Effects of physical exercise on cognitive function of older adults with mild cognitive impairment: A systematic review and meta-analysis

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A B S T R A C T

Background and Purpose: Mild Cognitive Impairment (MCI) is associated with a greater risk of dementia for older adults. However, systematic reviews have shown that some physical exercise (PE) seems to improve MCI symptoms and signs. Those reviews and meta-analysis could not explain what possible moderator influenced their results. This meta-analysis aims to identify the effect of PE over older people’s cognition with MCI and explore sources of heterogeneity.

Methods: Databases were searched from inception January 2020 for randomized clinical trials that evaluated the effects of PE over cognition of older persons with MCI. Random effect meta-analyses were performed for each cognitive outcome. Subgroup analyses and meta-regressions models explored the potential sources of heterogeneity.

Results: A total of 2077 participants (mean age = 71.8 years) from 27 studies were included. PE improves global cognitive function (SMD = 0.348 [95% CI 0.166 to 0.529]; p = 0.0001), executive function (SMD = 0.213 [95% CI 0.026 to 0.400]; p = 0.026) and delayed recall (SMD = 0.180 [95% CI 0.002 to 0.358]; p = 0.047). A trend towards beneficial effects of PE on verbal fluency (SMD = 0.270 [95%, CI -0.021 to 0.561]; p = 0.069) and attention (SMD = 0.170 [CI -0.016 to 0.357]; p = 0.073) were also observed. Subgroup analyses showed a relationship between modality and intensity of physical exercise and changes observed in global cognitive function, executive function, delayed recall, verbal fluency and working memory.

Discussion and Conclusion: PE can ameliorate cognitive deficits of older adults with MCI. The most pronounced effects appear to arise from other types of exercise that included mind-body exercises and moderate intensity.

1. Introduction

The worldwide increase in life expectancy culminated on the increased incidence and prevalence of degenerative diseases such as dementia (Salthouse, 2010). Prior to the diagnosis of dementia, older adults experience a transient state of cognitive function commonly known as mild cognitive impairment (MCI) (Petersen, 2004). Although pharmacological treatment has limited effects on cognitive function (Schneider et al., 2014), currently there are indications that MCI can be reversed, or at least have its progression to dementia decelerated, by lifestyle changes (Law, Barnett, Yau, & Gray, 2014; Schmitter-Edgecombe & Dyck, 2014). In fact, physical exercise (PE) has been shown to improve cognitive function in healthy and older persons with cognitive impairment (Bherer, Erickson, & Liu-Ambrose, 2013; Blondell, Hammersley-Mather, & Veerman, 2014; Carvalho, Rea, Parimon, & Cusack, 2014; Sofi, Valecchi, & Bacci, 2011).

Previous systematic reviews have addressed the effects of PE on cognitive function of older people with or without cognitive deficits showing positive effects of PE on cognitive gains (Cai & Abrahamson, 2016; Colcombe & Kramer, 2003; Falck, Davis, Best, Crockett, & Liu-Ambrose, 2019; Gates, Singh, Sachdev, & Valenzuela, 2013; Groot, Hooghiemstra, & Rajmakers, 2016; Jensen, Hasselbalch, Waldemar, & Simonsen, 2015; Kelly et al., 2014; Law, Barnett, Yau, & Gray, 2014; Law, Lam, Chung, & Pang, 2020; Öhman, Savikko, Strandberg, &...
Pitkäla, 2014; Sanders, Hortobágyi, la Bastide-van Gemert, van der Zee, & van Heuvelen, 2019; Song, Yu, Li, & Lei, 2018; Ströhle, Schmidt, & Schultz, 2015; van Uffelen, Chin A Paw, Hopman-Rock, & van Mechelen, 2008; Zheng, Xia, Zhou, Tao, & Chen, 2016). Of those, seven specifically address the topic of exercise and cognition in older adults with MCI (Cai & Abrahamson, 2016; Falck et al., 2019; Gates et al., 2013; Jensen et al., 2015; Law et al., 2020; Öhman et al., 2014; Sanders et al., 2019; Song et al., 2018; Ströhle et al., 2015; Zheng et al., 2016). Although all evidence showed increases in at least one cognitive domain, there are some points that still need evaluation since some studies have included individuals without diagnosed MCI (Law et al., 2014b; Cai & Abrahamson, 2016; Gates et al., 2013; Öhman et al., 2014; Zheng et al., 2016). Previous meta-analyses (MA), have found that PE has a greater effect than drugs on cognition of patients with MCI (Ströhle et al., 2015). Also, gains are greater in interventions lasting at least six months (Zheng et al., 2016). None of these two studies, however, evaluated exercise prescription parameters such as intensity, time or modality (Ströhle et al., 2015; Zheng et al., 2016). Other three reviews address the topic of PE and MCI. Results from (Sanders et al., 2019; Song et al., 2018) related PE to global cognitive function improvement, but none other cognitive domain in older adults with MCI (Sanders et al., 2019; Song et al., 2018). Law and collaborators (Law et al., 2020) revealed that PE can improve global cognitive function and that effect can be primarily attributed to its effects on working memory.

