THE EFFECT OF ORAL SUPPLEMENTATION OF L-THEANINE AND STRESS FORMULA VITAMIN ON THE STRESS REDUCTION

WIPORN MONGKONSRITRAGOON

MASTER OF SCIENCE
IN
ANTI-AGING AND REGENERATIVE SCIENCE

SCHOOL OF ANTI-AGING AND REGENERATIVE MEDICINE
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ACKNOWLEDGEMENTS

I would first like to thank my advisor Dr. Karnt Wongsuphasawat. He is consistently available whenever I had question about my research or writing. He also steered me in the right direction whenever he thought I needed it.

I would also like to thank the expert who involved in the validation of all statistics and analysis of this independent study Asst. Prof. Dr. Tawee Saiwichai. Without his validation and advice, my study could not been successfully concluded.

I would also like to acknowledge Asst. Prof. Dr. Phakkharawat Sittiprapaporn as the main reader of this study, and I am gratefully indebted to his valuable comments on every detail.

Finally, I must express my very profound gratitude to my family for providing me with unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this independent study. This accomplishment would not have been possible without them. Thank you.

Wiporn Mongkonsritragoon

Independent Study Title	The Effects of Oral Supplementation of L-Theanine and Stress formula Vitamin on The Stress Reduction
Author	Wiporn Mongkonsritragoon
Degree	Master of Science (Anti-Aging and Regenerative Science)
Advisor	Karnt Wongsuphasawat, B. Pharm., Ph. D.

ABSTRACT

L-Theanine is an amino acid contained in green tea leaves which is known to block the binding of L-glutamic acid to glutamate receptors in the brain. Because the characteristics of L-Theanine suggest that it may influence psychological and physiological states under stress, thus this study aimed to elucidate possible effects of L-Theanine compared with Stresstab which known as multivitamins on acute stress which activated by a mental arithmetic task: an acute stressor. Then, twenty good health volunteerss underwent two separate trials: one in which they took L-Theanine and one in which they took multivitamin (Baseline). The experimental sessions were performed by randomized and single-blind experiment. Our study showed that L-Theanine and multivitamin can reduce the Heart Rate Variability (HRV) stress index at the each time point period of mental arithmetic task (Rest 1, Rest 2), which is in good agreement with the Multivitamins. When compared the difference of HRV stress index of stress reduction at Rest 1 group (20 minutes after stress task) and Rest 2 (40 minutes after stress task) between L-Theanine and Multivitamins, HRV Stress index both groups, the result showed that L-Theanine group gave a difference of HRV between Task and Rest 2 higher than Multivitamins group (8.05±4.31 and 1.6±1.17, $p<0.05$), significantly. Comparisons stress reduction between L-Theanine and Multivitamins group, result

showed that HRV stress index value in L-Theanine was decreased continuously in each time point period from Task = 55.65 (± 11.85), Rest 1 = 52.95 (± 12.21) and Rest 2 = 47.6 (± 12.99). Between group for dependent use paired t-test showed a significant difference in mental arithmetic task testing (Task) group and Rest 2 group at ($P<0.05$). Then in this study suggest the possibility the effect of oral intake of L-Theanine and Multivitamin could reduce the HRV stress index, activated by mental arithmetic task, in a dose and time dependent fashion. In addition, this study suggested that L-Theanine and Multivitamin have an anti-stress property and moderate mechanism via the inhibition of cortical neuron excitation.

Keywords: Heart Rate Variability (HRV)/Stress index/L-Theanine/Mental arithmetic task/Stresstab/Stress formula vitamin

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CHAPTER 1

INTRODUCTION

1.1 Research Background

Stress is kind of reaction to stimulation which can affect our physical or mental balance. Anxiety and stress are weakening conditions that can shorten one's life decreasing performance, well-being, and the total enjoyment of all activity too. Stress can also lead an inability to perform mental jobs and may also cause frustration, the outcome in reactions to situations, unfriendliness, and harm. Stress can damage the immune system while decreasing resistance to disease and create the possibilities for opportunistic diseases to happen. Stress can cause melancholy too. A pressure that is cause from stress can trigger fight response, creating hormones adrenaline and cortisol to surge through the body. A short term small of stress, known as "acute stress," it is exciting, keeps people active and alert. But long-term, or "chronic stress," can have detrimental effects on health (Carlson, 2013) and The American Institute of Stress (n.d.)

