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EFFECTS OF ACUTE AND CHRONIC, MULTIMODAL AND UNIMODAL, PHYSICAL EXERCISE ON BRAIN OF ELDERLY PEOPLE:A SYSTEMATIC REVIEW

EFFETTI DELL'ESERCIZIO FISICO ACUTO E CRONICO, MULTIMODALE E UNIMODALE, SUL CERVELLO DELLE PERSONE ANZIANE: UNA REVISIONE SISTEMATICA

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Abstract

Age-related cognitive decline is a growing health concern. The lack of adequate pharmacological treatments to reduce or prevent the loss of cognitive abilities associated with aging, has contributed to a growing interest in integrated interventions useful for promoting the proper functioning of cognitive abilities. Among these, physical exercise seems to be an effective strategy.
This study aims to systematically review studies examining the relationship between acute/chronic, multimodal/unimodal exercises and cognitive functions in elderly people, in order to clarify which type of exercise may be most appropriate for delaying or preventing cognitive decline.
For this purpose, a bibliographic search was carried out on two main database search, PubMed and Scopus. Studies from 2016 to 2020 were selected. The research strategy focused on three main categories: exercise, cognition and population. After applying the eligibility criteria, 15 studies were included in the review. 4 studies describe a multimodal approach, 11 describe the unimodal approach, 3 studies describe the effects of acute exercise and 12 focused on the effects of chronic exercise on cognitive functions. The evidence included in the study shows that exercise, whether unimodal or multimodal, has positive effects on cognitive function and is able to delay or prevent age-related decline. Acute and chronic exercise also induce beneficial effects, however, chronic exercise should be preferred so that the effects can be sustained.

Il declino cognitivo correlato all'età è una preoccupazione crescente. La mancanza di adeguate cure farmacologiche per ridurre o prevenire la perdita delle capacità cognitive associate all'invecchiamento, ha contribuito ad un crescente interesse per interventi integrati utili a favorire il corretto funzionamento delle capacità cognitive. Tra questi, l'esercizio fisico sembra essere una strategia efficace. Questo studio si propone di rivedere sistematicamente gli studi che hanno esaminato la relazione tra esercizi acuti/cronici, multimodali/unimodali e funzioni cognitive nelle persone anziane, al fine di chiarire quale tipo di esercizio può essere più appropriato per ritardare o prevenire il declino cognitivo. A tal fine è stata effettuata una ricerca bibliografica su due principali database di ricerca, PubMed e Scopus. Sono stati selezionati gli studi dal 2016 al 2020. La strategia di ricerca si è concentrata su tre categorie principali: esercizio, cognizione e popolazione. Dopo aver applicato i criteri di ammissibilità, sono stati inclusi nella revisione 15 studi. 4 studi descrivono un approccio multimodale, 11 descrivono l'approccio unimodale, 3 studi descrivono gli effetti dell'esercizio acuto e 12 focalizzati sugli effetti dell'esercizio cronico sulle funzioni cognitive. Le prove incluse nello studio mostrano che l'esercizio, sia unimodale che multimodale, ha effetti positivi sulla funzione cognitiva ed è in grado di ritardare o prevenire il declino correlato all'età. Anche l'esercizio acuto e cronico inducono effetti benefici, tuttavia, l'esercizio cronico dovrebbe essere preferito in modo che gli effetti possano essere duraturi.

Keywords
Aging, Physical Exercise, Cognitive Function
Invecchiamento, Esercizio Fisico, Funzioni Cognitive

Introduction

Aging is an irreversible process, characterized by a progressive deterioration of physiological functions and processes, that lead to the manifestation of cardiovascular diseases, hypertension, diabetes, osteoporosis, sarcopenia and sensory deficit (Dziechciaz & Filip, 2014). Aging is often associated to cognitive deficits (eg. gradual reduction of conceptual reasoning, memory and information processing speed), that limit the autonomy and reduce the quality of life of elderly people (Harada, Love, & Triebel, 2013).

