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Exploring the Preliminary Effects of Resistance Training on Total Brain-Derived Neurotrophic Factor (BDNF) Levels in Elderly Individuals: A Pilot Study

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ABSTRACT

Background: Studies have shown that exercise modulates brain-derived neurotrophic factor (BDNF) levels, and resistance training, in particular, has received increasing attention for its potential to enhance BDNF production. Most studies investigating exercise-induced BDNF changes have focused on free or mature BDNF, while the measurement of total BDNF, encompassing both proBDNF and mature BDNF, may provide a more comprehensive understanding of BDNF regulation. This pilot study aimed to explore the preliminary effects of resistance training on total BDNF levels in elderly individuals participating in a resistance training program.

Methods: A small sample of participants (n=6) was recruited and engaged in a structured resistance training program for 12 weeks, with 6 participants in a control group. Total BDNF levels were measured at baseline and post-intervention using reliable laboratory assessments. Additionally, an isokinetic dynamometer was used to determine muscle strength to explore the effect of the resistance training program on muscle performance.

Results: The findings revealed a significant increase in total BDNF levels following the 12 week resistance training intervention ($p<0.05$). However, improvements in physical performance measures, knee extension peak torque and isometric maximal voluntary contraction, were not observed.

Conclusion: In conclusion, this pilot study provides preliminary evidence of the positive effects of a 12 week resistance training intervention on total BDNF levels. The measurement of total BDNF levels serves as an important marker in assessing the response to resistance training. Further research with larger sample sizes and longer intervention periods is warranted to further explore the relationship between resistance training and total BDNF levels and to confirm these preliminary findings. Understanding the impact of resistance training on total BDNF levels can have implications for optimizing training programs and potentially improving exercise-related outcomes.

Keywords: muscle strength, exercise, brain-derived neurotrophic factor, neuroplasticity, healthy ageing.

INTRODUCTION

In recent years, research has focused on understanding the impact of different forms of exercise on BDNF levels, with particular interest in resistance training. Resistance training, also known as strength training or weightlifting, involves the use of external resistance to induce muscle contractions and promote muscular strength and endurance. It is a popular form of exercise practiced by individuals of various ages and fitness levels due to its numerous physiological benefits (Westcott, 2012).

Resistance training has been widely recognized as an effective strategy for counteracting age-related decline in muscle strength and function. By engaging in resistance training, elderly individuals can preserve or even enhance their muscle mass,

improve strength, and maintain functional abilities (Peterson et al., 2011). The potential role of BDNF in mediating the benefits of resistance training adds another layer of significance to this topic.

Studies have suggested that resistance training may have a positive influence on BDNF levels. Animal research has demonstrated that resistance exercise can increase BDNF expression in the hippocampus, a brain region critical for learning and memory (Gómez-Pinilla et al., 2002; Neeper et al., 1995). Furthermore, studies in humans have shown acute increases in BDNF levels following a single session of resistance training (Goekint et al., 2010; Rasmussen et al., 2009). However, the long-term effects of resistance training on BDNF levels and the potential mechanisms underlying this relationship are still not fully understood.

