Influence of Ultra-High Hydrostatic Pressurizing Brown Rice on Cognitive Functions and Mental Health of Elderly Japanese Individuals: A 2-Year Randomized and Controlled Trial

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Summary Brown rice contains many ingredients that might protect against cognitive decline and Alzheimer's disease. However, brown rice is very hard, difficult to cook, and is poorly digested; thus, it is difficult to eat long-term. To solve these problems, ultra-high hydrostatic pressurizing brown rice (UHHPBR) was prepared. We investigated the effects of dietary UHHPBR administration for 24 mo on cognitive function and mental health in the elderly. Healthy elderly participants ($n=52$) were randomized into UHHPBR and polished white rice (WR) groups. The UHHPBR group consumed 100 g of UHHPBR per day for 24 mo and the WR group consumed white rice. At baseline, and after 12 and 24 mo, cognitive functions were assessed using the Revised Hasegawa's Dementia Scale, Mini-Mental State Examination, Frontal Assessment Battery (FAB), and the Cognitive Assessment for Dementia, iPad version (CADi). Mental health condition was also assessed using the Apathy Scale and the Zung Self-Rating Depression Scale, and serum biochemical parameters were determined. From baseline to month 24, the mean change in the FAB-sub item 1 scores was higher in the UHHPBR group compared to the WR group. Furthermore, apathy scores decreased, as well as the time required to answer all questions of the CADi, and plasma epinephrine levels increased. These results indicate that a 2-y oral consumption of UHHPBR increases information processing speed (as a measure of cognitive function) and improves apathy in the elderly, suggesting a protective effect of UHHPBR administration against age-related decline in brain cognition and motivation.

Key Words ultra-high hydrostatic pressurizing brown rice, elderly, cognitive function, apathy, randomized and controlled trial

According to the 2016 report, the Ministry of Health, Labor and Welfare in Japan estimated that the number of elderly people aged 65 or older will be ~36.57 million in 2025, which accounts for 30.3% of Japan's total population (1). We should consider not only the present generation of baby boomers, but also the generation of their children that become elderly in 2040. Therefore, the ministry is paying efforts to promote an environment that can sustain good health and offer an extension of healthy life expectancy. Hence, healthy diets have been promoted, with a consideration for the development of food materials that can be incorporated into daily eating habits with ease. In this study, we focus on

whether being able to incorporate brown rice (BR) daily as a staple food can yield numerous health benefits.

Compared to polished white rice (WR), BR contains many ingredients that may be protective against the age-related decline of cognitive functions, such as ferulic acid, vitamin B6, vitamin B12, and others (Table 1) (2). However, BR requires a time-consuming cooking method, as its outer bran shell is very hard and poorly digested, and is difficult to eat long-term. Recently, to solve these difficulties, ultra-high hydrostatic pressurizing brown rice (UHHPBR), a non-thermal food processing technique, was developed (2, 3). The UHHPBR is easier to cook because of the high-water penetration into its hard shell, and it has a decreased characteristic odor and an improved texture; thus, it is easier to eat compared to the regular BR (3). Moreover, the number

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of common bacteria in UHHPBR is much lower than that in the regular BR. UHHPBR also improves the digestion and absorption of food, minimizing nutrient loss (3). The ultra-high hydrostatic pressure (UHP) treatment has brought some favorable and palatable characteristics of UHHPBR, making it easy to examine the effects of chronic intake of UHHPBR on human cognitive functions, which otherwise would have been difficult with normal BR. Therefore, using the UHHPBR, we conducted an interventional trial demonstrating the influence of the oral consumption of UHHPBR for 24 mo on the cognitive and emotional functions of elderly subjects.

Materials and Methods

Participants. Healthy elderly community dwellers,

Table 1. Nutritional content of white rice (WR) and ultra-high hydrostatic pressurized brown rice (UHHPBR).