Given the above mentioned, the present study intended to evaluate the relationship between cognitive outcomes and PE, exploring the role of intensity, modality, duration of intervention, frequency and time, including only older adults with confirmed MCI diagnosis. Thus, our aims were: 1) to establish the effects of exercise on cognitive function in older adults with MCI, comparing exercise vs. control groups; 2) to perform subgroup analyses to compare exercise response on cognitive function according to type (aerobic, resistance, multi-component or other types of exercise), intensity (light, moderate or vigorous) and methodological quality of study (low bias risk or high bias risk); 3) to identify moderators, including participant’s characteristics (age and sex) and exercise intervention variables (exercise protocol length, exercise weekly volume), that could influence the effects of exercise on cognitive function; and 3) to assess the potential influence of publication bias on the relationship between exercise and cognitive function in older persons with MCI.

2. Methods

This systematic review is in line with the Preferred Reporting Items for Systematic Review and Meta-Analyses: The PRISMA Statement (Moher, Liberati, Tetzlaff, & Altman, 2010). The protocol of the present study was initially registered at the International Prospective Register of Systematic Reviews, PROSPERO, on March 31st 2016 (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42016037182).

2.1. Eligibility criteria

We were included in this meta-analysis studies that: (1) Investigated participants (mean age ≥ 60 years) diagnosed with MCI accordingly to Mayo Clinic (Pettesen et al., 2015) or the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders criteria (American Psychiatric Association, 2013). The criteria consisted of: (a) self- or informant-reported memory or cognitive complaint; (b) scores below expected for the same age and schooling group in psychological tests; (c) preserved independence in functional abilities; and (d) no dementia diagnosis; (2) Assessed global cognitive function and any specific domains of cognition, including cognitive speed, verbal fluency, immediate recall, delayed recall, working memory, executive function or attention measured by neuropsychological tests or other objective measurements; (3) Have not included patients in with MCI resulted from another neurological condition or psychiatric disease; (4) Were randomized controlled trials (RCT); (5) Have used an exercise intervention, of any type, intensity, duration or frequency, but defined as a planned, structured, repetitive, and purposive physical activity aiming the improvement or maintenance of one or more components of physical fitness (Caspersen, Powell, & Christenson, 1985). (6) Have used as a control group: no treatment; balance, tone or stretching programs; or social and/or mental activities. (7) Were written in English.

2.2. Search strategy

Five electronic databases (Medline, Cochrane Central, Embase, PsycINFO, and SportDiscuss) were searched from their inception to January 2020. Search strategy used individually or combined keywords and synonyms, adjusted to fit requirements of each electronic database that included ‘physical exercise’, ‘exercise’, ‘aerobic exercise’, ‘strength training’, ‘resistance training’, ‘physical training’, ‘cognitive decline’, ‘dementia’, ‘cognitive impairment’, ‘cognition’, ‘mild cognitive impairment’, ‘mild neurocognitive disorder’, ‘cognitive decline’, ‘old’, ‘elderly’, ‘aged’ and ‘aging’. Outcome terms were not included to enhance search sensitivity. Additionally, reference lists of the included trials and in reviews of the literature were also screened for relevant trials. The detailed strategy for PubMed is shown on Table 1. The complete search strategy is available upon request.

2.3. Study selection

Two investigators (LFB and FS), independently screened titles and abstracts retrieved on electronic database searches determining potentially eligible articles according to a standard screening checklist based on eligibility criteria. After removal of duplicates, full-text versions of the remaining studies, including those potentially eligible and uncertain, were retrieved independently for complete review by two reviewers to determine eligibility. Disagreements were discussed between reviewers. For studies without sufficient information to evaluate their eligibility, the study authors were contacted via email twice. After contact, papers with insufficient information were excluded.

