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Note

Effect of Palatinose Administration on α1 Brain Waves in Human Volunteers

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The effect of palatinose intake on α1 brain wave generation was studied by human volunteer test. Twelve healthy volunteers were administered 40 g of palatinose or sucrose, and electroencephalogram (EEG) was made before and at 150 min after administration. The area of α1 wave generation on topographs increased after administration of either sugar, but there was a significant difference in the intensity between the palatinose and sucrose groups. Ten volunteers were administered 100 mg of theanine, which has a relaxing effect, in combination with 17.5 g of palatinose (T-P group), and EEGs were recorded before, at 60 and 150 min after administration. Though the area of generated α1 brain wave in the topographs increased in both groups (T-P and 17.5 g palatinose groups) after administration, the patterns of their increase differed. Nine volunteers were administered 5 g of palatinose, and EEGs were recorded before and at 150 min after the administration. The area of α1 wave generation increased slightly but less than that in 40 g palatinose group. The above results suggested that palatinose enhances generation of α waves and that its effect might be maintained longer than that of sucrose.

Keywords: palatinose, brain waves, α1 waves

Palatinose (1-O-α-D-glucopyranosyl-D-fructose, isomaltulose) is used as an ingredient for functional foods because of its physiological characteristics; for example, it is non-cariogenic (Minami *et al*., 1990; Ooshima *et al*., 1983a, b), causes a gradual increase in blood glucose level and a slight secretion of insulin (Kawai *et al*., 1989). Palatinose is a structural isomer of sucrose and a disaccharide composed of glucose and fructose with an α-1, 6 bond. Sucrose and glucose are known to change into blood glucose after ingestion and are utilized as the energy source for the brain. Recent studies have shown that the mental state (emotion, mood) in human is strongly related to the blood glucose level and glucose supply to the brain (Benton, 1998; Keul *et al*., 1982; Martin & Benton, 1999). Palatinose, which differs from sucrose in the time-course change of blood glucose level, is believed to have a different effect on the mental state of humans. This was the reason the effect of palatinose administration on mental concentration was investigated by Kashimura *et al*. (2003).

In today's stressful society there are various products promoting relaxation, and there are several ongoing studies about the relaxing effects of elements that directly appeal to the five senses: visual, images, music, flavor and taste (Kawano, 2000; Kawaki *et al*., 1998; Nagai, 2002). Various flavoring and seasoning ingredients are used in commercial foods claiming to have a relaxing effect, however, these sometimes do not meet people's preferences. Thus, there are studies focusing on substances such as theanine contained in green tea, which affect the release or decline of neurotransmitters in the brain, even when taken in a concentration which is not high enough to impart taste (Juneja *et al*., 1999; Kobayashi *et al*., 1998; Yokogoshi *et al*., 1998). With such a substance, the relaxing effect is perceived not during its ingestion but after a certain metabolic period has elapsed. It is likely that substances such as sugars, which are consumed by the brain cells, may affect emotion during their physiological process even after being absorbed and metabolized in the organs.

In this study, EEG analysis was used as a main index to estimate emotion including relaxation in human. EEGs are classified by their frequency into δ, θ, α and β waves. It is said that δ waves (0.5–3 Hz) are associated with deep sleep, θ waves (4–7 Hz) appear as people fall into drowsiness, α waves (8–13 Hz) appear in a relaxed state, and β waves (14 Hz ≤) are associated with an excited state; and that α waves are divided into α1 waves (≤10 Hz) and α2 waves (10 Hz ≤). In the resting and relaxing state the α1 wave tends to generate, and the α2 wave and the β wave tend to generate alternately in the concentrating and thinking states. In other words, low frequency EEGs tend to appear while the brain is not active as in deep sleep, and high frequency waves appear while the brain is excited and active as in learning. Various studies on the relationship between a relaxing effect and α wave generation have shown that α waves usually show quantitative change both in the generated site in the brain and in frequency when people feel relaxed. These quantitative changes sometimes vary according to the relaxing therapy and intake of foods (Kawano, 2000). Machi *et al*. (2001) and Chen *et al*. (2000) have studied how Qigong therapy or the use of different cathode ray tubes (CRT) affected the generation of α1 wave, and reported on the relationship of changes in heart rate, body temperature, skin resistance and EEG to a relaxed state. They confirmed in these studies that the area of α1 wave generation increased first in the occipital region and then toward the frontal region on the topographic map, and the power of the α1 wave increased in a relaxed state, which suggested that the area of α1

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wave generation could serve as a parameter of a relaxation effect.

