表2．運動介入前後の被験者の体組成変化

測定項目	介入前 平均	介入前 標準偏差	介入後 平均	介入後 標準偏差	p	
体重（kg）	64.4	(4.0)	61.9	(3.7)	0.01	*
BMI（kg/m²）	26.0	(1.7)	24.9	(1.8)	0.00	*
体脂肪率（%） 全身	35.6	(7.1)	32.9	(7.4)	0.00	*
体脂肪率（%） 上肢	32.7	(7.9)	30.3	(7.9)	0.02	*
体脂肪率（%） 下肢	36.0	(6.2)	34.5	(6.5)	0.00	*
体脂肪率（%） 体幹	35.9	(7.5)	32.4	(7.9)	0.00	*
除脂肪体重（kg） 全身	41.6	(6.6)	41.6	(6.0)	0.95	
除脂肪体重（kg） 上肢	2.1	(0.5)	2.1	(0.4)	0.40	
除脂肪体重（kg） 下肢	2.1	(0.5)	2.2	(0.4)	0.85	
除脂肪体重（kg） 体幹	23.1	(3.6)	23.0	(3.4)	0.45	
最大酸素摂取量（ml/kg/min）	20.1	(4.3)	22.0	(4.2)	0.145	
歩数（歩/日）	11448	(3179)	13387	(1767)	0.085	

表3．運動種目別における運動介入後の被験者の体組成変化

	水中運動群（n＝4） 介入前 平均	標準偏差	介入後 平均	標準偏差	陸上運動群（n＝4） 介入前 平均	標準偏差	介入後 平均	標準偏差	時間 p		交互作用 p	
体重（kg）	67.3	(2.6)	64.4	(2.0)	61.5	(2.7)	59.4	(3.5)	0.03	*	0.56	
BMI（kg/m²）	26.3	(2.0)	25.1	(2.1)	25.7	(1.6)	24.6	(1.8)	0.00	*	0.77	
体脂肪率（%） 全身	34.3	(10.3)	31.1	(10.6)	36.9	(2.5)	34.7	(2.5)	0.00	*	0.25	
体脂肪率（%） 上肢	31.1	(11.5)	28.2	(11.3)	34.2	(2.8)	32.3	(2.9)	0.00	*	0.35	
体脂肪率（%） 下肢	34.7	(9.1)	33.1	(9.5)	37.4	(1.4)	35.9	(1.7)	0.00	*	0.03	
体脂肪率（%） 体幹	34.7	(10.8)	30.4	(7.2)	37.1	(3.2)	34.4	(3.1)	0.00	*	0.17	
除脂肪体重（kg） 全身	44.4	(8.5)	44.4	(7.5)	38.8	(3.0)	38.8	(2.5)	0.95		0.91	
除脂肪体重（kg） 上肢	2.3	(0.6)	2.4	(0.5)	1.9	(0.1)	1.9	(0.1)	0.36		0.15	
除脂肪体重（kg） 下肢	7.6	(1.7)	7.6	(1.4)	6.8	(0.3)	6.9	(0.3)	0.86		0.86	
除脂肪体重（kg） 体幹	24.7	(4.0)	24.6	(3.7)	21.5	(2.5)	21.4	(2.3)	0.48		0.86	
最大酸素摂取量（ml/kg/min）	22.0	(3.9)	21.9	(2.5)	18.3	(4.4)	22.1	(5.9)	0.03	*	0.03	*
歩数（歩/日）	13145	(3179)	13163	(1593)	9752	(3858)	13610	(2148)	0.10		0.09	

＊p＜.05

Ⅳ．ま と め

本研究の目的は，メタボリックシンドローム該当者およびその予備群を対象に陸上運動もしくは水中運動を処方し，その運動効果を検討することにあった。その結果，10週間の運動介入後，水中運動群および陸上運動群の両群において，有意な減量効果（体重および体脂肪率の有意な減少）が認められた。本研究の結果からは，運動種目の違いによる運動効果の差は認められなかったが，長期的な運動介入を行った場合の運動効果は異なってくる可能性も考えられ，更なる検討が求められる。

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【付記】

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SHORT COMMUNICATION

Brain-Derived Neurotrophic Factor Treatment Increases the Skeletal Muscle Glucose Transporter 4 Protein Expression in Mice

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Summary

The purpose of the present study was to investigate whether peripheral brain-derived neurotrophic factor (BDNF) treatment induced metabolic adaptations in mouse skeletal muscle. BDNF (20 mg/kg/day) was injected subcutaneously for successive 14 days. BDNF treatment significantly reduced the total food intake and inhibited the weight gain in comparison to the control group. The glucose transporter 4 (GLUT4) protein expression in the gastrocnemius muscle was significantly increased by BDNF treatment in comparison to the control and pair-fed groups. Neither the oxidative nor the glycolytic enzyme activities in the gastrocnemius muscle changed after the BDNF treatment. These results suggest that the peripheral BDNF treatment promotes the skeletal muscle GLUT4 protein expression as well as hypophagia.

Key words

BDNF • GLUT4 • Hypophagia • Skeletal muscle

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Brain-derived neurotrophic factor (BDNF) is a part of the neurotrophin family and is produced in the nervous system and periphery. The BDNF controls the food consumption (Xu *et al.* 2003), lipid and glucose metabolism (Nakagawa *et al.* 2000, Tsuchida *et al.* 2002), and insulin resistance (Kuroda *et al.* 2003). Recent human studies have shown that circulating BDNF is associated with eating disorders (Nakazato *et al.* 2003, Monteleone *et al.* 2004), obesity (Monteleone *et al.* 2004, Suwa *et al.* 2006), glucose and lipid metabolism (Suwa *et al.* 2006, Levinger *et al.* 2008), type II diabetes mellitus (Suwa *et al.* 2006) and metabolic syndrome (Chaldakov *et al.* 2003, 2004). Based on these metabolic contributions, BDNF is considered to be a "metabotrophins" (Chaldakov *et al.* 2007).

Skeletal muscle metabolic characteristics such as glucose transporter 4 (GLUT4) expression and mitochondrial oxidative capacity are associated with skeletal muscle insulin-stimulated glucose uptake, whole body insulin sensitivity and prevalence of type II diabetes mellitus (He *et al.* 2001, Bruce *et al.* 2003, Doehner *et al.* 2010). Chronic BDNF treatment to diabetic mice significantly improves the glucose uptake in skeletal muscle (Yamanaka *et al.* 2007). Based on these results, the BDNF is hypothesized to regulate the skeletal muscle metabolism. This study examined whether chronic BDNF treatment to mice affects skeletal muscle metabolic characteristics such as GLUT4 protein expression and glycolytic and oxidative enzyme activities.

Sixty-nine- to 72-day old female ICR mice were

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used for the current study. All mice were fed a standard rodent chow (CE-2, CLEA Japan, Inc., Tokyo, Japan). All experimental procedures were approved by the Nakamura Gakuen University Animal Experiment Committee.

Because BDNF treatment reduces food intake (Nakagawa *et al.* 2003), the effects of BDNF treatment was studied in comparison with both *ad libitum*-fed control and pair-fed mice. The mice were divided into an *ad libitum*-fed (AL, n=8), a pair-fed (PF, n=8), or a BDNF-treated (BDNF, n=8) group. The mice of the BDNF group were subcutaneously administered daily with 20 mg/kg body mass BDNF (Dainippon Sumitomo Pharma, Osaka, Japan) in saline for 14 successive days. This dose of BDNF has been shown to enhance the skeletal muscle glucose uptake (Yamanaka *et al.* 2007). In the AL and PF groups, a comparable volume of saline was administered subcutaneously.

