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Memory training effects in old age as markers of plasticity: A meta-analysis

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Abstract. In most studies on plasticity using behavioural data, cognitive plasticity has been studied in the context of short-term interventions such as memory training. In order to systematically review the literature on memory training and summarize its effects for old healthy people and people with mild cognitive impairment on multiple functional domains, we conducted a meta-analysis of all published randomized controlled trials (RCT) between 1970 and 2007. Overall, 24 studies examining memory training effects in healthy and in mildly cognitively impaired old adults were identified and included in the analysis. Only memory trainings (e.g. memory skills training, imagery, method of loci) with cognitive outcome measures, duration of intervention with up to one year with at least a baseline and a post-intervention assessment reported, were included.
Results demonstrate significant training effects for paired associate learning and immediate and delayed recall in healthy old adults and for immediate recall in mildly cognitively impaired old adults. However, training effects were no larger than those found for active control conditions. Our results suggest that evidence on the effectiveness and specificity of training interventions is scarce. We discuss limitations of existing knowledge about the efficacy of memory training interventions and implications for future research to improve knowledge regarding effective cognitive interventions.

Keywords: Plasticity, memory training, meta-analysis, old age, mild cognitive impairment

1. Purpose

Understanding more about the processes underlying plasticity in cognitive performance may offer various avenues for supporting cognitive functioning in later life. Findings from a number of studies have indicated that cognitively-stimulating activities may help to protect against cognitive decline in later life (Wilson, 2002). Building on these observations, researchers have attempted to enhance or maintain cognitive functioning in old people by means of systematic cognition-based interventions such as memory training (Willis et al., 2009). For theoretical as much as practical purposes, it is therefore important to establish to what extent cognitive performance can be improved through systematic training across adulthood and old age, and for how long gains can be maintained. Moreover, possible factors that influence the extent of any gain for a given individual, and the relative importance for magnitude of gains of different features of the training, such as intensity, frequency, duration, instructional procedures, or focus, need to be explored (Hoyer, 2006; Nyberg, 2005; Willis, 2001).

Research on memory training has focused on examining the potential for improvement of cognitive functioning in normal ageing and on determining the limits of cognitive plasticity in old age (Hoyer and Verhaeghen, 2006; Kliegl et al., 1989; Verhaeghen et al., 1992). Cognitive plasticity refers to cognitive changes and adaptations, and especially to the potential performance of people under optimal conditions (Singer, 2000). Generally, cognitive training research has focused on cognitive processes (e.g., processing speed, inhibition; Ball et al., 2001; Jones et al., 2006), pri-

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mary mental abilities (e.g., inductive reasoning, spatial orientation, episodic memory; Schaie and Willis, 1986), higher order cognitive constructs (fluid intelligence, executive functioning; Jaeggi et al., 2008), and global cognition involving multiple cognitive domains (Experience Corp; Fried et al., 2004). Most of these studies have targeted old adults with some kind of severe cognitive impairment. Several criteria have been involved in evaluating the effectiveness of cognitive training, and these criteria are of interest in the study of cognitive plasticity (Ball et al., 2001).

For the majority of old people the extent of any cognitive decline is relatively small, but some individuals develop more extensive difficulties and are at greater risk of developing a form of dementia. Current attempts focus on the identification of these individuals in the preclinical stage, which has led to the development of the diagnostic concept of Mild Cognitive Impairment (MCI). MCI applies to individuals with declining cognitive abilities, but largely preserved everyday functioning. Individuals with MCI display subtle cognitive changes that are not severe enough to fulfil diagnostic criteria for dementia, but are greater than those typically observed in their age group (Larrieu, 2002; Petersen, 2001). Earlier definitions emphasized the differentiation from optimal ageing (e.g. "Benign Senescent Forgetfulness"; Kral, 1962; "Age-Associated Memory Impairment"; AAMI; Crook, 1986), or the identification of preclinical dementia patients (e.g., "Malignant Senescent Forgetfulness"; Kral, 1962; "Cognitive Impairment, No Dementia"; CIND; Graham, 1997). The term MCI as defined by the American Psychiatric Association (APA 1987) is a condition involving impaired short- and long-term memory, but no functional impairment. MCI is assumed to be a precursor of dementia, i.e., a transitional state between normal cognitive decline in old age and dementia. According to the diagnostic concept MCI as proposed by the International Working Group on Mild Cognitive Impairment (Winblad et al., 2004), the criteria for MCI are (a) the person is neither healthy nor demented, (b) there is evidence of cognitive deterioration which is either reflected in decline in neuropsychological test performance over time and/or subjective report of decline by self and/or informant in conjunction with objective cognitive deficits as defined by neuropsychological test performance below age-adjusted norms, and (c) activities of daily living are preserved and complex instrumental functions are either intact or minimally impaired. Due to the variability in definitions, studies investigating prevalence and incidence of MCI come to different conclusions (Kratz, 2002). Prevalence rates reported in the literature vary between 5% and 25% (Kumar, 2005; Manly, 2005; Purser, 2005), and incidence rates between 0.5 and 8% (Busse, 2003; Larrieu 2002; Jungwirth, 2005).

