored and reported a positive association between improvements in task performance and enhancement of neural structures including cortical thickness of the right inferior frontal gyrus triangularis (Kühn et al., 2017), and grey matter density within the right post-central gyrus (Lampit et al., 2015). These brain-behavior correlates indicate that larger improvements on tasks after training are associated with increases in neural matter.

3.4.2. Association between cognitive and functional brain changes

Eleven studies examined the association between cognitive and functional outcomes. Four fMRI studies reported positive correlations, indicating that larger training gains were associated with increased cerebral blood flow within the frontal cortex (Mozolic et al., 2010), increased resting-state connectivity between the hippocampus and

temporal gyrus (Lampit et al., 2015), and increased task-based activation in cortical parietal regions (Kim et al., 2017), thalamus and caudate (Brehmer et al., 2011). Some studies also reported inverse correlations, demonstrating that larger training gains were associated with decreased resting-state connectivity between the posterior cingulate and superior frontal gyrus (Lampit et al., 2015), decreased task-based activation within the right inferior frontal cortex, right inferior parietal cortex, left fusiform gyrus, insula (Brehmer et al., 2011), as well as decreased activation in the lateral medial frontal gyrus, and caudal superior frontal sulcus (Heinzel et al., 2016).

Six EEG studies explored the relationship between cognitive and neural changes. Of these studies, three reported positive correlations, indicating that larger cognitive improvements were associated with increases in theta power along midline frontal regions (Anguera et al., 2013), as well as increased centroparietal CNV amplitudes (Niu et al., 2016), and P3 amplitudes (Tusch et al., 2016). Similarly, one study found that reductions in reaction time (better performance) were associated with larger increases of high-gamma power within the left medial frontal gyrus and intraparietal sulcus (Akimoto et al., 2016). Gajewski and Falkenstein (2012) explored brain-behavior relationships for pre-test and post-test separately rather than examining the association between *changes* in both outcomes. The authors found that more errors and longer response times were associated with a more delayed N2 component (latency). Additionally, more error occurrences were associated with larger and more delayed Ne (error monitoring) amplitudes. One study reported no significant association between cognitive outcomes and functional neural outcomes (O'Brien et al., 2017).

4. Discussion

This systematic review aimed to connect and shed light on training-related cognitive and neural plasticity amongst healthy older adults as a function of EF training. The findings from 20 studies were examined. This section will first discuss training-related neural plasticity in terms of structural and functional changes, followed by training-related cognitive plasticity. Intervention characteristics that potentially moderate the effects of cognitive training will then be explored, and avenues for future research will be recommended.

4.1. Training-induced neural plasticity: structural changes

In terms of structural brain changes, two studies reported decreased cortical and subcortical volume amongst older adults over time (Lampit et al., 2015; Raz et al., 2013). This age-related deterioration in brain volume is consistent with numerous cross-sectional and longitudinal studies (e.g., Driscoll et al., 2009; Good et al., 2001; Raz et al., 2005; Scialli et al., 2003). However, four out of five studies in this review demonstrated that engagement in EF training attenuated the loss of, and even increased the volume of, grey matter. Additionally, two studies reported that individuals who demonstrated larger training-related improvements in task performance also demonstrated larger increases in grey matter volume (Kühn et al., 2017; Lampit et al., 2015). These findings are in line with cross-sectional and longitudinal studies reporting positive associations between grey matter volume and cognitive performance, whereby individuals possessing larger brain volumes perform better on measures including executive functioning and processing speed (e.g., Kramer et al., 2007; Van Der Werf et al., 2001). Two studies examined training-related changes in structural connectivity but reported inconsistent findings (Lampit et al., 2015; Lövdén et al., 2010b).

These findings should be taken with caution as the robustness and strength of evidence concerning training-related brain changes have been disputed. Thomas and Baker (2013) suggest that weak experimental designs (e.g., inadequate control groups), non-conservative statistical methods, and methodological artifacts (e.g., signal-to-noise ratio) are prominent within cognitive training studies and should be

improved upon to provide stronger evidence regarding training-related structural changes. Nevertheless, the findings from these imaging studies indicate the potential for EF training to induce neuroplastic and cognitive change, or at least protect against cortical and subcortical atrophy in older adulthood.