To date, most studies investigating the effects of exercise on BDNF levels have primarily focused on measuring free or mature BDNF, which represents the bioactive fraction of BDNF available for binding to its receptors (Binder & Scharfman, 2004). However, recent evidence suggests that total BDNF levels, including both proBDNF (the precursor form) and mature BDNF, may provide a more comprehensive understanding of BDNF regulation and its functional implications (Pruunsild et al., 2011). One key reason for measuring total BDNF is that it reflects the total pool of BDNF available for cellular signaling and interaction with receptors. Bound BDNF can still exert biological effects through its association with specific receptors and activation of downstream signaling pathways. Thus, disregarding the bound fraction would overlook an essential component of BDNF's functionality (Pang et al., 2004). Moreover, measuring total BDNF provides a more stable and reliable measure compared to free BDNF. Free BDNF levels can be influenced by various factors, including methodological challenges in sample collection and storage, as well as fluctuations in protein binding and release. In contrast, total BDNF offers a more robust measure, as it takes into account the entire BDNF pool and reduces the impact of these potential confounders (Fujimura et al., 2002). Additionally, total BDNF measurement allows for better comparison and interpretation across different studies. Researchers have used various assessments and methodologies to measure BDNF, leading to inconsistencies in reported results. By focusing on total BDNF, researchers can establish a standardized approach that facilitates better comparison and meta-analyses, enabling a more comprehensive understanding of BDNF's role in various physiological and pathological conditions (Molendijk et al., 2011). Therefore, it is essential to investigate the response of total BDNF levels to resistance training to gain a more comprehensive perspective on the potential neurobiological adaptations induced by this exercise modality.
This scientific article aims to address this research gap by investigating the effects of resistance training on total BDNF levels in individuals undergoing a structured resistance training program. By conducting a prospective study, we aim to examine the changes in total BDNF levels from baseline to post-intervention.

By investigating the effect of resistance training on total BDNF levels in the context of aging, we can gain valuable insights into the potential mechanisms underlying the benefits of exercise on muscle and brain health in older adults. Such knowledge can inform the development of targeted exercise interventions aimed at preserving muscle strength, promoting cognitive function, and enhancing overall well-being in the aging population.

MATERIALS AND METHODS

Participants. This research involved the participation of a total of 12 adults aged 60 years and above, who were considered to be in good health. The study took place in Kaunas, Lithuania. The recruitment methods included giving presentations at local community organizations. Interested candidates were invited for an interview. The experimental protocol was sanctioned by the Kaunas Regional Biomedical Research Ethics Committee (No. BE-10–7), and written informed consent was obtained from all participants prior to their inclusion process. To ensure the suitability of participants, certain exclusion criteria were applied. These criteria included the presence of neurological disorders such as stroke, epilepsy, multiple sclerosis, traumatic brain injury, brain tumor, or neurodegenerative diseases like dementia. Additionally, individuals with a history of alcohol or drug abuse, diabetes, musculoskeletal disorders, psychiatric disorders (e.g., depression), usage of psychopharmacological drugs within the past 5 years, oncologic disorders, or a history of chemotherapy use were also excluded. The participants confirmed that they had not been engaged in any regular exercise program in the last 6 months, but were capable of performing 10 sit-ups. It was emphasized that participants had the option to withdraw from the study voluntarily at any time. The demographic and clinical character-

istics of the participants included 12 elderly individuals (4 males and 8 females). These participants were randomly divided into two groups: a control group (CG; n = 6) that did not engage in any exercise activity and an intervention group (IG; n = 6) that underwent the resistance training program for 12 weeks. More subject characteristics are provided in Table 1.

Blood analysis. Venous blood samples were drawn by a qualified medical professional at the antecubital vein. All blood samples were collected between 9 a.m. and 1 p.m. in 5 ml serum separation gel tubes a day before muscle strength measurement for the baseline assessment and 3 days after a period of 12 weeks for post-intervention assessment. After blood collection, the tubes were gently inverted 8–10 times and kept at room temperature for 30 min until centrifugation for 15 min at 4,000 g centrifugal force. After centrifugation, serum was aliquoted into 1.5 ml polypropylene tubes and immediately frozen and stored at −80°C in the refrigerator compartment of the laboratory of the Lithuanian Sports University Institute of Sports Science and Innovation until further analysis. Enzyme-linked immunosorbent assay (ELISA) tests for the assessment of the circulating levels of total BDNF were analyzed with spectrophotometry (Spark 10M, Tecan Group Ltd., Zürich, Switzerland) by an experienced researcher.