About 24 h after the last administration, the mice were fasted for 4 h and anesthetized with pentobarbital sodium (60 mg/kg body weight i.p.). The gastrocnemius muscle was rapidly dissected, frozen in liquid nitrogen and stored at –80 °C until the analyses were performed.

The GLUT4 protein expression was determined by Western blotting and the enzyme activities including citrate synthase (CS), malate dehydrogenase (MDH), β–hydroxyacylCoA dehydrogenase (βHAD), hexokinase (HK), and lactate dehydrogenase (LDH) were measured spectrophotometrically as described previously (Suwa *et al.* 2008).

To compare the findings among the three groups, a one-way analysis of variance (ANOVA) was used. Fisher's PLSD was conducted if the ANOVA indicated a significant difference. A value of $P<0.05$ was considered to be significant.

The body mass prior to the treatment was similar in all three groups (AL; 27.5±0.5 g, PF; 27.9±0.6 g, BDNF; 27.6±0.2 g). The changes in the body mass in the PF (0.0±0.7 g) and BDNF (-0.3±0.4 g) groups were significantly lower than AL group (1.7±0.4 g) (Fig. 1A, $P<0.05$). Total food intake in the PF (49.7±2.1 g) and BDNF (49.7±2.1 g) groups were significantly lower than in AL group (58.7±1.9 g) (Fig. 1B, $P<0.01$). These results suggest that BDNF treatment inhibits the body mass increase because of reducing food intake.

The GLUT4 protein expression in the BDNF group was significantly higher by +37 % and +35 % than in the AL and PF groups, respectively (Fig. 2, $P<0.05$). Oxidative (CS, MDH and βHAD) and glycolytic (HK and LDH) enzyme activities were measured, and no differences were observed among the groups in any enzymes (data not shown).

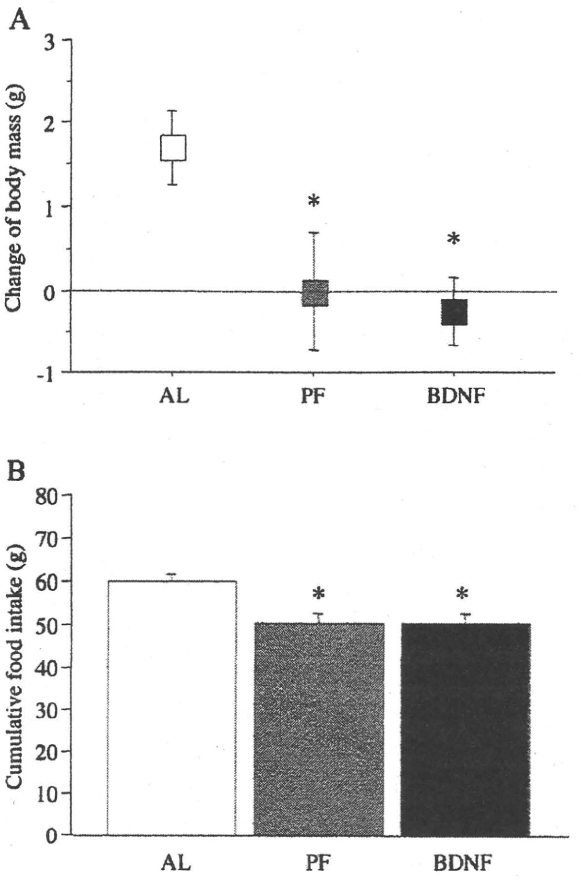

Fig. 1. A: Change of body mass during treatment. **B:** Cumulative food intake during the treatment. N=8 per group. Data are expressed as the mean ± S.E.M. *; P<0.05 vs. AL.

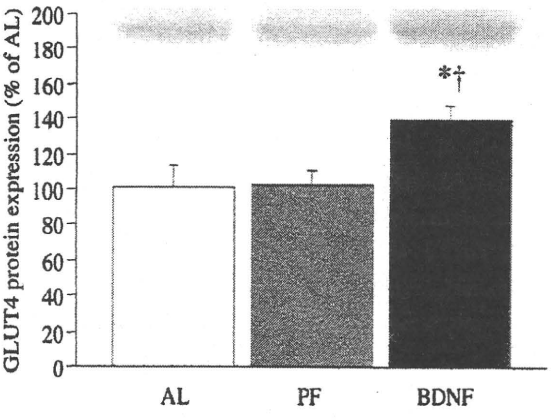

Fig. 2. GLUT4 protein expression of the gastrocnemius muscle in the 3 groups. N=8 muscles per group. Data are expressed as the mean ± S.E.M. *; P<0.05 vs. AL. †; P<0.05 vs. PF.

The current study demonstrated that the subcutaneous BDNF injection to mice significantly decreased the food intake in agreement with the previous study (Nakagawa *et al.* 2003). In humans, the serum BDNF level may demonstrate a possible link with such eating disorders as *bulimia nervosa* and *anorexia nervosa* (Nakazato *et al.* 2003, Monteleone *et al.* 2004). Circulating BDNF may therefore play a role in suppressing food intake. BDNF expressed in ventromedial hypothalamus neurons has been shown to apparently suppress food consumption downstream of the melanocortin-4 receptor (Xu *et al.* 2003). Because BDNF can cross the blood-brain barrier (Pan *et al.* 1998), the subcutaneous injection of BDNF reduces the food intake possibly *via* hypothalamus neurons.

The most important finding in the current study is that the BDNF treatment increases the GLUT4 expression. GLUT4 plays an important role in skeletal muscle glucose uptake (Röckl *et al.* 2008). GLUT4 protein abundance is strongly associated with capacity of skeletal muscle glucose uptake (Doehner *et al.* 2010), suggesting that skeletal muscle GLUT4 abundance is a potential limiting factor of whole body and skeletal muscle glucose metabolism. The increasing GLUT4 protein expression in the current study is thus considered to improve the glucose metabolism.

Although it has been generally accepted that the neurotrophins act by either paracrine or autocrine mechanisms (Davies 1996), BDNF also exists in the blood (Radka *et al.* 1996). More than 90 % of blood BDNF is stored in platelets, and platelets can release the BDNF (Fujimura *et al.* 2002). Platelets are assumed to release BDNF at nerves or other tissues expressing BDNF receptor tyrosine kinase B (Fujimura *et al.* 2002). In addition, circulating BDNF level is associated with eating behavior (Monteleone *et al.* 2004), metabolic disorders (Chaldakov *et al.* 2003, 2004, Suwa *et al.* 2006), physical activity (Nofuji *et al.* 2008), depression (Brunoni *et al.* 2008), Alzheimer's disease (Laske *et al.* 2006), and cognitive function (Gunstad *et al.* 2008). We therefore presume that circulating BDNF might possess several of physiological functions including GLUT4 biogenesis and thereby mimic the endocrine mechanism.

Although this is only a preliminary study, the results presented herein raise the possibility that BDNF treatment may potentially contribute to the therapy of obesity and type II diabetes mellitus, while also helping to treat related cardiometabolic diseases. Further studies are necessary to identify the therapeutic effects of BDNF for such diseases and to clarify the mechanism underlying the effects of BDNF for GLUT4 expression and hypophagia.

Conflict of Interest

There is no conflict of interest.