Nutrients	WR	UHHPBR
Protein	6.8 g	7.7 g
Carbohydrate	75.3 g	76.6 g
Dietary fiber	0.3 g	7.1 g
Lipid	1.3 g	3.0 g
GABA	2 mg	9.1 mg
Inositol	ND	202 mg
Ferulic acids	ND	12–50 mg
Calcium	2 mg	9 mg
Magnesium	20 mg	110 mg
Phosphate	140 mg	290 mg
Potassium	110 mg	230 mg
Sodium	2 mg	1.8 mg
Iron	0.5 mg	2.1 mg
Zinc	4 mg	1.8 mg
Vitamin B1	0.12 mg	0.51 mg
Vitamin B2	0.03 mg	0.04 mg
Vitamin B6	0.05 mg	0.32 mg
Vitamin E	0.40 mg	ND
Niacin	1.40 mg	7.46 mg

Values are shown for 100 g WR or UHHPBR. GABA, γ -aminobutyric acid. ND, not detected. Part of the data within this table are reprinted with permission from Oyo Yakuri [92(3/4): 69–73, 2017].

aged 65 y or older and living independently in the middle mountain area of the Shimane prefecture in Japan, participated in the study. The participants underwent medical examinations that included anthropometric, blood biochemistry, cognitive function and mental health tests. Participants were excluded if they had a life-threatening disease, required total parenteral feeding, and were using any psychotropic drug or supplement that might significantly influence cognitive function, or had a history of a hypersensitivity or allergy to rice.

After screening, 52 participants (mean age = 72.9 ± 0.8 y) were included in the present investigation and randomly assigned to two groups: the UHHPBR group ($n=27$, mean age = 70.5 ± 0.9 y) and the WR group ($n=25$, mean age = 75.4 ± 1.1 y). Following this, a randomized controlled trial was conducted. The UHHPBR group consumed 100 g of UHHPBR per day for 24 mo and the WR group consumed white rice instead of UHHPBR for the same 24 mo. The UHHPBR and WR was supplied from Elise Co., Ltd (Iinan-cho, Shimane, Japan). This study was conducted according to the principles of the Declaration of Helsinki and Good Clinical Practice. The protocol was approved by the Ethics Committee of Shimane University (approval number: 20150815-1), and all participants gave written informed consent before participation.

Anthropometrics and self-administered questionnaires. Hospital nurses measured body weight, height and blood pressure of participants. Following this, participants were requested to answer two self-reported questionnaires: a general questionnaire on lifestyle, including questions related to educational and medical histories, and a brief diet history questionnaire (BDHQ) (4).

Blood sampling and cognitive evaluations and mental health. At baseline, and after 12 and 24 mo of intervention, blood samples were obtained in the morning or afternoon, after ascertaining whether the participants had eaten breakfast or lunch. Serum separated from the whole blood samples was stored at -80°C within 8 h of collection. Cognitive function was assessed using the Revised Hasegawa's Dementia Scale (HDS-R) (5), Mini-Mental State Examination (MMSE) (6), Frontal Assessment Battery (FAB) (7), and the Cognitive Assessment for Dementia, iPad version (CADi) (8). Mental health

Fig. 1. Flow diagram of participants throughout the study.

Table 2. Baseline and month 24 characteristics of study subjects.

	Baseline		Month 24	
	WR	UHPBR	WR	UHPBR
Sex (male/female)	25 (12/13)	27 (13/14)	17 (7/10)	17 (8/9)
Age	75.4±1.1	70.5±0.9*	76.5±1.2	73.5±1.4
Height (cm)	153.6±1.5	158.7±2.1	153.4±1.9	158.4±2.9
Body Weight (kg)	53.2±1.8	63.0±2.9*	53.4±2.2	60.4±3.7
Body Mass Index (kg/m ²)	22.5±0.5	24.8±0.6*	22.6±0.7	23.8±0.7
Body fat (%)	25.4±1.8	29.5±1.3	29.8±1.5	29.1±1.4
Blood Pressure (mmHg)				
Systolic	144.2±5.8	143.6±3.2	134.9±5.3	138.3±5.0
Diastolic	76.4±3.2	80.0±2.0	75.5±3.1	78.1±2.5
Cognitive function				
HDS-R score	27.7±0.5	28.7±0.2	27.9±0.5	28.5±0.3
MMSE score	28.0±0.4	28.4±0.3	28.5±0.5	28.8±0.4
Frontal Assessment Battery score	14.4±0.3	15.2±0.4	14.9±0.4	16.0±0.5
CADi score	7.6±0.3	8.3±0.3	8.4±0.3	8.9±0.2
CADi time required (s)	162.0±12.3	125.3±8.7*	138.7±9.3	102.9±7.8*
ApoE4 no. (%)				
0	19 (86.4)	20 (80.0)	15 (88.2)	14 (82.4)
1	2 (9.1)	5 (20.0)	2 (11.8)	3 (17.6)
2	1 (4.5)	0 (0)	0 (0)	0 (0)
SDS (Depression Scale) score	33.0±1.4	32.7±1.3	35.3±2.1	29.6±2.1*
Apathy score	11.0±0.8	9.1±1.0	13.4±1.5	7.6±1.5*
Plasma biochemical parameters				
GOT (U/L)	25.4±1.3	26.7±1.2	27.9±3.1	27.2±2.7
GPT (U/L)	17.3±1.5	21.4±1.3*	20.4±2.5	20.2±1.7
γ-GTP (IU/L)	34.0±7.2	39.3±7.7	34.2±12.5	45.5±14.0
Albumin (g/dL)	4.1±0.05	4.1±0.04	4.1±0.05	4.1±0.07
Total-cholesterol (mg/dL)	189.4±5.4	195.4±5.6	193.6±9.1	190.6±7.9
Triglyceride (mg/dL)	127.1±11.5	152.2±20.9	134.9±18.6	130.8±22.3
Blood urea nitrogen (mg/dL)	18.2±1.3	15.9±0.5	16.8±1.0	15.7±0.9
Creatinine (mg/dL)	0.79±0.08	0.70±0.03	0.73±0.04	0.69±0.04
Glucose (mg/dL)	128.0±8.3	110.9±6.2*	111.1±9.9	107.2±3.9
HDL-cholesterol (mg/dL)	63.4±2.7	59.1±2.3	66.5±3.9	65.3±3.8
LDL-cholesterol (mg/dL)	100.6±5.5	105.7±5.6	100.2±6.6	99.1±8.0
HbA1c (NGSP) (%)	5.8±0.1	6.0±0.1	5.7±0.1	6.0±0.1*