2.4. Outcomes

Our primary outcome of interest was the mean change difference on cognitive outcomes in exercise group and control groups. The cognitive outcomes had to be evaluated by any validated neuropsychological test or test battery concerning global cognitive function or any specific domains of cognition, including cognitive speed, verbal fluency,
immediate recall, delayed recall, working memory, executive function or attention., in comparison with Control Group.

2.5. Data extraction

Two reviewers (LFB and FS) independently conducted the following data extraction: (1) Sample (number of participants, % of women, mean age); (2) Exercise protocol (type of exercise [aerobic, resistance, multi-component (i.e., a kind of exercise training that combines different regimes of exercise in the same exercise session incorporating both aerobic and/or resistance training and other forms of exercise training (Cadore, Rodriguez-Manas, Sinclair, & Izquierdo, 2013; Heubel et al., 2018)), or other types of exercise (i.e., PE that were not classified into these previous categories)], intensity of intervention [light, moderate and vigorous (see Supplementary Appendix A for details)], weekly volume [amount of minutes during the week destined to exercise intervention] and length of the trial, [total length of study intervention protocol]); (3) Methodological factors (study quality, risk of bias, instruments used to assess cognitive function); (4) Finally, the pre- and post-test means and standard deviations (SD) of global cognitive function or any specific domains of cognition for the Exercise and Control group were extracted. If a study did not have reported pre- and post-test means and standard deviations (SD), we used the mean change and SD or pre- and post-test means and confidence interval, if reported by authors. Also, for studies presenting incomplete outcome data, authors were contacted by e-mail, and if possible, procedures for estimation of missing data were performed. When a study reported more than one outcome measure for a cognitive domain, we selected the outcome proposed by the author as the main outcome for that domain.

2.6. Risk of Bias and quality assessment

All included studies were evaluated and classified independently by two reviewers (LFB and FS) according to the items set by Cochrane Collaboration’s tool for assessing the risk of bias within and across randomized trials (Higgins, Altman, & Gøtzsche, 2011). The following items were evaluated for each study: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting and (7) other bias. The overall judgment of each item for each study was characterized as ‘low’, ‘high’ and ‘unclear’ according to the levels of bias.

2.7. Meta-analysis

We used a random-effects meta-analysis due to the anticipated heterogeneity. The standardized mean difference (SMD) and 95% confidence intervals (CIs) were used as the effect size measure (ES). The meta-analysis was conducted in the following steps, for each cognitive function independently (Global function, immediate memory, delayed memory, working memory, executive function, verbal fluency, cognitive speed and attention): First, we calculated the SMD statistic together with 95% CIs to establish the effects of exercise on cognition of elderly with MCI across all studies. Next, we conducted subgroup analyses to compare exercise response according to type (aerobic, resistance or multi-component), intensity (light, moderate or vigorous) and methodological quality (low bias risk or high bias risk). Further, we conducted meta-regression analyses to investigate the potential moderators of the effects of exercise on each cognitive function. Potential moderators
were chosen a-priori according to previous literature and included: participants age, exercise protocol length, exercise weekly volume, proportion of women. Heterogeneity was assessed with the Cochran Q and I² statistics for each analysis (Higgins, Thompson, Deeks, & Altman, 2003). Publication bias was evaluated by Egger, Smith, Schneider, and Minder, (1997) and Begg and Mazumdar (1994) bias tests. In addition, whenever a publication bias was identified, we conducted a trim and fill adjusted analysis (Duval & Tweedie, 2000) to recalculate the effect size at each iteration. All analyses were run in Comprehensive Meta-Analyis software (CMA; Version 3, Biostat, Englewood, New Jersey).

