



Resistance Exercise Intensity Does Not Influence Neurotrophic Factors Response in Equated Volume Schemes

by

Leandro Lodo^{1,2}, Alexandre Moreira², Reury Frank P Bacurau¹, Carol D Capitani³,
Wesley P Barbosa¹, Marcelo Massa¹, Brad J Schoenfeld⁴, Marcelo S Aoki¹

The aim of the present study was to evaluate the effects of 2 different intensities of resistance training (RT) bouts, performed with the equated total load lifted (TLL), on the acute responses of neurotrophic factors (NFs) (brain-derived neurotrophic factor [BDNF]; and nerve growth factor [NGF]), as well as on metabolic (lactate concentration) and hormonal (salivary cortisol concentration) responses. Thirty participants (males, 22.8 ± 2.3 years old, 177 ± 6.8 cm, 75.5 ± 7.9 kg, n = 15; and females, 22.2 ± 1.7 years, 163.7 ± 6.5 cm, 57 ± 7.6 kg, n = 15) performed 2 separate acute RT bouts with one week between trials. One bout consisted of 4 sets of 5 submaximal repetitions at 70% of 1RM and the other of 4 sets of 10 submaximal repetitions at 35% of 1RM for each exercise. Both RT bouts were conducted using the bench press and squat exercises. The TLL in each bout (determined by sets x repetitions x load [kg]) was equated. Serum BDNF, serum NGF, salivary cortisol, and blood lactate concentration were determined pre- and post-RT. No significant pre- to post-exercise increase in neurotrophic factors ($p > 0.05$; BDNF; effect size = 0.46 and NGF; effect size = 0.48) was observed for either of the RT bouts. A similar increase in blood lactate concentration was observed pre- to post-exercise for both RT bouts ($p < 0.05$). Cortisol increased similarly for both RT bouts, when compared to the resting day condition ($p < 0.05$). In conclusion, the results suggest that, despite differences in RT schemes, a similar acute neurotrophic, metabolic and hormonal response was observed when the TLL is equated.

Key words: BDNF, NGF, Cortisol, Blood Lactate, Resistance Training.

Introduction

The finding that physical exercise is able to promote neuronal cell survival and differentiation, via upregulation of neurotrophins (Quiles et al., 2019), led to numerous studies to further investigate such promising outcomes (Erickson et al., 2011; Heisz et al., 2017; Hopkins et al., 2011). In recent years, the brain-derived neurotrophic factor (BDNF) emerged as a principal neurotrophin (NT) and has been investigated as a potential mediator of exercise-induced neuroplasticity (Quiles et al., 2019). The mechanism of action of the BDNF may be explained via induction of calcium calmodulin

kinase II and mitogen activating protein kinase, thereby facilitating an increase in the mitochondrial content of uncoupling protein 2 in neurons, and thus preserving cell calcium homeostasis, the production of ATP and free radical control (Gligoneska et al., 2012).

Interestingly, it has been demonstrated that the effects of resistance training (RT) are not restricted to a specific improvement in neuromuscular outcomes (e.g. strength development and muscle hypertrophy). For instance, Cassilhas et al. (2007) reported that a regimented 24-week RT protocol improved spatial

¹ - School of Arts, Sciences and Humanities, University of São Paulo, São Paulo, Brazil.

² - School of Physical Education and Sport, University of São Paulo, São Paulo, Brazil.

³ - School of Applied Sciences, University of Campinas, São Paulo, Brazil.

⁴ - CUNY Lehman College, Bronx, NY, USA.

learning and memory in elderly individuals. In a rodent model, in which male Wistar rats were chronically stimulated by RT, the improvement in mechanisms of spatial memory in the hippocampus was found to be training-specific (Cassilhas et al., 2016). While the potential positive effects of RT on neurotrophic factors (NFs) show promise for improving health and wellness, research remains equivocal on the topic. For instance, several human trials have failed to show an acute RT-mediated increase in the BDNF (Correia et al., 2010; Goekint et al., 2010; Rojas et al., 2010), while others observed elevations of this NF (Church et al., 2016; Yarrow et al., 2010). The contradictory findings regarding the effect of an acute bout of RT on BDNF concentration could be due to differences in the intensities and duration of previous studies. To ensure an adequate training stimulus that is able to positively modulate NF secretion, it is crucial to investigate the effect of the intensity of acute RT sessions on such responses. This issue could be particularly relevant for older individuals, who are particularly susceptible to alterations of key regions of the brain (and, consequently, present declines in several cognitive domains) (Phillips et al., 2017). It has been recommended that these adults perform RT at 60-80% of their 1RM, but that such relatively high training intensities may be challenging for those with joint-related pathologies and muscle weakness (Cook et al., 2017).

