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The effects of exercise on cognition in older adults with and without cognitive decline. A systematic review

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Abstract

Objective: to systematically review the effect of physical exercise on cognition in older adults with and without cognitive decline.

Data sources: randomized controlled trials were identified by literature searches in PubMed, EMBASE, CENTRAL, PsycINFO and AgeLine.

Study selection: papers were included on the basis of predefined inclusion criteria.

Data extraction: data on study population, exercise intervention and effectiveness were extracted. Two independent reviewers assessed methodological quality.

Data synthesis: 23 studies were included; 15 among cognitively healthy subjects and eight among subjects with cognitive decline. Seven studies were qualified as high quality studies, two in cognitively healthy subjects and five in subjects with cognitive decline. In cognitively healthy subjects, significant beneficial intervention effects were observed in five studies on information processing, executive function, or memory. Interventions in these studies included aerobic exercise only (n=2), strength exercise (n=1), strength and balance exercise (n=1), or all-round exercise including aerobic, strength, balance and flexibility training (n=1). In subjects with cognitive decline, five studies observed beneficial effects on general cognition, executive functions and memory. Interventions included aerobic (n=3) or strength exercise combined with flexibility or balance exercise (n=2).

Conclusions: Beneficial effects of various exercise programs on aspects of cognition have been observed in studies among subjects with and without cognitive decline. The majority of the studies, however, did not find any effect. The small number of included studies, lack of high quality studies, and the large variability in study-populations, exercise protocols and outcome measures complicate interpretation of the results. More high quality trials are needed to assess the effects of different types of exercise on cognitive function in older adults with and without cognitive decline.

BACKGROUND

Cognitive function declines as a normal consequence of the ageing process, even in the absence of pathology. However, in some cases the rate of cognitive decline is disproportionately high. Mild cognitive impairment (MCI) refers to the in-between stage in which a person experiences cognitive decline which is more serious than is expected on the basis of the normal ageing process, but does not meet criteria for dementia.[1] Although subjects with MCI have an increased risk to develop dementia[2, 3], the possibility exists that they remain in the stage of MCI or revert to normal cognition.[4, 5] In contrast, dementia goes together with irreversible progressive cognitive decline and leads to significant impairment in physical and social functioning.[6]

At the individual level, cognitive decline places a burden on subjects and their significant others, because of the detrimental effect on quality of life[7] and the association with a higher risk for functional limitations and disability.[8, 9] At the population level, cognitive decline, and especially dementia, puts an enormous burden on healthcare systems in terms of finances and manpower.[10] Obviously, effective interventions for preventing or slowing down the rate of cognitive decline in older adults would greatly benefit both the individual and society. In this respect, a number of meta-analyses and systematic reviews reported beneficial effects of physical activity and exercise on cognition in cognitively healthy older adults[11-13] and adults with cognitive impairments and dementia.[14, 15] Others failed to observe effects of physical activity interventions on cognition in people with dementia.[16, 17] Some of the reviews advised to carefully interpret the findings given the low number of included studies.

Various potential mechanisms for the enhancing effect of exercise on cognition have been hypothesized. In a systematic review on longitudinal studies exploring the effect of physical activity on cognition and dementia, Fratiglioni et al (2004) abstracted three hypotheses.[18] The cognitive reserve hypothesis assumes that physical activity and exercise improve the non-neural components of the brain, resulting in increased perfusion of the brain, which in turn leads to larger cognitive reserve. This cognitive reserve can be utilized in case of degenerative diseases, such as Alzheimer’s disease. The vascular hypothesis presumes that exercise reduces the risk of cardiovascular disease, which is a determinant of dementia. Finally, the stress hypothesis poses that exercise benefits cognition by decreasing stress since subjects susceptible to stress have a two-fold risk for dementia. In contrast to these hypotheses that are not based on a specific type of physical activity, the aerobic fitness hypothesis implies that the potential beneficial effects on cognition are induced by aerobic exercise via improvements in aerobic fitness. Although evidence exists that increased aerobic fitness is associated with subsequent morphological changes in the human brain[19], in a recent meta-analysis and review it could not be confirmed that improvements in aerobic fitness were responsible for the effects of aerobic exercise on cognition.[20, 21]

According to the hypotheses as described above, potential mechanisms underlying the effect of exercise on cognition are based on physical and mental processes. Moreover, the social aspects of exercise may also have its impact on cognition. The current lack of knowledge about exact mechanisms responsible for changes in cognitive function may explain the different findings in the literature for different populations. None of the reviews, however, concluded that exercise could have a detrimental effect on cognitive function. Thus, it is of importance to continue investigating the effects of exercise on cognition, both in adults with and without cognitive decline. Given the lack of support for the aerobic fitness hypothesis[20, 21] it is relevant to also include trials examining the effect of other forms of exercise on cognitive function in reviews.

The aim of the present systematic review is to summarize randomized controlled trials examining the effect different types of physical exercise on cognition in subjects with and without cognitive decline. This review differs from previous publications with respect to several issues, as previous publications included either cognitively healthy subjects[11-13, 21] or subjects with cognitive decline or dementia [14, 15, 17]; included all intervention studies irrespective of study design[12, 13, 15, 16]; did not perform a standardized quality assessment[11, 13, 15, 16]; included exercise programs with an aerobic exercise component only[11, 21]; applied a very broad definition of exercise also including recreational therapy[14, 17]; or focused on the potential mediating effect of cardiovascular risk factors.[15]

METHODS

Literature search

The databases PubMED, EMBASE, CENTRAL (Cochrane Central Register of controlled trials), PsycINFO and AgeLine were searched for relevant studies in February 2007. The search was updated on April 22, 2008. Groups of thesaurus terms as well as free terms were used to search the databases. Terms for older adults (thesaurus terms OR elderly, seniors, aging or ageing) were used in AND-combination with terms for exercise (thesaurus terms OR exercise*, physical activity, physical training, strength training, resistance training, aerobic training, cardiovascular training, endurance training, flexibility training, relaxation, Tai Chi, walking, or yoga) and search terms representing cognition, cognitive processes, cognitive decline or dementia (thesaurus terms OR cogniti*, memory, executive function* or executive control). Search results were limited by search terms for specific study design, e.g. clinical trial. Furthermore, additional articles were identified by manually searching the authors' own literature databases.

Inclusion criteria and selection process

In order to be included in the review, studies had to meet the following criteria, 1) design: randomised controlled trial; 2) population: cognitively healthy older adults or adults with cognitive decline or dementia, but no mental disorders other than dementia, such as depression; 3) intervention: physical exercise program; 4) outcome: cognitive function assessed using neuropsychological tests. Only full-text articles written in English were included. Titles, keywords and abstracts of articles identified through the search process were reviewed to identify eligible papers. Checking for eligible papers was done first by JvU to exclude articles out of scope. Subsequently, the first and second author (JvU and MC) independently reviewed all potentially relevant references for eligibility. Disagreements were discussed and resolved.