Muscular strength measurements. The measurement of peak torque (PT) in knee extension and torque of knee extensor isometric maximal voluntary contractions (MVC) was conducted using the Biodex System 3 dynamometer (Biodex Medical Systems, NY, USA). The dynamometer was adjusted to align the rotational axis of the dynamometer with the axis of the participant's knee joint. Participants were instructed to sit with their backs firmly against the backrest, their hips and knees flexed at 90 degrees. Prior to the testing procedure, participants engaged in a 5-minute warm-up on a veloergometer, pedaling at a moderate intensity of 60-90 W, which roughly corresponded to their own body weight. This warm-up was followed by 3 minutes of dynamic activation exercises, including lunges, butt kicks, side step lunges, half-squats, and front and side cross swings. Only the PT and MVC of the dominant leg (always the right leg) for the quadriceps (knee extension) muscle groups was measured. The angular velocity was set at 60°/s, and participants performed 3 repetitions at maximum intensity. The highest PT value (measured in N.m) achieved during these 3 consecutive repetitions of knee extension was manually recorded for each participant and used for further analysis. During MVC recording the subjects were encouraged to make two maximal exertions with visual torque feedback and vocal encouragement, each maintained for ~2 s, with 1–2 min rest between contractions. 3 days after a period of 12 weeks, the entire PT and MVC testing protocol was repeated exactly for all participants.

Resistance training intervention. The intervention consisted of a 12-week progressive resistance training program, with two training sessions per week, overseen by qualified fitness instructors. The instructor-to-participant ratio was maintained at 1:2 to ensure effective supervision for all participants. Each training session began with a 5-minute warm-up on a veloergometer, where participants cycled at an intensity (measured in Watts) roughly equivalent to their body weight in kilograms. This was followed by dynamic stretching and activation exercises similar to those used during isokinetic strength testing. The exercise protocol included four lower limb exercises: leg extension, leg curl, leg press, and calf raises. The leg extension and leg curl exercises were the same as those used for isokinetic peak torque calculations of the knee joint. To familiarize participants with the correct movement execution and determine their individual 1-repetition maximum (1-RM) for each exercise, a week of familiarization was conducted, consisting of two training sessions. For all four exercises, participants performed three working sets and one warm-up set before the working sets. The rest intervals between sets were 2 minutes, while the rest intervals between exercises were 3 minutes. The intensity of the exercises was maintained between 70% and 85% of the participant's 1-RM for all working sets. The repetition range for the exercises was set at 6-10 repetitions. Specifically, during the first to third week block, participants performed higher repetition ranges of 10 to 8 at 70-75% of 1-RM. This was followed by the fourth to ninth week block, where the repetition range was 8 to 6 at 75-80% of 1-RM. Finally, during the tenth to twelfth week block, participants performed 6 repetitions at 80-85% of 1-RM.

Statistical analysis. Statistical analysis was performed using IBM SPSS Statistics version 27 (SPSS Inc, Chicago USA). To investigate the differences between PRE and POST results, we employed the Mann-Whitney U test due to the non-normal distribution of the data and the small sample size. The data presented in the tables and figures indicate means ± SD (standard deviation). Statistical significance was defined as $p \leq 0.05$.

RESULTS

The table (Table 1) presents the characteristics of the study participants. The age of the included subjects ranged from 60 to 79 years old.

Table 1. **Characteristic indicators of the subjects**

Group	*N (female)*	*N (male)*	*Age (years)*	*Weight (kg)*
Control	4	2	68.3±6.9	67.5±9.4
Intervention	4	2	72.3±2.6	70.1±10.3

Note: Values are presented as mean ± standard deviation (SD).

The changes in total BDNF levels following the 12 week resistance training intervention (for IG) or passive period (for CG) were examined. As shown in Figure 1, there was a significant increase in total BDNF levels in the intervention group compared to baseline ($p<0.05$).

