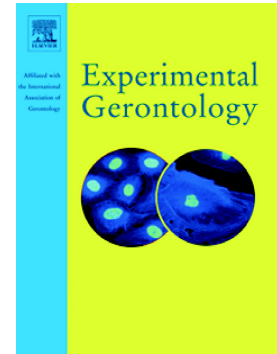


Functional and traditional training exercises improves muscle power and reduces proinflammatory cytokines in older women: A randomized controlled trial

Alan Bruno Silva Vasconcelos, Antônio Gomes de Resende-Neto, Albernon Costa Nogueira, José Carlos Aragão-Santos, Marcos Raphael Pereira Monteiro, Gilberto Santos Morais Junior, Gleiciane Gontijo Avelar, Enilton Aparecido Camargo, Otávio de Toledo Nóbrega, Marzo Edir Da Silva-Grigoletto



PII: S0531-5565(19)30774-0

DOI: <https://doi.org/10.1016/j.exger.2020.110920>

Reference: EXG 110920

To appear in: *Experimental Gerontology*

Received date: 5 November 2019

Revised date: 25 February 2020

Accepted date: 5 March 2020

Please cite this article as: A.B.S. Vasconcelos, A.G. de Resende-Neto, A.C. Nogueira, et al., Functional and traditional training exercises improves muscle power and reduces proinflammatory cytokines in older women: A randomized controlled trial, *Experimental Gerontology*(2018), <https://doi.org/10.1016/j.exger.2020.110920>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

FUNCTIONAL AND TRADITIONAL TRAINING EXERCISES IMPROVES MUSCLE POWER AND REDUCES PROINFLAMMATORY CYTOKINES IN OLDER WOMEN: A RANDOMIZED CONTROLLED TRIAL

Neuromuscular training improves muscle power and reduce inflammatory cytokines

Alan Bruno Silva Vasconcelos^{1#}; Antônio Gomes de Resende-Neto²; Albernito Costa Nogueira²; José Carlos Aragão-Santos¹; Marcos Raphael Pereira Monteiro²; Gilberto Santos Morais Junior³; Gleiciane Gontijo Avelar³; Enilton Aparecido Camargo¹; Otávio de Toledo Nóbrega³; Marzo Edir Da Silva-Grigoletto^{1,2}

¹Department of Physiology, Post Graduate Program in Physiology Sciences, Federal University of Sergipe, São Cristóvão, Brazil

²Department of Physical Education, Post Graduate Program in Physical Education, Federal University of Sergipe, São Cristóvão, Brazil

³Post-graduate Program in Health Sciences, University of Brasília (UnB-DF), Brasília, Brazil.

#Corresponding Author: Vasconcelos, ABS. Rua Ribeirópolis, nº 779, primeiro andar, Bairro Suíssa, Aracaju, Sergipe, Brazil. Phone number: +55 79 99112-5286 Email: abs.vasconcelos@gmail.com

Conflict of Interest: The authors declare no conflict of interest with the contents of this article.

Acknowledgments: The authors thank the Functional Training Group (FTG by UFS) from Department of Physical Education of Federal University of Sergipe for technical and methodological support; and “Conselho Nacional de Pesquisa e Desenvolvimento Científico” (CNPq). This study was financed in part by the “Coordenação de Aperfeiçoamento de Pessoal de Nível Superior” – Brasil (CAPES) – Finance Code 001. ABSV was a recipient of scholarship from CAPES and MRPM was a recipient of scholarship from FAPITEC/SE (Chamada MS/CNPq/FAPITEC/SE/SES – Nº 06/2018 – Programa pesquisa para o SUS: gestão compartilhada em saúde - PPSUS).

ABSTRACT

BACKGROUND: Aging is a natural process that, even in the nonattendance of complex diseases, is associated with a numerous behavioral change that attributes reduced muscle mass, power, strength and function. In addition, aging linked to low-grade inflammatory status, characterized by increased plasma concentrations of inflammatory cytokines such as TNF- α and IL-6. Physical exercise is the main non-pharmacological strategy for improving the physical fitness of the aged individuals. However, it is still controversial whether exercise can reduce aging-mediated inflammation. **OBJECTIVE:** To analyze the effects of functional (FT) and traditional (TT) training practice on muscle power and inflammatory profile in physically active older women. **METHODS:** The study has been performed for twenty-six weeks in which twenty-four weeks utilized for training sessions and two weeks for physical and biochemical assessments. Forty-three older women (age FT: 64.25 ± 4.70 , range: 60-75; TT: 64.90 ± 3.03 , range: 60-71; Control: 65.91 ± 5.79 , range: 60-75) were randomly divided into three groups: Functional (FT; n=16); Traditional (TT; n=16) training groups; and Control Group (CG; n=11) respectively. Muscle power tests were performed by push (Bench press) and squatting (Squat) actions. The jumping ability was performed through Counter Movement Jump (CMJ). In addition, Isometric strength were assessed by Hand Grip Test. Plasma cytokine concentration was measured using flow cytometry. **RESULTS:** Functional and traditional training activity sessions subjected to aged women demonstrated significant enhancement in their physical activity and muscle power. The trained individuals from above two groups showed significant improvements in all analyzed parameters excluding hand-grip. Functional and traditional training exercise reduced the plasma concentrations of TNF- α (FT: $p=0.0001$; TT: $p=0.0410$) and whereas FT group has reduced IL-6 ($p=0.0072$), but did

not affect the alterations of pre and post measurements of IL-2 (FT: $p=0.0651$; TT: $p=0.2146$) and IL-10 values (FT: $p=0.2658$; TT: $p=0.3116$). There was no significant difference in any of the test parameters between FT and TT groups. **CONCLUSION:** The functional and traditional training practices showed equivalent beneficial outcomes by increasing muscle strength and reducing systemic markers associated with inflammation.

KEYWORDS: Aging. Dynapenia. Inflamm-aging. Cytokines.

INTRODUCTION

Aging is a natural process that, even in the absence of disease, is associated with a variety of psychological and biological changes that can contribute to reduced muscle mass, power, strength and function, which leads to decreased ability to tolerate and recover from stressors, in addition to making the individual more vulnerable to falls and other accidents, for example (Fragala et al., 2019). Muscle power combines strength with speed and movement coordination, basic characteristics for performing basic daily tasks of the older people. In this perspective, declines in muscle power have been shown to be more important than muscle strength in the ability to perform daily activities (Byrne et al., 2016; Fragala et al., 2019).

In addition, aging appears to be linked to low-grade inflammatory status, characterized by increased plasma concentrations of inflammatory cytokines (Flynn et al., 2019). During the aging process there is a reduction in naive T cells and an increase in effector memory T cells (de Araújo et al., 2013; Xia et al., 2016). The continuous antigenic stimulation and associated clonal expansion and differentiation of effector T cells lead to the appearance of senescent T cells, these senescent cells have a high proinflammatory profile in blood and tissues, so they increase the release of cytokines such as TNF- α and IL-6 (de Araújo et al., 2013; Xia et al., 2016).