3. Results

3.1. Search results

Fig. 1 shows the detailed selection process flow diagram. The preliminary search according to the predetermined search strategy identified a total of 6308 studies. Four additional records were identified through other sources. From those, 1232 were duplicates and 4985 were excluded in title and abstract stage, remaining 91 for full-text eligibility assessment stage. Of these 88, 61 studies were excluded. Finally, 27 studies fulfilled the inclusion criteria and were included in our review (Baker et al., 2010; Brinke, Bolandzadeh, & Nagamatsu, 2015; Damirchi, Hosseini, & Babaee, 2018; Davis et al., 2013; Fiatarone Singh, Gates, & Saigal, 2014; Hildreth, Van Pelt, & Moreau, 2015; Hong, Kim, & Jun, 2017; Lam, Chau, & Wong, 2012; Lam, Chan, Leung, & Fung, 2015; Langoni et al., 2019; Lautenschlager, Cox, & Flicker, 2008; Law, Mok, & Yau, 2019; Lazarou, Parastatidis, & Tsoaki, 2017; Lu et al., 2016; Nagamatsu, Handy, & Hsu, 2012; Nagamatsu, Chan, & Davis, 2013; Qi, Zhu, Zhang, Wu, & Wang, 2019; Scherder, Van Paaschsen, & Deijen, 2005; Sungkarat, Boripuntakul, Chattipakorn, Watcharasaksilp, & Lord, 2017; Suzuki, Shimada, & Makizako, 2012; Suzuki, Shimada, & Makizako, 2013; Tao et al., 2019; van Uffelen, Chinapaw, van Mechelen, & Hopman-Rock, 2008; Varela et al., 2012; Wei & Ji, 2014; Xia et al., 2019). 27 studies provided complete data to enable inclusion within our meta-analysis (Baker et al., 2010; Begg & Mazumdar, 1994; Brinke et al., 2015; Damirchi et al., 2018; Davis et al., 2013; Duval & Tweedie, 2000; Egger et al., 1997; Fiatarone Singh et al., 2014; Heubel et al., 2018; Higgins et al., 2003, 2011; Hildreth et al., 2015; Hong et al., 2017; Lam et al., 2012, 2015; Langoni et al., 2015; Lautenschlager et al., 2008; Law et al., 2019; Lazarou et al., 2017).

3.2. Characteristics of included studies and participants

A total of 27 RCTs, accounting for 2077 participants with MCI were included for review. From those participants, 1094 were randomized to exercise group and 983 were used as intervention program in eight studies (Lam et al., 2012; Lazarou et al., 2017; Qi et al., 2019; Sungkarat et al., 2017; Tao et al., 2019; Wei & Ji, 2014; Xia et al., 2019; Zhu et al., 2018).

Global cognitive function, cognitive speed, verbal fluency, immediate recall, delayed recall, working memory, executive function and attention tests were used to evaluate cognition within included studies. Additional information regarding characteristics of each of the included studies can be fully assessed (see Supplementary Appendix B, which demonstrates characteristics of included studies and participants).

3.3. Risk of Bias and study quality

Seven studies were considered of low risk of bias (Baker et al., 2010; Davis et al., 2013; Fiatarone Singh et al., 2014; Langoni et al., 2019; Sungkarat et al., 2017; van Uffelen, Chinapaw et al., 2008; Zhu et al., 2018) and the remaining 20 studies presented high risk of bias (Brinke et al., 2015; Damirchi et al., 2018; Hildreth et al., 2015; Hong et al., 2017; Lam et al., 2012, 2015; Lautenschlager et al., 2008; Law et al., 2019; Lazarou et al., 2017; Lu et al., 2016; Nagamatsu et al., 2012, 2013; Qi et al., 2019; Scherder et al., 2005; Suzuki et al., 2012, 2013; Tao et al., 2019; Varela et al., 2012, 2014; Xia et al., 2019). Full detailed risk of bias and quality assessment are presented in Fig. 2.

3.4. Effect of interventions on Global Cognitive Function and its domains

A total of eighteen arms from sixteen unique studies including 1473 participants (706 in the intervention groups and 767 in the control groups) contributed to global cognitive function (GCF) analysis (Fig. 3). The primary analysis showed effects of PE training on GCF in older adults with MCI (n = 1473, SMD = 0.348 [95 % CI 0.166 to 0.529]; p = 0.0001). The results of the subgroup analysis established that other types of PE improved GCF (SMD = 0.531 [95 % CI 0.172 to 0.854]; p = 0.003), while aerobic (SMD = 0.186 [95 % CI -0.216 to 0.589]; p = 0.364), resistance exercise (SMD = 0.192 [95 % CI -0.350 to 0.735]; p = 0.488) and multicomponent programs did not (SMD = 0.379 [95 % CI -0.025 to 0.785]; p = 0.666). Subgroup analyses of studies with low and high risk of bias demonstrate a more prominent effects between studies with low risk of bias (SMD = 0.771 [95 % CI 0.343-1.200]; p = 0.0004). Meta-regression indicates a negative correlation between volume and GCF (β = -0.0048, R² = 0.33, p = 0.044) demonstrating that effects are higher in studies with low volume (see tables and figures, Supplementary Appendix C, which demonstrates meta-regression and publication bias risk for cognitive domains.

