

スクは高まるとする報告があり⁹⁾、テレビ視聴時間が増すと運動に使える時間が減少し、消費エネルギー量が減少する、テレビを見ながら食べものを口にする、テレビのコマーシャルや食事シーンの影響などが考えられている。よって休日の過ごしかたは、テレビの視聴などの時間を減らすことが望ましいと考えられた。

食行動では、T2DM 群で食品数が少なかったが、特に男性では根菜類・緑黄色野菜・海藻類の摂取頻度が少ないことが判明した。これらの食品には食物繊維が豊富に含まれている。食物繊維の効用には、食物繊維そのものがエネルギー源になりにくい、ほかの栄養素の消化吸収を阻害する、唾液・胃液の分泌を促進して満腹感をもたらすことなどが考えられている⁹⁾。また、食事療法として、高繊維食の摂取によって HbA_{1c} は有意な変化はないものの、糖尿病患者の空腹時血糖値や 1 日尿糖排泄量、血中インスリン濃度が低下し、同時に総コレステロール、中性脂肪、LDL コレステロールも低下するという報告もある¹⁰⁾。これらのことから、食物繊維の多い食品を摂取することが望ましいと考えられ、特に男性では根菜類・緑黄色野菜・海藻類の摂取を習慣化することが大切である。

喫煙習慣では、T2DM 群で喫煙率および喫煙指数が高いことが判明した。日本における大規模コホート研究では、喫煙習慣者は、男女とも糖尿病発症リスクが高まると報告しており、喫煙によるインスリン抵抗性や酸化ストレスの増加が指摘されている¹¹⁾。わが国では 2006 年より禁煙治療に保険が適用されるようになり、喫煙指数 200 以上の喫煙者はニコチン依存症という疾病に位置づけられた。煙草は単なる嗜好品でなく依存性薬物とみなし、特に喫煙指数の高い者への禁煙支援が急務である。飲酒習慣では、男女混合に解析すると T2DM 群で飲酒頻度が多かったが、男女別の解析では有意差を認めなかった。過度の飲酒量は、糖尿病発症の要因とする報告がある^{3,4)}。

今後はさらに対象者を増やし、飲酒量や飲酒行動に至る規定要因についても調査する必要がある。T2DM 群は健常群と比較して肥満度が有意に高いため、今回の研究で明らかになった生活習慣の特性が 2 型糖尿病のみの特性によるものなのか、肥満をきたしやすい群の特性を示したのかの判断は困難であるが、今後、耐糖能正常者で類似の肥満度を認める群との比較検討が必要であろう。健康に関する情報を知識として理解しても行動変容までに結びつけるのは容易ではない。健康行動の定着化のためには個別に対応し、

いかなる理由で実行しがたいのかに目を向け、今回明らかになったような健康行動実践の阻害要因を取り除くことが先決と考えられる。そのためには個人の実生活に即し、かつ QOL の保持可能な内容に従っての糖尿病療養指導が望まれる。

まとめ

2 型糖尿病患者の生活習慣とその関連因子を検証する目的で、T2DM 群と健常群の生活習慣について比較検討を行った。T2DM 群は健常群に比べて、睡眠・休養行動、運動行動、食行動、喫煙習慣が不良であったが、その背景には睡眠時間の不足感、眠りが浅く熟睡できない、休養日に気分転換ができない、運動施設や運動仲間恵まれていない、運動を行おうとする意志が低い、休日のテレビ視聴時間が長い、根菜類・緑黄色野菜・海藻類の摂取不足、喫煙指数が高値などの不良な理由が認められた。これらを基礎資料として、効果的な糖尿病療養指導のプログラム構築の必要性が示唆された。

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Decreased serum brain-derived neurotrophic factor in trained men

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ABSTRACT

The purpose of this study was to clarify the effect of physical activity on the level of serum brain-derived neurotrophic factor (BDNF). The serum BDNF level in trained men who have participated in regular sport activity ($n = 12$) was compared to that in sedentary subjects ($n = 14$). The physical activity levels expressed as total energy expenditure, move-related energy expenditure and walking count in the trained were significantly higher than those in the sedentary. The serum BDNF level in the trained men was found to be lower than that in the sedentary (19.54 ± 4.53 ng/ml vs. 23.63 ± 2.94 ng/ml, respectively, $P < 0.01$). The serum BDNF level showed a significant negative correlation with daily total energy expenditure ($r = -0.507$, $P < 0.05$), movement-related energy expenditure ($r = -0.503$, $P < 0.05$), and walking count ($r = -0.480$, $P < 0.05$). These results may suggest that vigorous habitual physical activity decrease the serum BDNF level.

