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ORIGINAL ARTICLE

Time course of recovery following resistance training leading or not to failure

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Abstract
Purpose To describe the acute and delayed time course of recovery following resistance training (RT) protocols differing in the number of repetitions (R) performed in each set (S) out of the maximum possible number (P).
Methods Ten resistance-trained men undertook three RT protocols [S × R(P)]: (1) 3 × 5(10), (2) 6 × 5(10), and (3) 3 × 10(10) in the bench press (BP) and full squat (SQ) exercises. Selected mechanical and biochemical variables were assessed at seven time points (from − 12 h to + 72 h post-exercise). Countermovement jump height (CMJ) and movement velocity against the load that elicited a 1 m s^{-1} mean propulsive velocity (V1) and 75% 1RM in the BP and SQ were used as mechanical indicators of neuromuscular performance.
Results Training to muscle failure in each set [3 × 10(10)], even when compared to completing the same total exercise volume [6 × 5(10)], resulted in a significantly higher acute decline of CMJ and velocity against the V1 and 75% 1RM loads in both BP and SQ. In contrast, recovery from the 3 × 5(10) and 6 × 5(10) protocols was significantly faster between 24 and 48 h post-exercise compared to 3 × 10(10). Markers of acute (ammonia, growth hormone) and delayed (creatine kinase) fatigue showed a markedly different course of recovery between protocols, suggesting that training to failure slows down recovery up to 24–48 h post-exercise.
Conclusions RT leading to failure considerably increases the time needed for the recovery of neuromuscular function and metabolic and hormonal homeostasis. Avoiding failure would allow athletes to be in a better neuromuscular condition to undertake a new training session or competition in a shorter period of time.

Keywords Muscle strength · Weight training · Hormonal response · Bench press · Back squat

Abbreviations

ANOVA	Analysis of variance
Basal AM	The same morning of the resistance training protocol at 8:00 h
Basal PM	The day before the resistance training protocol at 18:00 h
BP	Bench press
CK	Creatine kinase
CMJ	Countermovement jump
ES	Effect size
GH	Growth hormone
MPV	Mean propulsive velocity
Post 0 h	Immediately following each resistance training protocol (11:00 h)
Post 6 h	Same evening of resistance training, at 18:00 h
Post 24 h	24 h after the resistance training protocol
Post 48 h	48 h after the resistance training protocol
Post 72 h	72 h after the resistance training protocol

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RT	Resistance training
SQ	Full back squat
SD	Standard deviation
T/C	Testosterone/cortisol ratio
V1 load	The load that elicited a ~ 1.00 m s^{-1} mean propulsive velocity

Introduction

Knowledge of the mechanical and physiological mechanisms underlying resistance training (RT) is essential to improve our understanding of the stimuli that affect adaptation (Crewther et al. 2006). Among the main RT variables that can be manipulated to configure the mechanical stimulus (Kraemer and Ratamess 2006; Sánchez-Medina and González-Badillo 2011; Spiering et al. 2008), the actual number of repetitions performed in a set out of the maximum number that can be completed (i.e., proximity to muscle failure), recently termed '*level of effort*' (Sánchez-Medina and González-Badillo 2011) has received only minor research attention. The lack of studies addressing this question is likely due to the widespread assumption that, to be effective and maximize gains in strength and muscle mass, RT should be conducted to the point of muscle failure in each exercise set. However, recent studies suggest that how close each set is performed to failure is an aspect worth considering when RT is aimed at optimizing neuromuscular adaptations and improving athletic performance.

RT that avoids reaching muscle failure in each set (i.e., submaximal *level of effort*) has been shown to be an adequate strategy to achieve positive neuromuscular and morphological adaptations (Davies et al. 2016; Folland et al. 2002; Izquierdo-Gabarren et al. 2010; Pareja-Blanco et al. 2017; Sampson and Groeller 2016), and even most importantly, to enhance athletes' competitive performance (García-Pallarés et al. 2009, 2010; Izquierdo-Gabarren et al. 2010). Pareja-Blanco et al. (2017) recently compared the effects of two squat training programs that differed in the magnitude of repetition velocity loss allowed in each set (20 vs. 40%). It was found that while a 40% velocity loss (which led to muscle failure in 56% of the training sets) induced a greater hypertrophic response, it also resulted in a fast-to-slow shift in muscle phenotype, whereas a velocity loss of 20% (which corresponded to performing approximately half the possible number of repetitions per set) prevented this reduction in the fastest IIX fiber-type pool and resulted in similar or even superior strength gains, especially in high-velocity actions such as the vertical jump.

A high *level of effort* (i.e., reaching or approaching volitional failure in each set) is an important factor to maximize muscle growth (Morton et al. 2016). However, performing repetitions to failure causes a marked disruption of cellular homeostasis, as indicated by a near complete depletion of phosphocreatine stores, a significant reduction of adenosine triphosphate and muscle total adenine nucleotide pool, as well as very high increases in some muscle damage and acute and delayed recovery markers such us lactate, ammonia, testosterone, growth hormone (GH), cortisol and creatine kinase (CK), thereby suggesting that such protocols may require longer recovery times (González-Badillo et al. 2016; Gorostiaga et al. 2012, 2014; Sánchez-Medina and González-Badillo 2011). Recently, Bartolomei et al. (2017) have reported a slower time course of recovery following high-volume compared to high-intensity RT protocols. However, little is known about the time of course of recovery following RT protocols in which a certain number of repetitions are left in reserve in each set. González-Badillo et al. (2016) detailed the mechanical, biochemical and autonomic cardiovascular response to manipulating the actual number of repetitions performed in each set out of the maximum possible number. Although some study design issues such as randomization, total training volume per set and session and effect of circadian rhythm were not controlled or matched between groups in that study (González-Badillo et al. 2016), the authors found strong evidence that performing a half-maximum number of repetitions per set resulted in a lower impairment of neuromuscular performance and a faster recovery, which was monitored up to 48 h post-exercise. The rate of recovery following different types of RT protocols is especially important among competitive athletes because it can greatly influence subsequent workouts.

Given that the acute and delayed mechanical and biochemical response to failure vs. non-failure resistance exercise protocols in both upper- and lower-body muscle actions has not been addressed in detail, the purpose of this study was to analyze the time course of recovery following three distinct RT protocols in terms of the *level of effort* required maximum (to failure) vs. half-maximum number of repetitions per set in the bench press (BP) and full back squat (SQ) exercises. Several assessment time points from the evening before to 72 h post-exercise were established to evaluate the mechanical and biochemical response to each exercise protocol in an attempt to advance our understanding of the overall short-term recovery following RT.

