Published in final edited form as:
J Am Geriatr Soc. 2012 January ; 60(1): 136–141. doi:10.1111/j.1532-5415.2011.03761.x.

Extended Practice and Aerobic Exercise Interventions Benefit Untrained Cognitive Outcomes in Older Adults: A Meta-Analysis

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Abstract

Background—A recent NIH State of the Science conference on interventions to reduce or delay Alzheimer's disease and cognitive decline in older adulthood suggested cognitive engagement and aerobic exercise held promise for healthy individuals, but were inconclusive.

OBJECTIVES—This quantitative meta-analysis examines whether therapeutic interventions of extended practice of cognitive tasks or aerobic exercise have produced significant improvement on untrained cognitive outcomes.

DESIGN—The PSYCINFO, MEDLINE, and Abstracts in Social Gerontology databases were searched for English language cognitive interventions of exercise or extended cognitive practice ranging 1966-2010. The final search was in January 2011. Studies included were experimental interventions hypothesizing improvement on untrained cognitive outcomes with pre- and post-tests. Studies of varying quality were included and compared.

SETTING—Interventions generally took place in laboratories, gymnasium facilities, in the home and outdoors. Testing was administered by experimenters.

PARTICIPANTS—Forty-two studies with 3781 healthy older adults ages 55+ were analyzed.

MEASUREMENTS—Between-group effect sizes (ES), which account for practice effects on outcome measures, and within-experimental group ES were computed from untrained cognitive outcome domains including choice reaction time, memory, and executive function, which were compared. ES were also coded for training type and study quality. Multilevel mixed effects analyses accommodated multiple outcomes from individual studies.

RESULTS—Both extended practice (estimated *ES* = 0.33, 95% *CI*= [.13-.52]) and aerobic fitness (estimated *ES*= 0.33, 95% 95% *CI*=[.10-.55]) training produced significant between-group ES but did not differ in magnitude. Better study quality was associated with larger effect sizes.

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Author Contributions: Both authors contributed to study concept, acquisition, analysis and interpretation of data, and preparation of the manuscript.

Conflict of Interest: This research was supported in part by grant R01AG10569 from the National Institute on Aging.

Sponsor's Role: None.

CONCLUSION—Findings indicate that both aerobic and extended cognitive practice training interventions for healthy older adults improve performance on untrained cognitive tasks.

Keywords

cognitive intervention; cognitive training; meta-analysis; aerobic exercise; cognitive decline

INTRODUCTION

Recently, the National Institutes of Health published a State of the Science Conference statement on preventing Alzheimer's disease and cognitive decline.[1] It indicated the evidence is inadequate to support a conclusion that any interventions are adequate to either prevent or delay Alzheimer's disease. The conference review focused only on randomized controlled clinical trials with more than 200 participants. However, it suggested there are encouraging associations of positive effects of interventions that either maintain or improve cognitive function in healthy older adults, including cognitive engagement and aerobic exercise.

Both types of interventions are at an early evaluation phase for clinical practice adoption. Many studies are at Phase I or II, where hypothesized effects of the intervention and treatment protocol are developed (Phase I) or initial exploratory studies are conducted (Phase II). A few randomized controlled trials are at Phase III. In contrast, the State of the Science review was of Phase IV and V interventions: efficacy studies to extend established positive outcomes to specified populations (Phase IV) and focusing on cost-effectiveness and intervention efficiency (Phase V).[2]

Yet the cognitive training industry grossed an estimated $295 million in 2009. [3] It is therefore important to evaluate early-phase results of interventions for older adults. The assumption behind cognitive training is that the benefits will extend to untrained outcomes.[4] Several meta-analyses,[5,6] however, have found only small effects of untrained test improvement.

Nevertheless, some approaches may be effective for untrained outcomes. One kind of intervention similar to that of commercial products uses extended practice that is, completing hundreds to thousands of trials of basic tasks like phoneme span or choice response time either with or without strategy instruction. Extended practice is likely to result in untrained task improvement because the skills trained overlap with those used in other cognitive activities,[4] but its general effectiveness has not yet been confirmed.

Aerobic training interventions were also cited as promising for cognitive benefits.[1] A meta-analysis of aerobic exercise interventions found significant within-experimental group improvements in several cognitive domains.[7, 8] Aerobic training engages neuroplastic processes that produce general improvements in cognition in animals and humans,[9] including older adults.[10]

It is too early to compare the likely different mechanisms underlying cognitive changes associated with extended practice and aerobic exercise and it is unknown whether either is more effective. Cognitive processes thought to benefit from interventions have been suggested to be those most sensitive to aging, such as executive processes. However, memory has not been systematically evaluated with respect to aerobic interventions in older adults, [7] nor has it been shown to improve in strategy-based interventions.[11] Because memory declines systematically with age, it is important to establish whether it can be improved with extended practice or aerobic interventions.

