Effects of Endurance Exercise Training on Brain-Derived Neurotrophic Factor

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ABSTRACT

Williams, JS, Ferris, LT. Effects of Endurance Exercise Training on Brain-Derived Neurotrophic Factor. JEPonline 2012;15(4):11-17. As a member of the growth factor family, brain-derived neurotrophic factor (BDNF) has been identified as an important mediator of neuronal health. The purpose of this investigation was to determine the effects of an endurance training program on basal levels of BDNF. Eighteen physically active subjects completed a 12-wk supervised jogging class (3x/wk, 30 min/session, 65-70% HR max). A graded exercise test was conducted before and after the training program to determine maximal oxygen consumption (VO₂ max) and maximal work rate (WR max) on a cycle ergometer. Blood samples for basal serum BDNF and cortisol (COR) were also obtained before, at the mid-point, and after the training program. Training resulted in a significant increase (P<0.05) in VO₂ max and WR max. Both BDNF and COR were unchanged (P>0.05) in response to the training program. It was concluded that aerobic exercise training of this intensity, frequency, and duration did not provide an adequate training stimulus to result in a significant upregulation of basal BDNF.

Key Words: Growth Factors, Aerobic Training, Neuronal Health
INTRODUCTION

Brain-derived neurotrophic factor (BDNF) is an endogenous growth factor that plays a vital role in neuronal health. The binding of BDNF to a tyrosine kinase receptor results in neuronal survival, differentiation, and the promotion of synaptic transmission and long-term potentiation (2). The BDNF treatment of hippocampal slices from BDNF-knockout mice reverses deficits in long-term potentiation as well as improves basal synaptic transmission (9). The BDNF is also protective against ischemic insults and promotes neurogenesis (4). It is found and made in many locations throughout the body, especially the visceral epithelial cells, smooth and skeletal muscle fibers, and the brain and spinal cord (7,8).

The potential of exercise to affect neural function is becoming increasingly recognized. An acute bout of exercise has been shown to increase BDNF concentrations in humans (5,6,10). Furthermore, it appears that the increase in BDNF concentration in response to acute exercise is intensity-dependent (5,10). However, data describing the basal response of BDNF to an endurance exercise training program are unclear and lacking in humans (3,12,14). The purpose of this study was to determine the effects of a moderate intensity 12-wk jogging program on basal BDNF levels in young healthy human subjects.

METHODS

Subjects
The study population consisted of eighteen subjects (3 males and 15 females; age 20.0±0.3 yr; height 167.6±2.4 cm; weight 61.8±2.4 kg; BMI 21.9±0.4 kg/m²; mean ± SE) who were physically active, but not engaged in competitive sports. The participants were members of a formal university jogging class. Based on a detailed health history questionnaire, all subjects were nonsmokers and free of cardiopulmonary, metabolic, and musculoskeletal diseases. Thus, the subjects were in good health and free of any physical condition placing them at risk for participation in the study. The research design and data collection procedures were approved by the institutional review board. All subjects signed an informed consent form.

Procedures
A summary of the study timeline and procedures is shown in Figure 1. Participation in the study required three visits to the laboratory. During the first and third visits, the subjects performed a graded exercise test (GXT) on a stationary cycle. Prior to the GXT, blood samples were obtained for the determination of basal serum BDNF and cortisol (COR) levels. During the second visit, at the midpoint of the 12-wk training program, BDNF and COR levels were again obtained. All testing was performed at the same time of the day.

GXT Procedures
Testing was performed on an electronically-braked cycle ergometer (Lode, Corival). After a 5-min warm-up of unloaded cycling, the workload was set at 50 W and incremented by 25 W each minute to volitional fatigue. Pedal frequency was maintained at 70 rpm. Oxygen consumption (VO₂) and work rate (WR) were determined during the GXT on a breath-by-breath basis with samples averaged for 30-sec intervals (MedGraphics, CPX/D). The highest 30-sec average was defined as maximum. Volume and gas calibration of the metabolic system were performed before each test in accordance with the manufacturer’s specifications. Blood pressure was monitored during the GXT via auscultation. Heart rate and rhythm were obtained via standard electrocardiography (Quinton Instruments, Model 4000). The subjects were instructed to avoid strenuous exercise for 24 hrs and food and caffeine for 3 hrs before each GXT.
**Blood Sampling and Analysis**

A 10 ml sample of blood was withdrawn from the antecubital vein for the determination of basal serum BDNF and COR levels. The blood was allowed to clot (1 hr) and then centrifuged for 12 min at 1300 rcf (Eppendorf, Model 5804). The supernatant was decanted and stored in a -80 °C freezer until analysis. Serum BDNF was assayed via a sandwich ELISA kit (Chemikine). The sensitivity as reported in the ELISA kit literature was 7.8 pg mL⁻¹. Serum COR was assayed via radioimmunoassay (Diagnostic Products). The reported sensitivity was 0.2 µg/dL.

