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TWO MONTHS OF COMBINED PHYSICAL EXERCISE AND COGNITIVE TRAINING, OVER COGNITIVE FUNCTION IN OLDER ADULTS: THE RESULTS OF THE MEMTRAIN PROJECT PILOT PROGRAM

Laura Carbonell-Hernández; Eduardo Cervelló; Diego Pastor

Department of Sport Science. Miguel Hernández University of Elche, Spain.

ABSTRACT

Introduction: The MEMTRAIN project is a European Erasmus plus KA2 project were 5 sports associations from 5 different European countries and the Miguel Hernández University of Elche collaborate to create an exercise and cognitive training manual for older people. During the project, manual activities were tested in a pilot study. *Methods*: Fifty-four subjects from five different countries participated in the project, the treated group did a two-month exercise and cognitive pilot program developed in accord with manual instructions (n = 44). At the same time, a group which only did cognitive training tasks were used as a control group (n = 10). This study was developed in an ecological environment with real participants of the different sports associations. *Results*: After the pilot program, the participants in the pilot program improved their Inhibitory cognitive function measured with Stroop test and their Interference Index from the Stroop test. Moreover, there was an intragroup improvement in aerobic fitness, measured with six minutes walk test. No changes were observed in the word learning memory task, neither in agility Up & Go test. *Discussion*: Results showed that physical exercise program with cognitive training tasks as is proposed in MEMTRAIN manual maybe could improve the executive function of older adults opposite with only cognitive training tasks.

Keywords: exercise, older people, cognitive function, fitness

EFECTO DE DOS MESES DE EJERCICIO FÍSICO Y ENTRENAMIENTO COGNITIVO COMBINADOS SOBRE LA FUNCIÓN COGNITIVA DE ADULTOS MAYORES: RESULTADOS DEL PROGRAMA PILOTO DEL PROJECTO MEMTRAIN

RESUMEN

Introducción: El proyecto MEMTRAIN es un proyecto financiado con fondos europeos Erasmus Plus KA2 en el cual 5 asociaciones deportivas de 5 países europeos diferentes, junto a la Universidad Miguel Hernández de Elche, colaboraron para crear un manual de entrenamiento físico y cognitivo combinado para personas mayores. Durante el proyecto, las actividades del manual fueron testadas en un estudio piloto. *Método*: Cincuenta y cuatro sujetos procedentes de 5 países diferentes participaron en el proyecto. El grupo tratado participó durante dos meses en dos sesiones semanales de ejercicio físico y cognitivo combinado, siguiendo las instrucciones del manual (n=44). Al mismo tiempo, un grupo control realizó únicamente el entrenamiento cognitivo (n = 10). El estudio fue desarrollado en un entorno ecológico, donde los participantes realizaron las actividades y evaluaciones en sus propios centros de actividades, en sus respectivos países. *Resultados*: Tras el programa piloto, el grupo tratado mejoró su respuesta en el control inhibitorio de la función cognitiva, medido mediante el test Stroop, tanto en la fase incongruente como en el Índice de Interferencia. Además hubo una mejora intragrupo en la resistencia aeróbica, medida mediante la prueba de 6 minutos caminando. Sin embargo, ni la memoria verbal ni la agilidad medida con el test Up&Go cambiaron. *Discusión*: Los resultados muestran que el entrenamiento físico y cognitivo combinado, tal como es propuesto en el manual MEMTRAIN, podría mejorar la función ejecutiva de las personas mayores en mejor medida que tan solo el entrenamiento cognitivo aislado.

Palabras clave: ejercicio, personas mayores, función cognitiva, condición física

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Correspondence:
Diego Pastor
dpastor@umh.es
Department of Sport Science. Miguel Hernández University of Elche, Spain.

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INTRODUCTION

The time is unstoppable, and is one direction process for human life, in the end, becomes death. Human has fear of the end, and the process which leads us to this end is called aging. Aging is the inevitable effect of time which implies physiological changes during lifespan (Park & Yeo, 2013). Aging is common to all living organisms, and not necessary implies always a deleterious process (da Costa et al., 2016). "Senescence" is the specific word to define those changes of aging leading to disease, disability, and death (da Costa et al., 2016). Anyway, as "aging" is commonly used in literature to speak about the decline of physical function during lifespan as a consequence of time, we will use the aging term.