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Research article

Association of cardiorespiratory fitness with elevated hepatic enzyme and liver fat in Japanese patients with impaired glucose tolerance and type 2 diabetes mellitus

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Abstract
No study has so far determined whether a favorable level of cardiorespiratory fitness (CF) contributes to a reduced risk of elevated hepatic enzymes and a high degree of liver fat in patients having various metabolic risks. This study investigated the association between the maximal oxygen uptake (VO_2max) and the prevalence of elevated liver enzymes and high liver fat, while considering such factors as abdominal obesity, hyperinsulinemia and the other metabolic risks. The study enrolled newly diagnosed Japanese patients (n = 84; 52 males and 32 females; aged 25-69 years) with impaired glucose tolerance (IGT) and type 2 diabetes mellitus (Type2DM) who did not receive any intervention or pharmacological therapy. The subjects were divided into 3 groups according to the distribution of the VO_2max for each sex. The odds ratios (ORs) for the prevalence of elevated aspartate and alanine aminotransferase (AST and ALT) and high degree of liver fat adjusted for age, sex, disease type, daily ethanol intake, and current smoking were significantly lower in the moderate- and high CF groups in comparison to the low CF group. In addition, a significant OR for AST was maintained in the moderate and high CF group after adjusting for abdominal obesity and/or hyperinsulinemia. The significant ORs for the prevalence of elevated ALT and a high degree of liver fat were attenuated after adjusting for abdominal obesity and/or hyperinsulinemia. No significant OR for the prevalence of elevated gamma-glutamyl transferase (GGT) was recognized in all logistic models. These results indicated that CF was negatively and independently associated with the prevalence of elevated AST even in Japanese diabetic patients having various metabolic risks. It was concluded that the AST level might be useful as a simple marker reflecting physical inactivity in such subjects.

Key words: Cardiorespiratory fitness, hepatic enzyme, non-alcoholic fatty liver, abdominal obesity, insulin resistance.

Introduction

Hepatic enzymes are primary indices for the diagnosis of non-alcoholic fatty liver disease (NAFLD), which is noticed as one of phenotypes of metabolic syndrome (André et al., 2007). Furthermore, elevated hepatic enzymes have been noted as a predictor of metabolic syndrome, type 2 diabetes mellitus (Type2DM) and cardiovascular disease (André et al., 2006; Cho et al., 2007; Doi et al., 2007, Monami et al., 2008; Nakanishi et al., 2004; Rector et al., 2008; Sattar et al., 2004). Hepatic enzymes might therefore be a general marker reflecting the pathology of these diseases.

On the other hand, cardiorespiratory fitness (CF), which is a direct index of physical activity, plays a role of suppressing the onset of type 2 DM, metabolic syndrome, cardiovascular diseases and mortality (LaMonte et al., 2005; Lakka et al., 2002; Sawada et al., 2003; Sui et al., 2007; Lyerly et al., 2009). In addition, recent cross-sectional studies reported an inverse association between CF and NAFLD (Church et al., 2006; Lawlor et al., 2005; Nguyen-Duy et al., 2003; Perseghin et al., 2007). It is therefore naturally expected that a favorable level of CF might be related not only with a low prevalence of NAFLD, but also elevated levels of hepatic enzymes.

A recent study (Messier et al., 2010) has demonstrated that metabolically healthy but obese women who were in the upper quartile of insulin sensitivity values had significantly lower concentrations of ALT, AST, and GGT as well as a lower fatty liver index in comparison to individuals in the lower 3 quartiles. However, this study did not evaluate either the physical activity or CF. A survey performed on adults aged 17 yrs of age or older in US (n = 15676) (Clark et al., 2003) reported unexplained aminotransferase elevation, which was significantly associated with a higher body mass index, waist circumference, triglyceride levels, fasting insulin, and lower HDL. It is well-known that these indices are strongly influenced by physical activity; however, no description regarding lifestyle was made in that report. Furthermore, the most of those studies are conducted in normal populations, and no study has yet investigated the impact of the maximal oxygen uptake on both liver fat and liver enzymes while taking other metabolic risks into consideration in specific subjects having a number of metabolic abnormalities.

The current study therefore investigated whether the prevalence of high degree of liver fat and elevated liver enzymes could be associated with low level of CF in newly diagnosed impaired glucose tolerance (IGT) and Type2DM patients with various metabolic risks but not consuming excessive amounts of alcohol.

Methods

Subjects

One hundred fifty-seven Japanese outpatients (114 males and 43 females, aged 25 to 81 years) who were newly-diagnosed to have IGT and Type2DM based on a 75g oral glucose tolerance test (75g OGTT) participated in the present study. The pathological state was classified based

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on the diagnostic criteria of the Committee of Japan Diabetes Society (Kuzuya et al., 2002). Though 2-24 months passed from the time that the patients were noted to have an elevated blood glucose level at a group medical checkup, none of the subjects had received pharmacological therapy or intervention until the diagnosis.

The patients answered a questionnaire to assess their alcohol consumption and current smoking habits. The type, amount, and frequency of alcohol consumption were assessed, from which the total amount of alcohol consumption was calculated and converted to the daily ethanol intake. Sixty-five subjects whose daily ethanol intake was more than 20g in males and 10g in females (Hashimoto, 2004), were excluded from the analysis. In addition, any cases including missing data needed for an analysis (n = 8) were also excluded. Finally, the data of 84 patients (52 male and 32 female, aged 25 to 69 years) were used for the analysis of the present study. Informed consent was obtained from each patient and the study was approved by The Ethics Committee of Institute of Health Science in Kyushu University.

Anthropometric measurement and protocol for computed tomography

The BMI was calculated as the weight (kilograms) divided by height (meters) squared. The waist circumference was measured at the level of the umbilicus. The visceral (VFA) and subcutaneous fat areas (SFA) were assessed by computed tomography (CT; VIGOR LAU DATOR, Toshiba, Japan). The subjects were examined following overnight fasting and in the supine position. Scanning was performed using the usual clinical assessment settings, i.e., 120kV and 200mA, 400mm field of view, 5mm thickness, and 2sec scanning time. The regions of interest were determined by the clinical specialists by tracing an outline of the adipose tissue on the CT image at the umbilical level. The whole abdominal and visceral fat areas were computed automatically based on the pixels for the X-ray attenuation range of these areas (Tokunaga et al., 1983). The SFA values were derived by subtracting the VFA from the whole abdominal fat area. In addition, liver fat deposition was evaluated using a CT image including both the liver and spleen derived from the twelfth thoracic vertebra level to the second lumbar vertebra level. The analysis of the mean CT attenuation values derived for the liver and spleen were performed by clinical specialists in diagnostic imaging. The ratio of the liver/spleen attenuation value (L/S ratio) was defined as an index of liver fat (Church et al., 2006).

Measurements of clinical data

Following overnight fasting of at least 9 hrs, blood samples were drawn from antecubital vein for the analysis as below; sampling tubes of EDTA 2K-NaF and plain were used. A 75g OGTT was performed on the subjects' blood samples obtained at 30, 60, 120, and 180 minutes. The fasting insulin and fasting blood glucose concentrations were measured using a radioimmunoassay and an enzymatic method, respectively. The levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT) were determined as indices of the hepatic function, using a method recommended by the Japanese Society of Clinical Chemistry for determining the catalytic amounts of enzymes. Tests for hepatitis B or C virus and other liver diseases were performed on the subjects whose AST and/or ALT were over 100 IU/L. The levels of fasting triglyceride, total cholesterol, and high-density lipoprotein cholesterol were assessed using an enzymatic method. The resting systolic (SBP) and diastolic blood pressure (DBP) were determined 3 times following a 30-minute rest period using a mercury sphygmomanometer, with the lowest values used as the resting blood pressure. The subjects newly diagnosed to have IGT or Type2DM were instructed to undergo an anthropometric evaluation and a fitness test within 2 to 3 weeks following the diagnostic tests.

Criteria for abnormalities of parameters

The definition of elevated liver enzymes based on a statement by The Ministry of Health, Labour and Welfare in Japan, 2007. The abnormal criteria for each enzyme were as follows; elevated AST: AST > 30U/L, elevated ALT: ALT > 30U/L, and elevated GGT: GGT > 50U/L. Furthermore, a patient with an L/S ratio less than 0.9, which is a cutoff value usually adopted in domestic medical institutions (Hashimoto, 2006), was regarded as having high liver fat.