**Exercise Training Procedures**

The participants jogged outdoors for 30 min/exercise session, 3x/wk, for 12 wk at an exercise heart rate range that corresponded to 65-70% HR max as determined from the GXT. All the participants wore a heart rate monitor (Polar A1) that enabled them to maintain a jogging pace within the prescribed heart rate range. The training sessions were monitored for attendance and supervised by experienced exercise instructors.

**Statistical Analyses**

Differences between pre- and post-exercise training VO₂ max and WR max values were analyzed using paired t-tests. Serum BDNF and COR values over the course of the study were analyzed using
repeated measures ANOVA. Significant main effects were further analyzed with Student-Newman post hoc tests. The association between the pre- and post-exercise training changes in basal serum BDNF and COR and changes in VO$_2$ max and WR max were examined with Pearson correlation coefficients. The level of significance was set at $P<0.05$. All values are reported as mean $\pm$ SE. Statistical analyses were conducted using SigmaStat for Windows (Jandel Scientific Software, SPSS).

RESULTS

Analysis of the attendance records for the training group demonstrated an 87.5% compliance rate (i.e., 567 exercise sessions were completed of a possible 648). Post-training VO$_2$ max and WR max were significantly increased following the 12-wk jogging program compared to pre-training values (4.8% and 7.3%, respectively) (Figure 2). The baseline mean VO$_2$ max was 33.8 mL·kg·min$^{-1}$, which increased to 35.4 mL·kg·min$^{-1}$ post-training ($P<0.01$). The baseline mean WR max was 168.3 W, which increased to 180.5 W post-training ($P<0.001$). Mean basal values during the time course of the training program (beginning, midpoint, and endpoint) for BDNF and COR are shown in Figure 3. The mean basal BDNF values for the three measurement points were 14180.7, 15064.7, and 14820.8 pg·mL$^{-1}$, respectively. There were no significant differences among the three time points ($P>0.05$). The mean basal COR values for the three measurement points were 26.1, 20.4, and 25.7 µg/dL, respectively. There were no significant differences among the three time points ($P>0.05$). There was no significant correlation between the change in BDNF and the change in VO$_2$ max ($R = 0.32$, $P>0.05$), nor was there a significant correlation between the change in BDNF and the change in WR max ($R = 0.050$, $P>0.05$). Similarly, there was no significant correlation between the change in COR and either the change in VO$_2$ max ($R = 0.010$, $P>0.05$) or the change in WR max ($R = 0.10$, $P>0.05$).

![Figure 2. Maximal oxygen consumption, VO$_2$ max, (left panel) and maximal work rate, WR max, (right panel) before and after the 12-wk endurance training program. Values are means $\pm$ SE; *Significantly different from baseline; $P<0.01$.](image-url)
DISCUSSION

The primary purpose of this study was to determine the effects of a 12-wk endurance exercise program on BDNF concentrations in humans. Our key indicators of a training effect, VO\textsubscript{2} max and WR max, were significantly higher post-training compared to baseline suggesting that a training effect, however small, was achieved. The endurance training program did not significantly alter basal levels of BDNF.
BDNF and COR Responses

Our findings are in contrast to those of Baker et al. (1) Seifert et al. (14), and Zoldac et al. (15) where basal BDNF was elevated following an aerobic training program. The differences may be explained by the higher intensity training protocol (i.e., greater training frequency and percentage of heart rate or VO2max) used in the earlier studies. In addition, Schiffer et al. (13) has shown that infusion of lactate at rest increases BDNF concentrations, which supports the idea that higher intensity aerobic training may be necessary to upregulate basal BDNF. Previous data regarding the response to an acute bout of exercise suggests that an increase in BDNF is dependent upon the exercise intensity as well (5,10), and this finding may be similar for chronic exercise training. Castellano and White (3) were unable to demonstrate a significant increase in basal BDNF concentrations following either 4 or 8 wks of aerobic training (3x/week at 60% VO2 peak) in controls and multiple sclerosis patients. Schiffer et al. (12) demonstrated a 20% decline in basal BDNF in subjects that trained for 45 min, 3x/week for 12 wks at 80% of the HR at lactate threshold. The training intensity of these studies is more aligned with that of the present study. Basal COR levels were also measured from blood samples taken at the beginning, middle, and end of the training protocol while the subjects were resting. Stress, perhaps via a cortisol-mediated mechanism is thought to have deleterious effects on neural tissue and a dose-dependent decrease of BDNF in rodents following corticosterone administration has been demonstrated (11). The chronic training from this protocol resulted in no significant changes in basal COR levels and could not have affected our BDNF responses.

CONCLUSIONS

A 12-wk aerobic training program of moderate intensity completed by healthy subjects did not result in an increase in basal BDNF concentrations. It is possible that a higher training volume (i.e., intensity, frequency, and duration) is needed to elicit favorable results with respect to the regulation of this neurotrophin during exercise. Future studies should consider the differential effects of training volume with respect to both aerobic and strength training programs.

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REFERENCES


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