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Research article

Effects of Acute Loading Induced Fatigability, Acute Serum Hormone Responses and Training Volume to Individual Hypertrophy and Maximal Strength during 10 Weeks of Strength Training

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Abstract

This study investigated whether a strength training session-induced acute fatigue is related to individuals' strength training adaptations in maximal force and/or muscle hypertrophy, and whether acute responses in serum testosterone (T) and growth hormone (GH) concentrations during the training sessions would be associated with individual neuromuscular adaptations. 26 males completed the 10-week strength-training intervention, which included fatiguing dynamic leg press acute loading bouts (5 x 10 RM) at weeks two, four, six, and ten. Blood samples were collected before and after the loading and after 24h of recovery for serum T, GH, and cortisol (C) concentrations at weeks 2, 6, and 10. The cross-sectional area of the vastus lateralis was measured by ultrasonography. Isometric force measurements were performed before and immediately after loadings, and loading-induced acute decrease in maximal force was reported as the fatigue percentage. The subjects were split into three groups according to the degree of training-induced muscle hypertrophy after the training period. Increases in isometric force were significant for High Responders (HR, n = 10) (by 24.3 % ± 17.2, p = 0.035) and Medium Responders (MR, n = 7) (by 23.8 % ± 5.5, p = 0.002), whereas the increase of 26.2 % (±16.5) in Low Responders (LR, n = 7) was not significant. The amount of work (cm + s) increased significantly at every measurement point in all the groups. A significant correlation was observed between the fatigue percentage and relative changes in isometric force after the training period for the whole group (R = 0.475, p = 0.022) and separately only in HR (R = 0.643, p = 0.049). Only the HR group showed increased acute serum GH concentrations at every measurement point. There was also a significant acute increase in serum T for HR at weeks 6 and 10. HR showed the strongest correlation between acute loading-induced fatigue and isometric force gains. HR was also more sensitive to acute increases in serum concentrations of T and GH after the loading. Acute fatigue and serum GH concentrations may be indicators of responsiveness to muscle strength gain and, to some extent, muscle hypertrophy.

Key words: Strength training, muscle hypertrophy, strength gains, individual differences, acute loading-induced fatigue, serum responses of testosterone and growth hormone.

Introduction

Fatigue is a temporary and reversible decline in the ability to produce voluntary force. It is usually a result of a previous exercise and/or an exercise session, and can be used as an indirect measurement of the volume load (i.e. sets [no.] x repetitions [no.] x load [kg]) of the body. Strength training volume (reps x sets) has been proposed to be an important factor for hypertrophic adaptations (Figueiredo et al., 2018; Heaselgrave et al., 2019; Krieger, 2010; Ralston et al., 2017; Schoenfeld and Grgic, 2018). Volume has dose-response effects on post-workout increase in mTOR signalling (Ahtiainen et al., 2015; Terzis et al., 2010), muscle protein synthesis rate (Ogasawara et al., 2017), myogenic signalling (Drummond et al., 2010), acute neuromuscular fatigue and larger acute anabolic hormone response (e.g. Ahtiainen et al., 2004; Häkkinen and Pakarinen, 1993; Kraemer et al., 1999; Walker et al., 2015). A dose-response relationship between resistance training (RT) volume and training-induced hypertrophy has been observed for untrained men (Krieger, 2010; Schoenfeld et al., 2017), but not always (Schoenfeld et al., 2019).

Higher volumes of resistance training could be needed for maximizing the gains in muscle mass (Burd et al., 2010; Terzis et al., 2010). It is not known, however, whether an increase in acute fatigue during one training session could indicate also increased hypertrophic adaptations during the following training period. It is still unclear whether fatigue is a significant stimulus for muscle hypertrophy or just the consequence of training. Improper fatigue management seems to lead to decreased performance (e.g., Fry and Kraemer, 1997; Gorostiaga et al., 2012) and more fatigue produced by resistance training does not always mean larger strength gains (Pareja-Blanco et al., 2020). The amount of fatigue needed for muscle hypertrophy is still unclear, and large inter-individual variation is likely observed. In addition, a possible relationship between acute fatigue and training-induced adaptations in muscle mass has not yet been determined systematically.

The magnitude of fatigue depends largely on RT volume or duration (Hunter and Faulkner, 1997). High and low-intensity eccentric exercises with the same amount of work seems to induce similar fatigue (Gauche et al., 2009) and intensity seems to affect fatigue only when the number of repetitions is high (Nosaka and Sakamoto, 2001). Gender can also affect largely fatigue capacity (Yoon et al., 2007). Other factors such as rest time between sets and reps and exercise type, can also greatly affect fatigue (Hernandez et al., 2021). In addition, training to a failure induces greater acute fatigue than no-failure training, even when the volume is equated (Fonseca et al., 2020). Although the optimal training frequency has been shown to vary between different individuals (Damas et al., 2019), the individual responses to these modifications have not been studied thoroughly. Interestingly, individuals with the same genetics have been shown to exhibit different amounts of muscle damage (Gulbin and Gaffney, 2002) and twin studies

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(Marsh et al., 2020) have shown that genes may not play such a large role as previously estimated from cross-sectional studies in terms of training adaptations.

Increased fatigue during a training session seems to increase post-workout acute serum hormone concentrations for serum testosterone (T), cortisol (C), and growth hormone (GH) (Häkkinen and Pakarinen, 1993), which speculatively could positively affect training-induced long-term hypertrophic adaptations. Serum hormone concentrations of T over intensive and prolonged strength training and/or acute postexercise increases in serum anabolic hormone concentrations have been shown to be linked to muscle hypertrophy and/or gains in strength (e.g. Ahtiainen et al., 2003; Häkkinen et al., 1985; 1987; 1988; Häkkinen and Pakarinen, 1991; Kraemer et al., 1999; McCall et al., 1999; Seppänen and Häkkinen, 2022; Walker et al., 2015), although some studies have not shown similar results (Morton et al., 2016; West et al., 2009; 2010).