Data extraction and quality assessment

Data on the study population, exercise programs and outcome measures were extracted by JvU and MH. On the basis of program descriptions in the individual studies, programs were qualified as aerobic, strength, flexibility or balance exercise, or combinations thereof. Methodological quality of the included studies was independently determined by two reviewers (JvU and MC) using the Delphi list developed by Verhagen et al.[22], which has been used in a previous review on exercise interventions in the elderly. [14, 23]This list consists of nine quality criteria assessing different methodological aspects, see table 1. Criteria have a 'yes' (=1), 'no' (=0) or 'unclear' (=0) answer format. All criteria have the same weight and a quality score ranging from zero to nine was calculated for each study. High quality was defined as a score of five or higher.[24]

Study populations with and without cognitive decline

Cognitive decline was determined on the basis of the description of the population or the provided MMSE-scores. In the latter case, the standard cut-off point of 24 was applied.[25] If no specific information about cognitive status was reported, it was assumed that the population was cognitively healthy.

RESULTS

Study selection

The literature searches yielded a total of 1325 potentially relevant articles; 552 in Pubmed, 539 in Embase, 175 in CENTRAL, 14 in PsycINFO and 45 in Ageline. After removing references that were selected from more than one database, 1059 articles remained. The titles and abstracts of 79 references were checked for eligibility by JvU and MC after removing papers out of scope. Twenty-four references met the inclusion criteria. The abstracts of seven articles provided insufficient information to make a decision. Therefore, 31 articles were retrieved in order to screen the full text. Eight papers were excluded after all, because of the following reasons, no full-text paper (n=1); no RCT (n=1); study population also including subjects with depression and psychosis (n=1); multi-component intervention including non-exercise components (n=2); no neuropsychological tests (n=2); or describing same study and results as another included study (n=1). Finally, 23 papers were included; 15 among subjects without cognitive decline (No Cognitive Decline = NCD)[26-40] and eight among subjects with cognitive decline (CD).[41-48]

Quality assessment

Methodological quality of the included papers is summarized in Table 2. Only seven of the 23 studies were qualified as high quality studies; two out of 15 among NCD[31, 35] and five out of eight among CD.[41, 42, 44, 47, 48].

All studies used randomization, but only seven of them described that treatment allocation was concealed (NCD[31, 35] and CD[41, 42, 46-48]). Despite randomization, groups were not comparable at baseline in five studies (NCD[28, 30, 33] and CD[45, 46]). In five of the 17 studies reporting that study groups were similar at baseline, the number of participants per group was only fifteen or less (NCD[29, 34, 39] and CD[41, 48]), which complicates finding statistically significant between-group differences.

Eight studies, all performed among cognitively healthy subjects, did not clearly specify the inclusion and exclusion criteria.[27-29, 32, 35-37, 40]

In general, blinding was not consistently described. In eight studies, the outcome assessor was blinded (NCD[33, 35, 36] and CD[41, 42, 44, 45, 47]). Participants were blinded in two studies, one among cognitively healthy adults[38] and one in subjects with cognitive decline.[47] The exercise trainer was blinded in two studies as well (NCD[31] and CD[47]).

Eleven studies analyzed the data on an intention-to-treat basis for those with complete data (NCD[26, 27, 32, 35-37, 39] and CD[41, 43, 44, 48]). Only three studies, one among subjects without cognitive decline[31] and two among subjects with cognitive decline[41, 47] reported point estimates and measures of variability for the between group differences in outcome measures.

Study populations

The details of the study populations are summarized in Table 3. Age of the study populations ranged from 55 to 94 in cognitively healthy populations and from 67 to 99 in populations with cognitive decline. In both groups, the majority of participants were women. The sample sizes varied from 30 to 210 subjects in the 15 studies among cognitively healthy subjects and from 20 to 152 in the eight studies among subjects with cognitive decline. In general, samples were larger in studies including cognitively healthy elderly. Of the six studies including more than 100 subjects, four were performed in a cognitively healthy population[26, 31, 35, 40] and two in subjects with cognitive decline.[44, 47] In both groups half of the studies included 50 subjects or less.

Exercise programs

The exercise programs are summarized in Table 4. Of the 15 studies among cognitively healthy subjects, six consisted of aerobic exercise.[26, 29, 30, 32, 35, 38] In one of these studies aerobic exercise was combined with flexibility exercise.[38] Five programs covered strength exercise[27, 31, 33, 37, 39], which was combined with balance exercise in one of these studies.[33] Of the remaining four studies, three examined the combination of aerobic, strength and flexibility exercise[28, 36, 40] and one study compared aerobic, strength and balance exercise.[34] Intensity of aerobic exercise was operationalized in various ways: 60-70 % of heart rate reserve (n=3)[32, 34, 38]; 30-40% of heart rate reserve (n=1)[38]; 70% of maximum heart rate (n=3)[26, 28, 35]; ratings of perceived exertion (n=1)[30] or ventilatory threshold (n=1).[29] Two studies did not report on the specific exercise intensity.[36, 40] Five studies examined progressive resistance exercise (n=5).[27, 28, 31, 34, 39] In four resistance exercise studies progression was not reported.[33, 36, 37, 40]

Of the eight studies among subjects with cognitive decline, three comprised aerobic exercise.[45-47] Specific intensity was not reported. The other five studies combined strength exercise with flexibility or balance exercise.[41-44, 48] Three of them comprised progressive resistance exercise[41, 43, 44] and Dorner et al.[42] and Van de Winckel et al.[48] did not report progression.

Program duration ranged from 8-42 weeks (mean = 20) in NCD and from 6-52 weeks (mean 23) in CD. Mean session duration ranged from 20-65 minutes (mean = 51) in NCD, was not reported in three studies[30, 37, 39], and ranged from 30-60 minutes (mean = 42) in CD. In cognitively healthy populations, the frequency of almost two-thirds of the programs was three times per week (n=9 [26-28, 30-33, 38, 39]); this was the case in half of the studies in people with cognitive decline (n=4 [41, 42, 45, 46]). Only one program, among cognitively healthy subjects, was performed five times per week.[34]

The other programs were performed twice per week (n=3 in NCD[29, 36, 40] and n=3 in CD[43, 44, 47]) or once per week (n=2 in NCD[35, 37] and n=1 in CD[48]).