Despite interest in neural adaptations from RT and its possible benefits, the effect of manipulation of acute training variables (e.g. intensity, volume, pause, velocity of action) on the NF response has not been adequately addressed. To shed light on this topic, it is important to assess the effects of acute RT sessions, when performed with different intensities, but with an equated TLL, on neurotrophic factors. Therefore, the aim of this study was to investigate the effect of 2 acute RT sessions performed with different intensities (i.e. 35% 1RM and 70% 1RM), with the equated TLL, on neurotrophic factors. In addition, metabolic (lactate concentration) and hormonal (salivary cortisol concentration) outcomes were investigated to determine if the 2 bouts with different intensities, but the same TLL, would provoke similar physiologic responses. The authors hypothesized that the equated TLL would

promote a similar response in neurotrophic, metabolic and hormonal factors to both acute RT bouts.

Methods

Participants

Thirty participants, comprising 15 men (22.8 ± 2.3 years, 177 ± 6.8 cm, 75.5 ± 7.9 kg) and 15 women in the luteal phase of their menstrual cycle (22.2 ± 1.7 years, 163.7 ± 6.5 cm, 57 ± 7.6 kg), were selected for the present study. Participants had approximately 3 months of RT experience, performing 2-3 sessions per week. All participants were familiar with the exercises performed in this study. They each took part in this study after having the protocols explained to them and giving their written informed consent. This study was conducted in accordance with recognized ethical international standards (Helsinki) and the protocol was approved by the University's Ethics Committee (n° 35/2011).

Measures

1RM test for the chest press and for the squat

The 1RM test was performed in accordance with recommendations of the American Society of Exercise Physiologists (ASEP) (Brown et al., 2001). Participants performed 2 warm-up sets. The first set consisted of 3 repetitions at 50% of estimated 1RM, while the second set consisted of 3 repetitions at 70% 1RM. A 2-minute rest interval was afforded between sets. After completion of the warm-up sets, up to 5 consecutive trials were then performed to determine the 1RM, with a rest interval of 3 to 5 minutes in between. Briefly, the load was progressively increased until the participant could no longer perform a complete movement (prerequisite for the trial to be considered valid) with adequate technique. The researchers provided verbal encouragement to participants during the performance of each 1RM trial. To avoid accidents, 2 researchers served as spotters, 1 at each extremity of the bar, to assist participants if necessary. For the chest press 1RM, participants were instructed to grip the bar in a comfortable position, typically 10 to 20 cm greater than the distance between the acromion processes. Each trial began with the elbows extended. Movement was carried out by lowering the bar to the chest and then reversing the direction by extending the elbows until lockout. Testing for the

1RM squat followed the same protocol as for the chest press. Performance began with the knees fully extended. Participants then descended into a squat until the knees reached a 90° angle, then reversed direction by extending the knees until lockout. The angle of knee flexion was manually measured by a goniometer for each participant so that knee flexion was limited to 90° with the aid of a wood apparatus.

Total Load Lifted (TLL)

The TLL for each session (session at 35% of 1RM and session at 70% of 1RM, respectively, mild and moderate intensity) was equated by the total volume of the load lifted (TLL = repetitions x sets x load), as described by Uchida et al. (2009). The total volume was the same for 35% 1RM and 70% 1RM ($2,078.80 \pm 747.03$ kg), considering all the participants ($n = 30$).

Blood Lactate Concentration

To evaluate lactate concentration, a blood sample was obtained 5 minutes before each session and 5 minutes after the second and fourth sets of both the chest press and squat exercises. Capillary blood samples (25 μ L) were drawn from the ear lobe and immediately transferred to a microtube (containing 50 μ L of sodium fluoride), and stored at -80°C . The blood samples were analyzed electrochemically using the YSI 1500 Sport Analyzer (YSI 1500 Sport[®], EUA) previously calibrated in accordance with the manufacturer's instructions.

Salivary Cortisol

In each of the 2 experimental days, saliva samples were collected 15 minutes before (rest) and immediately after (post RT) the experimental protocol. Saliva sampling occurred before blood sampling (for lactate and NF analysis) in order to avoid additional stress associated with the blood drawing procedure. Furthermore, additional samples were taken on a rest day (baseline cortisol concentration - CON) at the same times as those of the initiation and termination of the resistance exercise experimental protocols. Cortisol concentration was determined in duplicate using an enzyme-linked immunosorbent assay (Salimetrics[®], USA), according to the manufacturer's instructions. The intra-assay coefficient of variation for cortisol concentration was approximately 4-5%. To account for diurnal variation, the samples were collected at the same time on each day (10:00-

12:00 am). Each participant provided their pre- and post-RT saliva samples at the same time of the day for both RT bouts and for the resting day condition (baseline).