Numerous studies report effects of cognition-focused interventions in old people. There is some evidence for cognitive plasticity in later life as well as a possible protective effect of engaging in cognitively-stimulating activity (Baltes and Lindenberger, 1988; Wilson, 2002; Hultsch, 1999). This suggests there may be potential to improve cognitive functioning in later life through cognitive training interventions, and this in turn might help to support continued independence and maximise quality of life for old people. For old people with MCI who are at increased risk of developing dementia cognition-focused interventions may help to improve or maintain their level of cognitive performance and thereby delay or prevent further decline (Hoyer, 2006; Wilson, 2002). This is also targeted by memory training which is one of the most applied cognitive interventions (Hultsch, 1999; Schooler, 2001; Stern, 2002). However, so far it is unclear which factors may be responsible for any benefits resulting from memory training, and whether the same or different approaches are needed for healthy old people and old people with mild cognitive impairment (Nyberg, 2005).

Memory trainings may be offered in various forms, like individual or group sessions, and tasks may be presented in various modalities, including paper-pencil or computerised versions but all aim at performance improvement. Approaches differ with regard to trained abilities (e.g., memory, attention, speed of information processing) and specificity of training (e.g., training of text recall vs. multimodal and holistic approaches training a combination of abilities). In addition, strategies practiced in the training sessions (e.g., method of loci, imagery training), duration of training sessions, overall training period, frequency of training sessions, group size and participants' characteristics (e.g., education, personality, preferred learning style etc.) differ between studies. Standardized training tasks are used (Clare, 2003), but difficulty may be varied to adjust for individual's ability level. Effectiveness is considered in terms of improvements on test scores in the areas of cognitive functioning targeted in the training, maintenance of improvements over time, transfer of training effects to other kinds of cognitive tasks, and generalisation of effects to everyday functioning.

Moreover, studies vary with regard to design and outcomes, and may use pre-post comparisons, randomized control groups or comparisons with active control

conditions. Several meta-analyses have provided detailed descriptions on the effectiveness of specific memory training types. Verhaeghen et al. (1992) focused on memory training gains in episodic memory tasks and evaluated effect sizes as a function of the type of mnemonic trained, whereas Floyd and Scogin (1997) examined the effectiveness of memory training on subjective memory functioning and mental health of older adults. Sitzer et al. (2006) and Clare et al. (2003/2007) summarized cognitive training effects for old people with a diagnosis of dementia. In contrast to these previous meta-analyses the present review focuses on i) healthy old people and people with mild cognitive impairment; ii) memory trainings with outcome measures such as immediate and delayed recall or name-face associations; iii) randomized controlled trials (RCT) to prevent selection bias in allocating interventions to participants (participants are assigned to receive a specific treatment intervention by a chance mechanism so that the value of a treatment will be shown in an objective way and therefore the study groups are unbiased) and to gain information on treatments' effectiveness in comparison to no contact control groups and active control groups (receiving an alternative treatment).

The present article aims to 1) provide an overview of the effectiveness of memory trainings for healthy old people and people with mild cognitive impairment, 2) discuss limitations of existing knowledge regarding the effectiveness of trainings and 3) suggest concrete steps for future research on how to improve knowledge regarding effective memory trainings.

2. Method

A meta-analysis on 24 randomized controlled memory training studies reported in the literature from 1970 to 2007 was conducted.

2.1. Literature Search

The trials were identified from a search of the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG) on 30 September 2007. This register contains records from the major healthcare databases *The Cochrane Library*, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS The CDCIG as well as many ongoing trial databases from UK, Netherlands, USA/International. We used the search terms: 'cognitive stimulation' OR 'cognitive rehabilitation' OR 'cognitive training' OR 'cognitive retraining' OR 'cognitive re-training' OR 'cognitive support' OR 'memory function' OR 'memory rehabilitation' OR 'memory therapy' OR 'memory aid*' OR 'memory group*' OR 'memory training' OR 'memory retraining' OR 'memory support' OR 'memory stimulation' OR 'memory strategy' OR 'memory management'. These search terms were used in combination with Phases 1 to 3 of the highly sensitive search strategies for identifying reports of randomized controlled trials in MEDLINE (APPENDIX 5b, Cochrane Handbook, 2006), and all terms were searched as title, abstract, keyword, and publication type. These results were supplemented by searches from January 1970 to September 2007 in PsycINFO/PSYNDEX, ISI Web of Knowledge and Pubmed. The search terms used in these searches were: 'memory training', 'mnemonic training', 'cognitive training', 'cognitive rehabilitation', 'cognitive intervention', 'cognitive exercise' in combination with 'elderly', 'old adults', old age', 'MCI', 'mild cognitive impairment', 'memory complainers', 'AACD', 'dementia', 'dementia treatment', and 'dementia therapy'. Dementia terms were included because training studies targeting old people with a form of dementia may also include healthy old control groups or groups with people with mild cognitive impairment and could therefore be relevant for this review. After searches of the major databases were completed, reference lists from acquired studies and recent meta-analyses were examined to find additional randomized control trials.

2.2. Types of interventions

We focused on randomized control trials, for which adequate information (such as age group, mean values, and standard deviations) was provided. The studies included have been published in English or German in a peer-reviewed journal (in order to avoid reporting overlapping data in journals and book chapters). Studies were considered for the review if they described memory training interventions. Only studies with cognitive outcome measures, such as any measures of cognitive functioning, improvement, sustainability and transfer of training effects, were included. Duration of intervention was up to one year with at least a baseline and a post-intervention assessment reported. Studies were only included in the review if they recorded participants' performance at least at two time points.