The purpose of this study was to investigate whether a strength training session-induced acute fatigue would be related to individuals' strength training-induced gains in maximal force and/or muscle hypertrophy. In addition, this study investigated whether individual acute responses in serum hormone levels after the heavy resistance training sessions would be associated with individual adaptations of maximal strength and/or muscle hypertrophy over a 10-week strength training period in male participants. We have earlier published one article (Räntilä et al., 2021) from our large research project, and the present paper includes new data related to acute neuromuscular and hormonal responses to single heavy resistance loading session(s) performed before and after 10 weeks of hypertrophic type of strength training.

Methods

Participants

Twenty-six healthy, physically active men between the ages of 19 - 30 years volunteered to participate in the study. The subjects were recreationally physically active but without a systematic strength training background. The exclusion criteria included regular endurance training or team sports more than once per week. They were advised not to take part in any endurance or team sports activities during the intervention.

After initial interviews, the participants' suitability for the intervention was examined using resting electrocardiography (ECG) and blood pressure measurements. A cardiologist reviewed the participants' ECG data before they were accepted into the study. In total, 32 participants underwent pre-screening, and of these, 26 (age 24.6 years ± 3.8, height 180 cm ± 7.3, weight 77.0 kg ± 10.0) were included in the study. Potential risks and discomforts of the study, and the possibility of dropping out from the research project at any time were informed to the subjects, and then they signed an informed consent document. Two subjects dropped out of the study because of health problems unrelated to the study. The study was approved by the Human Sciences Ethics Committee of the University of Jyväskylä and conducted in accordance with the Declaration of Helsinki.

Study design

A total of a 13-week intervention was designed, which included four measurement timepoints within the actual training intervention (Figure 1). The study also included two measurement points before the intervention. The actual intervention included ten weeks of progressive hypertrophic resistance training. The acute fatigue testing procedure was performed four times during the training intervention**:** 1) two weeks after the start of the intervention, 2) four weeks, and 3) six weeks after the start of the training intervention as well as 4) in the final tenth week of the training intervention. The measurement sessions for individual subjects were always performed at the same time of day during the study period.

After the training intervention, the participants were divided into three subgroups: high responders (HR), medium responders (MR), and low responders (LR). The responsiveness was categorized based on the degree of muscle growth (HR>15% n = 10, MR 15 - 4,5% n = 7, and LR <4,5% n = 7) in Vastus Lateralis Cross-sectional area (VLCSA) (measured by Panoramic ultrasonography), and the mean hypertrophic results from these three subgroups have been previously published (Räntilä et al., 2021). The level of responsiveness for the present paper was used to analyse whether changes in VLCSA and fatigue were correlated.

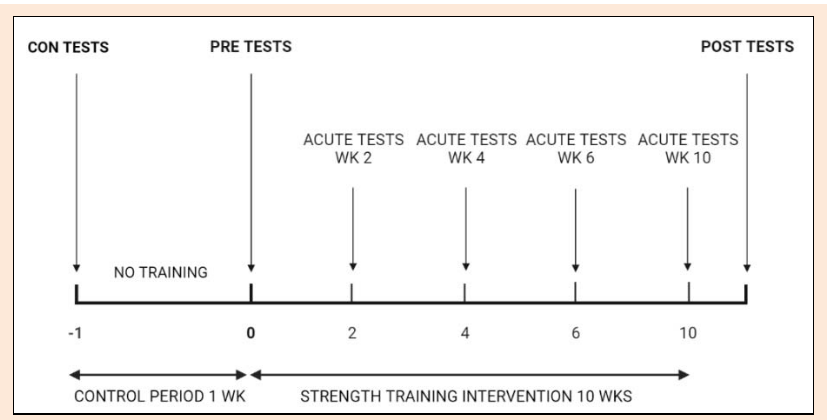

Figure 1. Overview of the experimental design of the study. CON refers to Control. The control tests lasted one week, the control period lasted one week, and the pre-tests were performed prior the intervention. The training intervention lasted 10 weeks and posts tests were done one week (wk) after the strength training intervention. Acute serum hormone responses were collected at wk 2, 6 and 10. The total length of the intervention was 13 weeks.

Table 1. **Training program. When only one variable increased (volume or intensity), it was expressed as a medium period, while during a heavy week, both variables increased (volume and intensity).**

	Medium period	Heavy period	Medium period
Length	3 weeks	4 weeks	3 weeks
Progression	Volume	Volume and intensity	Intensity
Progression Type	+1 set per week for LP and BP	Intensity increased +5% weekly in BP and LP. +1 set weekly for all assistant exercises.	+5% intensity every week in BP and LP.

BP = bench press, LP = leg press

Procedures

Training

All subjects completed the 10-week training intervention, which included 30 supervised training sessions three times per week. None of the subjects missed more than two training sessions during the intervention, and the average participation number in the training sessions was 29.1 ± 0.93.

The training program was planned so that the volume of training (the number of sets) increased over the first seven weeks, and thereafter, the volume remained approximately the same, and the training intensity increased (percentage loads from the 1RM) (Table 1).

Exercise selection choices were made to minimize learning effects over the intervention. Leg press and bench press were selected for the main exercises, and accessory exercises included knee extension, knee flexion, dumbbell bench press, seated French press, elbow flexion and extension, horizontal row, and core exercises. The summary of the training program is shown in Table 2.

The tempo of the lift was controlled for the eccentric phase (3s), and then the concentric part of the lift was performed as explosive as possible. Rest time was 3 minutes for the main exercises and 60s for the other exercises. The main exercises were horizontal leg press and bench press. Rest time remained unchanged during the intervention. Additionally, approximately 5 % of the overall training volume was performed using maximal isometric training contractions in the knee extension and knee flexion machines with the knee angle of 90°. The isometric bench press was performed at an elbow angle of 90°. The isometric training force values were shown to participants to encourage them to go over the previous values. Isometric training was also added to the program to maximize strength development, taking into account specificity, and to contribute positively also to hypertrophic adaptations. The subjects trained either unilaterally or bilaterally. The overall training volume was carefully equated between the groups. The subjects received and consumed one protein bar including 203 kcal, 7 g of fat, 20.1 g of carbohydrate, and 19.6 g of protein after each training session.

Data collection and analyses

VLCSA, isometric and dynamic strength tests, and blood samples were measured at the control-, pre- and post-tests. During the acute testing process blood samples, isometric strength testing, work, and fatigue percentage were collected. The measurements were performed at different times of day but always at the same time of day for each subject.

