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3 *Active recovery shows favorable IGF-I and IGF binding protein responses following heavy*  
4 *resistance exercise compared to passive recovery*  
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**1 ABSTRACT**

2  
3 IGF-I and IGFBPs have important physiological modulatory effects and this study sought to examine the  
4 influence of active vs. passive recovery following a heavy resistance exercise on IGF-I and IGF binding  
5 protein (IGFBP) recovery responses. It was hypothesized that increased IGF-I and decreased inhibitory  
6 IGFBPs during active recovery may be reflective of cascades promoting physiological recovery. 18  
7 untrained men ((AR n=7, PR n=11), age: 26±4 years, height: 174±8 cm, body mass: 75±13 kg) performed  
8 either a protocol-specific 10x10x30% 1RM active (AR) or passive recovery (PR) session following a  
9 heavy resistance exercise session performed on a leg press device (10x10 1RM). Maximal isometric  
10 force production (MVC) and IGF- and IGFBPs were measured pre, post, 1-hr post, and next morning. A  
11 significantly greater relative response in IGF-I was observed in AR than in PR at post recovery and next  
12 morning ( $p<0.01$  and statistical trend, respectively) while absolute concentrations of IGFBP-1 at next  
13 morning were significantly higher in PR than AR ( $p<0.05$ ), and relative IGFBP-1 response from control  
14 to next morning in PR was significantly greater than in AR ( $p<0.001$ ). IGFBP-1 may be inhibitory to  
15 IGF-I biological action, thus the lower concentration of IGFBP-1 after AR may be considered favorable  
16 in terms of recovery due to its positive relationship with glucose metabolism and maintaining metabolic  
17 homeostasis. These results suggest that some of the benefits of an active recovery bout may be mediated  
18 by favorable IGF-I system responses (increased IGF-I and decreased IGFBP-1) in the hormonal milieu  
19 that may assist facilitating the cascade of physiological recovery processes following acute heavy  
20 resistance loading exercise.

21 Key words: exercise, active recovery, passive recovery, IGF-I system, heavy resistance exercise, lower  
22 extremities

23

24

25

1

## 2 INTRODUCTION

3 Insulin-type growth factor I (IGF-I) is a 7.5 kDa polypeptide that stimulates both anabolic and metabolic  
4 effects via the IGF type I receptor (IGF-IR) [1]. IGF-I plays a direct role in whole-body glucose  
5 homeostasis and participates in processes that promote muscle hypertrophy [2]. IGF-I is positively  
6 associated with muscular endurance and aerobic fitness as well as positive health and fitness outcomes  
7 [3]. It uses both autocrine and paracrine actions that respond to the loading state of the muscle [4]. IGF-  
8 I is an important biomarker of metabolism [5], and it is bound to specific binding proteins (IGFBP 1–6)  
9 that either attenuate or potentiate the biological potency of IGF-I in

10

11 both blood circulation and tissues [6]. The majority of IGF-I in circulation is bound to IGFBP-3, which  
12 helps to control the distribution of the majority of IGF-I [7,8]. Endocrine and locally produced IGF-I [4]  
13 binds to other IGFBPs, especially IGFBP-1 in the extra-cellular fluid, and regulates the access of IGF-I  
14 to the IGF-IR [6]. The binding of IGF-I to these binding proteins may allow for an extended period of  
15 transport throughout the body, consequently increasing the potential for action. The IGF-I system is  
16 thought to mediate the cascade of cellular and physiological processes during recovery of intense  
17 exercise.

18

19 Heavy resistance training is characterized by significant loading of the muscles in which a marked acute  
20 decrease in force production capacity is typically observed after each loading session [9-11]. This heavy  
21 resistance training may trigger physiological cascades that play a key role in strength development,  
22 muscle hypertrophy, and overall recovery [12,13]. A single, heavy resistance exercise session has been  
23 reported to result in increased serum concentrations of hormones including testosterone, growth  
24 hormone, and cortisol as well as IGF-I [14-16]. In the days following a heavy resistance exercise  
25 protocol, perturbations in hormonal balance such as testosterone, cortisol and T/C ratio may be an

1 indicator of training stress and/or physiological responses leading to positive training adaptations [16],  
2 however, the same has not yet been established in terms of IGF-I and its binding proteins.

3

4 Recovery between sessions of loading is extremely important to promote positive training adaptations  
5 and for optimal performance of subsequent tasks. Both active and passive methods have been developed  
6 to facilitate recovery [17]. Methods for passive recovery include lying prone or remaining seated in order  
7 to reduce metabolic demand [18-20]. Active recovery methods are reported to facilitate recovery via an  
8 increase in blood flow and substrate clearance. Examples of such methods include upright standing [21],  
9 walking and aerobic running [22], as well as submaximal cycling [23]. Heavy resistance exercise  
10 protocol-specific active recovery has not, to our knowledge, been investigated. Protocol-specific active  
11 recovery may be justified in small gyms or e.g. during military operations where equipment, time, and  
12 mobility are limited. The extra total work required by active recovery may allow for an extended period  
13 of blood flow and/or further increases in e.g. hormones that may consequently increase the potential for  
14 positive adaptations and more optimal recovery. The IGF-I system was specifically chosen in this study  
15 due to its known metabolic influences on whole body physiology.