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Brain-derived neurotrophic factor (BDNF) is a member of the neurotrophin family of growth factors and found in the nervous system and periphery. BDNF is known to promote the growth, development, maintenance and function of survival of the neuronal system [2,4,30,35]. In addition, accumulating evidence suggests that BDNF may play important roles in memory, learning [20,21], mood disorder [7], food intake, and energy metabolism [23].

BDNF is also present in human and rat plasma, and much more concentrated in the serum [31]. Although the role of circulating BDNF remains unclear [9,22,32], since BDNF can cross the blood–brain barrier [28], consequently, the serum BDNF could reflect the expression and/or action of BDNF in the brain and other organs, and some clinical conditions. Indeed, serum BDNF is decreased in patients with severe Alzheimer's disease [17], depression [12,33], and eating disorders [24] in comparison to healthy controls. Furthermore, BDNF has a possible link with metabolic status [5,6]. A previous study demonstrated that serum BDNF was increased in patients with type 2 diabetes mellitus [34].

BDNF level is also affected by exercise. It has been shown in humans that there is a transient augmentation of serum BDNF concentration immediately after moderate exercise [10] and short

duration high-intensity exercise to exhaustion [36]. In animals, exercise training has been reported to increase BDNF mRNA in several brain areas [25–27]. Moreover, BDNF mRNA expression in the hippocampus was positively correlated with running distance. These findings suggest the possibility that daily physical activity may thus have an impact on the serum BDNF level. This study determined whether the serum BDNF level in trained men differs from that in age-matched control subjects.

Twelve Japanese trained males and 14 sedentary male volunteers participated in this study. All trained men had participated in regular sports activities more than four times and 16 h per week for more than 3 years. The control subjects had not participated in any regular exercise for more than 1 year. The trained group included distance runners ($n = 7$), a sprinter ($n = 1$), tennis players ($n = 3$), and a badminton player ($n = 1$). The details of the training frequency, volume and playing experience were obtained by questionnaires. We interviewed the subjects to obtain their medical history and current life style. Subjects who were on medication for any medical or psychological condition and/or smokers were excluded from this study. This study was conducted in accordance with the Declaration of Helsinki, and approved by the ethics committee of the Institute of Health Science, Kyushu University, Fukuoka, Japan. Written informed consent was received from all participants prior to participation.

After overnight fasting, venous blood samples were collected between 9:00 and 10:30 A.M. After the blood was centrifuged,

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the serum and plasma were stored at -80°C until analyses. The BDNF assessment was performed within 1 month of the sample collections. The serum and plasma BDNF level was measured using an enzyme-linked immunoassay (ELISA) kit (Promega, Madison, WI). Hemoglobin A_{1c} (HbA_{1c}) was measured by high-performance liquid chromatography. The fasting blood glucose (FBG) and the lipid profiles including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) were determined using enzymatic methods.

Morphologic and psychological measurements were conducted because the serum BDNF level has been reported to be affected by various conditions such as obesity [22] and depression [12,33]. The body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. The percentage of body fat (%Fat) was measured by electrical impedance (Tanita, Tokyo, Japan) [29]. Waist circumference measured at the level of the umbilicus was divided by the circumference of the hip measured at its greatest gluteal protuberance to calculate the waist-hip ratio (WHR). The psychological state such as depressive mood and anxiety was assessed using 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.

To evaluate physical activity, the participants attached the Lifecorder[®] (Suzuken Co., Nagoya, Japan) for 1 week just before the day of blood collection. The Lifecorder[®] is a small solid state recorder (62.5 mm × 46.5 mm × 26 mm, 40 g), containing an acceleration sensor, an amplifier, a microprocessor and memory. Based on the memorized intensity and times of movements, weight, and basal metabolic consumption, daily total energy expenditure (TEE) and movement-related energy expenditure (MEE) is calculated [32].

The data were presented as the mean ± standard deviation (S.D.). The comparisons between the control subjects and trained were performed using the unpaired Student's *t*-test. The relationship between two variables was examined using Pearson's correlation coefficient. A stepwise multiple regression analysis was performed to assess the influence of the following independent variables on serum BDNF level: age, BMI, GHQ score, WC, FBG, TC, TG. Statistical significance was defined as $P < 0.05$.