Serum BDNF and NGF

Blood sampling for serum BDNF and NGF analysis occurred 10 min before and 10 min after each session. Two mL of blood were collected from the participants antecubital vein upon arrival using a syringe without anticoagulant. Serum was then separated by centrifugation at $1,500 \times g$ for 10 min in a refrigerated centrifuge (4°C), aliquoted and stored at -80°C in microtubes until analysis. The serum BDNF level was measured by an enzyme-linked immunosorbent assay (ELISA) (Aviscera-Bioscience[®], USA; detection range was 1.56–100 pg/ml). The intra-assay coefficients of variation for BDNF and NGF were 3.8% and 5.2%, respectively. All samples were determined in duplicate and were run within the range of the standard curve. The NGF was measured in the same samples by ELISA, according to the manufacturer's instructions (Aviscera-Bioscience[®], USA).

Design and Procedures

Maximum repetition (1RM) tests were performed using the chest press and squat exercises to determine the intensity of each session (35% of 1RM and 70% of 1RM), following a randomized crossover design (1 week between trials). The 35% 1RM session consisted of 4 sets with 10 repetitions for both exercises used in the 1RM test (i.e. chest press and squat on the Smith Machine), while the 70% 1RM session consisted of 4 sets with 5 repetitions for the same exercises. Thus, the total volume of the load lifted (TLL) was equated between sessions. In both sessions, a 2-min rest interval was afforded between sets. To assess the NF acute response to RT schemes, a blood sample was taken pre- and post (10 min) each exercise session. To evaluate lactate concentration, a blood sample was obtained 5 min before each session and 5 min after the second and fourth sets of both chest press and squat exercises. Also, a salivary sample was obtained 15 min before and immediately after each session to analyze cortisol concentration. All training sessions were performed between the hours of 10:00 and 12:00 and a similar breakfast was provided to participants prior to both trials.

Statistical Analysis

Data are presented as the means \pm standard deviation (SD). Data were checked for normality (Shapiro-Wilk's test) and homoscedasticity (Levene's test). A mixed model 2-way analysis of variance with repeated measures was used to examine differences in salivary cortisol, lactate, BDNF, and NGF between RT protocols and time-points (pre- and post-exercise). In the event of a significant difference, a Bonferroni post-hoc test was used to identify the origin of any effects. SPSS (v. 20.0, SPSS Inc., Chicago, IL, USA) software was used for data analyses. Statistical significance was set at $p \leq 0.05$. The pre- to post-study magnitude of changes was assessed by Cohen's d effect sizes (ES) (Cohen, 1992), with thresholds of 0-0.19, > 0.20-0.49, > 0.50-0.79, and > 0.80 interpreted as *weak*, *small*, *moderate* and *large* effects, respectively.

Results

No significant difference for the BDNF was observed between the 2 schemes (35% of 1RM vs. 70% of 1RM; $p > 0.05$). A small effect size for the pre- to post BDNF (pooled data for both schemes – $d = 0.46$) response was noted.

No significant difference for the NGF was observed between the 2 protocols (35% of 1RM vs. 70% of 1RM; $p > 0.05$). A small effect size for the pre- to post NGF (pooled data for both schemes – $d = 0.48$) response was noted.

A similar increase in blood lactate concentration was observed at all points evaluated (Pre, Post BP, Post 4BP; Post 2PS and Post 4PS, respectively, $p < 0.05$) for 35% of 1RM and 70% of 1RM sessions. Blood lactate concentration increased equally over time for both RT sessions, with no difference between conditions ($p > 0.05$).

No significant difference for salivary cortisol concentration was observed between protocols (35% of 1RM vs. 70% of 1RM; $p > 0.05$). The difference in cortisol concentration did not reach statistical significance in the pre- to post-RT comparison for both groups (35% of 1RM vs. 70% of 1RM; $p > 0.05$). However, a greater post-RT salivary cortisol was detected for both protocols (35% of 1RM and 70% of 1RM; $p < 0.05$), when compared to the baseline resting condition (CON), at the same time of the day.