In this study, we investigated what role palatinose, a sugar which has a remarkable effect on the slow raising and maintaining of the blood glucose level, plays in the generation of α brain waves in human.

Materials and Methods

Materials Crystalline palatinose-IC was used as palatinose and granulated sugar GM as sucrose, both of them produced by Shin Mitsui Sugar Co., Ltd. (Tokyo). For theanine, Suntheanine™ (L-theanine content ≥98%) produced by Taiyo Kagaku Co., Ltd. (Yokkaichi), was used.

Subjects Eighteen healthy volunteers (21–40 years of age, 16 men and 2 women) participated in this study. The volunteers underwent electroencephalography prior to their participation in the study, and were confirmed not to have an abnormal EEG. Since the test substance was a sugar, the volunteers were asked not to take any food or drug, except water, for 12 h preceding the test, to exclude the influence of other factors on changes in blood glucose and EEGs. As this study was conducted in accordance with the code of ethics of the World Medical Association (Helsinki Declaration of 1964, as revised in 1989), the content and methods of the study were fully explained to the volunteers, and their informed consent was obtained in writing.

Design and procedure In Experiment 1, the effects of palatinose and sucrose were compared. First, EEGs were recorded for 5 min in 12 volunteers (21–40 years of age, 11 men, 1 woman) resting with their eyes closed, and the data obtained were used as the initial values. Next, the volunteers were administered 40 g of palatinose or sucrose dissolved in water (190 ml), then after a 130-min rest they were asked to work using a word processor for 20 min, and subsequently to rest with their eyes closed for 5 min to record EEGs. Each volunteer was subjected to the palatinose and sucrose tests on different days. The 40 g dose, which corresponded to the amount of sugar contained in a light meal and the common dose in the test for blood glucose curve, had been confirmed to induce an increase of blood glucose and to recognize discrimination between the two sugars. Using a word processor involved simple typing of randomly selected pages, which had been reported to produce fatigue of the brain and a change in the area of α wave generation on the topographic map (Chen *et al*., 2000). It had also been confirmed that with sucrose the level of glucose reached peak value at 30–60 min after the administration and returned to the initial value 90–120 min after administration, with some individual variations in the elapsed time. On the other hand, with palatinose, the level of glucose smoothly rose at 30–60 min after administration and decreased thereafter but did not fall to the initial value at 90–120 min (Kawai *et al*., 1989). Effects of α wave generation were thought to arise after the changes in blood glucose. It was therefore considered appropriate to compare the EEGs at 150 min after the administration of sugar, which was the period of recognition of the differences in blood glucose sustention between the two sugars.

In Experiment 2, the effect of palatinose alone was compared with the effect of palatinose combined with theanine. In 10 of the volunteers (21–40 years of age, 8 men, 2 women), EEGs were recorded for 5 min while they had their eyes closed and resting, and the data obtained were used as the initial values. Next, the volunteers were administered an aqueous solution containing palatinose alone or an aqueous solution containing palatinose and theanine (380 ml), and EEGs were recorded at 60 min and 150 min after administration while resting with their eyes closed. Each volunteer was subjected to these tests on different days. It was assumed that palatinose would be used as a sweetener for so-called "near water," which requires the concentration of the sweetener to be 4.5% (w/v); thus in the present test 17.1 g of palatinose was used to prepare 380 ml of palatinose solution in water. Theanine in combination with palatinose is known to induce the generation of α waves, which were reported to appear about 30 min after administration of 50 mg or 200 mg theanine and to persist for approximately 2 h (Kobayashi *et al*., 1998). In the present test 100 mg of theanine was used to prepare 380 ml of solution in water.

