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Journal of Aging and Physical Activity

Note: This article will be published in a forthcoming issue of the *Journal of Aging and Physical Activity*. This article appears here in its accepted, peer-reviewed form; it has not been copy edited, proofed, or formatted by the publisher.

Section: Original Research

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Journal: *Journal of Aging and Physical Activity*

Acceptance Date: January 21, 2018

DOI: https://doi.org/10.1123/japa.2017-0135

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Abstract

This study aimed at identifying the effects of self-paced cycling on the cognitive and functional status and fall risk on institutionalized older adults without cognitive impairment. Thirty-nine individuals were randomly assigned to an exercise (EG) or to a control (CG) group. The EG participants cycled at their self-selected intensity at least for 15 minutes daily during 15 months. The CG participants performed recreational activities. The Mini-Mental State Examination, Fuld Object Memory Evaluation, and Symbol Digit Modality Test were used for cognitive assessments. The Katz Index, the Timed Up & Go Test and the World Health Organization questionnaire were used to assess functional independence, mobility, and fall risk. Significant improvements were observed in the EG for global cognition and attention, visual scanning, and processing speed. Long-term self-paced cycling training seems to have a protective effect on cognitive status and attention, visual scanning, and processing speed in older institutionalized individuals.

Keywords: physical activity; cognition; institutionalized older adults; functional mobility; activity of daily living.

The biologic aging process is a major risk factor for disease and disability in the elderly with important physical and cognitive consequences (Koscak, 2017). The neurocognitive consequences from aging frequently result in long-term care assistance (Li & Porock 2014). These cognitive dysfunctions affect various domains and especially mental processing speed, attention, memory, and executive function (Harada, Natelson, & Triebel, 2013). Aging-related phenotypic expressions include, among others, gait dysfunction, and mobility limitations (Blackwood, Shubert, Forgarty, & Chase, 2016). These problems are not only neurological in origin but have musculo-skeletal contributions (Covinsky, Eng, Lui, Sands, & Yaffe, 2003) and, altogether, induce downstream effects which lead to a functional loss of independence in daily life activities (Harada et al., 2013; Covinsky et al., 2003) and an increase in the risk for falls (Barban et al., 2017).

Dementia and functional decline are two of the main factors linked with the decision to institutionalize older adults (Hajek et al., 2015). In addition, the mere process of institutionalization, for whatever reason, is associated with an increased risk of functional and cognitive deterioration; this may be related to acute changes in the psychosocial situation of the individual (Gonzalez-Colaço et al., 2014; Jerez-Roig, de Brito, Torres de Araujo, & Costa, 2017). Therefore, finding strategies to palliate this cognitive and functional decline is of crucial importance, especially in institutionalized individuals.

There is increasing evidence that the regular practice of physical exercise can reduce morbidity and the impact of age-related functional decline; in fact, this may be one of the most important forms to prevent and treat chronic diseases (Bean, Vora, & Frontera, 2004). Physical exercise is a non-pharmacological strategy that is gaining special interest in reducing the risk cognitive decline in older people (Lautenchlager et al., 2008).

Diverse physical exercise modalities have been studied with the objective of preserving or maintaining cognitive performance. The most common is aerobic training type, strength type

(Northey, Cherbuin, Pumpa, Smee, & Rattray, 2017), and the multicomponent type (Northey et al., 2017; Bouaziz et al., 2017), which combines the aforementioned types with balance activities (Suzuki et al., 2012), flexibility (Nouchi et al., 2014), and proprioception (Tarazona-Santabalbina et al., 2016).

Among these modes of exercise, aerobic training is particularly attractive because when practiced regularly, has beneficial effects on cardiovascular, metabolic, general function, and quality of life (Bouaziz et al., 2017). Improvements in attention, mental processing speed, and executive function have also been observed with this exercise modality (Smith et al., 2010). Various mechanisms may help to explain the beneficial effects of this type of training on cognitive function. These include an increase in brain volume, increase in size of the anterior hippocampus, neurogenesis, promotion of cardiovascular changes in the peripheral and cerebral vascular system, enhanced angiogenesis, and decrease of peripheral risk factors (Karssemeijer, Bossers, Aaronson, Kessels, & Olde Rikkert, 2017).

Of the different modalities of aerobic physical exercises that are prescribed for elderly people, cycling is particularly attractive for its performance feasibility and its effects on cognitive and functional outcomes (Bouaziz, Schmitt, Kaltenbach, Geny, & Vogel, 2015). Nevertheless, there is controversy on the intensity at which this exercise should be performed. While most experts recommend vigorous to moderate aerobic exercise, others indicate that higher intensity requires more attention to physical exercise at the expense of cognitive processes and this may reduce its benefits (Tivadar, 2017).