Table 1 shows the morphologic, psychological and metabolic characteristics of the subjects. There were no differences in age, height, weight, BMI, %Fat, FBG, HbA_{1c}, HDL-C or TC and the scores of the GHQ and STAI between the two groups. A difference observed

Table 1
Characteristics of the subjects

	Control (n = 14)	Trained (n = 12)
Age (years)	22.4 ± 1.2	21.8 ± 0.9 ns
Height (cm)	171.7 ± 7.0	172.5 ± 7.2 ns
Weight (kg)	60.9 ± 7.7	62.6 ± 8.0 ns
BMI (kg/m ²)	20.6 ± 2.1	21.0 ± 2.0 ns
%Fat	17.1 ± 4.3	15.0 ± 2.6 ns
WHR	0.85 ± 0.08	0.77 ± 0.05*
TC (mg/dl)	173.8 ± 26.4	159.5 ± 19.8 ns
HDL-C (mg/dl)	61.4 ± 14.3	69.2 ± 12.8 ns
TG (mg/dl)	91.1 ± 41.2	59.2 ± 23.7*
HbA _{1c}	4.8 ± 0.2	4.7 ± 0.03 ns
FBG (mg/dl)	91.4 ± 8.9	88.7 ± 7.0 ns
GHQ-30	4.6 ± 4.4	5.8 ± 3.0 ns
STAI (Trait)	42.5 ± 9.4	42.4 ± 7.0 ns
STAI (State)	40.7 ± 9.1	39.3 ± 7.8 ns

Data are expressed as the mean ± S.D. BMI, body mass index; %Fat, percentage of body fat; WHR, waist-hip ratio; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; HbA_{1c}, Hemoglobin A_{1c}; FBG, fasting blood glucose; GHQ-30, 30 items version of the General Health Questionnaire; STAI, self-ratable State-Trait Anxiety Inventory; ns, non-significant.

* Significantly different between the groups ($P < 0.05$).

Table 2
Physical activity level of the subjects

	Control (n = 14)	Trained (n = 12)
TEE (kcal/day)	2199.6 ± 228.3	2532.7 ± 270.5*
MEE (kcal/day)	261.5 ± 108.6	556.0 ± 174.5*
WC (steps/day)	9171.0 ± 2861.2	15517.9 ± 4227.6*

Data are expressed as the mean ± S.D. TEE, total energy expenditure; MEE, movement-related energy expenditure; WC, walking count.

* Significantly different between the groups ($P < 0.05$).

between the two groups in the TG and WHR. The average TEE, MEE, WC in the trained group was distinctly higher than those in the control group (Table 2).

Fig. 1 indicates the serum BDNF level in the both groups. The serum BDNF level in the trained was significantly lower than that in the control subjects (19.54 ± 4.53 ng/ml vs. 23.63 ± 2.94 ng/ml). No difference was detected in the plasma BDNF levels between the groups (controls: 1440.61 ± 1090.28 pg/ml vs. trained: 1143.64 ± 600.53 pg/ml). Correlation analyses were conducted with the measurements obtained from all of the subjects. Significant negative correlations between serum BDNF and TEE ($r = -0.507$, Fig. 2A), MEE ($r = -0.503$, Fig. 2B), WC ($r = -0.480$, Fig. 2C) and GHQ scores ($r = -0.551$) were detected. GHQ-30 provides six subscales: general illness, somatic symptom, insomnia, social dysfunction, anxiety and dysphoria, and depression. Only the scale of anxiety and dysphoria was associated with serum BDNF level ($r = -0.52$). The serum BDNF was not significantly associated with age, height, weight, BMI, %Fat, WHR, FBC, HbA_{1c}, HDL-C, TG, TC and STAI score. None of measurements significantly correlated with plasma BDNF level. In a multiple regression model with serum BDNF as the dependent variable (model $r^2 = 0.46$, $P < 0.01$), GHQ score ($\beta = -0.48$, $P < 0.01$) and WC ($\beta = -0.42$, $P = 0.01$) were significant independent predictors, but there were no significant contributions from age ($P = 0.51$), BMI ($P = 0.17$), FBG ($P = 0.65$), TC ($P = 0.90$) and TG ($P = 0.61$).

This is the first report to investigate the serum BDNF level in trained men. The serum BDNF level in trained men was lower than that in age-matched subjects and was negatively correlated with the physical activity level. The serum BDNF level has been reported to change according to age [37], body weight, BMI [22] and depressive state [16]. In the current study, no significant difference was observed in age, anthropometric and psychological parameters between the two groups, suggesting such parameters were not related to the difference of the serum BDNF level between the groups.

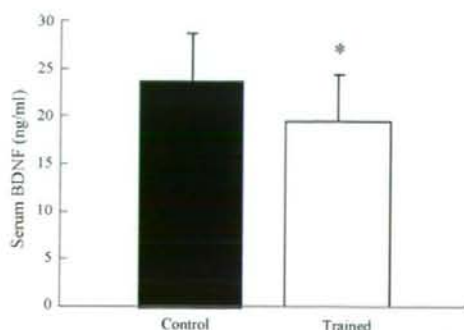


Fig. 1. The serum BDNF level in the control (n = 14) and the trained groups (n = 12). Data are expressed as the mean ± S.D. *: $P < 0.05$ vs. control.

