Neuroscience Letters 486 (2010) 146–149

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Does a period of detraining cause a decrease in serum brain-derived neurotrophic factor?

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ARTICLE INFO

Article history:
Received 5 August 2010
Received in revised form 1 September 2010
Accepted 11 September 2010

Keywords:
BDNF
Neurotrophin
Humans
Aerobic training
Detraining

ABSTRACT

Brain-derived neurotrophic factor (BDNF) is one of the neurotrophins promoting cognitive function and contributing to neurogenesis and neuroprotection. Available evidence suggests that exercise influences serum BDNF concentrations, but that the effect is transient. The purpose of this study is to determine whether a period of aerobic training, followed by a period of detraining, can influence basal serum BDNF levels in humans. Sixteen young, sedentary subjects were assigned to an experimental group ($n = 9$) and a control group ($n = 7$). The experimental group performed an aerobic training program during 8 weeks, followed by 8 weeks of detraining, during which subjects returned to their previous, sedentary activity level. The control group remained physically inactive during 16 weeks. In both groups, performance on short-term (Digit Span test) and mid-term memory (Recall of Images) was assessed. Aerobic training significantly increased the VO_2 peak in the experimental group, and these values returned to baseline after 8 weeks of detraining. Basal serum BDNF was not influenced by 8 weeks of aerobic training and detraining did not seem to have an effect on basal peripheral BDNF concentrations. Both training and detraining did not clearly influence short-term memory performance on the Digit Span test and no differences were present between the experimental and control group on the mid-term memory test. Future studies should focus on patient groups and elderly to further investigate the effect of training and detraining on neurotrophic factors and cognitive function, and on the effects of training and detraining on the BDNF response to acute exercise.

Brain-derived neurotrophic factor (BDNF) is a neurotrophin that is involved in central neuroprotection and neurogenesis [3,8], and it is suggested to play a role in the regulation of cognitive function [2,30]. Next to its role in proliferation, differentiation and survival of neurons during development, evidence indicates that BDNF also contributes to food intake and energy metabolism [15] and functions as a metabotrophin in the hippocampus [12].

BDNF can be influenced by several external stimuli, such as antidepressants, stress and physical exercise [1,13,23]. The past few years, physical exercise and its beneficial effects on both physical and cognitive function has been thoroughly discussed as a means to mediate BDNF [29]. In humans, a growing number of studies examined the effects of different forms of exercise and training on peripheral BDNF [4,9–11,13,16,21,22,24,25,28,32,34]. From these studies it is clear that an acute exercise bout will increase circulating BDNF levels, but that a longer training period not necessarily increases circulating BDNF concentrations (for review see Knaepen et al. [13]). Schulz et al. [25] were the first to investigate the effects of an aerobic training program on serum BDNF in multiple sclerosis (MS) patients and showed that 8 weeks of training (cycling) did not result in significant changes of basal peripheral BDNF concentration [25]. These results have been confirmed by other studies, in both patients and healthy subjects [4,24]. Only the study of Zoladz et al. [34] demonstrated an effect of 5 weeks aerobic training on plasma BDNF, although no control group was included in this study. Up to now, aerobic training seems not able to influence basal levels of peripheral BDNF. Yet, Seifert et al. [26] recently showed that after 12 weeks of aerobic training, the release of BDNF from the brain is enhanced, but this increase could only be detected in the jugular vein and no differences were seen in the plasma BDNF concentration in a peripheral artery [26].

The beneficial effects of exercise on cognition have been demonstrated in many studies [7] and it seems that the ability of exercise

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doi:10.1016/j.neulet.2010.09.032

to improve cognitive function involves the action of BDNF on metabolic processes to impact several aspects of hippocampal function [12]. The question also remains whether the effects of exercise on cognition last in periods when patients are unable to continue their physical exercise.

To our knowledge, the effect of detraining on BDNF in humans has not yet been studied. In rodents, Radak et al. [19] investigated the influence of a period of detraining on brain function, BDNF and oxidative stress. They found that BDNF in the hippocampus of rats increased with an 8-week period of training, while it decreased to levels that were even lower than those found in the sedentary control group when training stopped (8 weeks detraining). The purpose of this study was to investigate whether an 8 weeks aerobic training program is able to change basal serum BDNF concentration in sedentary subjects, and whether a period of detraining reverses this change.

Subjects were recruited among sedentary students of the Vrije Universiteit Brussel (except students in physical education and physiotherapy). In total 16 subjects volunteered to participate, all aged between 18 and 30 years old. No musculoskeletal complaints or cardiovascular risk factors were present. None of the subjects was physically active for more than 1 h per week, and none of them had followed a training program during the past 2 years. Overall, 9 subjects participated in the experimental group, the control group consisted of 7 subjects.

All experiments were conducted in accordance with the Declaration of Helsinki and approved by the institutional review board of the Vrije Universiteit Brussel, Belgium. Written informed consent was obtained from all participants.

Subjects were tested on 3 occasions during the 16 weeks experiment: at baseline, after 8 weeks, and at 16 weeks. At each time point, a blood sample was taken and memory performance was determined. Next to this, all subjects performed a graded exercise test (GXT) to exhaustion to determine their VO_2 peak. Training guidelines were based on the results of the GXT.