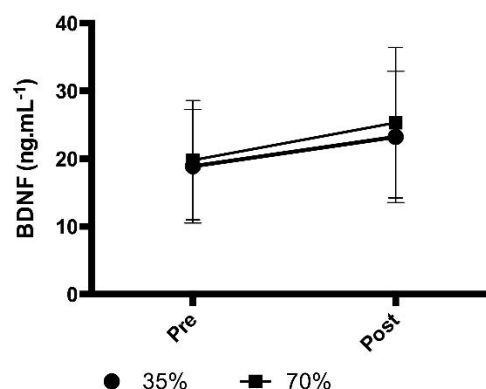


Figure 1

Brain-derived neurotrophic factor (BDNF) blood levels (pre and post-RE session) for the 35% 1RM and 70% 1RM protocols. Results presented as means \pm SD. PRE – before exercise; Post – post-exercise.

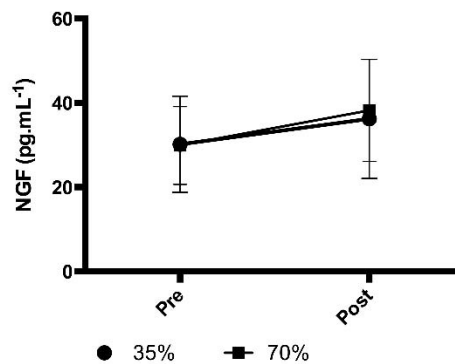


Figure 2

Nerve growth factor (NGF) blood levels (pre and post-RE session) for the 35% 1RM and 70% 1RM protocols. Results presented as means \pm SD. PRE – before exercise; Post – post-exercise.

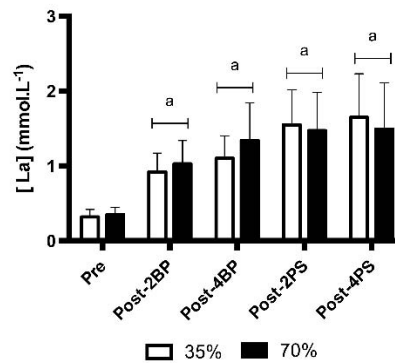


Figure 3

Blood lactate levels (Pre, Post 2BP, Post 4BP; Post 2PS and Post 4PS) for the 35% 1RM and 70% 1RM protocols. Results presented as means \pm SD. PRE – before exercise; Post 2BP – post 2nd bench-press set; Post 4BP – post 4th bench-press set; P 2PS – post 2nd parallel squat; Post 4PS – post 4th parallel squat. ^a*p* < 0.05 vs. Pre.

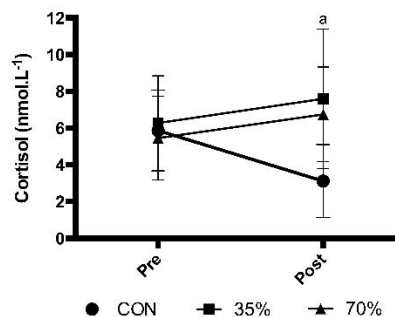


Figure 4

Salivary cortisol concentrations (pre and post-RE session) for the 35% 1RM and 70% 1RM protocols. Results presented as means \pm SD. PRE – before exercise; Post – post-exercise. ^a*p* < 0.05 vs CON.

Discussion

The main finding of the present study was a similar acute neurotrophic, metabolic and hormonal response, despite the difference in the RT bout, when the TLL was equated. It has been previously suggested that an optimal combination of volume and intensity might be an important factor to stimulate increases in BDNF concentration after a RT session (Goekint et al., 2010; Quiles et al., 2019). The current study is the first to investigate the effect of exercise intensity on neurotrophic factors using submaximal RT sessions with the equated TLL. The current findings indicate that both protocols (35% and 70% of 1RM) failed to induce a significant change in the post-exercise BDNF level, suggesting that intensity per se might not be a major factor for eliciting an increase in this neurotrophic factor, at least when investigating submaximal RT protocols. Other studies have also failed to show a significant alteration in BDNF concentration pursuant to acute high intensity RT protocols (Correia et al., 2010; Rojas Veras et al., 2010). In contrast, Marston et al. (2017) investigated whether the inconsistency of the human neurotrophic response to RT, observed between studies, was related to the low intensity of some RT programs by comparing the effects of 2 RT protocols (a "strength protocol" consisting of 5 sets of 5RM, with 3 min rest intervals, using 7 exercises vs. a "hypertrophy protocol" consisting of 3 sets of 10RM, with a 1 min rest interval using the same 7 exercises) on the BDNF level. Although mechanical work was matched between the 2 protocols, a significant increase in the BDNF level was observed only immediately after the hypertrophy-oriented protocol when compared to the strength-oriented protocol. Based on their findings, those authors concluded that a reps-to-fatigue hypertrophy-based RT protocol successfully increased peripheral BDNF. The results indicate that a traditional hypertrophy-oriented scheme optimizes stimulation of peripheral BDNF, compared to a traditional strength scheme, performed with equated mechanical work. From this perspective, it seems reasonable to consider that, besides intensity per se, a complex interaction occurs following manipulation of training variables. Additionally, a volitional fatigue protocol could explain some of their findings, which oppose the findings of the