16

17 Effective recovery processes may involve metabolic and hormonal milieu cascades that facilitate muscle  
18 recovery, and IGF-I's role in tissue remodelling and in metabolic modulation, merits investigation. Thus,  
19 the purpose of this study was to examine the influence of active vs. passive recovery on the acute IGF-I  
20 and IGF binding protein responses and maximal isometric force production to a high volume and  
21 strenuous lower body heavy resistance loading session. Based on the previous studies of active vs.  
22 passive recovery strategies, we hypothesize that active recovery conditions lead to more favourable  
23 hormonal milieu during the recovery following the resistance exercise when compared to passive  
24 recovery.

1

## 2 MATERIALS AND METHODS

3 **Subjects.** Participants ( $n = 18$ ) in this study were voluntary healthy men, recruited via newspaper and  
4 online advertisements. The target group was healthy physically active, but not formally trained men,  
5 exclusion criteria included: body mass index  $> 28 \text{ kg} \cdot \text{m}^{-2}$ , illness, disease, injury or use of medications  
6 that would contraindicate participation in the study. Health questionnaires were reviewed, and the  
7 subjects were cleared for participation in the study by a physician prior to testing. The subjects were  
8 randomly assigned to either a passive recovery group (PR) or an active recovery group (AR). For the  
9 present sub-study, complete data was available from eleven subjects of the PR group (mean  $\pm$  SD, age:  
10  $25.7 \pm 3.9$  years, height:  $181.0 \pm 7.7$  cm, body mass:  $78.4 \pm 10.9$ , body mass index:  $23.9 \pm 2.4$ ,  $\text{VO}_{2\text{max}}$   
11  $60.8 \pm 4.9 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) and seven subjects of the AR group (age:  $25.4 \pm 3.1$  years, height:  $180.1 \pm 7.7$  cm,  
12 body mass:  $80.5 \pm 15.5$ , body mass index:  $24.7 \pm 3.4$ ,  $\text{VO}_{2\text{max}}$   $59.7 \pm 10.2 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ). Groups were not  
13 equal due to scheduling conflicts. The subjects were instructed to avoid caffeine and tobacco for at least  
14 4 hours prior to each testing session. Subjects were also instructed not to participate in strenuous exercise  
15 or to drink alcohol the day before the strenuous loading and during the two days of experimental testing.  
16 The subjects were in a morning-fasted state each testing day. The subjects gave resting blood samples  
17 and were familiarized with all testing methods  $\sim 2$  weeks prior to the heavy resistance exercise protocol  
18 described below. In these familiarization measurements, maximal oxygen uptake, maximal bilateral  
19 isometric force production, and maximal dynamic leg press were also determined (methods below).

20

21 **Ethics statement.** Ethical approval of both methodology and consent procedures was granted by the  
22 Central Finland Health Care District (K-S shp:n Dnro 34/2007), and the Surgeon General of the Finnish  
23 Defence Forces. The study was conducted according to the provisions of the most recent Declaration of  
24 Helsinki. All subjects received written and oral information about the study design and measurement

1 procedures including information on the possible risks and benefits of participation. All subjects signed  
2 an informed consent document prior to participation in this study. The data presented in this manuscript  
3 is from a larger study regarding neuromuscular and hormonal responses to heavy resistance exercise  
4 followed by loading-specific active or passive recovery. A previously published manuscript discusses  
5 the responses of serum luteinizing hormone, serum testosterone, serum cortisol, and sex hormone binding  
6 globulin as well as maximal bilateral isometric force (also reported in the present manuscript) and  
7 countermovement jump height [24].

8

9 **Heavy resistance exercise protocol.** The heavy resistance exercise included a 10 x 10 repetition  
10 maximum (RM) sets of bilateral leg presses in a horizontal sitting position (David 210, David Health  
11 Solutions Ltd, Helsinki, Finland) with 2 min of rest between sets. The starting load was ~70% (to the  
12 closest 2.5 kg) of individual 1RM. After the first set, the workload was adjusted so that each subject was  
13 able to perform 10 repetitions during each set of the loading protocol. If the load became too heavy for  
14 the subject to complete the set alone, assistance by trained laboratory personnel was provided so the  
15 subject could complete it. The range of motion for each repetition was from a knee angle of 65° to a knee  
16 angle of 180° (full extension). The loading started at the same time of day (11:00) for all subjects and  
17 lasted for ~60 min (including post-loading blood sampling and maximal isometric strength  
18 measurements). A break of 10 min between the 5<sup>th</sup> and 6<sup>th</sup> set allowed for additional measurements (data  
19 not presented). The heavy resistance exercise protocol has previously been described [30].

20

21 **Recovery protocols.** AR and PR protocols started immediately after force measurements and blood  
22 sampling after the heavy resistance exercise. Subjects in the AR group completed a low load protocol of  
23 10 x 10 x 30% 1RM leg press with 5 min of passive rest between sets lasting ~60 min. Subjects in the  
24 PR group were seated in a chair for 60 min. These subjects were permitted to read, listen to music, or

1 work on the computer. The only physical movement permitted for PR subjects was walking to and from  
2 the bathroom, if necessary.