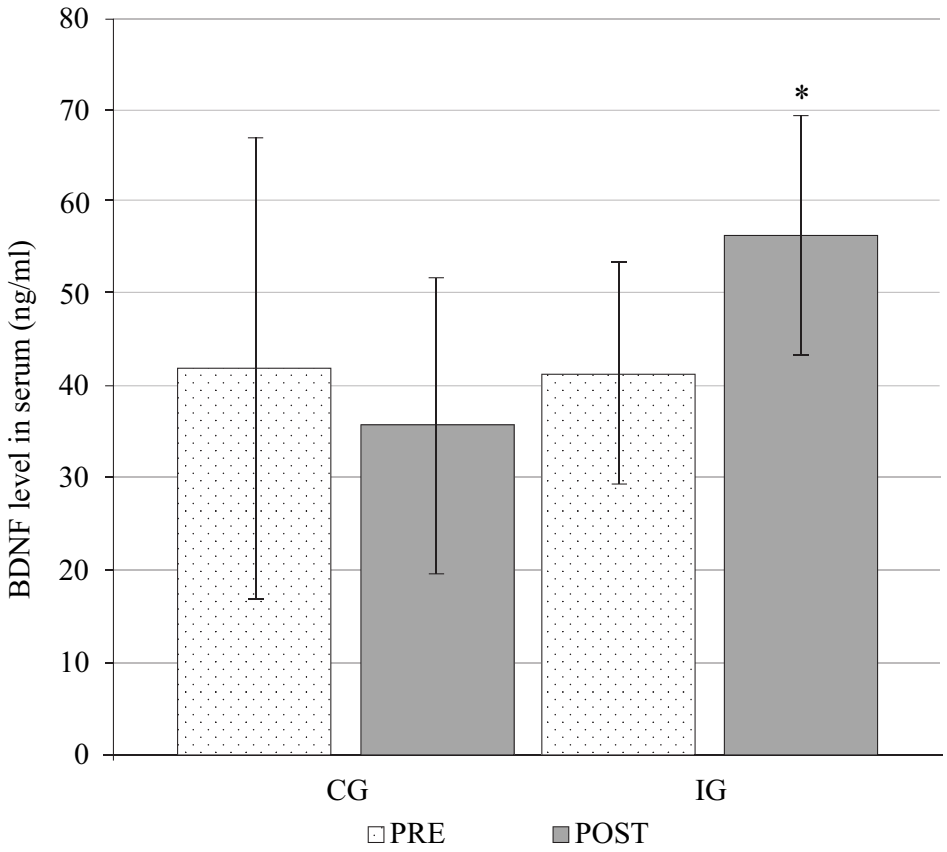

Figure 1. **Changes in BDNF blood levels. CG – control group, IG – intervention group. PRE – baseline values before training program. POST – post-intervention values. * - p<0.05 comparing intervention group PRE and POST values.**

The effect of the 12 week resistance training intervention on knee extension peak torque was assessed in the intervention group. Figure 2 displays the mean peak torque values at baseline and post-intervention. Surprisingly, there was no significant change in knee extension peak torque following the resistance training program ($p>0.05$).