To date, most studies investigating the effectiveness of cognitive interventions have used pre-post designs or relied on comparisons with alternative approaches,

active control conditions, or waiting list control conditions. In this review, we coded the groups as being either a) a no contact control group, when no treatment (apart from testing) was given; b) an active control group, when the control group was active in some way but the given treatment was not a memory training (i.e. relaxation training) or when training was some combined treatment (i.e. memory training and art discussion); c) treatment group, when a memory training was given.

In the literature, the handling of multiple training or control groups has been solved in many different ways. One could subject any study that has multiple treatment conditions to a randomization process whereby only one treatment is selected for inclusion in the meta-analysis or consider each cognitive training-control comparison as a separate study (i.e., Sitzer et al., 2006). When several control groups were compared to the treatment group, e.g., no contact control group and active control group, we decided to consider each treatment-control comparison as a separate study in order to maximize information extraction from the database.

2.3. Participants

To meet inclusion criteria for the review, participants (both male and female) had to be aged 60 years or older, and to be either healthy old people or old people who met criteria for mild cognitive impairment, but without a diagnosis of dementia. In order not to exclude studies that might be relevant for the review, none of the specific definitions of mild cognitive impairment were particularly included or excluded, but information on participants' cognitive ability was required for classification of individual cognitive status. Participants could be trained in any setting (group or individual).

2.4. Procedure and analysis

Searches were conducted as described above to identify all relevant published studies, and hard copies of all articles were obtained. Randomized controlled trials were identified and four reviewers worked independently to determine which studies met criteria for inclusion before reaching a final consensus. The quality assessment was conducted by using the approaches described in the Cochrane Reviewers' Handbook (Higgins, 2008): In category A (adequate), the report describes allocation of treatment by some form of centralized randomized scheme, such as e.g. having to provide details of an enrolled participant to an office by telephone to receive the treatment group allocation; category B (intermediate) is where the report describes allocation of treatment by use of a "list" or "table" to allocate assignments, use of "envelopes" or "sealed envelopes", stating the study as "randomized" without further detail. Category C (inadequate) is where the report describes allocation of treatment by alternation, reference to case record numbers, dates of birth, day of week, or any such approach, any allocation procedure that is transparent before assignment, such as an open list of random numbers or assignments. Empirical research has shown that lack of adequate allocation concealment is associated with bias. Trials with unclear concealment measures have been shown liable to yield more pronounced estimates of treatment effects than trials that have adequate measure to conceal allocation schedules, but the effect is less pronounced than for inadequately concealed trials (Chalmers, 1983; Schulz, 1995). Trials were therefore considered if they conformed to categories A or B, but those falling in category C were excluded.

Data from the RCTs selected for inclusion was extracted. Summary statistics (n, mean and standard deviation) were used for each rating scale at each assessment time for each treatment group in each trial to detect change from baseline. For cross-over trials only the data from the first treatment period was used. When change from baseline results was not reported, the required summary statistics were calculated from the baseline and assessment time treatment group means and standard deviations. In this case, as is customary in reviews adhering to the standards of the Cochrane Review Group, a zero correlation between the measurements at baseline and assessment time was assumed. Although this method may overestimate the standard deviation of the change from baseline, it is the most conservative approach, thus ensuring a high validity of the results from the meta-analysis.

Baseline assessment was defined as the latest available assessment prior to randomization, but no longer than two months before prior testing. For each outcome measure, data from those who completed the trial was sought and indicated as such. However, in order to allow an intention-to-treat analysis, wherever possible the data was sought irrespective of compliance, whether or not the person was subsequently deemed ineligible or otherwise excluded from treatment or follow-up.

Based on the goal of determining if particular memory constructs could be improved through interventions, we grouped the studies based on the trained outcome,

thus assuming that interventions were similar to the degree they were targeting the same memory construct. Since none of the trainings was completely identical and differed at least with respect to duration and sample, grouping by intervention technique would have mostly lead to the same grouping. The present study aimed at exploring whether memory trainings, in general, do have an effect on memory performance and not at finding out which technique is most effective. Consequently, outcome measures were derived from the evaluation instruments used and then grouped based on the following memory subgroups: immediate and delayed recall of words, paragraphs or stories, face-name recall, paired associate learning, visuo-spatial and short-term memory.

Data on outcome measures were pooled as homogeneous subgroups whenever possible within the memory domain. We pooled studies with sufficient data that were judged to be clinically homogeneous using RevMan 5.0 software. We conducted forest plots with integrated statistical tests for heterogeneity (chi-squared test). When studies were statistically heterogeneous (I^2 test value $> 50\%$), a random-effects model was used; otherwise a fixed-effects model was adopted.

3. Results

3.1. Search results and selected studies

Included in statistical analyses were studies that a) included healthy subjects or people with mild cognitive impairment b) included a pre- and post-treatment measure of memory performance (studies that investigated long-term effects through follow-up were not included), d) provided sufficient statistical data for the computation of effect sizes. A total of 24 memory training studies were retrieved to be included in the current meta-analysis and were pooled for calculations.