current study that observed a lack of change in BDNF in submaximal acute RT protocols. An alternative interpretation for the results from Martson et al. (2017) was offered by Quiles et al. (2019), who suggested that the hypertrophy protocol in that study had more training volume, in comparison to the strength protocol (despite the fact that Martson and colleagues alleged that this difference was significant although negligible in magnitude). Thus, the results of Martson et al. (2017) may be justified by the training volume theory. However, this assumption was not confirmed by the study of Lira et al. (2018); those authors hypothesized that a full-body resistance exercise would induce a greater increase in serum BDNF, in comparison to split-body resistance exercises (i.e. for upper body and lower body). This hypothesis was not confirmed since lower body resistance exercises induced a greater increase in BDNF, suggesting that the volume accomplished by larger muscle groups was more important for the increase in BDNF than the overall volume performed in the RT session.

The effect size analysis for pooled data indicates that the small, non-significant, effect on BDNF ($p > 0.05$; pooled data for both schemes; $d = 0.46$) observed in the present study is in accordance with the suggested ability of this neurotrophic factor to respond to acute metabolic stress (e.g. mild increase in blood lactate concentration), in this case imposed by submaximal RT protocols. With regard to the discrepant results in the BDNF response to RT observed in different studies, other factors could be involved, such as rest intervals between sets, a work-to-rest ratio, the type of equipment used to perform the exercise, age, body composition and the amount of muscle mass involved during the RT bout. For example, Correia et al. (2010) and Rojas Veras et al. (2010) reported no pre-to-post change in BDNF. It should be noted that both these studies used isokinetic work as an RT model, with a few monoarticular exercises performed in the experimental session, limiting the muscle mass recruited. The time of collecting the blood sample could also be important for understanding these conflicting results; for example, in the study by Yarrow et al. (2010), both groups (traditional RT and eccentric RT pooled data) experienced a significant increase in serum BDNF, immediately after a RT session. However, BDNF concentration was gradually reduced over

the following 60 min, decreasing 53–57% when compared to the peak value (1 min after the RT session) under both conditions. Note that, in the present study, blood samples for BDNF analysis were collected at the 10th min after RT. Therefore, it is possible that the BDNF concentration reported herein may not represent the true post-RT peak value and, in turn, may partially explain the lack of a significant change in this neurotrophic factor. Dominguez-Sánchez et al. (2018) observed a 9.3% increase in the BDNF serum level in overweight adults submitted to RT consisting of 6 exercises repeated between 25–30 times each at 50–70% of 1RM. Those authors mentioned that the discrepancy among their and other results could be due the fact that all the subjects that participated in their study were overweight. In fact, since BDNF was negatively correlated to body weight (Lommatzsch et al., 2005), Dominguez-Sánchez et al. (2018) stated that a proportional increase in BDNF could be expected in their subjects. One other explication for the lack of BDNF response observed in the present study is that the blood level of BDNF may not reflect the parallel increase that occurs locally in the brain and muscle, as noted by Forti et al. (2014). This hypothesis remains speculative and requires further investigation. Forti et al. (2014) also hypothesized that the lack of a RT-induced BDNF elevation might be due to a short-lived BDNF response, which occurs acutely following exercise. Taking all factors into account, it is reasonable to speculate that it might be necessary to: 1) reach a certain “intensity and/or volume threshold” within a RT session (Church et al., 2016; Martson et al., 2017; Quiles et al., 2019), 2) recruit a significant amount of muscle mass (Church et al., 2016; Martson et al., 2017), 3) implement a reps-to-fatigue protocol (Pareja-Blanco et al., 2017; Lira et al., 2018), and 4) conduct a time course of blood sampling to properly assess the effect of RT on the acute BDNF response (Yarrow et al., 2010).