Patients whose VFA levels were more than 100 cm^2 were defined as having excess visceral fat (The Examination Committee of Criteria for "Obesity Disease" in Japan, 2002). The fasting insulin equivalent was determined to be 7μU/mL, a 75th percentile value of fasting insulin in Japanese male workers (Tamakoshi et al., 2003) as the basic criteria for hyperinsulinemia in this study.

Evaluation of cardiorespiratory fitness

Graded exercise tests were performed by a skilled examiner using a cycle ergometer (Monark, Stockholm, Sweden) to evaluate the CF. The heart rate, electrocardiogram, and blood pressure were monitored and recorded during the test. The exercise intensity was increased 3 or 4 times every 4 minutes until the heart rate reached 70% of the maximum or higher. Maximal oxygen uptake (VO_2max), which is regarded as an index of CF, was determined according to the nomogram of Åstrand & Rhyming (1954), a modality that is generally used to predict the VO_2max.

The distributions of VO_2max were divided into tertiles in each sex. The details regarding the range in each group were as follows; the lowest tertile (Low-CF group): $VO_2max \leq 31.8$ml/kg/min in males and $VO_2max \leq 26.2$ in females; the intermediate tertile (Moderate-CF group): $31.8 < VO_2max \leq 35.6$ in males and $26.2 < VO_2max \leq 30.2$ in females; and the highest tertile (High-CF group): $VO_2max > 35.6$ in males and $VO_2max > 30.2$ in females.

Statistical analysis

An analysis of variance (ANOVA) was performed to compare continuous variables of the subjects classified by CF level. TG, fasting glucose and insulin, AST, ALT, and GGT had a skewed distribution and were therefore analyzed following log-transformation. A comparison of categorical variables was analyzed using chi-square analysis. The odds-ratio (OR) and 95% confidence inter-

val (95%CI) for the prevalence of any abnormalities in each group were calculated using 4 logistic regression models. First, ORs adjusted for age, sex, disease type, daily ethanol intake, and smoking as basic confounding factors for the prevalence of these abnormalities were calculated (Model-1). After the analysis using Model-1, the ORs were adjusted for abdominal obesity or hyperinsulinemia (Model-2 and 3), finally, adjustments for both abdominal obesity and hyperinsulinemia were added (Model-4). All statistical analyses were performed using the SPSS version 14.0 software program (SPSS Japan Inc.). Statistical significance was set at a value of $p < 0.05$.

Results

Characteristics of the subjects divided by the CF level

Characteristics of all subjects and those classified by CF levels are indicated in Table 1. The distribution of the subjects' VO_2max was observed to have shifted slightly to a lower level and the whole range was narrower than that in the Japanese healthy population.

The mean value of the VFA in all the subjects ($160.4 \pm 63.2 cm^2$) was substantially higher than the Japanese criteria for abdominal obesity ($\geq 100 cm^2$). The mean value of the fasting insulin level ($7.4 \pm 4.7 \mu U/ml$) was as high as the mean value of the top quartile in Japanese male workers (Tamakoshi et al., 2003). Prevalence of elevated AST, ALT and GGT in all subjects was 23, 49 and 31%, respectively. The subjects having elevated AST accounted for 48, 14 and 7% in the high, moderate and low CF group, respectively. The elevated ALT in each group accounted for 74, 41 and 32%, in addition, the elevated GGT was accounted for 37, 35 and 21%, respectively. Further, prevalence of high liver fat in all subjects was 21%, and 41, 14 and 11% in each fitness level, respectively. The Abdominal and liver fatness, fasting insulin, AST and ALT levels showed a gradual decrease according to the increase of CF level.

Analysis of the prevalence of abnormalities in the groups classified by CF level

As indicated in Table 2, The ORs for the prevalence of elevated AST in the moderate- and high CF group were significantly low in all models in comparison to the low CF group; the ORs ranged from 0.06 to 0.14. The ORs for an elevated ALT in the moderate- and high CF group were also significantly low in model 1, which ranged from 0.15 to 0.25. Model 2 showed a significant OR for elevated ALT only in high CF group. However, the significant ORs were attenuated after adjusting for only hyperinsulinemia (model 3), and after adjusting for both abdominal obesity and hyperinsulinemia (model 4). The ORs for an elevated GGT showed no significance in any group. The OR for high liver fat in the high CF group was significantly low in comparison to the low CF group (OR: 0.21) in model 1; however, the ORs in the other models adjusted for abdominal obesity and/or hyperinsulinemia showed no significance in any group.

Discussion

The main finding in the current study was that a favorable level of CF contributed to the attenuation of the elevated

Table 1. Comparison of characteristics of subjects classified by fitness level.

Continuous variables	All subject (M=52, F=32)		Fitness level Low (M=18, F=9)		Moderate (M=17, F=12)		High (M=17, F=11)		p
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (yrs)	50.9	10.7	47.4	11.5	53.6	10.4	51.4	9.6	N.S.
BMI ($kg \cdot m^{-2}$)	25.1	4.1	27.7	4.4	24.8	3.2	22.9	3.2	< .001
Waist girth (cm)	88.4	10.1	94.3	10.8	88.0	7.5	83.0	8.8	< .001
Daily ethanol intake (g)	3.0	5.2	1.7	3.6	3.9	5.5	3.4	6.1	N.S.
Type 2 DM (%)	60.0 (71.4)		20.0 (74.1)		21.0 (72.4)		19.0 (67.9)		
Current smoking (%)	26.0 (31.0)		10.0 (37.0)		6.0 (20.7)		10.0 (35.7)		N.S.
Visceral fat area (cm^2)	160.4	63.2	197.6	70.4	155.2	44.9	129.8	55.2	< .001
Subcutaneous fat area (cm^2)	172.1	86.0	202.1	104.1	165.7	78.6	149.8	66.7	N.S.
L / S ratio †	1.03	0.26	0.90	0.28	1.09	0.17	1.08	0.26	< .005
AST (U/L)	26.3	12.5	33.9	14.3	22.6	8.9	22.8	10.6	< .001
ALT (U/L)	38.8	31.0	57.6	39.3	29.3	17.3	30.5	25.3	< .001
GGT (U/L)	43.7	26.8	53.0	31.9	42.2	25.7	36.3	19.7	N.S.
VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$)	32.1	5.7	27.5	3.8	31.1	3.0	37.5	4.9	< .001
Total cholesterol (mg/dL)	217.6	35.9	211.0	39.1	226.6	31.2	214.7	36.8	N.S.
Triglyceride (mg/dL)	134.4	78.3	140.1	77.8	127.9	67.2	135.5	90.8	N.S.
HDL-C (mg/dL)	51.4	12.5	47.1	11.0	55.3	14.9	51.6	10.1	N.S.
Fasting glucose (mg/dL)	136.1	33.5	136.3	41.8	140.9	32.8	131.0	24.3	N.S.
Fasting insulin (μU/mL)	7.4	4.7	10.3	5.8	6.3	3.3	5.6	3.3	< .001
Systolic blood pressure (mmHg)	127	17	133	16	124	18	124	17	N.S.
Diastolic blood pressure (mmHg)	80	11	84	11	79	11	76	9	< .05

Abbreviations are denoted in text. Data are expressed as means±S.D. or number of patients. The percentage in each group is shown in parenthesis. One-way ANOVA or Chi-square test was performed for statistical analysis. N.S. not significant.

Table 2. Odds ratios for the elevated hepatic enzymes and NAFL in the groups classified by fitness level (n = 84).

