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Intense resistance exercise increases peripheral brain-derived neurotrophic factor

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ABSTRACT

Objectives: Brain-derived neurotrophic factor (BDNF) has been shown to increase in an intensity dependent manner in response to aerobic exercise. However, previous research investigating the use of resistance exercise to increase BDNF levels has been less conclusive, likely due to the low intensity nature of traditional resistance exercise programs. This study examined the influence of acute resistance exercise to-fatigue on serum BDNF levels and blood lactate.
Design: Acute crossover study.
Methods: Eleven untrained to intermediately trained males (age: 25.0 ± 1.3 year) and five untrained females (age: 23.2 ± 1.1 year) were recruited to undertake two bouts of resistance exercise. Strength (five sets of five repetitions, 180 s recovery) and hypertrophy (three sets of ten repetitions, 60 s recovery) based resistance exercise was implemented to-fatigue to examine the effect on serum BDNF and blood lactate levels immediately post-, and 30 min post-exercise.
Results: An interaction ($p < 0.01$; ES = 0.52) was observed between conditions immediately post-exercise, with hypertrophy resulting in significantly greater BDNF levels when compared with strength exercise. Changes in lactate and BDNF from baseline to post- exercise were positively correlated following hypertrophy exercise ($r = 0.70$; $p < 0.01$), but not correlated following strength exercise ($r = 0.18$; $p = 0.56$).
Conclusions: The use of a to-fatigue hypertrophy based resistance exercise protocol provides the necessary stimulus to increase peripheral serum BDNF. Mechanistically, the presence of lactate does not appear to drive the BDNF response during resistance exercise.

1. Introduction

Alzheimer's disease (AD), characterised by memory loss and cognitive dysfunction, is a leading cause of death in older adults. Age is the most significant predictor of AD diagnosis; nevertheless, the development of AD neuropathology likely starts decades prior to presentation of clinical symptoms.[1] Following the clinical onset of AD symptoms, progression can be rapid and unpredictable. To date, no effective treatment or cure exists for AD, thus research attention is focusing on the identification of effective preventative strategies to delay or prevent AD. Increasing evidence indicates physical activity, specifically structured exercise, can benefit cognitive health [2] and could potentially be used as a preventative strategy for AD. Mechanistic studies support a relationship between exercise and enhanced brain health in older adults. Specifically, results from exercise interventions have demonstrated upregulation of brain-derived neurotrophic factor (BDNF), a neurotrophin involved in the growth and repair of neural tissue.[3] In human studies, aerobic exercise has been shown to increase circulating levels of BDNF [4,5] and provide a protective influence to cognitive function.[2,4] The influence of aerobic exercise on BDNF appears to be dose dependent with greater levels of peripheral BDNF associated with an increased intensity of aerobic exercise.[4–6] To date, the majority research examining the influence of exercise on BDNF is focused on aerobic based exercise.[4–6] As resistance exercise is routinely prescribed to an ageing population,[8] understanding the influence of this exercise modality on BDNF is essential.

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Within the literature, resistance exercise has been shown to improve cognitive function;[9] however, from these studies it is not possible to determine if these effects were mediated by increases in BDNF. Unlike aerobic based exercise interventions, previous studies of resistance exercise and BDNF are equivocal. Some studies report increases in peripheral BDNF follow acute resistance protocols,[10] whereas others report no change[11,12]: These differing results may potentially be due to the intensity of the exercise.[4,13] Indeed, BDNF expression is indirectly associated with lactate,[4] a biomarker of physical fatigue which is elevated in response to higher exercise demands.[14] Furthermore, blood lactate accumulates with each repetition,[15] and has shown reduced clearance from the muscle with shorter periods of recovery.[16] It is possible through the manipulation of acute resistance training variables such as sets, repetitions, load, and recovery that the necessary stimulus could be provided to increase peripheral BDNF and enhance cognitive function. Manipulation of resistance exercise variables has been shown to elicit differing responses in blood markers; for instance, high load, low repetition, long recovery resistance exercise elevates serum testosterone levels,[13] a hormone linked to cognitive function.[17] Alternatively, moderate load, moderate repetition, short recovery resistance exercise stimulates human growth hormone[13]; which has been previously associated with peripheral BDNF.[18]

The use of exercise to prevent cognitive decline appears promising; however, the lack of data currently available in this field restricts its prescription. The purpose of this study was to examine the peripheral BDNF response to two different, yet intense, sessions of resistance exercise. We recruited individuals less than 30 year as in this population greater intensity of exercise is possible,[19] thus providing a greater effect for proof of BDNF induction principle and potential translation to older populations in future studies. Furthermore, as preventative strategies of cognitive decline should ideally span many decades: this cohort represents individuals at the beginning of this continuum. A secondary aim of the current study was to compare the lactate response to each exercise condition and determine the association between changes in lactate and BDNF. We hypothesised that the greatest magnitude change in BDNF and lactate would be observed following hypertrophy resistance exercise.