The primary analysis pooled from a total of nineteen arms from fifteen unique studies, including 1072 participants, showed significant small effect for executive function (EF) domain (n = 1072, SMD = 0.213 [95 % CI 0.026 to 0.400]; p = 0.026) (Fig. 4). The results of the subgroup analysis established that other types of PE improved EF in older adults with MCI (SMD = 0.499 [95 % CI 0.093 to 0.905]; p = 0.015), while aerobic (SMD = 0.130 [95 % CI -0.177 to 0.438]; p = 0.407), resistance exercise (SMD = 0.136 [95 % CI -0.259 to 0.532]; p = 0.499) and multicomponent programs did not (SMD = 0.039 [95 % CI -0.811 to 0.889]; p = 0.928). In addition, moderate (SMD = 0.448 [95 % CI 0.075 to 0.821]; p = 0.018) showed positive effects of exercise on EF. Light and vigorous intensity did not promote gains in EF for this population (SMD = 0.039 [95 % CI -0.818 to 0.897]; p = 0.928 and SMD = 0.066 [95 % CI -0.258 to 0.390]; p = 0.688 respectively). The meta-regression analysis demonstrated a
negative correlation between length of trial and EF presented ($\beta = -0.0035$, $R^2 = 0.32$, $p < 0.047$) indicating that higher effects on shorter studies (Supplementary Appendix C).

A total of 1569 participants (744 in the intervention groups and 825 in the control groups) included from a seventeen arms analysis of fifteen unique trials contributed to delayed recall (DR) results (Fig. 5). There was evidence of benefit of the physical exercise intervention in DR for older adults with MCI ($n = 1569$, SMD = 0.180 [95% CI 0.002 to 0.358]; $p = 0.047$). Subgroup analysis demonstrated that other types of exercise improved DR (SMD = 0.593 [95% CI 0.269 to 0.917]; $p = 0.000$). Neither aerobic (SMD = 0.071 [95% CI -0.192 to 0.335]; $p = 0.596$), resistance exercise (SMD = -0.037 [95% CI -0.444 to 0.369]; $p = 0.856$) nor multicomponent programs (SMD = 0.006 [95% CI -0.377 to 0.390]; $p = 0.973$) had significant effects. Again, moderate (SMD = 0.661 [95% CI 0.233–1.090]; $p = 0.002$) showed positive effects of exercise on DR. Light and vigorous intensity did not promote gains in DR for this population (SMD = 0.260 [95% CI -0.177 to 0.698]; $p = 0.244$ and SMD = -0.014 [95% CI -0.348 to 0.319]; $p = 0.930$ respectively).

Although not significantly, the primary meta-analysis showed a trend towards beneficial effects of PE on verbal fluency (VF) for older persons with MCI ($n = 1115$, SMD = 0.270 [95% CI -0.021 to 0.561]; $p = 0.069$). Subgroup analysis demonstrate that PE at moderate intensity (SMD = 0.890 [95% CI 0.133 to 0.165]; $p = 0.021$) resulted in a positive prominent effect. Attention (ATT) ($n = 467$, SMD = 0.170 [CI -0.016 to 0.357]; $p = 0.073$) also demonstrated a trend towards improvements of PE for participants with MCI. Even thought primary meta-analysis did not supported the effects of PE for working memory (WM) for older individuals with MCI ($n = 849$, SMD = -0.012 [95% CI -0.323 to 0.299]; $p = 0.939$), subgroup analysis revealed a significantly effect during moderate intensity (SMD = -0.064 [95% CI -1.260 to -0.030]; $p = 0.039$). There was no further evidence of benefit of the physical exercise in any other studied cognitive domain including: cognitive speed ($n = 642$, SMD = 0.023 [95% CI -0.150 to 0.196]; $p = 0.794$) and immediate recall ($n = 679$, SMD = 0.090 [95% CI -0.085 to 0.264]; $p = 0.314$) (Supplementary Appendix D).

