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Non-pharmacological interventions on cognitive functions in older people with mild cognitive impairment (MCI)

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ABSTRACT

Mild cognitive impairment (MCI) can be a stage of pre-dementia. There is no consensus about pharmacological treatment for this population, so it is important to structure non-pharmacological interventions for increasing their cognitive reserve. We intended to analyze the effects of non-pharmacological interventions in the cognitive functions in older people with MC, in form of a systemic review. Data sources were the Web of Science, Biological Abstracts, Medline, Pub Med, EBSCHost, Scirus and Google Scholar. All studies were longitudinal trials, with MCI sample, aged > 60 years, community-dwelling, and having cognitive functions as dependent variable. Seven studies, from 91 previously selected ones, were identified according to the inclusion criteria. Six studies used cognitive intervention, improving memory and one study used physical activity as intervention, improving executive functions. The results show evidence that physical activity and cognitive exercise may improve memory and executive functions in older people with MCI. But yet, more controlled studies are needed to establish a protocol of recommendations regarding the systemization of exercise, necessary to produce benefits in the cognitive functioning in older people with MCI.

1. Introduction

MCI is known as the limit between normal aging and dementia, characterizing those seniors with cognitive decline, but with normal global operation (Winblad et al., 2004). Still, seniors with MCI present larger risk of developing dementia (Amieva et al., 2004; Petersen et al., 2006), with conversion rate of 10–40%/year for Alzheimer dementia (AD), compared with 1–2%/year, in healthy seniors (Verghese et al., 2003; Amieva et al., 2004; Schmidtke and Hermeneit, 2008). It is important to point out, then, that seniors with MCI may not develop dementia and, in other cases, they may even reverse that situation to a normal cognitive function (De Rotrou et al., 2005).

MCI can be considered as a stage of pre-dementia (Dubois et al., 2007). Identifying and treating older adults with MCI is important to prevent and reverse the progression of AD, which impacts on reducing functional decline (Chertkow et al., 2006). There is no consensus in the literature about pharmacological interventions, and it is not recommended the use of medicines for MCI-treatment (Feldman and Jacova, 2005; Chertkow, 2008). Thus, it is of great importance to structure non-pharmacological interventions, which increase the seniors' cognitive reserves.

The practice of physical activities, particularly aerobic exercises, and cognitive activities have benefits associated with cognitive functions of cognitively preserved seniors (Antunes et al., 2001; Ball et al., 2002), evidenced by longitudinal studies of cohort (Laurin et al., 2001; Kramer et al., 2004). This association has still been enough to reduce cognitive decline and risk for developing dementia (Wilson, 2002; Lindstrom et al., 2005).

However, there is no evidence on the mechanisms, acting in the physical or cognitive intervention on cognitive decline and on risk for dementia. This finding showed that it is not possible to conclude about this relationship of cause and effect in preventing or delaying the progression for dementia, in elderly with MCI (Wilson, 2002; Verghese et al., 2003).

Given the above and considering the growing interest in understanding the benefits of non-pharmacological interventions, the purpose of this systematic review was to analyze the studies that have investigated the effect of these interventions in the cognitive functions in older people with MCI and to discuss its main findings.

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2. Methods

2.1. Search strategy and selection criteria

A targeted search was carried out to develop this systematic review in the following databases: Web of Science, Biological Abstracts, Medline, Pub Med, EBSCHost, Scirus and Google Scholar. The keywords and Boolean operators used were: (MCI OR mild cognitive decline OR mild cognitive disorder OR mild cognitive disturb) AND (cognition cognitive performance OR memory executive function OR attention OR) AND (OR physical activity OR physical exercise motor cognitive intervention OR intervention OR cognitive fitness training OR aerobic strength). The keywords should appear alone or combined among them in the title or abstract.

In addition to the databases searching, we conducted a manual search from the reference list of selected articles, both held in May 2009. The articles selection was based, in order, the following inclusion criteria: longitudinal studies, case–control and open studies which reported sample with age over 60, community-dwelling and with, at least, one specific group of MCI subjects; and studies containing cognitive functions as dependent variable.