Acute loading and testing

The acute testing and measurements were performed four times during the actual training period. Maximal isometric leg press was performed before and after the loading. Blood samples for serum hormones were also collected at weeks two, six, and ten. Blood samples were collected before the loading, right after the loading, 15 minutes post the loading, and the next day. The acute loading session in different weeks was always conducted at different times of day but always the same time of the day for every individual subject.

Table 2. **Training program and exercise selection. Isometric training included maximal intensity work for 5s, followed by 15s rest. This was repeated three times and counted as one set. If a subject could not complete 10 reps on the dynamic leg press, the rest of the reps were completed with forced repetitions.**

Training session		Weeks 1-3	Weeks 4-7	Weeks 8-10
#1	**Dyn LP**	5 x 10RM	5 x 10RM	5 x 10RM
	Iso Knee Extension	2 x 60s	2 x 60s	2 x 60s
	Iso Knee Flexion	2 x 60s	2 x 60s	2 x 60s
	Iso BP		2 x 60s	2 x 60s
	Dyn Lat Pulldown		3 x 12 x 70%	3 x 12 x 70%
#2	**Dyn LP**	3 x 10 x 70%	5 x 5 x 80%	4 x 8 x 80%
	Dyn Knee Extension	3 x 12 x 60%	3 x 12 x 65%	4 x 8 x 80%
	Dyn Prone Knee Flexion	3 x 12 x 60%	3 x 12 x 60%	3 x 8 x 80%
	Dyn DB BP	3 x 10 x 50%	3 x 10 x 70%	4 x 8 x 80%
	Dyn Seated French Press with DB	2 x 10 x 60%	2 x 12 x 60%	Dyn DB incline BP 2 x 6 x 70%
	Dyn Horizontal Row	3 x 12 x 60%	3 x 12 x 65%	3 x 8 x 80%
	Isometric Back Extension	2 x 45 s	3 x 45 s	3 x 45 s
#3	**Dynamic BP in smith**	3x10x70%	5 x 5 x 80%	4 x 6 x 80%
	Dyn Horizontal Row	3 x 12 x 60%	Seated OP 3 x 12 x 50%	Seated OP 2 x 10 x 50%
	Dyn Zotmann curl with DB	3 x 12 x 60%	2 x 15 x 50%	3 x 12 x 50%
	Dyn Row with DBs		2 x 12 x 65%	
	Dyn Triceps Push Down		2 x 12 x 65%	3 x 6 x 80%
	Dyn LP	3 x 10 x 70%	Dyn LP 1,5 rep 2 x 8 x 50%	4 x 6 x 70%

s = seconds, RM = repetition maximum, Dyn = dynamic, Iso = isometric, RM = repetition maximum, DB = dumbbell, OP = overhead press, BP = bench press, LP = leg press.

The acute measurements were performed at different times of day but always at the same time of the day for each individual subject (Table 3). Subjects came to the laboratory and gave a blood sample. After that, they started to do warm-up. After the warm-up, they did first the isometric testing in the leg press followed by the leg press loading. The loading consisted of five sets and ten reps of leg press with ascending weights. The third set was done so that the subject had one more repetition in reserve. Thereafter, the load was raised so that the subjects could not do the required ten reps by themselves. The last two sets were done to concentric failure and these sets were completed with forced repetitions. Rest time was three minutes after every set. Subjects performed the testing and loading either unilaterally or bilaterally. For the unilateral group, the left and the right leg were calculated together when the data was analysed. Thereafter, the subjects gave blood samples and right after that, they did the isometric leg press testing. After 15 minutes, they gave the final blood sample, and the testing was finished. The time between the loading and isometric testing was attempted to keep as short as possible. A desirable recovery time before the post-isometric testing was three minutes.

Table 3. Timetable for acute measurements.

TIME (min)	TESTS
0	Pre blood samples
5	Warm up
20	Pre isometric strength testing
30	Dynamic leg press loading 5 x 10 RM
60	Post blood samples
65	Post isometric strength testing
	Rest
75	Post 15min blood samples

Work

The amount of work done during the intervention was measured in the acute loading tests every second week. The work was calculated during the dynamic leg press loading, which consisted of five sets and ten reps of leg press with ascending weights. The loading exercise was–performed using the leg press (David 210, David Health Solutions Ltd, Helsinki, Finland), which has a custom-built device attached to it. It measured the length (cm) and duration of every rep (s) and calculated the overall time and distance for every set. The device measured only when the sled in the leg press was moving. Short stops at the end of concentric or eccentric portions of the lift were not included in the overall results. In the starting position of the leg press, each subject was seated on the device with a knee angle of 60°. The movement started with the concentric portion of the lift. Subjects were required to lift the load to a fully extended position. Work (W) was calculated by multiplying the force (F) by the movement of the object (d) ($W = F \times d$). For the unilateral group, the results of the left and right leg were calculated together. Subjects did five sets during the measurements, and the calculated work average of those five was used.

Muscle cross-sectional area

B-mode axial-plane ultrasound (model SSD-a10, Aloka Co Ltd, Japan), using a 10-MHz linear-array probe (60 mm width) with extended-field, was used to assess the vastus lateralis cross-sectional area (CSA). The subjects lay supine, and their leg position was controlled with legs strapped to polystyrene supports. A custom-crafted convex-shaped probe was used to ensure a perpendicular angle of the probe. The probe was moved manually, slowly, and continuously along the marked line on the skin. Anatomical landmarks were marked from the middle section between the joint space on the lateral side of the knee and to the greater trochanter. 40 % of the femur length was marked. and a line was drawn from the lateral to the medial diaphysis of the right thigh. After scanning, the software uses the captured images to automatically combine a complex image of the muscle's CSA. Great care was taken not to compress the muscle tissue. Three panoramic CSAs samples were collected for each measurement. The CSA was then determined using the Image-J - program (version 1.37, National Institute of Health, USA). Within Image-J the polygon selection tool was used for the analysis. This enables manual tracing along the muscle border. The inner line of the fascia was closely followed, and when it was not observed, the predicted route was chosen according to previous. Great care was used to complete the analyses, the mean value from the three pictures was used in the analyses. The same investigator did all measurements and analyses. Panoramic ultrasonography had an intraclass correlation coefficient of 0.997 with a standard error of measurement of 0.38 cm^2 (Ahtiainen et al., 2010).

