

Comparison of high-intensity vs. high-volume resistance training on the BDNF response to exercise

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Church DD, Hoffman JR, Mangine GT, Jajtner AR, Townsend JR, Beyer KS, Wang R, Monica MB, Fukuda DH, Stout JR. Comparison of high intensity vs. high volume resistance training on the BDNF response to exercise. *J Appl Physiol* 121: 123–128, 2016. First published May 26, 2016; doi:10.1152/jappphysiol.00233.2016.—This study compared the acute and chronic response of circulating plasma brain-derived neurotrophic factor (BDNF) to high-intensity low-volume (HI) and low-intensity high volume (HV) resistance training. Twenty experienced resistance-trained men (23.5 ± 2.6 y, 1.79 ± 0.05 m, 75.7 ± 13.8 kg) volunteered for this study. Before the resistance training program (PRE), participants performed an acute bout of exercise using either the HI [3–5 reps; 90% of one repetition maximum (1RM)] or HV (10–12 reps; 70% 1RM) training paradigm. The acute exercise protocol was repeated after 7 wk of training (POST). Blood samples were obtained at rest (BL), immediately (IP), 30 min (30P), and 60 min (60P) post exercise at PRE and POST. A three-way repeated measure ANOVA was used to analyze acute changes in BDNF concentrations during HI and HV resistance exercise and the effect of 7 wk of training. No training \times time \times group interaction in BDNF was noted ($P = 0.994$). Significant main effects for training ($P = 0.050$) and time ($P < 0.001$) in BDNF were observed. Significant elevations in BDNF concentrations were seen from BL at IP ($P = 0.001$), 30P ($P < 0.001$), and 60P ($P < 0.001$) in both HI and HV combined during PRE and POST. BDNF concentrations were also observed to increase from PRE to POST when collapsed across groups and time. No significant group \times training interaction ($P = 0.342$), training ($P = 0.105$), or group ($P = 0.238$) effect were noted in the BDNF area under the curve response. Results indicate that BDNF concentrations are increased after an acute bout of resistance exercise, regardless of training paradigm, and are further increased during a 7-wk training program in experienced lifters.

neurotrophin; resistance exercise; muscle; training status

NEW & NOTEWORTHY

There have been a number of investigations examining the BDNF response to exercise; however, our understanding of changes in the BDNF response to resistance training has been primarily limited to frail, older adults. This is the first study that has compared two different resistance training paradigms in experienced, resistance-trained adults and have demonstrated that training, independent of resistance training paradigm, can modify the BDNF response to an acute bout of resistance exercise.

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BRAIN-DERIVED NEUROTROPHIC factor (BDNF) is a neurotrophin of the nerve-growth factor protein family, whose downstream effects are mediated through tropomyosin-related kinase (Trk) receptors (38). BDNF is present throughout the nervous system and a crucial mediator in the formation of neuronal circuits throughout the brain where it promotes neuronal survival, neurite outgrowth, and synaptogenesis (12). BDNF-associated adaptations to hippocampal architecture have been associated with positive changes in memory and learning (11, 30, 31, 41) and has been reported to ameliorate the response to stressful stimuli (20, 22). Despite its notable role in the central nervous system, expression of BDNF and its high-affinity receptor TrkB are broad, being found in skeletal muscle, cardiac, liver, and adipose cells (26). Although its role in the skeletal muscle is less clear, increased expression of skeletal muscle BDNF has been shown to increase fat oxidation in an AMP-activated protein kinase-dependent mechanism (28). However, BDNF synthesized in the skeletal muscle does not appear to contribute to systemic circulating levels but rather acts in a paracrine or autocrine fashion (28). Preliminary data indicate that the brain is the primary source, providing ~80% of circulating plasma BDNF in response to exercise (34).

