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Original article

Effects of white rice containing enriched gamma-aminobutyric acid on blood pressure

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ABSTRACT

Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter with beneficial effects including antihypertension and antistress properties. In this study, we examined the effects of GABA-enriched white rice (GABA rice) on blood pressure (BP) in 39 mildly hypertensive adults in a randomized, double-blind, placebo-controlled study. The participants were divided into a test group ($n = 22$) who consumed rice with 11.2 mg GABA/100 g of rice and a placebo group ($n = 17$) who consumed rice with 2.7 mg GABA/100 g of rice. For 8 weeks, the participants took 150 g of either the GABA rice or the placebo rice. Hematological examinations were performed on both groups at 0, 4, and 8 weeks after the start of rice consumption. Home BP was self-measured two times daily, morning and evening, from 1 weeks before to 2 weeks after the intervention. Although the hospital BP and evening BP measurements of the participants showed no significant change, consumption of the GABA rice improved the morning BP compared with the placebo rice after the 1st week and during the 6th and 8th weeks. These results showed the possibility that the GABA rice improves morning hypertension.

1. Introduction

An increase in average blood pressure (BP), that is, hypertension, is a major cause of cardiovascular disease, and it can result in an increased risk of cardiovascular mortality. Several studies have shown that variations in BP are linked to the progression of organ damage and can trigger vascular events.[1] Similar to hypertension, the combined effects of smoking, dyslipidemia, diabetes, and other lifestyle-related disorders contribute to the early onset of severe diseases such as coronary atherosclerosis, angina pectoris, myocardial infarction, coronary artery disease, cardiac failure, and arrhythmia.[2]

Functional foods that can reduce the occurrence of hypertension are being extensively studied and developed. For example, several fish-derived peptides were found to be effective in reducing BP in rats by inhibiting the activity of angiotensin-converting enzyme.[3] Glycoside extracts of *Eucommia* leaf was reported to induce an antihypertensive effect by relaxing vascular smooth muscles through a direct action on the parasympathetic nervous system.[4] Various functional foods that can effectively reduce hypertension using gamma-aminobutyric acid (GABA) as the principle active component are also being developed.[5,6]

GABA is an amino acid that is present in high concentrations in mammalian brains, and it is also known to be present in plants. GABA is biosynthesized from glutamic acid by the action of glutamic acid decarboxylase (GAD), and it is metabolized by transamination by the catalyzing effects of GABA transaminase to yield succinic semialdehyde or succinic acid, which then enters the citric acid pathway.[7] GABA has been demonstrated to be a typical inhibitory neurotransmitter in the central nervous system. However, it is also active and found in the peripheral nerve or tissues. GABA receptors have also been found in heart muscles.[8] In addition, GABA is found to have antistress effects.[9] However, GABA does not pass through the blood–brain barrier,[10] and because the peak concentration of GABA in blood lasts only for approximately 30–60

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minutes, after which it is rapidly metabolized, its mechanism of action following oral ingestion is not fully understood.

Japanese food is well-known worldwide for being healthy and of high nutritional value, and in 2013, Japanese food was designated as an intangible cultural heritage by the United Nations Educational, Scientific and Cultural Organization.[11] Because of its high nutritional value, rice is considered the most important item in Japanese food. Previous research has demonstrated the unique properties of rice in preventing lifestyle-related diseases.[12] Sprouted brown rice in particular has been shown to contain high amounts of vitamins, and it is also rich in GABA.[13]

With the addition of water to brown rice, GAD and glutamic acid (which are both present in brown rice) will react with each other to produce large amounts of GABA rapidly. Taking advantage of this fact, Satake Co., Ltd. (Hiroshima, Japan) developed a new variety of white rice enriched with GABA (GABA rice).[14,15] The GABA rice was developed to retain all of the nutritional content that is already present in the white rice, and in addition, its GABA content was enriched than the ordinary white rice. The GABA rice can be consumed easily on a daily basis for prolonged periods. Considering such merits, daily consumption of the GABA rice can lead to a high GABA intake, resulting in overall health benefits.

In this clinical study, we tested the effects of rice containing enriched GABA content on BP (GABA rice), and found that the GABA rice improved the morning BP of study participants who ate it every day.

2. Methods

2.1. Study participants

Forty-six volunteers (age, 40–64 years) were recruited. None of the participants had any history of recent gastrointestinal disorders, pregnancy, significant diseases, surgery, severe allergic reaction to food, or current use of any medication including antihypertensive medication. The mean values of the participants' characteristics and body composition are presented in Table 1.