In both groups, the majority of the exercise-programs was group-based: NCD (n=12) and CD (n=7). Exercise sessions for cognitively healthy subjects were supervised by trained exercise leaders (n=5)[34-36, 38, 40] or a physical therapist.[33] Exercise programs for subjects with cognitive decline were led by physical therapists[43, 48], exercise physiologists or sport scientists[41, 42], trained instructors[47] or researchers.[46] In the remaining study among subjects with cognitive decline, participants were supervised individually.[45] In cognitively healthy subjects, two studies examined the effect of individual exercise[30, 31] and one study did not report on this issue.[37]

Dropout and attendance

Dropout from the study, defined as no post-intervention measurements available, was reported in 19 studies, see table 5 (NCD: n=12; all, except for [30, 31, 34] and CD: n=7; all, except for [45]). In the 12 studies in cognitively healthy subjects, the median drop-out rate was 6 percent of all randomized participants. The lowest reported rate was zero[27, 29, 36, 37] and the highest rate was 26 percent.[38] In subjects with cognitive decline, the median drop-out rate was 15 percent, ranging from 0[41] to 38 percent.[46]

Attendance to the exercise intervention classes in percentages was reported in 13 studies, see Table 4 (NCD: n=8[26, 28, 31-33, 35, 36, 40] and CD: n=5[41-44, 47]). Some of these studies only included subjects who attended at least a certain percentage of sessions, or only subjects who completed the exercise program. Average session attendance ranged from 69-96 percent in cognitively healthy adults and 63-92 percent in subjects with cognitive decline. Of these 13 studies, eight included a control program with session attendance ranging from 56-100 percent (NCD: n=4[26, 28, 32, 35] and CD: n=4[41, 43, 44, 47]).

In most studies, it was not described whether subjects who discontinued the exercise programs were included in the attendance rates. Three studies however, two in subjects without[27, 38] and one in subjects with cognitive decline[46], reported that only subjects attending 70-75 percent of the sessions were included in their analyses. Two other studies reported that they only analyzed data of subjects who completed the program.[40, 42] One study[47] reported including subjects who discontinued the exercise programs in the attendance rates and the analysis.

Effects

The effects of the exercise programs on neuropsychological outcomes are described in Table 5. No detrimental effects of the exercise programs on cognitive function were observed. Five out of the 15 studies in cognitively healthy subjects observed significant beneficial effects on some of the included measures for cognition [27, 30, 33, 34, 40] No significant effects were observed in the two high quality studies in cognitively healthy subjects.[31, 35] Quality scores of the studies in which effects were observed were three points out of nine[27, 33, 34], or two points out of nine.[30, 40] Significant effects were also observed in five out of the eight studies in subjects with cognitive decline.[41, 45-48] Three of these were qualified as high quality studies (≥ 5 points/ 9)[41, 47, 48] and the other two had three points.[45, 46]

In cognitively healthy adults, improvements were observed in memory (Corsis block-tapping test, Rey–Osterrieth figure, face recognition, digit span)[27, 30, 40], information processing abilities (organization, auditory processing)[34] and executive function (word fluency).[33] Effective interventions in this group included aerobic exercise (n=2)[30, 34], strength exercise[27] alone or combined with balance exercise (n=1)[33], and all-round exercise including aerobic, strength, balance and flexibility training (n=1).[40]

In subjects with cognitive decline, improvements were observed in general cognitive function (MMSE)[41, 48], executive functions (category fluency, trail making, clock drawing)[45, 46, 48]. One study[47] observed a beneficial effect on memory (15 word learning test), but only in men who attended at least 75 percent of the sessions. Effective interventions among subjects with cognitive decline included aerobic exercise (n=3)[45-47] and strength exercise combined with flexibility or balance exercise (n=2).[41, 48]

DISCUSSION

This review suggests that different kinds of exercise may benefit cognitive function irrespective of baseline cognitive status. In one third of the studies among subjects without cognitive decline and two thirds of the studies in subjects with cognitive decline, beneficial effects of aerobic or strength exercise on certain aspects of cognition have been observed. However, due to methodological shortcomings further study on this topic is needed.

In the literature, ample attention has been paid to the specific pathways by which aerobic exercise may benefit cognition. A well-known hypothesis is the aerobic fitness hypothesis, assuming that changes in aerobic fitness contribute to the changes in cognitive performance.[11, 20] Indeed, in the present review beneficial effects of aerobic exercise were observed in subjects with and without cognitive decline. Etnier et al (2006)[20] and Angevaren et al (2008)[21], however, examined the association between aerobic fitness and cognition and concluded that the aerobic fitness hypothesis was not supported by intervention studies. Other, more specific, potential physiological mechanisms for an association between exercise and cognitive function include cerebrovascular integrity, neurotransmitter function, hormone function and morphological changes in the brain as a result of exercise.[49] Furthermore, the potential beneficial effects of being part of a social network should not be overlooked.[18] Thus, besides aerobic exercise, other forms of exercise may also be beneficial for cognition.

In the present review, beneficial effects of strength exercise were observed in two studies among cognitively healthy and two studies among subjects with cognitive decline. Moreover, in both groups nearly significant effects on cognition were observed in studies examining the effect of strength exercise[37] and strength and flexibility exercise.[43] Literature on the specific pathways by which strength exercise may influence cognition is barely available. The possibility exists that strength exercise improves the ability to participate in aerobic exercise. In their meta-analysis, Colcombe and Kramer (2003) do find larger effects on cognition of combined aerobic and strength exercise than of aerobic exercise only.[11] Another possibility is that strength exercise affects other factors, such as described in the paragraph above, thereby contributing to improved cognitive function.

Considering its complexity, the study of potential pathways by which different exercise programs may benefit cognition in future studies is very relevant. Knowledge about all potential pathways is essential in order to design effective exercise programs for cognitive function. Kramer and Erickson provided an overview of the cellular and molecular mechanisms for the association between exercise and cognition that are addressed in animal research, including increased production of brain derived neurotrophic factor and insulin-like growth factor.[50] Findings from animal studies provide directions for future study of the physiological mechanisms that may underlie the effect of exercise on cognitive function in humans.

Limitations

In general, publication bias endangers the external validity of reviews and meta-analyses. Also in the present review, publication bias cannot be ruled out. However, the poor methodological quality and the predominantly small sample sizes of the included studies are the most important limitations of the present review. Especially if sample sizes are small, it is difficult to show significant between-group differences. In this case statistical techniques, such as regression, provide insight into the direction and precision of these differences. However, 15 studies used (M)AN(C)OVA to analyze between-group differences and only provided p-values. Furthermore, only half of the included studies performed an intention-to-treat analysis. Intention-to-treat analysis provides optimal information about the effectiveness of an intervention, since data of all randomized subjects are included in the analysis. None of the five studies among cognitively healthy subjects that observed a significant beneficial effect met the criterion for a high quality study. Among subjects with cognitive decline, three out of the five studies that found a beneficial effect on cognition were qualified as high quality studies.

The possibility exists that actual methodological quality of the studies was underestimated because of inappropriate reporting. Especially treatment allocation and blinding of subjects and exercise trainers was not well described. Due to the nature of the intervention, i.e. exercise programs, blinding is difficult. However, both subjects and participants can be blinded by including a ‘placebo’ activity program not aimed at improving aerobic fitness or strength, and by telling subjects and instructors that the difference in effect between the programs is of interest. We urgently recommend to comply with the CONSORT statement guidelines for the standardized reporting of RCT’s.[51]

We determined study populations with and without cognitive decline on the basis of description of the population or mean MMSE scores in the absence of a description. This was the most feasible method to discriminate between groups on the basis of available information in the included studies. The applied cut-off point for the MMSE of 24 is commonly used to distinguish subjects with and without cognitive decline for research purposes[25], but in reality the distinction is not that clear. To illustrate this, the study population in which the mean MMSE was 25, [33] was qualified as cognitively healthy. However, considering the standard deviation of five points, this study may have included subjects with cognitive decline as well. Vice versa, it is likely that the study population of Dorner et al (2007)[42], which was categorized as ‘cognitive declined’, also included cognitively healthy subjects given the mean MMSE score (SD) of 21 (5). In future exercise intervention studies in older adults, a clear description of the study population should be provided in order to provide more useful information for reviews, meta-analyses and practice.