Elevations in circulating BDNF concentrations have been demonstrated after an acute bout of both aerobic and resistance exercise (13, 27, 35, 43). A fourfold increase in resting BDNF secretion rates ($58 \text{ ng} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$ to $206 \text{ ng} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$) were reported after 3 mo of endurance training at ~65% of $\dot{V}O_{2 \text{ max}}$ (37). In addition, increases in circulating BDNF concentrations observed during exercise and in the recovery period appear to be associated with both duration and intensity of exercise (4, 13, 27, 35, 37). Ferris and colleagues (13) demonstrated that 30 min of cycling at 10% above subjects' ventilatory threshold resulted in higher concentrations of BDNF than when cycling at 20% below. However, the total amount of work performed was greater during the higher intensity protocol. In addition, Cho and colleagues (4) reported greater elevations in circulating BDNF concentrations during a maximal aerobic capacity test with greater duration of exercise. These data suggest that the greater volume, or the combination of greater volume and/or higher intensity, may have provided the stimulus for a greater BDNF response to exercise.

The vast majority of research investigating the BDNF response to physical activity has primarily examined endurance exercise. The BDNF response during resistance exercise has not been studied to the same extent. In a limited number of investigations, some investigators have reported no change in the acute BDNF response to resistance exercise (18, 35),

Table 1. Resistance training program

Program Variable	Preparatory Phase Both Groups	High Volume	High Intensity
Exercise prescription			
Training duration	2 wk	8 wk	8 wk
Training intensity	80–85% 1RM	70% 1RM	90% 1RM
Training volume	4 sets x 6–8 repetitions	4 sets x 10–12 repetitions	4 sets x 3–5 repetitions
Rest time	1–2 min	1 min	3 min
Exercises			
	Day 1	Day 2	Day 3
Back squats	Bench press	Back squats	Bench press
Deadlifts	Incline bench press	Deadlifts	Incline bench press
Leg press	Dumbbell flies	Barbell lunge	Incline dumbbell fly
Lat pull downs	Seated shoulder press	Seated row	Seated shoulder press
Barbell bent-over rows	Lateral dumbbell raise	Dumbbell pullover	Lateral dumbbell raise
Barbell biceps curls	Triceps extension	Dumbbell biceps curl	Triceps extension

whereas others have suggested that training can augment the BDNF response to resistance exercise in previously untrained college-aged men (43). Most of the studies examining the BDNF response to resistance training have been performed in older and frail adults. These studies have generally reported that limited resistance training (3 times/wk for 10–12 wk) may be sufficient to increase BDNF concentrations in older adults (5, 15, 31). The majority of these studies have examined serum BDNF, which includes platelets that store and release BDNF in response to exercise. In consideration that plasma is free of platelets, and BDNF turnover in the plasma is ~6 min (33), changes in plasma BDNF would be more indicative of an acute response to a training stress. Furthermore, ~60–80% of plasma BDNF is thought to be produced in the brain (34). To the best of our knowledge, no studies have been performed on the plasma BDNF response to resistance training in experienced, resistance-trained men. Thus the primary purpose of this investigation was to compare the acute BDNF response to two common resistance training paradigms before and after 7 wk of training in experienced, resistance-trained adults. We hypothesize that resistance exercise will increase BDNF concentrations to both training protocols. In addition, we further hypothesize that 7 wk of training will augment the BDNF response to exercise.

METHODS

Experimental design. Before the onset of the study, all participants were required to complete a 2-wk preparatory base resistance training program. Subsequently, participants were then randomly assigned to one of two training groups: a high-intensity, low-volume training group (HI; $n = 10$; 22.6 ± 2.3 y; 87.0 ± 15.1 kg; 1.80 ± 0.05 m; $15.9 \pm 7.2\%$ body fat) or a high-volume, moderate intensity training group (HV; $n = 10$; 24.5 ± 2.6 y; 89.5 ± 12.9 kg; 1.66 ± 0.34 m; $20.6 \pm 6.0\%$ body fat). All groups completed an 8-wk resistance training program using a 4-day split routine. Blood samples were collected during the first training session of week 1 (PRE) and week 8 (POST). These visits constituted the acute training protocols, during which participants performed the HI [3–5 reps; 90% of one repetition maximum (1RM)] or HV (10–12 reps; 70% 1RM) training paradigm.