3

4 **Study timeline.** The study timeline is illustrated in Figure 1. Resting blood samples and MVC were  
5 measured throughout the experimental protocol at control (07:00), pre-loading (11:00), post-loading  
6 (12:00), post-recovery (13:00), and the next morning (07:00).

7

8

\*\*\* *Figure 1 here* \*\*\*

9

10 **Maximal bilateral isometric force.** An electromechanical bilateral isometric leg extension device  
11 (horizontal leg press, designed and manufactured by Biology of Physical Activity in the Faculty of Sport  
12 and Health Sciences at the University of Jyväskylä, Finland) was used to measure maximal bilateral  
13 isometric strength (MVC) both during familiarization as well as before and after the heavy resistance  
14 exercise session (see study timeline). The subjects' knee angle was 107° measured using the greater  
15 trochanter, lateral tibiofemoral joint space, and lateral malleolus as reference points, while the hip angle  
16 was 110°. For reference, full extension of the leg was considered to be 180°. Subjects were instructed to  
17 produce force "as fast and as hard as possible" for approximately 3 s. The arms were kept crossed over  
18 the chest. In total, five submaximal warm-up trials (3 x ~50% and 2 x ~85%) were performed before the  
19 maximal performance. Subjects were verbally encouraged. Warm up trials were used only before the  
20 morning measurements (i.e. control and morning time points), while subsequent MVCs were performed  
21 without warm-up. Subjects performed at least three MVC [9] with 1 minute of rest between repetitions.  
22 If the maximum force produced during the latter trial was 5% greater than the previous trial, an additional  
23 trial was performed. Force data was collected at a sampling frequency of 2000 Hz, and then filtered with  
24 a 20 Hz low pass filter. Force data was analyzed using customized scripts (Signal 4.04, CED, UK). The



1 best performance trial, in terms of absolute maximal force was used for statistical analysis. The reliability  
2 of MVC has previously been reported as  $r = 0.98$ ,  $CV = 4.1\%$  [25].

3

4 ***One repetition maximum (1RM).*** One RM of the lower extremities (maximal dynamic bilateral  
5 horizontal leg press in a seated position) was measured using a David 210 dynamometer (David Sports  
6 Ltd., Helsinki, Finland) [9]. Prior to attempting 1RM, the subjects completed a warm-up consisting of 5  
7 x 70% 1RM, 1 x 80-85% 1RM and 1 x 90-95% of estimated 1RM, with one minute of rest between sets.  
8 Following this warm-up, no more than 5 attempts to reach 1RM were allowed. Leg press repetitions  
9 started from a knee angle of approximately  $65^\circ$ . Subjects were instructed to grasp handles located by the  
10 seat of the dynamometer and to keep constant contact with the seat and backrest during leg extension to  
11 a full extension of  $180^\circ$ . Verbal encouragement was given to promote maximal effort. The greatest weight  
12 that the participant could successfully lift (knees fully extended) to the accuracy of 2.5 kg was accepted  
13 as 1RM.

14

15 ***Maximal aerobic capacity ( $VO_{2max}$ ).*** Maximal aerobic capacity was measured for each subject to  
16 determine individual aerobic fitness levels for matching groups using a graded running test on a motor-  
17 driven treadmill (Telineyhtymä, Kotka, Finland). The graded  $VO_{2max}$  test was preceded by a 5-min  
18 warm-up, using a walking speed of  $5.0 \text{ km}\cdot\text{h}^{-1}$  for the first two min and  $8.0 \text{ km}\cdot\text{h}^{-1}$  for the last three min  
19 of the warm-up on a level grade. After the warm-up, the individual constant speed ( $9.5 - 12 \text{ km}\cdot\text{h}^{-1}$ ) was  
20 set according to individual endurance training history. The first stage was completed at a level grade for  
21 two min, after which the grade of the treadmill was increased by two degrees every two min. The rate of  
22 perceived exertion (RPE) in every 2 min was assessed by the Borg's scale [26].

23

1 All subjects were verbally encouraged to continue until volitional fatigue.  $\text{VO}_2\text{max}$  was defined as the  
2 highest 30-s  $\text{VO}_2$  during the test.  $\text{VO}_2\text{max}$  was accepted when 3 of 4 criteria were met: (1) the 60 s  $\text{O}_2$   
3 (oxygen consumption) value reached plateau or started to decrease, (2) respiratory exchange ratio (RER)  
4 was over 1.13, (3) heart rate (HR) was within 10 beats from the predicted maximal HR ( $\text{HR}_{\text{max}}$ , predicted  
5  $\text{HR}_{\text{max}} = 220 - \text{age}$ ) or failed to increase with added workload, and (4) Borg's RPE value was greater  
6 than 17 [27].  $\text{HR}_{\text{max}}$  was determined as the highest HR value recorded during the maximal graded running  
7 test. Subjects completed a 5-min cool-down period following the test during which walking speed was  
8 individually chosen between 3.0 - 4.0  $\text{km}\cdot\text{h}^{-1}$ . Breath-by-breath  $\text{O}_2$  was measured throughout the test  
9 using a portable gas analyzer (Oxycon Mobile®, Jaeger, Hoechberg, Germany) that was calibrated using  
10 known gas concentrations according to manufacturer instructions prior to each test. Beat-by-beat HR was  
11 measured throughout the test using a heart rate monitor (Suunto t6, Vantaa, Finland).