Cognitive decline related to aging is a growing public health concern. The World Health Organization (WHO) predicts that the total number of people with dementia will greatly increase until it reached a number of 152 million in 2050 (WHO, 2010). This rapid increase will have a significant impact on health systems. The lack of adequate pharmacological treatments to prevent and/or reduce the progression of the loss of cognitive abilities (Fink et al., 2018), has contributed to a growing interest in integrated interventions useful to promote the proper functioning of cognitive abilities, physical and mental health, functional autonomy in the absence of chronic diseases and the ability to adapt to changes and compensate the limitations. Among the various interventions, physical exercise (PE) seems to be an effective strategy (Troisi Lopez et al., 2020).

PE, defined by WHO as "a subcategory of physical activity that is planned, structured, repetitive, and purposeful in the sense that the improvement or maintenance of one or more components of physical fitness is the objective" (WHO, 2010), is involved in increasing the health potential in both the biological and psychological dimensions and in general well-being (Mandolesi et al., 2017, 2018). The positive effects of PE are innumerable and include reducing the risk of cardiovascular disease, stroke, hypertension, diabetes, osteoporosis, obesity, cancer, improves anxiety management, sleep quality and depression (Gremeaux et al., 2012; Seals, Nagy, & Moreau, 2019). Finally, there is some evidence that PE is able to produce a direct effect on the brain, inducing an increase in vascularization and in the production of neurotrophic factors, which facilitate neuronal repair and growth and the neuroplasticity processes (Ding, Vaynman, Akhavan, Ying, & Gomez-Pinilla, 2006; Gelfo, Mandolesi, Serra, Sorrentino, & Caltagirone, 2018; Knaepen, Goekint, Heyman, & Meeusen, 2010). Indeed, the brain is able to change in relation to various environmental factors and among these, PE plays a pivotal role because its constant practice induces neuroplasticity phenomena both at a structural and functional level which reflecting on cognitive functioning. It has also been shown that PE is an important neuroprotective factor in gaining cognitive reserves, preserving or delaying cognitive decline (Gelfo et al., 2018; Lista & Sorrentino, 2010).

Over the last few years, several studies focused on which type of PE induces the best phenomena of brain plasticity and consequently improves cognitive skills. Most of them showed that aerobic PE, with resistance programs diversified by intensity, duration and oxygen consumption, is the one that most determines positive effects on the brain and in particular on the neuronal circuits underlying the purposeful motor behaviour (Mandolesi et al., 2018). These circuits include large cortical portions, from the occipital cortex to the frontal areas, which are the seat of executive functions, such as attention and short-term memory (Montuori et al., 2019; Sorrentino et al., 2019). A number of studies have also examined the effects of chronic or immediate post-exercise on cognitive abilities, demonstrating that both types of PE produce improvements in cognitive functions (Loprinzi, 2019; Loprinzi, Moore, & Loenneke, 2020; Zhou et al., 2019). However, the mechanisms responsible for these changes are different, indeed while the chronic exercise produces lasting significant changes not only in physical fitness but also in cognitive functions, acute exercise, based on a single exercise session, produces small and non-lasting changes in cognitive functions (Loprinzi, Lovorn, Hamilton, & Mincarelli, 2019). Furthermore, there are several studies that examinated the effects of multimodal and unimodal or traditional exercise on physical and cognitive functions in adults and in typically and atypically development children (Foti et al., 2011; Mandolesi, Petrosini, Menghini, Addona, & Vicari, 2009). The main feature that distinguishes these two types of exercise is that the multimodal exercise is based on mind-body intervention that combines PE and mental processes with deep breathing and relaxation (Wells, Granetzke, & Paolini, 2019). Although these are different both interventions are associated with an improvement in physical fitness, memory, executive function, attention, heart rate, blood pressure, respiratory rate, fasting blood glucose, auditory and visual reaction times (Firth et al., 2018; Vitetta, Anton, Cortizo, & Sali, 2005).

Starting from the evidence above mentioned, this study aims to systematically review studies examining the relationship between acute/chronic, multimodal/unimodal exercise and cognitive functions in elderly people, in order to clarify which type of PE may be the most appropriate to improve physical fitness and cognitive processes.