Methods

Subjects

Ten highly resistance-trained men volunteered to participate in this study (age 21.5 ± 4.0 year, body mass 72.4 ± 8.4 kg, height 175.2 ± 7.2 cm, body fat 11.9 ± 2.5%, RT experience 8.2 ± 3.5 year, 1RM BP strength 87.2 ± 15.2 kg, 1RM SQ strength 105.7 ± 35.2 kg). The

subjects were informed in detail about the experimental procedures and the possible risks and benefits of their participation. The study, which complied with the Declaration of Helsinki, was approved by the Bioethics Commission of the University of Murcia, and written informed consent was obtained from all subjects. Subjects were informed that they could resign from participation at any time.

Experimental design

A randomized controlled experimental design was used, with all subjects serving as their own controls. Participants undertook three RT protocols, performed 4 weeks apart: (1) three sets of five repetitions not to failure with a load corresponding to 75%1RM [3 × 5(10)]; (2) six sets of five repetitions not to failure with 75%1RM [6 × 5(10)]; and (3) three sets of ten repetitions to failure with 75%1RM [3 × 10(10)], always using 5 min inter-set recoveries. All three RT protocols were comprised of the BP followed by the SQ exercise. These two exercises were performed in a Smith machine, and carried out exactly as described elsewhere (Sánchez-Medina and González-Badillo 2011; Sánchez-Medina et al. 2010, 2013, 2017). To quantify the degree of neuromuscular fatigue induced by each protocol, subjects underwent a battery of mechanical and biochemical measurements (explained later in detail) at seven different time points: (1) the day before the RT protocol at 18:00 h (Basal PM); (2) the same morning of the RT protocol at 8:00 h (Basal AM); (3) at 11:00 h, immediately following each RT protocol (Post 0 h); (4) that same evening at 18:00 h (Post 6 h); and the morning (10:00 h) of the following 3 days: (5) 24 h (Post 24 h); (6) 48 h (Post 48 h); (7) 72 h (Post 72 h) (Fig. 1). Those times of day (i.e., 10:00 h and 18:00 h) were selected since they were common training hours in the schedule of this group of elite athletes that usually perform twice-a-day practices. The RT protocols [3 × 5(10), 6 × 5(10) and 3 × 10(10)] were designed to evaluate the main effects of total training volume (60 vs. 120 repetitions), degree or *level of effort* (training to failure vs. non-failure) and time course of recovery after exercise (Basal PM, Basal AM, Post 0 h, Post 6 h, Post 24 h, Post 48 h and Post 72 h) on neuromuscular fatigue and biochemical responses.

In the 12 months preceding this study, subjects had been training 2–3 RT training sessions per week and were capable of performing both exercises (SQ and BP) with excellent technique. No physical limitations, health problems or musculoskeletal injuries that could affect testing were found after a medical examination. None of the subjects was taking drugs, medications or dietary supplements known to influence physical performance.

Experimental protocol

During the 5 days that each experimental trial lasted (the day of the RT protocol, the one before and the three following days), the subjects stayed in the facilities of the sports research and training center where they slept and ate all meals. A 2800–3000 kcal day^{-1} diet composed of 55% of energy intake from carbohydrates, 25% from fat and 20% from protein, evenly distributed across three meals each day (breakfast at 8:30 h, lunch at 13:30 h and dinner at 20:00 h) was consumed. Subjects refrained from physical activity other than that required by this experiment and withdrew from alcohol, tobacco and any kind of caffeine intake from 4 days before to 3 days after the corresponding RT protocol. The day before every RT protocol, each subject's height was measured to the nearest 0.5 cm during a maximal inhalation using a wall-mounted stadiometer (Seca 202, Seca Ltd., Hamburg, Germany). Body weight was determined and fat percentage estimated in a fasted state using an eight-contact electrode segmental body composition analyzer (Tanita BC-418, Tanita Corp., Tokyo, Japan). All subjects had already taken part in other neuromuscular assessments similar to those performed in the present study. Nevertheless, participants underwent three familiarization sessions before the start of this study (Fig. 1) to avoid the bias of progressive learning on test reliability.

Testing procedures

Determination of reference loads for the assessment of neuromuscular performance

Since exercise-induced neuromuscular fatigue could manifest differently depending on the loads being used, in the present study we set to examine the mechanical response by analyzing changes in movement velocity against low, medium and high loads. Thus, countermovement jump (CMJ) height was chosen as an indicator of neuromuscular performance against low loads. In addition, the load that elicited a ~ 1.00 m s^{-1} (V1 load) mean propulsive velocity (MPV) was chosen as the reference against medium loads (Sánchez-Medina and González-Badillo 2011; Sánchez-Medina et al. 2017), and the load corresponding to 75% 1RM was selected for assessing performance against high loads. The last familiarization session, performed in the morning (10:00 h) of the third day prior to the beginning of each experiment, included the determination of these individual loads (V1 and 75% 1RM) in both exercises (Fig. 1). During that session, participants underwent a standardized warm-up that consisted of 5 min of treadmill jogging at 10 km h^{-1} and 5 min of joint mobilization exercises followed by two sets of six and four repetitions in the BP and SQ exercises with fixed loads of 20 and 30 kg (2 min recoveries), respectively.