This meta-analysis evaluates improvements of healthy older adults on untrained cognitive tasks after extended cognitive practice compared with findings from aerobic exercise. It extends earlier findings from aerobic exercise interventions[7, 8] that evaluated improvement within the experimental group to analysis of between-group effect sizes (ES) that include pre- and post-test control group means to account for improvements from retesting at post-test that may be independent of the intervention.[12] It examines performance changes on memory tasks, choice response time (RT) and executive tasks, all of which are sensitive to aging. The role of study quality is also analyzed as an outcome predictor. Aerobic training studies represent a somewhat older literature (range of publication dates from 1966 - 2009; median 1993) than extended practice studies (1984-2010; median 2005), and the more recent literature may reflect greater sophistication in study design, so the interaction between type of intervention and study quality on outcomes was also evaluated.

The questions addressed included 1) whether ES computed from between experimental and control group comparisons show different patterns than within-experimental group comparisons; 2) whether ES differ between extended cognitive practice and aerobic exercise interventions, 3) whether ES differ for outcomes from different cognitive domains, 4) whether ES varies with study quality, and 5) whether the two interventions produce ES that vary with study quality.

METHODS

Study Selection

Database searches, restricted to English language, human studies, and older adults, were of PSYCINFO, Abstracts in Social Gerontology, and MEDLINE. There were no restrictions on publication dates, and included articles published online through December 2010. Keywords included “aerobic”, “aging” “cognition”, “cognitive”, “cognitive plasticity”, “cognitive rehabilitation”, “intervention”, “maintenance”, “older adult”, “physical fitness”, “plasticity”, “transfer”, and “training”, both individually and in combination. There were 715 abstracts returned from the databases, and of these, 239 articles were determined to be potentially appropriate for inclusion. Additional articles were found manually. Articles used in the meta-analysis of adult aerobic training programs[7] were also obtained for computation of ES with practice effects removed. The final search was on January 5, 2011.

Inclusion and Exclusion Criteria—Inclusion criteria were (a) original research reporting extended cognitive domain practice of basic tasks such as *N*-back or aerobic fitness interventions hypothesizing cognitive improvements, (b) healthy, cognitively unimpaired community-residing age 55+ adult participants (if younger adults were included, only ES for the older participants were computed), (c) experimental and control groups, (d) multiple session training, and (e) pre- and post-tests of untrained cognitive tasks. Studies with subjective outcomes were excluded, though studies with both subjective and untrained cognitive outcomes were included with only the cognitive outcomes evaluated. Interventions teaching only strategies such as mnemonics or inductive reasoning were not included as they do not generalize[11]. Included articles not directly cited are listed in the appendix.

Study Quality—To assess quality, a 5-point scale adapted from items used elsewhere[5] was applied. One point was assigned for a) randomization, b) an active control group, c) a description of inclusion/exclusion criteria, d) provision of attrition information, including whether there were dropouts or no attrition, and e) indication of follow-up either in the original study or a subsequent report. Scores ranged from 0 to 5.

Effect Size Calculation

Two *d*'s[13] for pre- vs. post-training effects corrected for small sample bias were computed for each outcome. These were the between-group pre-post effect (*between* ES), to control for cognitive test-taking practice in the experimental and control groups, and the within-experimental group pre-post effect (*within* ES). Two studies included both no-contact and active control groups[14, 15] and one had two sets of older age groups[16] so that two between ES for the same outcome were computed. Effects reflecting better performance with lower values were rescaled. ES were computed from reported means and measures of variability, or estimated from figures, t ratios, F ratios for 1 degree of freedom (df) main effects, or reported probabilities associated with 1 df test statistics. When only a description of findings across groups was available, significant pre-post change of $p < .05$ and non-significant change of $p < .50$ was used to transform z to r to d's.[14]

Outcomes likely to reflect ceiling or floor effects in healthy older adults were excluded, including accuracy measures in RT studies, RT tasks with memory loads of 1, 1-back tasks, and Trails-A. Tasks within a study reflecting essentially identical constructs at different levels of difficulty were averaged using $d+$ computations, for example, RT at memory loads of 2 and 4.[17]

Thirty-two ES were computed based on estimated probabilities, 14 between, and 18 within, from four studies. Several studies had insufficient information to compute parallel between- and within-group ES. For example, Dustman et al[14] provided only within-group significant p-values. Multiple outcomes per study are included to reflect different cognitive domains resulting in 421 ES, 218 between and 203 within, computed.