The clinical intervention was carried out as a randomized, double-blind, placebo-controlled trial. At randomization, the 46 participants were randomly and blindly assigned to two groups evenly distributed according to the sex ratio, average age, and systolic BP (SBP). As shown in Table 2, the test rice was rich in GABA (containing 11.2 mg GABA per 100 g of rice) and the placebo rice had a lower concentration of GABA (containing 2.7 mg GABA per 100 g of rice). For 8 weeks, the participants took 150 g of either the GABA rice or the placebo rice. Hematological examinations were performed at baseline (Week 0), Week 4, and Week 8 during the intervention. The schedule of this clinical study is shown in Fig. 1.

Hematological examinations were consigned to Sapporo Clinical Laboratory Inc. (Sapporo, Japan). The body composition and hospital and home BPs were measured using InBody (Biospace Co., Tokyo, Japan) and OMRON digital BP monitors (OMRON Healthcare, Kyoto, Japan), respectively.

All participants provided written informed consent before undergoing any study-related tests, and the protocol was approved by the Ethics Committee of Hokkaido Information University (Certificate No. 2013-04). The study protocol conformed to the Helsinki Declaration.

Table 1
Characteristics of the placebo group and the test group participants.

Characteristics	Placebo	Test
Number of participants	$n = 17$	$n = 22$
Number of males (%)	7 (41.2%)	12 (54.6%)
Age (y)	54.35 ± 5.9	52.5 ± 6.8
Height (cm)	160.6 ± 7.1	166.0 ± 9.1
Body weight (kg)	62.5 ± 10.8	67.3 ± 12.5
Body fat rate (%)	28.8 ± 7.2	25.4 ± 8.2
Body mass index (kg/m^2)	24.2 ± 3.7	24.3 ± 3.3
Systolic blood pressure (mmHg)	135.5 ± 15.3	138.0 ± 14.8
Diastolic blood pressure (mmHg)	82.0 ± 10.0	85.4 ± 10.5

Values are presented as mean ± standard error. Statistical analysis was performed by one-way analysis of variance with age, height, body weight, and body mass index, and by Chi-square test for sex.

Table 2
Components of the GABA-enriched white rice (GABA rice) and the placebo rice.

Component	Placebo rice (per 100 g)	GABA rice (per 100 g)
Calories (kcal)	341	342
Water (g)	15.6	15.5
Proteins (g)	6.1	6.2
Lipids (g)	0.9	1.1
Carbohydrates (g)	77.1	76.8
Ash (g)	0.3	0.4
Sodium (mg)	–	–
Potassium (mg)	56.3	98.8
GABA (mg)	2.7	11.2

GABA = gamma-aminobutyric acid.

2.2. Test meal preparation

A nonglutinous rice (brand name: Yumepirika) cultivated in Hokkaido, Japan was used a test meal in this study. The GABA rice was produced by an air heating and humidifying process developed by Mizuno et al.[14,15] The temperature and humidity of grain were controlled using testing equipment (LGB03; Satake) scaled down of actual equipment to increase the quantity of GABA, and then the product (grain) was hulled and milled. The quantity of GABA was analyzed by the automatic amino acid analysis method, based on the procedure described by Ohisa et al[16] but with some modifications. The production and the packing of rice were carried out at Satake Corporation in a quality-controlled manufacturing plant in compliance with the Food Sanitation Act (the Ministry of Health, Labor, and Welfare of Japan). The quality and safety of the test samples were thoroughly examined by Satake Co., Ltd.

2.3. Measurement and analysis of home BP

Home BP was self-measured by the participants two times a day, in the morning (between urination and breakfast) and in the evening (before going to bed). At each measurement, after taking a 5-

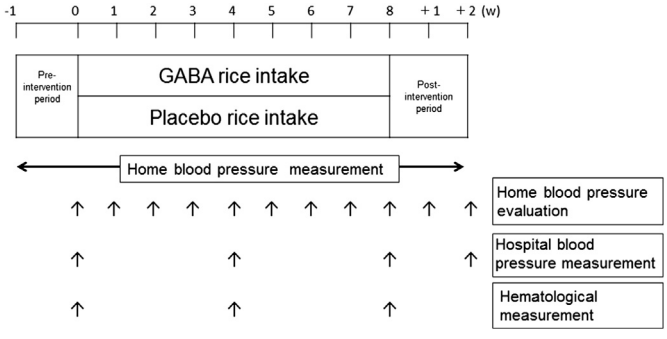

Fig. 1. Schedule (in weeks) for this clinical study. Home blood pressure was recorded two times daily (morning and evening) and was evaluated one time per week until the 2nd week after the intervention. Hospital blood pressure was recorded at baseline (0 weeks), the 4th week, the 8th week, and 2nd week after the intervention. Hematological measurements were obtained at baseline (0 weeks), the 4th week, and the 8th week.