Methods

The search for scientific articles was carried out on the following databases: PubMed and Scopus starting from January 1th 2016 to 2020. The search strategy focused on three main categories: exercise, cognition and population. The respective keywords, for each of the above categories, were: “exercise”, “physical activity”, “exercise intervention”, “aerobic”, “resistance training”, “mind body”; “cognition”, “cognitive function”, “executive function”, “attention”, “memory”; “elderly” (Figure 1).

Studies examining the relationship between PE and cognition in healthy elderly people (age≥ 60 years) were included in the review. Studies describing, chronic (defined number of attacks in the set period), acute (single attack) (or both), multimodal (mind-body exercise), or unimodal (traditional physical exercise) exercise intervention, were considered eligible. The exclusion criteria were: populations of older adults with diagnosed cognitive deficits, articles in a language other than English, reviews, abstracts or theses. The duplicates were removed, the search results were reviewed and deleted by title and abstract using the eligibility criteria. All potential and relevant studies were further evaluated by reading the complete manuscript. Studies that did not meet the eligibility criteria were excluded (Figure 2).

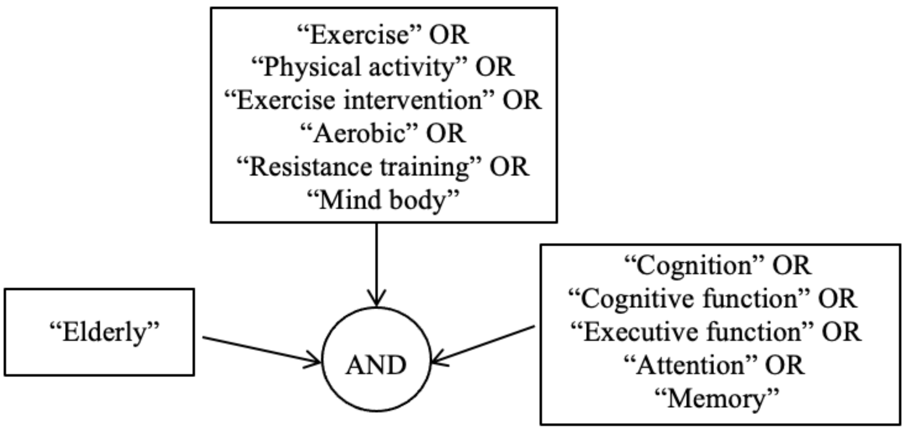

Figure 1. Search strategy adopted for the papers selection

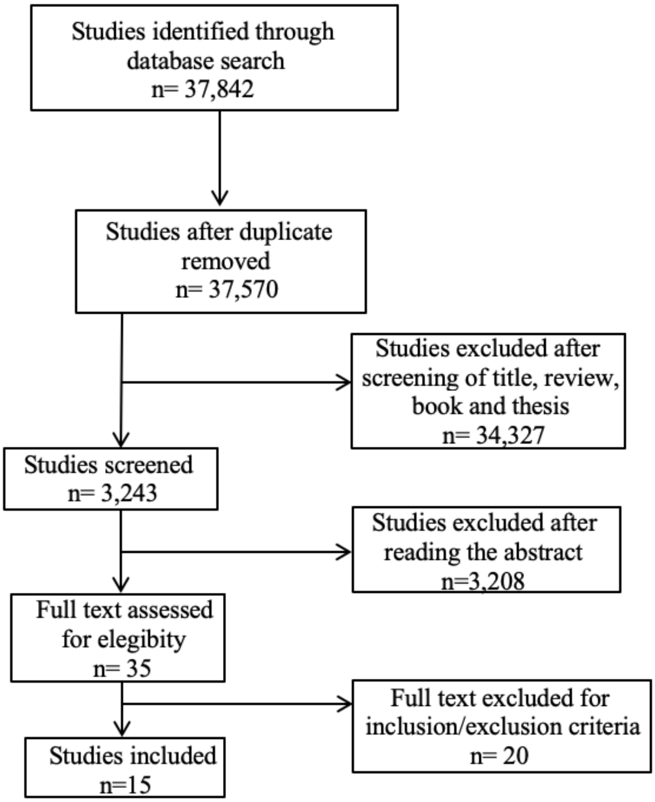

Figure 2. Flow chart of adopted research methodology

Tab. 1 Included Studies

Articles	Population		Intervention		Measures	Results
	Age	**Number**	**Type**	**Frequency**		
(Gothe, Keswani, & McAuley, 2016)	62	118	Yoga, stretching	8 weeks, 3 times, 1hour	Salivary cortisol, 14-item Perceived Stress Scale, State Trait Anxiety Invento-ry, letter version of the running memory span test, task switch-ing.	Improved accuracy on executive function measures and an atten-uated corti-sol response compared to their stretch-ing.