Finally, the classification of neuropsychological tests according to neuropsychological focus is disputable, since cognitive functions are interwoven and neuropsychological tests in general do not measure one single aspect of cognition.[52] In the results section, tests were categorized into cognitive domains as reported by the authors of the included studies. Since cognitive decline is often associated with a decline in memory, it is remarkable that no effect of exercise on memory was found in studies among subjects with cognitive decline. Only one study observed a beneficial effect of aerobic exercise on memory, but in men attending at least 75 percent of the sessions only.[47] This is in contrast to a previous review, including intervention studies irrespective of design, in which a beneficial effect of exercise on memory was observed among elderly with dementia.[12] A logical explanation may be that memory was extensively assessed in only two of the studies in elderly with cognitive decline.[45, 47] One study[48], included a measure of short-term memory only. Five studies examined effects on immediate recall of three words – included in the MMSE - in which the presence of a ceiling effect is likely. Moreover, three-word recall alone is a measure that is probably not sensitive to small changes in memory. Therefore, future studies among subjects with cognitive decline should include a more thorough assessment of memory using neuropsychological tests that are responsive to change.

In conclusion, the finding that some beneficial effects of different kinds of exercise on cognition are observed in both subjects with and without cognitive decline is very relevant. Unfortunately, because of the diversity in exercise programs, measures of cognition, and study populations in included studies, it is impossible to draw valid conclusions about which type of exercise program (content, intensity, frequency and duration) is most effective, for what aspect of cognition and for which specific population. It should also be noted that in the majority of the included papers no effects of exercise on cognition were observed. Moreover, methodological quality of included studies was poor. More high quality studies are needed in order to address these issues and gain better insight into the effect of various exercise programs on cognition in populations that differ in cognitive status.

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List of titles for all Tables

Table 1. Criteria considered for quality assessment according to Verhagen et al.[22]

1a. Was a method of randomization performed?
1b. Was the treatment allocation concealed?
2. Were the groups similar at baseline?
3. Were the eligibility criteria specified?
4. Was the outcome assessor blinded?
5. Was the exercise trainer blinded?
6. Was the participant blinded?
7. Were point estimates and measures of variability presented for the primary outcomes?
8. Did the analysis include an intention-to-treat analysis?

Table 2. Quality assessment sorted by study population and quality score

First author, year	1a. randomization?	1b. treatment allocation concealed?	2. group similarity at baseline?	3. specified eligibility criteria? [a]	4. blinded outcome assessor?	5. blinded exercise trainer?	6. blinded participants?	7. point estimates and measures of variability?	8. intention-to-treat analysis?	score
Study population without cognitive decline										
Lachman, 2006	Y	Y	Y	Y	?	Y	N	Y	?	6
Oken, 2006	Y	Y	Y	?	Y	?	N	N	Y	5
Blumentahl, 1991	Y	?	Y	Y	?	?	N	N	Y	4
Okumiya, 1996	Y	?	Y	N	Y	?	N	N	Y	4
Stevenson, 1990	Y	?	Y	Y	?	?	Y	N	N	4
Tsutsumi, 1997	Y	?	Y	Y	?	?	N	N	Y	4
Cassilhas, 2007	Y	?	Y	?	?	?	?	N	Y	3 *
Molloy, 1988	Y	?	N	Y	Y	?	N	N	?	3 *
Moul, 1995	Y	?	Y	Y	?	?	?	N	?	3 *
Perrig Chiello, 1998	Y	?	Y	N	?	?	N	N	Y	3
Fabre, 2001	Y	?	Y	?	?	?	N	N	?	2
Hassmen, 1997	Y	?	N	Y	?	NA	?	N	?	2 *
Madden, 1989	Y	?	?	?	?	?	?	N	Y	2
Williams, 1997	Y	?	Y	?	?	?	?	N	N	2 *
Emery, 1990	Y	?	N	?	?	?	N	N	N	1

Study population with cognitive decline										
Van Uffelen, 2008	Y	Y	Y	Y	Y	Y	Y	Y	?	8 *
Baum, 2003	Y	Y	Y	Y	Y	?	N	Y	Y	7 *
Dorner, 2007	Y	Y	Y	Y	Y	?	N	N	N	5
McMurdo, 2000	Y	?	Y	Y	Y	?	?	N	Y	5
Van de Winkel, 2004	Y	Y	Y	Y	N	N	?	N	Y	5 *
McMurdo, 1994	Y	?	Y	Y	?	N	?	N	Y	4
Scherder, 2005	Y	?	N	Y	Y	?	N	N	?	3 *
Stevens, 2006	Y	Y	N	Y	?	N	N	N	N	3 *

NA= not applicable; Y= yes; N= no; ? = unclear; [a] If only exclusion criteria were reported, this was rated as ‘unclear’; * significant beneficial effect on some of the included measures for cognition.

Table 3: Description of study populations[a]

Author, year	- number of participants (n)[b]; gender (%women); mean age (sd) and/or range - baseline cognitive status (if available)	eligibility criteria
Study population without cognitive decline		
	Aerobic exercise	
Oken, 2006	- n=135; 75%; 72(5), range 65-85 - healthy adults; no MMSE	- exclusion: actively practicing yoga or tai-chi in last 6 months; performing aerobic exercise > 210 min/week; insulin-dependent diabetes; uncontrolled hypertension; evidence of liver or kidney failure; significant lung disease; alcoholism or drug abuse; symptoms or signs of congestive heart failure; symptomatic ischemic heart disease; significant valvular disease; significant visual impairment.
Blumenthal, 1991	- n=101; 50%; 67 yrs, range 60-83 - healthy adults; no MMSE	- inclusion: age ≥ 60; healthy and free from coronary disease; not participating in regular exercise.
Stevenson, 1990	- n=72 ; 55%; 64(4) yrs, range 60-81 - healthy adults; no MMSE	- inclusion: age ≥ 60; community-dwelling; absence of cardiovascular disease, hypertension, diabetes; normal findings in physical examinations + blood tests; absence of coronary disease; normal echocardiogram; no abnormal findings on cycle ergometer stress test.
Fabre, 2002	- n=32 ; 84% ; 66(2) yrs, range 60-76 - healthy adults without signs of	- inclusion: member of club (?); age ≥ 60. - exclusion criteria: depression; positive ECG during exercise testing; no breathing through mouth during