Participants. Twenty physically active, resistance-trained men agreed to participate in this study. After an explanation of all procedures, risks, and benefits, each participant provided his written informed consent to participate in the study. This investigation was approved by the New England Institutional Review Board, and all procedures were in accordance with the ethical standards of the 1964

Helsinki Declaration and its later amendments. All participants were free of any physical limitations (determined by medical history questionnaire and PAR-Q) and had been regularly participating (at the time of recruitment) in resistance training for a minimum of 2 y (5.7 ± 2.2 y).

Before the present investigation, all participants described their training habits to be different from the present training regimen in terms of exercise order and groupings. Approximately 82% of the participants described their normal repetition range to be either lower (VOL = 77%) or higher (INT = 87%) than what they were assigned to in the study, with about 43% typically using a 6–10 RM range and another 21% using an alternating (or pyramid) structure for specific multiple joint structural and assistance exercises. Additionally, 50% of the participants reported using either longer (VOL = 54%) or shorter (INT = 47%) rest periods, whereas ~29% did not track their rest times previously. The remaining participants employed a similar training scheme (i.e., intensity, volume, and rest) to what they were assigned to in the study.

Preparatory phase of training. All participants completed a preparatory resistance training protocol during the 2 wk before the training intervention (see Table 1). This phase encompassed a total of six workouts: four workouts (Monday, Tuesday, Thursday, and Friday) during the first week and two workouts (Monday and Tuesday) during the second week. The purpose of the preparatory training program was to instruct proper lifting technique, familiarize participants with all exercises, and ensure the participants initiated the study with a comparable training base. Compared with the training intervention groups, the exercises (and their order) were identical, but the volume (6–8 RM) and rest intervals (1–2 min) differed. Participants were instructed not to participate in any other form of physical activity throughout the duration of the study.

Anthropometric assessments. Anthropometric measurements for all participants were conducted ~24 h before all strength measures. Height (± 0.1 cm) and body mass (± 0.1 kg) were determined using a Health-o-Meter Professional scale (model 500 KL, Pelstar, Alsip, IL) with the participants standing barefoot, with feet together, and in their normal daily attire. Body fat percentage was determined using whole body-dual energy X-ray absorptiometry (DXA) scans (Prodigy TM; Lunar, Madison, WI). All measurements were performed by the same certified radiological technician using standardized subject positioning procedures.

Strength testing. To determine appropriate training load for both HI and HV, strength in the bench press and squat exercises was assessed. Participants were scheduled for testing at a standard time of day. A general warm up consisting of riding a cycle ergometer for 5 min at a self-selected resistance preceded strength testing. Standardized procedures, as previously described (19), were used for the 1RM barbell bench press and barbell back squat, respectively. Subjects performed

two warm-up sets at 40–60% and 60–80% of his perceived 1RM, respectively, before performing 3 or 4 subsequent trials to determine the 1RM. A 3–5 min rest period was provided between each trial. For all other exercises, the 1RM was assessed using a prediction formula based on the number of repetitions performed to volitional fatigue using a given weight (3). Trials not meeting the range of motion criteria for each exercise or using improper technique were discarded.

Resistance training intervention. Participants reported to the Human Performance Lab (HPL) four times per week, at the same time of day, to complete their assigned training program (see Table 1). Both groups performed the same exercise routine but differed in the intensity of exercise, number of repetitions performed, and rest interval between sets. Specifically, the HI training program required participants to perform four sets of 3–5 repetitions with 90% of their 1RM, with 3-min rest period between sets, whereas the HV group performed four sets of 10–12 repetitions with 70% of their 1RM, with a 1-min rest period between sets. During the resistance training program the load was increased for participants (regardless of group) when the required number of repetitions (for a particular exercise) were achieved on two consecutive workouts. On average, three to four participants were being trained by study personnel at one time during the course of the resistance training program. All study personnel were certified strength and conditioning specialists.