The paucity of studies investigating the NGF response to an acute RT session precludes comparisons with the observations of the present study. In this study, RT sessions with different protocols were unable to promote a significant change in NGF serum concentration ($p > 0.05$; a small effect size for the pre- to post NGF pooled data for both schemes; $d=0.48$). Even after a 15-

week resistance training intervention, NGF concentration remained unchanged in females with fibromyalgia (Jablochkova et al., 2019). Taken together, these data indicate that NGF secretion was not affected in response to acute and chronic RT interventions, at least under the described circumstances. Interestingly, Bonini et al. (2013) reported that the NGF serum level was significantly higher in 96 Italian pre-Olympic athletes than in control participants.

It is worth mentioning that besides the positive effects of neurotrophins on cognitive function and memory, the circulating NGF level has been consistently associated with atopic diseases and asthma. Bonini et al. (2013) did not find any differences in serum NGF in a sample consisting of 44 allergic and 52 non-allergic athletes. Thus, although their results suggest that long-term training processes are associated with a higher NGF serum level in athletes, they admit that the limited number of observations could have obscured an effect of allergy on the NGF level (Bonini et al., 2013). As such, with regard to NGF, the issue of training status also requires further investigation. Similar to the current results, in a recent investigation, no significant change in serum NGF concentration was detected in females after a RT bout.

Cortisol is a stress hormone of which concentration does not seem to be differentially affected by RT sessions of different intensities, but with an equated TLL, at least when submaximal repetition zones are performed (as implemented in the current study). In a recent study (Pareja-Blanco et al., 2017), the cortisol response was investigated for 2 different RT protocols (leading to failure: 3 x 12RM and not leading to failure: 3 x 6 reps performed with the 12RM load in the bench press and squat exercises), with an unmatched TLL. No change in the cortisol concentration between the pre- to post-RT acute protocol not leading to failure was observed. In contrast, a significantly greater cortisol concentration was detected for the post-RT protocol leading to failure, when compared to the RT scheme not leading to failure. Corroborating the current findings, RT sessions not designed to induce muscular failure seem to impose a mild level of stress, which in turn, is insufficient to modulate the stress hormones response. In the present study, the alteration in the level of cortisol did not

reach statistical significance between the time-points investigated. However, both RT sessions (35% and 70% of 1RM) induced a significant increase in the cortisol level, as compared to the same time of day on a baseline resting condition (CON). On the other hand, RT based on maximum repetition schemes influences the cortisol concentration (Pareja-Blanco et al., 2017) and also the BDNF (Church et al., 2016) response. However, it is important to acknowledge that the RT session designed to achieve muscular failure also presented a higher TLL (Pareja-Blanco et al., 2017). To the best of the authors' knowledge, no previous study has investigated the acute relationship between cortisol and BDNF using submaximal equated RT schemes as an experimental design model. The current results suggest that despite the difference in the intensity of submaximal RT protocols (35% and 70% of 1RM), neither cortisol nor BDNF were affected when the TLL was equated. It has been reported that chronically the BDNF level is inversely correlated to the cortisol level (Begliomini et al., 2008). For instance, depression presents a low serum BDNF level and an elevated cortisol level (McEwen et al., 2015). In contrast, 3 months of yoga practice induced an increase in BDNF concentration in relation to cortisol concentration in depressed individuals (Naven et al., 2016). Additionally, it has been suggested that the beneficial effects of exercise on chronic stress could be mediated by decreases in cortisol levels in structures, such as the hippocampus, allowing an increase in BDNF-mRNA and protein (Gligoroska and Manchevska, 2012). Accordingly, Begliomini et al. (2008) found that, under physiological conditions, males present the highest circulating BDNF level early in the morning, in a pattern very similar to the cortisol circadian rhythm. Those authors believed that this similar pattern maintained the homeostasis between factors able to insult and protect the neurons.

Acknowledgements

The authors would like to thank CNPq Brazil for financial support (Grant #470758/2012-0). LL would to thank CAPES for his scholarship.

References

- Adlercreutz H, Härkönen M, Kuoppalmi K, Näveri H, Huhtaniemi I, Tikkanen, Remes K, Dessypris A, Karvonen J. Effects of training on plasma anabolic and catabolic steroid hormones and their response during physical exercise. *Int J Sports Med*, 1986; 7(1): 27-28

Lactate is considered an indirect marker of exercise intensity and glycolytic metabolism (Kelleher et al., 2010; Zajac et al., 2015). In this study, the lactate concentration increased in a similar manner in response to both RT sessions (35% and 70% of 1RM). A previous study investigated 2 different RT systems (the multiple-sets system: 3 sets of repetitions maximum at 75% of 1RM for the bench press, peck-deck and decline bench press, and; the pyramidal system: 3 sets of repetitions maximum at 67%, 74% and 80% of 1RM for the same 3 exercises), under equated TLL conditions (Charro et al., 2010). A similar concentration of lactate and cortisol was reported. It is important to note, however, that in Charro's study (2010) the maximum repetition was performed at a similar range of intensity in both RT systems. The present study used submaximal repetitions, and the intensity range (35% and 70% of 1RM) was significantly different to that of the previous study (Charro et al., 2010). Taken together, the results of the present study and Charro's data (Charro et al., 2010) indicate that the TLL is a major determinant in the lactate response.