Coding of Outcome Domains—Choice response time (RT) included direct measures as well as paper and pencil measures such as pattern comparison. Executive function included digits backwards, dual or switch task RT's or RT costs, fluency, letter-number sequencing, N-back accuracy, Stroop, or Trails-B. Memory included recall or recognition, as well as RTs under memory load conditions.

Other domains were not analyzed because there were many fewer ES. Reasoning included inductive or matrix reasoning tasks with 10 between and 9 within ES. Simple RT included direct measures or tapping (8 between, 9 within). Visuospatial measures included enumeration, mental rotation, rotation span, and visual short term memory (5 between, 8 within). There were measures of crystallized intelligence (3 between, 3 within) and cognitive task composites (2 between, 1 within).

Data Analysis

Multilevel modeling using maximum likelihood estimation was used to contrast ES across training interventions, quality, cognitive domains, and the training x quality interaction as fixed effects. ES varied in number and type of outcome and were nested within studies. The intercept-only model tested whether the average ES for transfer across all studies differed from zero and for significant between-study remaining random variance, which would justify analyses with additional hypothesized ES predictors. A second model added main effects of training (extended practice, aerobic), quality (dummy coded as low or high; see below), and domain (choice RT, executive, memory, each dummy coded against all other domains). A third model added a test of the training x quality interaction. Statistical significance was set at $\alpha = .05$. Means and 95% CIs were estimated from Model 3. Analyses were separate for between and within ES.

RESULTS

There were 42 studies in the analysis, 25 of which reported extended cognitive practice. Information about study characteristics is in Table 1. The total sample of participants across all studies was 3781, with a mean age of 69.2. Quality ratings were recoded due to positive skewness. Ratings of 0-2 represented low (13 studies with 70 between and 70 within ES) and 3-5 represented high quality (29 studies with 148 between and 133 within ES). About two thirds of the participants were in the extended practice studies, but this was due to the inclusion of one experimental group and the no-contact controls from a study[18] with 1292 participants.

The two training approaches did not differ in study characteristics, with *F*'s (1, 41) in the range of .62 to 1.83 for sample size, mean age, and quality rating. Dummy coded quality ratings were also not significant across training type, χ^2 (1) = 1.4. The only difference between training types was in the number of sessions, F (1, 41) = 22.3, $p < .001$, with more for aerobic exercise ($M = 51.9$) than extended practice ($M = 17.6$).

Model 1, the baseline model with three significant parameters, intercept, between-study error, and residual, indicated that the estimated *d* across all studies differed significantly from zero for both the between ES (-2LL = 261, 3 parameters) and within ES (-2LL = 254, 3 parameters). The between ES intercept of 0.31 was smaller than the within effect intercept of 0.49, suggesting that practice effects from baseline testing inflate the apparent training benefit. Significant between-study random variance justified additional explanatory fixed effects in Model 2 including training, quality, choice RT, executive function, and memory. Model 2 had significantly better fit than Model 1 for between ES (-2LL = 249, 8 parameters, $\chi^2/df_{diff} = 12/5$, $p<.05$) and not for within ES (-2LL = 250, 8 parameters, $\chi^2/df_{diff} = 4/5$, *ns*). However, random between-study variance was reduced by 22% and 4%, for between and within ES, respectively.

Model 3, which adds the training type x quality interaction, was a significantly better fit for the within but not between ES, see Table 2. There was a further reduction of random variance by 8% and 16%, for between and within, respectively; however, random variance remained significantly different from zero. Model 3 was selected for comparisons across methods of computing ES (Table 2).

For both ES, the coefficients for study quality and training x quality differed significantly from zero, see Table 2. High quality studies produced larger ES than the low quality ones. The interaction for between ES indicated no quality difference in ES for aerobic training; however, high quality extended practice studies produced larger ES. Paradoxically for within ES group, low quality aerobic exercise studies had larger ES than high quality studies and the reverse was true for extended practice. This suggests that the within ES improvement is due to low quality aerobic studies using measures with stronger practice effects than high quality studies.

The test of differences in ES for extended practice versus aerobic training was not significant for either ES. The main effects of choice RT, executive, and memory domains did not produce significantly larger ES compared to those of all other outcomes. All ES did differ significantly from zero, however, suggesting that untrained outcomes benefitted from the interventions.

