

## Review Article

# Does Exercise Impact Cognitive Performance in Community-dwelling Older Adults with Mild Cognitive Impairment? A Systematic Review

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## ABSTRACT

**Background:** The prevalence of dementia and other cognitive disorders is expected to rise dramatically as the global population ages. Older adults who present with mild cognitive impairment (MCI) have an increased risk of developing more advanced dementia. However, there is currently no pharmacological treatment to slow the progression or reverse MCI. Thus, identifying effective non-pharmacological approaches to maintain or improve cognition is urgent.

**Aim:** The purpose of this systematic review is to summarize the evidence surrounding the impact of exercise interventions on the cognitive performance levels of community-dwelling older adults who have MCI.

**Methods:** Computerized database and ancestry search strategies located distinct intervention trials between 1990 and 2015.

**Results:** Thirteen national and international studies with 1,171 participants were reviewed. Types of exercise intervention varied. The most common interventions were aerobic exercise, including walking, and Tai Chi. Most studies had an intervention duration of 10 weeks to 6 months, while only 4 studies lasted 12 months. Cognitive outcomes were

mostly measured post intervention with no follow-up. Only one intervention was guided by health behavior theory. Results indicated that physical exercise can benefit cognitive function among older adults who have MCI, including improvements in global cognition, executive function, memory, attention and processing speed. Physical exercise also can positively impact the physiology of the aging brain. However, the evidence surrounding the characteristics of effective physical exercise interventions in terms of exercise type, intensity, duration and frequency remains limited.

**Conclusion:** Future rigorously designed large intervention studies with longer duration are needed to explore the effect of physical exercise programs on cognitive performance in older adults with MCI. Theory-based interventions with sex difference data and follow-up data are preferred. Moreover, clearly reported intervention design, participants' baseline activity level, compliance and acceptance and intervention fidelity control should be encouraged to facilitate the appropriate interpretation of future studies.

**Key Words:** mild cognitive impairment; exercise; older adults; community-dwelling; cognition

## Introduction

The US population of persons 65 years older or older is expected to increase substantially in upcoming decades, moving from 43 million to 92 million by the year 2060.<sup>1</sup> The prevalence of dementia and other cognitive disorders is predicted to rise substantially. Major population-based studies reported an average prevalence of mild cognitive impairment (MCI) of 18.9%.<sup>2-7</sup> The average incidence rates are 47.9 (range 21.5-71.3) per 1000 person-years.<sup>8</sup> Older adults who present with MCI have a greater risk of developing dementia, with a conversion rate of 10%-40% per year to Alzheimer's disease (AD).<sup>6</sup> With a worldwide ageing population, the societal impact of MCI is rising. So far, there is no pharmacological treatment to slow the progression or reverse MCI.<sup>6</sup> Given the high prevalence rate and conversion rate to dementia, identifying effective non-pharmacological approaches to maintain or improve cognition is urgent to control the epidemic of dementia.

Epidemiological studies have proposed that physical exercise is associated with various cognitive benefits.<sup>9,10</sup> Physical exercise reduces cognitive decline associated with

aging, and may reduce the risk for MCI and dementia in older adults who maintain higher levels of physical activity.<sup>9,10</sup> However, cognitive benefits of physical exercise among older adults with MCI are still unclear.

There are a number of mechanisms by which exercise may impact the aging brain.<sup>11</sup> Exercise has a demonstrated impact on cardiovascular function, and multiple cardiovascular risk factors, such as hypertension and circulatory health, are associated with risk for cognitive decline.<sup>12</sup> Increased risk for cognitive impairment has also been linked to diabetes, depression, and high levels of inflammatory markers, conditions which can be impacted by level of physical activity.<sup>13</sup> Exercise may also increase the release of protective agents such as neurotrophines, and impact the nervous system and brain physiology in ways that promote cognitive performance.<sup>14-17</sup>

There is an established body of literature surrounding the influence of interventions focused upon physical experience on cognitive function in older adults both within and without cognitive impairment. The purpose of this manuscript is to systematically describe what is known regarding the impact of exercise interventions on community dwelling older adults with