	dementia; no MMSE	testing; disease during exercise.
Hassmen, 1997	- n=40; 50%; 66 yrs, range 55-75 - healthy adults; no MMSE	- inclusion: no self-reported medical problems or impairments; no use of medication in past 6 months; not participating in regular exercise.
Madden, 1989	- n=85; 48%; 67(4) yrs, range 60-83 - no MMSE	- exclusion: uncontrolled hypertension; diabetes; heart disease; taking beta blockers or psychotropic medicine; contraindications for exercise.
	Strength exercise	
Lachman, 2006	- n=210; 78%; 75(7) yrs, range 60-94 - no MMSE	- inclusion: age ≥ 60; community-dwelling; sedentary; limitations in minimal 1 of 9 physical function areas of Short Form-36 physical function scale. - exclusion: contraindications for exercise; current treatment for cancer; kidney disease requiring dialysis; recent fracture; uncontrolled diabetes or seizures; regular use of wheelchair; current rehabilitation case; current fainting or dizzy spells; sudden loss of coordination; blindness.
Tsutsumi, 1997	- n=42; 79%; 69(6) yrs, range 61-86 -healthy adults; no MMSE	- inclusion: age ≥ 60; community dwelling; medically healthy; no regular exercise in past 6 months. - exclusion: cardiovascular disease; taking medication for hypertension.
Cassilhas, 2007	- n=62; ?; 68 (5.9) yrs - healthy adults; MMSE ≥ 24	- exclusion: cardiovascular pathologies; psychiatric conditions; use of psychotropic drugs; < 8 yr of schooling; MMSE < 24.
Molloy, 1988	- n=50; 100%; 83 yrs, range 73-90 - mean MMSE (sd) = 25 (5)	- inclusion: women; resident nursing home; women; age ≥ 70; ability to walk without assistance; no disability or disease that compromised ability to exercise.
Perrig Chiello, 1998	- n=46; 39%; 73 yrs - no MMSE	- inclusion: subjects from Longitudinal Interdisciplinary Aging Study, interested in resistance exercise.
	Aerobic and strength exercise	

Okumiya, 1996	- n=42; 57%; 79(5) yrs, range 75-87 - mean MMSE (sd) = 28 (3)	- inclusion: aged >= 75; community-dwelling.
Williams, 1997	- n=187; 100%; 72(5) yrs - no MMSE	- inclusion: community dwelling; age ≥ 60; took part in initial phase of Randwick falls and fractures study. - exclusion: ill; immobile; hospitalized; medical condition involving neuromuscular, skeletal or cardiovascular system precluding taking part in exercise; attending exercise classes with intensity equivalent to intervention.
Emery, 1990	- n=48; 83%; 72(6) yrs, range 61-86 - no MMSE	- inclusion: living in inner-city community; not participating in regular exercise.
	Aerobic versus strength exercise	
Moul, 1995	- n=30; 63%; 69(1) yrs, range 65-72 - no MMSE	- inclusion: no current symptoms or signs suggestive of heart disease; < 2 moderate or vigorous aerobic or resistance exercise sessions > 20 min/week; permission from physician to participate.
Study population with cognitive decline		
	Aerobic exercise	
Van Uffelen, 2008	- n=152; 44%; 75 (3) yrs, range 70-80 - mild cognitive impairment; median MMSE (25th–75th ‰) = 29 (28-29)	- inclusion: community-dwelling; age 70-80 yrs; memory complaints; objective memory impairment; able to perform moderate intensity physical activity without using walking devices. - exclusion: ADL disabilities; dementia; psychiatric impairment; depression; epilepsy; multiple sclerosis; Parkinson's disease; kidney disorder requiring haemodialysis; high dose vitamin B supplementation; using medication for rheumatoid arthritis or psoriasis; alcohol abuse; living in or on waiting list for a nursing home.
Scherder, 2005	- n=43; 88%; 86(5) yrs, range 76-94 - mild cognitive impairment; 12 item MMSE ≥ 7	- inclusion: resident of combined home for the elderly/ nursing home; 12 item MMSE 7-10 indicating mild/moderate cognitive deterioration OR 12 item MMSE 11-12 + decreased memory performance; meeting MCI-criteria.[1]

		- exclusion: probable AD; history of alcoholism; cerebral trauma; hydrocephalus; neoplasm; epilepsy; disturbances of consciousness; focal brain disorders.
Stevens, 2006	- n=75; 75%; 81 yrs - demented; 9 ≤ MMSE ≤ 23	- inclusion: resident aged care facility; mild to moderate dementia OR 9 ≤ MMSE ≤ 23; physical capable to gentle regular exercise; able to respond to verbal and physical response.
	Strength exercise	
Baum, 2003[a]	- n= 20 ; 75% ; 88 yrs, range 75-99 - mean MMSE 21; range 10-29; 50% MMSE ≤ 21	- inclusion: age ≥ 65; residents of a long term care facility, assisted living + nursing home for ≥ 3 months; ability to ambulate alone, with assistive devices or one caregiver. - exclusion: unstable acute or chronic illness; inability to follow a two-step command; assaultive behavior pattern; not wanting to discontinue any current physical therapy.
Dorner, 2007	- n=30; ?; 87(6) yrs, range 77-98 - cognitive impairment; mean MMSE (SD) = 21 (5); n=13 diagnosed with dementia	- inclusion: able to walk > 5 meters with or without walking aid - exclusion: MMSE < 10; severe acute disease
McMurdo, 2000	- n=133; 81%; 84(7) yrs, range 70-97 - mean MMSE (sd) = 19 (6)	- inclusion: resident of home for the elderly; age ≥ 70. - exclusion: MMSE < 12.
Van de Winckel, 2004	- n=25; 100%; 82(4) yrs - demented (AD n=22; MID n=3); mean MMSE (sd) = 12 (5).	- inclusion: hospitalized patients with dementia; MMSE score < 24; able responding to requests; able to mimic movements; able hearing music. - exclusion: apathetic patients; inability to maintain seated position for 30 minutes.
McMurdo, 1994	- n=65; 83%; 83(8) yrs, range 67-98 - mean MMSE (sd) = 15 (4)	- inclusion: resident of home for the elderly; ability to toilet, dress, walk independently. - exclusion: severe communication difficulties.