At first, the intention was to present as inclusion criteria randomized studies. However, it was observed at the inclusion phase of studies that only two studies selected had randomization of subjects in groups.

3. Results

Initially, the literature search resulted in 91 articles. It was verified, checking the titles, that 28 articles were related to the theme. Analyzing then the abstracts, 10 articles did not present cognitive functions as dependent variable; 5 were review articles; 5 articles used pharmacological interventions and one article presented, on its final sample, a heterogeneous group constitution, and they were excluded from the final analysis. Based on the criteria proposed for this study, only 7 articles composed the group of publications considered for the proposed analysis.

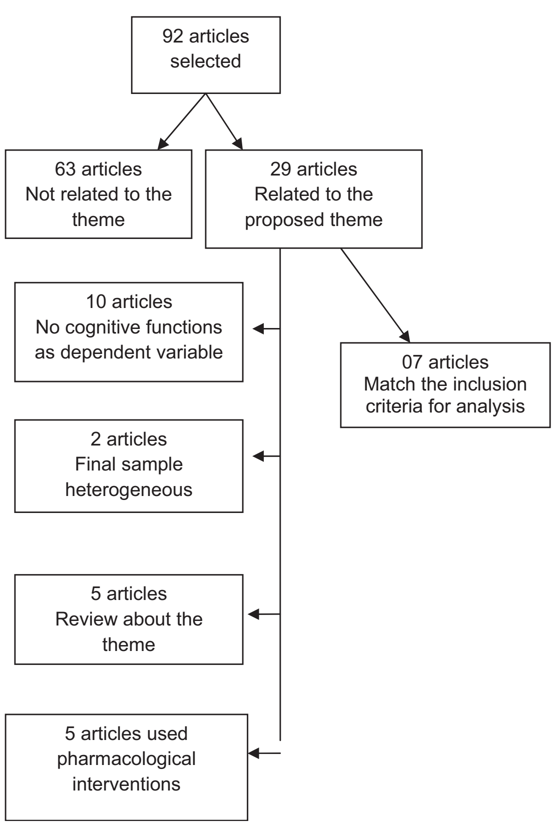

Fig. 1. The scheme of the selection stages of the articles.

Fig. 1 represents graphically the stages of the selection of the articles. The articles analysis was focused on the intervention and results of the group which presented MCI. Table 1 shows the main characteristics and results of the selected studies.

4. Discussion

The purpose of this review was to analyze the studies which interventions focused on cognitive functions of older people with MCI and to discuss their main findings. The seven reviewed studies evidenced positive effects of non-pharmacological (cognitive and/or motor) intervention on cognition in older subjects with MCI. In particular, the non-pharmacological interventions caused impact on older people with MCI. Memory, attention and executive functions, as cognitive functions aspects, were measured by validated and reliable instruments.

Regarding memory, to investigate the effect of the intervention, all studies used instruments that assess the episodic memory. Probably, this type of memory was selected due to its tendency to decrease with the age and its relationship with the difficulties of operating in the environment and of gain new knowledge (Erven and Janczura, 2004).

The attention single-handedly did not benefit from the interventions presented here. The concentrated and sustained attention were measured (Cipriani et al., 2006; Talassi et al., 2007), through the Visual Search test (Spinnler and Tognoni, 1987). The interventions proposed by those authors consisted of specific cognitive exercises of attention that did not demonstrate benefits for older people with MCI.

On the other hand, when attention is associated with memory, the benefits of non-pharmacological intervention become more evident. Cross-sectional studies on cognition have been indicating that episodic memory and control of attention are cognitive components severely affected in elderly with MCI (Tierney et al., 1996). A recent review (Chun and Turk-Browne, 2007) showed that memory and attention are interdependent, in other words, memory presents limited capacity and the attention determines the content to be stored.

