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THE EFFECTS OF L-THEANINE ON MENTAL RELAXATION AND FATIGUE PERCEPTION

Key Words: L-theanine, alpha wave, relaxation, fatigue

Forward

Due to increasing complexity in our society and difficulties from excessive work and interpersonal relationships, stress is increasing so that the population complaining of chronic stress without having any particular disorder is rising. Fatigue is very subjective and since there aren't any particular diagnostic tests for it, it is known to be difficult to define.1) However normally, fatigue is classified into physiological, pathological and mental types. Physiological stress is fatigue felt after extreme physical activity where the muscles and limbs feel heavy. Sometimes, there are symptoms of sleepiness and in most cases, this fatigue goes away with adequate rest.2) However, office workers that must work according to fixed schedules without regard to their own volition often feel continuous physiological fatigue.3) Pathological fatigue requires appropriate treatment depending on the diagnosis of the initial signs of organic disorder, such as thyroid, diabetes, etc. Mental fatigue is the most common form and is related to stress, mental nervousness, insecurity, conflict, depression and other factors in everyday life.2)

There is not a lot of epidemiological data available in Korea regarding persistent or chronic stress but the percentages of workers complaining of chronic stress at one industrial site was reported at 20.7% for men and 26.4% for women.4) In one of the research reports regarding fatigued patients visiting primary treatment clinics in Korea, patients that visited clinics complaining mainly of fatigue made up 4.7% of all patients and this is the 6th most voiced complaint of all patients. Of these, organic disorders diagnosed to be related to fatigue made up 46%.5) In another study, the rate of occurrence of fatigue that was severe enough to be a hindrance to everyday life made up 11.4% of patients that visited primary clinics and another 1.22% could be suspected of chronic fatigue syndrome.6) In one study carried out on general physical examinees that were not patients, it was reported that as many as 44% had fatigue symptoms.7) By looking at reports like this in Korea, it can be seen that fatigue is already an important social factor and various methods such as adjustments in lifestyle and activity therapies can be tried for physiological and mental fatigue that is not accompanied by a physical disorder. However, the clear symptoms or treatment results for which herbal medicine is efficacious have not yet been established.

As an example, green tea is known to be effective in relieving nervousness and clearing the mind and it can be expected to be effective in relieving stress and reducing mental fatigue as those results have

been proven somewhat in recent studies. This is based on the functioning of L-theanine which is an amino
acid contained in green tea. L-theanine is an amino acid that is found only in tea (camellia sinesis) and
similar types (C. taliensis C. irrawaiensis) and is a main component that gives green tea its unique taste. 8,
9) L-theanine is gamma-glutamil-ethylamide and the refined chemical structure after being extracted from
tea was first studied in 1949.9) A considerable amount of L-theanine is included in high-quality green tea
but it still makes up more than half of the beneficial amino acids in green tea regardless of its grade.10) If
L-theanine is taken orally, it is known to be quickly absorbed into the intestine and to bring about various
physiological results. The physiological results of L-theanine that have been reported include mental
relaxation, lowering of blood pressure and improved learning abilities.8-13) Also, tea contains more
caffeine than coffee or cocoa but in 1971, Kimura, et al1) showed that L-theanine has a counter effect to
the stimulating effects of caffeine. After that, Kakuda, et al, confirmed and reported the counter effect that
L-theanine has to caffeine through brain wave measurements in animal experiments.

The mechanisms for this effect have not been clearly shown but L-theanine is presumed to have an effect
on dopamine that affects the nerve cells or on the nerve transmitter substances in the brain, such as serotonin, and that it participates in suppression effects. 8, 14, 15)

These writers carried out this study on people that had been feeling fatigue continuously for one month or more by administering functional beverages containing 200mg of L-theanine and investigated
whether there were results in terms of mental relaxation and fatigue perception. This study was carried
out in order to find out if L-theanine is a component that can be used effectively in people feeling mental
stress or fatigue.