Generally, stress is related to both external and internal factors. External factors include the physical environment, including your job, relationships with others and all the situations, challenges, difficulties, and expectations people confronted with on a daily basis. Internal factors determine body's ability to respond to, and deal with, the external stress-inducing factors. Internal factors that influence ability to handle stress include nutritional status, overall health and fitness levels, emotional well-being, and the amount of sleep and rest.

From the previous times, it should be the study drinking green tea brings relaxation. The substance that is responsible for a sense of relaxation, is theanine (Yamane et al., 1991; Cooper, Morre & Morre, 2005). L-Theanine, one of the major amino acids contained in green tea and the main component responsible for the exotic

taste of ‘green’ tea. It was found that L-Theanine administered intraperitoneally to rats reached the brain within 30 min without any metabolic change. The biochemical characteristic of L-Theanine administered was proposed by Yokogosh, Kobayashi, Mochizuki & Terashima, (1998); Yokogoshi, Mochizuki & Saitoh (1998) and they reported that L-Theanine could pass through the blood–brain barrier, and that it increased by 1 h at the latest in serum, the liver, and the brain after administration, thereafter decreasing sharply in the serum and liver but only beginning to decrease in the brain 5 h after administration. Theanine also acts as a neurotransmitter in the brain and decreased blood pressure significantly in hypertensive rats. In general, animals always generate very weak electric pulses on the surface of the brain, called brain waves. Brain waves are classified into four types, namely α, β, δ and θ-waves, based on mental conditions. Generation of α-waves is considered to be an index of relaxation. In human volunteers, α-waves were generated on the occipital and parietal regions of the brain surface within 40 min after the oral administration of L-Theanine (50–200 mg), signifying relaxation without causing drowsiness (Juneja, Chu & Okubo, 1999; Kakuda, Nozawa & Unno, 2000; Mason 2001).

Stresstabs® is Stress formula vitamin supplement. It works by providing extra vitamins to the body and Stresstabs® has been trusted brand to help reduce everyday stress. Stress robs the body of essential nutrients and may contribute to sleeplessness, lack of concentration and irritability. Mostly all natural mineral can help to increase the body's resistance to physical, emotional and mental stressors and promotes balance in the body after stress occurs. The result is the ability to relax, revitalize and rejuvenate the body naturally. Stress formula vitamin and ingredient in Stresstabs Energy is included in the proper subcategory. The body to facilitate energy, cardiovascular health and cellular health, but adding more of these vitamins in supplement form will not promote better health uses these ingredients naturally. The useful of Stress formula vitamin of Stresstabs is Immune Strength. Zinc and vitamin C are commonly supplemented to reduce the chance of catching the common cold or reduce the time it takes to recover from the common cold (Stresstabs’s product information, n.d.)

Now a day consumers are looking for all natural supplement that effect on increasing energy and reduce stress level that would be better than served with a cup of 100 baht coffee. Coffee contains caffeine and caffeine increases energy for up to 12 hours but Stress formula vitamin and L-Theanine are taken once a day and the vitamins in the supplement will be pushed out of the body in just a few hours. By the way the effect of reducing the stress level, their mechanisms are still unclear. Then in this study have emphasized to L-Theanine and Stress formula vitamin and study by comparing the effect of reducing of stress between these supplements.

1.2 Research Objectives

1.2.1 To compare effect of L-Theanine and Stress formula vitamin on stress reduction amongst healthy subjects.

1.2.2 To examine the possible effects in a laboratory setting using a mental arithmetic task as an acute stressor compared between L-Theanine and Stress formula vitamin.

1.3 Beneficial Outcomes of the Study

1.3.1 Can take the results from this study to be the data for reference to compare L-Theanine and Stress formula vitamin with their effect on stress reduction and better understand more about the effect of L-Theanine and Stress formula vitamin on stress reduction.

1.3.2 Can to be a reference data for another research in the future

1.4 Hypothesis

L-Theanine might be better than Stress formula vitamin on stress reduction.