Different theories are nowadays used to explain aging, theories related with human genetics, with external or internal damage, or combinations of them (da Costa et al., 2016). The consequence of this not clearly understood process is the decline of physiological function, leading to a reduction in adaptability, an increase in disease, and finally to death (Park & Yeo, 2013).

As a consequence of aging, all systems are modified, with individual and social health consequences. For example, cardiovascular diseases like the coronary artery, hypertension or heart failure are dangerously increased in older adults (Lakatta, 2002). At the same time, there is a gradual decline in muscle function, with a muscle wasting process leading to muscle atrophy and sarcopenia in older adults (Miljkovic, Lim, Miljkovic, & Frontera, 2015; Ryall, Schertzer, & Lynch, 2008).

Not only the cardiovascular and muscle system, but also the nervous system experiment an aging decline leading a loss of cognitive and brain function (Bherer, Erickson, & Liu-Ambrose, 2013). This cognitive decline can lead to cognitive dysfunctions like dementia, Alzheimer or Parkinson disease (Lautenschlager, Cox, & Cyarto, 2012). Aging process will affect neurotrophic factors (Bherer et al., 2013), brain structures (Fletcher et al., 2016) and brain plasticity (Erickson, Gildengers, & Butters, 2013) leading to a loss of function.

All these changes are the result of the interaction between environment, lifestyle, and genotype for all subjects (da Costa et al., 2016). That means, lifestyle and environment are in our hand to reduce functional and physiological aging decline, and one of our possibilities to improve the aging process is physical exercise (WHO, 2016). Physical exercise is defined as physical activity program planned and oriented to improve any dimension of fitness or physical performance.

Physical exercise has an impact in all physiological systems, for example, aerobic training is an essential component in cardiac rehabilitation programs, and is well related with cardiac performance in old people (Vigorito & Giallauria, 2014). Well, programmed exercise can reduce arterial pressure, increasing peak VO_2, reducing submaximal exercise heart rate… (Vigorito &

Giallauria, 2014). In addition, well-oriented resistance training can improve muscular function during elderly, with high increased in strength (Peterson, Rhea, Sen, & Gordon, 2010) and gains in muscle mass with and specific increase in satellite cells (Verdijk et al., 2009).

Moreover, physical fitness is related with cognitive function (Colcombe & Kramer, 2003), fitness reduces the brain mass loss with aging (Fletcher et al., 2016), and physical exercise can increase gray matter volume (Erickson, Leckie, & Weinstein, 2014). This improvement will also improve motor performance of older people (Levin, Netz, & Ziv, 2017), reducing the risk of falls and improving balance (Lelard & Ahmaidi, 2015).

Furthermore, cognitive training also has positive effects over different cognitive domains (Fabre, Chamari, Mucci, Masse-Biron, & Prefaut, 2002). The combination of physical exercise and cognitive training programs seems to be also beneficial to improve cognitive function (Lauenroth, Ioannidis, & Teichmann, 2016). In fact, when physical exercise is combined with cognitive therapies, seems to be a complimentary enhanced in cognitive function (Gheysen et al., 2018).

With the challenge of an aging population, European Union (EU) started time ago, different plans and responses (European Commission, 2018), guiding principles for active aging, elaborating an Active Ageing Index, and other initiatives to improve health lifespan and aging. In the last two years, Erasmus+ KA2 projects from EU has funded the MEMTRAIN project (Práve ted´! o.p.s., 2018). MEMTRAIN project has been a collaborative project from six different European partners to build a manual of physical exercise and cognitive therapy for older people. Five of these European partners proposed different physical exercise and cognitive activities, and every one of these five partners elaborated a pilot program with some subjects from their countries.

In this ecological environment, the MEMTRAIN project decided to analyze some variables of physical performance (Up & Go test to measure agility and 6 minutes walk test to measure endurance) and cognitive responses (Stroop test with time-response register and Rey Auditory Verbal Learning Test). This kind of studies about exercise programs and cognitive function usually are developed in a laboratory environment, easier to measure the variables, but far from a real application of exercise programs. In this study, the subjects participated in MEMTRAIN pilot program, in different countries, with different technicians, with different activities. All the activities had the same objectives, structure and training orientation, but were developed in completely different ecological environments. All the instructors were professional technicians, non-researchers, and all the test were evaluated in the ecological training place by the usual instructor.