Method

1. Study Subjects
Twenty healthy volunteers aged 30 to 55 years who had had persistent fatigue for more than one month previously without any specific disorder were recruited openly. After receiving the posted test participation consent forms from all the subjects, they were examined through their medical histories,
questionnaires and basic clinical tests (diabetes, liver functioning, anemia, thyroid functioning) and those
having chronic disorders or psychiatric depression and anxiety were not included in the study. Two of the
first 31 volunteers were suspected of having psychiatric depression and anxiety disorder with scores of 8
or more on the Hospital Depression-Anxiety Survey and were removed. Six people were suspected of having chronic disorders and another three were not able to keep their appointments for the brain wave
test and were removed so that the testing was finally completed on a total of 20 people who finished the
study.

2. Questionnaire
In order to discern depression and anxiety, the Hospital Depression-Anxiety Scale, which is known to be useful in discerning depression and anxiety in primary examinations, was used. Where the
score for each came to eight or more, this was regarded as psychiatric depression or anxiety disorder and
that person was removed from the study.16) The fatigue severity scale, which has been confirmed to be
useful in domestic studies and which has been recognized in overseas studies to be reliable and suitable,
was translated and used to measure the degree of fatigue.17-19) In addition, the quantity of stress that can
have an effect on fatigue was also evaluated using the modified Bepsi stress survey.20)

3. Ingredients and Dosage Method
The form of the test beverage was a liquid substance with a transparent yellow color. SuntheanineTM (containing over 98% L-theanine) of Taiyo Kagaku Co. of Japan was used for the main

component L-theanine. 100ml of the test beverage contained 200mg of Suntheanine and 10ug of GABA
and in the placebo beverage there was 10ug of GABA and the contents, taste and color were manufactured to be the same as the test beverage. The dosage quantity and dosage method were determined so as to administer one bottle (100 ml/bottle) at one time on the test date according to the
testing schedule in a random allocation sequence and the subjects were instructed not to consume any
beverage (coffee, black tea, green tea, etc.) that contained caffeine at least on the same day before the
exam. Beverages that were taken before the exam were recorded.

4. Test Design
The random allocation was achieved by making random allocation tickets using an allocation code provided by a random allocation program and the test beverages and placebo beverages were assigned in that order. The double-blind method was maintained by attaching the same images and labels
to the test beverages and placebo beverages when producing the test beverages so that the subjects and the
clinical test researchers were rendered blind and the persons in charge of testing efficacy and the subjects

did not know information about the products being taken when carrying out the efficacy testing. When judging the results and safety of the final test products after evaluating the results for each subject, the researcher performed code breaking. Thus, the researcher was to store one sealed random allocation ticket in the sealed condition and to open it only when there occurred some serious abnormal reaction. The allocation details of the unique codes were not revealed until the clinical test was completed. The researcher supplied products to each subject in sequence starting with unique code #1 of the test samples.
When there was a loss or damage to the test samples, the blind testing was to be maintained by using extra samples (separate unique codes). The cross-over test was performed insofar as possible on the same day of the week and same time. The test schedule times were communicated in advance to the participants so that they would be sure to follow it.

5. EEG Measurement
The brain wave measurements were performed on the study subjects using a ceegraph 4 of Bio-Logic Co., by a technician expert in measuring brain waves and were measured along twelve channels.
The actual brain wave measurements were carried out starting 15 minutes after drinking the beverage in order to adjust to the environment and achieve stabilized brain waves and this continued for 60 minutes.
The measurement room was divided into a closed environment room and a recording room and the closed environment room was maintained at 25 degrees Celsius and at an illumination of 40 lux. In order to reduce artifacts as much as possible, the subjects were asked to cooperate by lying on a bed in a comfortable position with their eyes open and mouths closed. The brain wave analysis was carried out as a power spectrum analysis and the time-series signals of the brain waves were converted to frequencies.
As the purpose of this study was to find out the degree of tension alleviation of the patients, the power ratio between the alpha wave that contains the characteristics of tension relaxation and the beta wave that reflects aroused condition characteristics were looked at. In other words, after obtaining the total power spectrum of a patient's brain waves, the power value of the alpha wave and beta wave areas was obtained by calculating the power ratio of the alpha waves to the beta waves.