1.5 Operational Definitions

Baseline**:** The recording at 20 minutes rest then start recording for Baseline

Task: Take L-Theanine or Stress formula vitamin and performed a mental arithmetic task for 10 min, then recording HRV

Rest 1: The recording HRV again after resting 10 minutes

Rest 2: The recording HRV again after resting 40 minutes from task

HRV: The analysis for stress measurement are come form many information and finally all data were calculating as the stress index value

1.6 Conceptual Framework

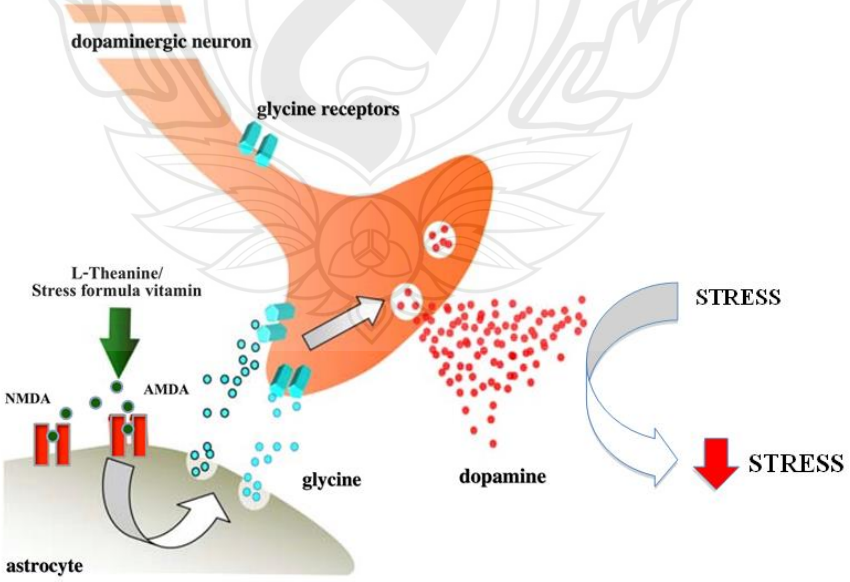

Figure 1.1 Conceptual Frameworks

The possibility hypothsis is L-Theanine and Stress formula vitamin can act as the sympathetic activity during acute stressor induced by mental arithmetic stress task and L-Theanine can reduce psychological and physiological stress responses.

1.7 Limitation on this Independent Study

Limitation in term of the duration of the study and some volunteer has headache after taking supplement and have to exclude from this study.

1.8 Term of Definitions

1.8.1 L-Theanine is a kind of amino acid that contains in green tea leaves which is known on blocking the binding of L-glutamic acid to glutamate receptors in the brain.

1.8.2 Stresstabs is Stress formula vitamin supplement. It works by providing extra vitamins to the body and Stresstabs® has been trusted brand to help reduce everyday.

1.8.3 Stress is a feeling of strain and pressure. The small number of stress may be wished, beneficial, and even healthy. The stress plays an important role in motivation, adaptation, and reaction to the environment. Excessive number of stress led to harmful to body. Stress also can increase the risk of strokes, heart attacks, ulcers, and mental disorders such as depression. (Sapolsky & Robert, 2004).

1.8.4 Arthemetic task is the computerized mental arithmetic task based human stress level detection using physiological signal, it served as physical or psychological stressors.

1.8.5 HRV stress index is Stress index is expressed as the combination of index with Pulse diversity, measured data analysis, distribution and autonomic nervous balance by measuring Heart Rate Variability (HRV) which determined by breathing, baroreceptor, chemoreceptor and variation of autonomic nerves' activity.

CHAPTER 2

LITERATURE REVIEW

2.1 Stress

Stress is often described as a feeling of being overloaded, wound- up tight, tense and worried. We all experience stress at times. It can sometimes help to motivate us to get a task finished, or perform well. But stress can also be harmful if we become over-stressed and it interferes with our ability to get on with our normal life for too long. Stress is becoming the single greatest cause of occupational disease (Leigh & Schnall 2000) and can have far-reaching consequences for both the worker and the workplace. Stress occurs when external demands and conditions do not match a person's needs, expectations or ideals or exceed their physical capacity, skills, or knowledge for comfortably handling a situation (French, Caplan & Harrison, 1982). The chronic exposure of employee to stressful situations such as work poor supervisory, overload, were effected to low input making decision and prospectively linked to a range of emasculation health outcomes, including depression, anxiety, emotional imbalance, immune deficiency disorders and cardiovascular disease (Sapolsky & Robert, 2004; Michie & Williams, 2003). Stressful working conditions have indirect effect to employee well being by limiting an individual's ability to make positive changes to lifestyle behaviors or by directly contributing to negative health behaviors (Landsbergis et al., 1998).