3.5. Publication bias analysis

Publication bias was identified for Verbal Fluency (Begg and Mazumdar Tau = 0.50, $p = 0.02$; Egger Intercept = 3.00, $p = 0.018$). The effect, however, no studies were trimmed, and the effect was not modified by the Duval and Tweedie’s trim and fill test (Supplementary Appendix C).

4. Discussion

This systematic review with meta-analysis examined the effect of PE on cognitive function in older people with MCI. The tested hypothesis is that PE improves cognitive function in older people with MCI. We have, therefore, confirmed this hypothesis, suggesting that an active lifestyle could positively affect cognitive function during aging process, preventing, or at least delaying, the progression of MCI to Alzheimer disease or other dementias (Law et al., 2014a; Schmitter-Edgecombe & Dyck, 2014).

Five previous MA have visited this hypothesis. However, Gates and colleagues (Gates et al., 2013) and Zheng and colleagues (Zheng et al., 2016) included non-RCT studies and older people without judicious diagnosis of MCI. Considering the same inclusion criteria adopted in the present study, Strohle and colleagues (Strohle et al., 2015) and Song and colleagues (Song et al., 2018) also presented positive effects of PE on at least some domain of cognitive function. Both studies, however, did not show subgroup analysis or meta-regression that help explain possible moderator of PE effects. More recently, Law and colleagues (Law et al., 2020) reported that PE can reduce global cognitive decline in people with MCI. Although a similar research question was applied,
we included two different databases (Embase and SportDiscuss) and specific eligibility criteria (older adults diagnosed with MCI accordingly to Mayo Clinic or the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders criteria).

Overall, our results indicate that PE training improve GCF, EF and DR. A positive trend towards improvements for VF and ATT was also observed, but did not reach statistical significance. It is already recognized that PE promotes several mechanisms interfering on brain and aging process. Changes in molecular and/or cellular pathways support the underlying mechanisms of the PE on cognition. A previous systematic review with meta-analysis from our group showed exercise-induced alterations on inflammatory (reduction in TNF-α and IL-6 concentrations) and neurotrophic (increased expression of BDNF) biomarkers in individuals with MCI (Stigger, Marcolino, Portela, & Plentz, 2018). Also, PE may increase the blood flow to the brain and the growth of blood vessels (Black, Isaacs, Anderson, Alcantara, & Greenough, 1990; Ogoh & Ainslie, 2009). Therefore, improvements in cognition following PE seems to be, in some way, related to changes in neurovascular and on molecular cascades, which in turn promote neurogenesis and synaptic plasticity (Stillman, Cohen, Lehman, & Erickson, 2016). Moreover, it is known that PE modulates the pre-frontal cortex’s rest activation and connectivity in healthy elderly, which is critically involved in both cognition and motor control (Churchill et al., 2002; Eggenberger, Wolf, Schumann, & De Bruin, 2016; Shibuya & Kubooyama, 2007; Voss, Prakash, & Erickson, 2010). It is possible to assume that such plasticity might happen throughout the brain cortex, thus reflecting in cognition improvements.

We also demonstrated that other types of PE, such as mind-body exercises (MBE), and moderate intensity are responsible for more prominent effects on cognitive domains. In our subgroup analysis, positive

<table>
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<th>Study name</th>
<th>Outcome</th>
<th>Std diff in means</th>
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![Fig. 3. Forest plot of comparison of Physical Exercise on Global Cognitive Function.](image)

![Fig. 4. Forest plot of comparison of Physical Exercise on Executive Function.](image)
significant effects were observed for EF, DR, VF and WM following moderate intensity PE. A high number of the included studies classified as other types of PE used (MBE) as intervention for people with MCI (Lam et al., 2012; Sungkarat et al., 2017; Tao et al., 2019; Xia et al., 2019). Our finding corroborates with previous studies that reported positive effects in various cognitive functions following MBE interventions for cognitively intact or older adults with MCI (Wang et al., 2018; Wu et al., 2019; Zheng et al., 2017; Zou, Loprinzi, Yeung, Zeng, & Huang, 2019). Although defined as aerobic exercises with moderate intensity (Yang et al., 2020), when compared to usual aerobic exercises such walking and cycling, or even to muscular strength, or other traditional multi-component programs that simply combine different types of exercise (eg. Aerobic, resistance, balance, muscular and flexibility), MBE could be considered as a multielement intervention program. MBE is characterized by slow and coordinated movement, psychosomatic relaxation, body awareness, and mental concentration (Zou et al., 2019). In addition, MBE had been previously demonstrated to induce activations of prefrontal cortex, motor cortex and occipital cortex and improved blood supply to the brain (Xie et al., 2019). Also, MBE are known to improve the individual’s cardiopulmonary function (Miller & Taylor-Piliae, 2014). At least in healthy older adults, higher cardiorespiratory fitness has lower rates of cognitive decline (Barnes, Yaaffe, Satariano, & Tager, 2003; Lam et al., 2012). Considering older adults at early stages of Alzheimer disease, cardiorespiratory fitness was associated with higher whole brain volume and better global cognitive performance (Burns et al., 2009).