The objective of the study was to know the impact in physical and cognitive function of two months of MEMTRAIN pilot study once the project finished, compared with a control group that trained only cognitive tasks in also an ecological environment.

METHOD

Participants

This study involved 61 subjects (55 women and 6 men), but only 54 finished the study (48 women and 6 men). They were from Irish, Italian, Polish, Slovene and Czech nationality. The age range was between 58 and 84 years of age (67.28 ± 5.51). Subjects were included in a pilot program of physical exercise and cognitive training that is part of the European project Erasmus plus: Memtrain (n = 44, the Treated Group). Every national partner used their own participant in their ecological facilities. The Czech partner was selected to also create a control group (n = 10, Control Group). That means the participants were not randomized, and the two groups (Control Group and Treatment Group) were not homogeneous. This not controllable ecological limitation was keeping in mind for the statistical analysis. We can see in Table 1 the participant distribution in countries and its age.

TABLE 1
Age participant distribution by countries.

	Age	**SD**	**n**
Slovenia	64.6	3.5	11
Poland	64.8	1.2	6
Italy	70.5	6.6	13
Ireland	68.6	5.9	14
All Treated Group	67.6	5.6	44
Czech Republic (Control Group)	66.2	5.4	10

The study was designed in accord with Helsinki Declaration, and approved by the Ethics Committee of the university. Before initiating the research, participants received information about the program and its risks and signed an informed consent approved by the university's ethics committee.

Intervention program

The intervention pilot program was carried out in different countries 2 days a week for two months. Subjects from the treated group (n = 44) performed a 60-minute session where the activity consisted of performing aerobic exercise for 40 minutes and, finally, practiced cognitive games for 20 minutes. The control group (n = 10) was established in the Czech center, which only performed the 20 minutes of cognitive games activity. The type of activities carried out can be observed in the Erasmus + Meimtrain manual (https://memtrain.eu/wp-content/uploads/2018/09/Training-manual_final.pdf). There are consisted of dance, Nordic walking, seniors athletics or functional exercises. The cognitive training consisted of coordinative tasks with bilateral movements at different rhythms, and memory and mathematical games with words and images. All the information is explained in the manual.

The different groups did different physical activities. The Poland group did dance, the Irish group did athletics, the Italian participants trained functional exercises, and the Slovenian group did nordic walking. All the activities were managed by a local instructor, who was ordered to reach intensity enough to improve aerobic fitness. There was no control of intensity far away from the prescription.

One week at the beginning of the program, and one week in the end, local instructors evaluated all the variables to the subjects. First, the RAVL-Test was evaluated, and the Stroop test was measured in the middle of RAVL-Test, so it also was used as interference. After the cognitive tasks, the Up & Go test was measured, and the 6 minutes walk was the last test.

Measurement variables

The variables measured in this study were agility and dynamic balance, aerobic fitness, executive function, and short and long term word learning memory.

- *Up & Go Test:* To measure agility and dynamic equilibrium, the "8 foot Up and Go test" was used. With a chair and a cone separated perpendicularly at a distance of 8 feet (2.44 meters). The subject, at the signal of "already", walked as fast as possible until reaching the cone to surround it and return as quickly as possible to the chair. The time it took to make the gesture was timed. Subjects repeated the test three times, taking time from the best trial.
- *6 Minutes Walk Test:* To measure aerobic fitness, the test "6 Minutes Walk Test" was used, where 10 cones were placed at a distance of 5 yards (4.57 meters) between them, so cones traced a rectangular area of 50 yards (47.7 meters). At the "already" signal, the participants walked around the area as fast as they could (without running) for 6 minutes. The total distance they were able to cover during those 6 minutes of walking were counted. Both the agility test and the aerobic fitness test are two tests belonging to a battery Senior Fitness Test (Rikli & Jones, 2013).
- *Stroop Test:* To measure the executive function, a digital application of the Test Stroop was used (Martín et al., 2012), created for the Erasmus + Memtrain project, which allowed us to record the response times of each response. The test consists of 3 phases of words and graphics of colored

