J Musculoskelet Neuronal Interact 2023; 23(1):43-51

Journal of Musculoskeletal and Neuronal Interactions JMNI

Original Article

Cross education is modulated by set configuration in knee extension exercise

Juan Fariñas[1], Jessica Rial-Vázquez[1], Eduardo Carballeira[2], Manuel A. Giráldez-García[1], David Colomer-Poveda[2], Marta Sevilla-Sánchez[2], Gonzalo Márquez[2], María Rúa-Alonso[1], Iván Nine[1], Asier Aracama[1], Miguel Fernandez-del-Olmo[3], Eliseo Iglesias-Soler[1]

[1]Performance and Health Group, Department of Physical Education and Sport, Faculty of Sports Sciences and Physical Education, University of A Coruna, A Coruña, Spain;
[2]Department of Physical Education and Sport, Faculty of Sport Sciences and Physical Education, Campus Bastiagueiro, University of A Coruna, Oleiros, Spain;
[3]Area of Sport Sciences, Faculty of Sports Sciences and Physical Education, Center for Sport Studies, King Juan Carlos University, Madrid, Spain

Abstract

Objectives: The main aim of this study was to determine the effects of set configuration during five weeks of unilateral knee extension resistance training on untrained knee extensors performance. **Methods**: Thirty-five subjects were randomly assigned to traditional training (TTG; n=14), rest-redistribution (RRG; n=10) and control group (CON; n=11). TTG and RRG groups trained the dominant knee extensors twice a week with the 10-repetition maximum (RM) load. TTG performed four sets of eight repetitions with three min-rest between sets and RRG 32 repetitions with 17.4 seconds of rest between each one. Before and after interventions, anthropometry, muscle thickness (MT), pennation angle (PA), 1RM, number of repetitions with 10RM pretest load (N10RM), maximum propulsive power (MPP) and maximum voluntary isometric contraction (MVIC) were measured. **Results**: 1RM of the untrained leg increased only in the TTG group ($p<0.001$, 10.3% compared with Pre-test). 1RM, MPP and N10RM increased in the trained leg in both TTG ($p<0.001$) and RRG ($p<0.001$). No changes occurred in MT or PA. **Conclusions**: These results suggest that, when it is not possible to perform bilateral exercises (e.g., leg injury), traditional set configurations should be recommended to improve maximal voluntary force in the untrained leg.

Keywords: Cross Education, Set Configuration, Unilateral Strength Training, Untrained Limb

Introduction

Unilateral resistance training (RT) increases maximal voluntary force of the trained muscles and also the untrained homologous contralateral muscles, a phenomenon known as cross-education (CE)[1,2]. Because CE is not usually accompanied by increases in muscle mass of the untrained homologous muscles, it is believed that adaptations in the untrained hemisphere underlie this phenomenon, which may arise from the subtle but concurrent activation of the untrained hemisphere during the unilateral contractions[1-3]. CE occurs in upper and lower limb, regardless of sex and age and with isometric, concentric, and eccentric RT[4,5]. The overall magnitude of CE is estimated to be around 12% of the baseline force value[5], although there are several training variables that could modify the benefits that the untrained limb gets from unilateral RT[6,7].

It has been recently shown that CE occurs only after high- (75% of one repetition maximum (1RM)) but not low-load unilateral RT (25% of 1RM), suggesting that training load could influence the magnitude of CE[8]. Similarly, the type of

The authors have no conflict of interest.

Corresponding author: Eliseo Iglesias-Soler, Performance and Health Group, Department of Physical Education and Sport, Faculty of Sports Sciences and Physical Education, University of A Coruna, A Coruna, Spain.
Facultade de Ciencias do Deporte e a Educación Física. Avda. Ernesto Che Guevara, 121 - Pazos-Liáns 15179, Oleiros, A Coruña
E-mail: eliseo.iglesias.soler@udc.es

Edited by: G. Lyritis
Accepted 12 September 2022

contraction could influence CE. Indeed, eccentric, compared with concentric or isometric contractions, results in greater CE[5,9]. It has been speculated that the greater CE with high-load and/or eccentric unilateral RT could be related to the greater untrained hemisphere activation or reductions regarding corticospinal inhibition occurring during high-intensity or eccentric contractions, thus increasing the adaptations experienced by the untrained hemisphere[2,10].

Another factor influencing the amount of ipsilateral hemisphere activation that could modify CE is the evolution of fatigue during unilateral contractions[11–13]. It has been shown that ipsilateral hemisphere activation increases during sustained fatiguing contractions[13], thus suggesting that fatiguing RT protocols could enhance the magnitude of CE. Although fatigue is not a training variable *per-se*, it is influenced by the different training variables that conform the RT protocol, like for example, set configuration, which refers to the number of repetitions performed in each set with respect to the maximum feasible for a load[14]. In this regard, traditional set configurations performed to or close to muscle failure are associated with greater levels of fatigue compared with set configurations with more frequent inter-set rest intervals (i.e. Cluster set configurations), as indicated by the greater reductions in power and concentric velocity, greater blood lactate concentrations, greater blood pressure response and greater heart rate peaks[15–17].

However, despite the proved effect of fatigue during unilateral contractions over ipsilateral hemisphere activation[11], the influence of fatigue during unilateral RT protocols over CE is unclear. Previous studies comparing the effects of different set configurations over CE suggest that a minimum threshold of fatigue is needed to increase the maximal voluntary force of the untrained biceps brachii[1]. However, a recent study suggests that unilateral knee-extensor high-load RT to failure (3 sets to failure with a 75% of 1RM i.e., maximum amount of fatigue achievable for each set) does not enhance the magnitude of CE compared with a RT protocol in which only around half of the theoretical maximum number of repetitions were done (6x5, 75% of 1RM), suggesting that more fatigue does not always translate to greater CE. Although the discrepancies between studies about the influence of fatigue over CE could be related to different sensitivity of the untrained upper[1] or lower limb[8,14] to fatigue, these different conclusions may be consequence of the models of "high" or "low" fatigue set configurations used in each study. Indeed, in the study by Colomer et al.[8], the "low fatigue" RT protocol (6x5, 75% of 1RM) was very similar to the "high-fatigue" protocol tested in Fariñas et al.[1] (5x6 10RM). These loads were probably above the minimum threshold of fatigue needed to maximize CE. Therefore, is not possible to detect the effect of fatigue over CE and to conclude that fatigue does not influence CE on the lower limbs.