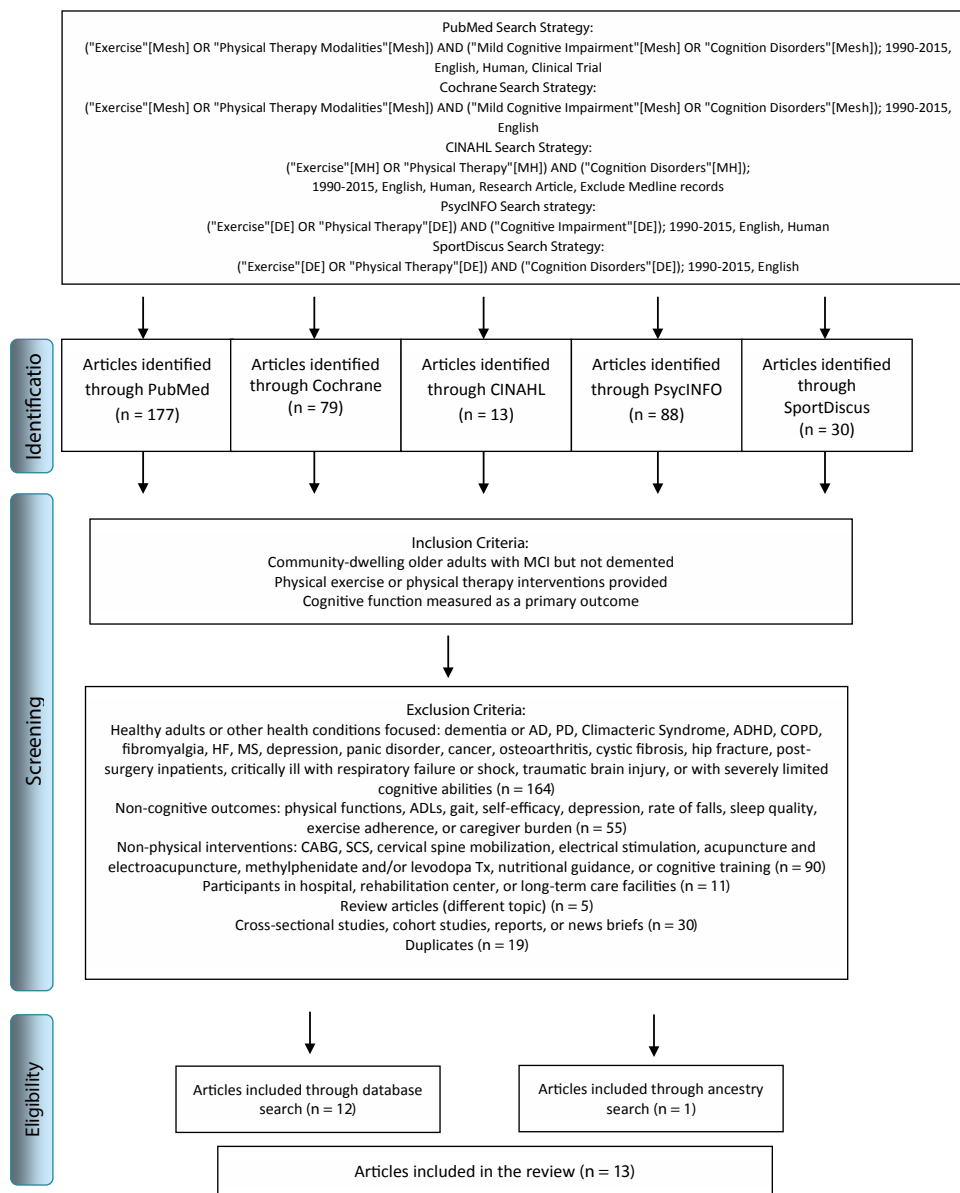
identified MCI, and provide insight regarding the impact this evidence can have on nursing and primary care practice.

## Method

We conducted a review of studies published from 1990 to 2015. Databases searched included CINAHL, PubMed, PsycINFO, SportDiscus, and Cochrane Library. MeSH Terms or Medical Headings used in the search included MCI/cognitive impairment, cognition disorders, exercise, or physical therapy modalities (see Figure 1). Searches were limited to English language and human studies in all databases and clinical trials in PubMed. Additionally, relevant sources cited in identified publications were included in the review (ancestry method). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines provided a structure for manuscript review.<sup>18</sup> Papers were included if: (i) participants were community-dwelling adults with the average age of 60 or

older; (ii) participants had MCI; (iii) they reported experimental or quasi-experimental studies; (iv) physical exercise or physical therapy interventions were described; and (V) they directly measured cognitive performance as an outcome.