words that are combined in different ways. The first phase, called Congruent phase (Con.), is formed by the words blue, green, red and yellow written in black ink on a white background. In the second phase, Neutral phase (Neu.), groups of 4 Xs (XXXX) appear, colored in blue, red, green and yellow. The objective of this phase is to choose the color in which the X's are colored, and this is how the subjects are informed. The last phase was Incongruent phase (Inc.), is formed by the names of the colors (blue, green, red and yellow), but colored with "non-congruent" colors, that mean, for example, word Green with blue ink. The subject must respond to the color they see, and not the word they read. All phases have unlimited words and the duration of each one is 45 seconds, with breaks of 25 seconds, counting the number of successful responses and the response time. Subjects practice twice the first time they did it before they were measured. Every subject used always the same device to make tests. The three phases were done in the same order (Con.-Neu.-Inc.) at the pre and post-test, and also in the two training trials. The Interference index was calculated with the successful responses of the three phases: Interference Index = Inc. – [(Con. x Neu.) / (Con. + Neu.)]. This index represents the relation between the real performance of the incongruent phase respect the expected performance of the neutral and congruent phases, with higher values explaining a better inhibitory control function (Martin et al., 2012).

- *Rey Auditory Verbal Learning Test:* To evaluate short- and long-term memory, Ray's AVLP was used (Savage & Gouvier, 1992). It consists of administering a list of 15 words during 5 learning trials (trials 1 to 5), a distraction list, a reminder of learning (trial 6), a 20-25 minute phase where another interference task is performed (we used the Stroop test) and a final reminder of learning (trial 7). The subjects were informed about the test before to start. Two different lists previously described (Geffen, Butterworth, & Geffen, 1994) were used for pre and post-tests. Each country used a different order.

Statistical analyses

As groups were ecological non-randomized groups, and Control Group (CG) was smaller than Treatment Group (TG), to compare groups and control the initial differences, and ANCOVA was performed for each test, the variables included in the ANCOVA fulfilled the assumptions of linearity and homogeneity of regression slopes. Two coverable were used in ANCOVA, the initial values of tests, and the age of subjects, because the cognitive response can be modulated by age. The effect size in the ANCOVA analysis is expressed as partial eta-squared (η_p^2), Eta-squared effect sizes are grouped as small (≤ .01), medium (≤ .06) and large (≤ .14) as Cohen described (Cohen, 1988). In addition, a paired

T-test was used for related samples to analyze the intragroup differences. The Cohen effect size for T-Test was analyzed with d of Cohen (Cohen, 1988, 1992), and the magnitudes of standardized effects sizes were considered as small (< 0.2), moderate (< 0.6), large (< 1.2) very large (< 2.0) and extremely large (> 2.0). The level of significance was established at p < 0.05. Not all subjects did all test. Analysis has been done with the data available.

RESULTS

All the data of the study are presented in table 2.

TABLE 2
Pre and post values for all variables.

TESTS DATA	TREATED GROUP				CONTROL GROUP			
	PRE		POST		PRE		POST	
	X	SD	X	SD	X	SD	X	SD
Con. Successes	28.63	8.13	29.97	8.94	29.71	11.41	34.20	40.80
Neu. Succeses	30.49	7.02	32.00	6.37	28.00	13.35	34.20	4.32
Inc. Succeses	17.67	8.06	19.95	7.73	12.00	8.50	9.90	8.17
Con. Time	1475.76	388.69	1408.56	379.10	1295.67	180.12	1258.33	158.93
Neu. Time	1386.25	304.58	1339.80	249.11	1135.06	143.85	1267.11	167.69
Inc. Time	2139.17	736.77	1950.67	602.42	2215.36	1059.30	2167.51	951.33
Interference Index	3.15	7.06	4.75	6.31	-0.47	13.70	-7.17	7.33
RAVLT 5 Trial	11.25	2.37	11.74	2.80	12.80	1.93	12.00	1.94
RAVLT 6 Trial	9.76	2.82	10.21	2.82	11.30	2.83	10.80	1.99
RAVLT 7 Trial	10.64	3.34	40.74	2.84	9.60	2.80	10.50	2.64
Up&Go	6.31	1.56	6.19	1.52	6.23	1.61	5.94	1.76
6 Min. Walk	645.63	86.77	657.63	79.40	542.90	125.79	545.30	132.65

After the pilot programs, and controlling the previous differences between different European groups in previous performance, number of subjects and age, with the ANCOVA analysis, there were differences between groups in the Interference Index and the Incongruent phases successes (Table 3).

TABLE 3
ANCOVA positive results.