12

13 ***Blood samples and serum hormones.*** Fingertip blood samples were taken for analysis of blood lactate  
14 using a Biosen S\_line Lab+ lactate analyzer (EKF Diagnostic, Magdeburg, Germany). Basal venous  
15 blood samples were collected after 12 hours of fasting between 07:00-08:00 on both testing days. A  
16 qualified lab technician collected blood samples from the antecubital vein using sterile needles into serum  
17 tubes (Venosafe, Terumo Medical Co., Leuven, Belgium). The technician reviewed analyses of the basic  
18 blood count (Sysmex KX-21N, Kobe, Japan) to check for abnormalities prior to further analysis. Whole  
19 blood was centrifuged at 2500 g (Megafuge 1.0R, Heraeus, Germany) for 10 min after which serum was  
20 removed and stored at  $-80^\circ\text{C}$  until analysis. Blood samples were used for determination of IGF-1 and  
21 IGF binding proteins 1-6. Serum and dialysate samples were analyzed for several IGF-I system  
22 components, and all samples for a particular analyte were run in the same assay batch to minimize intra-  
23 assay variance. Serum Total IGF-I was analyzed on the Immulite 1000 (Siemens Healthcare Diagnostics,  
24 Malvern, PA; LKGF1 kit, reported sensitivity of 20 ng/mL). Serum and dialysate Free IGF-I was

1 analyzed with an ELISA from Beckman Coulter (Brea, CA; DSL-10-9400 kit, reported sensitivity of  
2 0.015 ng/mL), and quantified on a Dynex MRX Revelation absorbance reader (Dynex Technologies,  
3 Chantilly, VA). Serum and dialysate IGFBP-1 through BP-6 were analyzed on a multiplexed bead-based  
4 fluorescent assay from Millipore (Billerica, MA; HIGFBP-53K multiplex kit, reported sensitivity of  
5 0.013, 0.325, 0.145, 0.573, 1.15, and 0.078 ng/mL, respectively), and quantified on the Luminex 200  
6 Instrument. Intra-assay CVs for the respective assays were as follows: Total IGF-I = 4.4 %; Free IGF-I  
7 = 8.7 %; BP-1 through BP-6 ranged 6.2-12.5 %. The average of two fasting blood samples (from the  
8 familiarization session and the morning of the experiment) were used to determine control values We  
9 recognize that loading-induced changes in plasma volume may influence hormonal concentrations [28],  
10 however, plasma volume changes were not used to correct hormone concentrations in the present study  
11 as plasma volume did not change significantly Furthermore, we believe that biological responses are  
12 dependent on an increase/decrease in interaction with receptors that is possible regardless of changes in  
13 plasma volume [29].

14

15 ***Nutrition.*** Caloric intake on the day of the heavy resistance exercise protocol was restricted for all  
16 subjects. Subjects were given an energy bar (commercially available: 700 kJ/170 kcal, proteins 7 g,  
17 carbohydrates 21g, fats 2.5g) following fasting blood measurements and approximately 3 hours prior to  
18 the start of the loading. The energy bar was accompanied by 0.5 L of water. A second energy bar and  
19 0.5 L of water was consumed approximately three hours after the loading. Otherwise subjects were  
20 allowed to drink a limited amount of water *ad libitum*. **Subjects were allowed to eat an unsupervised**  
21 **meal in the evening before the 10-12 hour fast preceding their blood samples the following morning.**  
22 **Subjects were instructed to eat their typical evening meal.**

23

24

1 **Statistical methods.** Standard statistical methods were used for calculation of means and standard  
2 deviations (SD). A repeated measures ANOVA with Bonferroni post hoc was completed for all variables.  
3 The “n” for successful biochemical analyses of IGFBP-2 and IGFBP-5 was so small that the results are  
4 not considered reliable and are not reported here. The criterion for significance was set at \* =  $p < 0.05$ ,  
5 \*\* =  $p < 0.01$  and \*\*\* =  $p < 0.001$ . Statistical analysis was completed with PASW Statistics 18 (SPSS  
6 Inc., Chicago, IL, USA). Relative responses are presented as e.g.  $\Delta\% = ((\text{post loading} - \text{control}) / \text{control})$   
7 \*100.

## 10 RESULTS

11 No significant differences were observed between physical characteristics of the two groups. Blood  
12 lactate concentrations changed in both groups ( $p < 0.001$ ) and increased significantly in both AR and PR  
13 groups by post loading ( $p < 0.01$  and  $p < 0.001$ , respectively). At post recovery, blood lactate values  
14 returned to almost resting values ( $2.1 \pm 1.3$  and  $2.3 \pm 1.3 \text{ mmol} \cdot \text{l}^{-1}$ ), which decreased further back to control  
15 values by the following morning ( $0.8 \pm 0.2$  and  $0.7 \pm 0.4 \text{ mmol} \cdot \text{l}^{-1}$ ). No differences in absolute or relative  
16 ( $\Delta\%$ ) blood lactate responses were observed. Blood glucose concentrations remained statistically  
17 unaltered, in both absolute and relative terms, from control to morning in both groups (Table 1).