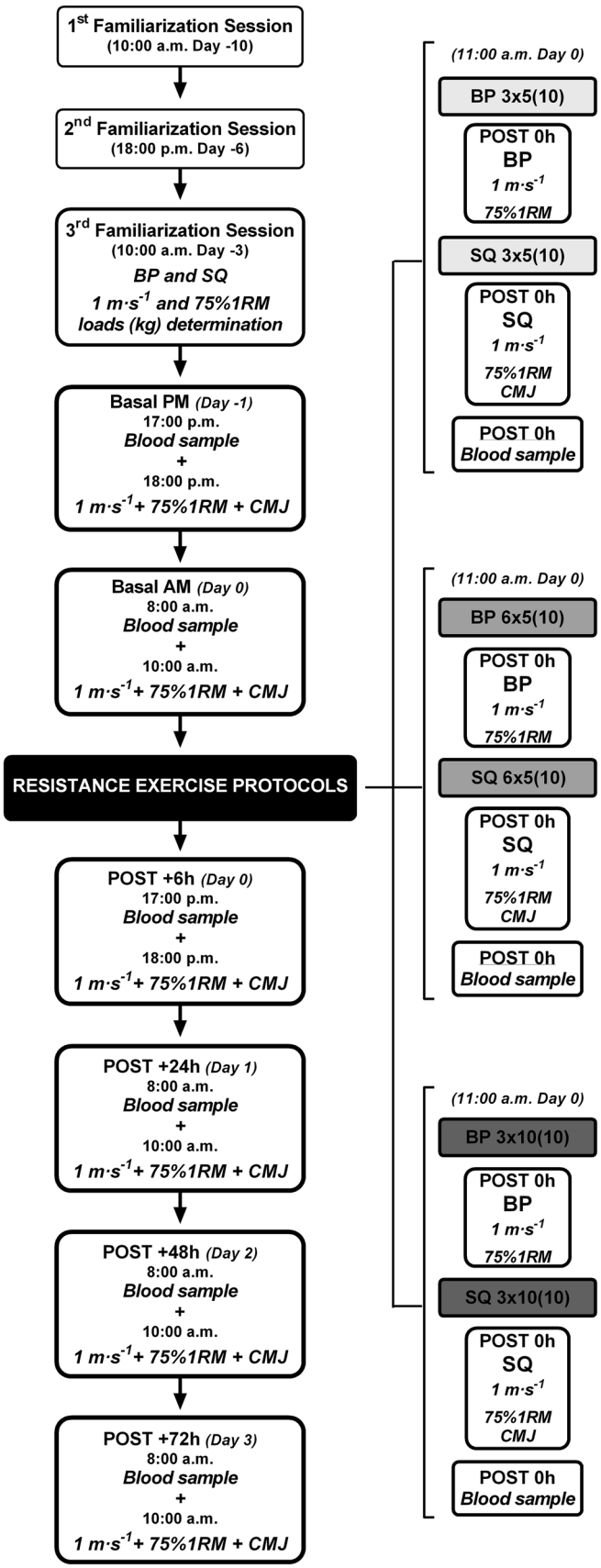

Fig. 1 Schematic representation and timeline of study design

Then, the individual loads (kg) that elicited a bar MPV of ~ 1.00 m s^{-1} (0.99 ± 0.02 for BP and 1.01 ± 0.02 m s^{-1} for SQ) and those corresponding to 75% 1RM (0.58 ± 0.02 for BP and 0.74 ± 0.03 m s^{-1} for SQ) were determined using a progressive loading test (Sánchez-Medina et al. 2013, 2017). A linear velocity transducer sampling at 1000 Hz (T-Force System, Ergotech, Murcia, Spain) was used to monitor the velocity of each repetition performed during the course of the present study. A detailed description of the BP and SQ testing protocols as well as validity (mean error for velocity < 0.25%; displacement accuracy ± 0.5 mm) and reliability data (ICC = 1.00; CV = 0.57% for MPV) of this measurement system has been reported elsewhere (Sánchez-Medina and González-Badillo 2011). Loads that elicit a velocity of ~ 1.00 m s^{-1} are very close to those that maximize the mechanical power output for isoinertial upper- and lower-body multiarticular RT exercises (Izquierdo et al. 2002; Sánchez-Medina et al. 2010, 2013, 2017). A load of 75% 1RM has been described as the minimal load that allows positive adaptations for maximum strength development in highly resistance-trained athletes (García-Pallarés et al. 2009, 2010; Ratamess et al. 2009). Standard CMJs were also performed at the seven established time points. Five CMJs separated by 1-min rests were performed by each subject, the highest and lowest values discarded, and the resulting average kept for analysis. CMJ height was measured using an infrared timing system (Optojump Next, Microgate, Bolzano, Italy). Strong verbal encouragement and velocity feedback in every repetition was provided throughout all sessions to motivate participants to give a maximal effort. Subjects were instructed to always perform the concentric phase of each repetition at maximal intended velocity.

Mechanical measurements of fatigue

The velocity attained against the V1 and 75% 1RM loads in the BP and SQ exercises, as well as the CMJ height, were taken as pre-exercise reference measures against which to compare the values obtained at the different time points (Basal PM, Basal AM, Post 0 h, Post 6 h, Post 24 h, Post 48 h and Post 72 h) established for the analysis of the time course of recovery following each RT session [3 × 5(10), 6 × 5(10) and 3 × 10(10)].

Biochemical measurements of fatigue: blood collection and analysis

At 8:00 a.m. in a fasted morning state (Basal AM, Post 0 h, Post 24 h, Post 48 h and Post 72 h) and at 17:00 p.m. (Basal PM and Post 6 h) venous blood samples were obtained from an antecubital vein (25 mL). Blood samples were mixed with ethylenediaminetetraacetic acid (EDTA) in plastic tubes. The plasma was immediately separated by centrifugation (MPW-350R, MedInstruments, Poland) and stored at − 20 °C for future analysis. Serum total testosterone (TT), cortisol (C) and GH were assayed by chemiluminescence using an automated Advia Centaur kit (Bayer Diagnostics, Tarrytown, NY, 7.7% intra-assay coefficient variation) for TT and an Immulite 2000 kit (Siemens, Los Angeles, Calif., intra-assay coefficients of variation below 7%) for C and GH. Serum CK was determined spectrophotometrically using a commercially available kit (Spinreact, Sant Esteve, Spain). Ammonia was measured using PocketChem BA PA-4130 (Menarini Diagnostics, Florence, Italy). The device was calibrated before each exercise session according to the manufacturer's specifications. Reliability was calculated by assessing twice 15 different samples over the physiological range (35–150 µmol/L). Coefficient of variation ranged from 3.0 to 5.2% for ammonia.

Statistical analyses

A Kolmogorov–Smirnov test was used to establish if data had a normal distribution. Two-way (RT protocol × time) ANOVA for repeated measures was performed to detect inter-group differences at each time point and for baseline comparisons (i.e., Basal AM vs. Basal PM) in all the studied variables. The Greenhouse-Geisser adjustment for sphericity was calculated. After a significant F test, pairwise differences were identified using Bonferroni significance post hoc procedure. Cohen's formula for effect size (ES) was used, and the results were based on the following criteria; > 0.70 large effect; 0.30–0.69 moderate effect; ≤ 0.30 small effect (Cohen 1988). The level of significance was set at $p < 0.05$. All values are presented as mean ± standard deviation (SD). Data analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY, USA).