We defined MCI using an combination of four major definitions from the Mayo Clinic, the National Institute on Aging-Alzheimer's Association workgroup (NIA-AA), and the Fifth edition of the Diagnostic and Statistical manual of Mental Disorder (DSM-5). Core clinical criteria according to these definitions includes: (i) self- or informant-reported memory or cognitive complaint; (ii) objective memory or cognitive impairment; (iii) essentially preserved general cognitive functioning; (iv) preserved independence in functional abilities; and (v) no dementia diagnosis.<sup>6</sup> While older adults are usually defined as those aged 65 years or older, it is common to find that research articles defined the cut-offs as 55-60.<sup>19-21</sup> Thus, we



*Note.* AD=Alzheimer's disease; PD=Parkinson's disease; ADHD=Attention Deficit Hyperactivity Disorder; COPD=Chronic Obstructive Pulmonary Disease; HF=Heart Failure; MS=Multiple Sclerosis; CABG= coronary artery bypass grafting; SCS= spinal cord stimulation.

**Figure 1:** Flowchart of selection of studies.

established 60 as the cut-off for the inclusion of studies in this review. The definition of exercise is intentional physical activity for improving health and fitness, based on the American College of Sports Medicine position stand.<sup>22</sup>

Table 1 displays identified studies in regards to the study characteristics: (i) study design: publication year, country, study design, sample (number, background demographic characteristics); (ii) intervention characteristics: setting, duration, delivery mode, theoretical framework, cognitive measures and time points; and (iii) key cognitive findings.

## Results

### Search Outcome

The initial computerized search yielded 387 citations. After screening abstracts, 19 duplicates and 355 articles that did not meet the inclusion criteria were rejected. The reasons for exclusion were primarily because of (i) participants did not have MCI, (ii) participants were institutionalized, (iii) non-experimental studies, (iv) non-physical interventions, or (v) cognitive performance were not measured. One additional study was identified through ancestry searches on previously published review articles and all potential primary studies. A total of 13 studies included in this review (see Figure 1).

#### Sample Characteristics

Four of the 13 studies were conducted in the United States (US), with the remaining 9 undertaken in Japan, Hong Kong/China, Australia, Canada, Brazil, and Spain. The 13 studies represented a total of 1,171 participants with mean ages from 70-78 years. Study sample sizes ranged from 11-389. The range of % male was from 0 to 63%, with an average of 38%.

#### Methodological Attributes

Of the 13 studies included, nine were randomized control trials (RCTs); two were non-randomized control trials (29, 30); and the remaining two were uncontrolled pretest-posttest studies.<sup>3,19-21,23-28, 31</sup>

Five of the 13 studies used aerobic exercise (e.g. walking) as the targeted intervention.<sup>19,21,27,28,32</sup> Four studies used Tai Chi exercise.<sup>20,26,29,31</sup> One study conducted functional task exercises, i.e. incorporated unilateral movement, bimanual movement, tasking switching and body mid-line crossing exercise.<sup>20</sup> One study used resistance training only.<sup>24</sup> The remaining two involved multi-component physical training, i.e. incorporated resistance training, aerobic exercise, and coordination/balance training.<sup>25,30</sup> In control groups, activities that were used included usual daily activity, stretching exercise, balance and/or toning training, non-exercise related health education, active cognitive training, low-intensity placebo physical activity, and recreational activities.<sup>19-21,23,25-30</sup>

Only one of the 13 studies was health behavior theory based (i.e., social cognitive theory).<sup>21</sup> The study provided individualized home-based physical activity program that aimed to encourage participants to perform at least 150 minutes of moderate-intensity physical activity per week. To enhance adherence, the study also delivered a social cognitive theory-based behavioral intervention package via a workshop, a manual, newsletters and telephone calls, which consisted of information

on exercise programs, rewards, goal setting, time management, barriers to activity, and safe exercise. Lautenschlager and the colleagues reported a high adherence rate of 78.2%.<sup>21</sup>

Most commonly measured cognitive outcomes were global cognition in 9 of the 13 studies; executive function in 7 studies, verbal learning and memory in 5 studies, and memory (i.e., delay or immediate recalls) in 4 studies. Other cognitive outcomes included attention, visual attention and task switching, processing speed, and brain activation measured by peripheral oxyhemoglobin or brain-derived neurotrophic factor (BDNF) level.