Other mechanisms may be related to this inflammatory process, such as chronic viral infections, such as cytomegalovirus, lead to an expansion and increased cytotoxicity of memory T cells and promote the release of proinflammatory cytokines, accumulation of intra-abdominal fat on white adipose tissue leads to activation of adipocytes and macrophages to secrete proinflammatory cytokines and oxidative stress also plays a major role in determining and maintaining the low-grade inflammation observed in aging (de Araújo et al., 2013; Xia et al., 2016). This condition has been defined as inflamm-aging and can make older people more susceptible to infections and even chronic diseases (Franceschi et al., 2006; Flynn et al., 2019).

Due to the undesirable physical consequences of aging, prevention strategies are necessary to promote a healthy and independent life. Neuromuscular stimulation with strength training has been consistently demonstrated as an effective way to attenuate physical fragility by improving muscle quality, bone density, insulin sensitivity, control of chronic health conditions, quality of life, psychological well-being and reduced risk of falls and fractures in the older people (Garatachea et al., 2015; Hunter et al., 2016). Strength training can improve the metabolic capacity of skeletal muscle, improving glucose homeostasis, preventing intramuscular lipid accumulation, increasing glycolytic enzyme capacity, increasing amino acid uptake and protein synthesis, and increasing anabolism in the older people (Fragala et al., 2019).

Although conventional methods show morphological and metabolic benefits clearly evidenced in the literature (Westcott, 2012), currently the prescription of fitness programs for the older people is focused on functional fitness to development and maintenance of daily activities (Liu et al., 2014; Nishimura et al., 2017). In this perspective, the functional training (FT) is based on the application of multisegmental exercises performed at maximum concentric speed and aims at the integrated

development of physical capabilities (muscle strength and power, dynamic balance, motor coordination, agility, flexibility and cardiovascular fitness) in order to promote multisystemic adaptations and ensure autonomy during the performance of daily functions (Resende-Neto, 2019).

Thus, FT is considered by many authors as the most promising method for promoting multisystemic adaptations and meeting the individual's daily needs, because of its basic premise of using resistance training not only for strength development but also for dynamic balance, motor coordination, flexibility, muscle power and cardiorespiratory endurance, aiming to increase the ability of individuals to perform daily activities safely and efficiently (Resende-Neto et al., 2019a; La Scala Teixeira et al., 2017).

However, the benefits of FT on reducing the inflammatory profile in older women are not well known in the current literature. Moreover, there is also a lack of investigations comparing FT with conventional methods on muscle power, making a more robust analysis of the neuromuscular responses found difficult. In addition, longitudinal studies with more than 16 weeks of training are also scarce. The objective of a 24-week training was to identify more clearly the chronic adaptations arising from the different strength training methods. As shown in a recent meta-analysis (Sardeli et al., 2018), few studies evaluating plasma concentration of inflammatory cytokines have a longer follow-up of 16 weeks. In addition, according to Sardeli et al. (2018) the reduction of proinflammatory cytokines is related to the increase in muscle mass in older women, so it was decided for an intervention period of 24 weeks, since Damas et al. (2018) suggests that the hypertrophic process is only accentuated after 20 weeks of strength training.

Thus, this clinical trial aimed to analyze the effects of functional and traditional training on muscle power and inflammatory profile in physically active older women. Our hypothesis is that functional training will be as efficient as traditional training for increasing muscle power and reducing plasma concentrations of proinflammatory cytokines in older women.

METHODS

Study Design

It is an experimental longitudinal study lasting twenty-six weeks, aiming to analyze two types of differentiated physical training, controlling the action of intervening factors and describing the behavior of the dependent variables this proposed clinical trial complies with the model proposed by CONSORT (<http://www.consort-statement.org>).

Sample

The intervention was publicized through leaflets, social networks and on the site of the local university, being necessary for participation, meeting the criteria: age over 60 years, having practiced some type of regular physical exercise in a period of six months prior to beginning of the study, presenting a medical fitness certificate and being physically independent. Among the women eligible for the research, the following exclusion criteria were adopted: hypertension \geq stage 2 (systolic \geq 160 mmHg and diastolic \geq 100 mmHg), uncontrolled cognitive and musculoskeletal disorders that could restrict the practice of high intensity exercises, being these criteria evaluated by a specialized medical team. The characterization data of the groups can be observed in table 1.

Table 1. Characteristics of participants. Values presented in mean and standard deviation ($M \pm SD$):

Variables	Control (n=11)	TT (n=16)	FT (n=16)	<i>p</i> value
Age (years)				
<i>Mean ± SD</i>	65.91 ± 5.79	64.88 ± 3.03	64.25 ± 4.70	
<i>CI 95%</i>	62.02 – 69.80	63.26 – 66.49	61.75 – 66.75	0.6426
Weight (kg)				
<i>Mean ± SD</i>	74.11 ± 12.02	71.69 ± 10.21	67.84 ± 11.32	
<i>CI 95%</i>	66.04 – 82.18	66.25 – 77.13	61.80 – 73.87	0.3398
Height (m)				
<i>Mean ± SD</i>	1.53 ± 0.04	1.56 ± 0.06	1.51 ± 0.04	
<i>CI 95%</i>	1.49 – 1.56	1.52 – 1.59	1.49 – 1.53	0.0575
BMI				
<i>Mean ± SD</i>	31.77 ± 5.75	29.62 ± 4.99	29.56 ± 4.41	
<i>CI 95%</i>	27.91 – 35.64	26.96 – 32.29	27.21 – 31.92	0.4657
Abdomen (C)				
<i>Mean ± SD</i>	100.30 ± 13.14	94.21 ± 10.99	91.66 ± 11.49	
<i>CI 95%</i>	91.48 – 109.10	88.35 – 100.10	85.53 – 97.78	0.1781
Waist (C)				
<i>Mean ± SD</i>	96.41 ± 14.61	89.31 ± 12.30	88.47 ± 14.47	
<i>CI 95%</i>	86.59 – 106.20	82.76 – 95.87	80.76 – 96.18	0.2997
Hip (C)				
<i>Mean ± SD</i>	106.2 ± 14.94	105.90 ± 8.38	100.50 ± 9.25	
<i>CI 95%</i>	96.12 – 116.20	101.40 – 110.30	95.57 – 105.40	0.0925
Waist-hip (r)				
<i>Mean ± SD</i>	0.90 ± 0.03	0.84 ± 0.09	0.87 ± 0.07	
<i>CI 95%</i>	0.88 – 0.93	0.79 – 0.89	0.83 – 0.91	0.1077
Medical history^a				
<i>Hypertension</i>	45.4%	37.5%	43.7%	0.9017
<i>Type 2 diabetes</i>	18.1%	12.5%	18.7%	0.8743
<i>Osteoarthritis</i>	18.1%	18.7%	12.5.7%	0.8743
<i>Dyslipidemia</i>	36.3%	37.5%	43.7%	0.9080

Note: BMI – Body mass index; C – Circumference; r – Ratio; SD – Standard Deviation. * $p < 0.05$ in comparison to control. # $p < 0.05$ in comparison to TT. One-way ANOVA followed by Bonferroni post hoc. ^aThe medical history were analyzed by the chi-square test with Yates's correction.