	Model 1 [a]			Model 2 [b]			Model 3 [c]			Model 4 [d]		
	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
Elevated AST												
Moderate CF	**.11**	**.02-.55**	**.007**	**.12**	**.02-.58**	**.009**	**.13**	**.02-.78**	**.025**	**.14**	**.02-.85**	**.033**
High CF	**.06**	**.01-.36**	**.002**	**.06**	**.01-.42**	**.004**	**.07**	**.01-.49**	**.008**	**.07**	**.01-.58**	**.013**
Elevated ALT												
Moderate CF	**.25**	**.06-.94**	**.041**	.28	.07-1.07	.063	.48	.11-2.02	.314	.52	.12-2.29	.390
High CF	**.15**	**.04-.58**	**.006**	**.20**	**.05-.83**	**.027**	.29	.07-1.25	.096	.39	.09-1.79	.226
Elevated GGT												
Moderate CF	.99	.28-3.47	.981	1.08	.31-3.81	.906	1.15	.29-4.65	.842	1.30	.32-5.25	.714
High CF	.52	.14-1.90	.320	.66	.17-2.53	.545	.60	.14-2.52	.488	.78	.18-3.37	.740
High liver fat												
Moderate CF	.35	.08-1.49	.155	.37	.09-1.63	.191	1.04	.18--5.86	.963	1.06	.19-5.92	.950
High CF	**.21**	**.05-.99**	**.048**	.28	.06-1.33	.109	.62	.10-3.63	.592	.77	.12-4.77	.778

These odds ratios are referring for that in the low CF group. Abbreviations are denoted in text. [a]: Adjusted for age, sex, disease type, daily ethanol intake and current smoking. [b]: Added adjusting for abdominal obesity to the Model 1. [c]: Added adjusting for hyperinsulinemia to the Model 1. [d] Added adjusting for abdominal obesity and hyperinsulinemia to the Model 1. CI: confidence interval.

AST, independent of the pathology frequently observed in the diabetic subjects. The prevalence of elevated AST was below one fourth of all subjects, whereas one half of them were included in the low CF group. On the other hand, the association of elevated ALT or high liver fat with CF depended on the presence of abdominal obesity and/or hyperinsulinemia in diabetic subjects. No association found between CF level and elevated GGT.

It is highly important to identify the difference in the strength of association with CF among these enzymes. This remains a matter for speculation, but might be due to a difference in the location of these enzymes. While ALT and GGT exist mainly in hepatic cells, AST exists not only in the hepatic cells, but also in cardiac and muscle cells. In the current study, the prevalence of elevated AST among the subjects with a high degree of liver fat was 50%, which was obviously lower than that in the subjects demonstrating both high liver fat and elevated ALT or GGT (88.9 and 72.2%, respectively). It is speculated that AST might therefore reflect either cell injury or inflammation beside hepatic tissue in such subjects having various metabolic abnormalities. At this point, the robust inverse relationship between CF and elevated AST can be attributed to the findings of recent studies reporting an inverse association of directly measured CF and such inflammation markers as C-reactive protein, fibrinogen and cytokine, etc (Kullo et al., 2007; Jae et al., 2008). In addition, a recent clinincal study showed a significant correlation between the carotid intimal media thickness and hepatic enzymes, including AST (Abdou et al., 2009). However, these explanations remain mere speculation. Further accumulation of evidence is thus needed to clarify the association between the CF and AST levels in the future.

On the other hand, ALT which mainly exists in the hepatic cells might be directly affected by higher levels of liver fat, which is related to both abdominal fat and insulin resistance (Messier et al., 2010). Results from recent animal experiments, which examined the effect of daily aerobic exercise (Rector et al., 2008), the cessation of exercise (Rector et al., 2008) and a genetically low aerobic capacity (Thyfault et al., 2009) to the hepatic oxidative capacity, are all consistent with the hypothesis that regular aerobic exercise or a favorable CF improve the hepatic oxidative capacity. Such evidence could therefore help us to explain both the low prevalence of high liver fat and the elevated ALT levels observed in the high CF group. However, the prevalence of both abnormalities was dependent on abdominal obesity and/or hyperinsulinemia rather than on the CF level in diabetic subjects; the result in the current study agreed with that in the prior-mentioned study (Messier et al., 2010).

No association between CF and elevated GGT found in the logistic model adjusted for basic confounders including disease type. Considerable number of prospective studies reported elevated GGT was a strong predictor of Type 2 DM (André et al., 2005, André et al., 2006, André et al., 2007, Doi et al, 2007, Lee et al., 2003, Nakanishi et al., 2004). The GGT level was closely correlated with the insulin level in the present study ($r = 0.452$, $p < 0.0001$, data not shown). Taking these evidences into consideration, it was speculated that GGT level in diabetic subjects was affected by insulin resistance rather than aerobic capacity strongly reflecting muscle oxidative capacity and cardiac function.

The present study has some limitations. The design of the study was cross-sectional and thus unable to identify causality between CF and elevated hepatic enzymes or high liver fat. In addition, the results of the current study were derived from diabetic patients; it should not be regarded as phenomena in healthy population. The VO_2max data was calculated using heart rate during exercise, thus few errors in the values of VO_2max might occur, though VO_2max measurements were performed by a skilled examiner. The daily ethanol intake was self-reported, and may therefore be biased or inaccurate. Tests for hepatitis B or C virus were only performed for the patients who were suspected of having these viruses. At least a 3-year treatment regimen by the subjects' primary doctor and at least a 1-year follow-up of lifestyle modification was performed for almost all subjects after the assessment of the present study; however, no onset of hepatitis B or C was recognized.

Conclusion

The current study is thus considered to demonstrate, for the first time, a favorable level of cardiorespiratory fitness could contribute to a reduced risk of elevated aminotransferase and high liver fat in Japanese patients newly diagnosed as IGT or type 2 DM. An independent and inverse association between the CF level and the prevalence of an elevated AST level was observed, the possibility that AST may potentially be useful as a simple marker concerning physical inactivity should therefore be assessed. Prospective cohort studies in the general population, exercise-intervention for high-risk populations, and a biochemical approach are required to address the effect of physical activity on both the hepatic enzyme levels and liver fat levels in the future.

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Key points

- The prevalence of elevated AST was negatively, and strongly associated with the CF level independent of abdominal obesity, hyperinsulinemia, and the other confounders in the subjects with glucose intolerance.
- The association between the CF level and both an elevated ALT level and a high degree of liver fat, as defined by the L/S ratio of CT images depended on abdominal fat and/or hyperinsulinemia in the subjects with glucose intolerance.
- No association was recognized between CF and elevated GGT in the subjects with glucose intolerance in the subjects with glucose intolerance.
- Having a favorable level of CF could lead to a reduced risk of hepatic-related abnormalities even in diabetic patients having the other metabolic risks.