Intervention settings included community settings participants' homes or both. Intervention setting was not clearly described in three studies.<sup>19-21,23,25-32</sup> Nine of the studies (69%) had intervention duration of 6 months or less, ranged from 10 weeks to 6 months; the remaining 4 interventions lasted 12 months.<sup>20,23,25,27</sup> Ten of the studies (77%) measured cognitive performance immediately post interventions, while only 3 studies measured follow-up outcomes at 3 months or 12 months post intervention.<sup>21,23,28</sup>

#### Efficacy of Interventions

In general, nine of the 13 studies (69%) reported some positive findings on cognitive improvement in global cognition, executive function, and/or memory.<sup>19,21,23,24,29,30,32</sup>

#### Global cognition

Nine of the 13 studies (69%) examined the effect of physical exercise on global cognition using the MMSE (Mini-Mental State Examination), ADAS-Cog (Alzheimer's Disease Assessment Scale cognitive subscale), CDR-SOB (Clinical Dementia Rating Sum of Boxes), NCSE (Chinese version of Neurobehavioral Cognitive Status Examination), and MoCA (Montreal Cognitive Assessment).<sup>20,21,23,25,26,28-31</sup>

A positive effect was observed in 5 of these 9 studies.<sup>21,23,25,29,30</sup> Li and the colleagues's study was a pilot RCT on the effect of a 14-week Tai Chi Quan: Moving for Better Balance (TJQMBB) program on global cognitive function with a total sample of 44 older adults. An Australian study randomized 170 participants with MCI for either a 6-month home-based physical activity motivation program (50-min sessions, three times a week) or an education group. At the end of the intervention, the exercise group showed an improvement of 0.26 points on ADAS-Cog, whereas the control group showed a deterioration of 1.04 points.<sup>21</sup> Another RCT in Hong Kong/China studied the effect of a 10-week functional task exercise program on cognition as compared to an active control group (existing cognitive training).<sup>23</sup> The program consisted of 13 sessions of 30-min simulated functional task exercise. After the intervention, participants showed an improvement on global cognitive function measured by the NCSE. Suzuki and the colleagues from Japan examined the effects of a 12-month multicomponent exercise program (90 min a day, 2 days a week; aerobic exercise, strength training, balance and dual tasking).<sup>25</sup> After the intervention, participants showed an improvement on MMSE but not on ADAS-Cog. A latest non-randomized control trial reported positive effect of a 4-month multimodal physical training program (muscular resistance, aerobic fitness and

**Table 1:** Study Characteristics and Findings.

Author (year)/ Location/Study Design	Sample characteristics -Subjects -Age range (mean) -Gender (% male) -MCI diagnostic criteria	Intervention: -Setting -Content/delivery mode -Duration	Measures/ Time Points	Findings
Baker (2010) USA RCT	N= 29 (TX n=19; Control n=10) Age 55-85 (70) Male 48% Mean MMSE (25.6-28.6); mean DRS	VA memory clinic and local YMCA Intervention: high- intensity aerobic exercise at 75% to 85% of HR reserve; 45-60 min/d, 4d/ wk Control: stretching activities, HR at or below 50% Duration: 6 mos	EF by SDMT, Verbal Fluency, Stroop, TMT-B, and Task Switching Memory by Story Recall, List Learning, and DMS Baseline, 3 mos, and 6 mos	Intervention vs. control: no sig findings at 3 mos For women, improved performance on multiple tests of EF at 6 mos For men, a favorable effect only on TMT-B performance
Chang (2011) USA Uncontrolled pre- post (pilot study)	N= 11 Average age 85 Male 9% MMSE(15-27), Digit Symbol-Coding on the WAIS-III(≤6), Digit Span on the WAIS-III(≤6), Stroop Color and Word test (≤39), or Hopkins Verbal Learning Test (≤39) With chronic pain; w/o depression	Senior centers and residential complexes Intervention: Sun-style 12-from TC; 20-40 mins/ session x twice a wk Duration: 15 wks	Cognitive function by the five screening tools, and physical and mental function by SF-36 Baseline, 15 wks	Post- vs. Pre-: no sig dif in cognition a sig dose-response relationship
Doi (2013) Japan Uncontrolled pre- post	N= 16 Age >65 (75) Male 63% Ethnicity: Japanese MMSE >23; w/o ADL impairment	Setting unclear Intervention: DTW and NW sessions: NW-1, DTW-1, NW-2, DTW-2, NW-3, DTW-3; 60s each Duration: one session	Changes in oxy-Hb in the prefrontal area EF by Stroop interference Baseline, posttest	During DTW vs. NW: higher oxy-Hb values Oxy-Hb in LIFG but not RIFG was sig correlated with EF during DTW, while no sig correlation during NW. No change in MMSE scores in both groups Intervention vs. control at 12 mos: no sig between-group dif on any cognition parameters
Lam (2012) Hong Kong, China RCT	N= 389 (TX n=171; Control n=218) Age >65 (77-78) Male 24% Ethnicity: Chinese CDR 0.5 or aMCI	Community centers, residential homes, or participant's homes Intervention: 24 forms simplified TC; ≥ 30 min/d, ≥3 d/wk Control: Stretching and toning exercise Duration: 12 mos	Cognitive functions by ADAS-Cog, digit span, delay recall, CVFT, TMT, and MMSE Baseline, 5, 9, and 12 mos	Intervention vs. control at 12 mos, completers only: greater improvement in delayed recall
Lautenschlager (2008) Australia RCT	N= 170 (TX n=85; Control n=85) Age 60-77 (69) Male 58% SMC only, aMCI, or Non- aMCI	Intervention: home-based PA motivation program, three 50-min sessions per wk; workbook, PA diary, newsletters, and telephone calls Control: education and usual care Duration: 6 mos	Cognition by ADAS-Cog Baseline, post-intervention, and 12 mos and 18 mos follow-up	Intervention vs. control over time: greater improvement of ADAS-Cog scores