In Experiment 3, the palatinose dose was reduced, and the results were compared with those of Experiment 1. First, EEGs were recorded in volunteers (21–23 years of age, 8 men, 1 woman) as already described. Next, the volunteers were administered 5 g of palatinose in water (190 ml); then they were asked to use a word processor for 20 min from 130 min after the administration, and subsequently to rest for 5 min with their eyes closed to record EEGs. The dose of 5 g is thought to correspond to the amount of sugar generally used for a cup of coffee or black tea.

Measurement and analysis of EEGs EEGs were recorded with a digital electroencephalograph (SYNAFIT EE 5521, NEC San-ei Instruments, Ltd., Tokyo), using the referential derivation method (unipolar recording) and 19 channels, with the left and right earlobe electrodes as reference electrodes according to the international 10–20 electrode system. Sampling frequency was 200 Hz. Of the recorded EEGs, the α1 wave zone (9–10 Hz) was decomposed by fast Fourier transform (FFT) at intervals of 5.12 s, then EEG mapping was performed for 5 min with 2.56 s as a unit, and EEG topographs were analyzed using ATLAS (Kissei Corp., Tokyo).

In the analysis of EEG topographs, the area in which α1 waves above a certain potential appeared was calculated from each topograph obtained in the course of every 5 min, and the mean α1 generation area with the subject resting with closed eyes was determined by averaging these areas. Using the initial mean area of α1 wave generation, which represented the ordinary state as 1, the relative value of the mean area of α1 generation after the administration was computed. Since the initial EEGs as the basic intensities were measured each time and for each subject, differences in physical conditions and the date might be negligible. It is well known that α waves appear in the occipital region while the subject rests with his/her eyes closed. Workload on the subject changes not only the power of α wave generation but also the area of α wave generation, and the removal of the workload also changes these values.

Results and Discussion

Comparison of α waves after palatinose and sucrose intake (Experiment 1) Figure 1 shows extracts (the first 30 s) of the time-course topograph as the initial intensity, and of the time-course topograph obtained 150 min after the administration of palatinose in one subject. The deep red part represents the area of α1 waves of high power, which was small in the initial topograph and enlarged in the post-dose topograph. Figure 2 shows the rela-

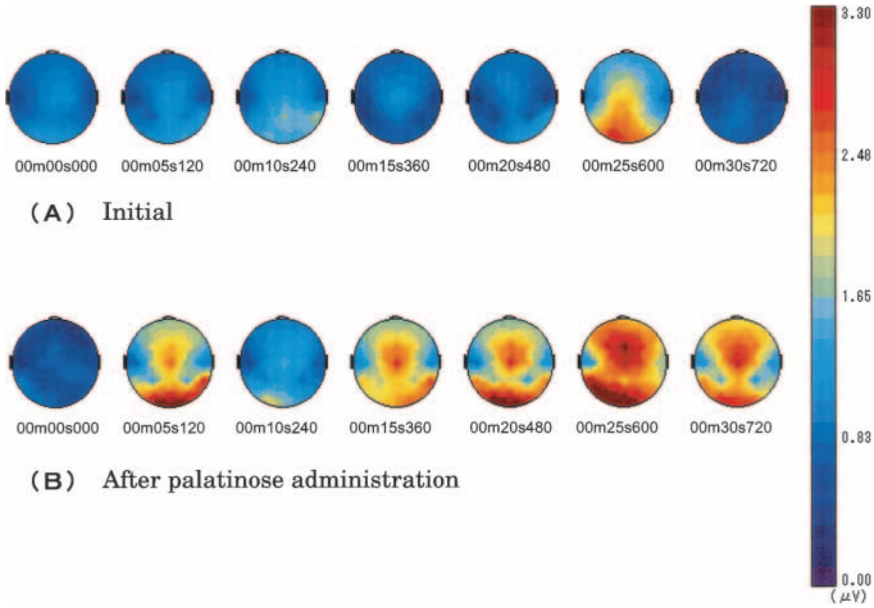

Fig. 1. Typical example of topography of α1 waves. (A) is the first 30 s of the time-course topographs for the initial intensity, and (B) is 150 min after palatinose administration.