Therefore, the aim of the present study was to analyze the effect of two different set configurations equated in load, total volume and work-to-rest ratio but potentially leading to different levels of fatigue, on maximal voluntary isometric and dynamic force, muscle endurance and muscle architecture of the trained and untrained knee extensors after five weeks of unilateral RT. Specifically, we compared the effects of a traditional set configuration (Traditional training group (TTG), 4 sets of 8 repetitions with three minutes of rest between them) with those of a special type of cluster set configuration in which every repetition is interspersed by short rest intervals (Rest redistribution group (RRG), 32 repetitions with 10RM load and 17.4 seconds of rest between them). We hypothesized that very low fatigue experienced by the RRG[8] would constrain opportunities to achieve the stimulus threshold to produce strength increases in untrained limb, reducing the amount of CE compared with the TTG.

Material and Methods

Experimental design

A randomized controlled study was conducted in order to test the effect on CE of two unilateral RT training programs differing in set configurations but equated regarding load, total volume, total resting time and therefore with the same repetition-to-rest ratio.

Figure 1A shows the design of the study. Before the start of the intervention period subjects came five times to the laboratory (Pre-tests) where the following procedures were done: i) anthropometric measurements; ii) muscle architecture measurements using echography; iii) a dynamic knee extension progressive load test; iv) a maximal number of repetition test with a submaximal load (10RM test); and v) maximum voluntary isometric contractions tests (MVIC). After five weeks of RT subjects came again five times to the laboratory to repeat the same procedures (Post-tests). Variables obtained from each testing session are described below. All measurements were obtained in both limbs and order was randomized for Pre-test sessions and replicated in Post-test sessions with the difference in the 10RM test, where subjects were asked to perform as repetitions as they could with the 10RM pretest load (N10RM). Subjects performed three familiarization sessions before the Pre-test sessions in order to standardize body position during exercise and get familiarized with isometric (first session) and dynamic (second and third sessions) knee extensions.

After the Pre-test sessions, subjects were assigned to three groups following a randomized block design to warrant equity regarding sex distribution and baseline 1RM of dominant limb: i) the traditional training group (TTG; n=14), that performed a traditional set configuration program with sets close to muscular failure; ii) the rest redistribution group (RRG; n=10), that followed a rest redistribution set structure program in which the total resting time of each session was the same as for traditional program but divided in shorter resting bouts between each repetition[18]; and iii) a control group (CON; n=11) which continued with their daily habits for the duration of the study. Subjects of the experimental groups trained with their dominant leg twice per week during five weeks for a total of 10 training sessions with at least 48 hours of rest between sessions. The velocity performed in each repetition in test and intervention sessions was recorded

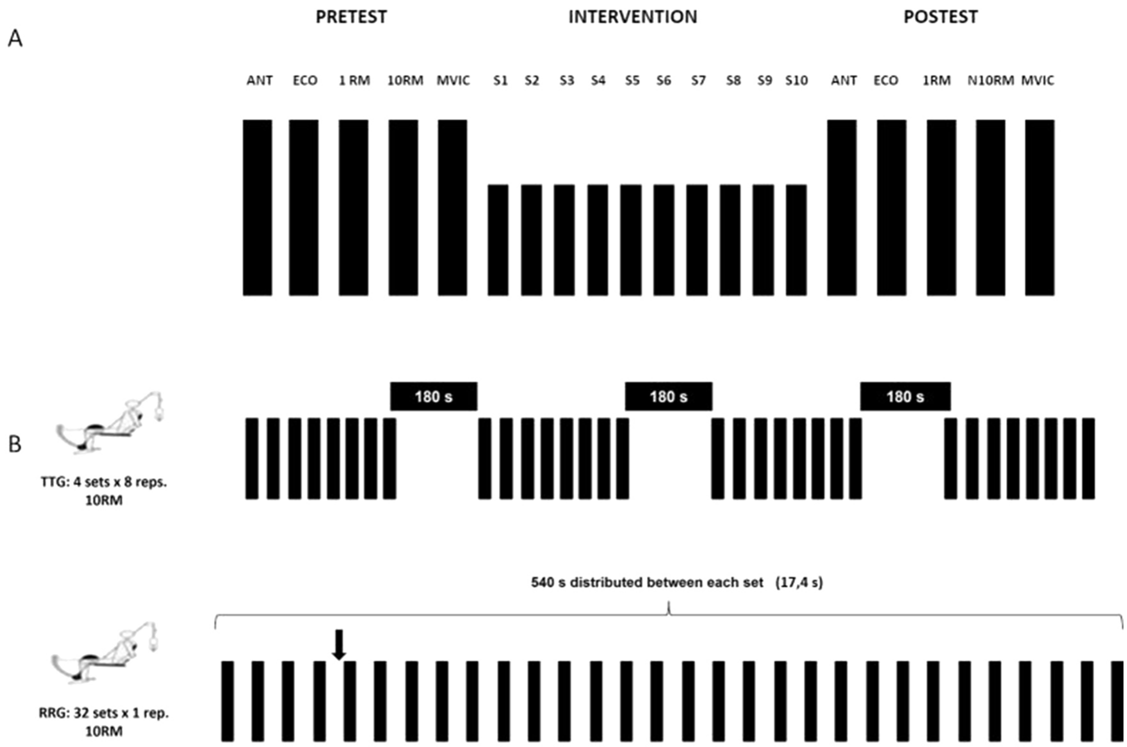

Figure 1. A) Study design; B) intervention protocols. TTG: traditional training group; RRG: Rest redistribution group; 10RM ten repetition maximum; Rep: repetition; ANT: anthropometric measurement; ECO: muscle architecture session; 1RM: one repetition maximum; 10RM: ten repetition maximum; MVIC: maximum voluntary isometric contraction; S=session.

using a linear velocity transducer (T-Force System; Ergotech, Murcia, Spain; sampled at 1kHz) and subjects were asked to perform each repetition at maximum intended velocity. T-force system gave us values as velocity, work, power and time under tension, which will be used for different analysis.