Isometric strength testing

Maximal bilateral leg extensor strength was measured on a custom-built horizontal leg press (Biology of Physical Activity, University of Jyväskylä) in a seated position with the knee joint angle at 107°. The subjects were instructed to use their maximum effort and push "as fast and hard as possible". They were strongly encouraged in every trial. Subjects maintained their maximum force levels for approximately 3 seconds. Subjects had two trials unless they increased their force by over five percent. In this situation, they were allowed to perform the third attempt. Rest time was 2 minutes between trials. The isometric leg press has been shown to have an intraclass correlation coefficient of 0.98 (0.93 - 0.99) and a coefficient of variation of 3.48 (-3.34 - 10.31) (Petré et al., 2023).

Fatigue percentage

Fatigue percentage was measured during the acute tests. Isometric leg press tests were done prior to and right after the dynamic leg press loading. Maximal isometric force before and after was compared and the percentage change was reported as fatigue percentage. Fatigue percentage in the unilateral group was the mean average of fatigue percentage of the left and right leg.

Blood samples

Venous blood samples were drawn into serum tubes (Venosafe, Terumo Mediacl Co., Leuven, Belgium) from the antecubital vein by a qualified laboratory technician. Six millilitres (ml) of blood was drawn covering approximately 2.5 ml serum.

There were no restrictions on food and beverages during blood sample collections**.** The first sample was given right before the training session, the post-sample was drawn immediately after the loading, and after the 15-minute rest, the third blood sample was collected. 24 hours (h) after the end of the training session the subjects came to the lab to give a post 24-hour blood sample. If the training session was, for example, in the evening, the subject came the next evening to the lab to give the blood sample, and if the training session ended in the morning, the post-24 sample was also collected the next morning. The samples were centrifuged for 10 minutes at 3500 rpm (Megafuge 1.0R, Heraeus, Germany). Then samples were frozen (-80°C) and stored for later analysis. Serum T, C, and GH levels were analysed. Analyses were performed using immunometric chemiluminescence techniques (Immulite 2000) and hormone-specific immunoassay kits (Immulite, Siemens, Illinois, USA)). Analytical sensitivity was T = 0.5 nmol L−1, COR = 5.5 nmol L−1, and GH = 0.01 µg L−1, and the intra-assay coefficient of variation is T = 13%, GH = 5.8%, and COR = 7.9%. Serum creatine kinase (CK) activity was assessed with Konelab 20 XTi (Thermo Fisher Scientific, Vantaa, Finland). The analytical sensitivity for serum CK was 10 U/l and the inter-assay coefficient of variation was 2.8%. The hormone values presented are uncorrected for plasma volume changes.

Statistical analyses

All statistical analyses were performed using SPSS version 24 (IBM corp., New York, NY, USA). Standard statistical analyses were used to determine descriptive statistics, and all data are reported as the mean ± SD, unless otherwise stated. Test of normality (Shapiro-Wilk) was done before the analysis and acceptable levels of skewness and kurtosis were also checked. Hormone data were not normally distributed. Repeated-measures ANOVA was used and when a significant F-value was found using the ANOVA with repeated measures with a Greenhouse-Geisser correction, the post hoc tests using the Bonferroni correction was used to locate the pair-wise differences. One-way ANOVA was used to analyse the differences between the subgroups (three groups). Associations between the different variables were tested with Pearson's product-moment correlation coefficients. The alpha level was set at $p \leq 0.05$.

Results

After the intervention subjects were split into three groups according to the magnitude of the increase in the VL CSA during the 10-week training period as follows (for details see Räntilä et al. 2021): High Responders >15%, (n = 10), Medium Responders 15 - 4, 5% (n = 7) and Low Responders <4,5% (n = 7). Absolute individual values in VL CSA and maximal isometric leg press force at Pre and Post training are shown in Figure 2.

Maximal isometric force in leg press increased from Pre to wk 4 (p = 0.003), pre to wk 6 (p < 0.0001), pre to wk 10 (p < 0.0001), wk 2 to wk 6 (p = 0.015), wk 2 to wk 10 (p < 0.0001) and from wk 4 to wk 10 (p = 0.040) for the whole group (Figure 3).

In the different responder groups, the increases in maximal isometric force were statistically significant in HR (by 24.3 %) from pre to wk 10 (p = 0.035) and MR (by 23.8 %) from pre to wk 10 (p = 0.002), while the increase of 26.2 % in LR was not statistically significant.

Mean values for leg press fatigue percentages increased significantly in the whole group from week 2 to week 4 (p = 0.046) and from week 2 to week 10 (p = 0.003) by +93% (±110) (Figure 4). No statistically significant changes took place in fatigue percentages in three different responder groups during the training period and no statistically significant differences occurred between the groups. The leg press fatigue percentage increased from week 2 to week 10 in LR by +143.7 (±139.9) (p = 0.009), in MR by +73.8 (±93.6.) and in HR: by +61.1 (±92.2). There were no significant correlations between changes in fatigue percentage in LR, HR or MR groups and changes in VLCSA. However, in the total group of subjects, a significant correlation was observed from week 2 to week 10 between relative changes in fatigue percent and relative changes in isometric force (R = 0.475, p = 0.022) (Figure 5) and as well as for HR (R = 0.643, p = 0.049).