The above research study designs were performed after being reviewed and approved by the clinical study research review committee set up in this hospital.

6. Handling of Statistics
The data obtained in this research was handled statistically by paired t-test and repeated ANOVA using SPSS 10.0. The level of significance was set at 5%.

Results

1. Characteristics of the Research Subjects

Of the 20 study subjects that completed the cross-over test and parallel test, 11 were men and 9 were women. The average age was 40.30 years and the average period of experiencing the fatigue disorder was 3.64 months. The average depression and anxiety scores were 5.0 and 4.85 respectively, the

Bepsi stress score was 1.86 and the fatigue score using FSS was an average of 3.55. (Table 1)

Table 1. Baseline Data of Subjects

Variables
Number (%)

Sex
Male 11 (55%)
Female 9 (45%)

Mean .SD

Age (year) 40 . 6.24
FSS index 3.55 . 1.44
Duration of fatigue 3.64 . 5.99

(month)
Hospital

Depression
5.00 . 2.34

Anxiety 4.85 . 2.03
Bepsi stress index 1.86 . 0.47

2.
The Correlation between Fatigue Level and Stress, Depression, Anxiety and Alpha/Beta Power Values
The fatigue level showed a significant positive correlation to stress and anxiety and also showed a positive correlation to the depression score but it was not significant. The Pearson correlation coefficients
between the level of fatigue and stress, anxiety and depression scores were 0.529, 0.416 and 0.123, respectively.

As a result of obtaining the Pearson correlation coefficient between the level of fatigue and the alpha/beta power values from 15-30 minutes we showed that in both the frontal and occipital regions,
there was a negative correlation and, in particular, at 20 and 30 minutes for the frontal region, a high negative correlation was shown. (Table 2).

3. The alpha/beta power values of the placebo group and the test beverage group
The alpha/beta power value of the test beverage group was measured at 0.90 at 55 minutes in the frontal region which was significantly higher compared to the 0.65 of the placebo group. The alpha/beta
power values of the test beverage group after 35 minutes showed a higher value in the occipital region
compared with the placebo group but this was not significant. (Table 3)

4.
The alpha/beta power values of the placebo group and test beverage group according to the degree of anxiety
Based on the average value for the anxiety score, the group was divided into those below the average value for a low anxiety group and those over the average for a high anxiety group so that the alpha/beta power value between the placebo group and the test beverage group was compared. The

results are as follows:

In the low anxiety group, the 55-minute alpha/beta power value of the test beverage group was higher in both the frontal and occipital regions compared to the placebo group but it was not significant.
(Table 4)

In the high anxiety group, an alpha/beta power value higher than the placebo group was shown continuously in the frontal region. This was significant from 25 minutes until 55 minutes. In the occipital
region, the alpha/beta power value of the test beverage group was continuously higher than the placebo
group starting at 35 minutes but this was not statistically significant. (Table 5)

5. Comparison of fatigue perception in the parallel study

The results of the double-blind random parallel study were shown for 8 people in the placebo group and 12 people in the test beverage group. There were more people that left the study early from the group scheduled to take the placebo in the parallel test and it is something that couldn't be corrected during the performance of the test due to the nature of the double-blind test. The result of performing the parallel test and comparing the basic FSS value with the FSS value measured after taking the beverage for one week is as follows:

The basic FSS value was 3.07 in the placebo group and 3.87 in the test beverage group. As such, it was a little higher in the test beverage group but this is not a significant difference. The FSS after taking the beverage for one week was 2.65 in the placebo group and 3.07 in the test beverage group and as a result the values were reduced by 0.42 and 0.80 respectively and the mentally perceived level of fatigue in each group was reduced. However, the result of performing the paired t-test showed that a statistically significant reduction was only seen in the test beverage group.