Law (2013) Hong Kong, China RCT	N= 83 (TX n=43; Control n=40) Age >60 (74) Male 40% SMC or suspected CI	Outpatient clinic Intervention: functional task exercise Control: active cognitive training Duration: 10 wks	Cognition by NCSE, CVVLT, CVFT, TMT-A, and TMT-B Baseline, post-intervention, and 6-mo follow-up	Intervention vs. control post intervention and 6-mo follow-up: greater general cognitive functions, memory, and EF
Li (2014) USA Non-randomized CT (pilot study)	N= 46 (TX n=22; Control n=24) Age ≥ 65 (76) Male 30% MMSE (20-25)	Senior centers Intervention: TJQMBB; 60-min session twice/wk Control: usual daily PA Duration: 14 wks	Global cognitive function by MMSE Baseline, post-intervention	Intervention vs. control at post-intervention: greater improvement on MMSE scores
Nagamatsu (2012) Canada RCT	N= 77 (TX1 n=26; TX2 n=24; Control n=27) Age 70-80 (75) Male 0% MoCA (<26/30) and SMC	Setting unclear TX1: resistance training (stretching, ROM, balance exercise, relaxation techniques); 60 mins, twice per wk TX2: aerobic training (outdoor walking program); 60 mins, twice per wk Control: balance and tone training; 60 mins, twice per wk Duration: 6 mos	EF by Stroop and TMT Working memory by verbal digits tests Associative memory by memorizing face-scene pairs Everyday problem solving ability by Everyday Problem Test Baseline, post-intervention	TX1 vs. control post intervention: greater improved performance on the Stroop Test and the associative memory task TX2 vs. control post intervention: no sig effect on cognitive function measures
Nascimento (2015) Brazil CT (Randomization unclear)	N= 45 (TX n=24; Control n=21) Age >60 (66-69) Male 41% MCI reported by subjects and caregivers; w/o depression	Setting unclear Intervention: multimodal physical training (muscular resistance, aerobic fitness, motor coordination/ balance) at 60%-80% of max HR; three 1-hr sessions per wk Control: usual activity Duration: 4 mos	Cognitive functions by MoCA Peripheral concentrations of BDNF Baseline, post-intervention	Intervention vs. control post intervention: improved cognitive functions, esp. the EF sig increased peripheral BDNF level
Suzuki (2013) Japan RCT	N= 50 (TX n=25; Control n=25) Age 65-93 (75) Male 54% aMCI	Community center Intervention: supervised multicomponent exercise (aerobic exercises, muscle strength training, postural balance retraining); 90 min/d, 2d/wk. Control: 3 sessions of education classes regarding health but not exercise specific Duration: 12 mos	Cognitive functions by MMSE, WMS-LM, DSC, LVFT and SCWT Baseline, 6 mos, 12 mos	Intervention vs. control over time from baseline to 12 mos: greater improvements on MMSE, logical memory of immediate recall (WMS- LM I), and LVFT
Tsai (2013) USA RCT (pilot study)	N= 55 (TX n=28; Control n=27) Age >60 (79) Male 27% Ethnicity: Caucasian 93% MMSE (18-28) and OA	Senior centers and residential complexes Intervention: Sun style TC classes, 3 sessions/wk Control: health and culture classes Duration: 20 wks	Cognitive functions by MMSE Baseline, every 4 wks, and post-intervention	Intervention vs. control post intervention: no sig dif in MMSE (p=0.096)