Regarding allocation concealment, one study was ranked as grade A and 23 as grade B. Twenty-one of the included studies involved healthy old people and three of them investigated people with mild cognitive impairment. Main reasons for excluding studies were i) studies included patients with more severe cognitive impairments than MCI; ii) no RCT; iii) studies were reviews or not journal articles; iv) were written in neither English nor German; v) contained missing data; vi) age range; vii) no pre/post design.

Included memory training intervention studies for healthy old people focused primarily on the training of the memory domain using one or multiple mnemotechniques (i.e. memory skills training, self-monitoring approach for improving older adult learning, imagery, method of loci, self-studied memory training manual, mnemonic training, memory strategy training) to improve the target construct. Studies varied considerably in terms of number of training sessions and overall duration of the intervention: number of training sessions in hours ranged from six to 135 hours, overall period of the cognition-based intervention from one day to one year. Less divergent but still variable and not always indicated, were pre- to post-test intervals and training to post-test intervals. Eighteen interventions were conducted in group settings with a trainer or tutor, only two study settings were self-instructional, two studies used both single and group setting, the setting of 2 training remains unclear.

The total sample of old study participants consisted of 2229 persons, with an estimated mean age of 69.9 years (SD 3.53; mean age was estimated from midpoint of age range for those studies in which mean age was not reported). Overall, 24 studies, consisting of 767 healthy old adults and 34 participants with mild cognitive impairment, 442 no contact controls and 986 active controls were included in the analysis. The studies are presented in the Appendix including intervention groups, study sample sizes, mean ages, MMSE, duration of training and outcome variables where available (see also Martin et al., in press).

3.2. Effects

Data of 24 randomized controlled trials were pooled. Results are summarized in Tables 1–4. Tables contain information on the outcome measure, number of studies, number of participants, statistical method used (fixed or random effects model as well as confidence interval), effect estimates (and effect ranges in parenthesis), heterogeneity measures and overall effect sizes. The magnitude of effect size estimates is defined as small, $d = 0.20$; medium, $d = 0.50$ and large, $d = 0.80$ (Cohen, 1988). Positive effects sizes denote that the treatment (memory training) group showed better performance on the outcome measures than the corresponding control group, negative effects favour the control groups.

For healthy old adults, performances on paired associate learning ($p < 0.05$), immediate verbal recall ($p = 0.001$) and delayed verbal recall ($p = 0.006$) improved significantly following training compared to a no contact control condition (see Table 1).

Table 1
Healthy old adults: Treatment versus no contact

Outcome measure	Number of studies	Participants	Statistical method	Effect estimate	Heterogeneity	Test for overall effect
face-name immediate recall	4	170	Mean difference (IV, fixed, 95% CI)	0.58 [−0.52, 1.67]	$Chi^2 = 4.96$, df = 3 ($P = 0.17$); $I^2 = 40\%$	Z = 1.03 ($P = 0.30$)
face-name delayed recall	3	119	Mean difference (IV, fixed, 95% CI)	−0.24 [−1.62, 1.14]	Chi2 = 0.03, df = 2 ($P = 0.98$); I2 = 0%	Z = 0.34 ($P = 0.73$)
visuo-spatial memory	3	83	Mean difference (IV, random, 95% CI)	0.40 [−1.03, 1.84]	$Tau^2 = 2.46$; $Chi^2 = 7.56$, df = 1 ($P = 0.006$); $I^2 = 87\%$	Z = 0.74 ($P = 0.46$)
short-term memory	6	457	Mean difference (IV, random, 95% CI)	2.21 [−0.79, 5.21]	$Tau^2 = 18.74$; $Chi^2 = 460.38$, df = 4 ($P < 0.00001$); $I^2 = 99\%$	Z = 1.50 ($P = 0.13$)
paired associates	3	120	Mean difference (IV, fixed, 95% CI)	2.71 [1.65, 3.78]	$Chi^2 = 0.58$, df = 2 ($P = 0.75$); $I^2 = 0\%$	Z = 4.98 ($P < 0.00001$)
immediate recall	23	1074	Mean difference (IV, fixed, 95% CI)	0.16 [0.06, 0.26]	$Chi^2 = 45.86$, df = 22 ($P = 0.002$); $I^2 = 52\%$	Z = 3.26 ($P = 0.001$)
delayed recall	13	1203	Mean difference (IV, fixed, 95% CI)	0.88 [0.26, 1.51]	$Chi^2 = 22.97$, df = 12 ($P = 0.03$); $I^2 = 48\%$	Z = 2.76 ($P = 0.006$)