Blood sampling. Blood samples were obtained at four time points: baseline (BL), immediately postexercise (IP), 30 min postexercise (30P), and 60 min post-exercise (60P). Participants reported to the Human Performance Lab (HPL) 3 h postprandial at a standardized time of day consistent with their normal training schedule. All blood samples at POST were taken at the same time of day as PRE to avoid the confounding influence of diurnal variations. All blood samples were obtained using a Teflon cannula placed in a superficial forearm vein using a three-way stopcock with a male Luer lock adapter and plastic syringe. The cannula was maintained patent using an isotonic saline solution (Becton Dickinson, Franklin Lakes, NJ). Blood samples at BL were obtained after a 15-min equilibration period. Participants were instructed to lie in a supine position for 15 min before the 30P and 60P blood draws.

All blood samples were collected into a Vacutainer tube containing no containing K₂EDTA. The Vacutainer tube was kept cold throughout processing in an attempt to reduce the variations in BDNF concentrations during processing. A small aliquot of whole blood from the tube was removed and used for determination of hematocrit and hemoglobin concentrations. The blood was centrifuged at 3,000 *g* for 15 min. The resulting plasma was placed into microcentrifuge tubes and frozen at –80°C for later analysis.

Blood analyses. Hematocrit concentrations were analyzed from whole blood via microcentrifugation (CritSpin, Westwood, MA) and microcapillary techniques. Hemoglobin concentrations were analyzed from whole blood using an automated analyzer (HemoCue, Cypress, CA). Coefficient of variation for each assay was 1.53% for hematocrit and 0.55% for hemoglobin. Plasma volume shifts were calculated using the formula established by Dill and Costill (9).

Multiplex ELISA was used to quantitate plasma BDNF concentrations using MAGPIX (Luminex, Austin, TX) and a commercially available kit (EMD Millipore, Billerica, MA) according to manufacturer's guidelines. To eliminate interassay variance, all samples were analyzed in duplicate by a single technician. The coefficient of variation for BDNF was 7.84%.

Nutrient intake and dietary analysis. Participants were instructed to maintain their normal kilocaloric intake habits throughout the investigation. Kilocaloric and macronutrient intake were monitored via weekly food diaries. Consequently, all participants were required to record all food and beverage intake over the course of 3 days (2 weekdays and 1 weekend day) during the initial and final week of (weeks 1 and 8) of the training program. The FoodWorks Dietary Analysis software version 13 (The Nutrition, Long Valley, NJ) was used to analyze dietary recalls.

Statistical analysis. Before hypothesis testing, the Shapiro-Wilk test was used to evaluate the assumption of normality for dependent variables. As our data were not normally distributed, we opted to log-transform BDNF measurements (using the natural logarithm). To examine group and training differences in the BDNF response to exercise before and after the 7-wk training program, a three-way [training (PRE, POST) × time (BL, IP, 30P, 60P) × group (HI, HV)] repeated-measures analysis of variance (ANOVA) was performed. The effect of training on AUC measures, calculated using the trapezoidal methods, was examined using a two-way [training (PRE, POST) × group (HI, HV)] repeated-measures ANOVA. In the event of a significant interaction or main effect, Bonferroni post hoc tests were performed. Interpretations of effect size were evaluated (6) at the following levels: small effect (0.01–0.058), medium effect (0.059–0.137), and large effect (>0.138). For all analyses, a criterion alpha level of $P \leq 0.05$ was used to determine statistical significance, and statistical software (SPSS V.21.0, Chicago, IL) was used. All data are reported as mean ± SD.

RESULTS

The effect of these different training paradigms on strength and anthropometric changes have been reported elsewhere (25). For the purposes of this study, no differences were noted at PRE between the groups in the 1RM squat ($P = 0.694$), 1RM bench press ($P = 0.934$), body mass ($P = 0.715$), lean body mass ($P = 0.611$), or percent body fat ($P = 0.136$). Relative energy intake did not change significantly over the course of the investigation for HI (PRE: 38.2 ± 11.1 kcal·kg⁻¹; POST: 31.1 ± 5.3 kcal·kg⁻¹) or HV (PRE: 31.7 ± 7.0 kcal·kg⁻¹; POST: 29.2 ± 8.1 kcal·kg⁻¹).