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通信制生活習慣改善法が睡眠改善に及ぼす効果とその関連要因

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目的　研究目的は，1）睡眠と睡眠に関連する生活習慣における1か月間の通信制習慣改善法の効果を例数を増やして確認すること，および2）その改善効果に影響を与える要因を検討することの2点であった。

方法　対象者は，職域で通信制睡眠習慣改善プログラムに参加した，入眠潜時（就眠時刻−就床時刻）と睡眠効率（睡眠時間/就床時間）に問題がある睡眠困難者178人であった。介入法は，小冊子の自己学習と自己設定した目標行動のセルフモニタリングという最小限の行動技法からなる簡便な方法であった。期間は1か月間で，やりとりは全て郵送で行われた。介入前後に自己記入式の質問票調査を実施した。介入前後の睡眠指標と睡眠に関係の深い生活習慣の変化を検討した。また，本法の効果に影響する要因を検討するために，対象者を入眠潜時および睡眠効率の平均改善値をカットオフ値として有効群63人と比較群115人に2分し，介入前の基本特性，睡眠指標，生活習慣および介入による変化を群間で比較した上で，さらにロジスティック回帰分析を行った。

結果　介入後に，全体で睡眠時間が5.71時間から6.05時間に増加，入眠潜時は18分短縮し，睡眠効率は5.6ポイント向上するなど，先行研究と同等の短期効果が確認された。習慣については9項目中8項目で望ましくない行動を選択する人の割合が減少した。目標行動としての選択や達成率で群間の差はなかったが，習慣改善個数は有効群2.63個，比較群2.06個と改善群が有意に多かった。ロジスティック回帰分析により，「ベースライン時の入眠潜時」が大きい者，および「定期的な運動の改善」をした者の2要因が睡眠改善に影響していることが明らかとなった。

結論　本法における短期効果が確認された。また，本法は介入前に入眠潜時が長く入眠困難を持つ者に対してより有用であること，睡眠指標の改善には特に定期的な運動習慣が重要な役割を持つことが示唆された。本研究の結果から，行動療法による睡眠改善教育は簡便な形であっても実施可能であり，その効果が期待できると考えられた。

Key words：睡眠改善，通信制，生活習慣改善法，行動療法

I　緒　　言

厚生労働省の調査によると，20歳から59歳の約4割は睡眠時間が6時間未満であり[1]，睡眠による休養が十分でない人の割合は21.2%にのぼることが報告されている[2]。健康日本21では，休養・こころの健康づくりのために睡眠改善が目標の一つとされ，平成15年には「健康づくりのための睡眠指針〜快適な睡眠のための7箇条〜」[3]が発表された。また，睡眠に関連した事故の発生[4]からマスメディアでも睡眠時無呼吸症候群を中心に睡眠の問題が多く取り上げられるなど社会の関心も高まっている。さらに近年，睡眠時間と血圧[5]，糖代謝[6〜9]，脂質代謝[10]など生活習慣病の危険因子との関連[11,12]が明らかになってきたことから，睡眠状態の改善は公衆衛生上重要な課題となっている。

睡眠障害の治療としては一般的には薬物療法が用いられているが，薬を用いない治療法として，慢性の不眠に対する行動療法がある。欧米においては1960年代より積極的にその治療研究が行われ，1990年代末にアメリカ睡眠学会[13]やNIH[14]（米国国立

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衛生研究所）は，行動療法について薬物療法よりも優れていると総括した。行動療法は行動科学を応用した心理療法であり，不適切な習慣行動の変容を目的としている。不眠の場合は，それを維持・強化していると思われる不適切な生活習慣や的外れの努力を修正することで，睡眠を改善させようとする[15]。最近のレビューでは，本法は性，年齢に無関係に有効であるだけではなく，慢性疼痛や癌など他疾患の合併の有無に関係なく改善効果があることも明らかになってきた[16,17]。

このように睡眠改善に対する行動療法の有効性についてはほぼ評価が確定している。しかし，一般的にその普及は難しいと考えられており，その理由としては行動療法の実施に時間や専門的知識と熟練を要する点があげられている[15]。これらの課題に対して，行動療法の治療構造の明確さを生かし，自己マニュアルや通信指導，コンピュータによる簡素化した指導法の研究が多くの問題において行われてきた[18~21]。足達らは自己学習と自己設定した目標行動のセルフモニタリングという最小限の行動技法から成る1か月間の通信指導プログラム（以下通信制習慣改善法）を作成し，職域においてメニュー式通信プログラムとして実施してきた[22]。睡眠については，この方法による介入によって，睡眠指標と睡眠に関連した生活習慣（以下習慣とする）が改善し[24]，1年後も効果が維持されたことを報告した[25]。さらに，入眠潜時（就眠時刻—就床時刻）と睡眠効率（睡眠時間/就床時間×100）に問題がある者（以下，睡眠困難者とする）47人では，睡眠改善効果が大きく習慣改善個数が睡眠効率，起床に要する時間との関連があることを報告した[26]。しかし，対象者が少数であり，通信制習慣改善法がどのような集団に効果的であるか，またどの習慣の改善が睡眠改善に影響を及ぼすかという検討は行っていなかった。

そこで今研究では例数を増やし，先行研究で得られた睡眠指標の改善と同等の結果が得られるかどうかを確認するとともに，その改善効果に関連する要因の検討を行った。

Ⅱ　研究方法

1.　対象と方法

対象者の選別は次のように行った。朝日新聞健康保険組合が2001-2004年の毎年11月に実施した通信制習慣改善法の睡眠コースの参加者は計371人で，終了者は324人（87.3%）であった。その中で開始時と終了時の就床時刻，入眠時刻，覚醒時刻，起床時刻の4つのデータが得られたのは250人であり，そこから睡眠困難者を選別した。睡眠困難者とは，開始時における入眠潜時が30分以上，または睡眠効率が85%未満のいずれかを満たしたものであった。重複参加者については初回参加時のデータのみを採用した。解析対象者は，睡眠困難者178人（男性67人，女性111人，平均年齢35.5±9.2歳）であった。なお，これらの中には先行研究[26]の対象者47人も含まれる。

次に本プログラムの睡眠指標の改善に影響を与える要因を検討するために，対象者の入眠潜時および睡眠効率の改善の平均値で対象者を2分した。すなわち，最終分析対象者178人のうち，入眠潜時18分以上短縮および睡眠効率が5.6%以上改善した63人を有効群，それ以外の115人を比較群とし，両群の基本特性，前後の睡眠指標と生活習慣，気分の変化を検討した。

プログラムの流れは図1に示した通りである。参加者には，習慣の自己評価および目標設定を行わせた。教材「ぐっすり眠る」とセルフモニタリングシートを送付し，自己学習後，1か月間選んだ目標をセルフモニタリングさせた。1か月後に質問票とセルフモニタリングシートを管理者へ返送させた。継続の強化子として開始2週間後には，記録を続けるように励ましの手紙を送付し，終了者には1,000～2,000円の記念品を贈呈することを事前に提示した。参加者とのやりとりはすべて郵送で行われ，管理者は1人であった。

2.　調査項目と解析法

睡眠指標については，就床時刻，入眠時刻，入眠潜時，覚醒時刻，起床時刻，起床に要する時間（起床時刻—覚醒時刻），睡眠時間，就床時間，睡眠効率（睡眠時間/就床時間×100）の9項目を調査した。習慣は9項目，睡眠に関連する気分（以下気分とす

図1　睡眠改善プログラムの流れ

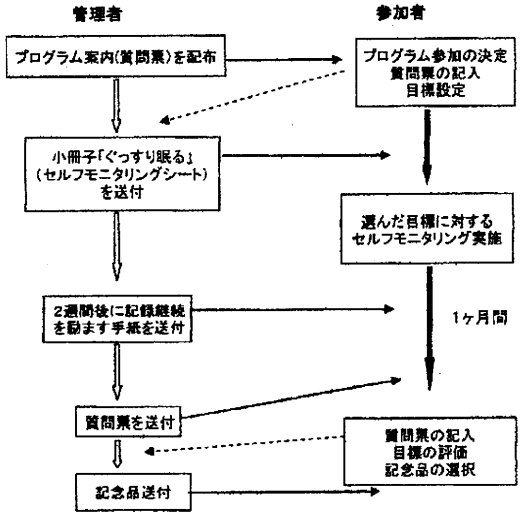

表1　睡眠に関連した生活習慣および気分のアンケートの項目

	質　問	回　答		
習慣	1. 就寝直前まで仕事や勉強をしている	あまりない	時々ある	よくある
	2. 夕食を食べてから寝るまで	3時間以上	2時間程度	1時間程度
	3. コーヒー，お茶などのカフェインの摂取は	1日3杯以内	1日4〜5杯	1日6杯以上
	4. 寝つきをよくするために飲酒する	していない	時々ある	よくある
	5. 休日はいつもより1時間以上寝坊	あまりない	時々ある	よくある
	6. ベッドでテレビを見たり仕事をする	あまりない	時々ある	よくある
	7. 目覚めたらすぐに起きる	よくある	時々ある	ほとんどない
	8. のんびりした入浴は	よくある	時々ある	ほとんどない
	9. 定期的な運動は	行っている		行っていない
気分	1. 目覚めの気分	良い	半々	悪い
	2. 熟睡感	ある	半々	ない
	3. 昼間の眠気	ない	半々	ある