The executive functions (EF) were also assessed by some studies presented here (Scherder et al., 2005; Belleville et al., 2006; Talassi et al., 2007; Wenisch et al., 2007; Kurz et al., 2009). Planning, initiation, sequencing and monitoring of actions, involving attention, concentration, abstraction, selectivity, mental flexibility, self-control and working memory, are involved in EF (Green, 2000). The frontal lobe is particularly involved in EF (Duke and Kaszniak, 2000), and it seems to be most vulnerable in the aging process. Only two studies (Scherder et al., 2005; Belleville et al., 2006) observed significant results after the intervention on the assessed executive functions.

That fact can be explained by the chosen evaluation not access the components worked in the intervention. That may be the case of one of the study here selected (Wenisch et al., 2007). They evaluated the executive functions using the Trail Making Test, which accesses mental flexibility, and using the Verbal Fluency test, which accesses initiation ability. However, the intervention had influence on components as planning, sequencing and self-monitoring. Therefore, the chosen evaluation did not show significant difference for being incompatible with the chosen intervention.

Another aspect to be emphasized is the difference between cognitive stimulation, training and rehabilitation. A literature review (Clare et al., 2003) defined cognitive stimulation as the

Table 1
A summary of the included studies.

Reference Groups	Evaluation	Intervention	Components of interv.	Significant results in
Kurz et al. (2009)				
MCI = 18	CERAD	Cognitive rehabil.	Memory training, organization, planning, physical training and relaxation exercises	MCI: episodic verbal and non verbal mem.
MCI cont. = 12	MMSE	4 weeks		MCI control: episodic verbal memory
MILD AD = 10	CVLT RCF	22 h/week group		
Talassi et al. (2007)				
MCI = 30	MMSE	Cognitive rehabil.	Computerized training (TNP software), occupational therapy, behavior training	MCI: nonverbal episodic memory
MCI cont. = 7	Digit span	Computer prog.		
AD = 20	VF	3 weeks		
AD cont. = 5	RBMT	4/week	Control = physical rehabil. (if a physical pathology was present), occupational therapy and behavior training	
	Visual search	30–45 min		
	RCF	individual		
	CDT			
Belleville et al. (2006)				
MCI = 20	MDRS	Cognitive training	Combination of a visual condition and an arithmetic task;	MCI and NCD:
MCI cont. = 9	MMSE	Computer prog.		episodic memory and executive function.
NCD = 8	BEM	8 weeks	Face-name associations;	
NCD cont = 8	RCF	1/week	Text organization;	
	Naming	120 min	Memorization of familiar	
	Brown Petersen	places and texts		
	VF	group		
Wenisch et al. (2007)				
MCI = 12	MMSE	Cognitive training	Explanation about memory operation; Techniques of reality orientation; journal reading and discussion; cognitive exercises.	MCI: episodic mem.
NCD = 12	CEP	12 weeks, 1/week		
	Wechsler	90 min		
	Trial making t.			
	VF	group		
Cipriani et al. (2006)				
AD = 10	MMSE	Cognitive rehabil.	Shared attention	MCI: episodic mem.
MCI = 10	VF	Computer program	Short and work memory	
MSA = 3	Visual search	4 weeks, 4/week	Perception, visuospatial	
	Dig. Sy. Test	13–45 min	Language	
	RBMT	individual	Non-verbal intelligence	
Scherder et al. (2005)				
MCI	MMSE (brief)	Physical training	WG = slow waking	WG and HFEG > control in executive function, but not at T3
WG = 15	Trial making test		HFEG = bending and moving fingers, facial expressions	
HFEG = 13	Naming	6 weeks, 3/week		
Control = 15	WMS-R	30 min	Control: 1. Social visits and normal social activities	
	VLMT	individual		
	RBMT			
	T1, T2, T3			
Rapp et al. (2002)				
MCI = 9	CERAD	Cognitive training	Multi-faceted intervention	MCI: episodic mem. at T2 and T3
MCI cont. = 10	MMSE	6 weeks	Information about memory and dementia	
	Welsch	1/week		
	WMS-R	2 h	education on memory skill; relaxation skills training	
	T1, T2, T3	group		