Changes in plasma BDNF concentrations during PRE and POST are depicted in Fig. 1. No training × time × group interaction for plasma BDNF concentration was noted ($F = 0.026$, $P = 0.994$, $\eta^2 = 0.002$). However, significant main effects for training ($F = 4.434$, $P = 0.050$, $\eta^2 = 0.207$) and time ($F = 14.233$, $P < 0.001$, $\eta^2 = 0.456$) were identified. When collapsed across group and training, the acute exercise protocol resulted in significant elevations in BDNF concentrations from BL at IP ($P = 0.001$), 30P ($P < 0.001$), and 60P ($P < 0.001$). Circulating BDNF concentrations, when collapsed across group and time, were significantly elevated ($P = 0.050$) from PRE to POST. AUC analysis revealed no significant training × group interaction ($F = 0.956$, $P = 0.342$, $\eta^2 = 0.053$) in the BDNF response between HI and HV (see Fig. 2). In addition, no main effect for training ($F = 2.938$, $P = 0.105$, $\eta^2 = 0.147$) or group ($F = 1.499$, $P = 0.238$, $\eta^2 = 0.081$) were noted for the BDNF AUC response.

Relative to BL, plasma volume shifts were not significantly different between the two groups at PRE ($P = 0.741$) or POST ($P = 0.332$). At PRE, plasma volume decreased at IP, $-8.8 \pm 8.6\%$; increased at 30P $5.2 \pm 7.7\%$; and increased at 60P, $4.7 \pm 6.4\%$. At POST, plasma volume decreased at IP, $-11.9 \pm 5.3\%$; increased at 30P, $3.2 \pm 4.0\%$; and increased at 60P, $5.8 \pm 10.4\%$. Blood variables were not corrected for plasma volume shifts because of the importance of molar exposure at the tissue receptor level.

DISCUSSION

The primary objectives of this study were to characterize and determine whether the BDNF response was different between HI and HV resistance exercise and training. The major findings of this study indicated that BDNF concentrations were signif-

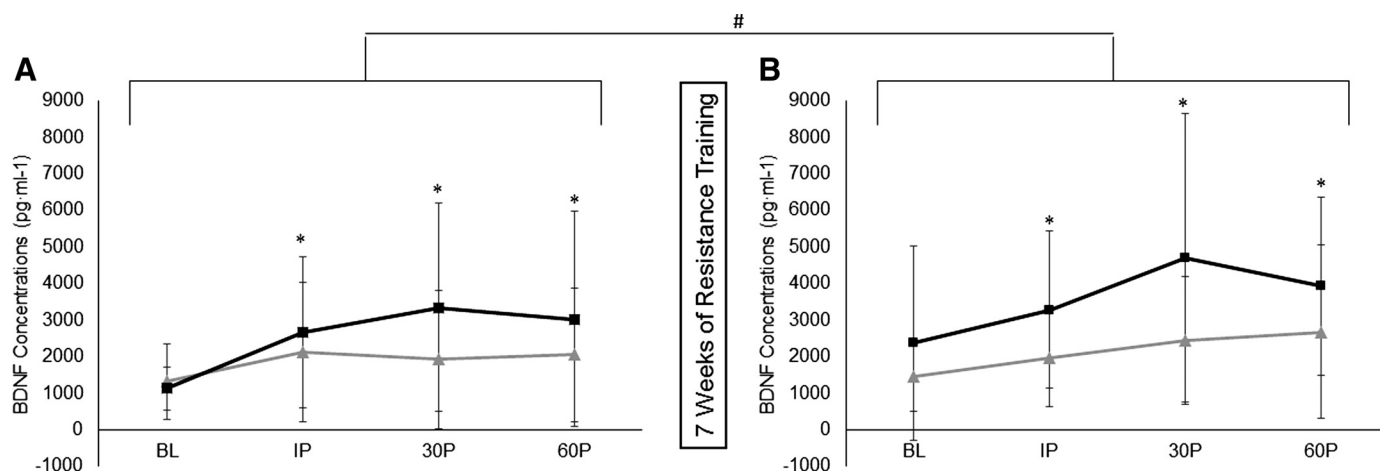


Fig. 1. Temporal circulating brain-derived neurotrophic factor (BDNF) concentrations at rest (BL), immediately after (IP), 30 min after (30P), and 60 min after (60P) either a high-intensity, low-volume (HI; light line with triangles) or low-intensity, high volume (HV; dark line with squares) resistance exercise protocol before (PRE; A) and after (POST; B) 7 wk of resistance training. Data are presented as mean \pm SD. *Significant difference compared with BL when groups are collapsed across group and training session. #Significant difference at POST compared with PRE when collapsed across time and group.