[a] Ordered from high to low quality within categories of content exercise program; [b] number as reported in abstract; AD= Alzheimer's disease; GDS= geriatric depression scale; MCI= mild cognitive impairment; MID= multi infarct dementia; MMSE = mini mental state examination; SD= standard deviation

Table 4: Description of exercise programs and session attendance [a]

Author, year	Program (P); Intensity (I); Frequency + duration (F/D); Organisation (O)/ Supervision (S) vs comparison [b]	Attendance (**A**erobic, **S**trength, **F**lexibility, **B**alance, **E**xercise, **C**ontrol, **NIC=** non-intervention control)
Study population without cognitive decline		
	Aerobic exercise	
Oken, 2006	**P: aerobic exercise**. walking outdoors on 400-m track. I: level 6-7 perceived exertion scale, 70% of Hrmax. F/D: 6 mnths, 1x/wk, 60 min + encouraged to exercise individually ≥ 5x/wk. O/S: group-based, personal trainer. **vs. Iyengar yoga**. (7-8 poses were taught per week to a total of 18 standing and seated poses, each pose held for 20-30 sec, rest between poses 30-60 sec, emphasis on breathing for relaxation; session ending with 10 min deep relaxation in supine position using progressive relaxation, visualization + meditation). I: low. F/D: 6 mnths, 1x/wk, 90 min + daily home practice encouraged. O/S: group based, Iyengar trained teacher. **vs. waiting list control group**.	A-E: mean (SD) = 69 (19)% Yoga: mean (SD) = 78 (20)% NIC: NA
Blumenthal, 1991 [c]	**P: aerobic exercise**. 10 min warm-up; 30 min bicycle ergometry + 15 min brisk walking or jogging with supplemented arm ergometry for 5 min; 5 min cool-down. I: 70% Hrmax. F/D: 16 wks, 3x/wk, 60 min. O/S: group-based, ? **vs. nonaerobic yoga exercise:** I: low. F/D: 16 wks, 2x/wk, 60 min. O/S: group-based, ? **vs. waiting list control group**	A-E: 96% Yoga: 100% NIC: NA
Stevenson, 1990	**P: aerobic + flexibility exercise**. 15 min warm-up (stretching + calisthenics); 30 min stationary cycle ergometry; 15 min cool-down (slow walking and stretching). I: moderate intensity, 60-70% HRR. F/D: 9 mnths, 3x/wk, 60 min. O/S:	AF-E: ? AF-Elow: ?

	group-based, exercise session leaders. **vs. same program, but low intensity**, 30-40% HRR.	only subjects attending ≥ 70% of sessions included
Fabre, 2002	**P: aerobic exercise**. 5 min warm-up; 45 min interval training (brisk walking, jogging); 10 min cool-down. I: individualized conform heart rate (ventilatory threshold). F/D: 8wks, 2x/wk, 60 min. O/S: group-based, ? vs comparison (factorial design): **mental training** (8 wks, 1x/wk, 90 min), **aerobic + mental training**, **social activity control group**.	A-E: 'very good' C: 'very good' (non-attenders excluded)
Hassmen, 1997	**P: aerobic exercise**. Walking. I: low, very light (9)-somewhat hard (13) according to Borg RPE scale. F/D: 3 mnths, 3x/wk, ? min. O/S: individual exercise, not applicable. **vs. home assignments**.	A-E: ? C: ?
Madden, 1989 [c]	**P: aerobic exercise**. 10 min warm-up; 30 min bicycle ergometry + 15 min brisk walking or jogging with supplemented arm ergometry for 5 min; 5 min cool-down. I: 70% HRR. F/D: 16 wks, 3x/wk, 60 min. O/S: group-based, ? **vs. non aerobic yoga exercise**: 16 wks, 2x/wk, 60 min. **vs. waiting list control group**.	A-E: 90% Yoga: 90% NIC: NA
	Strength exercise	
Lachman, 2006	**P: strength exercise**. 35 min videotaped program of 10 exercises using elastic bands. 10 min warm-up; 25 min resistance exercises; 5 min cool-down. I: using bands with higher resistance when > 10 repetitions possible without significant fatigue. F/D: 26 wks, 3 x/wk, 35 min. O/S: individual at home, 2 visits by physical therapist or trainer. **vs. waiting list control group**.	S-E: mean (SD) = 93 (38)%, range 0-218% of 78 required sessions. NIC: NA
Tsutsumi, 1997	**P: strength exercise**. 12 resistance exercises on machines: leg extension, leg curl, shoulder press, bench press, lateral pull-down, fly, triceps, press-down, arm curl, back extension, seated row, abdominal flexion. I: high: 2 sets of 8-	S-E: nearly 100% STlow: nearly 100%

	10 reps at 75-85% of estimated repetition maximum. Increasing during the programs. F/D: 12 wks, 3x/wk, ? min. O/S: group-based, ? **vs. same program, but low intensity**. I: 2 sets of 8-10 reps at 55-65% of 1 repetition maximum. **vs. non intervention control group**	NIC: NA
Cassilhas, 2007	**P: strength exercise.** 10 min warm-up; 6 resistance exercises on machines: chest press, leg press, vertical traction, abdominal crunch, leg curl, lower back. I: 2 sets of 8 reps at 80% of repetition maximum. F/D: 24 wks, 3x/wk, 60 min. O/S: group-based, ? **vs. same program, but moderate intensity.** I: 2 sets of 8 reps at 50% of repetition maximum. **vs. control**. Same program, but without overload. I: 2 sets of 8 reps without overload. F/D: 24 wks, 1x/wk, 60 min.	S-E: > 75% STmoderate: > 75% C: > 75%
Molloy, 1988	**P: strength + balance exercise**. I: low. F/D: 3 mnths, 3x/wk, 10-35 min. O/S: group-based, physiotherapist. **vs. non-intervention control group**.	SB-E: 71%, range 31-94 NIC: NA
Perrig Chiello, 1998	**P: strength exercise**. 10 min warm-up; 8 resistance exercises on machines: leg press, bench press, leg curls, seated row, leg extension, preacher curls, trunk curls, back extension. I: ? F/D: 8 wks, 1x/wk, ? min. O/S: ?,? **vs. waiting list control group**.	S-E: ? NIC: ?
	Aerobic and strength exercise	
Okumiya, 1996	**P: aerobic + strength + flexibility exercise**. 5 min warm-up; 50 min aerobic exercise (low intensity aerobic exercise e.g. walking, dodge ball; calisthenics e.g. stretching and ROM exercise; exercises aimed at neuromotor coordination; muscle strengthening exercises for extremities, abdominal wall, back); 5 min cool-down. I: low. F/D: 6 mnths, 2x/wk, 60 min. O/S: group-based, physical educator, medical doctor, 5 nurses. **vs. non intervention control group**.	ASF-E: 86%, range 59-100 NIC: NA

Williams, 1997	**P: aerobic + strength + flexibility + balance exercise**. 5 min warm-up; 35 min conditioning (predominantly aerobic exercise); 15 min stretching seated on floor or chair; 5-10 min cool-down. I: emphasis on social interaction and enjoyment, no measures of intensity. F/D: 42 wks, 2x/wk, 60 min. O/S: group-based, trained exercise leaders. **vs. non intervention control group**.	ASFB-E: 72% in those who completed program (n=71), range 32-100% NIC: NA
Emery, 1990	**P: aerobic + strength + flexibility exercise.** 15 min warm-up; 25 min aerobic walking + muscle strengthening; 5 min cool-down. I: 70% Hrmax (220- age) + increasing no of reps. F/D: 12 wks, 3x/wk, 60 min. O/S: group-based, ? **vs. social activity control group + waiting list control group** (pooled in analyses)	ASF-E: range 61-94% C: range10-94%
	Aerobic versus strength exercise	
Moul, 1995	**P: aerobic exercise**. Walking. I: 60% HRR, after 8 weeks 65%. F/D: 16 wks, 5x/wk, 30-40 min. O/S: group-based, exercise leader. **vs. strength exercise**. I: progressive resistance using weights. **vs. flexibility exercise** I: low.	A-E: ? S-E: ? F-E: ?
Study population with cognitive decline		
	Aerobic exercise	
Van Uffelen, 2008	**P: aerobic exercise**. Walking. Warming-up, moderate intensity walking exercises with walking pace and distance gradually increasing during program, cooling-down. I: moderate. F/D: 1 year, 2x/wk, 60 min. O/S: group-based, trained instructors. **vs. flexibility + balance exercise**. I: low.	median (25^{th}-75^{th} percentile) = 63 (2-81)%, 'and did not differ between programs'
Scherder, 2005	**P: aerobic exercise.** self paced slow walking with aid. I: low. F/D: 6 wks, 3x/wk, 30 min. O/S: ?,? **vs. flexibility exercise.** hand-face exercise. hand exercise =bending and stretching fingers + sliding wooden club by	A-E: ? F-E: ?