Notes: NCD: no cognitive decline; MSA: multiple system atrophy; WG: walking group; HFEG: hand/faces exercises; MMSE: mini-mental state examination; CERAD: Consortium for the estimation of a reg. for AD; CVLT: California verbal learning test; RCF: Rey complex figure; WMS-R: Wechsler memory scale, revised; VF: verbal fluency test; RBMT: Rivermead behavioral memory test; MDRS: Mattis dementia rating scale; BEM: Batterie d' efficience mnesique; CEP: cognitive efficiency profile; VLMT: verbal learning memory test; T1: pre-treatment; T2: post-treatment; T3: 6 weeks without treatment

involvement in group activities which have the goal of increasing the non-specific cognitive and social operation. Cognitive training involves teaching theoretical techniques and abilities with the aim of improving cognitive functions. And lastly, the cognitive rehabilitation is defined by individualized programs focused on specific activities of the daily life. The most effective would be a continuous stimulation of the preserved cognitive functions and, at the same time, produce an effective improvement in the cognitive deficit (Laurin et al., 2001; Cipriani et al., 2006). It is possible to observe, in the present review, three studies with which interventions characterized as cognitive rehabilitation (Cipriani et al., 2006; Talassi et al., 2007; Kurz et al., 2009) and three studies with interventions characterized as cognitive training (Rapp et al., 2002; Belleville et al., 2006; Wenisch et al., 2007).

Computerized cognitive training, specifically designed for dementia, has been developed to rehabilitate the cognitive areas and functions related to the tasks of daily living (Hofmann et al., 1996; Hoffmann et al., 2003). The advantage of this method is that it is based on the patient's neuropsychological decline (Talassi et al., 2007). From the studies that used cognitive intervention, three were with computerized programs (Belleville et al., 2006; Cipriani et al., 2006; Talassi et al., 2007).

Longitudinal studies of cohort have been shown that the seniors' participation in cognitive activities throughout life seems to be a protective factor against the cognitive decline (Verghese et al., 2003; Kramer et al., 2004). However, it is not clear whether cognitive activity has a protective effect on cognitive decline development with age or if reduced participation in the cognitive activities is a marker of early dementia (Verghese et al., 2003; Massoud et al., 2007).

Physical activity as non-pharmacological intervention produces organic benefits, decreasing the risk of developing chronic degenerative diseases (Singh-Manoux et al., 2005; Bucksch and Schlicht, 2006). Those diseases increase the risk factors for dementia (Yaffe et al., 2004). In addition, physical activity has beneficial effects in the components of the functional capacity (Sebastião et al., 2005), which are important for a better independence in daily living activities (Guimarães et al., 2004).

Although this conclusion, only one study from the present review (Scherder et al., 2005) had physical activity as main intervention. There was another study (Olarazan et al., 2004) that also studied the effect of physical activity on cognitive functions of older people with AD and MCI. The results were positive after the intervention. However, the authors did not analyze the results of both groups separately, so it is not clear which group responded better to the training; therefore this study was excluded from the present analysis.

Poon et al. (2005) also joined AD and MCI in the same group and analyzed the results together. But it could not be included in the present analysis.

As previously mentioned, only one study from this review (Scherder et al., 2005) involved motor intervention (walking and hand/face exercises), it presented significant improvement of EF, corroborating other findings (Stones and Dawe, 1993). It seems that physical activity, particularly walking, increases the cerebral blood flow (Hawkins et al., 1992), thus improving the performance of the executive functions is associated with frontal lobe functioning (Emery et al., 1998). The hand/face exercise also seems to be associated with frontal lobe functioning (Coan et al., 2001). Scherder et al. (2005) concluded that physical activity has selective effect on cognition, specifically on executive functions. But its effect was not significant after 6 months of the end of the intervention, in other words, without intervention the treatment effect does not remain (Scherder et al., 2005). This conclusion emphasizes the need for continuous intervention to minimize the losses after treatment.