2.1.1 The signs of stress

When facing with the stressful event, human bodies will respond by activating the central nervous system and induce the hormones release such as adrenalin and cortisol. These hormones cause physical changes and help us to react quickly and effectively to get through the stressful situation. This phenomenal sometimes called the

‘fight or flight’ response. The hormones will effect to heart rate, breathing, metabolism and muscle tension and blood pressure. Finally the pupils dilate and our perspiration rate increases. During these physical changes, this sign help us try to arrange with stressful situation, they can cause other psychological symptoms if the stress is ongoing and the physical changes don’t settle down.

These symptoms can include:

1. Headaches, pain and other ache
2. Sleep disturbance, insomnia
3. Stomach ache, digestion problem, diarrhea
4. Difficulty concentrating
5. High blood pressure
6. Anger, petulant
7. Depression
8. Fatigue
9. Overwhelmed and out of control
10. Low self-esteem, lack of confidence
11. Moody, Anxiety
12. Weakness of immune system
13. Heart disease

2.1.2 Type of Stress

There are different types of stress; acute stress, episodic acute stress and chronic stress. Each type of stress has its own characteristics, symptoms, duration and treatment approaches.

2.1.2.1 Acute stress

The most common of stress is acute stress. It comes from demands and pressures of the recent past and anticipated demands and pressures of the near future. Acute stress is thrilling and exciting in small doses, but too much is exhausting. For example, riding a roller coaster in a theme park, for instance, is a situation that brings about acute stress, yet brings excitement. Overstate on short-term stress can lead to psychological anxiety, stomach problem, tension headaches and other symptoms.

Acute stress is short term and acute stress doesn't have enough time to do the extensive damage associated with long-term stress. The most common symptoms are:

1. Emotional anxiety and depression, sometime combination of anger or petulant

2. Muscular problems, the tension of muscular lead to pulled muscles and tendon and ligament problem then occur headache, back pain, jaw pain.

3. Digestion problem, stomach, gut, bowel problems for example acid stomach, heartburn, diarrhea, constipation, irritable bowel syndrome and flatulence.

4. Transient over arousal, it may leads to elevate the blood pressure, increase heartbeat rapidly, heart palpitations, dizziness, migraine headaches, cold hands or feet, shortness of breath and chest pain.

2.1.2.2 Episodic acute stress

Another form of episodic acute stress comes from ceaseless worry. “Worry warts” see disaster around every corner and pessimistically forecast catastrophe in every situation. The world is a dangerous, unrewarding, punitive place where something awful is always about to happen. These “awfulizing” also tend to be over aroused and tense, but are more anxious and depressed than angry and hostile. The symptoms of episodic acute stress is the symptoms of extended over stimulate: persistent tension headaches, migraines, hypertension, chest pain and heart disease. Treating episodic acute stress requires intervention on a number of levels, generally requiring professional help, which may take many months. The episodic acute stress is normally seen in people who make self-inflicted, insensible demand or unrealistic which get all enlarge and bring too much stress in their attempt to accomplish these goals. Episodic stress is not like chronic stress because this type of stress causes from time to time which not as frequently as acute stress does.

Episodic stress is typically observed in people which personality “Type A” and involves with over aggressive, competitive, demanding, tense and hostile. These symptoms of episodic stress are found in Type A persons. These include long-term periods of intermittent depression, anxiety and emotional disorders, aggressiveness, impatience, a harrying sense of time urgency and persistent physical symptoms similar

to found in acute stress. Friedman et al. (1985) and Ragland and Brand (1988) found Type A's to be much more likely to develop coronary heat disease than Type B's, it will show the opposite symptom of behavior. Following their responses, and their manner, the participant can separate into one of two groups:

Type A behavior: Aggressive, Impatient, Competitive, Ambitious,.

Type B behavior: Relaxed, Non-competitive.