In relation to this, Varela, Ayán, Cancela, and Martín (2012) observed that the intensity of pedaling was not a determinant factor for this type of physical exercise on cognitive functional outcomes in elderly people with cognitive impairment.

Zak, Swine and Grodzicki (2009) suggested that cycling at a self-selected pace is an easy-going exercise routine with a positive impact on the health status of older people.

Therefore, permitting individuals to self-select the cycling pace, instead of monitoring the intensity of the activity to control the same movements within a pre-established range, could be an interesting alternative when prescribing aerobic exercise in institutionalized populations. To the authors' knowledge, information is still scarce on the effects of cycling at a self-selected pace on the cognitive function and functional outcomes in elderly persons without known cognitive impairment.

Recent systematic reviews and meta-analysis (de Asteasu, Martínez-Velilla, Zambom-Ferraresi, Casas-Herrero, & Izquierdo, 2017; Kelly et al., 2014; Young, Angevaren, Rusted & Tabet, 2015) indicate that, besides the scarce scientific information available to date, there are other relevant details related with the prescription of aerobic exercise for healthy older people. A particular unsettled issue is the duration of the physical exercise sessions. Most protocols suggest that each session should last between 40 to 60 minutes; few studies have focused on the effects of shorter exercise sessions. In this regard, Vidoni et al. (2015) observed that the practice of physical exercise at low-intensity in sessions of 75 minutes per week is sufficient to obtain cognitive and physical beneficial results (fitness) in elderly sedentary persons. Therefore, performing frequent (daily) cycling sessions of short duration may be an interesting strategy in institutionalized elderly people without known cognitive impairment. On the other hand, the length of the training program constitutes a second aspect to consider since very few studies have focused on the effects of these interventions beyond 52 weeks.

Thus, it is of relevant and practical interest the study of a program consisting of cycling sessions at a self-selected pace performed in a short-duration/long-term regimen and examine its effects on the cognitive function and the grade of mobility and functional autonomy of the individual. We hypothesize that this type of program, maintained for a period of 15-months and performed in selected institutionalized elderly individuals without cognitive impairment, may be an effective strategy that may improve various functional and cognitive outcomes in this population.

Methods

Participants

This study analyzed data from the Geriatric and Fitness (GER-FIT) Study, a multicenter longitudinal intervention study of cognitive function, aging and exercise, in older persons living in long-term home care institutions. Participants in this study were recruited through a collaboration agreement between the University of XX (Spain) and "XX S.A", a company for the management of residential care homes for the older adults. Individuals with the following criteria were included: (a) age over 65 years (b) absence of clinical diagnosis of dementia (c) Mini-Examen Cognoscitivo (MEC) score > 24 (Lobo et al., 1999) (d) ability to stand and walk for at least 30 meters without shortness of breath (e) able to walk safely and independently without aid, and (f) resident in geriatric long-term care home facility in XX (Northwest Spain). Excluded were individuals with a clinical diagnosis of dementia or other medical conditions that hindered or prevented a full and complete participation in the evaluation tests.

All the participants and their families were previously informed about the characteristics of the research protocol. The study was approved by the Clinical Research Ethical Committee of XX (CEIC 2009/345) and all participants gave their informed consent.

Outcome measures

Age, sex, education level, and medical information of each individual were obtained through the medical records of each residential-care center.

The neuropsychological tests were conducted by a team of experts who evaluated the participants. The assessment included memory tests, evaluation of language, attention and executive functions, functional independence and mobility, and primary clinical outcomes. The data was collected two weeks before and two weeks after the intervention period ended with the exception of the cognitive status (MEC), which was assessed every three months. The same evaluator's team performed all of the measurements (single-blinded for the group allocation). The following tests were administered:

Mini-Examen Cognoscitivo (MEC), which is the Spanish-adapted version of the Mini-Mental State Examination**.** This test was used to assess the impact of the intervention on the participant's cognitive function as well as identify the rate of cognitive decline experienced by the participants throughout the research. This tool is composed of 13 elements distributed into 5 sections which represent different cognitive domains (orientation, registration, attention and calculation, recall, language and copying). The maximum possible score is 35 points. The cutoff score for dementia is 24.

The Fuld Object Memory Evaluation (FOME). This test was used to assess the effects of the intervention on the memory of the participants (Fuld, Masur, Blau, Crystal, & Aronson, 1990). The FOME consists of 10 common objects contained in a bag. Following tactile identification and visual processing of the objects, there is a 60-second distracting interval filled with a rapid semantic retrieval task (first names). Next, there is a recall trial and four additional learning trials separated by 30- second rapid semantic retrieval trials. After each recall trial, the subject is reminded of the omitted item(s). Two FOME scores namely total storage (TS) (possible range 0-50) and delayed recall (DR) (0-10) were derived to assess encoding and recall of episodic memory respectively, with lower scores indicating greater impairment. For the purpose of this study, an adapted version of the FOME for Spanish-speaking populations was used (La Rue, Romero, Ortiz, Liang, & Lindeman, 1999).