Subjects

Healthy sport science students (n=35, six women and 29 men; 23±2 years) without contraindications to perform resistance training volunteered for the study. All subjects were asked to refrain from alcohol, caffeine and nutritional supplements consumption and to keep their daily habits. Table 1 shows the main characteristics of the sample. Subjects signed a written informed consent with a detailed explanation of the process before starting the study. The study was approved by the local institutional ethical committee in full accordance with the Declaration of Helsinki for human experimentation.

Procedures

Anthropometric measurements

Body weight and height were measured with a calibrated digital scale (Omron BF-508, Omron Healthcare Co., Kyoto, Japan) and a stadiometer (Seca 202, Seca Ltd., Hamburg, Germany) respectively. Body mass index (BMI) was calculated as body mass divided by the height squared (kg·m^{-2}) and rounded to the nearest 0.1 kg·m^{-2}.

Muscle architecture

Muscle thickness (MT) and pennation angle (PA) were measured from images taken with a liner probe with a frequency of 13-8 MHz, using an ultrasound device (LGE Logiq e BT12, GE Healthcare, Milwaukee, WI, USA). Two images were taken: i) a transversal image at mid-belly of the vastus lateralis (VL) to analyze MT and ii) a longitudinal image in order to analyze PA. For MT, an average of 3 thickness measurements[19] along aponeurosis in a mid-belly image was taken using a motion analysis software (Kinovea 0.8.15, Kinovea.org, France). PA was measured from the angle formatted by deeper aponeurosis and muscle fiber using the same software.

One repetition maximum load test

All dynamic unilateral force measurements were performed in the same knee extension machine used for training (Technogym, Gambettola, Italy). Two belts were used to fix subjects to the machine by chest and hip. The hip was

Table 1. Subjects characteristics (mean±SD).

Variable	CON	RRG	TTG
n	11	10	14
Age (yr)	22 ± 2	22 ± 2	23 ± 3
Sex	2 ♀ 9 ♂	2 ♀ 8 ♂	2 ♀ 12 ♂
Weight (kg)	73 ± 10	74 ± 11	73 ± 9
Heigh (cm)	173 ± 7	174 ± 8	172 ± 7
BMI (kg·m^{-2})	25 ± 3	24 ±2	25 ± 2
Laterality	3 Left-footed 8 Right-footed	1 Left-footed 9 Right-footed	2 Left-footed 12 Right-footed

TTG: Traditional training group; RRG: rest redistribution group; CON: control group; BMI: body mass index. ♀: female; ♂: male.

at an angle of 90° to isolate the leg extensors muscles, and subjects were asked to cross their arms on their chest.

Unilateral knee extension 1RM load for each leg was measured with a progressive load test in which load increments were based on velocity loss[14]. Subjects performed 3 repetitions as fast as they could with 20 kg. The highest mean propulsive velocity (MPV) of the three repetitions was taken as maximum reference velocity. Initial load increments were of 10 kg and subjects performed three repetitions with each load until a 25% loss in MPV compared with the maximum reference velocity. Rest was of one minute between each load. Then, load increments were reduced to five kg and subjects performed two repetitions with each load until a velocity loss of 50% compared with the maximum reference velocity was observed. Rest was of two minutes between loads. Thereafter, load increments were reduced to 2.5 kg and single repetitions were done separated by three minutes of rest between progressive attempts until the 1RM was achieved. This progressive protocol also allowed us to identify the load associated with maximum mean propulsive power (MPP), taking for the analysis the maximum MPP obtained by the linear velocity transducer for this load. All this procedure has been previously used, with adequate levels of reliability for lower limbs[20].

Ten repetition maximum test

Subjects completed 10 repetitions with the 50% of the 1RM and rested for three minutes. Then, a first attempt was carried out with the 10RM load estimated during the familiarization sessions. If the subject performed more than 10 repetitions, the load was increased between two and five kg and a new trial was carried out after five minutes of rest. If the subject was not able to complete 10 repetitions, the load was reduced. Reliability of this protocol has been previously reported[14]. This test also allowed us to obtain the total work (10RMW) as summatory of the work performed in each repetition.

Maximum voluntary isometric contraction test

Since four subjects did not attend the Post-test evaluation of MVIC, the sample for this analysis was of 31 subjects. Knee and hip angles were fitted at 90° and ankles were fastened with two rigid straps to a force transducer (Digitimer Ltd., Welwyn Garden City, UK) to measure MVIC force (band-pass-filtered 5-2,500Hz, amplified x1,000 and sampled at 2kHz). Subjects performed three unilateral four-seconds MVICs with three minutes of rest between attempts. MVIC was defined as the greatest value recorded throughout this protocol.

Training protocols and records during sessions

Before each familiarization, testing and training session, the subjects warmed cycling 5 minutes at 80 revolutions per min on a cycle ergometer (Monark 828E; Monark Exercise AB, Vansbro, Sweden) with a resistance of 1.25W per kg of body mass.