CONCLUSION

Both extended practice and aerobic interventions produced significant improvement in untrained cognitive outcomes. However, the between ES, which accounted for practice, were significantly smaller than the corresponding within ES, as confirmed by a separate multilevel analysis contrasting them. The finding of improvement for extended practice in this meta-analysis is inconsistent with previous work[6]; the substantial increase in currently available studies implies that those findings were affected by low statistical power.

The lack of ES differentiation between aerobic exercise and extended cognitive practice suggests that both are similarly effective in improving untrained cognitive performance in older adults despite different “dosages”. However, the mechanisms are likely to be very different between intervention types.

For comparison, ES from all studies in a previous meta-analysis[7] of aerobic exercise were computed, with the mean within ES essentially replicating the previous report's mean. Importantly, the between ES for those studies[7] estimated from a multilevel intercept-only model was 0.24, 95% CI (.09-.40), consistent with the results of this meta-analysis.

The overall between ES for extended practice 0.33, 95% CI (.13-.52) and for aerobic exercise 0.33, 95% CI (.11-.55) interventions might be considered negligible in terms of potential clinical relevance. However, for comparison, between ES for Modafinil (*Provigil),* prescribed for narcolepsy but used off-label for enhanced cognitive performance[19] was computed. The multilevel estimate for 28 cognitive outcomes including working memory and short term memory in a study of young adults[20] compared to placebo was 0.23 for both high and low dosage.

Neuroplasticity may be associated with untrained cognitive improvements for both types of training. Aerobic interventions produce neurogenesis in animal models and increased hippocampal volume in young and middle-aged adults[9] as well as older ones. [21] The neuroplastic mechanisms for extended practice findings are not as well defined,[22] with mixed findings of changes correlated with performance improvements.[21,23] Improvements in untrained memory performance in this analysis suggests that memory can be improved with training, in contradiction to studies using traditional mnemonic strategy training.[11,12] Memory strategy training is likely to be more effortful than nonstrategic approaches, age declines in executive abilities may affect strategy application, and its efficacy may be limited by an approach that does not consider individual differences.[4]

None of the cognitive domains of choice RT, executive function, or memory produced greater ES. A lack of advantage of any of the domains, however, may be associated with how well the outcomes represent the domains and may be because many studies included only one task to represent a domain.[24] It is also not currently possible to differentiate benefits of specific approaches to particular domains because many extended practice studies combine training from multiple domains, for example, working memory and processing speed.[25] Finally, it remains to be determined whether domain-specific benefits are more likely in aerobic than in extended practice interventions, which could not be evaluated here because of varying cell sizes associated with interaction tests.

Studies with higher quality ratings showed larger between ES, ($M = 0.43$) compared to ($M = 0.22$) for lower quality interventions, confirming the importance of rigorous methods. Analysis of individual components of the quality score suggested that the association between quality and outcomes was not driven by specific criteria, such as randomization.

Limitations

Publication bias, whereby studies with null results are excluded because they were not published, is often considered a limitation in meta-analysis. However, it was common to find studies here with null results for outcome measures. Other explanations for benefits could not be extracted, such as effects due to the social stimulation associated with participating, (e.g., interacting with training staff on a regular basis in extended practice, or exercising in a group).[26]

No formal test of differences between ES of studies using active versus wait-list controls could be made because few studies included active controls. Inclusion of age as a covariate in separate analyses suggested ES did not vary by age, but there was not much variability in age across studies. Training dosage in session number and overall duration for both aerobic and extended practice studies was analyzed as a covariate, but was not significant. A better comparison would involve similar doses of these two approaches. Duration of training benefits[27] could not be evaluated because too few of the studies included follow-ups. Several extended practice studies, e.g.,[25] evaluated three month to one year effects after training discontinuation and found reduced ES. Although cognitive outcomes have not been evaluated after discontinuation of aerobic exercise participation, it is likely that effects will fade, given that physical deconditioning occurs. This raises questions of whether continual practice is required for maintenance.

Assuming continued engagement in either type of training is necessary, how to encourage participation over the long term is poorly understood; participants in most of the studies were selected for their willingness to remain at least until posttest. Older adults, even in multiyear aerobic intervention studies, e.g.,[28] are likely to eventually discontinue participation. Thus it is important to identify approaches that encourage persistent engagement in cognitively beneficial activities.