	moving fingers. facial activity = producing 7 facial expression used with rehabilitation after paralysis of the facial nerve.	C: ?
	I: low. F/D: 6 wks, 3x/wk, 15 min. O/S: ?,?	
	vs. control: half social visits, half no intervention.	
Stevens, 2006	**P: aerobic exercise**. gentle aerobic exertion moving joints and muscles. I: ? F/D: 12 wk, 3x/wk, 30 min. O/S: group-based, researchers.	A-E: ? C: ?
	vs. social visits.	NIC: ?
	vs. non intervention control group.	only subjects attending ≥ 75% of AT or C sessions included
	Strength exercise	
Baum, 2003 [a]	**P: strength + flexibility exercise.** I: starting with ROM without resistance, progressing to 1 set of 5 repetitions, and 2 sets of 10 repetitions, using balls, soft ankle and wrist weights and elastic bands. F/D: 52 wks, 3x/wk, 60 min. O/S: group-based, exercise physiologist.	SF-E: 80% C: 56%
	vs. recreational group with art therapist/ social worker, activities such as drawing, playing cards.	
Dorner, 2007	**P: strength + balance exercise.** 10 min warm-up; strength = 25 min elastic resistance bands and soft weights; balance = 10 min exercise balls, balance disks and blocks of 20 cm high; 5 min cool-down. I: 1 set 10-15 reps. F/D: 10 wks, 3x/wk, 50 min. O/S: group-based, sport scientist.	SB-E: 92% in those who completed program (n=30) NIC: NA
	vs. non intervention control group	
McMurdo, 2000	**P: strength + flexibility + balance exercise**. seated exercise on music. I: increasing number repetitions, longer muscle contractions. F/D: 6 mnths, 2x/wk, 30 min. O/S: group-based, ?	SFB-E: 81%, range 33-100 C: 89%, range 35-100
	vs. reminiscence therapy	

Van de Winckel, 2004	**P: strength + flexibility + balance exercise**. seated dance. I: ? F/D: 12 wks, 1x wk/ 30 min. O/S: group-based, physiotherapist. **vs. individual daily conversation with physiotherapist.**	SFB-E: ? C: ?
McMurdo, 1994	**P: strength + flexibility exercise**. 10 min warm-up; 25 min seated isometric exercise; 10 min cool-down. I: increasing number of repetitions. F/D: 6 mnths, 2x/wk, 45 min. O/S: group-based, physiotherapist. **vs. reminiscence therapy**.	SF-E: 72%, range 18-98% C: 62%, range 29-100%

[a] Ordered from high to low quality within categories of content exercise program; [b] unless stated otherwise, frequency + duration, organization and supervision of the comparison interventions match these characteristics of the exercise interventions; [c] cross-over design, in table only data before cross-over considered HRR= heart rate reserve; Hrmax= maximum heart rate; low= low intensity; MET = metabolic equivalents; NA= not applicable; no= number; reps = repetitions; ROM = range of motion; RPE= rating of perceived exertion; SD= standard deviation.

Table 5: Description of neuropsychological outcome measures, domains of cognition, and between-group differences (exercise vs. control) [a]

Author, year	outcome measures	Cognitive focus as reported by authors	n randomized (R) n analyzed (A) (**A**erobic, **S**trength, **F**lexibility, **B**alance, **E**xercise, **C**ontrol, **NIC**= non-intervention control)	Between group differences *(cursive results just fail to reach p<0.05)*
Study population without cognitive decline				
	Aerobic exercise			
Oken, 2006	1. Stroop color word test 2. 10 word learning test 3. letter number sequencing (WAIS) 4. spatial attention task 5. simple reaction time 6. choice reaction time	1. attention 2-3: working memory 4. shifting spatial attention	R: 135 (47 A-E/ 44 yoga/ 44 NIC) A: 118 (38 A-E/ 38 yoga/ 42 NIC)	-
Blumenthal, 1991 [b]	1.short memory (Randt memory test) 2. digit span (WAIS-R) 3. Benton revised visual retention test 4. selective reminding test 5. digit symbol subtest (WAIS-R) 6. trail making test	1-4: memory 5-7: perceptual motor function 8-10: miscellaneous	R: 101 (33 A-E/ 34 yoga/ 34 NIC) A: 97 (31 A-E/ 34 yoga/ 34 NIC)	-

	7. 2 & 7 test 8. nonverbal fluency test 9. verbal fluency test 10. Stroop color word test			
Stevenson, 1990	1. visual reproduction, digit span, verbal memory, verbal pairs test (mental status test (Strub and Black), based on WMS)	1. attention/concentration, orientation, short term memory, higher cognitive functioning	R: 97 A: 72 (39 AF-E/ 33 AF-Elow)	-
Fabre, 2002	1. recall, learning, orientation, manipulation, ,mental problems, verbal fluency, denomination, visual reproduction (BEC 96 questionnaire) 2. orientation, mental control, immediate recall, digit span, reverse digit span, visual reproduction, paired associates learning (WMS)	1. cognitive problems, i.e. praxi, nosi, language 2. amnesic deterioration	R: 32 (8 A-E/ 8 C/ 8 A-E+C/ 8 C) A: idem	-
Hassmen, 1997	1. immediate (1 trial)/ delayed recall: 16 one-syllabus words 2. face recognition: 18 faces + 18 distracter faces 3. simple reaction time task 4. choice reaction time task 5. digit span test: starting with 3 digits, longest series after 10 min.	1-2: memory	R: 40 (20 A-E/ 20 C) A: ?	- better face recognition task in men in A-E (p<0.04) - better digit span test in women in A-E (p<0.001)