Symbol Digit Modalities Test (SDMT). The effects of the intervention on the level of attention, visual scanning, and processing speed of the participants was assessed by means of the SDMT (Smith, 2002). This test requires individuals to identify nine different symbols corresponding to the numbers 1 through 9, and to practice writing the correct number under the corresponding symbol. Then they manually fill the blank space under each symbol with the corresponding number. A second oral administration is then completed. The participant is given a blank copy of the test and asked to state the correct number for each corresponding symbol. The participant is given 90 sec. to complete each of these administrations. A written and oral score is calculated by totaling the number of correct answers for each section.

Katz Index (KI) Functional Independence. The impact of the intervention on the participant's ability to perform activities of daily living (ADL) independently was assessed by means of the Spanish validated version of the KI (Álvarez et al., 1992). The index ranks adequacy of performance in the six functions of bathing, dressing, toileting, transferring, continence, and feeding. Patients are scored yes/no for independence in each of the six functions. A score of 6 indicates full function, 4 indicates moderate dependence and 2 or less indicates severe functional dependence.

Timed "Up & Go" Test (TUG). The effects of the intervention on the participant's functional mobility were assessed by means of the TUG (Posiadlo & Richardson, 1991). This test measures the time required for an individual to stand up from a chair with armrests, walk 3 meters, turn, walk back to the chair, and sit down. No practice trial was included; the mean number of seconds required to performing the test across 2 trials was considered the outcome variable.

World Health Organization Falls Questionnaire. The number of falls was assessed by means of an item of the Spanish-adapted version of the World Health Organization questionnaire (Vidan-Astiz, Vellas, & Montemayor, 1993) that registers every fall from the beginning of the intervention to its completion.

Once the baseline data was obtained the participants were randomly assigned to an exercise (EG) or control (CG) group using a computer-generated sequence. The participating individuals were randomized in a 1:2 ratio so as to achieve a similar number of patients in each group at the end of the intervention. The reason for this was that a greater number of deceases were expected in the non-exercise group considering the long-term duration of the program; a higher level of daily physical activity is associated with better survival among older frail populations (Landi et al., 2008). The flow of recruitment to assessment is represented in Figure.1.

Individuals in both groups continued to carry out the usual routine activities offered by the residential-care institutions to the attendees including simple exercises of joint mobility, reading and morning visits, watching television, brief walks and afternoon visits, etc. This routine included one daily hour of recreational activities of the individual’s choice (playing cards, playing board games, doing crossword puzzles, crafts, etc) performed freely and without supervision. During this time the participants in the EG performed the exercise intervention.

Participants enrolling in the EG were encouraged to cycle continuously in a recumbent bike at their self-selected intensity at least for 15 minutes every day during 15 months. A physiotherapist monitored the sessions and registered the amount of time that each patient exercised daily as well as his/her adherence to the program. The participants who did not complete a minimum of 70% of the total sessions each were excluded from the data analysis. This criterion for valid attendance was set up to guarantee a minimum weekly practice (Varela et al., 2012).

Statistical analysis

The descriptive analysis was performed using measures of central tendency (means±SE) and percentage. The analysis of associated medical conditions was performed identifying the five more frequent in the study sample. The continuous variables were tested for normality with the Kolmogorov–Smirnov test ($p>.05$). The baseline differences between the groups (control and experimental) were done with the chi-squared test for qualitative variables and the unpaired Student's t- test for quantitative variables; homoscedasticity was analyzed with the Levene's test (p>.05; equal variances). We used two methods to analyze the effects of training. The first was an intention-to-treat analysis, while the second was a complete- case analysis, in which participants with valid data at two time points were included in the analysis.

A repeated measures procedure was used in an analysis of variance (ANOVA 2X2; Group: EG vs. CG; Session: Pre vs. Post) followed by a post-hoc Tukey test and covariance (ANCOVA 2X2; Group: EG vs. CG; Session: Pre vs. Post; Covariables: age, gender, educational level, pathologies in both the intention to-treat and complete-case analyses. For intention-to-treat data, a mixed model with repeated measures in SPSS was used while for complete-case data, a general linear model for repeated measures ANCOVA in SPSS was used.

The statistical analysis was performed using IBM-SPSS V.22 for Mac. A P value of less than .05 was considered to indicate statistical significance.

Results

Of a total of 1169 institutionalized individuals that were invited to participate, 218 initiated the evaluation process. One hundred and forty-four individuals presented medical conditions that contraindicated participation and were excluded. Randomization was thus performed in 74 participating individuals (EG n=25; CG n=49). During the intervention period 33 participants abandoned the study (EG n=6; CG n=7). Dropouts were related to death (CG n=4), serious medical events (EG n=3; CG n=3), and transfer to another residential-care facility (EG n=3; CG n=6). Fifteen individuals in the CG were not included in the final analysis (six participants missed the final evaluations and nine performed physical exercise of their choice).