2.1.2.3 Chronic stress

As the acute stress can be thrilling, dangerous, unhealthy and exciting but chronic stress is not. It is the strongly stress that made people away day after day, year after year. Chronic stress destroys human bodies, minds and human life. It destroys destruction through long-term wearing-down and chronic stress can occur when a person can't find the way out of a distressed situation. Chronic stress involves with relentless demands and pressures for apparently prolonged periods of time. Some chronic stresses occur from traumatic, early childhood experiences that become internal and remaining forever painful until present time. Even though sometimes people can get chronic stress, and they may do not notice it so much, then it continues to wear people down and has a negative effect on their relationships and their health.

The worst aspect of chronic stress is that people get used to it. They forget it's there. People are immediately aware of acute stress because it is new; they ignore chronic stress because it is old, familiar, and sometimes, almost comfortable. Chronic stress can lead to people suicide, violence, heart failure or heart attack, stroke and even though cancer. People wear down to a final, fatal breakdown. Because physical and mental resources are depleted through long-term attrition, the symptoms of chronic stress are very difficult to treat and it require extended medical as well as need to get the behavioral treatment and stress management too. (Adapted from The Stress Solution Pocket Books by Miller, Lyle and Alma (1993) Several studies have suggested that psychological stress that influenced by occupational stress induced production of reactive oxygen species (ROS) (Irie, Asami, Nagata, Miyata, & Kasai, 2001; Inoue et al., 2010). Chandola, Siegrist & Marmot (2005) proposed that job stress is as one of the major risk factors for coronary heart disease (CHD). Oxidative damage is a one of major risk factor for CHD, atherosclerosis and hypertension increased vessel wall

oxidative stress (Kao et al., 2010). Inoue et al. (2010) reported that oxidative damage may be one of mechanisms linking job stress with CHD.

2.1.3 How to manage the stress

The method learn to handle stress in healthy ways is very important. It is easy to learn simple techniques that help and these include recognizing and changing the behaviors that lead to stress, as well as using the techniques for reducing stress when it has occurred.

2.1.3.1 Identify warning signs

It is very helpful to be able to identify early warning signs in your body that tell you when you are getting stressed. The warning sign is vary from person to person, but might include behaviour like tensing jaw, grinding teeth, getting headaches and sometime have symptom with feeling irritable and short tempered.

2.1.3.2 Identify triggers

There are often known triggers that raise our stress levels and make it very difficult for managing. If you know what triggers are, it can object to anticipate stress and practice calming down beforehand, or even find the ways of removing the trigger. Triggers might include late nights, deadlines, seeing particular people, hunger or over-tired children. The method routines to manage with stress are including below:

1. Regular exercise and need to relaxation when fighting with stress
2. Spending time with people you care about, and who care about you, is an important part of managing progressing stress in your life.
3. Regular meal times, waking and bedtimes
4. Spend time with your friends and family, especially those you find uplifting rather than people who place demands on you.
5. Share your thoughts and feelings with others when opportunities arise. Don’t ‘bottle up’ your feelings.
6. Make sure you are eating healthy food and getting regular exercise.
7. Take time to do activities you find calming or uplifting, such as listening to music, walking or dancing.
8. Avoid using alcohol, tobacco or other drugs to cope.

2.1.3.3 Practice relaxation to manage the stress

Notice when you are using unhelpful self-talk, and instead try saying something, calming down yourself to reduce the levels of stress. Try more helpful self-talk like ‘I’m coping well given what’s on my plate’, or ‘Calm down’, or ‘Breathe easy’. Keeping things in perspective is also important. When we are stressed, it’s easy to see things as worse than they really are. Try self-talk such as ‘This is not the end of the world’ or ‘In the overall scheme of things, this doesn’t matter so much’. Then practice to relaxation, it will help your body and nervous system to settle and readjust. Consider trying some of the following things:

1. Learn a formal technique such as progressive muscle relaxation, meditation or yoga.

2. Make time to absorb yourself in a relaxing activity such as gardening or listening to music.

3. Plan things to do each day that you look forward to and which give you a sense of pleasure, like reading a book.

2.2 L-Theanine

In recent years, various healthful effects of the ingredients contained in green tea have been scientifically verified (Yamane et al., 1991; Cooper et al., 2005). L-Theanine, one of the major amino acids contained in green tea, has been a focus of attention due to its physical characteristics. As a biochemical characteristic of this substance, Yokogoshi, Kobayashi et al. (1998), Yokogoshi, Mochizuki et al. (1998) reported that L-Theanine could pass through the blood–brain barrier, and that it increased by 1 h at the latest in serum, the liver, and the brain after administration, thereafter decreasing sharply in the serum and liver but only beginning to decrease in the brain 5 h after administration. Furthermore, another study reported that L-Theanine could influence the secretion and function of neurotransmitters in the central nervous system even at 30 min after oral administration (Terashima, Takido & Yokogoshi, 1999). L-Theanine binds to the glutamate receptor subtypes (AMPA, kainate, and NMDA receptors) and it blocks the binding of L-Glutamic acid to the glutamate