Thus, we used a block randomization design with blocks of size three to distribute equally forty-eight active older women according to their lower limb power in: Traditional Training (TT: n=16), Functional Training (FT: n=16) and Control Group (CG: n=16). In a spreadsheet in Excel software we organized the files from the best to the worst lower limb power values/results and we started from top to bottom the

distribution of the participants in the groups. We opted for this type of distribution to guarantee homogeneity of the groups. The allocation was concealed, performed by an independent researcher.

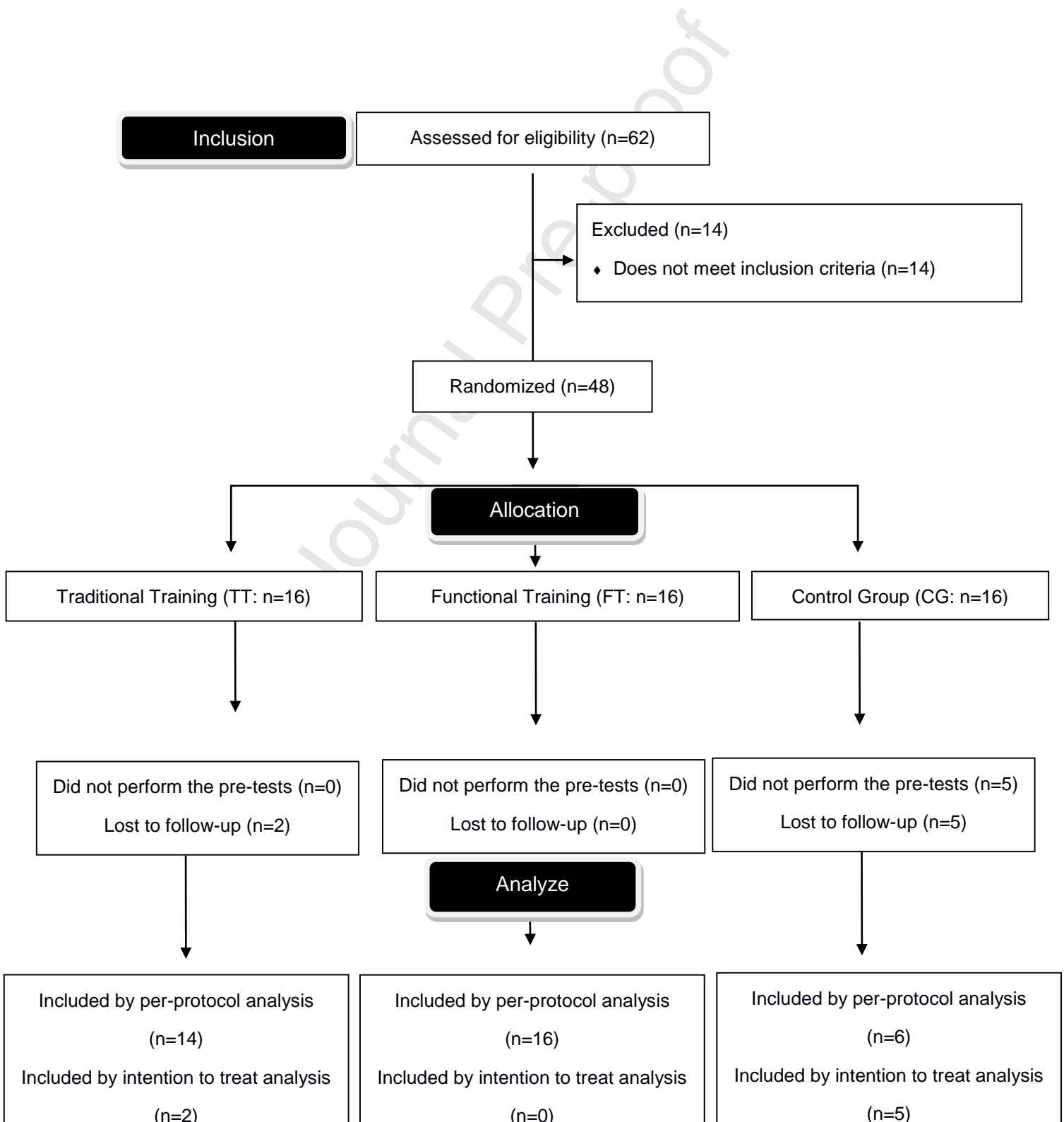


Figure 1. Sample procedure flowchart.

All participants were informed about ethical standards, objectives, procedures and risks related to the study and, after acceptance, signed the free and informed consent form. The data were kept anonymous and the Committee of the Federal University of Sergipe approved the accomplishment of the present study (CAAE: 96105118.6.0000.5546) and followed all the ethical aspects of the Declaration of Helsinki. This study is registered in the Brazilian Clinical Trials Registry (ReBEC) as RBR-89KCHG.

Exercise protocols

Participants in the experimental groups went through two weeks of familiarization and completed 72 training sessions. The 45-min sessions were performed three times a week, on non-consecutive days. The exercises were performed according to individual physical capacity and the effort was monitored and normalized during and after each training set by the OMNI-GSE scale (Da Silva-Grigoletto et al., 2013).

The FT participants performed exercises specific to their daily needs, each session being divided into four sets: (1) five min of mobility for the main joints (ankle, hip and glenohumeral) and general warm-up exercises that included ten repetitions of

squats and jumps; (2) 15 min of intermittent activities, organized in a circuit that demanded, mainly, agility, coordination, and muscular power (OMNI-GSE: 6-7); (3) 20 min of multiarticular exercises for lower and upper limbs, and intense recruitment of spinal stabilizing muscles, also organized in a circuit (OMNI-GSE: 7-8); and (4) five min of intermittent activities (Resende-Neto et al., 2019a).

In TT, the participants performed traditional exercises predominantly analytical in machines (Physicus, PLP, Auriflama, São Paulo, Brazil) and with isolated neuromuscular work, each session being also divided into four sets: (1) five min of mobility and general warm-up exercises; (2) 15 min of interval running (30 seconds running and 30 seconds walking) that mainly required muscular and cardiorespiratory endurance (OMNI-GSE: 6-7); (3) 20 min of resisted exercises for lower and upper limbs (squatting on the smith machine, articulated paddling, leg press 45°, vertical bench press, flexor table, forward pull, plantar flexion and stiff - OMNI-GSE: 7-8); (4) five min of intermittent activities (Resende-Neto et al., 2019a).