Results

No significant differences were detected in any of the neuromuscular and biochemical variables under study between the RT protocols [3 × 5(10), 6 × 5(10) and 3 × 10(10)] at the basal time points (Basal PM and Basal AM) (Figs. 2, 3, 4) ($p > 0.05$). Similarly, no significant differences were observed in any mechanical or biochemical variable at any time point following exercise (i.e., POST 0 h, POST 6 h, POST 24 h, POST 48 h and POST 72 h) between the two protocols not leading to failure [i.e., 3 × 5(10) and 6 × 5(10)] ($p > 0.05$), except for the GH concentration at Post 0 h ($p = 0.03$) (Fig. 4c).

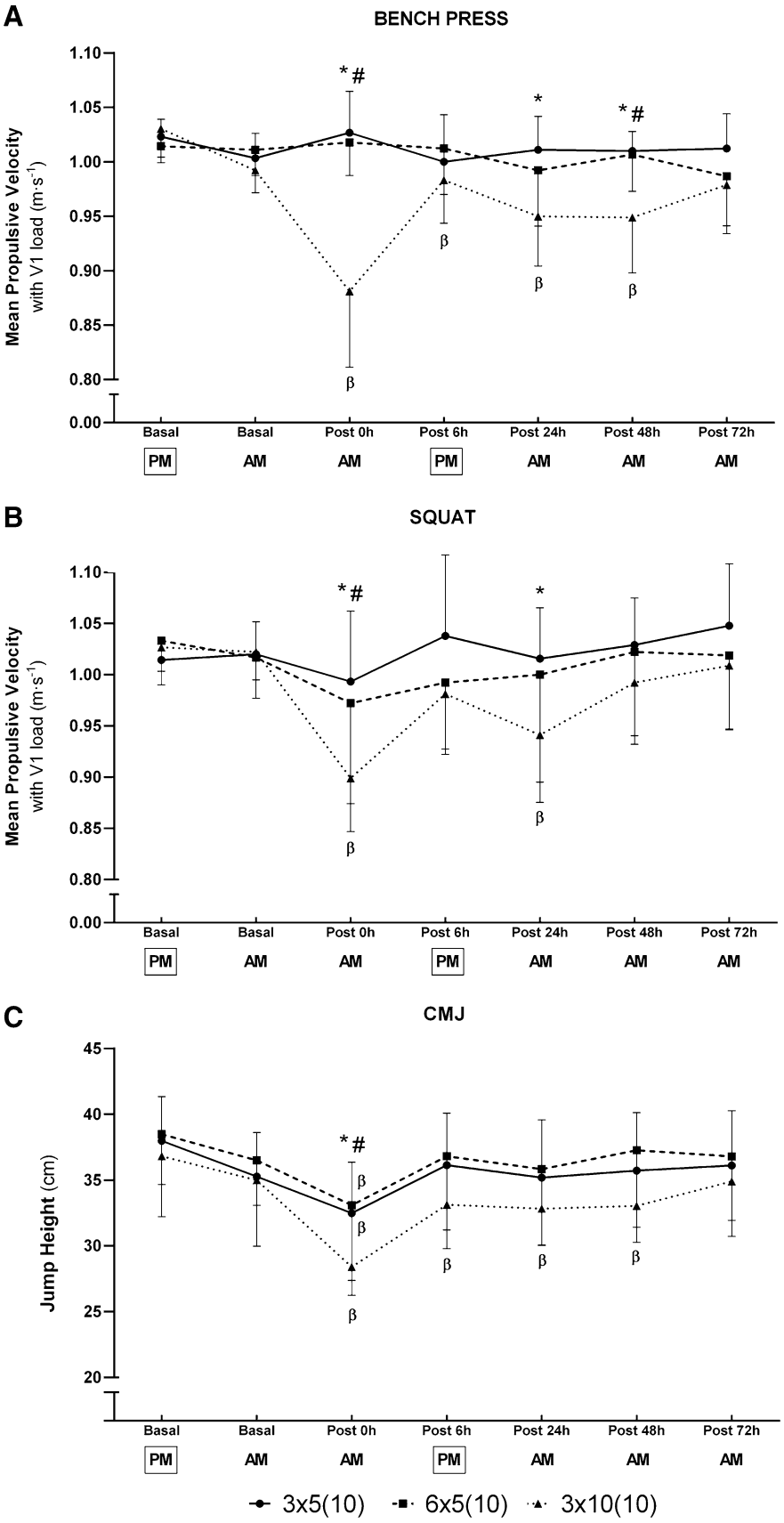

Fig. 2 Time course of bar mean propulsive velocity against the V1 reference load in the BP (**a**) and SQ (**b**) exercises, and CMJ height (**c**) at the seven time points established for the assessment of neuromuscular recovery (Basal PM, Basal AM, Post 0 h, Post 6 h, Post 24 h, Post 48 h and Post 72 h) following each of the three RT protocols under study [3 × 5(10), 6 × 5(10) and 3 × 10(10)]. Values are mean ± SD. Statistically significant differences: $^{*}p < 0.05$ when comparing 3 × 5(10) vs. 3 × 10(10) at the corresponding time point, $^{\#}p < 0.05$ when comparing 6 × 5(10) vs. 3 × 10(10) at the corresponding time point, $^{\beta}p < 0.05$ when comparing the value at a given time point to its respective basal value (AM or PM)