van Uffelen (2008) Australia RCT	N= 152 (TX n=77; Control n=75) Age 70-80 (74-76) Male 56% SMC, MMSE $\geq$ 24, and objective memory impairment (10 WLT delayed recall $\leq$ 5 and % savings $\leq$ 100)	Community centers Intervention: group- based moderate-intensity walking, twice weekly Control: low-intensity placebo activity program Duration: 12 mos	Cognitive functions by AVLT, SCWT-A, DSST, and VFT Baseline, 6 mos, 12 mos	Intervention vs. control: no sig effect of walking on cognition at 6 mos or 12 mos
Varela (2012) Spain RCT (pilot study)	N= 48 (TX1 n=17; TX2 n=15; Control n=15) Age >65 (78) Male 44% Clinical Dx of MCI; mean MMSE 20-22	Residential care homes TX1: supervised aerobic exercise (cycling) at 40% of HR reserve; three 30- min sessions per wk TX2: same aerobic exercise at 60% of HR reserve Control: recreational activities Duration: 3 mos	Cognition by MMSE Baseline, 3 mos, 6-mo follow-up	Interventions vs. control: no sig between-group dif on MMSE at 3 mos or 6-mo follow-up

Note: Unless otherwise stated, all reported findings are significant at  $p < 0.05$  level. RCT = randomized control trial; N = number who completed the study; TX = intervention group; Sig = significant; Dif = difference; WAIS-III = Wechsler Adult Intelligence Scale-Third Edition; EF = executive function; MMSE = Mini-Mental State Examination; SDMT = Symbol Digit Modalities Test; DMS = Delayed-Match-To-Sample; YMCA = Young Men's Christian Associations; VA = Veterans Affairs; TC = Tai Chi; DTW = dual-task walking; NW = normal walking; Oxy-Hb = oxygenated hemoglobin; LIFG = left inferior frontal gyrus; RIFG = right inferior frontal gyrus; SMC = Subjective memory complaints; CI = cognitive impairment; ADAS-Cog = Change in Alzheimer Disease Assessment Scale-Cognitive Subscale; NCSE = Chinese version of Neurobehavioral Cognitive Status Examination; CVVLT = Chinese version Verbal Learning Test; CVFT = Category Verbal Fluency Test; TMT-A = Trail Making Test A; TMT-B = Trail Making Test B; TJQMBB = Tai Ji Quan: Moving for Better Balance; PA = physical activities; MoCA = Montreal Cognitive Assessment; ROM = range of motion; WMS-LM = Logical Memory subtest of the Wechsler Memory Scale-Revised; OA = osteoarthritis; DSC = digit symbol coding; LVFT = letter and categorical verbal fluency test; BDNF = brain-derived neurotrophic factor; SCWT = Stroop color word test; AVLT = auditory verbal learning test; SCWT-A = Stroop color word test-abridged; DSST = digit symbol substitution test; VFT = verbal fluency test; WLT = Word Learning Test; CDR = Clinical Dementia Rating; aMCI = amnesic-MCI; Dx = diagnosis.

motor coordination/balance) on general cognitive function (esp. executive function) measured by MoCA.<sup>30</sup>

In contrast, the remaining 4 studies did not yield significant improvements on global cognitive function post interventions. A RCT with a large sample size (N=389) conducted in Hong Kong/China did not show improvements on MMSE or ADAS-Cog after a 12-month Tai Chi exercise (at least 30 minutes per day, 3 days a week).<sup>20</sup> Two other RCTs were pilot studies with a sample size of 55 and 48.<sup>26,28</sup> Tsai and the colleagues led 20-week Sun Style Tai Chi classes (3 sessions per week) in intervention group, and controlled with health and culture classes. Varela and the colleagues conducted a supervised aerobic exercise program (low-intensity and moderate-intensity cycling) for 3 months. The remainder was an uncontrolled pretest-posttest study with a sample of only 11 older adults who were involved in a 15-week Sun-style Tai Chi program (20-40 min per session, twice a week).<sup>26,28,31</sup>

### Executive Function, Memory, Attention and Other Cognitive Domains

Seven of the 13 studies (54%) evaluated the effects of exercise on executive function. Four of these 7 studies (65%) found modest positive effects. Commonly used assessment tools included the verbal fluency test, Stroop Color and Word

Test, and Trail Making Tests A and/or B (TMT).<sup>19,20,23-25,27,32</sup> Seven of the 13 studies (54%) tested the effects of exercise on memory which was measured by story recall, list learning, delayed-match-to-sample (DMS), Hopkins verbal learning test, auditory verbal learning test, and digit span test.<sup>19, 20, 23-25, 27, 31</sup> Four of these 7 studies (57%) demonstrated efficacy (20, 23-25).