After applying the criterion of 70% adherence, the final sample totaled 39 participants (EG n=17; CG n=22) (Figure 1).

No significant differences were found in the baseline sociodemographic and clinical characteristics of participants (Table 1). The drop-outs registered in both groups were not found to be different from the participants who completed the study on any of the baseline variables, with the exception of the performance of ADL (KI: $p<0.035$; ES; d: 0.41).

Table 2 shows the effects of the intervention on the participants who finished the intervention. The comparison between the initial and final results obtained after the administration of the tests indicated that self-paced cycling had a significant impact on the participants' global cognition and attention, visual scanning, and processing speed. The analysis of variance showed that self-paced cycling was significantly more effective than the recreational activities for the aforementioned outcomes. This effect was also observed after adjusting for confounding variables. The course of the cognitive function of the sample, which was assessed every three months throughout the study, can be observed in figure 2. The participants on the EG experienced a continuous and progressive improvement on this variable while the people on the CG showed an inverse trend.

The effects of the intervention in the intention-to-treat analysis are shown on table 3. The obtained results showed that there were no significant effects within the groups (changes from pre to post).

The intervention had distinct effects in both groups with significant differences between them. The results of the ANOVA showed that the participants in the CG, compared to those enrolled in the EG, experienced improvements on their global cognition and attention, visual scanning, processing speed, and encoding and recall of episodic memory, while the former showed a worsening in these variables. The ANCOVA showed that these results were maintained after adjusting for confounding variables.

No significant changes were observed on the frequency of neuropsychiatric disturbances, functional independence, functional mobility, and fall risk of the participants regardless of the group to which they were assigned and the type of analyses performed.

Discussion

In this study, self-paced cycling performed on a daily basis proved to be an effective exercise strategy for stabilizing or improving cognitive function in institutionalized older people without known cognitive impairment.

These findings are in line with previous observations of a positive relationship between aerobic exercise (including cycling) and cognitive improvement in healthy older people (Conner et al., 2017). This, however, still remains to be confirmed (Young et al., 2015). The particularity of the study presented herein lies on the fact that the participants cycled at a self-selected speed, which, in the vast majority of the cases, resulted in performing exercise at a low intensity. This resulted in a significant improvement in their cognitive function. We speculate that, among other reasons, exercise may improve cognition due to an augmentation in cerebral blood flow (Laitman & John, 2015) since steady-state cycling global increases brain blood flow (Barnes, 2015). The improvement in the cognitive function experienced by the participants in the EG may be the result of performing exercise at a low intensity.

A point of controversy is the duration and intensity of physical exercise programs. Some have reported that, regardless of the intensity at which cycling is performed, short term exercise programs do not impact on cognitive function of older people (Varela, et al., 2012; Tang, Eng, Tsang, & Liu-Ambrose, 2016). Others report that the effects of exercise on cognition depend as much on the intensity as its duration (Duzel, van Praag, & Sendtner, 2016). Different studies performed in animal models and in humans indicate that long-term low exercise intensity programs can improve cognitive function (Inoue et al., 2015; Tamura et al., 2015). Our observation on the improvement of cognitive function may be the result of long term exercising at a self-selected intensity.

Another interesting result is that the participants who exercised improved their level of attention, visual scanning, and processing speed. As indicated in previous reports (Voelcker-Rehage, & Niemann, 2013), physical exercise can stimulate several brain regions (including frontal, temporal and parietal lobe areas as well as the motor cortex) that participate in these cognitive functions.

From our results we may speculate that self-paced cycling may be an appropriate physical exercise strategy for maintaining the functional level of these brain regions older people. The SDMT is a coding task of rapid transcription of numbers to match symbols and, as other neurocognitive functions that require substitution tasks, they rely on processing speed, learning, memory, and world retrieval. As such, they are strongly related to executive function (Benedict et al., 2017). In accordance with previous studies (Clark et al., 2004; Hoffman et al., 2016), the SDMT may be an instrument able to detect changes in executive function. On this basis, daily performance of a self-paced cycling program can be considered a useful physical exercise training modality having a positive impact on the executive function of older people without known cognitive impairment. It is known that regular engagement in aerobic exercise can optimize executive function even in healthy older people (Guiney & Machado, 2013). Regarding the specific effect of cycling and its performance intensity on executive function no definitive conclusion can be made. Nevertheless, there is evidence that, in older people, aerobic exercise improves complex cognitive tasks including executive function (Northey et al., 2017). Some have suggested that, for healthy older people, cycling at high intensity results in greater significant improvement than cycling at low intensity (Lucas et al., 2012). Others observe that passive cycling (performed at a low intensity) has a positive impact on the executive function in patients with Parkinson's disease (Ridgel, Kim, Fickes, Muller, & Cotter, 2011). Both of these reports were based on the performance of acute bouts of cycling. We believe that the effect of long-term cycling exercise programs at different intensities on the executive function of healthy older people without known cognitive impairment is still unsettled and additional studies are needed.