Figure 1B shows a schematic view of the training protocols. Both training groups used a 10RM load, but TTG completed four sets of eight repetitions with three-min-rest between sets whereas RRG performed 32 repetitions with 17.4 seconds of rest between each repetition. To ensure accurate resting times, a verbal countdown was performed by controlling time with a handheld stopwatch during all sets[21]. The velocity performed in each repetition was recorded using a linear velocity transducer (T-Force System; Ergotech, Murcia, Spain; sampled at 1kHz). Only the velocity recorded during the propulsive phase was considered for further analysis. Propulsive phase was defined as the concentric phase period in which load acceleration (a) is above gravity acceleration (i.e., a> -9.81 m·s^{-2}). Additionally, this device allowed us to calculate the concentric time under tension (TUT) as the sum of the length of the concentric phase of all the repetitions. The whole of the range of motion was considered for this calculation (i.e., propulsive and non-propulsive phase) because during non-propulsive phase agonist muscles maintain a level of activation that may affect to the stimulus

Table 2. Changes in the performance of the untrained limb.

Variable	GRUPO	Pre-test ± SD	Post-test ± SD	Time	Group	Time×Group
1RM (kg)	CON	64.4 ± 19.4	64.4 ± 19.2	p=0.001	p=0.997	p=0.009
	RRG	64.0 ± 19.0	66.0 ± 19.2	$F_{1,32}$=12.293	$F_{2,32}$=0.002	$F_{2,32}$=5.493
	TTG	61.4 ± 16.0	67.4 ± 15.8*	η^2=0.284	η^2<0.01	η^2=0.262
N10RM (reps)	CON	10 ± 0	10 ± 1	p=0.139	p=0.038	p=0.052
	RRG	10 ± 0	10 ± 2	$F_{1,32}$=2.302	$F_{2,32}$=2.794	$F_{2,32}$=3.251
	TTG	10 ± 1	11 ± 1	η^2=0.069	η^2=0.191	η^2=0.173
10RMW (J)	CON	1601.6 ± 507.5	1627.5 ± 585.7	p=0.234	p=0.701	p=0.302
	RRG	1742.0 ± 434.3	1735.8 ± 623.9	$F_{1,32}$=1.476	$F_{2,32}$=0.256	$F_{2,32}$=1.245
	TTG	1678.5 ± 435.0	1872.6 ± 417.0	η^2=0.045	η^2=0.023	η^2=0.074
MPP (W)	CON	235.1 ± 70.6	243.9 ± 80.7	p=0.003	p=0.987	p=0.052
	RRG	233.7 ± 88.3	238.5 ± 90.5	$F_{2,32}$=10.271	$F_{2,32}$=0.013	$F_{2,32}$=3.254
	TTG	226.6 ± 70.4	256.0 ± 77.6	η^2=0.249	η^2=0.001	η^2=0.174
MVIC (N)	CON	1144.0 ± 324.1	1284.0 ± 339.2	p=0.019	p=0.953	p=0.742
	RRG	1188.2 ± 457.1	1249.6 ± 464.0	$F_{1,28}$=6.353	$F_{2,28}$=0.049	$F_{2,28}$=0.302
	TTG	1118.0 ± 414.7	1216.9 ± 446.9	η^2=0.209	η^2=0.004	η^2=0.025
MT (cm)	CON	2.5 ± 0.3	2.5 ± 0.4	p=0.212	p=0.380	p=0.101
	RRG	2.4 ± 0.3	2.6 ± 0.5	$F_{1,22}$=1.653	$F_{2,22}$=1.013	$F_{2,22}$=2.548
	TTG	2.7 ± 0.5	2.6 ± 0.5	η^2=0.07	η^2=0.084	η^2=0.188
PA (º)	CON	16.1 ± 2.5	16.0 ± 1.9	p=0.118	p=0.811	p=0.416
	RRG	16.0 ± 2.1	17.1 ± 2.0	$F_{1,22}$=2.641	$F_{2,22}$=0.211	$F_{2,22}$=0.913
	TTG	15.2 ± 2.5	16.6 ± 3.0	η^2=0.107	η^2=0.019	η^2=0.077

1RM: One repetition maximum; N10RM: repetitions with 10 repetition maximum Pre-test load; 10RMW: total work with 10RM load; MMP: maximum mean propulsive power; MVIC: maximum voluntary isometric contraction; MT: muscle thickness PA: pennation angle $p \leq 0.05$ *for post-hoc pairwise comparisons within the group; ** $p \leq 0.001$ for post-hoc pairwise comparisons within the group. Data are means ± SD.*

involved in the CE phenomenon. Mean propulsive velocity loss was used as indicator of fatigue[22], calculated as the difference between the first repetition and the last repetition of each training session[1], in order to compare the same number of repetitions between protocols, and expressed in both absolute (i.e., first repetition velocity-last repetition velocity) and relative ([(first repetition velocity-last repetition velocity)/first repetition velocity]×100) terms. At the end of each set (after eight grouped reps in RRG), when the eccentric phase of the last repetition was completed, subjects were asked to assign a value of the OMNI-RES scale to their perceived exertion[23]. RPE mean values of each session were calculated for further analysis.

Statistical analysis

Statistical analysis was performed with SPSS version 20 (IBM, Armonk, NY, USA). Sample descriptive values are shown as mean ± standard deviation (SD). Normality and homogeneity of variance between groups were confirmed for all variables by Shapiro-Wilk's and Levene's tests respectively. A one-way analysis of variance (ANOVA) was conducted to compare baseline characteristics (i.e. height, body mass, age and BMI) between groups. A t-test for independent samples was used to determine differences between groups during intervention sessions regarding mean velocity loss, RPE and TUT.