* いずれの項目も，3択のうち最も右側の回答を最も望ましくない回答とした

る）は3項目であった（表1）。これらの項目は，プログラム前後に自己記入された質問票（A4 1枚）を用いて調査した。生活習慣と気分の項目については「あまりない，時々ある，よくある」など3択式で回答させた。また，セルフモニタリングシートから目標14項目の選択率および介入後の目標達成率を調査した。

有効群と比較群で有意差がみられる項目を抽出するために，以下の解析を行った。ベースライン特性の群間比較として，睡眠指標には対応のないt検定を，習慣と気分の項目に関しては3択のうち最も望ましくない習慣や気分を持つ者の割合の比較にχ^2検定を用いた。介入前後の睡眠指標変化の比較に分散分析，習慣と気分の割合の変化についてはMcNemar検定を用いて検討した。また，介入後により望ましい選択肢を選択した者を改善ありとみなし，各群における習慣と気分が改善した者の割合をχ^2検定で比較した。次に，プログラムの効果に影響を与える要因の検討を行うために，有効群であることを従属変数，年齢，性別および群間で差のあった項目を独立変数とした強制投入法によるロジスティック回帰分析を行った。有意水準を危険率5％未満とし，統計解析にはSPSS for Windows12.0を使用した。

3. 倫理的配慮

プログラムの募集時に得られたデータの研究使用について紙面で説明し，それに同意した者のみが研究に参加した。なお，本研究は日本予防医学協会の倫理委員会の承認を受け実施された。

Ⅲ 研究結果

1. ベースライン時の特性

表2に示したように有効群は，男性23人（36.5％），女性40人（63.5％）の計63人で平均年齢34.8±9.9歳，比較群は男性44人（38.3％），女性71人（61.7％）の計115人，平均年齢35.9±9.6歳で男女比，平均年齢に群間差はなかった。

睡眠指標においては，有効群で睡眠時間が有意に短く，就眠時刻が遅く，入眠潜時が長く，睡眠効率が低い結果となり，比較群と比較して睡眠状態が不良であった。習慣に関しては有意な差はみられなかった。

2. 介入前後の変化

1) 睡眠指標の変化

全体ではベースラインから睡眠時間が19.8分，睡眠効率が5.8ポイント増加し，入眠潜時は18分，起床に要する時間は7.2分短縮した（$P<0.05$）。各群の睡眠指標の変化を表3に示した。有効群では睡眠時間が44.6分，睡眠効率が14.8ポイント増加し，入眠潜時は46.4分，起床に要する時間は20分短縮した（$P<0.05$）。比較群においては有意な変化はなかった。

2) 習慣の変化（表4）

対象者全体では，9項目中8項目の習慣で，最も望ましくない回答を選択した者の割合が有意に減少した。目覚めの気分が悪いと回答した者，および熟睡感がないと回答した者の割合も有意に減少した。また，改善した習慣の個数は，有効群2.63個，比較群2.06個で改善群が多かった（$P<0.05$）。習慣を改善した人の割合に群間差があったのは2項目で「ベッドで仕事をしたり，テレビを見たりする」が有効

表2　ベースライン時の特性

		全体		有効群		比較群	
		n	Mean(*SD*)/n(%)	n	Mean(*SD*)/n(%)	n	Mean(*SD*)/n(%)
	年齢（歳）	178	35.54(*9.24*)	63	34.79(*9.9*)	115	35.96(*9.6*)
	男性		67(*37.6%*)		23(*36.5%*)		44(*38.3%*)
睡眠指標	就床時刻（時）	178	24.42(*1.14*)	63	24.36(*1.17*)	115	24.45(*1.13*)
	就眠時刻（時）	178	25.30(*1.13*)	63	25.53(*1.12*)	115	25.18(*1.13*)*
	入眠潜時（分）	178	52.84(*31.50*)	63	70.20(*40.77*)	115	43.43(*19.60*)**
	覚醒時刻（時）	178	7.01(*1.02*)	63	6.90(*0.95*)	115	7.08(*1.05*)
	起床時刻（時）	178	7.51(*1.05*)	63	7.48(*0.98*)	115	7.53(*1.09*)
	起きるのに要する時間（分）	178	29.73(*32.84*)	63	34.65(*35.36*)	115	27.04(*31.22*)
	睡眠時間（時間）	178	5.71(*0.93*)	63	5.37(*1.07*)	115	5.90(*0.79*)**
	就床時間（時間）	178	7.09(*0.90*)	63	7.12(*1.10*)	115	7.07(*0.77*)
	睡眠効率（%）	178	80.81(*10.10*)	63	75.97(*12.10*)	115	83.46(*7.67*)**
習慣	就寝直前まで仕事や勉強をしている	167	29(*17.4%*)	55	10(*17.9%*)	110	19(*17.1%*)
	夕食後寝るまで1時間程度である	178	22(*12.4%*)	63	10(*15.8%*)	115	12(*10.4%*)
	コーヒー，お茶などカフェインを1日6杯以上飲む	178	16(*9.0%*)	61	7(*11.1%*)	115	9(*7.8%*)
	寝付きをよくするために飲酒する	178	20(*11.2%*)	61	5(*7.9%*)	115	15(*13.0%*)
	休日はいつもより1時間以上朝寝坊する	178	131(*73.6%*)	63	45(*69.8%*)	115	87(*75.7%*)
	ベッドでテレビを見たり仕事をする	178	63(*35.4%*)	63	26(*41.3%*)	115	37(*32.2%*)
	目覚めてすぐに起きることはほとんどない	177	73(*41.0%*)	63	29(*46.0%*)	113	44(*38.6%*)
	のんびりと入浴することはほとんどない	178	76(*42.7%*)	63	30(*47.6%*)	114	47(*40.0%*)
	定期的に運動をしていない	172	132(*76.7%*)	59	51(*85.0%*)	112	81(*72.3%*)
気分	目覚めの気分	109	40(*36.7%*)	41	17(*41.5%*)	68	23(*33.8%*)
	熟睡感	108	36(*34.3%*)	40	18(*45.0%*)	68	18(*26.5%*)
	昼間の眠気	107	33(*30.8%*)	39	15(*38.5%*)	68	18(*26.5%*)