When the effects of the intervention were analyzed for each group separately the performance of self-paced cycling did not carry significant changes in encoding and recall of episodic memory. However, when an intragroup comparison was performed, the participants in the EG group showed a tendency towards improvement while the participants in the CG group worsened. A possible explanation for this different pattern of outcome between the participants in both groups may lie in a possible threshold effect for age-related changes due to physical exercise (Young, Dowell, Watt, Tabet, & Rusted, 2016). In this regard, it has been suggested that exercise improves memory by preventing the volumetric changes in the hippocampus, a strategic brain region for memory (Briedermann et al., 2016). Erickson et al. (2011) reported an increase in the size of the hippocampus with improvement of memory in healthy older people who performed aerobic exercise at a moderate intensity. These authors suggested that the hippocampal volume changes were related to an increment in physical fitness. Therefore, it could be hypothesised that the exercise intensity at which self-paced cycling was performed was not sufficient enough to provoke significant changes in the participants' fitness level. As a result, although this type of physical exercise may have been the cause for which the participants in the EG group showed a tendency towards improvement in their memory function, the observed changes would not have been of sufficient magnitude to reach statistical significance.

When an intention-to-treat analysis was performed separately for each group, no significant changes were observed in any of the analyzed variables. Given that the participants who did not accomplish at least 70% of the exercise sessions were not considered completers, this result remarks the importance of exercise adherence. When an inter-group analysis was performed, our statistical analysis indicated that self-paced cycling was significantly more effective than the performance of unsupervised recreational activities in improving cognitive, executive, and memory function. Therefore, the results of this study implies that in institutionalized people without known cognitive impairment, the preservation of their cognitive function could be achieved by taking part in prolonged regimes of self-paced cycling. These effects would have been of a greater magnitude if the compliance to the program was higher.

We did not find improvement on functional mobility or functional independence in the participants. The TUG and KI scores obtained indicated a low functional mobility and a moderate impairment of ADL performance. In accordance with this, the participants could be considered as frail older adults (Robinson et al., 2013; Zasadzka, Borowicz, Roszak, & Pawlaczyk, 2015). In this population it has been found that functional mobility (as assessed by the TUG) are not significantly improved by exercising (Chou, Hwang, & Wu, 2012). Similarly, Giné-Garriga, Roqué-Figuls, Coll-Planas, Sitjá-Rabert & Salviá (2014) carried out a systematic review to determine the efficacy of exercise on improving performance-based measures of physical function in frail older adults and found no consistent effects of these type of interventions on the performance of ADL. Thus, the lack of effect on the functional mobility and independence may be related to the characteristics of the sample.

Finally, fall risk did not seem to be affected by the proposed intervention, a finding that is in accordance with the lack of improvement in the functional mobility. The characteristic of the participants as well as the type of exercise performed may explain the absence of significant changes observed on fall risk. On one hand, it has been stated that exercise interventions may only be effective for preventing falls in older adults with cognitive impairment (Guo, Tsai, Liao, Tu, & Huang, 2014). On the other, the training program proposed did not include strength or balance exercises which are key elements that, combined with endurance exercise, seem to be the best strategy to reduce falling risk rate (Cadore, 2013).

Finally, it should be mentioned that in this study there was a high drop-out rate, especially in the control group; this has been observed in other long duration studies performed in similar populations. (Van Schaik et al., 2014). Although it has been suggested that, in institutionalized persons, the factors associated with a higher probability of dropping out are older age, worse cognitive function, depression, and higher grade of disability (Beishuizen et al., 2017), in this study only this last factor showed a significant difference between the completers and non-completers. In addition, most dropouts were due to transfers to other residential-care facilities, disease or death; these reasons are frequent in other studies performed on residents in more than one facility (Mody et al., 2008).

Few studies have sought to identify the effects of self-paced cycling on older people; to the authors' knowledge, the present study is the first performed on people without cognitive impairmentt. Cancela, Pallín, Orbegozo & Ayán (2017) observed that self-paced cycling did not result in significant improvements on the functional mobility and functional autonomy in community dwelling people with mild cognitive impairment, a finding that implies that this strategy is not effective when trying to improving both aspects related to aging decline. Previous reports from this multicenter longitudinal study (Cancela, Ayán, Varela, & Seijo, 2016) showed that self-paced cycling was an effective strategy in order to improve cognitive status, memory, and functional mobility, but not functional autonomy in people with dementia.