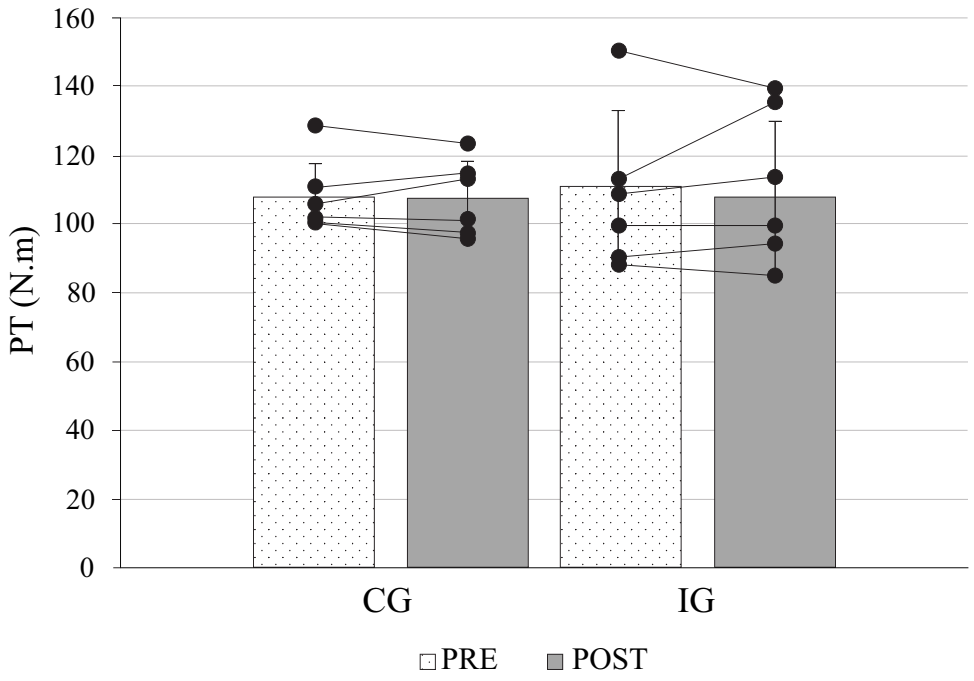

Figure 2. **Knee extension peak torque (PT) changes. CG – control group, IG – intervention group. PRE – baseline values before training program. POST – post-intervention values.**

Figure 3 illustrates the mean MVC torque values at baseline and post-intervention. Surprisingly, there were also no significant changes in MVC torque following the resistance training program ($p>0.05$).

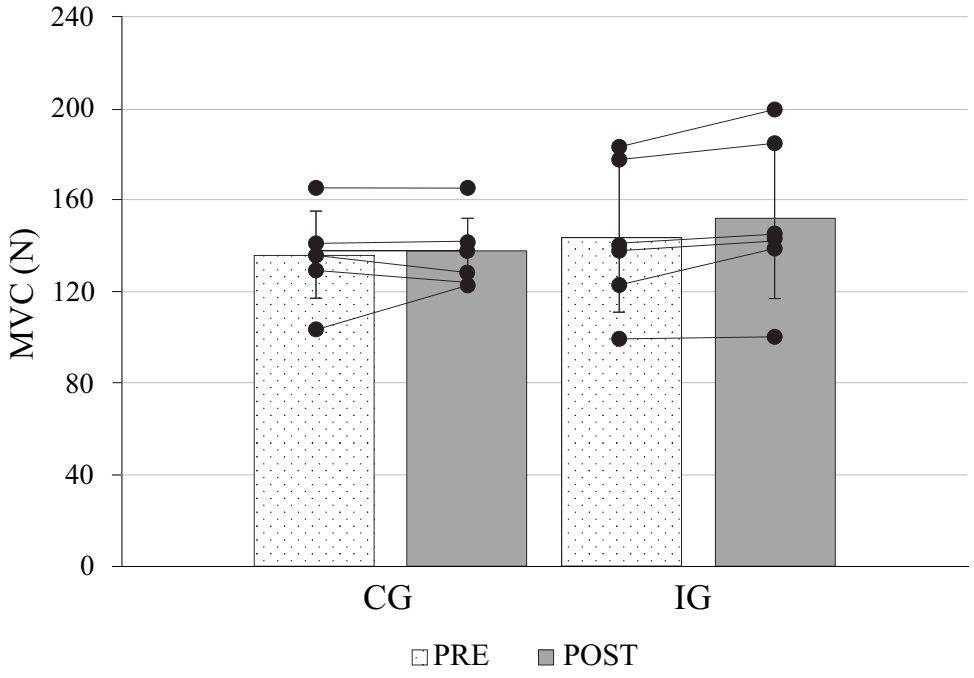

Figure 3. **Torque of knee extensor isometric maximal voluntary contractions (MVC). CG – control group, IG – intervention group. PRE – baseline values before training program. POST – post-intervention values.**

DISCUSSION

The present study investigated the effects of a 12 week resistance training intervention on BDNF levels, knee extension PT and MVC torque in elderly individuals. The results revealed a significant increase in total BDNF levels following the resistance training program, indicating that resistance training may induce neurobiological adaptations associated with enhanced BDNF production (Figure 1). However, no significant changes were observed in knee extension PT or MVC torque, suggesting that the resistance training program did not lead to notable improvements in muscle strength.