Interestingly, week volume demonstrated a negative correlation with GCF. Although our results are not in line with World Health Organization guidelines (adults aged ≥ 65 years should perform at least 150 min/week of moderate-intense or 75 min/week of vigorous aerobic physical activity or an equivalent combination of both) (WHO, 2011), they corroborate previous studies showing that interventions with lowest volumes (40 – 45 min per week) presented better results on cognitive function in individuals with cognitive impairment (Groot et al., 2016).

### 4.1. Strengths and limitations

The strengths of this review relate to careful selection of the population and the interventions of the included works drastically reduce the risk of selective bias found in other works. There was a team effort to ensure that only works with clear MCI criteria were included and that only results derived exclusively from PE were analyzed in an attempt to address the weaknesses pointed out by Horr and colleagues (Horr, Messinger-Rapport, & Pillai, 2015) in his review of the quality of non-pharmacological interventions in MCI. Also, we established different types physical exercise at any intensity, rather than only aerobic or resistance, choosing to perform subgroup analysis. The limitations of this work can be summarized as following: First, the small number of publications found for each domain of cognitive function, the unavailability to perform subgroup analysis in different subclasses of the MCI and comparator interventions. Second, the quality of the included trials could have affected our results considering that: (1) subgroup analysis showed that exercise had positive effects for DR and EF considering studies with low risk of bias (SMD = 0.404 [95 % CI -0.011 to 0.820]; p = 0.056; SMD = 0.304 [95 % CI 0.033 to 0.576]; p = 0.027 respectively) while high risk did not; (2) significant different effects were observed for GCF comparing low and high risk of bias studies; and (3) for cognitive speed, results of low risk of bias studies favors PE while high risk of bias studies favors control group (SMD = 0.022 [95 % CI -0.035 to 0.484]; p = 0.091; SMD = -0.291 [95 % CI -0.58 to -0.004]; p = 0.046 respectively). The randomization process was unclear in nearly half of the included studies. Only two trials published its protocol and in three included studies it was not possible to observe if there was selective reporting of results. Finally, but common to other exercise studies, participants and professions providing the intervention could not be blinded. Third, considering that it was not possible to separate included older adults within DCL subgroups, a “ceiling effects” could mask improvements of analyzed cognitive domains. Different MCI classifications involve great variability of cognitive deficits, including impairments in memory or/and other domains of cognitive functions, but not necessary in both or several domains (Petersen, 2004). Fourth, control groups of several included studies received balance and tone training, recreational/social interventions or instructed to maintain...
current level of physical activity. Although control activities probably were less effective than intervention programs, we can not exclude that they could have beneficial effects on cognitive performance. Fifth, the absence of control of intensity observed in eight of included studies and way that intensity is reported in different studies. Most of MBE intensity of intervention protocol was not clear.

5. Conclusions

Physical exercise ameliorates cognitive deficits of older people with MCI. Also, there was a relationship between modality and intensity of physical exercise and changes observed in global cognitive function, executive function, delayed recall, verbal fluency and working memory. The practical implication of this meta-analysis is that cognitively-engaging exercises such as Tai Chi Chuan, Badanjin and Dance appear to have a stronger effect than non-cognitively-engaging exercise for older adults with MCI. Also, moderate-intensity exercise practice has higher effects than low and vigorous intensity. Thus, prescribing a physical exercise as a routine for older individuals with MCI, considering such aspects, should be considered aiming in cognitive function.

We consider that larger studies with robust methodology, reduced risk of bias and established criteria for MCI diagnosis, are still required. Also, aiming to help health professionals to prescribe PE, those studies should explore the possible PE moderators, such as intensity, volume and type, on cognitive function.

Conflicts of Interest

All authors declare no conflict of interests.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.archger.2020.104048.

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