In conclusion, the findings presented herein suggest that the performance of continuous long-term self-paced cycling seems to have a protective effect on the cognitive and executive function (specifically in attention, visual scanning, and processing speed) of institutionalized people without known cognitive impairment.

We acknowledge various limitations. First, the final sample size was relatively small. Second, due to its lengthy duration, the management of the intervention period was complex, and it was difficult to complete isolate those participants in other organized activity in their center; this may have influenced our results. Third, although according to the MEC baseline scores the participants included in the present study seemed to have a preserved cognitive function (Park, Hwang, Kim, & Park, 2017), the low scores observed both in the SDMT and in the FOME could indicate the possible existence of memory dysfunction. Therefore, the results may not be directly applicable to institutionalized individuals without cognitive dysfunction.

Finally, a follow-up period after the intervention ended could have provided information on the maintenance of the beneficial effects over a longer period.

Conclusion

The performance of continuous long-term self-paced cycling is an effective strategy to preserve cognitive and executive function in institutionalized older people without known cognitive impairment. In this population, other exercises modalities should be proposed in order to achieve significant changes on memory function, functional independence, functional mobility, and fall risk.

Acknowledgments

This work was supported by the program ''INCITE'' Consellería de Industria Xunta de Galicia, Spain (grant no. 09SEC001374PR).

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"Self-Paced Cycling Improves Cognition on Institutionalized Older Adults Without Known Cognitive Impairment: A 15-Month Randomized Controlled Trial" by Varela S, Cancela JM, Seijo-Martinez M, Ayán C
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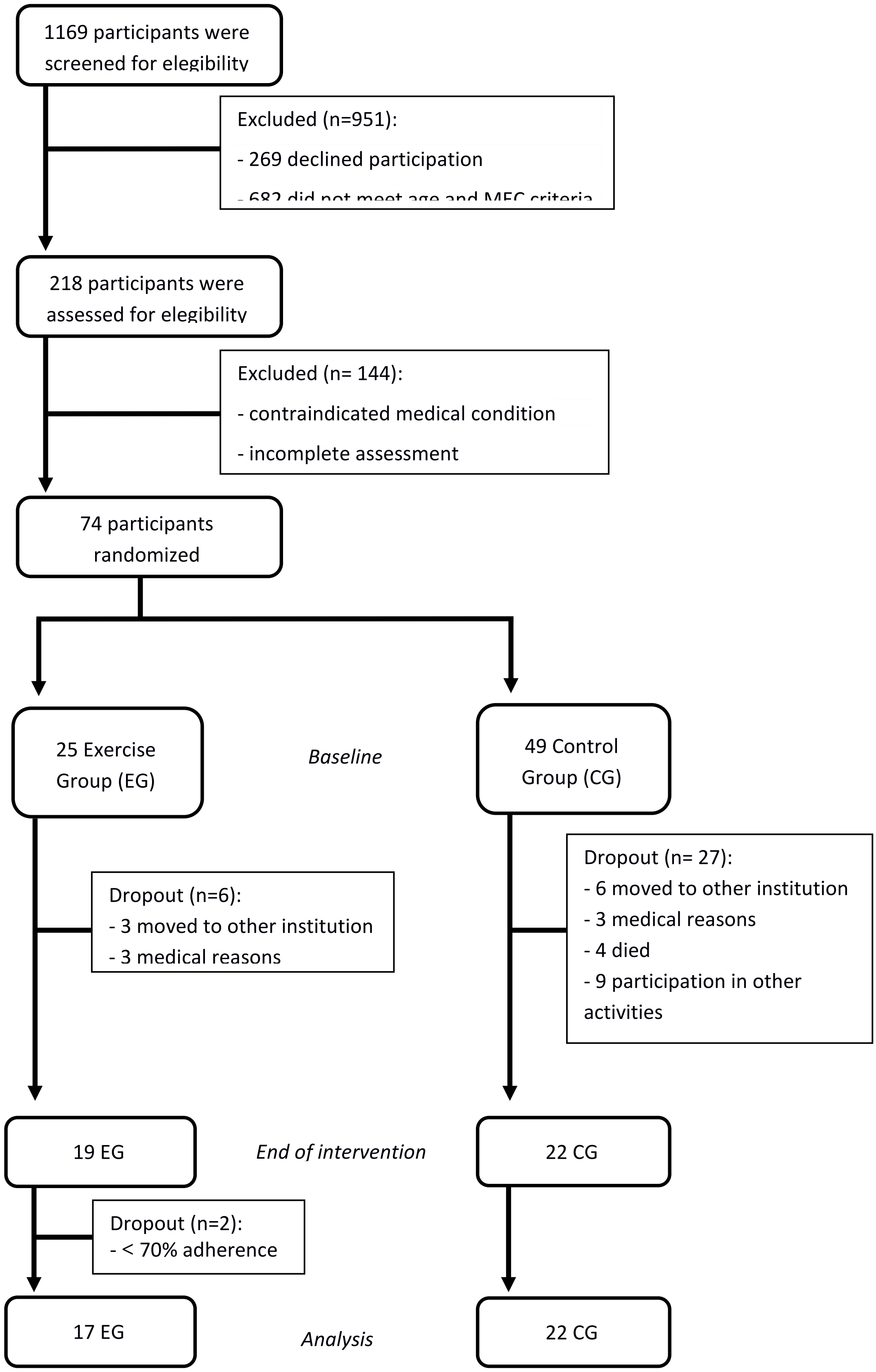

Figure 1: Flowchart for the number (n) of participants and sample loss.