Incongruent Successes	Mean	SD	F	Sig.	η_p^2
Treated Group	19.95	7.73	10.64	p = 0.002	0.188
Control Group	7.67	6.65			
Interference Index	**Mean**	**SD**	**F**	**Sig.**	η_p^2
Treated Group	4.75	6.31	24.62	p < 0.001	0.344
Control Group	-8.64	5.58			

The other measurements did not present significant results in the ANCOVA analysis: Congruent successes p = 0.17; Neutral successes p = 0.24; Congruent time p = 0.43; Neutral time p = 0.56; Incongruent time p = 0.64; RAVLT trial 5, p

= 0.22; RAVLT trial 6, p = 0.75; RAVLT trial 7, p = 52; Up & Go test p = 0.29; 6 minutes walk test, p = 0.18.

When we analyzed particularly each group with paired T-Test, we observed significant differences in Stroop test for the training group, in the most complex phase (Incongruent), for the successes (Table 4), and also in the time response (Table 5), despite this difference is not present in the ANCOVA, and we can not claim that this difference is produced by the program. However, it seems that, after the pilot exercise program, the participants were faster and responded more correct answers.

TABLE 4
Success in Incongruent condition

Training Group	n	Mean	SD	Sig.	Effect Size
PRE	44	17.67	8.06	p = 0.027	2.03
POST	44	19.96	7.73		
Control Group	**n**	**Mean**	**SD**	**Sig.**	**Effect Size**
PRE	7	12.00	8.51	p = 0.499	-0.72
POST	7	9.90	8.17		

TABLE 5
Response Time during Stroop test for Incongruent condition.

Training Group	n	Mean	SD	Sig.	Effect Size
PRE	44	2139.17	736.77	p = 0.002	-1.97
POST	44	1950.67	602.42		
Control Group	**n**	**Mean**	**SD**	**Sig.**	**Effect Size**
PRE	7	2215.36	1059.29	p = 0.748	-0.16
POST	7	2167.51	951.33		

In addition, the Interference Index presents a tendency (p = 0.088) to improve, that is not observed in the control group (Table 6). But analyzing with care the data, the positive ANCOVA result maybe is related to the decline in control performance, more than an improvement in the training group.

TABLE 6
Paired T-Test for Interference Index.

Training Group	n	Mean	SD	Sig.	Effect Size
PRE	44	3.15	7.06	p = 0.088	0.24
POST	44	4.75	6.31		
Control Group	**n**	**Mean**	**SD**	**Sig.**	**Effect Size**
PRE	7	-0.47	13.70	p = 0.236	-0.61
POST	7	-7.17	7.29		

Related with fitness, analyzing the paired T-Test, the participants in the Memtrain exercise pilot program improved their aerobic fitness measured by the Six Minute Walk Test (Table 7). The better previous performance of the Training group can be the reason to do not find significant results in ANCOVA and is coherent with older adults participants in exercise programs, that usually are people with better fitness than the non-participants (Picorelli, Pereira, Pereira, Felício, & Sherrington, 2014).

In contrast, there were not significant differences for Up & Go test in Training group (p = 0.402), neither in control group (p = 0.348).

TABLE 7
Paired T-Test for Six minutes walk test results.

Training Group	n	Mean	SD	Sig.	Effect Size
PRE	42	617.21	16.64	p = 0.024	1.09
POST	42	634.83	15.71		
Control Group					
PRE	10	542.90	39.78	p = 0.217	0.06
POST	10	545.30	41.95		

Verbal memory test seems to be not influenced with the training pilot program, as it did not change in the ANCOVA, neither in Paired T-Test.

DISCUSSION

Is well documented the improvement in physical performance with physical exercise in older adults, in the different dimension of fitness, like endurance (Vigorito & Giallauria, 2014), strength with resistance training (Peterson et al., 2010) or balance and postural control (Lelard & Ahmaidi, 2015). Moreover, is also well known the effect of physical exercise and fitness in the nervous system and cognitive function (Bherer et al., 2013; Colcombe & Kramer, 2003), especially in executive functions (Boucard et al., 2012). And those improvements are usually related with physiological changes like, for example, increased neurogenesis (Curlik & Shors, 2013; Yau et al., 2014), an increase in neurotrophic factors (Phillips, Baktir, Srivatsan, & Salehi, 2014), an improve in cerebral blood flow (Nishijima, Torres-Aleman, & Soya, 2016) or simply an increase in grey matter and white matter volume during aging (Erickson et al., 2014; Fletcher et al., 2016; Hayes, Salat, Forman, Sperling, & Verfaellie, 2015).