18  
19 Serum insulin-like growth factor-1 (IGF-I, Figure 2) changed significantly in the AR group ( $p = 0.002$ )  
20 and PR group ( $p = 0.008$ ) reaching statistically significant increase from control to post loading in the AR  
21 group ( $p < 0.05$ ), however in PR this increase was not statistically significant. No differences in absolute  
22 serum IGF-I concentrations were observed between groups. Significant differences in relative IGF-I  
23 responses were observed at post recovery and next morning with a significantly greater response  
24 observed in the AR group than the PR group ( $p < 0.01$  vs.  $p = 0.051$ , respectively). No statistical differences

1 in serum free IGF-I was observed from control to next morning in terms of both absolute and relative  
2 values.

3

4

**\*\*\* Figure 2 here\*\*\***

5

6 Absolute concentrations of serum insulin-like growth factor-I binding protein 1 (IGFBP-1, Figure 3)  
7 were statistically unaltered in AR ( $p = 0.365$ ) but not in PR ( $p < 0.001$ ). However, absolute concentrations  
8 of IGFBP-1 at next morning were significantly higher in the PR group than in the AR group ( $p < 0.05$ ). In  
9 relative terms, the IGFBP-1 response from control to the next morning in the PR group was significantly  
10 greater ( $p < 0.001$ ) than in the AR group.

11

12

**\*\*\* Figure 3 here\*\*\***

13

14 Serum concentrations of IGFBPs 3, 4, and 6 remained statically unaltered from control to morning. No  
15 differences were observed between the groups in absolute or relative terms.

16

17 Serum growth hormone (GH) concentrations increased significantly in PR from control to post loading  
18 from  $0.7 \pm 1.8$  to  $15.2 \pm 9.9 \mu\text{g} \cdot \text{l}^{-1}$  ( $p < 0.001$ ) but the increase in GH in AR was statistically insignificant  
19  $0.7 \pm 1.2$  to  $16.2 \pm 13.1 \mu\text{g} \cdot \text{l}^{-1}$  (Table 1). Nevertheless, the relative response in the AR group was greater  
20 than that of the PR group ( $p < 0.05$ ). No other differences were observed in absolute or relative response  
21 of GH between the groups.

22

23

**\*\*\* Table 1 here\*\*\***

24

1 Maximal bilateral isometric force (MVC) changed significantly in both groups (AR  $p=0.006$ , PR  
2  $p<0.001$ ), and decreased significantly ( $p<0.05$  and  $p<0.01$  in AR and PR, respectively) from the control  
3 measurements following the 10x10 RM bilateral leg press loading protocol in both AR and PR groups  
4 (Figure 4). By post recovery, MVC of the PR group had returned to the same level as in the control  
5 measurements, whereas MVC of the AR group remained significantly reduced ( $p<0.01$ ). No between  
6 group differences were observed in mean absolute or relative changes in MVC over the entire  
7 experimental period.

8  
9 **\*\*\*Figure 4 here\*\*\***

## 10 11 **DISCUSSION**

12 The present high-volume heavy resistance leg press exercise session and subsequent AR or PR protocols  
13 induced alterations in serum IGF-I concentrations, which may indicate that the protocol-specific AR is a  
14 slightly more favorable recovery method than PR to help support the performance of individuals involved  
15 in heavy resistance exercise or strenuous lifting tasks. Absolute concentrations of IGF-I were  
16 significantly higher than control values following the present heavy resistance exercise protocol in the  
17 AR group. *A significant increase in IGF-I concentrations in the AR group was observed at post-recovery*  
18 *(13.00). It should, however, be noted that there appears to be non-significant decrease from baseline in*  
19 *IGF-I in the PR group, which may influence the resultant significance and increased IGF-I in AR at post-*  
20 *recovery and this statistical difference was still marginally significant at morning.*

21  
22 Although significant differences in absolute IGF-I concentrations were not observed at any time point,  
23 the significant differences observed in relative IGF-I response at post recovery are of interest, when  
24 examined alongside the response of IGF-BPs. Endocrine and locally produced IGF-I [4] binds to other