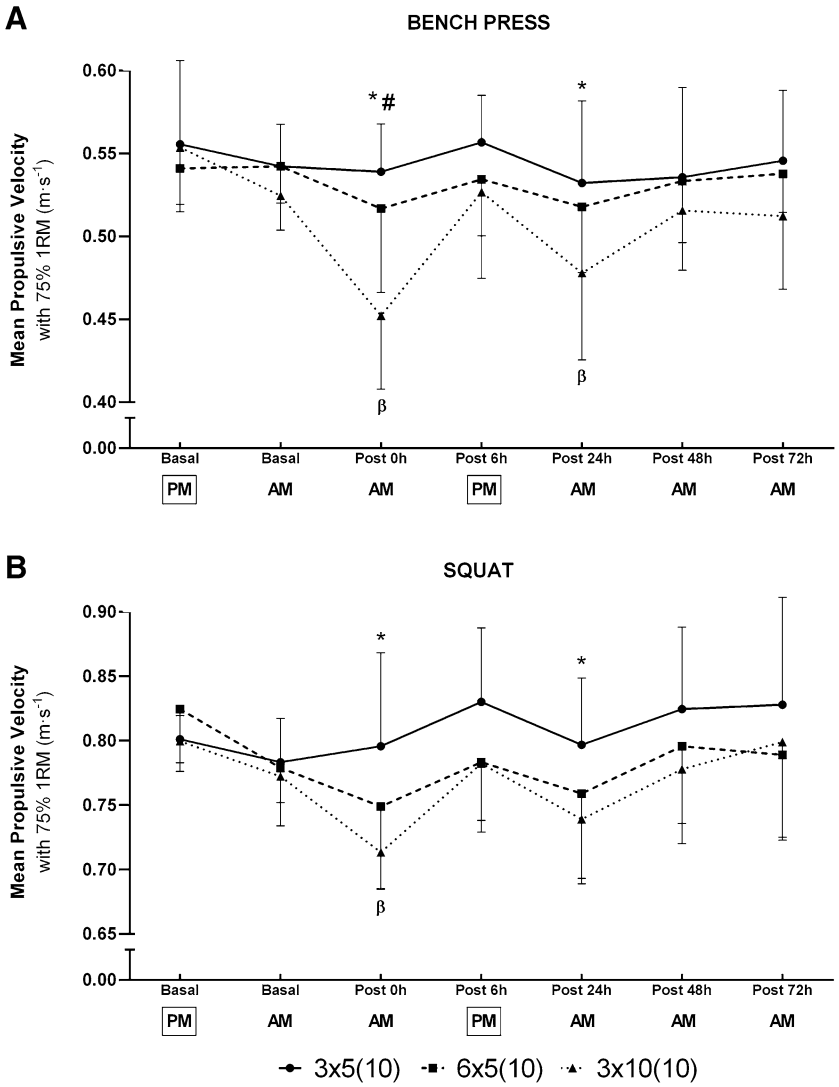

Fig. 3 Time course of bar mean propulsive velocity against the 75% 1RM reference load in the BP (**a**) and SQ (**b**) exercises, and CMJ height (**c**) at the seven time points established for the assessment of neuromuscular recovery (Basal PM, Basal AM, Post 0 h, Post 6 h, Post 24 h, Post 48 h and Post 72 h) following each of the three RT protocols under study [3 × 5(10), 6 × 5(10) and 3 × 10(10)]. Values are mean ± SD. Statistically significant differences: $^{*}p < 0.05$ when comparing 3 × 5(10) vs. 3 × 10(10) at the corresponding time point, $^{\#}p < 0.05$ when comparing 6 × 5(10) vs. 3 × 10(10) at the corresponding time point, $^{\beta}p < 0.05$ when comparing the value at a given time point to its respective basal value (AM or PM)

Changes in neuromuscular performance against the reference loads

Following the 3 × 10(10) protocol, the velocity attained against the V1 load in the BP showed significantly lower values at POST 0 h, POST 24 h and POST 48 h time points when compared to the 3 × 5(10) and 6 × 5(10) protocols ($p > 0.05$), except at POST 24 h when compared to 6 × 5(10) where it did not reach statistical significance ($p = 0.07$) (Fig. 2a). In the SQ, velocity against the V1 load was significantly reduced following the 3 × 10(10) protocol at POST 0 h and POST 24 h time points when compared to the 3 × 5(10) protocol ($p < 0.05$), and at POST 0 h when compared to 6 × 5(10) ($p < 0.05$) (Fig. 2b). When the velocity against the V1 load for the three RT protocols was compared to its respective morning or evening basal values (Basal PM or Basal AM) significantly lower values were observed only for the 3 × 10(10) protocol in both the BP and SQ exercises at POST 0 h and POST 24 h, as well as at POST 6 h and POST 48 h in the BP exercise ($p < 0.05$) (Fig. 2a, b). CMJ height was significantly lower immediately following the 3 × 10(10) protocol (POST 0 h) when compared to both 3 × 5(10) and 6 × 5(10) non-failure protocols ($p < 0.05$). When comparing the CMJ height values at each time point to their respective basal values (Basal PM or Basal AM), significant differences following the 3 × 10(10) protocol were detected at POST 0 h, POST 6 h, POST 24 h and POST 48 h ($p < 0.05$). In addition, significantly lower values were observed for 3 × 5(10) and 6 × 5(10) at POST 0 h when compared to their respective basal morning values (Basal AM) (Fig. 2c) ($p < 0.05$).

Following 3 × 10(10), velocity against the 75%1RM load was significantly reduced at the POST 0 h and POST 24 h time points when compared to 3 × 5(10) in both the BP and SQ ($p < 0.05$). Significantly higher values for the velocity against 75%1RM at POST 0 h were found for 6 × 5(10) when compared to the 3 × 10(10) protocol ($p < 0.05$). When the velocity against 75%1RM for the three RT protocols was compared to its respective