A two-way ANOVA with a repeated-measures factor (i.e. time) and interindividual factor (i.e. group) was performed for the following variables: 1RM, N10RM, 10RMW, MPP, MVIC, MT and PA. Effect sizes of ANOVA are presented as partial eta square (η^2) for each factor considering effects as low (η^2<0.06), mid (0.06≤η^2<0.14) and high (η^2≥0.14)[24]. When a significant interaction was detected, *post hoc t*-test with Bonferroni's adjustment was used. Furthermore, Hedge's *G* with corresponding 95% Confidence Interval (95% CI) were calculated to analyze the effect sizes of significant post-hoc pairwise comparisons when appropriate (i.e. if a significant time × group interaction was detected). The magnitude of the effect size was interpreted using the following scale[25]: trivial ($g \leq 0.2$), small ($0.2 \leq g \leq 0.5$), medium ($0.5 \leq g \leq 0.8$), and large ($g \geq 0.8$). The significance level was set at $p \leq 0.05$

Results

There were no significant baseline differences (p>0.05) between groups for height, body mass, age and BMI. The velocity loss from the first to the last repetition of each training

Table 3. Changes in the performance of the trained limb.

Variable	Group	Pre-test SD	Post-test ± SD	Time	Group	Interaction
1RM (kg)	CON	63.0 ± 18.8	63.2 ± 8.5	p<0.001 $F_{2,32}$=61.04 η^2=0.644	p=0.772 $F_{2,32}$=0.216 η^2=0.017	p<0.001 $F_{2,32}$=12.46 η^2=0.452
	RRG	63.6 ± 17.7	74.4 ± 20.2*			
	TTG	62.3 ± 17.0	70.7 ± 18.6*			
N10RM (reps))	CON	10 ± 0	10 ± 1	p<0.001 $F_{2,32}$=24.941 η^2=0.446	p=0.011 $F_{2,32}$=5.284 η^2=0.254	p=0.003 $F_{2,32}$=7.059 η^2=0.313
	RRG	10 ± 0	12 ± 2* ‡			
	TTG	10 ± 0.3	13 ± 2* ‡			
10RMW (J)	CON	1617.9 ± 479.8	1697.4 ± 530.7	p<0.001 $F_{2,32}$=45.173 η^2=0.593	p=0.324 $F_{2,32}$=1.168 η^2=0.07	p=0.003 $F_{2,32}$=6.907 η^2=0.308
	RRG	1668.8 ± 445.8	2262.6 ± 530*			
	TTG	1699.8 ± 483.7	2163.7 ± 614.0**			
MPP (W)	CON	243.1 ± 75.6	238.1 ± 75.23	p<0.001 $F_{2,32}$=35.507 η^2=0.534	p=0.892 $F_{2,32}$=0.115 η^2=0.007	p<0.001 $F_{2,32}$=11.316 η^2=0.422
	RRG	231.3 ± 77.8	282.8 ± 84.5*			
	TTG	221.0 ± 71.8	273.9 ± 8.7*			
MVIC (N)	CON	1198.5 ± 438.8	1280.2 ± 338.0	p=0.001 $F_{1,28}$=14.568 η^2=0.378	p=0.797 $F_{2,28}$=0.230 η^2=0.019	p=0.352 $F_{2,28}$=1.09 η^2=0.083
	RRG	1246.1 ± 461.9	1383.2 ± 586.4			
	TTG	1058.3 ± 309.1	1293.9 ± 383.4			
MT (cm)	CON	2.6 ± 0.4	2.5 ± 0.4	p=0.647 $F_{1,22}$=0.215 η^2=0.01	p=0.809 $F_{2,22}$=0.215 η^2=0.019	p=0.394 $F_{2,22}$=0.973 η^2=0.081
	RRG	2.5 ± 0.3	2.6 ± 0.2			
	TTG	2.7 ± 0.4	2.6 ± 0.4			
PA (°)	CON	14.9 ±3.1	16 ± 1.9	p=0.636 $F_{1,22}$=.230 η^2=0.01	p=0.55 $F_{2,22}$=0.615 η^2=0.053	p=0.142 $F_{2,22}$=2.133 η^2=0.162
	RRG	16.1± 2.6	17.2 ± 2.8			
	TTG	17.1± 2.8	15.9 ± 1.8			

*1RM: one repetition maximum; N10RM: repetitions with 10 repetition maximum Pre-test load; 10RMW: total work with 10RM load MMP: maximum mean propulsive power; MVIC: maximum isometric voluntary contraction; MT: muscle thickness measured; PA: Pennation angle. * p ≤ 0.05 for post-hoc pairwise comparisons within the group; **p ≤ 0.001 for post-hoc pairwise comparisons within the group: ‡ p ≤ 0.05 for post-hoc comparisons with CON at post-test. Data are means ± SD.*

session was greater in the TTG (-20.38%) compared with the RRG (1.77%, *p*<0.001; ES=2.86 95% CI=[1.72, 4.00]). RPE during training sessions was greater during TTG (7.66±1.16 a.u) compared with RRG (5.75±1.29 a.u; p=0.01; ES=1.51; 95% CI=[0.62, 2.40]). Similarly, TUT was also greater for TTG (470.5±64.4 min) compared with RRG (424.1±30.1 min); *p*=0.046 ES=0.84; 95% CI=[0.03; 1.66]).

Descriptive values and ANOVA results of the untrained limb are presented in Table 2. After the training period, 1RM increased by 10.3% in comparison with pre-test in the TTG (p<0.001; ES=0.25; 95% CI=[0.09, 0.42]) but not in RRG or CON. No changes occurred in MPP, N10RM, 10RMW, MVIC, MT and PA.

Regarding the trained limb, descriptive values and ANOVA results are presented in Table 3. Compared with Pre-test, 1RM increased in TTG (13%; *p*<0.001; ES=0.44; 95% CI=[0.291, 0.596]) and RRG (17%; *p*<0.001; ES=0.47; 95% CI=[0.30, 0.65]). MPP also increased significantly in TTG (23%; *p*<0.001; ES=0.58; 95% CI=[0.34, 0.81]) and RRG (22%, *p*<0.001; ES=0.57; 95% CI=[0.32, 0.82]). Similarly, N10RM increased in TTG (30%; *p*<0.001; ES=0.70; 95% CI=[0.42, 0.99]) and RRG (20%; *p*=0.001; ES=0.39; 95% CI=[0.13, 0.65]) and both increases were significantly different compared with CON (TTG: *p*=0.006; ES=1.23; 95% CI=[0.31, 2.15]; RRG: *p*=0.036; ES=2.65; 95% CI=[1.57, 3.73]).