1 IGFbps, in particular to IGFBP-1 in the extracellular fluid to regulate the access of IGF-I to the IGF-IR  
2 [6]. In the present study, no significant changes in absolute levels of IGFBP-1 were observed in AR or  
3 PR from control to next morning. At next morning, however, both the absolute and relative responses of  
4 IGFBP-1 were significantly different between AR and PR showing a higher serum concentration and  
5 higher relative response of IGFBP-1 in the PR group (and no change in AR). It is unclear, with the present  
6 data, as to why the IGFBP-I response was delayed at next morning. As IGFBP-1 is considered to be  
7 inhibitory to IGF-I biological action, however, the lower concentration of IGFBP-1 after AR may be  
8 considered favorable due to its positive relationship with glucose metabolism and maintaining metabolic  
9 homeostasis, which is linked to muscle recovery [31,32]. It is possible that the larger IGFBP-1 response  
10 is a result of exercise duration as IGFBP-1 appears to have a dose-response relationship with exercise  
11 where higher concentrations of IGFBP-1 have been observed following 2 versus 1 hour of exercise [33].  
12 The present high-volume heavy resistance exercise, in addition to AR, resulted in approximately 2 hours  
13 of work, while the PR group completed less than one hour of work. The changes in IGFBP-1 as observed  
14 post exercise (in this case, roughly 18 hours post loading) are in agreement with the study of Nindl et al.  
15 (2009), which demonstrated that IGFBP-1 appears to be associated with overall exercise stress and  
16 subsequent recovery.

17

18 In the present study, serum concentrations of IGFBP-3, IGFBP-4, and IGFBP-6 were statistically  
19 unaltered from control to morning. As mentioned in the methods, the “*n*” for IGFBP-2 and IGFBP-5 was  
20 so small that the results were not included in this manuscript. We should recall that the majority of IGF-  
21 I in circulation is bound to IGFBP-3, which helps to control the distribution of IGF-I [7,8], however, the  
22 concentrations of IGFBP-3 remained statistically unaltered.

23

1 Interestingly, the greater response of IGF-I and higher concentration IGFBP-1 is not reflected in the  
2 present changes in serum concentrations of free IGF-I, although increases in IGFBP-1 and IGFBP-2 have  
3 previously been associated with decreases in free IGF-I [6]. While it has been established that IGFBPs  
4 collectively determine the bioavailability of IGF-I, the specific roles of each BP and their response to  
5 physical loading have not yet been fully elucidated. The present results are, however, in agreement with  
6 a previous study [34] indicating that the influence of a heavy resistance exercise protocol on the IGF-I  
7 system is not just observed in the changes of IGF-I concentrations itself, but in the way that IGF-I is  
8 divided among its binding protein family. It is important to note that the timing of measurements may  
9 also significantly affect the perceived hormonal response as the present results contrast somewhat with  
10 those previously presented [35].

11

12 Growth hormone (GH) concentrations increased significantly in response to the heavy resistance exercise  
13 protocol and were roughly 22-fold higher at post loading than at control. Following AR and PR, GH  
14 concentration decreased to the level of the control measurements. No significant differences were  
15 observed between groups. GH response is significant in high volume, hypertrophic-type resistance  
16 loading sessions that cause substantial fatigue [13,16], and in those that utilized both concentric and  
17 eccentric motions [36]. The present bilateral leg press loading required both concentric and eccentric  
18 action as subjects were instructed to perform leg press in a controlled manner. The GH response in our  
19 study does not appear to have played a significant role in the differences that were observed in IGF-I and  
20 IGFBP-1 responses following AR.

21

22 The observed acute decreases in force production capabilities measured by MVC were expected  
23 following the present heavy resistance exercise session. The similarity in the mean decrease in MVC  
24 between the AR and PR groups post-loading implies that both groups experienced the exercise in similar



1 ways. As no between group differences were observed in mean absolute or relative changes in MVC over  
2 the entire experimental period, there does not appear to be a difference between AR and PR from the  
3 perspective of neuromuscular performance recovery over the present 18-hour time period. This is further  
4 supported by blood glucose levels that remained statistically unaltered through the experimental period  
5 as well as similar blood lactate profiles in both AR and PR throughout the loading. The relative similarity  
6 between the AR and PR groups in terms of neuromuscular and blood lactate responses, as well as in  
7 blood glucose profiles suggests that the level of exertion between the groups was indeed similar. In light  
8 of these findings, it is interesting to note the differences in hormonal responses observed during the  
9 present experimental loading and recovery.

10

11 It is important to note that our subjects' nutrition was controlled during the experimental loading and  
12 through recovery. They were, however, allowed to eat their typical (unsupervised) evening meal before  
13 the 10-12 hour fast preceding their blood samples the following morning. As this meal was unsupervised,  
14 we cannot comment on the energy intake of their evening meal. There is a possibility that the energy  
15 intake of the groups may have differed, e.g. the AR group may have responded with a greater energy  
16 intake due to the greater energy expenditure requirements of their protocol. This may have been a driving  
17 factor to the suppressed IGFBP-I concentrations observed at morning in AR. In response to energy intake,  
18 a rise in insulin mediates a reduction in IGFBP-I, and has been shown in obese women and non-obese  
19 women, to suppress IGFBP-I concentration.