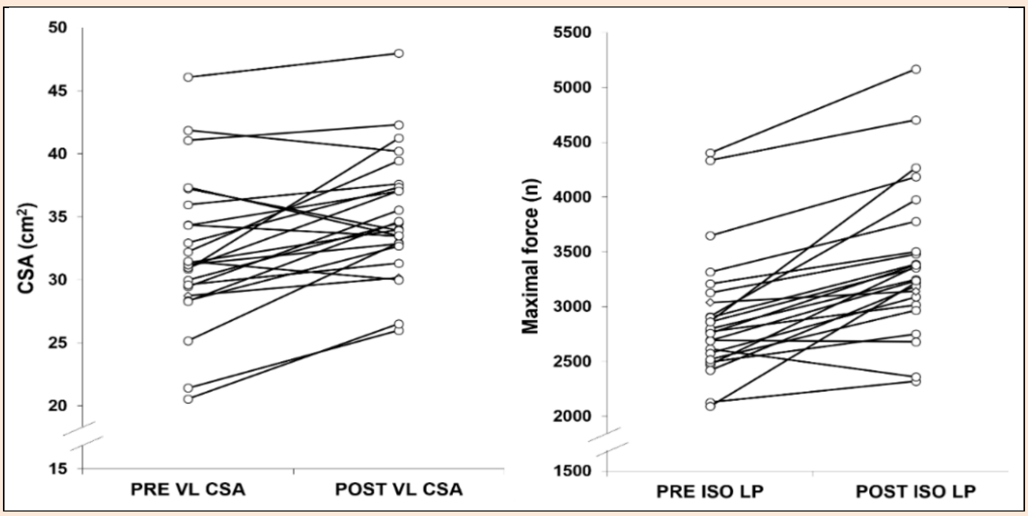

Figure 2. Individual absolute values in VL CSA pre to post (on the left) and individual absolute values in maximal isometric bilateral leg press force pre to post (on the right) after 10 weeks of hypertrophic strength training. PRE=Pre training intervention measurements, POST= post training intervention measurements.

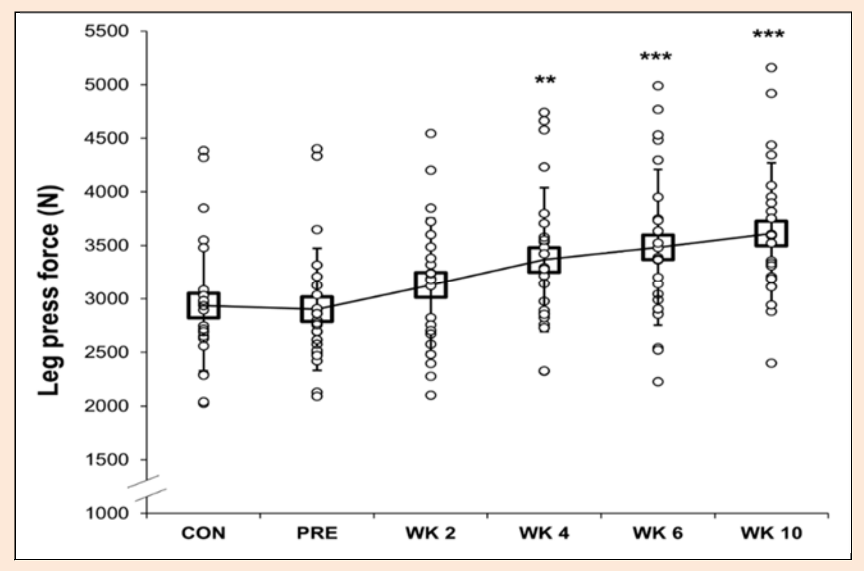

Figure 3. Maximal isometric bilateral leg press force values during CON and PRE, and repeatedly during the 10-week strength training period for the whole group including individual values. CON=Control measurements, PRE=Pre training measurements. * = compared to Pre. **P ≤ 0.01, ***P ≤ 0.001.

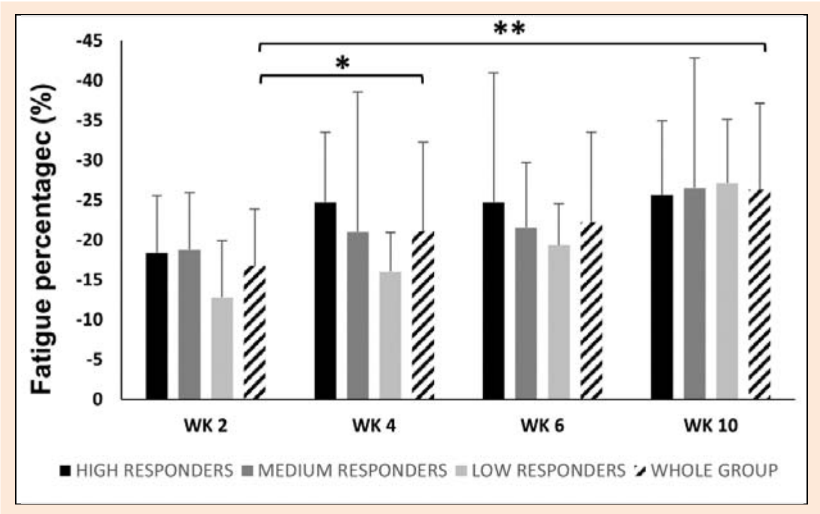

Figure 4. Fatigue percentages after the acute loading protocol in the leg press at different time points in three different responder groups and in the total group during the 10-week hypertrophic strength training intervention. *P ≤ 0.05, **P ≤ 0.01.

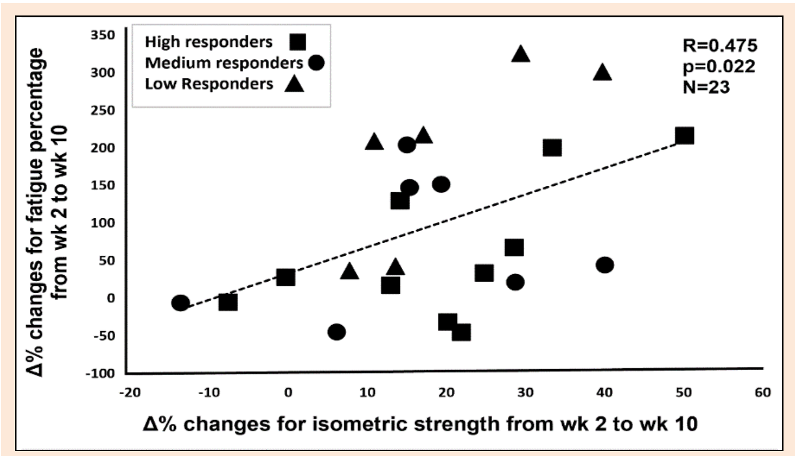

Figure 5. The correlation between the relative changes in maximal isometric force and fatigue percentage from week 2 to week 10 in the total subject group.