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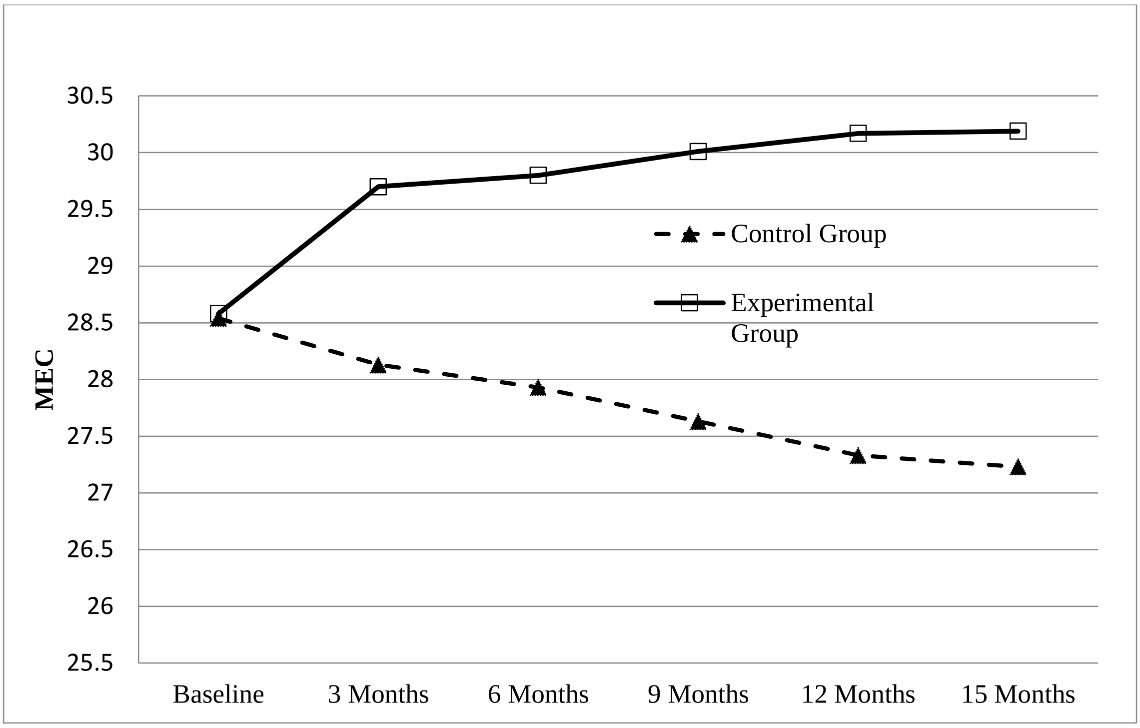

Figure 2: Cognitive status throughout the study.

"Self-Paced Cycling Improves Cognition on Institutionalized Older Adults Without Known Cognitive Impairment: A 15-Month Randomized Controlled Trial" by Varela S, Cancela JM, Seijo-Martinez M, Ayán C
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Table 1: Descriptive analysis of demographic, medical and medications.

	Baseline			
	%; mean±sd		Comparison of Group Means (P value)	
	Control (n=22)	Experimental (n=17)	t/ χ^2	*p*
Age (Years)	83.59±7.05	77.94±8.79	t=1.063	.298
Gender (Female)	31.81%	47.05%	χ^2=1.254	.263
Education level				
No studies	18.20%	23.50%		
Primary	54.50%	47.10%		
Secondary	13.60%	23.50%	χ^2=3.766	.288
University	13.60%	-		
No report	-	5.90%		
Main pathologies				
First	HBP	HBP		
Second	Cardiovascular disorder	Diabetes I-II		
Third	Diabetes I-II	Schizophrenia	χ^2=16.667	.546
Fourth	Arthrosis / arthritis	Cardiovascular disorder		
Fifth	Depression / Anxiety	Depression / Anxiety		
Medication				
Antihypertensive/betablockers	40.91%	38.10%		
Antidepressants	13.64%	14.29%		
Diuretics	18.18%	14.29%		
Hypnotic, anxiolytics, sedatives	13.64%	19.05%		
Oral hypoglycemic	27.27%	33.33%		
NSAIDS	18.18%	9.52%	χ^2=21.875	.347
Bronchodilators	9.09%	4.76%		
Lntiarrthymics	31.82%	33.33%		
Laxatives	4.55%	9.52%		
Antiparkinsonian	9.09%	4.76%		
Corticosteroids	4.55%	4.76%		

Abbreviation. HBP: High blood pressure; t= unpaired Student's t- test; χ^2= chi squared test.