20 Therefore, this response should be observed with caution. Additionally, energy restriction may cause  
21 decreases in circulating IGF-I [37], but the short nature of this energy restriction may have negated the  
22 chance for visible decreases in IGF-I concentrations. It is also essential to remember that an increase in  
23 serum concentrations of hormones may not entirely reflect hormone kinetics at a local skeletal muscle  
24 level, thus these serum hormone responses should be interpreted with some caution. For example, a

1 positive IGF-I response may be associated with a greater increase in lean body mass, which could be of  
2 interest if e.g. the pattern of increased IGF-I repeatedly occurs with AR over a prolonged period of time.  
3 It should be noted, however, that hormonal responses observed may not always be associated with  
4 increased strength (e.g. [38], although a number of studies have demonstrated positive association  
5 between anabolic hormone concentrations or exercise-induced hormone responses and gains in strength  
6 and/or muscle cross-sectional area during systematic prolonged resistance training (e.g. [39-42]). In  
7 addition, when examining changes in serum hormonal concentrations, one needs to consider the  
8 difference between statistical significance and clinical or physical performance significance as statistical  
9 significance does not necessarily imply clinical or physical performance significance and vice versa.  
10 Nevertheless, the present results indicate that AR could be favored over PR due to differences in  
11 responses of IGF-I, and IGFBP-1.

12

### 13 **CONCLUSIONS**

14 The results of this study provide valuable insight into the efficacy of recover modalities following heavy  
15 resistance loading sessions that may help to support the physical performance of individuals involved in  
16 highly strenuous muscle strengthening tasks. From an IGF-I perspective, the present protocol-specific  
17 AR appeared to be a more favorable recovery method for the heavy resistance loading session than PR  
18 due to the observed greater serum concentrations of IGF-I and difference in response of IGFBP-1  
19 observed between AR and PR. Further studies could investigate whether or not this type of response has  
20 long-term effects as well as the influence of nutritional intervention combined with AR and PR as feeding  
21 after loading is considered standard protocol for both elite and recreational athletes. This provides  
22 additional information regarding the IGF1 system including how IGFBPs respond to strenuous exercise.

23

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 2 irreplaceable expertise and assistance in completing this project. We also wish to thank our hard working  
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7

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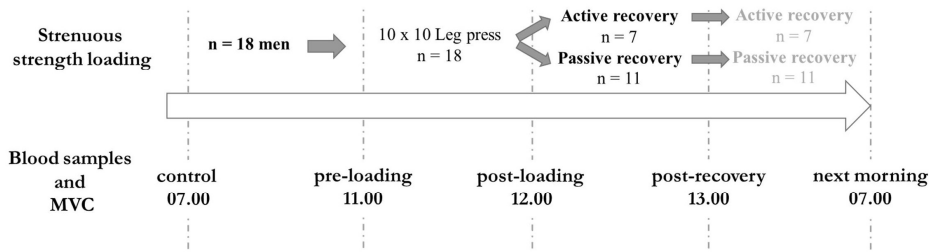
11 **TABLE 1.** Blood glucose, blood lactate, serum growth hormone (GH), insulin-like growth factor binding  
 12 protein 3 (IGFBP-3), insulin-like growth factor binding protein 4 (IGFBP-4), insulin-like growth factor  
 13 binding protein 6 (IGFBP-6) (mean  $\pm$  SD). b = significantly different from PR (relative changes). For  
 14 absolute values within group differences from control are marked as follows: \* $p < 0.05$  and \*\*\* $p < 0.001$ .

15 AR = active recovery, PR = passive recovery.

	Group	Control 07:00	Pre Loading 11:00	Post Loading 12:00	Post Recovery 13:00	Next Morning 07:00	P-value
<b>Blood glucose</b> ( $\text{nmol} \cdot \text{L}^{-1}$ )	AR = 5	4.6 $\pm$ 0.2	4.8 $\pm$ 0.4	4.8 $\pm$ 0.6	4.4 $\pm$ 0.4	4.8 $\pm$ 0.3	0.154
	PR = 9	4.3 $\pm$ 0.4	4.6 $\pm$ 1.3	5.0 $\pm$ 1.1	4.6 $\pm$ 0.5	4.6 $\pm$ 0.5	0.407
<b>Blood lactate</b> ( $\text{mmol} \cdot \text{L}^{-1}$ )	AR = 7	0.9 $\pm$ 0.4	1.2 $\pm$ 0.5	10.9 $\pm$ 3.0 **	2.1 $\pm$ 1.3	0.8 $\pm$ 0.2	<0.001
	PR = 11	0.7 $\pm$ 0.3	1.0 $\pm$ 0.3 **	11.1 $\pm$ 4.6 ***	2.3 $\pm$ 1.3	0.7 $\pm$ 0.4	<0.001
<b>GH</b> ( $\mu\text{g} \cdot \text{l}^{-1}$ )	AR = 7	0.7 $\pm$ 1.2	0.3 $\pm$ 0.4	16.2 $\pm$ 13.1 <sup>b</sup>	7.5 $\pm$ 6.6	0.1 $\pm$ 0.0	0.058
	PR = 11	0.7 $\pm$ 1.8	0.8 $\pm$ 0.7	15.2 $\pm$ 9.9 *	5.6 $\pm$ 5.5	0.3 $\pm$ 0.8	0.001
<b>Free IGF-I</b> ( $\text{ng} \cdot \text{ml}^{-1}$ )	AR = 6	1.05 $\pm$ 0.41	1.12 $\pm$ 0.37	0.96 $\pm$ 0.46	1.16 $\pm$ 0.47	1.03 $\pm$ 0.24	0.209
	PR = 9	1.22 $\pm$ 0.70	1.14 $\pm$ 0.58	0.82 $\pm$ 0.65	1.16 $\pm$ 0.89	0.98 $\pm$ 0.84	0.305
<b>IGFBP-3</b> ( $\text{ng} \cdot \text{ml}^{-1}$ )	AR = 7	885 $\pm$ 418	780 $\pm$ 352	887 $\pm$ 506	719 $\pm$ 269	746 $\pm$ 252	0.439
	PR = 11	896 $\pm$ 302	785 $\pm$ 230	872 $\pm$ 225	822 $\pm$ 309	881 $\pm$ 335	0.619
<b>IGFBP-4</b> ( $\text{ng} \cdot \text{ml}^{-1}$ )	AR = 7	27.8 $\pm$ 10.1	28.4 $\pm$ 12.9	31.7 $\pm$ 13.2	25.6 $\pm$ 9.0	25.5 $\pm$ 9.4	0.063
	PR = 11	34.6 $\pm$ 23.2	38.5 $\pm$ 31.4	38.7 $\pm$ 33.6	33.8 $\pm$ 22.0	25.6 $\pm$ 10.3	0.044
<b>IGFBP-6</b> ( $\text{ng} \cdot \text{ml}^{-1}$ )	AR = 7	159 $\pm$ 25	145 $\pm$ 17	158 $\pm$ 19	145 $\pm$ 22	164 $\pm$ 29	0.024
	PR = 11	150 $\pm$ 46	142 $\pm$ 41	148 $\pm$ 40	138 $\pm$ 37	146 $\pm$ 41	0.175