(Desjardins - Crépeau et al., 2016)	72	76	Aerobic and resistance training program, dual-task (DT) training program	12 weeks, 3 times, two 60 minute session of physical exercise, one 60 minute cognitive stimulation	Rey Auditory-Verbal Learning Test and recall, Color-Word Interference Test trail-making test.	Improvements in measures of functional mobility, improved speed of processing and inhibition abilities, but only participants who took part in the DT training independently of physical training.
(Johnson et al., 2016)	71	31	Aerobic exercise or resistance exercise	1 time	Stroop test, Borg Rating of Perceived Exertion scale, Mini Mental State Examination (MMSE),-Seven-Day Physical Activity Recall (7-d PAR).	Independently of mode or duration of exercise, participants improved in the Stroop Inhibition task immediately post-exercise.
(Falbo, Condello, Capranica, Forte, & Pesce, 2016)	72	36	Aerobic exercise, physical-cognitive dual task (DT) training	12 weeks, 2 times, 1hour	Random Number Generation (RNG) task.	Inhibitory performance increase after training with physical-cognitive DT focus.
(Shimada et al., 2017)	78	24	Aerobic exercise,	3 month, 2 times, 90	Positron emission	Significant post-

Tab. 1 Included Studies

Articles	Population		Intervention		Measures	Results
	Age	**Number**	**Type**	**Frequency**		
			strength training, and physical therapy.	min-session	tomography, fluorodeoxy-glucose gait analysis.	intervention increase in regional glucose metabolism in the left posterior entorhinal cortex, left superior temporal gyrus, and right superior temporo-polar area, significantly greater step length in the right foot after 3 months of physical activity.
(Donath et al., 2017)	69	22	Aerobic cycling exercise at 70% of the heart rate reserve.	3 days, 30 min-session	Executive function testing (Eriksen-Flanker-Test, Stroop-Color-Test, Digit-Span, Five-Point-Test).	Between day 1 and 2 were found for reaction times (Flanker- and Stroop Color testing) and completed figures (Five-Point test) at pre and post testing.
(Rosano et al., 2017)	75	26	Walking at moderate intensity, lower extremity resistance lower extremity resistance exercises, balance exercises, stretching and	24 month	Volumes of total hippocampus, dentate gyrus and cornu ammonis measured at baseline and at 24-month follow-up.	Significant left hippocampus, left cornu ammonis and right hippocampus in intervention group.

Tab. 1 Included Studies

Articles	Population		Intervention		Measures	Results
	Age	Number	Type	Frequency		
			behavioural counselling and health education program based on seminars regarding health-related matters and upper extremity stretching exercises.			
(Gothe, Kramer, & McAuley, 2017)	62	118	Hatha yoga, stretching	8 weeks	Attention Network Task, Trail Making Test parts A and B, and Pattern Comparison Test—at baseline and after the 8-week intervention.	Significantly faster reaction times on the Attention Network Task's neutral, congruent, and incongruent conditions, improvement of visuospatial and perceptual processing on the Trail Making Test part B and pattern.
(Marston et al., 2019)	60	45	High-load, long rest resistance training or moderate-load, short rest resistance training	12 weeks, 2 times	CogState computerised battery.	The verbal memory performance was improved in resistance training groups.