A substantial investment is being made in commercial “brain fitness” activities.[3] Our findings suggest that improvement in untrained cognitive performance is observed, however, we do not endorse use of commercial products which resemble extended practice interventions, because few have been tested for those benefits.[29]

Questions about training efficacy remain, including whether benefits are observed in subpopulations with health problems, or with varying education or ability. It is unclear when interventions should be first engaged, or whether they should be tailored to individuals’ cognitive needs rather than to general abilities that decline with age. Direct health benefits of aerobic exercise must be acknowledged, though extended practice improvements may also be associated with health improvements.

Acknowledgments

The authors would like to thank all of the authors for their research on which this meta-analysis is based.

This research was supported in part by grant R01AG10569 from the National Institute on Aging. This research is based on data from all included studies in the meta-analysis.

APPENDIX

Supplemental references in alphabetical order included in the meta-analysis, but not cited in the article. Those marked with a [cp] *used extended targeted practice and those with an* [a] *had an aerobic program.*

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Table 1

Participant, Training, Quality, and Outcome Characteristics[a]

Characteristic	All Studies (n = 3781)	Aerobic Exercise (n = 1016)	Extended Practice (n = 2765)
N of Studies	42	17	25
Participants			
Total N	3781	1016	2765
Median N	39 (13-1292)	34 (13-187)	40 (13-1292)
Mean age	69.2 (55+)	67.9 (55+)	69.9 (55+)
Training			
Mean weeks	13.2 (2-52)	23.8 (8-52)	5.9 (2-12)
Mean session N	30.5 (3-79)	49.6 (18-152)	17.1 (3-45)
Mean quality	2.9 (0-5)	2.5 (0-5)	3.1 (1-5)
N of low quality studies	13	7	6
Untrained Outcomes			
Mean outcome N	5 (1-16)	5 (1-12)	5 (1-16)

[a]Ranges are in parentheses.

Table 2

Estimated Model 3 Fit Indices, Effect Sizes, and 95% Confidence Intervals

Fit Indices	**BG**	**EG**
-2LL (parameters)	245(9)	241(9)
χ^2 /df$_{diff}$ [a]	4/1	9/1 *[b]
Fixed Effects		
Intercept	-0.09 (.27) **[c]	.06 (.18) **
Training	0.19 (.15)	0.26 (.17)
Quality	0.41 (.13) **	0.39 (.14) **
Choice RT	0.06 (.15)	0.12 (.16)
Executive Function	0.27 (.14)	0.25 (.15)
Memory	0.12 (.14)	0.18 (.16)
Training × Quality	-0.38 (.19) *	-0.67 (.21) **
Variance Components		
Between-Study Error	0.09 (.03) ***	0.14 (.03) ***
Residual	0.12 (.02) ***	0.11 (.01) ***

		BG			EG		
Group Category	***k***	***n***	***d***	**95% CI**	***n***	***d***	**95% CI**
Training type							
Aerobic exercise	17	89	0.325	(0.10, 0.55)	83	0.560	(0.32, 0.81)
Extended practice	25	129	0.327	(0.13, 0.52)	120	0.535	(0.31, 0.76)
Quality							
Low quality	13	70	0.218	(-0.01, 0.45)	70	0.520	(0.27, 0.77)
High quality	29	148	0.434	(0.24, 0.63)	133	0.575	(0.36, 0.79)
Cognitive outcome domain[d]							
Choice RT	20	41	0.355	(0.03, 0.68)	41	0.608	(0.26, 0.96)
Executive Function	30	90	0.459	(0.15, 0.77)	85	0.674	(0.34, 1.01)

		BG			EG		
Group Category	***k***	***n***	***d***	**95% CI**	***n***	***d***	**95% CI**
Memory	23	59	0.386	(0.07, 0.70)	47	0.637	(0.29, 0.98)
Training × Study quality							
Aerobic × low quality	7	39	0.312	(0.03, 0.60)	39	0.700	(0.40, 1.00)
Aerobic × high quality	10	50	0.338	(0.10, 0.58)	44	0.421	(0.15, 0.69)
Extended practice × low quality	6	31	0.124	(-0.14, 0.39)	31	0.340	(0.05, 0.63)
Extended practice × high quality	19	98	0.529	(0.33, 0.73)	89	0.729	(0.50, 0.96)

Abbreviations: BG, between group effect sizes; EG, experimental group effect sizes; k=number of studies; n=number of effect sizes; d=effect size; CI=confidence interval

[a] χ^2/df_{diff} compared to model 2.

[b] $p<.05$

[*] $p<.05$

[**] $p<.01$

[***] $p<.001$.

[c] Model coefficients are listed with standard errors (SE) in parentheses.

[d] The cognitive outcome domains of simple RT, reasoning, crystallized intelligence and composite measures had insufficient observations for separate estimation.