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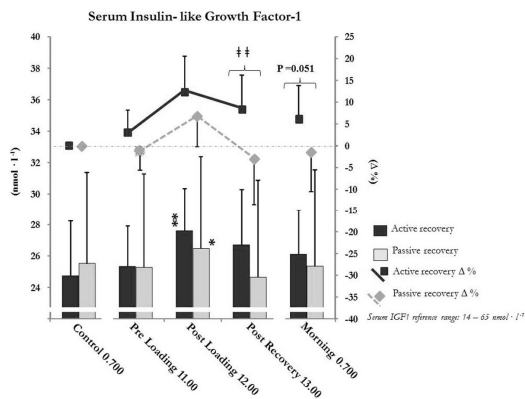
**FIGURE CAPTIONS (figures uploaded in separate jpg files)**



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**Figure 1.** Study timeline.

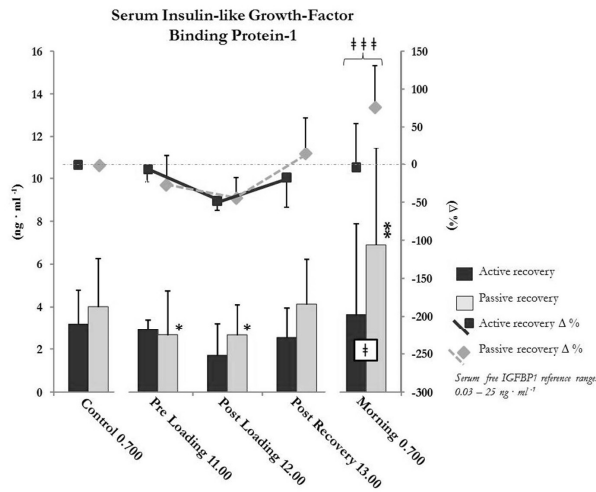
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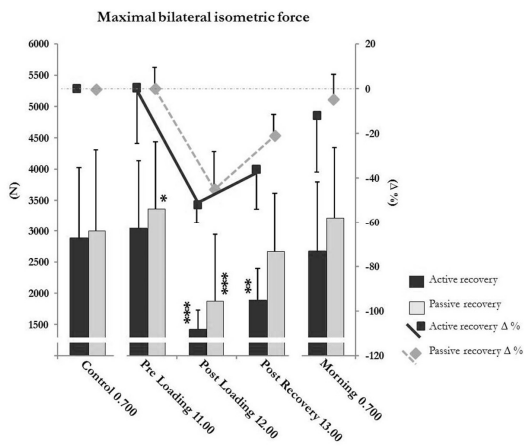
**Figure 2.** Absolute mean ( $\pm$ SD) values insulin-like growth factor I as columns and relative changes as lines. For absolute values within group differences from control are marked as follows: \* =  $p < 0.05$ . Significant difference between groups for relative changes # =  $p < 0.01$ . AR,  $n = 7$  and PR,  $n = 11$ .

11



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3 **Figure 3.** Insulin like growth factor binding protein-1 (IGFBP-1) absolute values as columns and relative  
 4 changes as lines (mean ± SD). Significant difference between the groups for relative changes † = p<0.05,  
 5 ††† = p<0.001. AR, n = 7 and PR, n=11.



6  
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8 **Figure 4.** Absolute mean (± SD) values of maximal bilateral isometric force as columns and relative  
 9 changes as lines. For absolute values within group differences from control are marked as follows:  
 10 \*p<0.05 and \*\* p<0.01. AR: n=7 and PR: n=11.