4.2. Training-induced neural plasticity: functional changes

4.2.1. Resting-state activation

Training-related changes in resting-state activation were explored in two studies which reported increased cerebral blood flow within frontal regions (Mozolic et al., 2010) as well as increased connectivity within memory-related regions including the hippocampus and superior temporal gyrus (Lampit et al., 2015). These findings are in line with previous research reporting positive correlations between functional connectivity and cognitive performance, whereby higher degrees of connectivity within memory-related networks (e.g., hippocampus) were associated with better performance on executive functioning and memory tasks (e.g., Damoiseaux et al., 2007; Wang et al., 2010). These higher-order networks (e.g., default mode network) are critical for attention, memory, and executive functioning, and have been found to be particularly vulnerable to age-related connectivity decline (Ferreira and Busatto, 2013). In addition to training-related increases, Lampit et al. (2015) reported connectivity decreases between the posterior-cingulate and superior frontal gyrus, as well as an inverse correlation between behavioral training gains and activity in this network. The authors suggested that this decreased activation may be a positive finding as increased activation in these regions have been observed in amnestic mild cognitively impaired individuals compared to healthy older adults. However, with small sample sizes and the limited number of studies that have investigated resting-state connectivity, further investigations are warranted to provide stronger evidence regarding the neural correlates of training-related connectivity increases and decreases.

4.2.2. Task-based activation

Studies examining task-based functional activation revealed a pattern of training-related activity increases within subcortical regions including the insula (Kim et al., 2017), striatum (Dahlin et al., 2008), thalamus, and caudate (Brehmer et al., 2011) as well as some frontal and parietal regions. However, training-related decreases in activation were mainly observed within cortical frontal and parietal areas including the DLPFC, anterior cingulate gyrus, frontal gyrus, and supramarginal gyrus (Brehmer et al., 2011; Heinzel et al., 2016; Kühn et al., 2017). Additionally, these studies reported positive correlations between behavioral training gains and increased activity within the thalamus, caudate, and supramarginal gyrus. Negative correlations were found between behavioral training gains and activation within frontal and parietal regions.

This pattern of training-related changes aligns with Park and Reuter-Lorenz's Park and Reuter-Lorenz, (2009) Scaffolding Theory of Aging and Cognition (STAC). This theory implicates the aging brain's adaptive response to recruit additional neural resources from frontal—particularly prefrontal—and parietal regions to act as compensatory 'scaffolds' to support less efficient brain regions (e.g., hippocampus, posterior regions) in achieving a particular goal or task. In their revised model (STAC-r), Reuter-Lorenz and Park (2014) consider life course factors that serve to enhance or deplete neural resources, which offers the possibility that cognitive interventions directly influence brain structure and function. The authors suggest that training may create scaffolds during learning or task acquisition; however, training may also improve efficiency of primary structures and networks, paradoxically reducing reliance on scaffolding. Thus, it is a possibility that, prior to training, older adult participants are required to recruit additional frontal and parietal resources as compensatory scaffolding to complete cognitive tasks. As behavioral performance and primary structures and networks become more efficient (evidenced as

increased activation) as a result of training, additional recruitment of frontal and parietal regions is no longer necessary to perform the same tasks (evidenced as decreased activation). It should be noted that this interpretation is based on speculation as only one study reported both increased subcortical activation as well as decreased frontal and parietal activation (Brehmer et al., 2011). It is clear, however, that integrative methods combining neural and behavioral outcomes need to be applied within cognitive training studies to provide stronger evidence regarding the neural mechanisms of cognitive training.

Most studies employing electrophysiological methods reported a training-related increase in neural activation across frontal, central, and posterior regions, indexed by increased high-gamma and theta power (Akimoto et al., 2016; Anguera et al., 2013) as well as increased amplitudes for numerous ERP components (e.g., Gaál and Czigler, 2018; Gajewski and Falkenstein, 2012, 2018; Niu et al., 2016; Tusch et al., 2016). In addition, larger behavioral improvements on cognitive tasks were associated with larger increases in P3 amplitude (Tusch et al., 2016), midline frontal theta power (Anguera et al., 2013), and high gamma power (Akimoto et al., 2016). In conjunction with behavioral improvements, activation increases may reflect a greater appropriation of neural resources to better match task demands. However, it should also be noted that three studies reported a more anteriorly-distributed P3 component (rather than the typical posterior distribution), which may indicate the use of compensatory scaffolding (Gaál and Czigler, 2018; Tusch et al., 2016; Wild-Wall et al., 2012). Additionally, some studies reported training-related activation decreases within frontal and frontocentral sites (Anguera et al., 2013; Küper et al., 2017; O'Brien et al., 2017) which may signify reduced reliance on additional fronto-parietal recruitment.

4.3. Cognitive plasticity

Regardless of the type of training provided across the included studies, cognitive improvements were generally limited to trained tasks, however near-transfer was also observed, albeit less consistently, on untrained tasks of the same cognitive construct. Limited improvements were reported on measures from untrained constructs (i.e., far-transfer) including attention, memory, processing speed, reasoning, executive functioning, and global cognition, though these improvements were not consistent across studies.