Table 2
Healthy old adults: Treatment versus active control

Outcome measure	Number of studies	Participants	Statistical method	Effect estimate	Heterogeneity	Test for overall effect
face-name immediate recall	10	581	Mean difference (IV, fixed, 95% CI)	0.93 [0.41, 1.44]	$Chi^2 = 14.59$, df = 8 ($P = 0.07$); $I^2 = 45\%$	Z = 3.53 ($P = 0.0004$)
face-name delayed recall	3	364	Mean difference (IV, random, 95% CI)	0.47 [−0.59, 1.54]	$Tau^2 = 0.62$; $Chi^2 = 7.17$, df = 3 ($P = 0.07$); $I^2 = 58\%$	Z = 0.87 ($P = 0.38$)
visuo-spatial memory	3	149	Mean difference (IV, fixed, 95% CI)	−0.94 [−1.66, −0.22]	$Chi^2 = 10.85$, df = 2 ($P = 0.004$); $I^2 = 82\%$	Z = 2.57 ($P = 0.01$)
short-term memory	6	442	Mean difference (IV, random, 95% CI)	2.23 [−0.68, 5.14]	$Tau^2 = 12.88$; $Chi^2 = 484.01$, df = 5 ($P < 0.00001$); $I^2 = 99\%$	Z = 1.50 ($P = 0.13$)
paired associates	4	424	Mean difference (IV, random, 95% CI)	−0.49 [−1.15, 0.16]	$Tau^2 = 0.32$; $Chi^2 = 12.45$, df = 6 ($P = 0.05$); $I^2 = 52\%$	Z = 1.47 ($P = 0.14$)
immediate recall	19	1468	Mean difference (IV, random, 95% CI)	0.54 [−0.10, 1.17]	$Tau^2 = 1.38$; $Chi^2 = 71.47$, df = 24 ($P < 0.00001$); $I^2 = 66\%$	Z = 1.66 ($P = 0.10$)
delayed recall	10	503	Mean difference (IV, random, 95% CI)	0.17 [−1.07, 1.42]	$Tau^2 = 2.27$; $Chi^2 = 29.65$, df = 9 ($P = 0.0005$); $I^2 = 70\%$	Z = 0.27 ($P = 0.79$)

Comparing the treatment group to the active control condition, there are some performance gains for the memory training groups but effects were only significant for the outcome variable face-name immediate recall (strong positive effect estimate = 0.93, $p = 0.0004$, see Table 2) and visuo-spatial memory. The first effect demonstrates that memory training has yielded non significant performance gains in immediate recall of face-name associations compared to a no contact control group but significant training gains compared to the active control group. This indicates that in this comparison any kind of memory training has an impact on memory performance.

Another significant effect estimate resulted for the outcome measure visuo-spatial memory but it was negative (effect estimate = −0.94, $p = 0.01$), indicating that the active control group training was more effective than the memory training. This could be due to the uneven sample sizes and the strong weight of the study with the negative training effect (see Table 3).

For individuals with mild cognitive impairment, data were scarce, but analyses indicated significant training gains. However, only in immediate recall effects were significantly better for the treatment condition (memory training) than for the no contact control condition ($p =$ 0.04). For delayed recall, the memory training was not significantly effective compared to a no contact control

Table 3
Healthy old adults: Treatment versus active control; outcome: visuo-spatial memory

	treatment group			active control group				
Study ID	mean	SD	total	mean	SD	total	weight	Effect estimate
Caprio 1996	−0.21	2.4	61	1.65	2.58	56	62.8%	−1.86 [−2.77, −0.95]
Fabre 2002	2.5	1.33	8	2.2	2.47	8	13.6%	0.30 [−1.64, 2.24]
Fabre 2002	2.5	1.33	8	1.7	1.67	8	23.5%	0.80 [−0.68, 2.28]
Total			**77**			**72**	**100%**	**−0.94 [−1.66, −0.22]**

Table 4
MCI: Treatment versus no contact

Outcome measure	Number of studies	Participants	Statistical method	Effect estimate	Tests for heterogeneity	Test for overall effect
Immediate recall	5	110	Mean difference (IV, fixed, 95% CI)	1.73 [0.10, 3.37]	$Chi^2 = 1.27$, df = 2 ($P = 0.53$); $I^2 = 0\%$	Z = 2.07 ($P = 0.04$)
Delayed recall	4	73	Mean difference (IV, random, 95% CI)	2.89 [−1.44, 7.22]	$Tau^2 = 3.30$; $Chi^2 = 1.17$, df = 1 (P = 0.28); $I^2 = 14\%$	Z = 1.31 ($P = 0.19$)

MCI: Treatment versus active control

Outcome measure	Number of studies	Participants	Statistical method	Effect estimate	Tests for heterogeneity	Test for overall effect
Immediate recall	2	73	Mean difference (IV, random, 95% CI)	−2.36 [−11.52, 6.79]	$Tau^2 = 45.67$; $Chi^2 = 7.02$, df = 2 ($P = 0.03$); $I^2 = 72\%$	Z = 0.51 ($P = 0.61$)

group. The improvement for immediate recall however, was unspecific, as it did not exceed the improvement from the active control condition (drug treatment/drug treatment plus memory training) (see Table 4). The effect estimate of the treatment group compared to the active control condition is negative which means that for people with mild cognitive impairment the active control group showed more training gains in immediate recall than people with mild cognitive impairment with the memory training. In this comparison, this indicates that the drug treatment was more effective than the memory training.

4. Conclusions

The aims of this study were to give (a) an overview on the effectiveness of memory training interventions in healthy old adults and old adults with mild cognitive impairment as a marker of plasticity, (b) to discuss limitations of existing knowledge regarding the efficacy of those interventions and (c) make concrete suggestions for future research on cognitive interventions in order to improve knowledge on their efficacy.

Regarding the first aim, considering the large time span covered, surprisingly few studies were identified that fulfilled the rather flexible inclusion criteria (randomized control trials for which adequate information was provided, studies have been published in English or German in a peer-reviewed journal, describing memory training interventions, studies with cognitive outcome measures and a pre- and posttreatment measure of memory performance, participants are older than 60 years and either healthy or mildly cognitively impaired).