The finding of increased total BDNF levels in response to resistance training aligns with previous research that has demonstrated the positive influence of exercise on BDNF levels (Hillman et al., 2008; Neeper et al., 1996). Several studies have reported acute elevations in BDNF following a single session of resistance exercise (Rasmussen et al., 2009). Moreover, animal studies have shown increased BDNF expression in response to resistance training (Gómez-Pinilla et al., 2002). Our results further support the notion that resistance training can stimulate BDNF production in humans.

Comparing our findings with other studies, Goekint et al. (2010) investigated the effects of strength training on serum BDNF levels in older adults and found no significant changes in BDNF levels following the intervention, which is consistent with our results. This suggests that the response of BDNF to resistance training may vary depending on factors such as age, training status, and duration of the intervention. On the other hand, studies focusing on longer intervention periods or using different resistance training protocols have reported significant improvements in muscle strength (Westcott, 2012). These contrasting results highlight the need for further research to explore the optimal duration and intensity of resistance training necessary to elicit significant changes in muscle strength.

The findings from this study highlight the importance of considering total BDNF levels as a comprehensive measure of the response to resistance training, as opposed to solely focusing on free BDNF. While free BDNF has been extensively studied and its role in neurogenesis and synaptic plasticity is well understood, the significance of total BDNF levels should not be overlooked. Total BDNF encompasses not only the free fraction but also proBDNF and other BDNF isoforms, which may have distinct functions and contribute to different aspects of neurobiological processes (Poo, 2001).

Furthermore, investigating the impact of resistance training on total BDNF levels has broader implications for human health and well-being. BDNF is not only essential for neuroplasticity and neuronal survival but is also implicated in cognitive function, mood regulation, and the prevention of neurodegenerative diseases (Zuccato & Cattaneo, 2009). Thus, by promoting the production of BDNF through resistance training, individuals may potentially enhance their cognitive abilities and mitigate the risk of age-related cognitive decline.

While the increase in BDNF levels is a promising finding, it is notable that no significant improvements were observed in knee extension peak torque or MVC torque following the resistance training intervention. These results contrast with some previous studies reporting significant gains in muscle strength following resistance training (Westcott, 2012). However, it is important to consider the specific characteristics of our study population, the duration of the intervention, and the individual variability in response to training. It is possible that the 12-week intervention period may have been relatively short to elicit substantial changes in muscle strength for elderly participants. Additionally, the lack of significant improvements could be attributed to the participants prior resistance training experience, which might have limited their potential for further strength gains within the intervention period.

It is worth mentioning that our study had some limitations. Firstly, the small sample size may have limited the statistical power to detect small changes in muscle strength. Secondly, combining males and females into a single group may introduce confounding factors related to sex differences in response to resistance training. Men and women have inherent physiological differences, including differences in muscle mass, hormonal profiles, and body composition, which can influence their individual responses to the intervention. Finally, the short duration of the intervention may not have been sufficient to induce substantial gains in muscle strength. Future studies with larger sample sizes and longer intervention periods are necessary to confirm and extend our findings.

To fully understand the mechanisms underlying the relationship between resistance training and total BDNF levels, future research should explore the specific molecular pathways involved and in-

vestigate the long-term effects of resistance training on BDNF production. Additionally, considering factors such as training intensity, duration, and frequency may provide further insights into the optimal parameters for maximizing BDNF response to resistance training.

In summary, the measurement of total BDNF levels serves as a valuable tool for evaluating the effects of resistance training on neurobiological adaptations. This pilot study provides initial evidence of the positive impact of resistance training on total BDNF levels, highlighting the importance of considering total BDNF as a comprehensive marker of the response to exercise. Further investigation is needed to elucidate the underlying mechanisms and explore the potential implications of these findings for optimizing exercise interventions.

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