Relationship between serum brain-derived neurotrophic factor and physical activity in young men

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1. Introduction

The metabolic syndrome (visceral obesity, dyslipidaemia, hyperglycaemia, and hypertension), depression and dementia have become one of the major public-health challenges worldwide. In the context of such diseases, brain-derived neurotrophic factor (BDNF) has gotten a lot of attention recently. BDNF is a member of the neurotrophin family of growth factors and found in the nervous system and periphery. BDNF is known to play an important role in the growth, development, maintenance and function of survival neuronal system (Thoenen, 1995). Recent evidences suggests BDNF may play important roles in memory, learning (Ma et al., 1998), depression (Duman, 2002), regulation of food intake, and energy metabolism (Nakagawa et al., 2000). Various studies have shown possible links between low levels of BDNF and some conditions such as Obsessive-compulsive disorder, depression, and Alzheimer’s disease (AD) while it is still not know their causality. It was demonstrated that heterozygous BDNF knockout mice, which have reduced BDNF levels, exhibit hyperphagia accompanied by significant weight gain in early adulthood (Lyons et al., 1999). In post-mortem human studies, the relative levels of BDNF mRNA and proteins are decreased in hippocampus in severe AD (Phillips et al., 1991) and depressed suicide patients (Chen et al., 2001) as compared with aged controls. Moreover, the level of serum BDNF, as well as brain, was decreased in severe AD (Laske et al., 2005) and depressed patients (Karege et al., 2002). As BDNF can cross the blood-brain barrier in both directions (Pardridge et al 1994), serum BDNF could reflect the expression and/or action of BDNF in brain and other organs. Unlike brain BDNF, significance of the serum BDNF has been so far ambiguous. Clarification of significance of the serum BDNF would contribute to understanding of the pathogenesis of such diseases and treatment.

Exercise is increasingly recognized as an intervention that can improve metabolic profiles (Hamdy et al. 2001) and reduce central nervous system dysfunctions such as cognitive decline, depression and stress (Adlard and Cotman, 2004). It has previously been reported in animals that acute exercise and training significantly increased the
BDNF mRNA and protein level in the brain (Neeper et al 1996; Gomez-pinillia et al 2001; Radak et al., 2006). In humans, blood BDNF concentration was augmented after acute moderate or high intensity exercise (Gold et al., 2003, Vega et al., 2006). It would therefore be of great interest to assess the level of serum BDNF in athletes. In this study, we determined whether serum level of BDNF in male athletes differ from those of age-matched male normal control subjects, and is associated with daily physical activity.

2. Methods

Male 14 healthy volunteers who have no sports activities (age: 22.4 ± 1.2 years) and 12 athletes (age: 21.8 ± 0.9 years) were participated in this study. The athletes group includes distance runners (n = 8), a sprinter (n = 1), tennis players (n = 3), and a badminton player (n = 1). All athletes have participated in regular sports activities (over 16 hours per week for more than 3 years). Control subjects have not participated in any regular exercise (for more than 1 year). The serum BDNF level was measured using an enzyme-linked immunoassay (ELISA) kit (Promega, Madison, WI). To evaluate physical activity, the participants attached the Lifecorder® (Suzuken Co., Nagoya, Japan) for 1 week just before the day of blood collection. Hemoglobin A1c was measured by high-speed liquid chromatography. The blood glucose and the lipid profiles including total cholesterol, high-density lipoprotein cholesterol, and triglyceride were determined using the enzymatic method. To measure the mental health of the subjects, the 30 items version of the General Health Questionnaire (GHQ-30) and the self-ratable State-Trait Anxiety Inventory (STAI) were performed in all subjects.

3. Results

We found that the serum BDNF in the young athletes was lower than that in age-matched subjects (Fig.1). On the other hand, no significant difference was observed in age, height, weight, body mass index, % body fat, fasting blood glucose, hemoglobin A1c, total cholesterol, high-density lipoprotein cholesterol and psychological parameters (GHQ-30, STAI) between the two groups. Triglyceride was lower in the Athletes than that in the control. On the other hand, physical activity levels (total energy expenditure, move-related energy expenditure, total time of physical activity and walking count) in the athletes were significantly higher than that in the control. The serum BDNF level was negatively correlated with the total energy expenditure (Fig.2), move-related energy expenditure, walking count and total time of physical activity.

4. Discussion

This is the first report to show that the level of serum BDNF was lower in athletes than that in control subjects and it was negatively
correlated with the daily physical activity levels. The following are the likely reasons why the level of serum BDNF was decreased in athletes.

It has been shown that more than 90% of blood BDNF proteins are stored in platelets, from which it can be released through activation or clotting processes at the site of traumatic injury to facilitate the repair of peripheral nerves or other tissues that contain TrkB (Radka et al., 1996; Fujimura et al., 2002). It has been reported that aerobic physical exercise generated reactive oxygen species such as superoxide anion and hydrogen peroxide are able to cause muscular damage and inflammation (Alessio and Goldfarb, 1988; Liu et al., 2005). Muscle also is damaged by mechanical stress. On the other hand, BDNF is known for a functional role in the periphery e.g. in repair processes at the site of traumatic injury. These evidences raise the possibility that release of BDNF from platelets to damaged tissues might increase in order to facilitate the repair.

In animals, BDNF has been shown to improve glucose, lipid metabolism and increase energy expenditure (Nakagawa et al., 2000). We already reported that the serum BDNF level in newly diagnosed female patients with type 2 diabetes mellitus is higher than that in healthy subjects and associated with the total and abdominal subcutaneous fat mass and lipid and glucose metabolism (Suwa et al., 2006). It is therefore likely that the BDNF level increased in obese diabetic patients to compensate for such pathophysiologic conditions because of its potential roles in improving energy metabolism and suppressing food intake. On the other hand, it is well established that exercise induce body fat reduction and improvement of lipid and glucose metabolism. In deed, energy expenditure in the athletes was significantly higher than that in the control subjects and triglyceride in the athletes was lower than that in the control subjects. Taken together, it is reasonable that BDNF which suppresses food intake and enhances glucose and lipid metabolism is decreased. In conclusion, we have shown that the serum BDNF level was decreased in the young male who performed a daily sport activity. In addition, the serum BDNF level was found to be associated with daily physical activity level.

5. Main references
Neeper SA, Gomez-Pinilla F, Choi J,


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**Fig.1. The serum BDNF level in the control subjects and athletes.**

**P<0.01**

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*Fig2. Relationship between the serum BDNF level and total energy expenditure in all subjects.*

- ■ Control  ▲  Athletes