Note. *p* <. 05

Table 2: Inferential analysis using ANOVA (2X2) of the benefits that the long-term physical exercise program provoked in the experimental group. Complete-case analysis.

	Control MEC>24 n= 22		Experimental MEC>24 n=17		
	Pre	Post	Pre	Post	F; *p*
Global Cognition (MEC)	28.54±2.80	27.23±3.42	28.58±2.50	30.19±3.77*	$F_{(1,38)}$=2.826; *p*=.03
Fuld object Memory					
Encoding memory	23.86±14.33	21.80±13.21	26.17±14.32	27.00±11.71	$F_{(1,38)}$=0.725; *p*=.39
Symbol Digit Modality Test	7.71±5.35	6.66±4.04	9.15±7.69	10.03±7.33*	$F_{(1,38)}$=1.004; *p*=.04
Neuropsychiatric Symptoms (NPI)	5.06±4.04	4.35±3.85	5.50±3.15	4.18±3.89	$F_{(1,38)}$=0.449; *p*=.50
Katz Index	1.36±1.81	1.50±2.02	1.29±1.57	1.18±1.98	$F_{(1,38)}$=0.002; *p*=.96
Functional Mobility (TUG)	21.80±10.93	21.97±6.57	19.47±9.72	19.20±8.93	$F_{(1,38)}$=0.537; *p*=.46
Falls	1.85±0.37	1.50±0.51	1.40±0.51	1.00±0.35	$F_{(1,38)}$=0.526; *p*=.47

Abreviations: MEC: Mini-Examen Cognoscitivo; TUG: Timed-up-and-Go test; NPI: Neuropsychiatric Inventory.

Note. Values are expressed as Mean ± SD; **p* <. 05.

Table 3: Inferential analysis using ANOVA/ANCOVA (2x2) of the benefits that the long-term physical exercise program provoked in the experimental group. Intention to treat analysis.

	Intention to Treat											
	Control n=49		Experimental n=25		Mean Difference From Baseline (95% CI)		Group Difference ANOVA(2x2)			Group Difference ANCOVA(2x2)[a]		
	Pre	Post	Pre	Post	Control	Experimental	$F_{(1.38)}$	*p*	ES	$F_{(1.74)}$	*p*	ES
Global Cognition (MEC)	28.29±2.14	26.32±1.89	28.35±2.33	30.36±2.47	-1.97 (-1.84 to -2.10)	2.01 (1.98 to 2.04)	3.435	.01	.031	5.987	.01	0.33
Fuld object Memory												
Encoding memory	23.45±12.35	19.91±12.12	24.15±13.15	25.28±13.56	-3.54 (-1.98 to -5.10)	1.13 (1.01 to 1.25)	2.124	.04	.030	2.789	.04	.031
Recall of episodic memory	9.65±7.10	9.33±6.97	10.11±8.08	10.36±8.88	-0.32 (-0.13 to -0.51)	0.25 (0.13 to 0.37)	1.267	.05	.012	1.987	.04	.021
Symbol Digit Modality Test	7.34±5.01	5.36±5.15	8.56±5.24	9.77±5.48	-1.98 (-0.86 to - 3.10)	1.21 (0.86 to 1.56)	2.132	.01	.029	2.678	.01	.033
Katz Index	4.61±1.99	4.05±1.67	4.40±2.33	4.75±2.01	-0.56 (-0.23 to -0.46)	0.35 (0.06 to 0.64)	0.456	.65	.011	0.657	.45	.015
Functional Mobility (TUG)	21.35±10.11	22.03±11.76	19.89±9.67	19.46±8.65	0.68 (0.28 to 1.08)	-0.43 (-0.25 to -0.61)	0.988	.30	.015	1.128	.25	.018
Falls	1.70±0.27	1.15±0.25	1.50±0.45	1.02±0.21	-0.55 (-0.17 to -0.93)	-0.48 (-0.24 to – 0.72)	0.777	.36	.021	0.967	.29	.025

Abreviations: MEC: Mini-Examen Cognoscitivo; TUG: Timed-up-and-Go test; NPI: Neuropsychiatric Inventory. ES: Effect Size-Eta square.

Note. Values are expressed as Mean ± SD; [a]Mixed-effect models with repeated measures and analysis of variance F test used. Covariables Including: age. gender. educational level. pathologies and baseline measure adjusted.