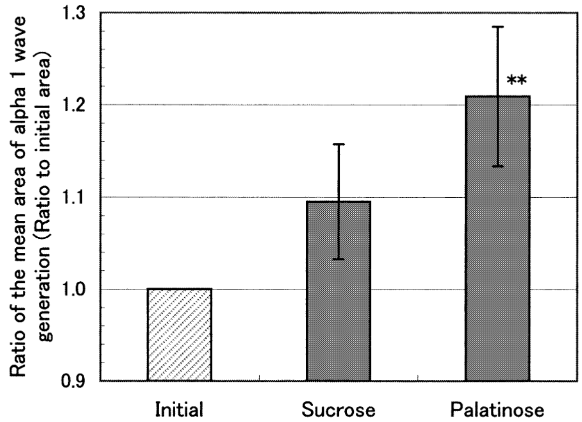

Fig. 2. Comparison of the α1 wave generation after sucrose and palatinose intake. The values are the relative values of the mean area of α1 wave generation 150 min after the sugar administration of 40 g, and are the ratio to the initial mean area. The values are the mean±SE of 12 subjects. $^{**}p<0.01$, compared with values of the sucrose administration group.

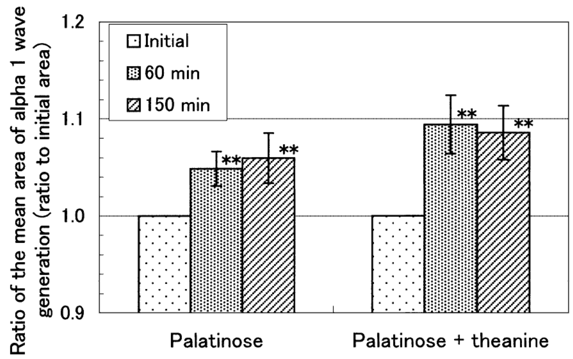

Fig. 3. Combined effect of palatinose and theanine on α1 wave generation. The values are the relative values of the mean area of α1 wave generation 60 min and 150 min after administration of palatinose (17.1 g) alone and combined administration of palatinose (17.1 g) and theanine (100 mg), and the ratio to the initial mean area. $^{**}p<0.01$, compared with the values of each initial value. The values are the mean±SE of 10 subjects.

tive values of the mean area of α wave generation after the administration of 40 g palatinose or sucrose. The initial value was represented by 1, and the area of α wave generation was increased 150 min after the administration of either sugar. This indicated that, compared with the initial condition of fasting and stress, the post-dose absence of stress and relaxing effect produced an increase of the area of α wave generation.

To analyze the relative values of the area of α wave generation, a paired *t*-test was used for comparison within the same group of subjects, and revealed that there was a significant difference ($p<0.01$). Although EEGs were recorded only at 150 min after the administration of sugar, if the generation of α waves had correlated with the blood glucose level, a higher value of generation of α waves might have been observed while the glucose level was high at 60–90 min after the administration. However, palatinose significantly increased the generation of α1 waves as compared with sucrose at 150 min after the administration when the glucose supply to the brain was already past the peak level, this suggests that palatinose also plays a role in maintaining a relaxing effect in addition to supplying glucose to the brain.