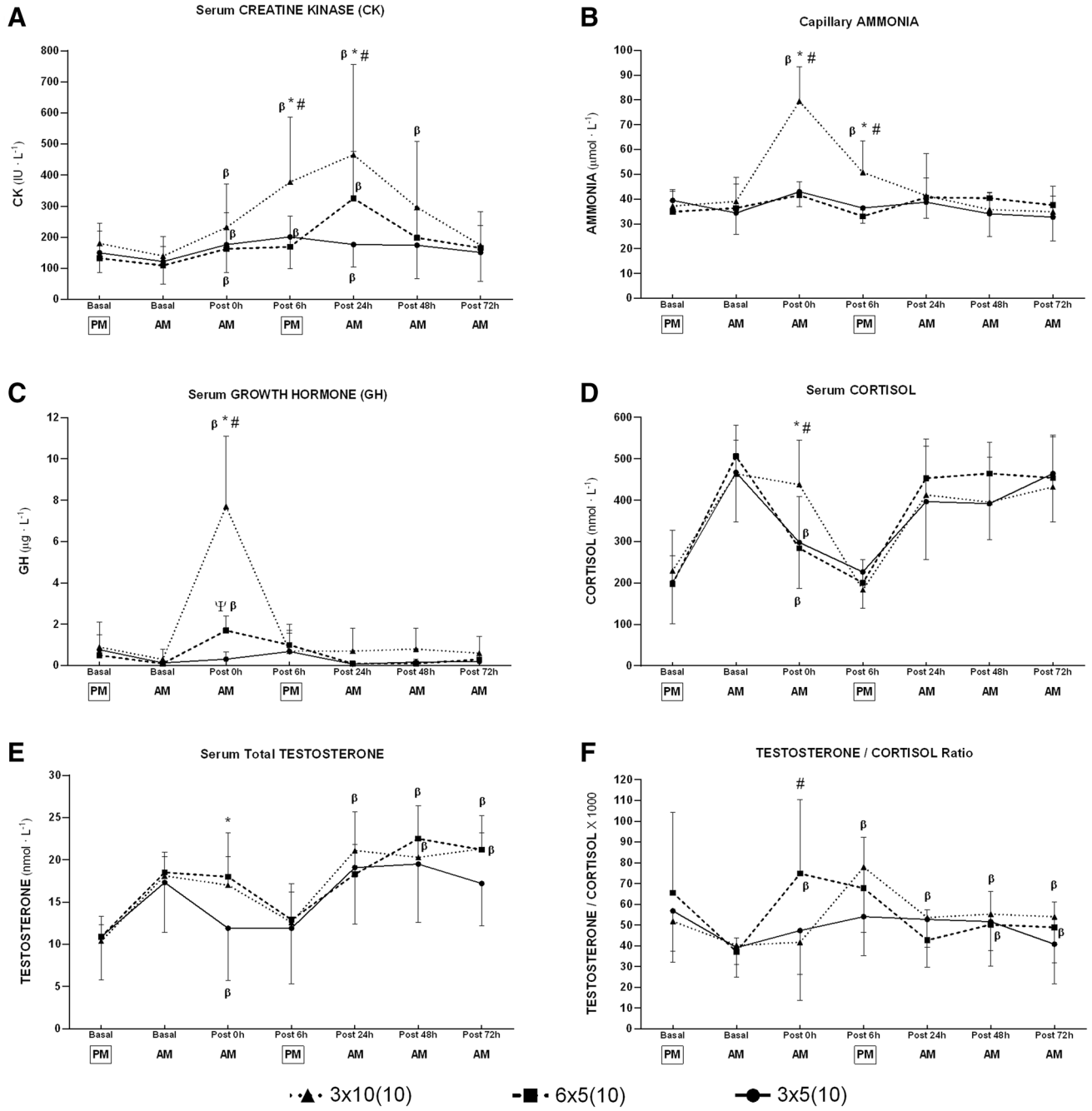

Fig. 4 Time course of the selected biochemical markers at the seven time points established for the assessment of neuromuscular recovery (Basal PM, Basal AM, Post 0 h, Post 6 h, Post 24 h, Post 48 h and Post 72 h) following each of the three RT protocols under study [3×5(10), 6×5(10) and 3×10(10)]. Values are mean ± SD. Statistically significant differences: $^{*}p < 0.05$ when comparing 3×5(10) vs. 3×10(10) at the corresponding time point, $^{\#}p < 0.05$ when comparing 6×5(10) vs. 3×10(10) at the corresponding time point, $^{\Psi}p < 0.05$ when comparing 3×5(10) vs. 6×5(10) at the corresponding time point, $^{\beta}p < 0.05$ when comparing the value at a given time point to its respective basal value (AM or PM)

morning basal values, significantly lower values at POST 0 h and POST 24 h time points were detected for the 3×10(10) protocol in the BP, and at POST 24 h for 3×10(10) in the SQ ($p < 0.05$) (Fig. 3). No significant differences for this variable were observed between protocols when comparing values at Post 6 h vs. Basal PM ($p > 0.05$).

Biochemical measurements of fatigue

Serum creatine kinase

Following the 3×10(10) protocol, the CK values were significantly higher compared to the 3×5(10) and 6×5(10) protocols at POST 6 h and POST 24 h time points ($p<0.05$; ES = 0.64–1.59). No significant differences were detected in this enzyme between the 3×5(10) and 6×5(10) protocols at any time point ($p>0.05$). When the CK concentration following the three protocols was compared to its respective baseline values (Basal PM or Basal AM), significant differences ($p<0.05$; ES = 0.39–2.02) were detected for the 3×10(10) and 6×5(10) protocols at POST 0 h, POST 6 h and POST 24 h time points, as well as for 3×10(10) at POST 48 h and for 3×5(10) at POST 0 h and POST 24 h ($p<0.05$; ES = 0.67 and 0.76, respectively) (Fig. 4a).

Ammonia

No significant differences were detected between protocols at any time point ($p>0.05$) except at POST 0 h and POST 6 h, where the 3×10(10) protocol resulted in significantly higher values than those observed following both non-failure 3×5(10) and 6×5(10) protocols ($p<0.05$; ES = 1.53–3.89). When the capillary ammonia values found following the three protocols were compared to their respective baseline values, significant differences were detected only for 3×10(10) at POST 0 h and POST 6 h ($p<0.05$; ES = 1.40 and 3.82, respectively) (Fig. 4b).

Blood concentration of steroid hormones

Growth hormone

No significant differences were detected between the three RT protocols at any time point ($p>0.05$), except at POST 0 h where the 3×10(10) protocols resulted in significantly higher values than those detected following 3×5(10) and 6×5(10) ($p<0.05$; ES = 2.86 and 3.90, respectively), with significantly higher values observed for 6×5(10) compared to 3×5(10) ($p=0.01$; ES = 2.56). When the GH levels observed following the three protocols were compared to their respective baseline values, significant differences were detected only for the 3×10(10) and 6×5(10) protocols at POST 0 h ($p<0.05$; ES = 3.79 and 3.77, respectively), (Fig. 4c).

Cortisol

No significant differences were detected between the three RT protocols at any time point for the cortisol concentration values ($p>0.05$) except at POST 0 h, where the 3×10(10) protocol resulted in significantly higher values than those detected following 3×5(10) and 6×5(10) ($p<0.05$; ES = 1.28 and 1.32, respectively). Additionally, the 3×5(10) and 6×5(10) protocols resulted in significantly lower values at POST 0 h than those detected at their respective basal AM time point ($p<0.05$; ES = 1.47 and 1.23, respectively), (Fig. 4d).