Among the presented articles, Scherder et al. (2005) did not find a positive result on memory. Another study (Molloy et al., 1988) did not observe positive results on memory. Both studies involved light physical activity, which may not have been enough to cause some physiological effects.

The improvement in cognitive performance of elderly with MCI suggests that they retain a cognitive reserve. It was observed in one of the studies, that the MCI group, after cognitive intervention period, reached values that did not differ significantly from the healthy group baseline value (Wenisch et al., 2007). However, this study did not have a control group with MCI and without intervention (the control group of healthy older people also participated in the intervention), which does not provide a safe interpretation of the results.

Only Scherder et al. (2005) chose for a placebo control group, in other words, a group that did not participate in the proposed intervention, controlling the effect of the social interaction of the intervention. The placebo group received visits, and the other control group continued their normal routine. At the end of the study a significant difference was not observed between the groups, so the authors have joined both groups into a single control group, which shows that, in this case, there was no interference of social interaction for cognitive functions.

There is evidence in the literature of the beneficial effects of a group intervention on cognition (Vance et al., 2005). Three studies presented here (Rapp et al., 2002; Belleville et al., 2006; Kurz et al., 2009) opted for intervention in group and had positive results, which lead us questioning about what, in fact, influenced the cognitive functions: intervention or socialization. But this influence seems to be relevant and it should not be seen as a limiting factor in studies, but as an intrinsic feature of physical activity.

The duration of intervention that have verified the effect of physical (Molloy et al., 1988; Colcombe and Kramer, 2003) and cognitive (Ball et al., 2002) exercise was 12–24 weeks. Nevertheless, the time of intervention adopted by the studies presented here ranged from 3 to 12 weeks, with frequency of 1–4 times a week. It may be one of the possible limitations of the studies: in short term intervention, the results would be products of learning the tests and not of the intervention.

There was no study, selected for the present review, comparing the two types of intervention, cognitive and motor, showing its effectiveness on MCI elderly. Fabre et al. (2002) carried out a study with older people with no decline and made this comparison. The authors analyzed the effect of four different interventions: motor, cognitive, motor and cognitive, and leisure. They observed the same improvement degree in the motor and cognitive intervention, suggesting that the combination among the methods could enhance the outcome. However, there was no result comparison with a group that did not engage in any activity, which affected the conclusions of the authors.

Although the presented articles have evidenced a significant improvement in cognitive decline, we can highlight some aspects that can generate limitations that affect the validity of the concluded estimates. Two articles did not show a control group, making it difficult to judge if the final effect was from the intervention or from learning the cognitive evaluations.

The use of reduced samples, not representative of the population, is another aspect that must be observed. The average was 12.2 ± 6.0 elderly in each group (range: 3–30). Aiming a non-tendentious characteristic sample, it is very important to randomize the sample for the selection or distribution in the groups, which did not occur in the selected studies.

Considering the great value of developing a program of cognitive and/or physical exercise objecting cognitive improvements, it seems to be very important to describe precisely the intervention, describe the exercises used in the intervention. Only the study of Talassi et al. (2007) did not describe the exercise of each type of intervention, which makes it difficult to replicate the intervention by the health professionals.

5. Conclusion

The studies presented here, in their majority, used interventions that were sufficient to temporarily improve episodic memory, abstraction, mental flexibility, self-control and working memory in older people with MCI. However, contradictions and divergences mark the number of studies on non-pharmacological interventions. Therefore, it was not possible to establish a protocol of recommendations regarding the systemization of exercise (cognitive or motor), necessary to produce benefits in the cognitive functioning in older people with MCI. However, the analysis of the intervention results is encouraging as for the potential effects on cognitive functions. Randomized controlled studies using longer interventions, motor intervention and with representative samples are crucial for the consistency of knowledge in the theme.

Conflict of interests statement

None.

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