In the 3rd set, consisting of strength exercises performed at maximum concentric speed, the participants trained in groups (FT) or pairs (TT), being supervised by experienced physical education professionals, whose responsibility was to guarantee an optimal standard of safety and motivation. In the case of the TT group, the addition of external load during the training period was based on a score 6 (easy) on the OMNI-GSE scale and with maintenance of 08 to 10 repetitions submaximal. For the FT group, the criterion previously mentioned for addition of external load in the possible exercises and in those performed with the body mass itself was followed, biomechanical modifications were applied in the exercises, according to level of skill and comfort, also for maintenance of 8 - 10 repetitions. The training density was 30 seconds of work per 30 seconds of transition/recovery between stations.

In the intermittent exercises (4th Set), the Interval Run in a space of 30 meters was performed, the participants were divided into five groups; of these, three formed a column behind a cone and the other two formed another column at a distance of 20 meters. Working time consisted of walking the distance with maximum speed and recovery was achieved while the other participants in the group performed the sprints. The total volume was 8 to 12 sprints per individual. The exercise program follows conceptual aspects suggested by Resende-Neto et al. (2019a) and was recently tested in a randomized controlled clinical trial (Resende-Neto et al. 2019b) in which a detailed description of the exercises can be found.

Collection procedures

The evaluators were blinded to the intervention performed by the participants and the test battery was applied at the pre and post training moments. To minimize interference between the tests, they were distributed on two consecutive days. On the first day were collected anthropometric measurements and biological material. On the second day, muscle power and maximal isometric strength tests were applied. Pre collections were performed at least 48h before the beginning of training, while post collections at least 48h after the last training session.

Anthropometry: Body weight was determined using a clinical scale (Filizola®, São Paulo, Brazil), with a maximum capacity of 150 kg. Height (cm) was determined with a stadiometer (Sanny, ES2030, São Paulo, Brazil). Waist and hip perimeters were evaluated according to the World Health Organization's protocol.

Muscle power: the Smith machine was used, contemplating the functional actions of pushing and squatting, with a fixed and variable external load [Push (4,8 and 12 kg), Squat (10, 20 and 30 kg)] and the speed was determined using a linear encoder

(speedometer) connected to the central unit of a data analysis program (Musclelab®, 3050e, Oslo, Norway). Initially the participants warmed up to 10 repetitions without load in the bench press exercise and used 5 kg for the squat at moderate speed. After three mins they performed 3-5 repetitions at the maximum concentric speed for each mentioned load. The highest performing repetition was chosen as the end result (Lawton et al., 2006; Lohne-Seiler et al., 201). These kinds of measurements being used systematically in our research group's studies and have excellent reliability (Feitosa-Neta et al., 2016; Aragão-Santos et al., 2019).

Sit and stand up (five repetitions): The purpose of this test is to evaluate the time spent by the individual to sit and stand up from a chair five times, understanding that this measure is associated with the lower limbs power and reaction capacity of the older people. The test will be timed from the evaluator's command until the individual sits and stands up from the chair (without using arms) five times. Three attempts will be made and the shortest time recorded (Guralnik et al., 1994).

Counter movement jump: Initially the participants performed five squats and five jumps as warm-up. The test was performed from a static standing position, with the hands on the waist, performing the jump preceded by a counter-movement, which consisted of a downward acceleration of the center of gravity, bending the knees to 90°, this angle being observed and visually controlled by the evaluator. Participants were instructed to perform three jumps as fast as possible and as high as they could, with a one-min rest between attempts. The best value was computed (Markovic et al., 2004).

Maximum isometric strength: this parameter was determined by the manual dynamometer (Hand Grip Test - Jamar Plus + ®; Sammons Preston, Rolyon, Bolingbrook, IL), with three attempts of five seconds of maximum voluntary

contraction, performed slowly and gradually, being accepted as the final result the sum of the highest value obtained in each hand, divided by two (Sagiv et al., 1985; Figueiredo et al., 2007).

Cytokines assessment: Inflammatory parameters were assessed at baseline and 24 weeks of follow-up. Blood collected by venipuncture was distributed into EDTA anticoagulant tubes, sodium citrate and serum separation accelerator tubes. The samples were centrifuged and frozen at -80°C until thawed for evaluation of immunological mediators. Cytokine concentrations were assessed by a flow cytometry method using an immunoassay kit (Human TH1/TH2 CBA II Cytokine Kit, BD Biosciences®, San Diego, CA, USA), according to manufacturer's protocol to obtain measurements for 4 different circulating mediators: interleukin(IL)-2, IL-6, IL-10 and tumor necrosis factor (TNF)- α . Briefly, lyophilized cytokine standards and serum samples were processed and results obtained from the BD FACSCalibur flow cytometer, channel FL4. Three hundred events were acquired for each cytokine used. Data were analyzed using FCAP software, version 3.0 (BD Biosciences®, San Diego, CA, USA). Standard curves for each cytokine were generated using a standard mix of mediators provided. The concentration in each serum was determined by interpolation from the corresponding standard curve. Whenever a given cytokine was evaluated by both kits, the mean value obtained was considered. All calibration curves have a linearity coefficient (R^2) of 0.98 or higher (in many cases 0.99), this ensures that the reagents and machine used were in good condition and the trial went on reliably. The test had an intra-assay coefficient of variation of 26.2%.

Statistical analysis

Sample size was calculated using the G*Power program (Erdfelder, Faul and Buchner, 1996; Kiel, Germany - version 3.1.9.2) using the outcome variables lower limb muscle power from the results obtained by Aragão-Santos et al. (2018) and cytokine concentration from the results of Tomeleri et al. (2018) and Chupel et al. (2017), expecting an average 10% increase in muscle power and a minimum 10% reduction in proinflammatory cytokines. Thus, adopting a α level of 0.05 and a power (1 - β) of 0.80, it would be necessary to include at least 36 volunteers (13 participants for each group).

Data were tabulated and analyzed using the Statistical Package for Social Sciences software (SPSS - version 22), adopting a significance level of 5% ($p \leq 0.05$), and expressed as descriptive statistics with mean, standard deviation and percentage of change. Homogeneity was tested from the Levene test. When parametric, data were analyzed using a repeated measures ANOVA (3x2) followed by Bonferroni post-hoc test. Nonparametric data were analyzed by Kruskal-Wallis test followed by Dunn's multiple comparisons test. All tests were two-tailed and the effect size (ES) was calculated according to the methodological procedures defined by Cohen (2009). The values for interpreting the effect size are: < 0.19 insignificant; 0.20 – 0.49 small; 0.50 – 0.79 moderate; 0.80 – 1.29 big; > 1.30 very big. The results were analyzed in accordance with the principle of the intention to treat analysis, whereby the baseline measurement for each individual who withdrawal from the study was carried forward to postintervention (Gupta, 2011).

RESULTS

The average participation rate was 68 sessions of 72 and the sample loss was six participants. The TT and CG obtained two and four participants loss, respectively,

because did not perform the minimum number of sessions. The TT presented significant improvements in the all tests. The FT group showed improvement in all tests except handgrip. There was no significant difference in any of the tests between TT and FT groups (Table 2).