receptors in cortical neurons (Kakuda, Nozawa, Sugimoto & Nino, 2002). Despite the lower affinity of L-Theanine with receptor subtypes than with L-Glutamic acid (about 80-fold lower with the AMPA and kainate receptors, and about 30,000- fold lower with the NMDA receptor), several reports demonstrating the neuroprotective effect of L-Theanine in cortical neurons via the antagonistic role (Kakuda et al., 2000; Nagasawa et al., 2004) suggest the functional role of L-Theanine in brain dynamics. These chemical and functional characteristics of L-Theanine in the brain suggest that it might down-regulate cerebral functions, at least to a moderate degree.

There are previous animal studies have reported that the administration of L-Theanine reduced blood pressure (Yokogoshi, Kobayashi et al., 1998) and inhibited the excitatory effects of caffeine (Kakuda et al., 2000). Since emotional or physiological states in humans are modulated by the chemical behaviors of neurotransmitters, psychological and physiological states could also be influenced by L-Theanine. Although empirical findings concerning the effects of L-Theanine on human participants have been limited, Kobayashi et al. (1998) reported that the oral administration of 200 mg of L-Theanine resulted in an increase of the a-band component of electroencephalograms (EEG) in the occipital and parietal scalp regions when participants rested in a relaxing state. Furthermore, the observed result that the a-band component of EEG increased more remarkably at 30 min after oral administration was consistent with the result in the animal study showing that neurotransmitters in the brain were affected by L-Theanine 20 min after its administration (Yokogoshi, Kobayashi et al., 1998; Yokogoshi, Mochizuki et al., 1998), and might indicate that there was a time-lag between when L-Theanine was administered and when it took effect.

However, the researchers examined the influence of L-Theanine on EEG only during a resting situation. It is well known that the extracellular level of glutamate in the brain is increased by acute stressors (Lowy, Gault & Yamamato, 1993; Moghaddam, 1993), and it seems likely that such a glutamate increase would also result in facilitation of the activity of the sympathetic nervous system. Considering the competitive role of L-Theanine against excitation of the glutamatergic phenotype, we hypothesized that L-Theanine might be able to reduce stress induced excitation of the peripheral sympathetic activity.

2.3 Stresstabs

Stresstab is stress formula vitamin supplement and works by providing extra vitamins to the body. Mostly all natural mineral can help to increase the body's resistance to physical, emotional and mental stressors and promotes balance in the body after stress occurs. The result is the ability to relax, revitalize and rejuvenate the body naturally. Stress formula vitamin and ingredient in Stresstabs Energy is included in the proper subcategory. The body to facilitate energy, cardiovascular health and cellular health, but adding more of these vitamins in supplement form will not promote better health uses these ingredients naturally. The useful of Stress formula vitamin of Stresstabs is Immune Strength. Zinc and vitamin C are commonly supplemented to reduce the chance of catching the common cold or reduce the time it takes to recover from the common cold. A stress formula vitamin is a preparation intended to supplement a human diet with vitamins, dietary minerals and other nutritional elements. A stress formula vitamin/mineral supplement is defined in the United States as a supplement containing 3 or more vitamins and minerals but does not include herbs, hormones, or drugs, with each nutrient at a dose determined by the Food and Drug Administration and the maximum daily intake that will not cause a risk for adverse health effects. People with dietary imbalances may include those on restrictive diets and those who cannot or will not eat a nutritious diet. Pregnant women and elderly adults have different nutritional needs than other adults, and their physicians may indicate it would be beneficial for them to take a stress formula vitamin.