Regarding de 10RMW, *post hoc* analysis showed significant changes for TTG (27%; *p*<0.001; ES=0.69; 95% CI=[0.39, 0.99]) and RRG (35%; *p*<0.001; ES=2.02; 95% CI=[1.04, 3.00]) in comparison with Pre-test values. No changes occurred in MVIC, MT and PA.

Discussion

We determined the effects of five weeks of unilateral RT using two different training protocols equated in load, total volume and work-to-rest ratio but leading to different levels of acute neuromuscular fatigue, on the trained and untrained knee extensors strength performance. In accordance with our hypothesis, present results show that despite similar effects of both training protocols on the trained knee extensors (i.e.: similar gains in maximal voluntary force), the traditional training set configuration, leading to a greater amount of acute neuromuscular fatigue, induced greater gains in the 1RM of the untrained knee extensors (i.e.: more CE) compared with a rest redistribution set configuration. Despite this increase in 1RM observed after traditional training, neither structural (MT and PA) nor muscular endurance or power parameters (i.e.: repetitions to failure and MMP with a submaximal load) of the untrained knee extensors were affected by any training protocol. Further and more specific research is needed in other to explore these kinds of variables.

Our results show an increase of 10.3% (6.3 kg) in the 1RM test of the untrained knee extensors in the TTG group. This result is in accordance with the magnitude reported by one of the last meta-analysis, which quantifies the magnitude of CE about an 11% in the lower limb[5]. However, the main aim of the present study was to determine the influence of acute neuromuscular fatigue derived from different set configurations on CE. CE is believed to occur in response to subtle adaptations in the untrained hemisphere, consequence of its concurrent activation during the unilateral contractions performed during training. Because untrained hemisphere activation increases during fatiguing submaximal contractions, it has been speculated that more fatiguing set configurations could increase the stimulus to the untrained hemisphere, therefore leading to greater CE[1]. However, only two studies have investigated this question before, with contradictory results. In a first study in the elbow flexors[1], it was found that a traditional set configuration leading to greater velocity losses (an accurate indicator of the level of neuromuscular fatigue and metabolic stress during resistance training) and RPE values, induced a greater CE than a rest redistribution set configuration, suggesting that fatigue could influence CE. However, a recent study examining this question on the knee extensors found that resistance training to muscular failure did not induce greater CE than a training protocol in which subjects only did half of the maximal theoretical number of repetitions possible with a 10RM load, suggesting no influence of fatigue on CE[8]. However, the two training protocols might have been above the minimum fatigue threshold needed to maximize untrained hemisphere activation during training, therefore obscuring the potential effects of fatigue on CE. Thus, more markedly different levels of fatigue could be needed to determine the influence of fatigue over CE in the knee extensors.

In this regard, in the present study we choose a low fatigue protocol based on rest redistribution, which is a type of cluster set configuration associated with a much lower acute neuromuscular fatigue than traditional set configurations[14,26]. Indeed, in accordance with previous literature[14,26], velocity loss (-20.4%), RPE (7.4 a.u.) and TUT (475.5s) were greater in TTG compared with RRG (1.8%, 5.75 a.u., and 424.1 min for velocity loss, RPE and TUT, respectively), which suggests that sessions using traditional set configurations with repetitions close to muscular failure, induced greater levels of neuromuscular fatigue. However, in accordance with our initial hypothesis, CE was absent in the RRG, which could be consequence of the low acute neuromuscular fatigue experienced by the RRG, which in turn would lead to a reduction of the untrained hemisphere activation during unilateral contractions, thus blunting CE.

Regarding the muscle endurance (N10RM and 10RMW) and structural (MT and PA) adaptations of the untrained limb, no changes were observed. These results are in line with those previously reported by Fariñas et al.[1] for the elbow flexors. The fact that the levels of muscle endurance was not transferred to untrained limb may by explained in two ways: i) muscle endurance may be mediated predominantly by metabolic processes , while 1RM improvements could have a higher neural implication in the adaptation processes[27] and ii) more time to cause significant improvements in endurance transfer might be needed. The absence of structural adaptations is also in agreement with previous literature that did not report changes in muscle thickness, muscle circumference or enzymatic activity in the untrained limb[1,28–30].

Therefore, increases in 1RM in the untrained limb without changes in either structural or endurance indexes after five weeks of unilateral RT based on sets close to muscular failure (i.e.: TTG), suggests that neural rather than structural mechanisms may be responsible of the CE phenomenon[31]. Reductions in intracortical inhibition of the untrained hemisphere or reductions in interhemispheric inhibition from the trained to the untrained hemisphere leading to increases in untrained limb voluntary activation and ultimately maximal voluntary force may underlie CE[32]. Therefore, a plausible scenario is that that the greater fatiguing stimulus during the traditional set configuration sessions, potentially leading to a greater untrained hemisphere activation, could enhance the adaptation-driving stimulus to the untrained hemisphere, leading to the greater CE in the TTG group observed in the present study. However, as previously discussed, despite the increase in 1RM for the untrained limb after traditional training, neither structural (MT and PA) nor muscular endurance or power parameters (i.e.: repetitions to failure and MMP with a submaximal load) of the untrained knee extensors were affected by any training protocol. Therefore, further and more specific research is needed in other to explore CE phenomenon for these variables.