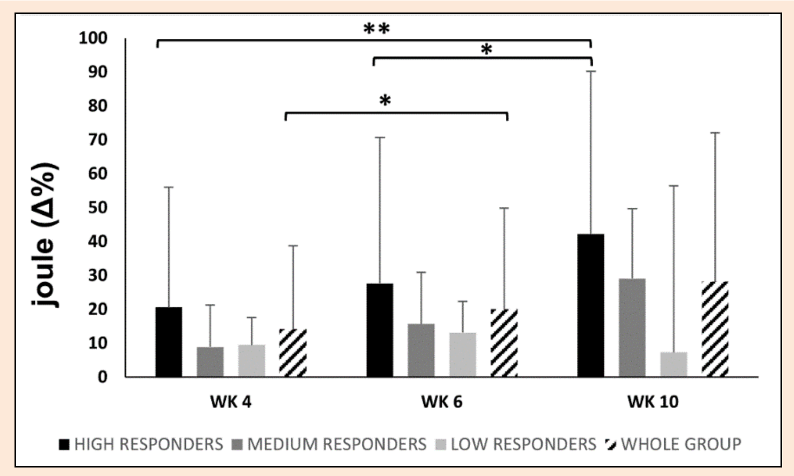

Figure 6. Relative changes in performed work during the acute loading protocol in the leg press exercise compared to initial week 2 tests in three different responder groups and in the whole group. *P ≤ 0.05, **P ≤ 0.01.

The amount of work performed during the acute loading protocol in the leg press exercise increased during the intervention in the whole group from WK 2 (102557 Joules (J)) to WK 4 (113355 J) ($p = 0.006$), to WK 6 (118165 J) ($p = 0.001$) and to WK 10 (129945 J) ($p<0.001$), from WK 4 to WK 6 ($p = 0.024$) and 10 ($p < 0.001$) as well as from WK 6 to WK 10 ($p < 0.001$). There were significant differences in the absolute amount of work during the intervention between HR and LR at week 2 (91265 J vs 120031 J), week 4 (103986 J vs 130736 J), and week 6 (108487 J vs 134480 J), but not at week 10.

Relative changes in leg press work in the whole group were statistically significant from week 4 to week 6 ($p = 0.011$) and HR had also statistically significant changes from week 4 to week 10 ($p = 0.005$), from week 6 to week 10 ($p = 0.025$) (Figure 6). In MR the changes were close to significance from week 4 to week 10 ($p = 0.053$) and from week 6 to week 10 ($p = 0.051$). There were no statistically significant changes in LR.

Serum T post loading concentrations increased significantly from 12.89 nmol/l (±4.20) to 15.33 nmol/l (±5.16) and up to week 16.62 nmol/l (±5.66) in the whole group (Table 4). Post 15 min values followed the same pattern, and the increase was in both cases significant. There were significant differences in post-loading concentrations between week 2 and week 10 ($p = 0.027$). In addition, the mean of post and post 15 concentrations was statistically significant from week 2 to week 10 ($p = 0.0034$). The increase in the concentrations from pre to post and post 15 were both statistically significant for week 6 and week 10. Fatigue percentage was also associated with serum T concentrations 24 h after the loading. The correlation was stronger during the intervention and at week 2 it was 0.42 ($p = 0.053$), at week 6 it was 0.48 ($p=0.020$), and at week 10 0.62 ($p = 0.002$).

In HR CK post 24h decreased significantly from week 2 (3483 ± 2653) to week 6 (254 ± 121) ($p = 0.011$) and from week 2 to week 10 (304 ± 138) ($p = 0.011$). There were statistically significant differences between CK post 24h results for HR and LR at week 6 (254 ± 121 vs 477 ± 139) ($p = 0.006$). CK delta changes from pre to 24h after the acute loadings differed significantly from week 2 (0% ± 39) to week 6 (89% ± 87) ($p = 0.002$) and from week 6 to week 10 (25% ± 48) ($p = 0.006$) for the whole group.

Serum C concentrations increased statistically significantly in week 10 from pre to post 15 for the whole group (Table 4). MR also showed significant changes from pre to post ($p < 0.001$) and from pre to post 24h ($p = 0.035$). LR also showed a significant rise in serum C from pre to post 24h ($p = 0.022$) and post to post 24h ($p = 0.0019$). After the initial weeks, HR had the smallest response in every measurement point in serum C after the loadings. In addition, HR was the only group to have a significant pre to post increase in serum T in week 6 ($p = 0.033$).

Table 4. Serum testosterone and cortisol concentrations (nmol/L) in the whole group measured at PRE, POST, POST 15, and POST 24h and relative changes right after, 15 min after, and 24 hours after the strength loading protocol two weeks after the start of the intervention and six and 10 weeks after the strength training intervention. Values are presented as mean and SD.

		WK 2		WK 6		WK 10	
			Δ% from PRE		Δ% from PRE		Δ% from PRE
Testosterone	**PRE**	11.5±3.8		12.9 ±4.8		13.9 ±5.4	
	POST	12.9 ±4.2	13.8 ±27.8	15.3 ±5.2 ***	23.6 ±23.8	16.6 ±5.7 ***	23.8 ±23.8
	POST 15	12.4 ± 4.5	6.4 ±27.3	14.3 ±5.0 **	19.2 ±24.2	15.8 ±5.7 **	15.9 ±19.2
	POST 24h	12.7 ±3.6	16.4 ±44	13.2 ±6.3	2.4 ±22.15	14.8 ±6.2	9 ±18.6
Cortisol	**PRE**	304 ±101.3		302.3 ±104.5		308.7 ±128.6	
	POST	290.9 ±154.8	-2.7 ±47.4	355.3 ±144	28 ±65.4	384.7 ±118	56.4 ±96.6
	POST 15	340.9 ±175.8	14.8 ±51.6	393.2 ±152	49.8 ±89.3	429 ±128.1 *	80.4 ±120.3
	POST 24h	318.2 ±142.5	8.4 ±40	291 ±118.8	2.1 ±42.2	304.5 ±93.8	23.2 ±90.7

*P ≤ 0.05, **P ≤ 0.01, ***P ≤ 0.001. All significances measured from pre.