The effects of stress formula vitamins are usually only studied in elderly people. A recent study assessed the relationship between stress formula vitamin supplementation and psychological functioning in healthy, non-elderly adults. Included in the study were 215 men aged 30 to 55 years who were employed full-time. The men received either a proprietary stress formula vitamin or a placebo for 33 days. Both groups were tested at the beginning of the study and at the end with a battery of mood, stress and health questionnaires and with physical and mental tasks that included mental arithmetic. The results revealed that after 33 days the group who received the stress formula vitamin reported significantly improved ratings of general mental health,

reduced subjective stress and increased ratings of ‘vigour’, with a strong trend towards an overall improvement in mood. The supplementation group also performed better on the cognitive function tests. The placebo group did not report significant changes in any area that was tested. These results seem to suggest that stress formula vitamin supplementation may improve ratings of stress, mental health and cognitive performance in adults who are otherwise healthy (Kennedy, Veasey & Watson, 2010). A growing literature has indicated that chronic stress formula vitamin supplementation can benefit cognition (Grima, Pase, Macpherson & Pipingas, 2012) and mood (Long & Benton, 2013). Randomised controlled trials have demonstrated that supplementation with stress formula vitamins containing minerals and herbs, over a period of 2 to 4 months, can enhance various domains of memory in those over the age of 50 (Harris et al. 2012; Macpherson, Silberstein & Pipingas, 2012; Summers, Martin, Cunningham, DeBoynton & Marsh, 2010). In men aged 50-69 years, 8- weeks stress formula vitamin/mineral and herbal (MVMH) supplementation has been shown to reduce symptoms of mood disorder, problems with day-to-day functioning and increase positive mood experience (Harris et al., 2011)

2.4 Previous Related Studies

Stress is defined as a state of mental, emotional strain and tension resulting from adverse or demanding circumstances (Exercise stress test, 2013). It is known that stress can induce increased blood pressure by stimulating the nervous system to produce the hormone. In the modern society is interested in natural, nutritional, healthy foods and many kinds of food ingredients have become widely used for promoting health benefits. Then L-theanine and stress formula vitamin became the popular items since its multiple roles in the central and autonomic nervous systems received attention. Animal studies have revealed that L-Theanine affected dopamine and serotonin concentrations in the brain, underlying its anxiolytic effect (Yokogoshi, Kobayashi et a., 1998; Yamada, Terashima, Okubo, Juneja & Yokogoshi, 2005). The study by Ito, Nagato and Aoi, (1998), crossover, randomized, placebo controlled design study, they have investigated the effects of orally administered L-Theanine (200 mg of Suntheanine standardized at

99% L-Theanine) compared with placebo on mental task performance stress conditions. The results showed that L-Theanine significantly changed both systolic and diastolic blood pressures in the high-response group after mental tasks compared with the placebo group. The assessment of the Profile of Mood States after mental tasks demonstrated that L-Theanine reduced the Tension-Anxiety scores when compared with placebo. According to the Yoto, Motoki, Murao and Yokogoshi (2012), the results suggest that L-Theanine able to reduce anxiety levels, also attenuates increased blood pressure in high-stress response (Yoto et al., 2012).

For the Stress formula vitamin supplement are commonly found in stress formula vitamin formulas, suggesting that stress formula vitamin supplementation may be able to improve mood and these food sources contain dietary antioxidants that can prevent, inhibit or repair damage caused by oxidative stress (Ames, 1983; Bourre, 2006). Oxidative stress is an imbalance or disruption in the redox state (oxidation/ reduction reactions) within cells causing impaired signaling and regulation, resulting in impaired functioning (Sohal & Orr, 2012). The maintenance of redox homeostasis is essential for healthy cellular function. Antioxidant vitamin C levels are particularly high in the brain and are needed for the transformation of dopamine into noradrenalin as well as the production of some neurotransmitters. Vitamin E is a lipid soluble antioxidant, which has neuroprotective effects against free radical damage, preventing cellular injuries to the brain related to oxidative stress (Cantuti-Castelvetri, Shukitt-Hale & Joseph, 2000). Vitamins E and A protect against lipid peroxidation, a damaging process affecting the permeability of cell membranes (Mariani, Polidori, Cherubini & Mecocci, 2005). Vitamin C works synergistically with B group vitamins and is vital for the metabolism and utilization of folate/folic acid (Huskisson, Maggini & Ruf, 2007). The Stress formula vitamin supplement or multivitamins were found to enhance immediate free recall memory but no other cognitive domains (Grima et al., 2012) and can be used as part of a treatment program for stress-related symptoms at the recommended dose (Schlebusch et al., 2000).