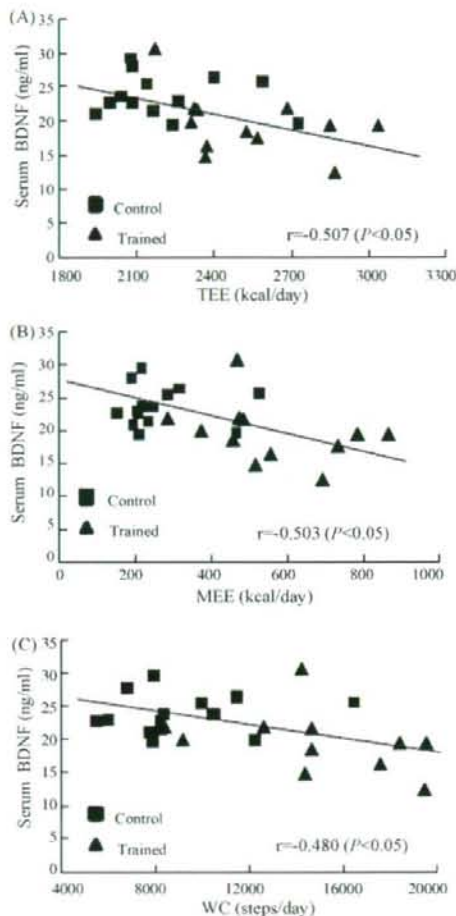


Fig. 2. Relationship between the serum BDNF level and total energy expenditure (A), move-related energy expenditure (B), and walking count (C). TEE, total energy expenditure; MEE, movement-related energy expenditure; WC, walking count.

The serum BDNF concentration increased immediately after moderate [10] and high-intensity [36] acute exercise and rapidly returned to basal concentration [10,36]. In the present study, the blood sample was collected at least 24 h after the last exercise. Therefore, the significant reduction of serum BDNF in trained men was the effect of chronic physical activity rather than that of acute exercise.

There is accumulating evidence in animals that exercise training increases the expression of BDNF mRNA and protein expression in several regions of the brain [25,26]. Since BDNF can cross the blood–brain barrier in both directions [28] and the cortex BDNF correlates with the serum BDNF [13], the serum BDNF is considered to reflect the expression and/or action of BDNF in the brain. Therefore, high level of serum BDNF in the trained was expected. In this study, however, BDNF concentration in the trained was lower than that in the control.

Why did the serum BDNF decrease in the trained men? One of the explanations is that BDNF utilization in some tissues might be increased to repair the injured tissues and then the release of BDNF from platelets might be increased. More than 90% of blood BDNF proteins are stored in platelets, from which it can be

released through activation or the clotting processes [9,31]. Since protein synthesis in platelet has not been confirmed, it is possible that platelets take up BDNF from the brain and/or other specific organs via the blood circulation. Physical exercise seems to increase accumulation of free radicals and reactive oxygen species such as superoxide anion and hydrogen peroxide as a response to the increased oxygen utilization [3] and they cause muscular damage and inflammation [1,18]. Exercise also induces mechanical stress, which causes injury to both muscles and nerves [15]. BDNF is known to play a role in repair processes at the site of traumatic injury [8]. Platelets appear to release BDNF upon activation at the site of traumatic injury to facilitate the repair of peripheral nerves or other tissues that contain the high-affinity BDNF receptor TrkB [9]. Interestingly, BDNF protein in the soleus muscle, where TrkB is expressed, significantly increased after training [11]. Such reports raise the possibility that the release of BDNF from platelets to damaged tissues increases in order to facilitate the repair process, and then the BDNF stored in platelets decreases.

Another possibility is that BDNF production is decreased because it is not necessary for the trained men. Several lines of evidence suggest that BDNF contributes to food intake and body weight control, acting as anorexigenic factor [14,19]. In addition, BDNF has been shown to improve glucose and lipid metabolism and increase energy expenditure [23]. 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 [34]. It is therefore likely that the BDNF level increases in obese diabetic patients to compensate for such pathophysiological conditions because of its potential roles in improving energy metabolism and suppressing food intake. On the other hand, it is well established that exercise induces body fat reduction and improvement of lipid and glucose metabolism. In the current study, the trained group showed high energy expenditure and low TG level. Taken together, it is reasonable that habitual physical activity enhances energy expenditure and then less BDNF is needed for controlling energy balance or eating behavior.

The limitations of this study were the cross-sectional design itself, the small sample size and the lack of the data of fitness levels such as maximal oxygen consumption. Further studies focused on such problems are called for.

In conclusion, the serum BDNF level was lower in trained men than that in sedentary subjects. In addition, the serum BDNF level was found to be correlated with the daily physical activity level. These results suggest that the daily physical activity affects the serum BDNF level.

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