icantly elevated after HI and HV resistance exercise in experienced, resistance-trained men. In addition, 7 wk of resistance training appears to increase circulating BDNF concentrations in response to the exercise protocol but did not change resting concentration. This appears to be the first study to compare two commonly used resistance training paradigms on the BDNF response in trained men.

Previous research on the acute BDNF response to resistance exercise has primarily used untrained individuals, and the results have been inconclusive (7, 18, 35, 43). Similar to the present study, Yarrow and colleagues (43) reported that resistance training can augment the BDNF response to exercise but not change resting concentrations. Other studies, using previously untrained or recreationally trained participants of similar age were unable to demonstrate any change in the BDNF response to an acute resistance exercise session (7, 18). These differences may be related to the duration or volume of exercise. Correia and colleagues (7) did not observe any change in BDNF concentrations after five sets of 10 repetitions

in the isokinetic knee extension exercise, ($60^{\circ}\cdot\text{s}^{-1}$). Similarly, Goekint et al. (18) used an exercise protocol of three sets of 10 repetitions (80% 1RM) in six different exercises (a total of 18 sets performed) and reported no change in the BDNF response to the exercise stimulus. However, these exercises were all performed with exercise machines. In contrast, the participants in the present study performed four sets of six exercises (a total of 24 sets) using free weight, multijoint structural movement exercises that recruited a larger muscle mass than the exercises used in the previously mentioned studies. Exercises that recruit a greater amount of muscle mass are associated with a greater endocrine and biochemical response compared with single-joint or confined movement exercises that recruit a smaller muscle mass (23). The difference in musculature recruited may provide a plausible rationale for the difference in the present study and those of Correia et al. (7) and Goekint et al. (18). It is also possible that a threshold stimulus of volume performed, muscle mass activated, and/or duration of activity is necessary to stimulate a resistance exercise-induced BDNF response.

The relationship of BDNF and resistance training has generally been examined in elderly or clinically relevant populations (14–16, 24, 36, 39). Previous research from our laboratory (16) and others (14, 24, 36, 39) have shown that resistance training does not significantly change resting BDNF concentrations. Recently Forti and colleagues (15) reported a significant increase in resting BDNF concentrations in elderly men (>65 y) who participated in a 3 day per week, 12-wk mixed, low-intensity (60 repetitions at 20% of 1RM, and 10–20 repetitions at 40% of 1RM with no rest) resistance training program. However, in that same study no changes were noted in resting BDNF concentrations in elderly men performing low intensity (1 set of 80–100 repetitions at 20% of 1RM) or higher intensity (2 sets of 10–15 repetitions at 80% of 1RM with 1-min rest between sets) training programs. In addition, no changes were noted in elderly women who participated in all three training programs. Walsh and colleagues (42) reported that 8 wk of resistance training in older adults (60–77 years) was unable to change either resting or the exercise response of BDNF. The ability of resistance training to elevate resting