Journal Pre-proof

Variables	Control (n=11)		TT (n=16)		FT (n=16)		p value		
	Pre	Post	Pre	Post	Pre	Post	Interaction	Time	Group
Hand Grip (kgf)									
<i>Mean ± SD</i>	19.18 ± 4.22	19.05 ± 4.23	23.78 ± 3.92	25.03 ± 3.28	21.91 ± 4.41	22.94 ± 4.32	0.1210	0.0121	0.0062
<i>CI 95%</i>	16.34 – 22.02	16.20 – 21.89	21.69 – 25.87	23.28 – 26.78	19.55 – 24.26	20.63 – 25.24			
<i>ES %Δ</i>		0.04 -0.67		0.42 5.25		0.29 4.70			
CMJ (cm)									
<i>Mean ± SD</i>	7.96 ± 3.17	7.72 ± 3.19	12.59 ± 2.15	14.51 ± 2.88*#	12.96 ± 3.36	15.26 ± 3.92*#	0.0207	0.0007	<0.0001
<i>CI 95%</i>	5.83 – 10.10	5.57 – 9.86	11.44 – 13.74	12.97 – 16.04	11.17 – 14.75	13.17 – 17.35			
<i>ES %Δ</i>		0.09 -3.01		0.89 15.25		0.77 17.74			
Sit and stand up (s)									
<i>Mean ± SD</i>	8.90 ± 1.24	8.81 ± 1.28	7.71 ± 1.43	6.04 ± 1.35*#	7.32 ± 1.85	4.99 ± 1.04*#	<0.0001	0.0001	<0.0001
<i>CI 95%</i>	8.07 – 9.74	7.95 – 9.67	6.95 – 8.48	5.32 – 6.76	6.33 – 8.30	4.44 – 5.55			
<i>ES %Δ</i>		0.09 -1.01		1.48 -21.66		1.68 -31.83			
Bench press (W)									
4 kg									
<i>Mean ± SD</i>	28.51 ± 9.28	28.63 ± 7.87	36.21 ± 9.76	40.06 ± 9.54	34.73 ± 8.13	36.99 ± 9.21	0.2243	0.0174	0.0224
<i>CI 95%</i>	22.28 – 34.74	23.34 – 33.92	31.01 – 41.42	34.98 – 45.15	30.39 – 39.06	32.08 – 41.91			
<i>ES %Δ</i>		0.02 0.42		0.49 10.63		0.32 6.50			
8 kg									
<i>Mean ± SD</i>	45.11 ± 19.85	41.07 ± 12.75	54.14 ± 16.74	62.72 ± 16.09*#	51.63 ± 12.69	58.02 ± 16.30*	0.0020	0.0105	0.0410
<i>CI 95%</i>	31.77 – 58.44	32.51 – 49.64	45.22 – 63.06	54.14 – 71.29	44.86 – 58.39	49.33 – 66.70			
<i>ES %Δ</i>		0.27 -8.95		0.64 15.84		0.52 12.37			
12 kg									
<i>Mean ± SD</i>	51.90 ± 13.26	52.61 ± 13.40	63.80 ± 20.90	70.55 ± 19.84	61.57 ± 19.95	66.53 ± 20.30	0.2746	0.0077	0.1098
<i>CI 95%</i>	42.99 – 60.81	43.61 – 61.61	52.66 – 74.94	59.98 – 81.12	50.94 – 72.20	55.72 – 77.35			
<i>ES %Δ</i>		0.07 1.36		0.41 10.57		0.30 8.05			
Squat (W)									
10 kg									
<i>Mean ± SD</i>	48.68 ± 11.75	47.95 ± 11.02	70.95 ± 16.02	77.49 ± 20.06*#	67.42 ± 16.73	76.13 ± 20.30*#	0.0159	0.0004	0.0005
<i>CI 95%</i>	40.79 – 56.58	40.54 – 55.35	62.41 – 79.49	66.80 – 88.18	58.50 – 76.33	65.31 – 86.95			
<i>ES %Δ</i>		0.08 -1.49		0.43 9.21		0.57 12.91			
20 kg									
<i>Mean ± SD</i>	83.44 ± 21.54	82.30 ± 20.70	120.7 ± 21.53	133.3 ± 26.39*#	117.30 ± 29.88	125.70 ± 32.08*	0.0250	0.0014	0.0002
<i>CI 95%</i>	68.97 – 97.90	68.40 – 96.20	109.2 – 132.1	119.2 – 147.4	101.40 – 133.20	108.60 – 142.80			
<i>ES %Δ</i>		0.07 -1.36		0.63 10.43		0.33 7.16			

30 kg

<i>Mean</i> ± <i>SD</i>	119.8 ± 42.77	121.1 ± 43.38	130.8 ± 33.44	172.3 ± 40.17	151.0 ± 33.27	109.1 ± 33.32	0.0730	0.0003	0.0084
<i>CI 95%</i>	91.01 – 148.5	90.44 – 151.7	137.6 – 175.7	151.1 – 193.9	133.9 – 169.3	151.2 – 186.9			
<i>ES</i> % Δ		0.04 1.08		0.51 10.01		0.64 11.54			

* $p < 0.05$ in comparison to pre-test # $p < 0.05$ in comparison to control group post-test. Two-way ANOVA followed by Bonferroni post hoc.

Journal Pre-proof

The TT and FT groups reduced the plasma concentrations of TNF- α and IL-6 cytokines, but did not change IL-2 and IL-10 values when comparing the pre and post-training. There was no significant difference in any of the tests between groups (Figure 2).