For the trained limb, both experimental groups showed significant improvements in the 1RM test. These results are similar to those observed in previous studies, which obtained comparable strength gains after training programs with different set configurations but equated in volume and work-to-rest ratio[14,16,18]. Furthermore, in agreement with previous research[18], these 1RM improvements were accompanied by increases in the levels of MPP, regardless of the set configuration that was used. However, no changes were observed in MVIC in either TTG or RRG, most probably due to the lack of specificity of the test (i.e.: subjects trained dynamic actions).

Despite the positive adaptations found in the maximal force and power capabilities of the trained knee extensors (i.e.: 1RM and MPP) after both protocols, no differences were observed in MT or PA. The absence of structural adaptations after five weeks of high load RT is in contrast with previous literature[33,34]. For example, Pareja-Blanco et al.[35] found that eight weeks of RT with a protocol leading to a 20% of velocity loss induced 4.3% increases in total quadriceps femoris volume. Although discrepancies with previous studies could be related to the shorter training duration of the present study, limiting the amount of hypertrophy, a detailed look at the data by Pareja-Blanco et al[35] shows a non-significant increase (3.4%) in VL plus vastus intermedius muscle volume. Therefore, it could be the case that the ultrasound measurements of VL muscle thickness used in the present study, could not be sensitive enough to detect the small hypertrophy present in the VL muscle after a RT protocol associated with only a 20% of velocity loss.

This study is not without limitations. Firstly, the length of the program was of only five weeks with a total of 10 training sessions. Recent studies have suggested a minimum of 13-18 sessions to maximize CE[32,36], therefore the short amount of training sessions could have limited the adaptations in the untrained knee extensors in both groups. Furthermore, we did not include a mid-intervention 10RM test, in order to maintain the exact load during training protocols, therefore the absolute load used during training could have been a progressively lower relative training load due to strength improvements, thus reducing the training stimulus.

Collectively our results suggest that traditional fatiguing RT protocols leading to high levels of velocity loss, but not cluster type set configurations associated with low levels of neuromuscular fatigue, lead to CE regarding maximum dynamic force (1RM), despite no differences in the increases between protocols in trained knee extensors. Further research is needed in order to test what is the velocity loss threshold for each set with 10RM load to cause CE phenomenon and how may it affect in longer training periods.

From a practical point of view, these results show the relevance of manipulating set configurations to obtain significant strength gains in untrained limbs. The CE phenomenon observed after training with traditional set configurations may be useful to reduce strength loss and neural adaptations after limb immobilization[37,38], providing an earlier return to sport practice and daily activities, comparing with traditional rehabilitation strategies[38]. Furthermore, after a stroke, training with less affected limb results in range of motion and strength gains in the most affected limb[39]. Thus, according with our results, training programs consisting of longer set configurations, with significant velocity loss and close to muscular failure, could be applied in some special groups with rehabilitation objectives.

Ethics approval

The study was approved by the University of A Coruna (Spain) Ethics Committee and conducted according to the Declaration of Helsinki.

Authors' contributions

Study design: EIS, MFDO, JF; Study conduct: JRV, EIS, JFR; data collection: JF, EC, AA, IN, MRA, MAGG; Data analysis: JF, EIS, GM, DCP, MSS; Data interpretation: EIS, JF; Drafting manuscript: JF, EI, GM, DCP; Revising manuscript content and approving final version: all authors included in the manuscript.

References

1. Fariñas J, Mayo X, Giraldez-García MA, et al. Set Configuration in Strength Training Programs Modulates the Cross Education Phenomenon. J Strength Cond Res 2019;(12):1.
2. Frazer AK, Pearce AJ, Howatson G, Thomas K, Goodall S, Kidgell DJ. Determining the potential sites of neural adaptation to cross-education: implications for the cross-education of muscle strength. Eur J Appl Physiol 2018;118(9):1751-1772.
3. Ruddy KL, Carson RG. Neural pathways mediating cross education of motor function. Front Hum Neurosci 2013;7(July):397.
4. Lee M, Carroll TJ. Cross education: Possible mechanisms for the contralateral effects of unilateral resistance training. Sport Med 2007;37(1):1-14.
5. Manca A, Dragone D, Dvir Z, Deriu F. Cross-education of muscular strength following unilateral resistance training: a meta-analysis. Eur J Appl Physiol 2017; 117(11):1-20.
6. Colomer-Poveda D, Romero-Arenas S, Hortobagyi T, Márquez G. Does ipsilateral corticospinal excitability play a decisive role in the cross-education effect caused by unilateral resistance training? A systematic review. Neurol (English Ed 2021;36(4):285-297.
7. Cirer-Sastre R, Beltrán-Garrido J V., Corbi F. Contralateral effects after unilateral strength training: A meta-analysis comparing training loads. J Sport Sci Med 2017;16(2):180-186.
8. Colomer-Poveda D, Romero-Arenas S, Fariñas J, Iglesias-Soler E, Hortobágyi T, Márquez G. Training load but not fatigue affects cross-education of maximal voluntary force. Scand J Med Sci Sport Published online 2020:0-2.
9. Munn J, Herbert RD, Gandevia SC. Contralateral effects of unilateral resistance training: a meta-analysis. J Appl Physiol 2004;96(5):1861-1866.
10. Kidgell DJ, Frazer AK, Rantalainen T, et al. Increased cross-education of muscle strength and reduced corticospinal inhibition following eccentric strength training. Neuroscience 2015;300(6):566-575.
11. Colomer-Poveda D, Romero-Arenas S, Keller M, Hortobágyi T, Márquez G. Effects of acute and chronic unilateral resistance training variables on ipsilateral motor cortical excitability and cross-education: A systematic review. Phys Ther Sport 2019;40:143-152.
12. Hendy AM, Chye L, Teo W-P. Cross-Activation of the Motor Cortex during Unilateral Contractions of the Quadriceps. Front Hum Neurosci 2017;11:1-11.
13. Liu JZ, Shan ZY, Zhang LD, Sahgal V, Brown RW, Yue GH. Human brain activation during sustained and intermittent submaximal fatigue muscle contractions: an FMRI study. J Neurophysiol 2003;90(1):300-312.
14. Iglesias-Soler E, Mayo X, Río-Rodríguez D, Carballeira E, Fariñas J, Fernández-Del-Olmo M. Inter-repetition rest training and traditional set configuration produce