Conclusion

The current data suggest that RT intensity is not a major determinant in the NF response when the TLL is equated in a submaximal repetition zone. However, as previously mentioned, the contradictory findings related to the acute effects of RT on BDNF may be explained by several inter-study differences, mainly due to the organization of acute training variables. The current results suggest that despite differences in RT submaximal bouts, a similar acute neurotrophic, metabolic and hormonal response was observed when the TLL is equated.

- Baechlet TR, Earle RW, Wathen D. *Essential of strength and conditioning*. Champaign, Human Kinetics, 395-425; 2000
- Begliomini S, Lenzi E, Ninni F, Casarosa E, Merlini S, Pluchino N, Merlini S, Pluchino N, Valentino V, Luisi S, Luisi M, Genazzani AR. Plasma brain-derived neurotrophic factor daily variations in men: correlation with cortisol circadian rhythm. *J Endocrinol*, 2008; 197(2): 429-435
- Binder DK, Scharfman HE. Brain-derived neurotrophic factor. *Growth Factors*, 2004; 22(3): 123-131
- Bonini M, Fioretti D, Sargetini V, Del Glacco S, Rinaldi M; Tranquili C, Bonini S. Increased nerve growth factor serum levels in top athletes. *Clin J Sport Med*, 2013; 5(3): 228-231
- Brown LE, Weir JP. ASEP Procedures recommendations I: accurate assessment of muscular strength and power. *J Exerc Physiol Online*, 2001; 4(3): 1-21
- Cassilhas RC, Tufik S, Mello MT. Physical exercise, neuroplasticity, spatial learning and memory. *Cell Mol Life Sci*, 2016; 73(5): 975-983
- Cassilhas RC, Viana VA, Grassmann V, Santos RT, Santos RF, Mello MT. The impact of resistance exercise on the cognitive function of the elderly. *Med Sci Sports Exerc*, 2007; 39(8): 1401-1407
- Charro MA, Aoki MS, Coutts AJ, Araujo RC, Bacurau RF. Hormonal, metabolic and perceptual responses to different resistance training systems. *J Sports Med Phys Fitness*, 2010; 50(2): 229-234
- Church DD, Hoffman JR, Mangine GT, Jajtner AR, Townsend JR, Beyer KS, Wang R, La Monica MB, Fukuda DH, Stout JR. Comparison of high-intensity vs. high-volume resistance training on the BDNF response to exercise. *J Appl Physiol*, 2016; 121(1): 123-128
- Cohen J. A power prime. *Psychol Bull*, 1992; 112(1): 155-159
- Correia PR, Pansani A, Machado F, Andrade M, Silva AC, Scorza FA, Cavalheiro EA, Arida RM. Acute strength exercise and the involvement of small or large muscle mass on plasma brain-derived neurotrophic factor levels. *Clinics (Sao Paulo)*, 2010; 65(11): 1123-1126
- Dominguez-Sánchez MA, Bustus-Cruz RH, Velasco-Orjuela GP, Quintero AP, Tordecilla-Sanders A, Correa-Bautista JE, Triana-reina HR, Garcia-Hermoso A, González-Ruiz K, Peña-Guzmán CA, Hernández E, Pena-Ibagon JC, Téllez-T LA, Izquierdo M, Ramirez-Vélez R. Acute Effects of high intensity, resistance, or combined protocol on the increase of level of neurotrophic factors in physically inactive overweight adults: The BrainFit Study. *Front Physiol*, 2018; 9(741):1-12
- Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, Kim JS, Heo S, Alves H, White SM, Wojcicks TR, Mailey E, Vieira VS, Martin SA, Pence BD, Woods JA, McAuley E, Kramer AF. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci U S A*, 2011; 108(7): 3017-3022
- Forti LN, Njemini R, Beyer I, Eelbode E, Meeusen R, Mets T, Bautmans I. Strength training reduces circulating interleukin-6 but not brain-derived neurotrophic factor in community-dwelling elderly individuals. *Age (Dordr)*, 2014; 36(5): 9704-9715
- Goekint M, De Pauw K, Roelands B, Njemini R, Bautmans I, Mets T, Meeusen R. Strength training does not influence serum brain-derived neurotrophic factor. *Eur J Appl Physiol*, 2010; 110(2): 285-293
- Greenberg ME, Xu B, Lu B, Hempstead BL. New insights in the biology of BDNF synthesis and release: implications in CNS function. *J Neurosci*, 2009; 29(41): 12764-12767
- Heisz JJ, Clark IB, Bonin K, Paulocci EM, Michalski B, Becker S, Fahnstock M. The effects of physical exercise and cognitive training on memory and neurotrophic factors. *J Cogn Neurosci*, 2017; 29(11): 1895-1907
- Hopkins ME, Nitecki R, Bucci DJ. Physical exercise during adolescence versus adulthood differential effects on object recognition memory and BDNF levels. *Neurosci*, 2011; 27(194): 84-94
- Kelleher AR, Hackney KJ, Fairchild TJ, Keslacy S, Ploutz-Snyder LL. The metabolic costs of reciprocal supersets vs. traditional resistance exercise in young recreational active adults. *J Strength Cond Res*, 2010; 24(4): 1043-1051
- Lira FS, de Freitas MC, Gerosa-Neto J, Cholewa JM, Rossi FE. Comparison between full-body vs. split-body resistance exercise on the brain-derived neurotrophic factor and immunometabolic response. *J Strength Cond Res*, 2018; doi: 10.1519/JSC.0000000000002653 [Online ahead of print]
- Lommatzsch M, Zingler D, Schuhbaeck K, Scholetcke K, Zingler C, Schuff-Werner P, Virchow JC.