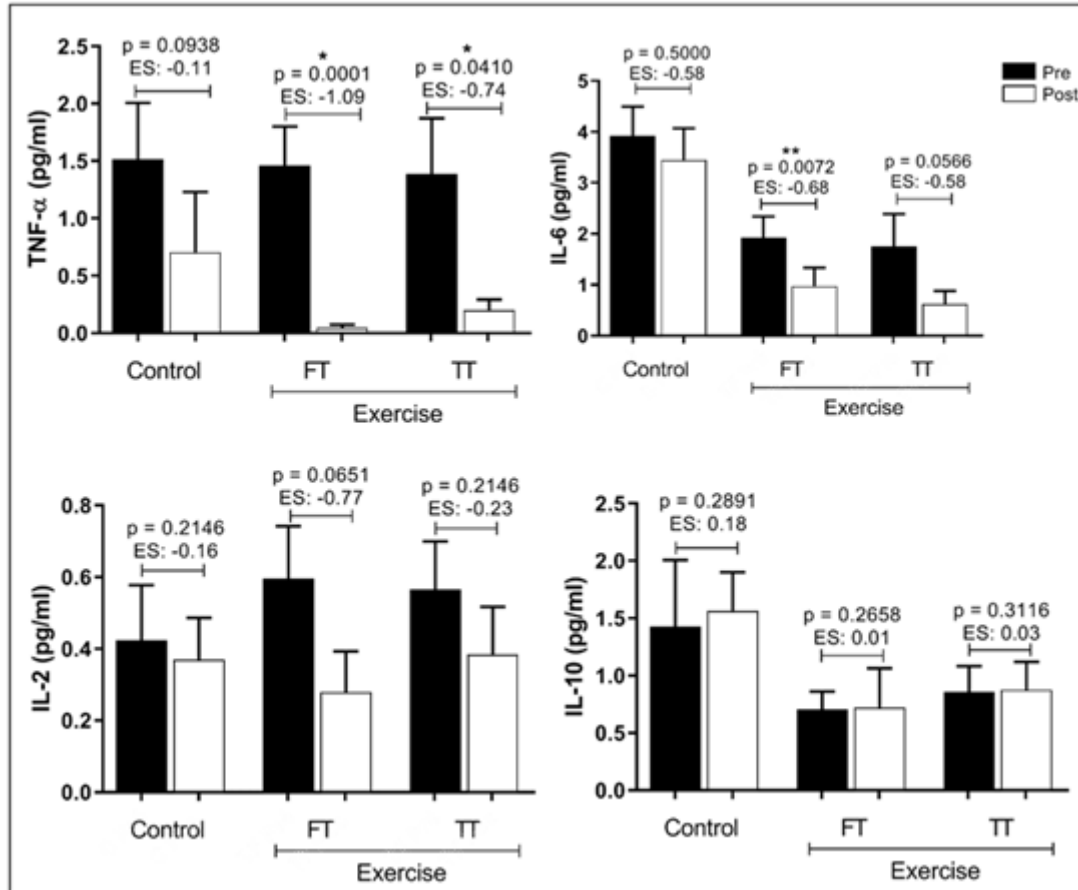


Figure 2. Plasma concentration of cytokines collected pre and post 24 weeks of functional (FT) or traditional (TT) training. The control group did not undergo a training protocol. * $p < 0.05$ in comparison to pre-test. Kruskal-Wallis test followed by Dunn's multiple comparisons test.

DISCUSSION

The results from this study confirmed previous concept that neuromuscular exercise improve muscle strength and power-related physiological parameters, as well as reducing the concentration of inflammatory biomarkers in older women (Lera Orsatti et al., 2014; Nunes et al., 2016; Tomeleri et al., 2018), while adding important

information regarding the effect of functional training practices on inflammatory biochemical markers. It was observed that both TT and FT practices promoted improvement of handgrip strength, jumping capacity, functionality and muscle power. In addition, a valued reduction in plasma concentration of proinflammatory cytokines such as, TNF- α and IL-6 detected.

It was well understood from the earlier literature's that both FT and TT practices promoted favorable enhancement in the functionality of senior women, including better muscle strength and physical phenomenon like fall risk, balance, and gait ability (Cadore et al., 2013; Lohne-Seiler et al., 2013; Liu et al., 2014; Bouaziz et al., 2016; Aragão-Santos et al., 2019).

Muscles are more likely to undergo physiological changes due to aging activity, hence, it reasoned to be the foremost index of weakened functionality (Reid and Fielding, 2012). The muscle power was evaluated through specific tests and indirectly by jumping ability. This capacity undergoes faster decreases than the maximum strength during the senescence process and its improvement is associated with functionality in the older people (Pereira et al., 2012; Reid and Fielding, 2012; Cadore et al., 2014). The present study data showed that both training protocols improved jumping ability, suggesting with better muscle powerfulness. This result seems coherent, considering that TT and FT have common characteristics, such as the multicomponent work and the maximum concentric velocity that can justify the positive adaptations (Ramírez-Campillo et al., 2014; Cadore and Izquierdo, 2018) to older women.

The handgrip strength presents a gradual and expressive decline after the age of 45 and reduction in the handgrip strength values are predictors of mortality and disability (Frederiksen et al., 2006; Bohannon, 2008). In our study, there is no significant difference in the results were found between the experimental and control

groups after the training practices intervention, supporting the previous findings of Fidelis et al. (2013) who elaborated that there was no significant difference in hand grip capability data between practitioners and non-practitioners of undergone physical test.

Our results demonstrated that FT-granted group showed a significant difference in the plasma concentrations levels of the IL-6 and TNF- α compared to the control group, while TT-applied group significantly reduced TNF- α and slightly decreased the IL-6 concentrations in comparison with subjects from control group. The both trained groups exerted no effects on IL-10 and IL-2 modulation. The above regulations in inflammatory cytokines profiles will reduce the inflammatory-mediated reactions and bring down the risk of morbidity and enhance the quality of life in the older people (Flynn et al., 2019).

TNF- α take part in muscle degradation process and induced the production of other cytokines such as IL-6 which play a vital role in weakening of muscle mass, strength and power. The other reliable factors could also pay way to the reduction in inflammatory markers of older subjects, including diminution in body fat composition and enhanced muscle activity.

It was well hypothesized in the earlier literature that physical exercise has capacity to reduce and lessen proinflammatory cytokines (Flynn et al., 2019; Macêdo Santiago et al., 2018; Sardeli et al., 2018), however, regarding IL-10 modulation, our study interrelated the former findings of Campo et al. (2015) who reinforced that there was no differences occurred in IL-10 concentration during a physical exercise training sessions in female cancer survivors. Regarding IL-2 modulation, our findings corroborate those of Kara et al. (2011) where young individuals were evaluated and no IL-2 modulation was found through physical exercise alone, being this modulation dependent on zinc supplementation.

However, our work mainly focused in analyzing the regulatory effect of proinflammatory cytokines in functional training practices, which based upon the principles of sports training with the intention of improving the individual's body function (Da Silva-Grigoletto et al., 2014; Stenger, 2018). The findings of this study should be considered with caution that few limitations are observed, such as test samples from healthy older women undergone training sessions were analyzed and interpreted, and this study did not validate the conception for older people possessing health disorders linked with loss of physical activity or distorted biochemical status. In addition, this study comprise physically active elderly women, capable of supporting high-intensity and high-volume training practices. Finally, the groups did not start the study with the same number of individuals, which can be considered a limitation.

It is worthwhile to highlight the importance of further studies analyzing the ability of physical exercise to modulate cytokines in older people with chronic diseases, such as diabetes, cancer and rheumatoid arthritis.

CONCLUSION

The functional and traditional training are efficient in improving the muscle power of physically active older women. The present study showed also that both training protocols with their particulars are effective in reducing systemic markers of aging-related inflammation. Thus, this work offers new alternatives for professionals in the field and can contribute to a better efficiency of health promotion programs through physical exercises.