Values are mean±SE. * $p<0.05$ compared with the polished white rice (WR) value. Differences between the WR and ultra-high hydrostatic pressurizing brown rice (UHPBR) group were analyzed by using analyses of covariance (ANOVA) adjusted for age. CADi, Cognitive Assessment for Dementia iPad version; GOT, Glutamate-Oxaloacetate Transaminase; GPT, Glutamate-Pyruvate Transaminase; γ-GTP, Gamma-Glutamyl Transpeptidase; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; HDS-R, Hasegawa's Dementia Scale-Revised; MMSE, Mini-Mental State Examination; NGSP, National Glycohemoglobin Standardization Program; SDS, Self-Rating Depression Scale.

condition was assessed with the Japanese version of Starkstein's Apathy Scale (9) and the Zung Self-Rating Depression Scale (SDS) (10). Participants were excluded if they had an MMSE score of less than 20.

Blood biochemical analysis. The serum biochemical variables were measured with an automated clinical chemistry analyzer TBA-c16000 (TOSHIBA, Tokyo, Japan), the serum HbA1c level was determined with high-performance liquid chromatography (HPLC) using the HLC-723G9 (TOSOH, Tokyo, Japan), and blood sugar was measured with the automatic analyzer GA08III

(A&T Co., Kanagawa, Japan). Apolipoprotein (APOE) ε4 single nucleotide polymorphism genotyping was determined as described previously (11).

The concentrations of monoamines (norepinephrine and epinephrine) in the serum were measured using the HPLC method as previously described by EICOM (Kyoto, Japan) (12). The serum was pretreated with clean column EG (EICOM, Kyoto, Japan). The HPLC equipment consisted of an EICOM HTEC-500 (EICOM, Kyoto, Japan), equipped with a data processor (EICOM EPC-500 PowerChrom) and an automatic injector

(EICOM M-514). The chromatographic separation was performed using an EICOMPAK CA-50DS column (2.1 mm×150 mm ID), linked to a precolumn (EICOM PREPAK PC-03-CA, 3.0 mm ID). PowerChrom software was used for data collection and analysis (EICOM, Kyoto, Japan). The mobile phase consisted of 0.1 M phosphate buffer (pH 5.7), containing: 12% methanol, 700 mg/L sodium 1-octanesulfonate, and 50 mg/L EDTA disodium salt. The flow rate was 0.23 ml/min, and the applied potential was +450 mV over an Ag/AgCl reference electrode. The column temperature was maintained at 25°C.

Statistical analysis. Results were expressed as means±SE. Student's *t*-test for dependent or independent samples was used to evaluate the differences in the demographic and baseline variables. Differences between the placebo and active group were analyzed using analyses of covariance (ANCOVA), adjusting for age. All analyses were carried out using PASW Statistics, Version 18.0. Chicago: SPSS Inc. All hypothetical tests were two sided, with a significance level of $p<0.05$.