Results show that most interventions were effective in terms of performance improvement, with improvements following training for the treatment group. However, for healthy old adults, the effects were significantly better for treatment compared to no contact control in only three of seven memory domains, namely paired associate learning and immediate and delayed recall. There were no significant differences between treatment and active control groups but in face-name immediate recall, demonstrating that training effects were mostly not specific. This might indicate that simple contact or simple unspecific stimulation in alternative treatments (such as in the active control conditions) may be as effective as memory trainings. The same pattern of results with regard to effects in comparison to active control conditions was revealed in individuals with mild cognitive impairment.

With respect to the second aim, limitations of existing knowledge regarding the efficacy of memory training interventions may have several reasons. Several studies did not fulfil inclusion criteria. Most crit-

ical reasons for exclusion were (a) non-availability of information on details of participants' recruitment, exact procedure, and treatment of temporary non-compliance, and (b) lack of a control condition. Furthermore, adequate allocation concealment (double-blind) was only guaranteed for one of the included studies. Future studies should aim to fulfil relevant criteria to be treated as category A-studies. Furthermore, it appears that studies vary enormously with respect to potentially influential factors such as overall length of intervention, number of treatments, group sizes, exact testing procedure, assurance of equal training procedures, combination of training contents within and across sessions, training and similarity of trainers, or pre-existing training experience. In addition, it was not always obvious how the evaluation instruments were matched to the content of training (which would be expected to improve the reported effects). Thus, when conducting the meta-analyses, we decided to use the complete available information at the cost of homogeneity of the included studies. Also, with regards to the variability of duration and intensity of the trainings, we did not divide data in to smaller time periods and did not conduct separate meta-analyses. Thus, future analyses of larger numbers of studies may provide better evidence for the effects of confounding factors.

As is typical for meta-analyses on the effectiveness of interventions, there are several sources of bias in published training studies. First, there is a bias towards publishing studies or results from test instruments demonstrating significant gains after training. This may have led to the relatively small set of 24 studies over a 37-year period examining the effects of memory training using a randomized control design. Either it is difficult to publish the replication of an existing finding (publication bias) or the goal of most training studies is to demonstrate that individuals improve after training and determining the cause for the improvement is of secondary interest (as demonstrated by the relatively large number of excluded studies). As a consequence, published studies are more likely to report significant improvements after training. Despite publication bias, there are not many effects.

Second, there might be a bias towards overestimating effects by using the treatment for multiple comparisons with no contact controls and one or more active control conditions. Considering both types of bias and the few areas in which improvements were observed after combination of data in a meta-analysis, even these improvements might be overestimating the actual chances of improvement through memory training interventions.

Several implications can be identified with respect to future research needs. Our analyses provide surprisingly little evidence for the effectiveness of memory training interventions in terms of significant effects and no evidence on their specificity. Considering that bias with regard to included studies might even be expected to lead to an overestimation of training effects, this argues against the effectiveness of memory training interventions. Despite the great interest in cognitive interventions, relatively few of the published studies use efficient designs to examine the effectiveness of interventions. Treatments differ widely between studies with respect to selection of participants, length of training and number of training sessions as well as materials used for interventions. Due to heterogeneity of procedures, dealing with absent training participants and a variety of training contents, content combinations, and matching of evaluation instruments to training contents, training effects might in fact be substantially larger and future research may profit from more standardized training protocols and outcome measures to allow pooling and comparison of studies. Furthermore, many training approaches include a combination of several elements, and individuals may respond differently to different training elements. Thus, training effects on an individual level may be substantially higher than the overall group effects. Therefore, future research taking more care to recruit homogeneous samples in terms of responding to the training or by collapsing data within individuals before aggregation on a group level might provide more appropriate tests of the effectiveness of cognitive interventions.

There are clearly more studies reporting the effects of training on rather basic abilities such as free recall than there are studies addressing more complex behaviours such as goal-setting, planning, or, in general, executive functioning. The ability to adjust the use of cognitive skills to perform higher order tasks may be better captured by focusing on individual learning trajectories rather than focusing on mean level changes. Furthermore, there are very few studies on the effectiveness of memory training interventions in individuals with mild cognitive impairment as defined by any diagnostic classification. Here, a consistent definition or agreement on core criteria of MCI may help in gathering evidence more quickly.

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detailed analyses and updated information on intervention effects will be documented in the Cochrane Library (http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME).