REFERENCES

- Aragão-Santos, J. C., De Resende-Neto, A. G., Nogueira, A. C., Feitosa-Neta, M. de L., Brandão, L. H., Chaves, L. M., et al. (2019). The effects of functional and traditional strength training on different strength parameters of elderly women: a randomized and controlled trial. *J. Sports Med. Phys. Fitness* 59. doi:10.23736/S0022-4707.18.08227-0.
- Bohannon, R. W. (2008). Hand-grip dynamometry predicts future outcomes in aging adults. *J. Geriatr. Phys. Ther.* 2001 31, 3–10.
- Bouaziz, W., Lang, P. O., Schmitt, E., Kaltenbach, G., Geny, B., and Vogel, T. (2016). Health benefits of multicomponent training programmes in seniors: a systematic review. *Int. J. Clin. Pract.* 70, 520–536. doi:10.1111/ijcp.12822.
- Byrne, C., Faure, C., Keene, D. J., and Lamb, S. E. (2016). Ageing, Muscle Power and Physical Function: A Systematic Review and Implications for Pragmatic Training Interventions. *Sports Med.* 46, 1311–1332. doi:10.1007/s40279-016-0489-x.
- Cadore, E. L., Casas-Herrero, A., Zambom-Ferraresi, F., Idoate, F., Millor, N., Gómez, M., et al. (2014). Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. *AGE* 36, 773–785. doi:10.1007/s11357-013-9586-z.
- Cadore, E. L., and Izquierdo, M. (2018). Muscle Power Training: A Hallmark for Muscle Function Retaining in Frail Clinical Setting. *J. Am. Med. Dir. Assoc.* 19, 190–192. doi:10.1016/j.jamda.2017.12.010.
- Cadore, E. L., Rodríguez-Mañas, L., Sinclair, A., and Izquierdo, M. (2013). Effects of Different Exercise Interventions on Risk of Falls, Gait Ability, and Balance in Physically Frail Older Adults: A Systematic Review. *Rejuvenation Res.* 16, 105–114. doi:10.1089/rej.2012.1397.
- Chupel, M. U., Direito, F., Furtado, G. E., Minuzzi, L. G., Pedrosa, F. M., Colado, J. C., et al. (2017). Strength Training Decreases Inflammation and Increases Cognition and Physical Fitness in Older Women with Cognitive Impairment. *Front. Physiol.* 8, 377. doi:10.3389/fphys.2017.00377.
- Cohen, J. (2009). *Statistical power analysis for the behavioral sciences*. 2. ed., reprint. New York, NY: Psychology Press.
- Da Silva-Grigoletto, M. E., Brito, C. J., and Heredia, J. R. (2014). Treinamento funcional: funcional para que e para quem? *Rev. Bras. Cineantropometria E Desempenho Hum.* 16, 714. doi:10.5007/1980-0037.2014v16n6p714.
- Da Silva-Grigoletto, M., Viana-Montaner, B. H., Heredia, J. R., Mata, F., Peña, G., Brito, C., et al. (2013). Validación de la escala de valoración subjetiva del esfuerzo OMNI-GSE para el control de la intensidad global en sesiones de objetivos múltiples en personas mayores.

- Damas, F., Libardi, C. A., and Ugrinowitsch, C. (2018). The development of skeletal muscle hypertrophy through resistance training: the role of muscle damage and muscle protein synthesis. *Eur. J. Appl. Physiol.* 118, 485–500. doi:10.1007/s00421-017-3792-9.
- de Araújo, A. L., Silva, L. C., Fernandes, J. R., and Benard, G. (2013). Preventing or reversing immunosenescence: can exercise be an immunotherapy? *Immunotherapy* 5, 879–893. doi:10.2217/imt.13.77.
- Feitosa-Neta, M. de L., Resende-Neto, A. G., Dantas, E. H., Almeida, M. B., Wichi, R. B., and Da Silva-Grigoletto (2016). Effects of functional training on strength, muscle power and quality of life in pre-frail older women. *Motricidade* 12, 61–68.
- Fidelis, L. T., Patrizzi, L. J., and Walsh, I. A. P. de (2013). Influência da prática de exercícios físicos sobre a flexibilidade, força muscular manual e mobilidade funcional em idosos. *Rev. Bras. Geriatr. E Gerontol.* 16, 109–116. doi:10.1590/S1809-98232013000100011.
- Figueiredo, I. M., Sampaio, R. F., Mancini, M. C., Silva, F. C. M., and Souza, M. A. P. (2007). Test of grip strength using the Jamar dynamometer. *Acta Fisiátrica* 14. doi:10.5935/0104-7795.20070002.
- Flynn, M. G., Markofski, M. M., and Carrillo, A. E. (2019). Elevated Inflammatory Status and Increased Risk of Chronic Disease in Chronological Aging: Inflamm-aging or Inflamm-inactivity? *Aging Dis.* 10, 147. doi:10.14336/AD.2018.0326.
- Fragala, M. S., Cadore, E. L., Dorgo, S., Izquierdo, M., Kraemer, W. J., Peterson, M. D., et al. (2019). Resistance Training for Older Adults: Position Statement From the National Strength and Conditioning Association. *J. Strength Cond. Res.* 33, 2019–2052. doi:10.1519/JSC.0000000000003230.
- Franceschi, C., Bonafè, M., Valensin, S., Olivieri, F., De Luca, M., Ottaviani, E., et al. (2006). Inflamm-aging: An Evolutionary Perspective on Immunosenescence. *Ann. N. Y. Acad. Sci.* 908, 244–254. doi:10.1111/j.1749-6632.2000.tb06651.x.
- Frederiksen, H., Hjelmberg, J., Mortensen, J., Mcgue, M., Vaupel, J., and Christensen, K. (2006). Age Trajectories of Grip Strength: Cross-Sectional and Longitudinal Data Among 8,342 Danes Aged 46 to 102. *Ann. Epidemiol.* 16, 554–562. doi:10.1016/j.annepidem.2005.10.006.
- Garatachea, N., Pareja-Galeano, H., Sanchis-Gomar, F., Santos-Lozano, A., Fiuza-Luces, C., Morán, M., et al. (2015). Exercise Attenuates the Major Hallmarks of Aging. *Rejuvenation Res.* 18, 57–89. doi:10.1089/rej.2014.1623.
- Gupta, S. (2011). Intention-to-treat concept: A review. *Perspect. Clin. Res.* 2, 109. doi:10.4103/2229-3485.83221.
- Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., et al. (1994). A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J. Gerontol.* 49, M85-94.