Testosterone

No significant differences were found between the three RT protocols at any time point for testosterone concentration except at POST 0 h ($p>0.05$), where the 3×10(10) protocol resulted in significantly lower values than those detected following 3×5(10) ($p=0.04$; ES = 1.07). When the serum total testosterone results of the three protocols were compared with their respective baseline values, significant differences were detected for the 3×5(10) protocol at POST 0 h, for the 6×5(10) protocol at POST 48 h and POST 72 h, as well as for 3×10(10) at POST 24 h, POST 48 h and POST 72 h ($p<0.05$; ES = 0.85–1.27) (Fig. 4e).

Testosterone/cortisol ratio

No significant differences were detected between the three RT protocols at any time point for the T/C ratio ($p>0.05$) except at POST 0 h, where the 6×5(10) protocol showed significantly higher values than those detected following the 3×10(10) protocol ($p=0.03$; ES = 1.30). When the T/C ratios for the three experimental groups where compared to their respective baseline values, significant differences were detected for 6×5(10) at POST 0 h, Post 48 h and Post 72 h, as well as for 3×10(10) at POST 6, POST 24 h, POST 48 and POST 72 h ($p<0.05$; ES = 0.73–1.78) (Fig. 4f).

Discussion

The present study described the acute and delayed time course of recovery (0–72 h) of selected mechanical and biochemical variables following three different RT protocols in which the '*level of effort*'' (actual number of repetitions performed in each set out of the maximum possible number) was manipulated while controlling the total number of repetitions per exercise and session as well as the effect of the circadian rhythm.

Our results seem to indicate that training to muscle failure [3×10(10) protocol], even when compared to completing the same total training volume [6×5(10)], resulted in a significantly higher acute (POST 0 h) decline of neuromuscular performance measured against low (CMJ), medium (V1) and high (75%1RM) loads, in both both upper- (BP) and lower-body (SQ and CMJ) muscle actions (Figs. 2, 3). In

contrast, the analysis of the time course of recovery following exercise shows that the two non-failure training protocols [3 × 5(10) and 6 × 5(10)] significantly speed up the mechanical recovery processes between 24 and 48 h compared to training to failure [3 × 10(10)]. This, in turn, would allow athletes to be in a better neuromuscular condition to undertake a new training session or competition in a shorter period of time. The results of the biochemical variables assessed in the present study also support these conclusions. Markers of acute fatigue such as ammonia and GH, but especially delayed fatigue markers such as CK, showed a time course of recovery which was markedly different between the levels of effort analyzed, showing again that training to muscle failure may significantly slow down (up to 24–48 h) the recovery of metabolic and hormonal homeostasis.

Taken together, our results seem to suggest that, even when the total training volume is maintained (i.e., the same number of repetitions is performed per exercise and session), the reduction of the recovery time in the subsequent 24–48 h period following non-failure RT approaches could be the mechanism underlying the superior neuromuscular, morphological and sport-specific performance improvements recently described in well- and highly-trained athletes (Davies et al. 2016; Folland et al. 2002; García Pallarés et al. 2009; Izquierdo-Gabarren et al. 2010; Sanborn et al. 2000), which would be especially important when concurrent endurance and strength training is required or several strength, endurance and technical capabilities must be developed simultaneously (García-Pallarés et al. 2009, 2010; Izquierdo-Gabarren et al. 2010).

The mechanical measurements used to assess neuromuscular fatigue in the present study in the BP and full squat exercises were conducted following strict protocols which have shown high reproducibility (Pallarés et al. 2014) and sensitivity (Mora-Rodríguez et al. 2015; Pallarés et al. 2013). However, it is well known that neuromuscular function is influenced by circadian rhythm (Mora Rodríguez et al. 2012, 2015). For instance, reductions in muscle power in the morning (8 h) in comparison to the evening (18 h) have been recently reported (4.8–9.4%; ES = 0.51–2.10). It thus seems appropriate that the comparison of results should be done with respect to reference baseline measurements performed at the same time of day (Basal AM or Basal PM), because neuromuscular performance may be influenced by the effects of the circadian rhythm and it can differ to a significant extent (2.8–7.3%) depending on the time of day chosen for its assessment (Mora Rodríguez et al. 2012, 2015; Pallarés et al. 2015). Furthermore, to ensure that the absolute load (kg) chosen for each RT protocol closely corresponded to the *level of effort* that was intended, load was carefully adjusted from each subject's load-velocity relationship at the beginning of each training protocol. Since 75%, 1RM and 10RM do not necessarily constitute the same loads for every subject, a velocity-based approach provides very useful information about the real effort performed during an exercise (Sánchez-Medina and González-Badillo 2011; Sánchez-Medina et al. 2013, 2017). Hence, we verified that the expected target velocities corresponding to 75% 1RM (~ 0.74 and ~ 0.58 m s^{-1} for the SQ and BP, respectively) were met.

In line with the results obtained by González-Badillo et al. (2016), who compared a non-failure vs. failure RT protocol, but considering that training volume was matched in two of our protocols [3 × 10(10) vs. 6 × 5(10)], reductions in the velocity attained against the V1 load in the SQ and BP were higher for 3 × 10(10) vs. 6 × 5(10) throughout the 72-h post-exercise recovery period, with the 3 × 5(10) protocol resulting in a lower movement velocity reduction in the 72 h following exercise. It is worth noticing that, while the velocity against the V1 load in both BP and SQ was already recovered at Post 6 h after 3 × 5(10), initial neuromuscular performance was not fully restored until Post 48 h following the 3 × 10(10) protocol. These results are even more evident for jumping ability. Thus, CMJ height did not return to pre-exercise values until Post 72 h following 3 × 10(10), whereas for 3 × 5(10) and 6 × 5(10) initial CMJ performance was already recovered at Post 6 h. This seems to indicate that the "explosiveness" or ability to rapidly develop force with the lower limbs may be considerably compromised up to at least 48 h (and even 72 h) following resistance exercise to failure. In this regard, in the present study, and to the best of our knowledge, it is the first time that we can observe the effect of training to failure on changes in movement velocity against low, medium and high loads (CMJ, V1 and 75% RM), each of which can be considered a different but complementary indicator of neuromuscular performance. These mechanical indicators of performance appear to be sensitive measures to monitor the recovery process following RT.