Fig. 2. The mean change in body fat percentage (%) from baseline to month 24 in the ultra-high hydrostatic pressurizing brown rice (UHHPBR) group and the polished white rice (WR) group. Vertical bars represent the SE. * $p<0.05$.

Results

Demographic and clinical characteristics at baseline. A total of 52 participants (25 men and 27 women) completed the baseline assessments and were randomized to either the UHHPBR or WR group. A total of 34 participants completed the study (Fig. 1), excluding the individuals who withdrew from the study ($86\pm1\%$), without a significant difference between the groups. The baseline characteristics of the two groups are shown in Table 2. The groups showed no significant differences in sex, blood pressure and serum biochemical parameters without age, body weight, body mass index (BMI), body fat and CADi time required. Thus, differences between the WR and UHHPBR group were analyzed using ANCOVA, adjusting for age. The mean total HDS-R, MMSE, and FAB scores of all participants were 28.2 ± 0.3 , 28.2 ± 0.2 , and 14.8 ± 0.2 , respectively, which was within the normal range. The APOE $\epsilon 2$, $\epsilon 3$ and $\epsilon 4$ allele frequencies were also not significantly different between the two groups.

Nutritional intake. There were no significant differences in the mean dietary nutritional intake over 24 mo between the UHHPBR and WR groups (data not shown). Side-effects that disturb daily life of the participants (such as allergic reactions, palpitations, and irritation in the stomach) were not present in either group.

Effect on body constitution and serum biochemical parameters. No significant differences were found between the two groups for height, body weight, BMI, or blood pressure at month 24 (Table 2). Similarly, the two groups did not differ in their blood biochemistry parameters without HbA1c (Table 2). At month 24, serum HbA1c levels are significantly higher in the UHHPBR group than the WR group ($p=0.007$), and however there was not a significant difference between the two groups for the mean change in serum HbA1c levels from baseline to month 24. The mean change in body fat percentage from baseline to month 24 was significantly lower in the UHHPBR than in the WR group ($p=0.044$) (Fig. 2).

Effect on cognitive evaluations and mental health. At month 24, the total FAB score tended to be greater in

Fig. 3. The mean changes in the FAB sub-item number 1 "conceptualization" score (A, left panel) and the CADi time required scores (B, right panel) from baseline to month 24 in the UHHPBR group and WR group. Vertical bars represent the SE. * $p<0.05$.

Fig. 4. The mean changes in the Apathy Scale scores (A, left panel) and the serum epinephrine levels (B, right panel) from baseline to month 24 in the UHHPBR group and WR group. Vertical bars represent the SE. * $p<0.05$.

Table 3. Serum norepinephrine and epinephrine levels of study subjects at baseline and month 24.

	Baseline		Month 24	
	WR (n=20)	UHHPBR (n=20)	WR (n=17)	UHHPBR (n=17)
Norepinephrine (pg/100 μ L)	35.2 $\pm$ 7.9	55.7 $\pm$ 4.4	128.0 $\pm$ 22.3	129.2 $\pm$ 7.3
Epinephrine (pg/100 μ L)	6.8 $\pm$ 6.0	1.8 $\pm$ 0.6	25.6 $\pm$ 6.9	31.2 $\pm$ 3.3*

Values are mean $\pm$ SE. * $p<0.05$ compared with the polished white rice (WR) value. N indicates the number of subjects. Differences between the WR and ultra-high hydrostatic pressurizing brown rice (UHHPBR) group were analyzed by using analyses of covariance (ANCOVA) adjusted for age.

the UHHPBR group than in the WR group ($p=0.062$) (Table 2). When the scores for the HDS-R, MMSE, and FAB sub-items were analyzed, the mean change in the FAB sub-item number 1 "conceptualization" score from baseline to month 24 was significantly greater in the UHHPBR group than the WR group ($p=0.041$) (Fig. 3A). Additionally, the mean change in the total time required to answer all questions of the CADi from baseline to month 24 was significantly shorter in the UHHPBR group than in the WR group ($p=0.017$) (Fig. 3B). The Apathy Scale and SDS scores were significantly lower in the UHHPBR group than in the WR group at month 24 ($p=0.012$ for Apathy score, $p=0.022$ for SDS scores) (Table 2). Furthermore, the mean change in the Apathy score from baseline to month 24 was significantly smaller in the UHHPBR group than in the WR group ($p=0.005$) (Fig. 4A).