Combined effect of palatinose and theanine (Experiment 2) Figure 3 shows the relative values of the α wave generated area at 60 min and 150 min after the administration calculated from the results of brain wave measurement in Experiment 2. The initial topographic area of α wave generation was defined as 1 in calculating relative value. For each subject, the post-dose change of area from the initial value was analyzed by two-way analysis of variance with repeated-measures, which did not show a significant difference regardless of the method of administration however, the relative value in the combined administration group was higher than in the palatinose administration group. A significant difference was detected in post-dose change of area ($p<0.01$) by

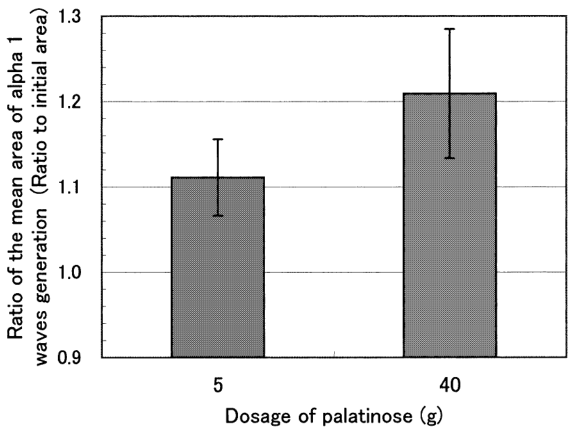

Fig. 4. The relative values for the area of α1 wave generation 150 min after the administration of 5 g and 40 g palatinose. The values are the ratio to the initial mean area, and are the mean±SE for 9 subjects in Experiment 3 (5 g of palatinose intake) and for 12 subjects in Experiment 1 (40 g of palatinose intake).

either administration, which confirmed that either was effective in increasing the area of α wave generation. Comparison between at 60 min and 150 min showed the relative values of the α wave generation area to be the same level, which suggests that palatinose could sustain the glucose supply to brain cells.

It takes 60 min or slightly less for the glucose level to peak after the administration of a sugar, so that the supply of sugar to the brain at 60 min must be greater than at 150 min after the administration. From the values at 60 min and at 150 min after the administration, therefore, the course of change between those time points can be estimated. Since theanine was reported to reach the brain about 30 min after the administration in a rat experiment and administration of 50 mg or more theanine significantly enhanced the α waves power (Kobayashi *et al.*, 1998), it seemed likely that the administration of 100 mg theanine in the present study would produce a sufficient α wave enhancing effect after 60 min, and that this effect would decrease thereafter. Accordingly, it was inferred that the greater increase in the area of α wave generation in the combined palatinose and theanine group vs the palatinose alone group was attributable to theanine, and the decrease in the area of α wave generation at 60 min to 150 min after the administration in the combined administration group was due to a decrease in the effect of theanine.

Administration of 5 g palatinose (Experiment 3) Figure 4 shows the relative values for the area of α wave generation 150 min after the administration of 5 g palatinose, as compared with those after the administration of 40 g palatinose in Experiment 1. After the administration of 5 g palatinose, the area of α1 wave generation increased as compared with the initial value. Comparison of the area of α wave generation 150 min after the administration between 5 g and 40 g doses by *t*-test revealed no significant difference. However, the small dose of 5 g palatinose could increase the α1 wave generation area. The area of α1 wave generation at 150 min after the administration of 5 g palatinose was larger than that after the administration of 17.1 g palatinose in Experiment 2. This can be explained by the fact that, α wave generation was stronger after the workload than without workload, and volunteers did not get a workload in Experiment 2.

From the present study, the administration of palatinose was confirmed to influence the generation of α1 wave, and sustained the effect as well as the effect on mental concentration (Kashimura *et al.*, 2003). Although it is not reasonable to conclude that palatinose has a relaxing effect based only on the record of EEGs and calculation of the increase in the area of high-power α wave generation on the topographic map, the present approach may provide an index of the relaxing effect. We already knew that palatinose does not increase blood glucose level immediately but sustains a relatively slow increase in this level. We believe that this sustention of blood glucose level relates to the sustention of α wave generation effect because of the slower glucose supply to brain cells than in the case of sucrose administration. It is under consideration to measure time-course changes in the glucose supply to the brain after palatinose administration as well as changes in the concentrations of neurotransmitters in the brain to determine the effect and action mechanism of palatinose on the brain.

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