In their theoretical framework of adult cognitive plasticity, Lövdén et al. (2010a) outline the mechanisms underlying cognitive training and improvements on trained tasks. The authors propose that plasticity occurs as a consequence of a prolonged discrepancy between functional supply (current neurocognitive capacity) and environmental demands (e.g., task difficulty)—a disparity they term ‘supply-demand mismatch.’ When learning a new task, there is an initial mismatch between supply and demand. After repeated practice, that functional supply responds to the increasing demands; thus, improvements occur as the current range of functioning increases to meet the high demands of the training task. However, once matched, functional supply remains stable and no longer needs to change as there is no longer any discrepancy between supply and demand. This has been supported by cognitive training studies reporting an asymptotic pattern of change, whereby large cognitive and neural improvements observed in the early stages of the training intervention tend to plateau over time (e.g., Lampit et al., 2015). From a neurocognitive perspective, it may be the case that training initially fosters the reduction of reliance on compensatory mechanisms (as described by the STAC and STAC-r models), however, once there is equilibrium between supply and demand, training may serve to promote maintenance mechanisms whereby preservation (as opposed to changes) of brain integrity is the main goal (Nyberg et al., 2012).

Although the ultimate goal of cognitive training is to generalize improvements to untrained tasks and everyday activities, very little is known regarding the mechanisms underlying cognitive transfer. Thus, a

possible account for the limited transfer effects reported across studies may be that the trained task did not tap into the same neural mechanisms or networks as the untrained task(s). For instance, Dahlin et al. (2008) demonstrated that, in order for cognitive transfer to occur, the trained and untrained tasks must engage overlapping brain regions at pre-test and must also share the same pattern of training-related changes in these regions. This premise has been supported by numerous training studies (e.g., Heinzel et al., 2016; Salminen et al., 2016).

Similarly, in a recent framework of transfer, Taatgen (2013) posited that all tasks comprise a combination of primitive information processing elements (PRIMs). Some elements are task-specific and some are task-general. Through practice, task-specific processing elements are combined and executed in parallel which allows for more efficient processing on that task. Transfer occurs when the trained and transfer tasks are structurally similar (in terms of task-general elements), even if low-level task features differ (i.e., task-specific elements). Limited or lack of transfer may therefore suggest that training and transfer tasks did not share sufficient task-general elements. Thus, it appears that transfer is more likely to occur when there are structural and neural commonalities between training and transfer tasks, though additional studies employing neuroimaging techniques are needed to further this field of research. By building upon the empirical and theoretical work in this area, cognitive researchers will be able to begin to develop a more comprehensive framework of cognitive training and transfer.

4.4. Potential moderators of cognitive training effects

Firstly, it should be noted that the following qualitative comparisons of intervention characteristics are based on a limited number of studies; findings should therefore be taken with caution. In particular, although adaptive training has been reported to promote larger training and transfer effects compared to nonadaptive training (e.g., Brehmer et al., 2011; Cuenen et al., 2016), the efficacy of training adaptiveness was not explored as only two studies included in this review employed nonadaptive interventions.

A comparison of type of control group did not yield any distinct patterns across studies. However, strengthened structural pathways were observed after training when compared to a passive control group (Lövdén et al., 2010b) but not when compared to an active control group (Lampit et al., 2015). Similarly, two working memory training studies employed far-transfer measures tapping inhibitory control and reasoning—one reported far-transfer when comparing against a passive control group (Heinzel et al., 2016), whereas the other reported no transfer when compared to an active control group (Brehmer et al., 2011). This may suggest that some non-focal factor(s) such as general cognitive stimulation, social interaction, or expectation effects are potentially driving cognitive and neural plasticity rather than the training itself (e.g., Schmiedek, 2016). However, this was not a prominent pattern that emerged across all included studies as behavioral and neural enhancements were reported by studies comprising passive and/or active controls. Similarly, previous meta-analyses have reported that type of control group is not a significant moderator of cognitive training effects (e.g., Karbach and Verhaeghen, 2014; Lampit et al., 2014; Toril et al., 2014).

In terms of training dose, 8 h of training may not be enough to induce structural plasticity but appears to promote increases in functional activation (Mozolic et al., 2010). Training-related increases in neural volume were observed after 12 h of training (e.g., Kühn et al., 2017). However, compared to changes in grey matter, plasticity of structural pathways potentially require more extensive training. Based on the included studies, strengthening of axonal and myelin integrity was observed after 100 h of multidomain training (Lövdén et al., 2010b) but not 36 h of multidomain training (Lampit et al., 2015).