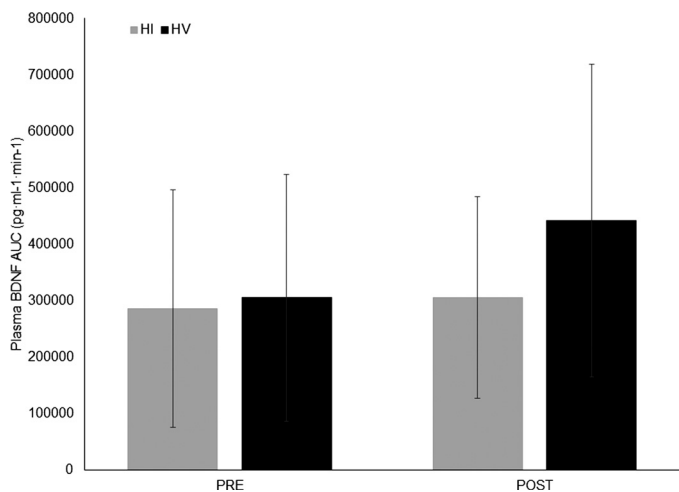


Fig. 2. Area under the curve (AUC) of plasma BDNF before (PRE) and after (POST) 7 wk of either a high-intensity, low-volume (HI) or low-intensity, high-volume (HV) resistance training program.

BDNF concentrations may be a function of both age and training status. Younger, and more experienced, resistance-trained adults appear not to be as sensitive as an older, untrained population to stimulate changes in resting BDNF. However, we observed a significant effect of training on circulating BDNF, supported by the strong effect sizes observed in the temporal ($\eta^2 = 0.207$) and AUC ($\eta^2 = 0.147$) responses. These results are in accordance with Yarrow and colleagues (43), who demonstrated 5 wk of resistance training was able to alter the BDNF response in untrained men.

Increases in circulating BDNF in response to metabolic challenges are suggested to have a role in regulating peripheral energy metabolism within the brain and in peripheral neurons (26). Elevations in circulating concentrations of BDNF resulting from an elevation in metabolic stress do provide support for a duration/volume threshold stimulus (13, 17, 34). Previous research has shown cortisol concentrations to be inversely related to BDNF (2, 21). We previously reported the cortisol response of the current study (25). The cortisol response at POST was attenuated in HV but not in HI. Although the attenuated cortisol response of HV may explain the increase in circulating plasma BDNF at POST, the similar cortisol response between PRE and POST for HI does not provide support. Therefore, it does not appear that cortisol influenced changes in the BDNF response observed in this study. Additional research is necessary to provide further insight to the mechanism governing BDNF changes to training.

The role of circulating BDNF is ambiguous. Much of our present understanding focuses on BDNF's role as a neurotrophin in the brain (40); however, its role in modulating peripheral neurogenesis is less understood. Current evidence indicates plasma BDNF is a proxy marker of BDNF production in the brain (34); however, BDNF can also be synthesized peripherally (40). The importance of the resistance training-induced increase in BDNF has been suggested to be related to improvements in cognitive function, memory, and mood (1, 8, 10). Further research is still needed to delineate the potential physiological role that BDNF has in the neuromuscular system, especially in apparently healthy, trained individuals.

Conclusions

This investigation appears to be the first study to explore the BDNF response to different resistance training paradigms in experienced, resistance-trained men. The results of this study demonstrate that the BDNF response is significantly elevated after both the high-intensity and high-volume training protocols, with no differences between the protocols. In addition, 7-wk of training did appear to increase the BDNF response to exercise. Future research appears warranted in examining the potential role that elevated BDNF concentrations may have on neuromuscular adaptations.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

D.D.C., J.R.H., G.T.M., J.R.T., D.H.F., and J.R.S. conception and design of research; D.D.C., J.R.H., G.T.M., A.R.J., J.R.T., R.W., and M.B.L.M. performed experiments; D.D.C., J.R.H., G.T.M., A.R.J., J.R.T., R.W., D.H.F., and J.R.S. analyzed data; D.D.C., J.R.H., G.T.M., A.R.J., K.S.B., D.H.F., and J.R.S. interpreted results of experiments; D.D.C. and J.R.H. prepared figures;

D.D.C. and J.R.H. drafted manuscript; D.D.C., J.R.H., A.R.J., J.R.T., K.S.B., R.W., M.B.L.M., D.H.F., and J.R.S. edited and revised manuscript; D.D.C., J.R.H., G.T.M., A.R.J., J.R.T., K.S.B., R.W., M.B.L.M., D.H.F., and J.R.S. approved final version of manuscript.

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