2. Methods

Sixteen individuals (males, n = 11, age 25.0 ± 1.3 year; females, n = 5, age: 23.2 ± 1.1 year) volunteered to participate in this study. All participants were untrained (n = 13) to intermediately trained (n = 3) as determined by previous guidelines.[8] Participants were considered low risk for moderate to intense exercise as per the Exercise and Sports Science Australia adult pre-exercise screening tool. Participants completed four exercise sessions (two familiarisation and two experimental sessions) with no less than four and no greater than 10 days between each session. All procedures were approved by the institutional Human Research Ethics Committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Participants were provided with written documentation of the possible risks and benefits related to their participation in this study and signed informed consent was obtained in writing.

Two initial laboratory sessions familiarised participants with the equipment and procedures involved in the study. During the first session, participants were provided verbal and visual instruction regarding the correct lifting technique for seven resistance exercises (bench press, latissimus dorsi pull-down [lat pull-down], leg press, leg extension, seated row, military press and dumbbell arm curl). Assessment of five- and 10- repetition maximum (RM) were conducted in a randomised and counterbalanced order in the following exercise sequence; 1) bench press, 2) seated row, 3) leg press, 4) military press, 5) lat pull-down, 6) leg extension, and 7) arm curl. During 5-RM testing, participants were asked to lift a weight, pre-selected by the researcher, which would result in only five repetitions being able to be completed as per previous guidelines.[20] During each exercise, range of motion was measured using a static measuring tape attached to weight machines and averaged over several repetitions in order to calculate mechanical work completed.[21] Range of motion during the arm curl was measured using a goniometer, and forearm length was measured using a tape measure. During the 10-RM visit, participants completed 10-RM testing using the same exercises and identical methodology to the 5-RM session, with the exception that the maximum weight that could be lifted with correct technique for ten repetitions was determined.

Table 1
Equations used to calculate total mechanical work, volume load and mean tonnage.

Equation no.	External measure	Equation
1	Mechanical work	$W = f \times d$
2	Mechanical work (leg press)	$W = (f \times \text{cosine} \times 45) \times d$
3	Mechanical work (arm curl)	$W = t \times \theta$
4	Volume load	$VL = m \times \text{repetitions}$
5	Mean tonnage	$MT = VL/\text{repetitions}$

Note: W = mechanical work, f = force, d = displacement, t = torque, θ = theta (angle in radians), VL = volume load, m = mass, MT = mean tonnage.

On the subsequent two laboratory sessions, participants completed either strength based or hypertrophy based resistance exercise protocols[13] in a randomised and counterbalanced order in the same sequence as during the RM testing. All sessions commenced with a five min self-paced warm-up on a rowing ergometer at low to moderate intensity followed by low resistance repetitions of all exercises. During the strength based session, participants completed five sets of five repetitions at their 5 RM resistance with 180 s of passive recovery between each set. During the hypertrophy based session, participants completed three sets of 10 repetitions at their 10 RM resistance with 60 s of passive recovery between each set.

Venous blood samples were collected prior to warm-up, immediately after the completion of the exercise, and 30 min post-exercise, for later BDNF quantification. Venous blood samples were obtained from the antecubital vein using a 21-gauge needle into serum separation tubes (SST Vacutainer®, Becton-Dickinson, U.S.A) and left to clot at room temperature before high-speed (1800 × *g*) centrifugation for 15 min to minimise platelets within the serum. After centrifugation, serum supernatant was transferred into 1.5 mL aliquots and stored at −80 °C for BDNF batch analysis. A further 4.0 mL of venous blood was collected into an ethylenediaminetetraacetic acid tube (EDTA Vacutainer®, Becton-Dickinson, U.S.A) once for platelet count. Prior to warm-up, immediately after the completion of the exercise, and 30 min post-exercise, 0.7 μL of blood was obtained in duplicate from the fingertip and analysed for blood lactate concentration using a handheld lactate analyser (Lactate Plus, Nova Biomedical®, U.S.A). Serum samples were analysed for total BDNF (precursor and mature isoforms) using a standard enzyme-linked immunosorbent assay technique. Serum BDNF was determined using a commercial kit (HBDP-33K, Milliplex®, Millipore™, Billerica, USA) as per manufacturer instructions. The manufacturer declares intra- and inter-assay coefficients of variation of less than 10%.

Total mechanical work, volume load and mean tonnage were calculated using the formulae defined in Table 1. We used equation one for all exercises involving vertical displacement (i.e. seated row, lat pull-down, leg extension, military press and bench press). Equation two calculated mechanical work of the incline leg press,