In relation to cognitive plasticity, 8 h of multidomain training did not promote any transfer (e.g., Akimoto et al., 2016), whereas 8 h of single-domain training promoted transfer to trained and near-transfer

tasks (e.g., Gaál and Czigler, 2018; Mozolic et al., 2010). However, more extensive multidomain training studies (at least 36 h) consistently reported far-transfer to executive control and global cognition (e.g., Gajewski and Falkenstein, 2012, 2018; Lampit et al., 2015). Thus, it may be the case that single-domain training predominantly promotes near-transfer as more extensive practice on one cognitive process likely enhances performance on tasks—trained or untrained—that tap into that particular cognitive domain. In contrast, training multiple cognitive processes may enhance performance in a range of cognitive domains, though longer training periods may be required as less time is spent exercising each cognitive process. This interpretation, however, should be taken with caution due to the limited number and variable nature of studies in this review; for instance, the training regime, measures, and focal cognitive processes differed in each study—some studies included a range of far-transfer measures tapping different domains whereas others did not include any. Nevertheless, this idea is consistent with previous reviews and meta-analyses which have reported that higher training doses (e.g., 20 h or more) as well as multidomain training elicits broader transfer to numerous cognitive domains over lower training doses (less than 20 h) and single-domain interventions (e.g., Lampit et al., 2014). Thus, it may be fruitful for future research to compare the scope for transfer between single- versus multidomain training interventions, as well as the optimal training dose required for each type of intervention to promote far-transfer.

The evidence reviewed appears to support the notion that functional brain changes occur before structural changes, both of which precede behavioral changes (e.g., Reuter-Lorenz et al., 2016). Based on the studies included in this review, 8 h of training may be sufficient to elicit functional neural changes but not structural changes which may require at least 12 h of training. In contrast to multidomain training, 8 h of single-domain training likely promotes enhancements on trained and near-transfer tasks, but not far-transfer tasks. Although multidomain training may require a more extensive training regime, this type of intervention could be more effective in promoting far-transfer, and, in effect, performance on functional everyday tasks. Further investigations into the time-course of training-related brain and behavioral changes are warranted to provide a more comprehensive understanding of the neural mechanisms underlying cognitive training and transfer.

4.5. Limitations and future directions

The evidence presented for cognitive plasticity in this review should be taken with caution as the included studies are not representative of all EF training in the extant literature—eligible studies were restricted to those that included a neural outcome measure. Although there are a number of similar studies that report limited evidence for cognitive plasticity, many studies have been successful in transferring training gains to untrained tasks (e.g., Borella et al., 2010; Karbach and Kray, 2009). Furthermore, each cognitive training intervention encompassed a variety of characteristics which differed across and within studies (e.g., training type, adaptiveness, training duration, control group). Such variables may have contributed to the inconsistent cognitive and neural findings reported. Despite this, cognitive EF training provides a promising approach to protect against age-related cognitive decline, though further research is required to establish the optimal training conditions that might promote broader transfer to untrained tasks. In particular, multidomain training interventions targeting multiple EFs are a worthwhile avenue of research. Multidomain training programs exercise numerous cognitive processes and likely activate a more widespread neural network, thereby having the potential to promote larger and broader transfer to untrained tasks than targeting a single cognitive domain alone. Additionally, EFs have been implicated in a wide range of cognitive processes required to perform essential tasks independently in older adulthood. For instance, performance on EF tasks has been found to predict prospective memory performance (memory for intentions or future actions such as remembering to take

medications or pay bills; e.g., Schnitzspahn et al., 2013) and driving performance (e.g., Adrian et al., 2011). Thus, if the ultimate goal of cognitive training is to promote the application of training gains to a broad range of everyday functional activities, training multiple EFs appears to be a viable approach to defend against cognitive decline.

Critically, many of the included studies only employed a passive control group to compare findings against. Passive controls only take part in the testing sessions and can only control for test-retest effects; thus, findings should be interpreted with caution as this type of control group cannot account for non-focal effects such as motivation, social interaction, expectancy, and general cognitive stimulation. It is therefore recommended that future studies employ appropriate active control groups in which participants engage in activities that produce the same non-focal effects as the training group but do not train the focal cognitive domain(s) of interest. Furthermore, future studies are encouraged to utilize neural measures to compliment behavioral measures, as this integrative method is likely to provide a more comprehensive insight into cognitive training and aging mechanisms.

4.6. Conclusion

This systematic review explored both cognitive and neural plasticity as a function of EF training within healthy older adults. Training-related cognitive improvements were generally restricted to trained tasks, with mixed findings regarding near- and far-transfer to untrained tasks. Training elicited structural brain changes, evidenced by increased volumetric tissue in cortical and subcortical regions, but mixed findings regarding enhancements in the structural integrity of neural pathways. In terms of functional brain changes, training generally appeared to strengthen activity and connections within higher-order neural networks, and in turn, reduced activation within frontal and parietal regions that may have been acting as compensatory mechanisms. As these findings were somewhat mixed, further EF training studies utilizing neural and behavioral outcomes are warranted to provide a more comprehensive and conclusive understanding of the mechanisms underlying cognitive training, transfer, and aging. Overall, EF training appears to be a promising intervention to protect against the cognitive and neural deterioration associated with aging, though there is still much to be learnt within this rapidly developing area of research.

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