(Zhou et al., 2019)	65	60	Tai Chi (24-42-56)	12 weeks, in phase one (Week 1-6), six 60-min exercise sessions, in second	Montreal Cognitive Assessment (MoCA) Time Up & GO (TUG), Balance, Six	All three TC groups showed significant improvements on overall cognitive ability at 6 or

Table 1 Included Studies

Articles	Population		Intervention		Measures	Results
	Age	**Number**	**Type**	**Frequency**		
				phase (week 7-12) five 90-min exercise session.	meter walk test.	12 weeks training period, TC-56 appears to have superior effects on arterial stiffness and static/dynamic balance.
(Arrieta et al., 2018)	84	112	Routine activities, individualized, progressive, multicomponent physical exercise program focused on strength, balance, and walking	Six month	Montreal Cognitive Assessment (MOCA), Rey Auditory-Verbal Learning Test, Trail making test A, Coding and Symbol Search test, Verbal and Semantic Fluency, anxiety and depression scale, BDNF.	A six-month individualized, progressive, multicomponent physical exercise intervention is effective at maintaining cognitive function and decreasing perceptions of loneliness among nursing home residents. Blood levels of BDNF were not affected by the intervention.

(Guadagni et al., 2020)	65	206	aerobic exercise program	12 month, 3 times/week	Symbol-Digit Modalities Test, Cart Sorting Test and Color-Word Inference Test from the Delis-Kaplan Executive Function system battery, Buschke Selective Reminding Test, Medical College of Georgia	The 6-month aerobic exercise intervention was associated with improvements in some cognitive domains and cerebrovascular regulation.

Table 1 Included Studies

Articles	Population		Intervention		Measures	Results
	Age	**Number**	**Type**	**Frequency**		
					Complex, Verbal Fluency Test from the Delis-Kaplan Executive Function system battery Auditory Consonant Trigram Test, Cerebrovascular regulation measures, maximal aerobic capacity.	

(Wheeler et al., 2020)	67	67	sitting, exercise + sitting, sitting, moderate-intensity walking, exercise + breaks, moderate-intensity walking, light-intensity walking	6-day washout	Blood for analysis of BDNF, computerised test battery (Cogstate, Melbourne, Australia) to assess psychomotor function, attention, executive function, visual learning and working memory.	A morning bout of moderate-intensity exercise improves serum BDNF and working memory or executive function in older adults.
(Coelho-Júnior et al., 2020)	45	67	Traditional resistance training (TRT) and combined power training (PT) and TRT (PTRT)	22 weeks, 2 times	Global cognitive function, short-term memory, and dual-task performance. Serum BDNF levels were assessed at baseline and after the intervention.	Overall cognitive function, short-term memory, and dual-task performance were similarly improved after TRT and PTRT. Serum BDNF concentrations were not altered by any training protocol.
(García-Garro et al., 2020)	68	110	Pilates exercises program	12-week, 2 times, 60 minutes	Global cognitive function (Mini-Mental State	Significant benefits in all measures

Table 1 Included Studies

Articles	Population		Intervention		Measures	Results
	Age	**Number**	**Type**	**Frequency**		
					Examination), verbal fluency (Isaacs test), executive function (Trail Making Test), functional flexibility (Back Scratch Test and Chair Sit-and-Reach Test), and lower-body strength (30 s Chair-Stand Test).	except for global cognitive function and functional flexibility (Back Scratch Test).

Results

In the initial search, 37.842 documents were collected. After the removal of duplicates and ineligible manuscripts for the above criteria, 15 articles (published from 2016 to 2020) were considered eligible for the study (Figure 2). Among the 15 identified articles, 3 describe acute exercise intervention and 12 describe chronic exercise intervention. Among the included studies, 4 describe a multimodal mind-body approach (yoga, tai chi and pilates), 11 describe a unimodal approach (aerobic exercise without specific cognitive and/or mental implication). All studies had an intervention and control condition and included an assessment of physical performance. The control condition included stretching, physical therapy, routine activities and walking. A description of the works included in the study is given in Table 2.

Discussion

This study, aims to systematically review studies investigating the relationship between acute/chronic, multimodal/unimodal exercise and cognitive functions in elderly people, in order to highlight which type of PE may be the most appropriate for improving both physical fitness and cognitive processes in healthy elderly people. For this purpose a small sample of relatively recent articles (15 articles), addressing this issue were identified.