In a RCT, Baker and the colleagues examined the effect of a 6-month high-intensity aerobic exercise on executive function and memory (45-60 min, 4 times a week).<sup>19</sup> Favorable effects of physical exercise were found in all executive function measures (verbal fluency, TMT-B and task switching) among female participants at the end of the intervention, while for males, a favorable effect only on TMT-B performance. No improvement on memory was found. In contrast, another RCT reported positive findings on memory (delayed recall) and negative findings on executive function at the end of a 12-month Tai Chi program.<sup>20</sup>

Three other RCTs reported consistent negative findings on executive function and memory post interventions which were a 12-month multicomponent exercise program, a 10-week functional task exercise program and a 6-month resistance training program.<sup>23-25</sup> The details of Suzuki and Law's studies were discussed above. Nagamatsu and the colleagues from Canada conducted a RCT comparing the effects of resistance

training and aerobic training intervention with active control group (balance and tone training), with the same training doses (60 min per session, twice per week). They found that, as compared to control group, Stroop test and associative memory task performance was improved in the resistance training group post intervention, but not in the aerobic training group.<sup>23-25</sup>

Two pretest-posttest studies with small sample size did not yield improvements in executive function or memory performance.<sup>31,32</sup> Chang's study was discussed above. Doi and the colleagues from Japan provided a walking intervention with alternated normal walking (NW) and dual-tasking walking (DTW; walking while performing a verbal letter fluency task). Changes in oxyhemoglobin levels were recorded while participants performed the NW and DTW tasks. Authors found that oxyhemoglobin level was higher during DTW than during NW, and oxyhemoglobin level in left inferior frontal gyrus (LIFG) was significant correlated with executive function during DTW but not during NW. Another objective measurement was the peripheral BDNF measured in Nascimento's study. Significant increase in the peripheral concentration of BDNF and cognitive functions were observed after the 16-week period of multimodal physical training, while no significant changes were observed in the control group.<sup>30</sup> In another RCT, van Uffelen and the colleagues tested the efficacy of a 12-month group-based moderate-intensity walking program as compared to a low-intensity placebo activity program among 152 older adults.<sup>27</sup> Authors did not find intervention effects on immediate and delayed recall and executive function post intervention.

Attention and processing speed were less commonly measured in included studies. Two studies (one pretest-posttest and one RCT) reported negative findings on attention after a 15-week Tai Chi program and a 12-month moderate-intensity walking program.<sup>27,31</sup> Similarly, three studies that measured processing speed did not yield efficacy.<sup>25,27,31</sup>

## Discussion

Physical exercise programs in this review consisted of several different types of exercise, including aerobic exercise, resistance training, functional task exercise, multicomponent exercise, and a mind-body exercise, Tai Chi, which was also considered a multicomponent exercise.<sup>29</sup> Results indicated that physical exercise can benefit older adults who have MCI, including improvement in the areas of global cognition, executive function, memory, attention and processing speed. Our findings of improved global cognition and executive function after aerobic exercise interventions were consistent with previous review articles.<sup>35-38</sup> This manuscript adds new evidence that other types of exercise, i.e. resistance training, functional task exercise, and multicomponent exercise, could have positive effect not only on global cognition and executive function, but also on memory and brain activation. However, at this time, specific evidence to direct primary care practitioners toward recommending an exercise type, intensity, duration and frequency to impact cognitive function appears limited.

In many studies, exercise intensity was quite high, up to moderate intensity, but the attendance to the training sessions or participants' acceptance of the exercise intervention was rarely described. The duration of interventions was relatively short,

from 10 weeks to 6 months. Participant's adherence to exercise after intervention period and the maintenance of positive effects on cognition was not examined in the included studies, and could be a significant issue when implementing these interventions in community settings. The cognitive tests used to measure cognitive outcomes were numerous. Tests measuring global cognitive function, executive function and memory were most commonly used. Recent studies have started to examine the effects of physical exercise on specific cognitive domains in addition to general cognitive function. More research is needed to measure the impact of community-based exercise interventions using tools that are accessible to the primary care nurse or physician, and targeting the aspects of cognition that are most meaningful to older adults with MCI.