Analysis

By measuring externally and recording the electric changes that are accompanied and produced by the activities of brain nerve cells, the movements that occur in varied ways due to the connection from or activity between the nerve cells of the brain, which is at the top of the central control and that oversees mental states, exercise and senses, can be measured. The electric activities of the brain come through filters, such as meninges, transfusion, skull, muscles and skin, and so when the electric potential is compared with the area where the brain waves first occurred, it is greatly reduced and recorded as the total amount of the electric activities in a certain wide area. Also, because the measurement measures the brain having complicated activity variations according to time or various conditions compared to the heart, the testing time becomes longer and the small electric potential variations are amplified and recorded so that artifacts can get mixed in easily. However, in spite of this kind of limitation, brain waves are an objective index to represent brain functioning, and, in particular the activity level of the brain, such as the increase or decrease in activity. Therefore, it can be said to be the most sensitive testing method 21) Jacobs22) has reported that brain waves are a sensitive quantitative measurement tool for stress and relaxation reactions and Siepmann, et al23) said the same about the effects of caffeine.

Brain waves are largely divided, depending on the frequency spectrum, into delta waves (delta wave: 0.2-4 Hz), theta waves (theta wave: 4-8 Hz), alpha wave (alpha wave: 8-13 Hz), beta wave (beta

wave: 13-30 Hz) and gamma wave (gamma wave: 30-50 Hz). It is known that delta waves appear when
sleeping, theta waves when tired, alpha waves when relaxed and beta waves when excited. When in a
relaxed state after closing one's eyes when awake, alpha waves are the main brain waves of healthy adults
and it is normal for these to mix with the beta waves. When awake, the theta and delta waves normally
cannot be seen. When closing one's eye while still, alpha waves are much more pronounced in the occipital region and beta waves increase when feeling anxiety or nervousness. Also, due to the visual stimulation when opening one's eyes, audio stimulation from sound and skin stimulation from pain, etc.,
activity of the whole brain increases so that the alpha waves decrease as a result. This condition of the
alpha wave falling is called .-attenuation. This is known to result from changes in the overall brain cortex activity that occurs because of the ascending reticular activating system or activity of the lower
part of the thalamus.

In this study, the brain waves of the study participants were measured with their eyes open while in a reclining position and while stable. This was to prevent sleep as it is easy to fall asleep while lying with one's eyes closed for an hour. There would have been artifacts introduced due to attenuation resulting from a certain amount of visual stimulation and eye blinking due to measuring with the eyes
open. While analyzing the brain waves, data were used to remove these kinds of artifacts through filtering.

Also, the brain waves are known to fluctuate widely according to the external environment and time so
that after applying the brain wave electrodes and administering the drink, the actual brain wave measurements and data collection were done after an adaptation time of about 15 minutes. The cross-over
tests were carried out as much as possible on the same day of the week and the same time. The measured
brain waves were analyzed on data obtained in the frontal region and occipital region respectively and the
alpha/beta power values obtained.

In Japan where green tea has been traditionally enjoyed, it was widely regarded that drinking green tea relaxes emotional nervousness but tests that could establish a basis for this kind of effect were
very rare. Ito, et al selected four people from a low anxiety group and four people from a high anxiety
group and administered placebo and L-theanine in 50mg and 200mg doses each in tests to analyze alpha
waves but there was almost no increase in alpha waves in the occipital and parietal regions when administering 50 mg. But he reported that when administering 200 mg, the alpha waves increased remarkably beginning 40 minutes after administration and this kind of effect was much more pronounced
in the high anxiety group and is similar to the results of this study. However, this effect was not significant in the occipital region in this study and there was a difference in the frontal region but this is
thought to be because the testing was done with the subjects' eyes open to prevent them from becoming
drowsy and in contrast with the testing by Ito, et al 24) where the eyes of the subjects were closed for
testing.