The studies on multimodal PE focused on mind-body interventions, which combine mental concentration, breathing control and body movement, determining a beneficial effect not only on the flexibility and stability of the body but also on the brain health. In the present study, were included four studied which described the effect of yoga, pilates and tai chi on cognitive functions. Gothe NP et al. (Gothe et al., 2016) examinated the cortisol level and self-reported stress associated to yoga practice. Although the study failed to show positive effects of yoga on cortisol levels by reducing it, in response to a stressful event such as cognitive assessments, the yoga group showed an attenuated response to cortisol and perceived stress, resulting in better accuracy on executive function assessment tasks. On the contrary, the control group (who practiced stretching) showed a high response to cortisol and a poor performance of task switching. Stress and anxiety can be two critical factors that impair the ability to perform tasks correctly and increase the cortisol level. Cortisol, although a widely used measure of stress, may influenced by age, gender, health status and behaviours, as well as the perception of stress (Fries, Dettenborn, & Kirschbaum, 2009). The ability to manage emotions induces an improvement both cortisol levels and cognition (Moore & Malinowski, 2009). Therefore, Yoga can be understood as a practice capable not only of improving physical fitness but promoting the stability of attention and awareness of the present moment, repeatedly bringing the attention back to the object of meditation as one's own breath. In a study on Hatha yoga (Gothe et al., 2017) was shown the improvement of processing speed information and a significantly faster reaction times on the attention network task. The improvement of these abilities could depend on the effects induced by this practice on the structure of the brain. Neuroimaging studies, reported increased volume of grey matter in several regions of the brain, including the frontal lobe, largely responsible for executive processes associated to yoga practice (Froeliger, Garland, & McClernon, 2012). In the literature, the effects of experience of new activities have been shown cognitive benefits on brain structure and function involving memory consolidation associated with specific brain networks (Hampson et al., 2006; Lardone et al., 2018; Liparoti et al., 2019; Minino et al., 2020; Rucco et al., 2019; Sorrentino et al., 2019). In addition to yoga, Tai Chi (Zhou et al., 2019), a moderate intensity exercise widely practiced in Chinese countries, seems involved in improvement of cognitive function. It is characterized by different styles that share common elements such as breathing control, extension / flexion of muscles, awareness of the body, mental concentration and coordination of the whole body expressed during the execution of choreographic movements defined "forms" (Zou et al., 2018). Specifically, three types of forms (24-form, 42-form, and 56-form) were performed by tai chi practitioners of the study, that involve different levels of strength, endurance and flexibility. All three Tai Chi groups showed significant improvements on overall cognitive ability assessed by Montreal Cognitive Assessment (MoCA). Tai Chi seems to be involved in improving cognitive function, attention span and visual-spatial capacity probably because the ability to perform sequences of continuous movements induces processes of neuronal plasticity, which results in better cognitive function. Like yoga and tai chi, pilates is also a mind-body practice that seems to be involved in improving cognitive functions. In particolar García-Garro PA et al. (García-Garro et al., 2020) demonstrated the beneficial effects of pilates on verbal fluency and executive functions. These findings have significant clinical implications and open up new possibilities for delaying cognitive impairment thereby improving the autonomy and quality of life of elderly people. The effects of mind-body exercise have already been addressed in a meta-analysis study that demonstrates how this practice is able to improve the cognitive performance of the elderly with or without cognitive impairment. Therefore, these practices could be considered as intervention to prevent cognitive decline in aging populations.