Findings in this review should be interpreted in the context of several limitations. First, the rigor of the included studies varied. Given the limited amount of research targeting community-dwelling older adults with MCI, we did not limit our search to RCTs only. Instead, non-randomized control trials and pretest-posttest studies were all included to achieve a broader view on what have been studied on this topic. For example, Chang's study did find some trend of positive effect of Tai Chi exercise on global cognition, cognitive processing speed and memory.<sup>31</sup> However, the small-scale pre-post study might not have had enough power to detect the effect of Tai Chi on cognitive function, especially those specific cognitive domains. Second, participants' age and health condition might effect study results. For example, older adults in Chang's study were of very old age (average age of 85) and were having a chronic pain condition. These facts may interfere with the compliance of exercise intervention and the detection of cognitive changes post interventions. Similar issues were found in another small-scale RCT with similar study design by the same research team.<sup>26</sup>

Moreover, gender-specific intervention effect was analyzed in only one study.<sup>19</sup> Relatively small sample sizes in most of the studies limited their ability to analyse the gender difference of intervention effects on cognitive function. Third, median adherence (<75%) to exercise program was reported in most of the studies. For example, van Uffelen and the colleagues reported a 63% adherence rate among 152 participants in a 12-month walking program. In addition, adherence rate in female participants was as low as 45%, in comparison to 75% in males.<sup>27</sup> Overall, 20% of participants didn't attend a single intervention session, who were, however, still included in final analysis of intervention effects. An additional analysis including completers only might be helpful to present more accurate results. Fourth, intervention fidelity control was described in only two studies.<sup>26</sup> For example, Li stated that the intervention teaching protocol was monitored by the first author per criteria described in the paper. Fifth, inclusion criteria of MCI participants were inconsistent.<sup>29</sup> As discussed previously, MCI is a concept in evolution. Some studies found that participants were not diagnosed correctly at baseline when they might have dementia already, which might blurred the effect of physical exercise intervention on cognitive changes. Last but not least, many studies didn't report the participants' baseline physical activity level. For example, some studies found that most participants were having moderate-intensity exercise at baseline,

which might result in less sensitivity to exercise intervention of a similar intensity.<sup>27,28</sup>

In this review, only one intervention was guided by health behavior theoretical frameworks to encourage participant adherence to exercise program. Recent meta-analyses show that interventions strongly guided by health behavior theory significantly impact the physical activity outcomes of participants.<sup>33,34</sup> For example, when examining social cognitive theory-based physical activity interventions, this health behavior theory explained 31% of the variance in physical activity.<sup>34</sup> However, the mechanism that explains these larger effects are not clear.<sup>33,34</sup> Theory-based strategies might be developed with greater care, fidelity and structure. In the implementation of exercise interventions among older adults, motivational/supportive contacts guided by health behavior theories may increase participants' adherence to exercise program.

The mixed findings of these studies indicate that more primary research is needed. To further understand the effect of physical exercise on cognitive function, RCTs with large sample sizes are needed. Physical exercise interventions guided by health behavior theories might be helpful in improving adherence during interventions or even after interventions. Future large studies may include gender as a predictor variable to better understand sex differences on intervention effects. Intervention duration of more than 6 months with follow-up data is needed to explore long-term effects of exercise interventions on cognitive function and the maintenance of positive effects over time.

Nurses are the largest segment of the health care workforce, and despite the potential that nursing care may have on impacting the outcomes of exercise-focused interventions, nurses were involved in only one of the 13 studies. Public health and community health nurses and home care nurses are well suited to provide exercise interventions to community-dwelling older adults, because (i) they see patients in their natural environment and can involve families and community members in the intervention, (ii) they have education that has emphasized the need to establish a trustful relationship with patients and provided individualized exercise plan, (iii) they have ongoing contact with patients over an extended period of time which may help motivate patients to adhere to interventions better. Thus, evidence encouraging the use of exercise interventions with the MCI population could potentially benefit from research specifically aimed at nursing practice.

In conclusion, the causal effect of physical exercise interventions on cognitive performance in community-dwelling older adults is unclear because of insufficient evidence. It remains unclear which intervention characteristics are more effective, in terms of exercise type, intensity and duration. Future rigorously designed large intervention studies with longer duration are needed to explore the effect of physical exercise programs on cognitive performance in older adults with MCI. Theory-based interventions with sex difference data and follow-up data are preferred. Moreover, clearly reported intervention design, participants' baseline activity level, compliance, acceptance and intervention fidelity control should be encouraged to facilitate the appropriate interpretation of future studies.

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