Consequently, resistance exercise characterized by great reductions in repetition velocity, as it occurs in the typical, to failure, body-building routines, may considerably increase the amount of time needed for recovery, as previously suggested (Gorostiaga et al. 2012; Sánchez-Medina and González-Badillo 2011; Izquierdo et al. 2006). It is for these reasons that leaving a certain number of repetitions in reserve in each exercise set or setting a velocity loss limit during RT (Pareja-Blanco et al. 2016; Sánchez-Medina and González-Badillo 2011) seems an appropriate measure to avoid performing unnecessarily slow and fatiguing repetitions that may not be contributing to the desired training effect.

Being aware of the diurnal variation of testosterone and cortisol due to their pulsatile nature (Mora-Rodríguez et al. 2012), we designed the present study with two baseline blood collection times to be used as control or reference points. One in the morning (8:00 h), against which to

compare most of the blood samples collected (i.e., 0, 24, 48 and 72 h post-exercise) and another at 17:00 h to compare with the blood collected 6 h following each RT protocol (Fig. 1). The hormonal response to manipulating the '*level of effort*'' and total work for the three RT protocols (each of which consisted on performing the BP followed by the SQ exercise) is presented in Fig. 4. Our hypothesis was that the protocol inducing the greatest fatigue [3 × 10(10)] would result in a less favorable anabolic hormonal milieu. However, testosterone concentration did not increase immediately after exercise in any of the protocols under study. Interestingly, it took 24 h for testosterone to increase after RT and it only remained significantly elevated above basal values following the two protocols with the higher total work (6 × 5 and 3 × 10 repetitions). Thus, our data seem to suggest that a certain amount of work is needed to reach the neuroendocrine threshold to increase testosterone secretion and that resistance exercise to failure sets do not diminish this response. Moreover, our data also seem to indicate that training to muscle failure does not provide a superior stimulus to increase blood testosterone levels than performing the same amount of total work distributed over a larger number of non-failure exercise sets to reduce neuromuscular fatigue and speed up recovery.

On the other hand, the protocol leading to muscle failure in each set [3 × 10(10)] resulted in an elevated cortisol response immediately after exercise in comparison to the other two protocols. However, this elevation was short lived and 6 h following exercise cortisol levels had returned to PM basal values in all protocols under study. It is unclear if this transitory elevation of cortisol following the 3 × 10(10) protocol may mediate the proteolytic actions of cortisol opposing those of testosterone (Kraemer and Ratamess 2005). Previous studies using similar RT protocols have resulted in inconsistent blood testosterone/cortisol responses. While longer sets to failure at a lower intensity (i.e., 3 × 12 at 70% 1RM) resulted in post-exercise increases in both testosterone and cortisol (Pareja-Blanco et al. 2016), shorter sets to failure at a higher intensity (i.e., 3 × 8 at 80% 1RM) did not affect testosterone or cortisol right after exercise (González-Badillo et al. 2016). The present results (3 × 10 at 75% 1RM) resemble the findings of that latter study. However, thanks to the inclusion of a work-matched protocol [6 × 5(10)] it emerges that total time under load may be a factor favoring the anabolic response to RT.

Interestingly, GH was very responsive to the *level of effort* of the three trials. Thus, large GH elevations were observed following the exercise to failure protocol [3 × 10(10)], modest elevations were found for the work-matched protocol with half the repetitions per set [6 × 5(10)], and no response was evident following the RT protocol with half the number of sets and repetitions per set [3 × 5(10)]. These responses were short-lived (Crewther et al. 2006) since 6 h following the exercise protocol concentrations returned to baseline levels. GH, far for being a marker of anabolism after RT, has been reported to increase as the number of repetitions in a set approaches fatigue. In fact, the GH elevations found following resistance exercise seem to be induced by increases in H^+ and lactate (Gordon et al. 1994). Furthermore, the elevation in blood lactate with exercise has been shown to be paralleled by an increase in blood ammonia (Gorostiaga et al. 2010, 2014). However, in the present study, blood ammonia remained elevated 6 h following the 3 × 10(10) protocol, a time when blood lactate was most likely back to resting levels. This elevation in ammonia coincided with the lack of recovery of movement velocity in the BP exercise, which seems a better index of neuromuscular recovery. Finally, CK concentration seemed to be the biochemical variable which was most related to the mechanical variables measured following the three RT protocols (Fig. 2). This is, MPV against the V1 load was not fully recovered until 72 h following the 3 × 10(10) protocol, coinciding with the time at which CK returned to basal levels. CK may be an indicator of damage in the membrane of the miocyte, which suggests that, when resistance exercise is conducted to the point of failure, muscle damage occurs. This, in turn, reduces the velocity at which muscle actions against a given load can be performed. On the other hand, these exercise to failure protocols are known to induce a larger hypertrophic effect (Pareja-Blanco et al. 2017).

A limitation of using blood hormone concentrations to obtain information about anabolic/catabolic effects is that changes in the concentration of these hormones may not reflect their actions at the tissue level. Factors such as the bioavailability of the free form of the hormone, the interaction between hormone and receptor as well as the potency of the evoked intracellular signal mediate the effects of hormones. For instance, increased hormone degradation and clearance rates and low receptor density and affinity would result in reduced anabolic effects for the same blood testosterone concentration. However, we expect little changes in those factors from week to week when using a cross-over experimental design (same subjects). Finally, some studies have suggested that exercise-induced increases in GH and testosterone concentrations do not enhance strength and hypertrophy adaptations and that other factors within the skeletal muscle might be responsible for stimulating anabolism (West and Phillips 2010). Rather than focusing in the anabolic aspects of the measured hormones, we monitored cortisol, blood ammonia, CK and even GH concentrations as markers of endocrine stress and muscle damage since recovery was the focus of our study.

In conclusion, when RT is conducted far from the point of muscle failure (i.e., submaximal *level of effort*, leaving several repetitions in reserve in each exercise set), a considerably faster recovery of neuromuscular performance

between 24 and 48 h following exercise is observed when compared with a training to failure protocol. The results of the metabolic and hormonal variables assessed in the present study also support these conclusions. Acute fatigue markers such as ammonia and GH levels, but especially delayed fatigue biomarkers such as CK, showed a markedly different time course of recovery following the protocols under study, showing again that training to muscle failure significantly slows down the recovery of metabolic and hormonal homeostasis up to 24–48 h post-exercise.

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