In addition to multimodal interventions, this systematical review also highlights the potential of the unimodal approach on the brain and cognitive functions. In recent years, several studies have focused on the effects of aerobic exercise, resistance exercises and mixed interventions (aerobic and resistance combined) on cognitive function and brain health in healthy and pathological adults. Aerobic exercises in the elderly people have shown effects on cognitive performance, regional brain volume, neurotrophin levels, and brain activation patterns. Indeed in Shimada H et al. (Shimada et al., 2017) people who performed aerobic exercise showed significant increases in regional glucose metabolism in the left posterior entorhinal cortex, left superior temporal gyrus and right superior temporopolar area, as well as improved physical performance assessed by gait analysis (Liparoti et al., 2020, 2019; Troisi Lopez et al., 2021; Rucco et al., 2020; Sorrentino 2016). The brain regions listed above, are part of a critical pathway which is at the basis of memory formation. Zola-Morgan and colleagues (Zola-Morgan, Squire, & Ramus, 1994) reported that the entorhinal cortex receives afferents from limbic areas, including the hippocampus and projects efferences to the neocortex and dentate gyrus of the hippocampus, and also receives afferents from the dorsal stream pathway (Andersen, Asanuma, Essick, & Siegel, 1990; Rossi et al., 2008; Zola-Morgan et al., 1994). An increase in the volume of the post-surgery hippocampus was also observed in the study of Rosano et al. (Rosano et al., 2017). It is interesting to note that this increase is lateralized, which indicates a greater susceptibility of one hemisphere than the other. Future studies with larger samples should focus on the effects of exercise on a specific hemisphere and the clinical implications it entails. Although these researches provide compelling evidence on the benefits of aerobic exercise on brain volume, it is not known whether such changes are accompanied by cognitive improvement in this cohort.

The studies reviewed investigated the effects of aerobic or mixed exercise (aerobic-resistance exercise) on executive function. From the analysis of these works it is clear that the elderly employed in aerobic physical exercise, show significant improvements within three specific domains of executive functions, inhibition, working memory and switching. Executive functions involve cognitive processes in the anterior and posterior brain regions that modulate the ability to independently manage the activities of daily living (Montuori et al., 2019). These are the basis of the ability to appropriately allocate attention between activities that are performed simultaneously and allows you to ignore irrelevant sensory inputs (Liparoti et al., 2019; Yogev-Seligmann, Hausdorff, & Giladi, 2008). Several studies have shown that in aging individuals may experience difficulty performing multiple tasks at the same time, particularly when performing another task such as walking. In this review emerge an improvement in executive functions associated with aerobic exercise tested, in most of the studies, through the use of the Stroop colour-word task. In particular, there is a better accuracy in performing task and in processing the information by inhibiting the superfluous ones, which translates into a reduction in reaction times associated with aerobic physical exercise.

This review also aimed to examinate the effect of acute and chronic PE. Specifically, three works described the effect of acute exercise intervention on cognitive function and twelve described the effects of chronic exercise intervention. Acute physical exercise is associated not only to improve of executive functions and working memory post-intervention, but also to promote the release of brain-derived neurotrophic factor (BDNF), identified as an initiator of brain neuroplasticity. Wheeler et al. (2020) (Wheeler et al., 2020) demonstrated an increase of BDNF after acute the aerobic physical exercise of moderate intensity. This is an important result because it is observed that is involved in increases proliferation of hippocampal cells therefore it may be implicated in improvement of memory skills. Various evidences supported the hypothesis of the beneficial effects of acute physical exercise on cognitive functions (Chang, Labban, Gapin, & Etnier, 2012; Tomporowski, 2003), however, the effects of a single bout exercise are generally small and may be unreliable (Chang et al., 2012; Donath et al., 2017). Conversely, chronic physical exercise is associated with long lasting effects on cognitive function which are the expression of consistent changes on brain regions involved in the expression of these functions (Guadagni et al., 2020; Rosano et al., 2017). Chronic physical exercises based on a moderate intensity program, in addition to being associated with changes in improvement of cognitive functions post-exercise, are also associated with the maintenance of these benefits over time. Therefore, in agreement with the guideline recommended by WHO (WHO, 2010), the optimal physical exercise for elderly people is the regular and moderate intensity physical exercise.

Conclusion

In conclusion regular physical activity can delay or prevent age-related decline and this review although draws on a small but substantial evidences, suggest that moderate intensity acute aerobic exercise has benefits on cognition, however it should be preferred the chronic moderate physical exercise which have long-lasting effects. Both unimodal and bimodal physical exercises appear to have beneficial effects on the brain and cognitive function, however, the evidence of multimodal exercises reported in this review is relatively few. The information reported in this review could be useful in identifying optimal programs aimed at improving not only physical but also cognitive fitness.

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