Madden, 1989 [b]	1. letter search: compare a visually presented probe letter with a set of letters held in memory composed of 2,4, or 6 different letters (Sternberg task, 90 min) 2. word comparison: deciding whether 2 words are synonyms (90 min)	1. working memory 2. retrieval from long-term memory	R: 85 (28 A-E/ 30 yoga/ 27 NIC) A: 79 (25 A-E/ 28 yoga/ 26 NIC)	-.
	Strength exercise			
Lachman, 2006	1. reverse digit span (WAIS)	1. working memory span	R: 210 (102 S-E/ 108 NIC) A: ?	-
Tsutsumi, 1997	1. mental arithmetic task: counting back with 7 from 3-digit number for 2 min 2. mirror drawing task: move cursor along track using a mouse that has to be moved in opposite direction	-	R: 42 (14 S-E/ 14 S-Elow/ 14 NIC) A: 41 (13 S-E/ 14 S-Elow/ 14 NIC)	-
Cassilhas, 2007	1. digit span: forward and backward (WAIS III) 2. Corsis block-tapping: forward, backward, similarities (WMS-R) 3. Toulouse-Pieron test: cancellation numbers, errors 4. Rey Osterrieth figure: copy, immediate recall	1. short term memory 2. visual modality of short term memory 3. attention 4. long term episodic memory	R: 62 (20 S-E/ 19 S-Emoderate/ 23 C) A: idem	- better digit span forward, Corsi_s block-tapping task backward, Corsi similarities, Rey–Osterrieth complex figure immediate recall in S-E vs control and S-E moderate vs control (all

				p<0.05) - better Toulouse–Pieron test item errors in S-Emoderate than control (p=0.01)
Molloy, 1988	1. total recall (4 trials), immediate free recall (trial 1), recognition test with 3 distraction slides (7 colour slides test) 2. digit symbol (WAIS) 3. forward + reverse digit span (WAIS) 4. logical memory (WMS) 5. word fluency test (Western Aphasia Battery) 6. MMSE	1. memory, language, visual perception 3. short-term memory 5. motivation, attention, concentration, retrieval from long-term memory	R: 50 (25 SB-E/ 25 NIC) A: 45 (23 SB-E/ 22 NIC)	less decline in word fluency test in SB-E (p=0.025)
Perrig Chiello, 1998	1. digit symbol test (WAIS) 2. immediate/ delayed recall + free recall: 8 two-syllabi words 3. immediate/ delayed recall: 8 distracter words	1: visuomotor coordination, attention, information processing speed. 2-3: memory	R: 46 (23 S-E/ 23 NIC) A: idem	*better immediate (p=0.07) + delayed recognition (p=0.08) in S-E*
	Aerobic and strength exercise			
Okumiya, 1996	1. MMSE 2. Hasegawa dementia scale revised 3. visuospatial cognitive performance test: eye-tracking	1-2: overall cognition 3: concentration, non verbal visuospatial	R: 42 (21 ASF-E/ 21 NIC) A: idem	-

	performance vigilance task	orientation, reaction time		
Williams, 1997	1. digit span subtest (WAIS-R) 2. picture arrangement subtest (WAIS-R) 3. Cattell's matrices	memory + fluid intelligence	R: 187 (94 ASFB-E/ 93 NIC) A: 149 (71 ASFB-E/ 78 NIC)	- improved digit span in ASFB-E (p= 0.004)
Emery, 1990	1. digit symbol (WAIS-R) 2. digit span (WAIS-R) 3. writing digits 4. writing words	1-4: fluid intelligence, i.e. problem solving, integration new information	R: 48 (15 ASF-E/ 15 C/ 18 NIC) A: 39 (14 ASF-E/ 25 C+NIC)	-
	Aerobic versus strength exercise			
Moul, 1995	1. immediate memory, recent memory, temporal orientation, problem solving and abstract reasoning, organization, auditory processing (Ross Information Processing Assessment)	1.information processing abilities	R: 30 (10 A-E/ 10 S-E/ 10 F-E) A: ?	better 'organization' and 'auditory processing' in A-E vs. S-E and A-E vs. F-E (p<0.05)
Study population with cognitive decline				
	Aerobic exercise			
Van Uffelen, 2008	1. immediate/ delayed recall (CVLT) 2. abridged stroop color word test 3. digit symbol substitution test 4. verbal fluency test: 3 trials of 1 min per letter	1. memory 2. attention 3. information processing speed 4. executive function	R: 179 (86 A-E/ 93 FB-E) A: 152 (77 A-E/ 75 FB-E)	ITT: no main effects PP: better CVLT delayed recall in men in A-E attending >75% of the sessions (n=33), (beta (95%CI) = 1.5(0.1-3.0); p=0.04)

				- interaction between attendance and CVLT delayed recall (p=0.06) and attendance and stroop color word test (p=0.04) in women in A-E (n=67)
Scherder, 2005	1. category naming: 1 min animals, 1 min professions 2. trail making A + B 3. digit span (WMS-R) 4. visual memory span (WMS-R) 5. immediate/ delayed recall + recognition (CVLT) 6. face recognition (RBMT) 7. picture recognition (RBMT)	1-2: executive functions 3-7: memory	R: 43 (15 A-E/ 13 F-E/ 15 C) A: ?	- better category naming in A-E vs. control (ES 0.16; p=0.02) + F-E vs. control (ES 0.12; p=0.04) - better trail making in A-E vs. control (ES 0.10; p=0.07) and F-E vs. control (ES 0.19; p=0.02)
Stevens, 2006	1. clock drawing test	1. progression symptoms dementia	R: N= 120 (?/ ?/ ?) A: N=75 (24 A-E/ 21C/ 30 NIC)	less decline in A-E vs. C (p=0.002)
	Strength exercise			
Baum, 2003 [a]	1. MMSE	-	R: 20 (11 SF-E/ 9 NIC) A: idem	better MMSE in SF-E (3.1 points ; ES (90% CI)=0.5 (.12-.95) ; p=0.02)
Dorner,	1. MMSE		R: 42 (21 SB-E/ 21 NIC)	-

2007			A: 30 (15 SB-E/ 15 NIC)	
McMurdo, 2000	1. MMSE 2. reaction time	-	R: 133 (77 SFB-E/ 56 C) A: 90 (52 SFB-E/ 38 C)	-
Van de Winckel, 2004	1. MMSE 2. short-term memory, orientation, visuoconstructional problems, category fluency, copying figures, free recall 8 words (Amsterdam Dementia Screening test 6)	-	R: 25 (15 SFB-E/ 10 C) A: 24 (15 SFB-E/ 9 C)	- improved MMSE in SFB-E (ES=0.5; p=0.02) - improved fluency in SFB-E (p=0.01)
McMurdo, 1994	1. MMSE 2. speed of response to visual stimulus (recognition movement time + time taken to respond to the stimulus)	1. cognitive state 2. choice reaction time	R:65 (36 SF-E / 29 C) A: 55 (32 SF-E/ 23 C)	*less decline on MMSE in SF-E (p=0.06)*

[a] Ordered from high to low quality within categories of content exercise program; [b] cross-over design, in table only intervention before cross-over considered; CVLT = California verbal learning test (or modification in another language); ES= effect size; ITT= intention to treat analysis; low= low intensity; PP= per protocol analysis; RBMT = Rivermead behavioral recognition test; WAIS-(R) = Wechsler adult intelligence scale (revised); WMS-(R) = Wechsler memory scale (revised).