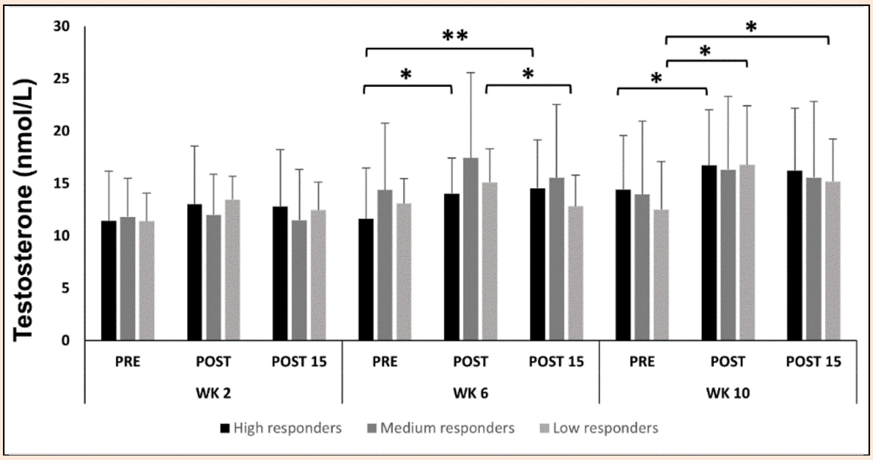

Figure 7. Acute responses in serum testosterone concentrations during the hypertrophic loading conditions for different subgroups at weeks 2, 6 and 10 during the 10-week strength training intervention. *P ≤ 0.05, **P ≤ 0.01. Pre = before loading, Post = right after loading, Post15 = 15 minutes after the loading.

The hypertrophic loading induced acute increases in serum T concentration were significant in HR from pre to post (p = 0.033) and pre to post 15 (p = 0.001) at week 6 and pre to post (p = 0.034) at week 10 (Figure 7). For LR, there was a significant decrease at week 6 from post to post 15 p = 0.005, and a significant increase at week 10 from pre to post (p = 0.004) and from pre to post 15 (p = 0.040). Relative changes were statistically significant for low responders for post 15 from week 6 to week 10 (p = 0.011) and for post to post 15 in week 6 (p = 0.008).

Serum GH concentration increased significantly from pre to post and pre to post 15 at weeks 2, 6, and 10 for the whole group (all p < 0.001). There were no significant differences in post and post 15min concentrations at different weeks. The relative changes were also significant for the whole group from week 2 to week 6 (p = 0.001) and to week 10 (p = 0.005). The same was observed for pre to post 15 concentrations with significant increases in week 2 to week 6 (p = 0.005) and in week 2 to week 10 (p = 0.005). In addition, the percentage increase from pre to post became larger during the intervention in the whole group. In week 2 the increase in GH concentration was 3642 % (±8583), in week 6 it increased by 16882 % (±17768) and in week 10 the increase was 26514 % (±29606).

For three subgroups serum GH concentration increased significantly for HR from pre to post and pre to post 15 at weeks 2, 6, and 10 (Figure 8). In MR, the increase was significant at week 6 from pre to post 15. In LR, the increase was significant from pre to post and pre to post 15 at week 6 and from pre to post 15 at week 10.

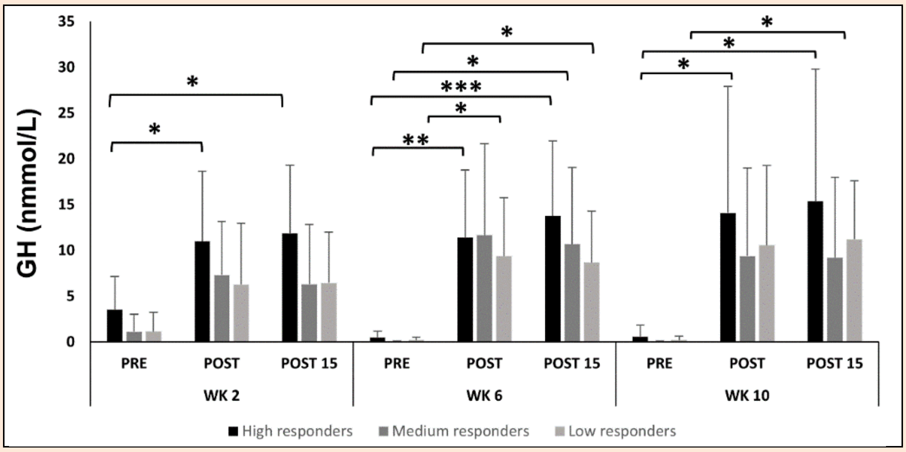

Figure 8. Acute responses in serum GH concentrations during the loading conditions for different subgroups at weeks 2, 6 and 10 during the 10-week strength training intervention. *P ≤ 0.05, **P ≤ 0.01, ***P ≤ 0.001. Pre = before loading, Post = right after loading, Post15 = 15 minutes after the loading.

Discussion

The primary findings of the present study showed that acute resistance loading-induced fatigue in the whole subject group correlated significantly with strength training-induced relative gains in maximal isometric force but not for muscle hypertrophy adaptations. The present results also showed that HR subjects were more sensitive to loading-induced acute rises in serum hormone concentrations of T and GH. Thus, the present findings may partially explain some of the inter-individual differences in strength training-induced adaptations.

Inter-individual fatigability differs already after several weeks of strength training (Ahtiainen et al., 2003;

Walker et al., 2013;2015). It would be a logical assumption that fatigability also affects the ability to adapt to the strength training stimulus. However, no significant correlations were observed between the level of fatigue and training-induced enlargements in muscle size. On the other hand, there was a significant correlation between fatigue and relative changes in maximal isometric force in the whole subject group and for the HR group, while the two other subgroups did not show significant correlations between these two variables during the intervention.

Increases in workload seemed to be more important than acute fatigue for hypertrophy, since LR did more work (cm + s) than HR (sig. differences at weeks 2, 4, and 6), but the amount of work performed no longer increased in LR from week 6 to week 10 as much as it did in both HR and MR. This may indicate that the amount of work and fatigue could have affected the prescribed workload. The fatigue percentage increased in LR much more in comparison to HR (+143.7 ±139.9 versus +61.1 ±92.2). Acute fatigue may have led the LR group to use a shorter range of motion, which affected the amount of work done by LR (cm + s). Thus, acute fatigue may influence the magnitude of hypertrophic adaptations through decreased work. RT-induced volume is one of the main drivers of hypertrophic adaptations (Schoenfeld et al., 2017), and hypothetically a high amount of acute fatigue, and consequently, decreased work, would influence hypertrophy adaptations. At the same time, HR increased their relative workload most from week 2 to week 10, when LR increased the least among all subgroups. A six-month study found no advantage in terms of high fatigue and high metabolite accumulation to strength gains (Welsh and Rutherford, 1996). Folland et al. (2002) showed that isometric strength gains can be obtained without a large amount of fatigue. However, we found a correlation between acute fatigue and training-induced gains in isometric strength, but not with hypertrophy.