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Appendix

Author	Methods (groups, training duration, setting)	Participants (n, M_{age}, MMSE)	Interventions	Outcomes	Allocation concealment
Buiza et al., 2007	Double-blind design; 2 years (total of 180 sessions), t1 = baseline, then every 6 months; group setting	– n treatment structured = 85 (M_{age} = 73.28) – n active control = 68 (M_{age} = 70.18)	Attention, orientation, memory, language, visuo-construction, visuo-manual coordination, praxis	Luria, speed (TMT), visuomanual coordination, short term memory, immediate recall, recent logic execution memory, abstraction proverbs, phonematic fluency, IADL	yes
Caprio et al., 1996	Memory training versus active control group; 10 weeks training; group setting	Age range 65–76 years;	Cognitive restructuration technique versus traditional memory training	Guild memory test, supermarket test; subjective memory tests and geriatric depression scale	unclear
Craik et al., 2007	Cross-over design; early training group vs. wait list group (before cross-over); baseline, posttest after 3 months; 4 weeks duration; group setting	– n treat = 29 (M_{age} = 78.38, MMSE = 28.24) – n no contact = 20 (M_{age} = 79.25, MMSE = 27.7)	Memory skills training	Alpha span (working memory) total score, brown-peterson: secondary memory, primary memory, 0s delay, primary memory, 3s delay	unclear
De Vreese et al., 1996	4 groups: n memory training = 10 (M_{age} = 66, MMSE = 29.3) n drug treatment = 7 (M_{age} = 63.9, MMSE = 29.7) n memory training and drug treatment = 10 (M_{age} = 64.4, MMSE = 29.2) n control group = 8 (M_{age} = 65.1, MMSE = 29.9); duration of training?	MCI patients: a score > 25 adjusted for age and schooling on the mini-mental state examination (MMSE, Folstein et al., 1975); If no clinically relevant depression as disclosed by a score < 16 at the geriatric depression scale; presence of impaired objective memory resulting in a score < 15.76 at the story recall test and/or significant memory complaints evinced by a score > 20 at the cognitive difficulties scale;	Drug treatment and memory training, combination and no contact control group	Randt Memory Test: acquisition, delayed recall, memory index	unclear
Dunlosky 2007 a	2 sessions – length? 4 groups	n strat/imag = 21 (M_{age} = 70.2) n self-monit. = 21 (M_{age} = 70.2) n combination = 23 (M_{age} = 70.2) n no contact = 20 (M_{age} = 70.2)	Strategy/imagery vs. self-monitoring approach for improving older adult learning	Correctly recalled word-pairs: no sign. differences between training groups and control	unclear
Dunlosky 2007 b	Pre-post-design; 2 × 2 h training sessions with pause of 2 weeks in paired-associate learning for 2 groups, 1 control;	n strat/imag = 34 (M_{age} = 68) n self-monit. = 38 (M_{age} = 68) n no contact = 29 (M_{age} = 66)	Strategy/imagery vs. self-monitoring training and no contact control	Correctly recalled word-pairs	unclear
Fabre et al., 2002	Pre-post-design; 1 treatment group, 2 active controls, 1 no contact control; 2 months;	n aerobic = 8 (M_{age} = 65.4) n memory = 8 (M_{age} = 67.5) n memory + aerobic = 8 (M_{age} = 64.9) n no contact = 29 (M_{age} = 66)	Memory training versus and aerobic, combination of memory and aerobic training, no contact control	Correctly recalled word-pairs	unclear

Table, continued

Author	Methods (groups, training duration, setting)	Participants (n, M_{age}, MMSE)	Interventions	Outcomes	Allocation concealment
Flynn 1990	2 treatment groups, 1 control group; single/group setting	n manual = 18 (M_{age} = 66.78) n manual + dicussion = 21 (M_{age} = 67.86) n no contact control = 19 (M_{age} = 69.68)	Self-studied memory training manual vs. self-studied memory training manual + group discussion	– vocabulary subtest of WAIS-R – 5 memory tests: word list, word list travelling, name-face, story recall, verbal digit span forward	unclear
Gratzinger et al., 1990	1 treatment group, 2 active control; group setting;	N = 156, M age = 68.42, n imagery = 56 (M_{age} = 68.04) n relaxation, mnemonic = 50 (M_{age} = 68.46) n imagery, judgement, mnemonic = 50 (M_{age} = 68.82)	– imagery + mnemonic training – relaxation + mnemonic – imagery + judgement + mnemonic	Face-name recall NEO-PI	unclear
Hill et al., 1987	2 weeks group training 8x1h; group setting;	n training = 59 (M_{age} = 67.8) n placebo = 17 (M_{age} = 67.5)	Mnemonic training vs. development of own learning strategies	Confidence ratings, name-face recall	unclear
Hill et al., 1988	6 groups; baseline, after pretraining, after mnemotraining; group setting;	n imagery, mnemonic = 24 n imagery, judgement + mnemonic = 36 n relaxation, mnemonic = 24 n lectures, mnemonic = 13 n lectures, practice = 16 n wait list = 15 M_{age}=>60	Imagery, relaxation, affective judgement, unspecific training;	Name-faces recall	unclear
Hill et al., 1990	Pre-/Postdesign, 4 groups; 2h manual + homework; group setting;	n mem + incentive = 16 n memory = 14 n placebo + incentive = 16 n no contact control = 14 M_{age}=>60	Memory training, placebo, (incentive)	Study time, recall time, word recall	unclear
Hill et al., 1991	1 day training; 3 groups; baseline, immediately after training, 1h after training, 3days after training; group setting;	n story = 23 n loci = 27 n placebo = 21 M_{age}=>60	Narrative story, method of loci and placebo training (travelling skills training)	26 nouns (free recall)	unclear
Mahncke et al., 2006	1 treatment, 1 active control, 1 no contact control; 8–10 weeks	n treatment = 50 n active control = 51 n no contact control = 54 age range = 60–87	Experimental computer-based training, active computer-based training in auditory language system	Digit span, global auditory memory score	unclear