The GXT to exhaustion was performed on a cycle ergometer. Subjects started at 50 W and resistance was increased by 25 W every 3 min to exhaustion. Heart rate and lactate were measured every 3 min. VO_2 peak was registered using a portable cardiopulmonary indirect breath-by-breath calorimetry system (MetaMax® 3B, Cortex Biophysik, Germany).

The experimental group followed an 8-week aerobic training program (3 sessions/week; 20–40 min walking, running, cycling, synchro, wave). Individual training guidelines were given, based on the heart rate and lactate during the GXT. To monitor participants, we used TGS (TechnoGym® System) keys. TGS allows to save all workout data of every subject into a personalized database. Following the 8-week training period, subjects were asked to return to their sedentary activity level. The control group was asked not to change their sedentary activity level during 16 weeks.

Blood for BDNF analysis was collected into pre-cooled serum tubes (BD Vacutainer® SST II Advance) and left to clot at room temperature for 1 h. After centrifugation (12 min, 3000 rpm), the resulting serum was decanted and stored at −80 °C until analysis. Serum BDNF was assayed in duplicate according to the manufacturer's instructions (ChemiKine® BDNF ELISA kit, Millipore®, Temecula, CA, USA). The BDNF ELISA kit has a detection range from 7.8 to 500 pg/mL. The intra-assay and inter-assay variations are ±3.7% (125 pg/mL) and ±8.5% (125 pg/mL), respectively.

To examine the effects on cognitive function, both short-term and mid-term memory were assessed. Short-term memory was determined using a Digit Span memory test [31]. Subjects were presented a series of numbers to memorise. Each number was shown for 1 s, 0.5 s later the next number appeared. The task was to recall the numbers, in the right or reverse order. To assess mid-term memory, a picture recall task was used [5,6]. Subjects were shown 12 pictures, each for 10 s. Subjects were asked to write down which pictures they remembered after a period of 30 min.

Table 1
Overview of the subject characteristics from the control and experimental group at baseline. No significant differences were present between groups.

Subject characteristics	Control group	Experimental group
N	7	9
Age (years)	21.3 ± 1.0	21.2 ± 1.1
Length (m)	1.75 ± 0.04	1.71 ± 0.03
Weight (kg)	70.7 ± 5.7	67.8 ± 3.8
BMI (kg/m^2)	22.8 ± 0.9	23.2 ± 1.0

Statistical analysis was performed using Statistica 6.0 software. Normality of data was checked using a Kolmogorov–Smirnov Goodness of Fit test. By using a mixed design ANOVA model we tested for differences within the groups during the training period (time effect) and between the experimental and control group (treatment effect). Post hoc analysis was applied by using the Duncan's multiple range post hoc test. Differences were considered to be significant when $p < 0.05$. All data are presented as mean ± standard error.

An overview of the subject characteristics at baseline can be found in Table 1. No significant changes were found in weight or BMI during the whole training and detraining period.

At baseline, no differences were found in VO_2 peak between the experimental and control group. Within the experimental group, VO_2 peak increased significantly (+11, 47%) as a result of 8 weeks of aerobic training. After 8 weeks of detraining, VO_2 peak returned to baseline level. In the control group, no change in VO_2 peak was observed during 16 weeks.

The protein level of BDNF was determined with ELISA in serum samples taken from a peripheral vein. No effect of training or detraining was found over the 16-week study, and BDNF concentration did not differ from values in the control group (no effect of group or time). Neither training nor detraining influenced peripheral BDNF (Fig. 1).

No differences between groups could be found on the short-term memory test at baseline. A period of training or detraining did not change performance on short-term memory compared to the control group (Fig. 2). Also for mid-term memory, no difference was present between the experimental and control group, meaning that training or detraining did not significantly influence performance on this test. Overall, for both groups, an improvement in mid-term memory performance was seen after 16 weeks compared to 0 and 8 weeks ($p = 0.03$), indicating a learning effect following memorization of images.

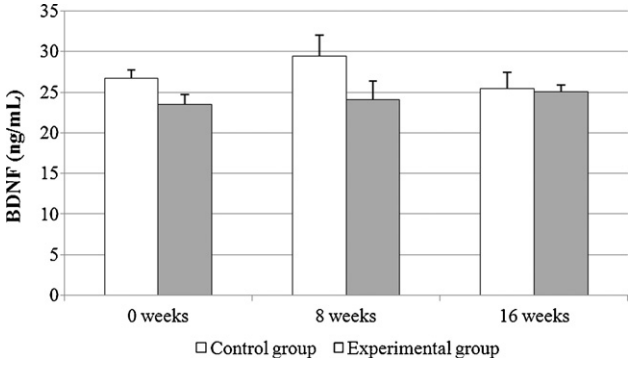

Fig. 1. Serum BDNF concentration (ng/mL) in the control and experimental group at baseline (0 weeks), after 8 weeks (training period), and after 16 weeks (detraining period). No significant difference was present between experimental and control group nor within groups.