In our study, MEMTRAIN pilot program increased the number of successful responses when we take into account the initial values and age, in the more complex tasks of the Stroop Test, that is, the Incongruent phase. Moreover, maybe the reaction time during incongruent phase was also improved, but initial differences do not less us to be sure about this change, and ANCOVA did not report significant results. The Stroop Test evaluates the inhibitory control cognitive function and, with the MEMTRAIN app, we also evaluate the response time of the subjects. Moreover, the Interference Index, as a measure of global inhibitory control of the Stroop test (Martin et al., 2012), also improved in the training group..

Recently it has been published a correlation between aerobic fitness and Stroop test (Hyodo et al., 2016), that's interesting because our training group seems to improved their aerobic fitness in the intragroup analysis, and presented better results in inhibitory control test. Two months of MEMTRAIN program seems to be enough to improve 6 minutes walk test, at least when we analyze intragroup changes. This test correlates with aerobic fitness (Burr, Bredin, Faktor, & Warburton, 2011; Ross, Murthy, Wollak, & Jackson, 2010; Zhang et al., 2017). Interestingly, improvements in cognitive function have been usually related with improvements in aerobic consumptions and endurance (Baker et al., 2010; Colcombe & Kramer, 2003; Erickson & Kramer, 2009; Griffin et al., 2011; Hayes et al., 2015). However this correlation is not always present in literature, and researchers sometimes fail to find a relation between the improvement in aerobic fitness and cognitive response (Young, Angevaren, Rusted, & Tabet, 2015). Moreover, we can not claim that this improvement is really related to our program because ANCOVA did not show these results, and groups were previously highly different. Maybe the improvements in treatment group are mediated by previous fitness differences.

Or maybe the improvements were produced by the combination of physical and cognitive training, as has been seen in other studies (Fabre et al., 2002; Lauenroth et al., 2016; Oswald, Gunzelmann, Rupprecht, & Hagen, 2006). But we can not conclude any possibility as we have only a control group with cognitive training. Moreover, the control group did not improve in any variable. Some studies have observed cognitive improvements after cognitive training (Kelly et al., 2014; Kim, Chey, & Lee, 2017). Maybe our cognitive techniques were not adequate, maybe 20 minutes two days a week is not enough to produce adaptations and improvements in cognitive tasks.

Finally, the Rey Auditory Verbal Learning test did not improve, this quality is considered declarative memory (Squire, 1992a), and it is related with the hippocampus function in the brain (Squire, 1992b). The hippocampus seems to be enhanced with exercise training and cognitive tasks (Curlik & Shors, 2013), it seems to increase its volume with aerobic exercise, at least in women (ten Brinke et al., 2015). Probably our pilot study was too short, or our aerobic fitness improves in a lesser degree that is necessary to improve the hippocampal structure and declarative memory. Or maybe declarative memory is not easy to improve with physical exercise. Indeed, maybe there is no relation between the aerobic fitness and memory (Young et al., 2015).

By the other hand, the two month pilot program neither was enough to improve Up&Go test, this test correlates with balance and gait tests (Herman, Giladi, & Hausdorff, 2011), and even with some executive functions (Herman et al., 2011), but the MEMTRAIN program seems to be not enough to improve this variable in two months. Maybe it was too short time period.

CONCLUSIONS

It seems that two months of physical and cognitive training using the MEMTRAIN manual can improve inhibitory control in older people compared with only cognitive training. These results must be corroborated with more studies, and more different cognitive protocols must be used to analyze the possible combinatory benefits of physical exercise and cognitive training.

LIMITATIONS

This study has been developed in an ecological environment. The subjects were participants in physical programs from Poland, Slovenia, Ireland, Italy, and the Czech Republic. In all these countries, the physical instructors were responsible to measure the tests, that mean the researcher group has low control over the protocols, and the evaluator was not always the same person, and that can imply some bias. Furthermore, the control group was only formed in Czech Republic, and they were old people who participate in cognitive training programs, as they were from only one country and not absolutely sedentary, maybe that implies another bias.

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