- Hunter, S. K., Pereira, H. M., and Keenan, K. G. (2016). The aging neuromuscular system and motor performance. *J. Appl. Physiol.* 121, 982–995. doi:10.1152/jappphysiol.00475.2016.
- Kara, E., Ozal, M., Gunay, M., Kilic, M., Baltaci, A. K., and Mogulkoc, R. (2011). Effects of exercise and zinc supplementation on cytokine release in young wrestlers. *Biol. Trace Elem. Res.* 143, 1435–1440. doi:10.1007/s12011-011-9005-1.
- La Scala Teixeira, C. V., Evangelista, A. L., Novaes, J. S., Da Silva Grigoletto, M. E., and Behm, D. G. (2017). “You’re Only as Strong as Your Weakest Link”: A Current Opinion about the Concepts and Characteristics of Functional Training. *Front. Physiol.* 8, 643. doi:10.3389/fphys.2017.00643.
- Lawton, T. W., Cronin, J. B., and Lindsell, R. P. (2006). Effect of interrepetition rest intervals on weight training repetition power output. *J. Strength Cond. Res.* 20, 172–176. doi:10.1519/R-13893.1.
- Lera Orsatti, F., Nahas, E. A., Maestá, N., Nahas Neto, J., Lera Orsatti, C., Vannucchi Portari, G., et al. (2014). Effects of resistance training frequency on body composition and metabolics and inflammatory markers in overweight postmenopausal women. *J. Sports Med. Phys. Fitness* 54, 317–325.
- Liu, C., Shiroy, D. M., Jones, L. Y., and Clark, D. O. (2014). Systematic review of functional training on muscle strength, physical functioning, and activities of daily living in older adults. *Eur. Rev. Aging Phys. Act.* 11, 95–106. doi:10.1007/s11556-014-0144-1.
- Lohne-Seiler, H., Torstveit, M. K., and Anderssen, S. A. (2013). Traditional versus functional strength training: effects on muscle strength and power in the elderly. *J. Aging Phys. Act.* 21, 51–70.
- Macêdo Santiago, L. Â., Neto, L. G. L., Borges Pereira, G., Leite, R. D., Mostarda, C. T., de Oliveira Brito Monzani, J., et al. (2018). Effects of Resistance Training on Immunoinflammatory Response, TNF-Alpha Gene Expression, and Body Composition in Elderly Women. *J. Aging Res.* 2018, 1467025. doi:10.1155/2018/1467025.
- Markovic, G., Dizdar, D., Jukic, I., and Cardinale, M. (2004). Reliability and factorial validity of squat and countermovement jump tests. *J. Strength Cond. Res.* 18, 551–555. doi:10.1519/1533-4287(2004)18<551:RAFVOS>2.0.CO;2.
- Nishimura, R. A., Otto, C. M., Bonow, R. O., Carabello, B. A., Erwin, J. P., Fleisher, L. A., et al. (2017). 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 135. doi:10.1161/CIR.0000000000000503.
- Nunes, P. R. P., Barcelos, L. C., Oliveira, A. A., Furlanetto Júnior, R., Martins, F. M., Orsatti, C. L., et al. (2016). Effect of resistance training on muscular strength and indicators of abdominal adiposity, metabolic risk, and inflammation in

postmenopausal women: controlled and randomized clinical trial of efficacy of training volume. *AGE* 38, 40. doi:10.1007/s11357-016-9901-6.

Pereira, A., Izquierdo, M., Silva, A. J., Costa, A. M., Bastos, E., González-Badillo, J. J., et al. (2012). Effects of high-speed power training on functional capacity and muscle performance in older women. *Exp. Gerontol.* 47, 250–255. doi:10.1016/j.exger.2011.12.010.

Ramírez-Campillo, R., Castillo, A., de la Fuente, C. I., Campos-Jara, C., Andrade, D. C., Álvarez, C., et al. (2014). High-speed resistance training is more effective than low-speed resistance training to increase functional capacity and muscle performance in older women. *Exp. Gerontol.* 58, 51–57. doi:10.1016/j.exger.2014.07.001.

Reid, K. F., and Fielding, R. A. (2012). Skeletal muscle power: a critical determinant of physical functioning in older adults. *Exerc. Sport Sci. Rev.* 40, 4–12. doi:10.1097/JES.0b013e31823b5f13.

Resende-Neto, A. G. (2019). Conceptualizing the Functional Training Exercise for Older People. *Int. J. Phys. Med. Rehabil.* 7, 3. doi:10.4172/2329-9096.1000524.

Resende-Neto, A. G., Oliveira Andrade, B. C., Cyrino, E. S., Behm, D. G., De-Santana, J. M., and Da Silva-Grigoletto, M. E. (2019a). Effects of functional and traditional training in body composition and muscle strength components in older women: A randomized controlled trial. *Arch. Gerontol. Geriatr.* 84, 103902. doi:10.1016/j.archger.2019.103902.

Resende-Neto, A. G., Silva-Grigoletto, M. E. D., Santos, M. S., and Cyrino, E. S. (2016). Treinamento funcional para idosos: uma breve revisão. *Rev. Bras. Ciênc. E Mov.* 24, 167–177. doi:http://dx.doi.org/10.18511/rbcm.v24i3.6564.

Resende-Neto, A. G. de, Nascimento, M. A. do, SÁ, C. A. D., Ribeiro, A. S., Santana, J. M. de, and Silva-Grigoletto, M. E. da (2019b). Comparison between functional and traditional resistance training on joint mobility, determinants of walking and muscle strength in older women. *J. Sports Med. Phys. Fitness.* doi:10.23736/S0022-4707.19.09751-2.

Sagiv, M., Hanson, P., Besozzi, M., and Nagle, F. (1985). Left ventricular responses to upright isometric handgrip and deadlift in men with coronary artery disease. *Am. J. Cardiol.* 55, 1298–1302. doi:10.1016/0002-9149(85)90492-8.

Sardeli, A. V., Tomeleri, C. M., Cyrino, E. S., Fernhall, B., Cavaglieri, C. R., and Chacon-Mikahil, M. P. T. (2018). Effect of resistance training on inflammatory markers of older adults: A meta-analysis. *Exp. Gerontol.* 111, 188–196. doi:10.1016/j.exger.2018.07.021.

Silva, F. O. C. da, and Macedo, D. V. (2011). Exercício físico, processo inflamatório e adaptação: uma visão geral. DOI: 10.5007/1980-0037.2011v13n4p320. *Rev. Bras. Cineantropometria E Desempenho Hum.* 13, 320–328. doi:10.5007/1980-0037.2011v13n4p320.

Stenger, L. (2018). WHAT IS FUNCTIONAL/NEUROMOTOR FITNESS?: *ACSM's Health Fit. J.* 22, 35–43. doi:10.1249/FIT.0000000000000439.

Tomeleri, C. M., Souza, M. F., Burini, R. C., Cavaglieri, C. R., Ribeiro, A. S., Antunes, M., et al. (2018). Resistance training reduces metabolic syndrome and inflammatory markers in older women: A randomized controlled trial. *J. Diabetes* 10, 328–337. doi:10.1111/1753-0407.12614.

Westcott, W. L. (2012). Resistance Training is Medicine: Effects of Strength Training on Health. *Curr. Sports Med. Rep.* 11, 209–216. doi:10.1249/JSR.0b013e31825dabb8.

Xia, S., Zhang, X., Zheng, S., Khanabdali, R., Kalionis, B., Wu, J., et al. (2016). An Update on Inflamm-Aging: Mechanisms, Prevention, and Treatment. *J. Immunol. Res.* 2016, 1–12. doi:10.1155/2016/8426874.

HIGHLIGHTS

- ❖ Aging is associated with to reduced muscle mass, power, strength and function
- ❖ Aging is linked to increased plasma inflammatory cytokines such as TNF- α and IL-6
- ❖ Functional and traditional training improve the muscle power of older women
- ❖ Functional and traditional training reduces inflammatory cytokines of older women

Journal Pre-proof