similar strength gains without cortical adaptations. J Sports Sci 2016;34(15):1473-1484.
15. Rúa-Alonso M, Mayo X, Mota J, Kingsley JD, Iglesias-Soler E. A short set configuration attenuates the cardiac parasympathetic withdrawal after a whole-body resistance training session. Eur J Appl Physiol 2020;120(8):1905-1919.
16. Rial-Vázquez J, Mayo X, Tufano JJ, Fariñas J, Rúa-Alonso M, Iglesias-Soler E. Cluster vs. traditional training programmes: changes in the force–velocity relationship. Sport Biomech 2020;00(00):1-19.
17. Mayo X, Iglesias-Soler E, Kingsley JD. Perceived exertion is affected by the submaximal set configuration used in resistance exercise. Int J Sport Exerc Psychol 2017;33(2):426-432.
18. Tufano JJ, Brown LE, Haff GG. Theoretical and Practical Aspects of Different Cluster Set Structures. J Strength Cond Res 2017;31(3):848-867.
19. de Boer MD, Seynnes OR, di Prampero PE, et al. Effect of 5 weeks horizontal bed rest on human muscle thickness and architecture of weight bearing and non-weight bearing muscles. Eur J Appl Physiol 2008;104(2):401-407.
20. Iglesias-Soler E, Carballeira E, Sánchez-Otero T, Mayo X, Jiménez A, Chapman ML. Acute effects of distribution of rest between repetitions. Int J Sports Med 2012;33(5):351-358.
21. Boffey D, Clark NW, Fukuda DH. Efficacy of Rest Redistribution During Squats: Considerations for Strength and Sex. J strength Cond Res 2021;35(3):586-595.
22. Sánchez-Medina L, González-Badillo JJ. Velocity Loss as an Indicator of Neuromuscular Fatigue during Resistance Training. Med Sci Sport Exerc 2011;43(9):1725-1734.
23. Hollander DB, Durand RJ, Trynicki JL, et al. RPE, pain, and physiological adjustment to concentric and eccentric contractions. Med Sci Sports Exerc 2003;35(6):1017-1025.
24. Richardson JTE. Eta squared and partial eta squared as measures of effect size in educational research. Educ Res Rev 2011;6(2):135-147.
25. Cohen J. Statistical Power Analysis for the Behavioral Scienses. Lawrence Erlbaum Associates; 1988.
26. Tufano JJ, Conlon JA, Nimphius S, et al. Effects of Cluster Sets and Rest-Redistribution on Mechanical Responses to Back Squats in Trained Men. J Hum Kinet 2017;58(1):35-43.
27. Izquierdo M, Ibañez J, González-Badillo JJ, et al. Differential effects of strength training leading to failure versus not to failure on hormonal responses, strength, and muscle power gains. J Appl Physiol 2006;100(5):1647-1656.
28. Beyer KS, Fukuda DH, Boone CH, et al. Short-term unilateral resistance training results in cross education of strength without changes in muscle size, activation, or endocrine response. J Strength Cond Res 2016;30(5):1213-1223.
29. Coratella G, Milanese C, Schena F. Cross-education effect after unilateral eccentric-only isokinetic vs dynamic constant external resistance training. Sport Sci Health 2015;11(3):329-335.
30. Farthing JP, Borowsky R, Chilibeck PD, Binsted G, Sarty GE. Neuro-physiological adaptations associated with cross-education of strength. Brain Topogr 2007; 20(2):77-88.
31. Carroll TJ, Herbert RD, Munn J, Lee M, Gandevia SC. Contralateral effects of unilateral strength training: evidence and possible mechanisms. J Appl Physiol 2006;101(5):1514-1522.
32. Manca A, Hortobágyi T, Carroll TJ, et al. Contralateral Effects of Unilateral Strength and Skill Training: Modified Delphi Consensus to Establish Key Aspects of Cross-Education. Sport Med 2021;51(1):11-20.
33. DeFreitas JM, Beck TW, Stock MS, Dillon MA, Kasishke PR. An examination of the time course of training-induced skeletal muscle hypertrophy. Eur J Appl Physiol 2011;111(11):2785-2790.
34. Folland JP, Williams AG. The Adaptations to Strength Training Increased Strength. Sport Med 2007;37(2):145-168.
35. Pareja-Blanco F, Alcazar J, Sánchez-Valdepeñas J, Cornejo-Daza PJ, Piqueras-Sanchiz F M-VR, Sánchez Moreno M, Bachero-Mena B, Ortega-Becerra M, Alegre LM. Velocity Loss as a Critical Variable Determining the Adaptations to Strength Training. Med Sci Sport Exerc 2020;52(8):1752-1762.
36. Barss XTS, Klarner T, Pearcey GEP, Sun Y, Zehr EP. Time course of interlimb strength transfer after unilateral handgrip training. Published online 2018:1594-1608.
37. Haggert M, Pearce A, Frazer A, Rahman S, Kidgell D, Siddique U. Determining the Effects of Cross-Education on Muscle Strength, Thickness and Cortical Activation Following Limb Immobilization: A Systematic Review and Meta-Analysis. J Sci Med. 2020;2(4):1-19.
38. Farthing JP, Krentz JR, Magnus CR a. Strength training the free limb attenuates strength loss during unilateral immobilization. J Appl Physiol. 2009;106(3):830-836.
39. Farthing JP, Zehr EP. Restoring symmetry: Clinical applications of cross-education. Exerc Sport Sci Rev 2014;42(2):70-75.