Effect on serum catecholamine. At both baseline, the WR and UHHPBR groups showed no significant differences in their serum catecholamine levels. At month 24, serum epinephrine levels were significantly greater in the UHHPBR group than in the WR group ($p=0.009$) (Table 3). The mean change in the epinephrine levels from baseline to month 24 was also significantly greater in the UHHPBR group than in the WR group ($p=0.022$) (Fig. 4B). Further, a mild/moderate but non-significant inverse correlation was observed between the mean change in the Apathy score and serum epinephrine levels ($r=-0.294$, $p=0.091$) (Fig. 5).

Fig. 5. Correlation between the mean changes in the Apathy Scale scores and the mean changes in the serum epinephrine levels from baseline to month 24 in the UHHPBR group and WR group.

Discussion

The aim of the present study was to evaluate the effect of oral intake of UHHPBR on cognitive functions and mental health in elderly. The results of the investigation suggest that UHHPBR prevails over WR for improved performance in neuropsychological tasks that explore cognitive and behavioral domains in the elderly, and that correlate with frontal lobe integrity and dementia. As assessed by the Apathy Scale and the SDS, the men-

tal health condition of the elderly in the UHHPBR group showed greater improvements than those in the WR group. These results suggest a protective effect of UHHPBR consumption against age-related decline in brain cognition and motivation. To the best of our knowledge, the present study is the first long-term, randomized, controlled trial evaluating the influence of dietary UHHPBR supplementation on cognitive functions and apathy in healthy elderly Japanese individuals. Additionally, the compliance rate during this study was high ($86 \pm 1\%$).

Abstract thinking is frequently impaired in elderly subjects with frontal lobe lesions (13, 14). Such individuals present difficulties conceptualizing two objects belonging to the same semantic category. In this study, dietary UHHPBR intake improved conceptualization ability, one of the functions of the frontal lobe (Fig. 3A), and decreased the total time required to answer all questions in the computerized cognitive function test (the CADi) (Fig. 3B). Although the mechanism through which UHHPBR consumption improves cognitive function in the elderly remains to be elucidated, we speculate that these effects are caused by improvements in the central executive system of working memory, which depends on the function of the dorsolateral prefrontal cortex. Dietary UHHPBR intake induced improvements in motivation, as indicated by lower scores in the Apathy Scale and SDS (15), suggesting that motivated behavior requires a combination of behavior-specific regions in the hypothalamus and important components of several frontal-subcortical circuits. Neuroimaging investigations on apathy and Alzheimer's disease (AD) revealed that the anterior cingulate cortex (ACC), prefrontal cortex, and parts of the basal ganglia play an important role in motivation (16–18). The frontostriatal circuit, linking the ventral striatum to the dorsal ACC via the ventral pallidum and thalamus, is believed to be crucially involved in effort-based decision-making and executive functions. Disruptions in this circuit have been hypothesized to play a critical role in apathy across neurodegenerative disorders (19). Amyloid- β (A β) deposition, a pathological characteristic of AD, has also been shown to correlate positively with apathy (20). Okuda et al. previously reported that UHHPBR decreases A β levels in the brains of senescence accelerated mouse-prone 8 (SAMP8), a mouse model of AD, with concurrent improvements in cognitive dysfunctions (21). Many other reports have linked the onset and duration of apathy to problematic lifestyles characterized by sleep deprivation (and general fatigue), poor diet, and lack of exercise; or to organic defects, such as a malfunctioning thyroid gland or limbic system (22). Apathy can also occur in dementias (such as AD, vascular dementia, and frontotemporal dementia), and prefrontal A β deposition correlates with apathy in AD. Therefore, the decrease in apathy scores in the UHHPBR group may reflect a possible role of UHHPBR in reducing amyloid burden.

Moreover, catecholaminergic systems are key modulators of motivated behaviors. It is well known that the hypothalamic-pituitary-adrenal (HPA) axis plays an important role in the regulation of stress-related

homeostasis and emotional states, such as apathy and depression (23, 24), suggesting that the improvement in motivation may involve serum catecholamine levels. In the present study, the mean change in the apathy scores from baseline to month 24 showed a mild/moderate inverse correlation with the mean change in serum epinephrine levels from baseline to month 24 (Fig. 5B). These results suggest that the long-term dietary intake of UHHPBR may improve apathy scores by modifying the activity of behavior-specific regions in the hypothalamus and/or HPA axis.