- The impact of age, weight and gender on BDNF levels in human platelets and plasma. *Neurobiol Aging*, 2005; 26; 115-123
- Martson KJ, Newton MJ, Brown BM, Rainey-Smith SR, Bird S; Martins RM, Peiffer JJ. Intense resistance exercise increases peripheral brain-derived neurotrophic factor. *Sci Med Sport*, 2017; 20(10): 899-903
- McEwen BS, Bowles NP, Gray JD, Hill MN, Hunter RG, Karatsoreos IN, Nasca C. Mechanisms of stress in the brain. *Nat Neurosci*, 2015; 18(10): 1353-1363
- Naveen GH, Varambally S, Thirthalli J, Rao M, Christopher R, Gangadhar BN. Serum cortisol and BDNF in patients with major depression-effect of yoga. *Int Rev Psychiatry*, 2016; 28(3): 273-278
- Pareja-Blanco F, Rodríguez-Rosell D, Sánchez-Medina L, Ribas-Serna J, López-López C, Mora-Custodio R, Yáñez-Gracia JN, González-Badillo JJ. Acute and delayed response to resistance exercise leading or not leading to muscle failure. *Clin Physiol Funct Imaging*, 2017; 37(6): 630-639
- Rasmussen P, Brassard P, Adser H, Pedersen MV, Leick L, Hart E, Secher NH, Petersen BK, Pilegaard H. (2009). Evidence for a release of brain-derived neurotrophic factor from the brain during exercise. *Exp. Physiol*, 2009; 94, 1062–1069
- Rojas Vega S, Knicker A, Hollmann W, Bloch W, Strüder HK. Effect of resistance exercise on serum levels of growth factors in humans. *Horm Metab Res*, 2010; 42(13): 983-986
- Uchida MC, Crewther BT, Ugrinowitsch C, Bacurau RF, Moriscot AS, Aoki MS. Hormonal responses to different resistance exercise schemes of similar total volume. *J Strength Cond Res*, 2009; 23(7): 2003-2008
- Yarrow JF, White LJ, McCoy SC, Borst SE. Training augments resistance exercise induced elevation of circulating brain-derived neurotrophic factor (BDNF). *Neurosci Lett*, 2010; 479(2): 161-165
- Zajac A, Chalimoniuk M, Maszczyk A, Gołaś A, Lngfort J. Central and peripheral fatigue during resistance exercise - a critical review. *J Hum Kinet*, 2015; 49: 159-169

Corresponding author:**Marcelo S Aoki, Ph.D.**

University of São Paulo

Av. Arlindo Bettio, 1000

03828-000 - São Paulo, SP, Brazil

Phone: 55-11-3091-8842

E-mail: aoki.ms@usp.br