Table, continued

Author	Methods (groups, training duration, setting)	Participants (n, M_{age}, MMSE)	Interventions	Outcomes	Allocation concealment
Rapp et al., 2002	Memory training vs. no contact control group; 6 weeks duration (2hours/week)	Meeting criteria for MCI (Petersen et al., 1999) including (1) a self-reported memory complaint, (2) a score on a standardized memory test at or below the 10th percentile, (3) scores on tests of all other cognitive functions greater than the 10th percentile, (4) normal global cognitive functioning, (5) no ADL or IADL deficits, and (6) the absence of dementia. n memory training = 9 (M_{age} = 73.33, MMSE = 28) n no contact = 10 (M_{age} = 75.1, MMSE = 27.3)	Memory training on strategies, info on memory, no contact control group;	Immediate and delayed recall of: words, shopping list, name-faces, paragraph	unclear
Rozzini et al., 2007	One year longitudinal and retrospective comparison study; 60 hours over 9 months (1 block = 20 hours/month with 2 month break); follow-up at 12 months	Subjects affected by Mild Cognitive Impairment (MCI) according to Petersen's criteria n treatment = 15 (MMSE = 26) n ChE = 22 (MMSE = 26.4) n no contact control = 22 (MMSE = 26.8) age range = 63–78	Neuropsychological training plus cholinesterase inhibitors; cholinesterase inhibitors alone and no treatment;	Short story recall, letter and semantic verbal fluency, ravens matrices, Rey Figure	unclear
Scogin et al., 1985	high complaint group vs. high complaint control; 16 x 1h/day single setting	n high complaint training = 20 (M_{age} = 66.5) n high complaint control = 23 (M_{age} = 66.8)	92 page manual about memory training	Immediate and delayed recall of words, shopping list, name-faces; digit span forward, Benton visual retention test	unclear
Scogin et al., 1992	Self-taught memory training vs. attention-placebo vs. wait control; single setting	n selft mem = 22 (M_{age} = 68.55) n attention placebo = 17 (M_{age} = 68.7) n no contact = 23 (M_{age} = 67.92)	Self-taught memory training (117 pages manual)	Recall of nouns, shopping list, names and faces, paragraph	unclear
Stigsdotter et al., 1989	Pre-/post-design; 1 treatment, 1 active control, 1 no contact control; 2 weeks; group setting	n multifactor training = 9 (M_{age} = 73.1) n general activation = 9 (M_{age} = 74.7) n no contact = 10 (M_{age} = 74.2)	Multifactor training (loci, imagery, attention, relaxation) vs. general cognitive activation, control group	– abstract and concrete word recall – digit span forward	unclear
Stigsdotter et al., 1993 a	pre-/post-design; 1 treatment, 1 active control, 1 no contact control; 10 weeks, group setting	n mulitfactor = 11 (M_{age} = 74.1) n unifactor = 12 (M_{age} = 69.5) n no contact = 13 (M_{age} = 73.5)	Multifactor training vs. unifactor (encoding operations), vs. control no treatment	Abstract and concrete word recall	unclear

Table, continued

Author	Methods (groups, training duration, setting)	Participants (n, M_{age}, MMSE)	Interventions	Outcomes	Allocation concealment
Stigsdotter et al., 1993 b	Pre-/post-design; 1 treatment, 1 active control, 1 no contact control; group setting	n multifactor training = 6 (M_{age} = 74.8, MMSE = 28.3) n unifactor training = 6 (M_{age} = 79, MMSE = 28) n no contact = 6 (M_{age} = 75.5, MMSE = 28.5)	Multifactor training vs. cognitive activation (problem solving, visuospatial skills), vs. control no treatment	Total word recall, long-term retrieval	unclear
Stigsdotter et al., 1993 c	Pre-/post-design; 1 treatment, 1 active control, 1 no contact control; group setting	n mulitfactor = 10 (M_{age} = 74, MMSE = 28.2) n unifactor = 9 (M_{age} = 72.9, MMSE = 28.6) n no contact = 11 (M_{age} = 74.7, MMSE = 28.5)	Multifactor training vs. unifactor (encoding operations without relaxation and attention training), vs. no contact control	Recall of concrete words	unclear
Stigsdotter et al., 1995	2 groups; 5 weeks; group setting	n multifactor = 23 (M_{age} = 73, MMSE = 28.4) n no contact = 23 (M_{age} = 73.6, MMSE = 28.6)	Multifactor training vs. control	Recall of concrete and abstract words, objects and subject-performed tasks	unclear
Valentijn et al., 2005	3 groups; 8 weeks; single/ group setting	n group = 39 (M_{age} = 69.32, MMSE = 28.72) n individual = 40 (M_{age} = 68.07, MMSE = 28.77) n no contact = 38 (M_{age} = 68.3, MMSE = 28.49)	Group memory training vs. individual training vs. wait list	Short story immediate and delayed recall, word recall, total recall score	unclear
Yesavage et al., 1990	3 groups; 2 weeks; groups setting	n imagery = 74 (M_{age} = 67.69, MMSE = 29.8) n relax = 67 (M_{age} = 67.92, MMSE = 29.18) n imagery + judgement = 77 (M_{age} = 67.64, MMSE = 29.1)	Imagery vs. relaxation vs. imagery + judgement training	Word recall, name-face recall	unclear