A major question remains as to why and how the consumption of UHHPBR, compared to WR, ameliorates the cognitive function of the elderly. BR is enriched with nutrients crucial for the maintenance of cognitive function and with potential neuroprotective benefits, such as ferulic acid, vitamin B6, vitamin B12, and folic acid. Contrarily, WR is simply the starch left after the nutrient-dense husk is removed. The cooking time of BR is longer than that of WR, requiring more water, and BR has a distinctive chewy texture and nutty flavor. Many people therefore prefer WR due to its fluffy texture and shorter cooking time; however, WR fails to offer the nutritional benefits of BR. As it is high in fiber and has a lower glycemic index than WR, BR can help stabilize blood sugar levels and promote digestion, indicating that BR may be a better option for diabetics (25).

In addition, BR contains nutrients that WR lacks, such as antioxidants (including tocopherols, tocotrienols, and gamma-oryzanol) (26). A large number of studies indicate that oxidative stress and inflammatory dysfunction in the brain may play an important role in age-related cognitive decline and neurodegeneration, particularly the neuronal loss caused by AD (27). Ferulic acid is an antioxidant with anti-inflammatory properties and is able to interfere with the biological pathways involved in cell death induced by oxidative stress, as well as inflammation due to A β aggregation (28). More interestingly, and consistent with other reports, the content of gamma-aminobutyric acid (GABA) increased 4–5 fold in UHHPBR compared to WR. We consider this to be due to the increase in water penetration into the deep bran-layer, increasing the amount of extractable GABA from the soft bran-layer of the BR after treatment with UHHP. The main inhibitory neurotransmitter in the brain and the spinal cord of mammals is GABA, and it is involved in the regulation of many physiological and psychological processes, inducing hypotensive, diuretic, and tranquillizing effects (29, 30). Strong clinical and preclinical evidence also implicates dysfunctions of the GABA system in the pathophysiology of several neuropsychiatric disorders, including anxiety and depression (31, 32), even though depression is largely seen as a dysfunction in monoamine neurotransmission and antidepressant strategies mainly focus on monoamines (33). GABA postsynaptically binds to GABAB receptors and is coupled mainly to inwardly rectifying K⁺ channels (34) and mediates slow inhibitory postsynaptic potentials (35). GABAB receptors are abundant in the brain, where they localize in interneuron populations and

some glial cells. Furthermore, there is a high expression of GABAB receptors in the limbic system (36), indicating a role in regulating emotional behavior. Therefore, normative activation and functioning of the GABAergic system is crucial for numerous learning and memory tasks. Targeting this system via consumption of UHHPBR, resulting in increases in GABA levels, may benefit several clinical populations. For example, activating the GABA-GABAB receptor system has been shown to promote mental relaxation and feelings of happiness (37), and to ease muscle tension (38). Many other investigations have also reported that GABA receptor activation rapidly and reliably decreases symptoms of anxiety (37–40).

GABA can cross the blood brain barrier (BBB), albeit conflicting, in small amounts (41). Evidence has been found for the presence of a GABA transporter in the BBB (42), thus indicating that GABA can enter and/or exit the brain through facilitated transport. Many consumers of GABA-supplements claim that they experience benefits from the food supplement version of GABA; however, it remains to be confirmed whether these GABA supplements confer benefits beyond a placebo effect.

Accordingly, future research needs to establish the effects of oral GABA administration on GABA levels in the human brain, as well as any resulting behavioral effects. It has also been proposed that GABA-rich food supplementation affects the central nervous system through the enteric nervous system. This gut-brain axis maintains a bidirectional communication system and whether this operates with GABA remains to be clarified. In summary, GABA levels were higher in UHHPBR than WR, and long-term daily intake of UHHPBR had preventive effects on age-related decline in brain cognition and depression in the elderly. Thus, UHHPBR could prove beneficial in protecting against neurodegenerative diseases such as AD.

Conclusion

Compared to WR, the nutrient-rich UHHPBR increased cognitive function (including rapid information-processing that explored conceptualization) and decreased apathy-related anxiety and depression, a characteristic of neurodegenerative disorders. The beneficial effects were related to the enriched nutrient content of UHHPBR, such as antioxidants, vitamins, minerals, and GABA. Finally, the results indicate that UHHPBR could be an ideal regular staple food with protective benefits against age-related cognitive decline and apathy.

Disclosure of State of COI

No conflicts of interest to be declared.

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