It has been confirmed that if L-theanine is taken, it enters the blood after being absorbed in the intestines and then passes through the brain blood barrier to enter the brain. 11, 25) At that time, it can be
inferred that this is brought about by the reduction in serotonin and an increase in norepinephrin so that
the administration of L-theanine creates a relaxed state but not a sleepy state.26) The effect of increased
alpha waves for L-theanine in this way appears to be much more effective for calming the central nerves
when anxiety is high.

Furthermore, in this study, in order to find out if there is an effect of L-theanine on the perception of the level of fatigue, the fatigue level was measured after taking 200 mg each day of L-theanine for seven days. The first basic level of fatigue value score showed that both the group that took the placebo
and the group that took L-theanine showed a reduction in the score for the perceived level of fatigue of
13.6% and 20.7%, respectively. However, the paired t-test showed that this was statistically significant
only in the L-theanine administered group and it is thought that L-theanine has a certain effect in improving the perceived level of fatigue. This kind of improvement in the perceived fatigue level is

thought to relate to a reduction in mental strain and so the result of investigating the correlation in the
cross-over test of this study between the alpha/beta power value from 15 to 30 minutes after taking the
placebo and the level of fatigue showed that in both the frontal and occipital regions there is a negative
correlation and the increase in the alpha/beta power value forms the basis for there being a relationship
with an improvement in the perceived fatigue level.

In this study, the result of looking at the improvements in mental relaxation and perception of the level of fatigue from L-theanine through double blind, cross-over and parallel testing showed that a functional beverage containing 200 mg of L-theanine causes an increase in alpha waves which are known
to be related to mental relaxation and concentration ability and, in particular, where it is accompanied by
light or severe anxiety, it can be confirmed that the alpha wave increase effect is much more enhanced.
Furthermore, there was a significant result even in the improvement of personal perception of the level of
fatigue. It is thought that, in the future, it will be necessary to carry out studies that can reveal the physiological causes and more wide-ranging effects of L-theanine on a larger number and wider range of
study participants.

Reference
[Translated References]

4.
Yeong-Bok Kim, Byeong-Woo Kim: “Statistical Analysis of the Causes of Chronic Fatigue in Laborers.” South
Cholla Medical College Journal, 1986; 23: pp. 605-17.
5.
Ho-Cheol Shin, Hwan-Seok Choi, Chang-Jin Choi, Sang-Wook Song: “Analysis of Patients Visiting Outpatient
Family Medical Clinics Complaining Mainly of Fatigue.” Family Medicine Journal, 1993; 14: pp.833-42.
6.
Cheol-Hwan Kim, Ho-Cheol Shin, Yong-Woo Park:“Causes of Chronic Fatigue and Chronic Fatigue Syndrome.” Family Medical Journal. 2000; 21: pp. 1288-97.
7.
Bang-Boo Yoon, Mi-Gyeong Oh, Seon-Gyu Kim, Jae-Yoon Lee: “Results and Relationships between Chronic
Fatigue and Clinical Exams in Health Examinees.” Family Medical Journal. 1999; 20: pp.978-90.
16. Se-Man Oh, Gyeong-Joon Min, Doo-Byeong Park: “Standardization Research Regarding Hospital Anxiety-
Depression Scale.” Neuropsychiatric Medical Journal. 1999; 38: pp. 289-96.
20. Jee-Hyeok Im, Jong-Myeon Bae, Soon-Shik Choi, Seong-Weon Kim, Hwan-Shik Gwang, Bong-Ryeol Huh:
“Suitability of the Korean Version of BEPSI Survey (Revised Version) as a Tool for Measuring Stress in Outpatients.” Family Medical Journal. 1996; 17: pp.42-9.
21. Seon-Ho Han, Saito S.: “Clinical Brain Waves”; 2nd Ed. Seoul: Il-Jo-Gak, 1992.
2A

a = Cross Over Study
b = parallel study
c = test medication
d = placebo medication
e = dosage/administration
f = 60 minutes
g = 7 days
h = 4 – 5 days
i = Exam 1
j = Rest period
k = Exam 2
l = Exam 3

[insert diagram bottom of page Vol.23, No. 5, 639]