Fatigue seems to be associated with a decrease in the total work capacity of the neuromuscular system (Pareja-Blanco et al., 2017; Párraga-Montilla et al., 2020). Häkkinen and Pakarinen (1993) noticed that the very high volume 10 x 10 x 70% hypertrophic strength loading led to an almost 25% decrease in ten reps repetition maximum. A quarter drop in force production ability is considered extreme fatigue, and it might not be sustainable in every training session. In our intervention, the force production ability decreased steadily at every measurement point. It dropped from -16.8% in the first measurement all the way to -26.3% in the last testing session. The optimal range for fatigue to maximize hypertrophic and strength adaptations still remains unclear. We need to note that in the present study, the amount of work was only measured during the leg press exercise. Thus, in overall, the amount of work between individuals may have varied a lot, which could in part explain rather large individual differences between the subjects. Martins-Costa et al. (2022) showed that the equation of workload, time under tension, was more important than the number of reps used, for gains in strength and skeletal muscle hypertrophy. Thus, in future interventions, it is important to quantify the amount of volume with the amount of work done, when the goal is to compare individual loading responses and training adaptations during the intervention.

HR**s** were more sensitive to acute rises in serum hormone concentrations of testosterone and GH right from the start of the training period. Walker et al. (2015) also showed higher acute serum GH response before versus after the training period for high hypertrophy responders compared to low hypertrophy responders. Thus, this may imply that HR may be more sensitive to increases in acute GH response after hypertrophic loading. Moreover, Ahtiainen et al., (2003) have noticed that athletes increased their serum TES levels during the acute loading conditions more than non-athletes. Sensitivity for acute hormone rises can affect the magnitude of adaptations, because, for example, resting serum TES, TES/COR, and TES/SHBG ratios and/or their changes have been shown to correlate significantly with increases in isometric and dynamic strength (Ahtiainen et al., 2003; Häkkinen et al., 1985; 1987; 1988). On the other hand, intramuscular androgen receptor content may also be important to skeletal muscle hypertrophy in addition to circulating serum hormones (Morton et al., 2018). Overall, it seems that serum hormone concentrations may be one of the indicators of an individual's ability to adapt to resistance training.

Interestingly, serum TES concentration did not recover to the baseline in 24h but remained somewhat higher, and there were large individual differences. Kotikangas et al. (2022) found that serum TES and COR did recover to baseline after 24h from loading. In turn, McCaulley et al. (2009) noticed that TES remained elevated, and COR decreased, compared to the baseline 24h after loading. Häkkinen and Pakarinen (1993) noticed that serum morning TES concentration decreased significantly, for at least to two days, after the extreme high-volume (10x10RM) hypertrophy loading. In the present study, recovery from loading was similar between the subgroups. Kotikangas et al. (2022) did not also report significant differences between groups 24 h after the loading. Fatigue percentage was also associated with testosterone concentrations 24 h after the loading with a growing correlation during the intervention, indicating that the amount of fatigue was associated with the next-day serum testosterone concentrations.

The HR response for CK was almost twice as high as that of the other subgroups. MacHado and Willardson (2010) also noticed that after hypertrophic loading CK activity in high responders was approximately 70% higher than that in normal responders. CK may contribute to fatigue by increasing the myoplasmic concentration of inorganic phosphate, when the resistance training stimulus is more prolonged (Dahlstedt et al., 2000). We observed that in HR CK-post 24h decreased significantly from week 2 compared to the following training weeks. After exercise, CK has been shown to increase up to 48 h (Marathamuthu et al., 2022), over 96 h (Paschalis et al., 2005), and even after seven days (Saka et al., 2009). However, in the present study, CK was measured only 24 h after the training session. Interestingly, after the initial weeks, the HR group also showed the smallest response in serum cortisol concentrations indicating that overall serum hormone responses in HR adapted during the training intervention.

It must acknowledge that the present study had some limitations, when attempting to draw evidence-based conclusions. First, fatigue was measured repeatedly but only during one training session, and it may not directly reflect the entire training intervention. In addition, the amount of work was measured only during the leg press exercise. Thus, it does not reflect the work performed by other exercises and/or machines. Future research could focus on recording work during all the exercises performed during the intervention. It would be intriguing to determine, how the prescribed volume varies among individuals during the training process. Secondly, our responders were divided into three subgroups based on the magnitude of hypertrophy in one muscle only (VLCSA) (see Räntilä et al., 2021). The ability to respond may vary greatly depending on the muscle group under investigation. Third, although we provided protein and carbohydrate supplements to our participants, we did not control for diet or recovery in any other way. Some of the differences in adaptations between individuals might have, at least in some part, been explained by nutritional intake or other lifestyle choices made individually.

Conclusion

The present study showed that acute loading-induced fatigue seems to have some role in contributing to strength gains, but not necessarily for muscle hypertrophy adaptations. HR showed the strongest correlation between acute loading-induced fatigue and relative changes in maximal isometric force compared to the other two subgroups that did not show any significant correlations. The present results showed also that HR subjects were more sensitive to loading-induced acute rises in serum hormone concentrations and these subjects demonstrated significant changes in every measurement point in the acute loading-induced serum GH concentrations. Thus, the present findings could partly explain the interindividual differences observed in strength training-induced adaptations.

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Key points

- High responders to strength training showed a strong correlation with acute fatigue and training-induced gains in isometric force
- High responders were more sensitive to acute increases in serum hormone concentration compared to other subgroups
- Low responders did more work compared to High responders, but high responders increased their workload more throughout the intervention.
- Progression in the amount of work might be more important than the overall workload
- Force production ability decreased during the acute loading tests from the first test of -16.8% to all the way down to -26.3%, while optimal fatigue range for muscle hypertrophy needs further investigation.

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