*1.　3択のうち最も望ましくない習慣および気分を選択した者の割合　　** <0.01, * <0.05

*2.　年齢，睡眠指標は student's t 検定，比率には χ^2 検定を使用

表3　睡眠指標の変化

	prc		post		群	経時変化	群×経時変化
	有効群 Mean(*SD*)	比較群 Mean(*SD*)	有効群 Mean(*SD*)	比較群 Mean(*SD*)	F値	F値	F値
就床時刻（時）	24.36(*1.17*)	24.45(*1.13*)	24.58(*1.21*)	24.39(*1.24*)	0.070	2.311	7.701*
入眠時刻（時）	25.53(*1.12*)	25.18(*1.13*)	24.97(*1.17*)	25.07(*1.29*)	0.466	41.386**	19.933**
入眠潜時（分）	70.20(*40.77*)	43.43(*19.60*)	23.55(*27.64*)	41.12(*22.76*)	1.307	269.069**	220.469**
覚醒時刻（時）	6.90(*0.95*)	7.08(*1.05*)	7.08(*0.88*)	7.08(*1.13*)	0.325	4.254*	3.630
起床時刻（時）	7.48(*0.98*)	7.53(*1.09*)	7.33(*0.84*)	7.54(*1.13*)	0.677	2.524	3.208
起きるのに要する時間(分)	34.65(*35.36*)	27.04(*31.22*)	14.61(*23.54*)	27.14(*24.92*)	0.422	16.055**	16.375**
睡眠時間（時間）	5.37(*1.07*)	5.90(*0.79*)	6.12(*1.10*)	6.01(*0.91*)	2.344	63.391**	35.243**
就床時間（時間）	7.12(*1.10*)	7.07(*0.77*)	6.75(*1.04*)	7.15(*0.85*)	1.787	7.721**	17.129**
睡眠効率（%）	75.97(*12.10*)	83.46(*7.67*)	90.73(*9.37*)	84.05(*7.65*)	0.100	186.425**	159.297**

ANOVA　　** <0.01, * <0.05

表4　生活習慣や気分の項目において最も望ましくない回答をした人の割合

		pre n/(%)	post n/(%)
生活習慣	就寝直前まで仕事や勉強をしている	29(17.4)	16(9.0)*
(n=178)	夕食後寝るまで1時間程度である	22(12.4)	12(6.7)*
	コーヒー，お茶などカフェインの摂取1日6杯以上	16(9.0)	14(7.9)
	寝付きをよくするために飲酒する	20(11.4)	12(6.7)*
	休日はいつもより1時間以上朝寝坊する	131(73.6)	98(55.1)**
	ベッドでテレビを見たり仕事をする	63(35.4)	41(23.0)**
	目覚めてすぐに起きることはほとんどない	73(41.0)	36(20.2)**
	のんびりと入浴することはほとんどない	76(42.7)	28(15.8)**
	定期的に運動をしていない	132(74.2)	123(69.5)*
気分	目覚めの気分	40(36.7)	23(21.1)**
(n=109)	熟睡感	36(33.3)	24(22.4)*
	昼間の眠気	33(30.8)	27(25.2)

McNemar 検定　　** <0.01, * <0.05

表5　睡眠改善効果に影響を与える要因

	OR	95%CI
性別（女性）	1.19	[0.53-2.67]
年齢（歳）	0.99	[0.96-1.04]
就眠時間（時間）	0.95	[0.62-1.43]
睡眠時間（時間）	0.66	[0.69-1.60]
睡眠効率（%）	1.10	[0.93-1.08]
入眠潜時（時間）	7.69	[2.09-28.26]**
ベッドで仕事したりTVを見る習慣の改善	1.63	[0.74-3.61]
定期的な運動習慣の改善	4.08	[1.24-13.39]*

** <0.01, * <0.05

1）強制投入法によるロジスティック回帰分析
- 就眠時間，睡眠時間，睡眠効率，入眠潜時はベースライン時
- 年齢，就眠時刻，睡眠時間，睡眠効率，入眠潜時については1単位増に対するオッズ比
  他の項目については各項目に該当なしを reference とした

群39.7%，比較群22.6%，「定期的な運動」が有効群16.9%，比較群5.2%と有効群が高かった（$P<0.05$）。睡眠に関連する気分は両群で有意な差はみられなかった。選んだ目標や各目標の達成率に群間差はなく，どの目標も70%以上の者が達成していた。

3）　ロジスティック回帰分析の結果（表5）

プログラムの効果に影響を与える要因の検討を行うために，有効群であることを従属変数とし，年齢，性別，ベースラインで群間差のあった睡眠指標4項目（就眠時刻，入眠潜時，睡眠時間，睡眠効率），改善者の割合に差のあった習慣2項目（ベッドでテレビを見たり仕事をしたりする頻度の改善，定期的な運動実施の改善）の計8項目を独立変数とした強制投入法によるロジスティック回帰分析を行った。その結果，「ベースラインの入眠潜時」（オッズ比（OR）：7.687, 95%信頼区間（CI）：[2.09-28.26]）と「定期的な運動の改善」（OR：4.082, 95% CI：[1.24-13.39]）の2項目が有意水準0.05%で有意な変数であった。

Ⅳ　考　　察

本研究では，介入前後の睡眠指標および生活習慣の変化から通信制習慣改善法による睡眠指標の変化の検討を行い，先行研究で得られた結果の再確認を行った。さらに対象者を睡眠指標の改善値の平均により2群に分け，その効果に関連する要因の検討を行った。

その結果，本研究の178人の対象者全体で睡眠時間，睡眠効率，入眠潜時，起床に要する時間が改善し，先行研究の47人で報告した短期効果が確認された。

本プログラムは，全て非対面で行われ，手順が標準化されているため管理者の負担が少なく，同時に多数への介入が可能であるという公衆衛生的な利点を持つ。序文で述べたように，一般的に睡眠への行動療法介入は難しいとされるが，本研究の結果は，ここで用いたような比較的簡便な方法であっても，睡眠改善に効果が期待できる可能性を示唆するものと考えられた。

次にプログラムの効果に影響を与える要因の検討を目的に行ったロジスティック回帰分析の結果からは，「ベースラインの入眠潜時」，「定期的な運動」の2項目が抽出された。これは本プログラムが，介入前の入眠潜時が長く入眠困難のある人により効果

的であること，プログラムによって定期的な運動を行うように変化した人でより睡眠が改善したことを意味している。

行動療法に含まれる各技法の改善効果については，刺激統制法[27]が最も確実で効果が大きいとされ，次いで睡眠制限法[28]が比較的簡便に用いることができる方法として推奨されている。弛緩法は古くから研究対象となり効果は明らかとされるが，漸進的筋弛緩等の本格的な方法は普及が難しいために照明や入浴などの睡眠衛生教育に一般化される傾向にある[15,29]。

本プログラムでは，そのうち弛緩法と刺激統制法を一般的な睡眠健康教育と並列して例示し，目標行動として選択させたが，これらは睡眠の改善に影響する項目として抽出されなかった。その理由として，本法で用いた方法は標準的な弛緩法や刺激統制法ではなく，その一部のみを改善の対象習慣として介入したにすぎなかったからと考えられた。したがって本研究の分析法から技法の影響は明らかにできず，今後の課題と考えた。

運動が睡眠に与える影響については，本研究が運動への特異的な介入ではないため，睡眠が改善したことにより二次的に身体活動が増加した可能性を否定できず，睡眠と運動の関連の方向性は明らかではない。しかし，先行研究において運動介入が睡眠潜時を短縮し，睡眠時間を増加させるのに有効である可能性が報告されている[30]。また，本邦においても中高年女性勤労者に対し週に1回1時間の運動教室および家庭での10分程度のストレッチによる3週間の介入により入眠潜時が短縮した[31]と報告されている。今回の結果は運動の睡眠に対する効果を間接的に支持するものであると考えられた。

本研究の限界としては，統制群を欠くこと，評価を自己報告のみに依存していること，睡眠指標として中途覚醒回数，中途覚醒時間を欠いていること，運動やカフェイン摂取等習慣の各項目の定義を欠いていることがあげられる。これらは，多忙な職域の現場で行った実用的な方法であったことに起因している。そのためデータの精度には制限がある。今後，睡眠日誌の導入や統制群の設定による本プログラムの効果の確認が重要な課題と考えた。

V　結　　語

通信制習慣改善法による介入により対象者の睡眠指標は改善した。さらに睡眠指標の変化に影響を与える要因の検討により本法が入眠潜時の長い者，すなわち入眠困難のある者に，より有効である可能性が示唆された。また，定期的な運動は，睡眠指標の改善に影響を与えると考えられた。

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