2.5 Instruments

2.5.1 L-Theanine and Stress formula vitamin.

Materials come in tablet form. The tablet was taken with 200 ml. non-carbonated water. The safety of the oral administration of L-Theanine has been has been proven in numerous medical reports like those at NYU and Harvard, L-Theanine does not present significant side effects and confirmed by many toxicological research (Yoto et al., 2012). We decided to use this particular dose because many research reported that it has a significant anti-anxiety effect in humans (Lu et al., 2004, Ritsner et al., 2011, Heese et al., 2009)

In this study we used NUTRAKAL Zen® (L-Theanine 50mg tablet) and StressTab® (Multivitamins tablet)

2.5.2 HRV and stress measurement tool

With HRV's usefulness as an evaluation tool of autonomic nerves, it is widely used on stress researches. As Selye and Cannon, etc. put it, it is because stress reaction appears as biochemical physiology response in a human body through the response between HPA axis and autonomic nerves. The failure or abnormality of autonomic nerves is related to many of stress symptoms and diseases including depression, fibromyalgia, sensitive, colon syndrome, anorexia, dizziness, orthostatis low blood pressure, diabetes, low pressure, anxiety, asthma, high blood pressure, insomnia and irregular pulse, etc.

Stress consists of many types, and HRV is being widely used, in particular, for researches on chronic occupational stress. If death from overwork or Sudden Cardiac Death, or SCD taken for example, the failure of heart rhythm control is a major cause in the case of SCD and it is HRV that evaluates heart rhythm control.

The trend of existing researches on occupational stress is as follows:

1. Man-made causes/mental work load: influence on HRV of experimental demand (Work Demands)

2. Dynamics research on cardiovascular diseases: influence on CHD on cardiovascular control failure

3. Occupational stress - industrial and medical research: how mental and social work character influences directly or indirectly in three ways. Albeit significant results from those approaches, they failed to determine pathophysiology of mental and social causes including occupational stress on SCD, coronary artery diseases. Still, as HRV analysis methods develop, because autonomic nerves could be the evaluation of physiological mechanism to control heart functions, it aims to evaluate the influence of environmental stress employees go through (Belkic et al., 2000, Brisson, Larocque, Moisan, Vézina & Dagenais, 2000).

2.5.2.1 HRV Stress index analysis:

HRV analysis for stress measurement are come form many information and finally all data were calculating as the stress index value. In this study we use Max Pulse scanning device as tool for analysis of HRA. Max Pulse is a device in assisting health-care practitioners, technicians, and individuals in the early detection of cardiovascular related issues. The test will also help assess nutraceutical and/or pharmaceutical needs. Through periodic screenings and lifestyle changes (i.e. exercise, diet, and supplementation etc.), one is able to monitor the effectiveness of these changes and how they relate to the person's cardiovascular, autonomic and overall health status. The source information for HRV analysis is continuous beat-by-beat (not averaged) recording of heartbeat intervals. There are many ways to measure and record those intervals. However two such methods are found to be the most appropriate for this. Pulse wave analysis is way of measuring heartbeat intervals. It is a simple and least invasive method of measurement based on photoplethysmograph (PPG). PPG is a signal reflecting changes in a blood flow in tiny blood vessels typically spotted in fingertips or earlobes. Typical PPG sensor emits infrared light towards the skin area of an earlobe or finger. The blood passing through this area through numerous tiny vessels absorbs certain portion of that light while remaining light is detected by a special photocell. The amount of absorbed light is proportional to the amount of blood passing by. Since the blood flow is not constant due to pulsations caused by heartbeats the sensor generates a very specific waveform reflecting those changes in blood flow. This waveform is usually called as a pulse wave. A special algorithm to derive beat-by-beat heartbeat intervals can process this waveform. The Result analysis for stress index in this study have the detail for measurement stress response bellow;

2.5.2.2 Plus Change and Pulse diversity.

Pulse change means a graph recording the change in heart rate. Pulse diversity represents the complexity of graph, it means the diversity of heart rate forms and also reflected resistance of the external environment such as stress.

2.5.2.3 Autonomic nervous system.

Graph represents to the tested measurement of sympathetic activity (LF) and Para-sympathetic activity (HF) and the ratio balance between LF/HF compared with the standard deviation of normal subjects value in the system.

2.5.2.4 Distribution of heart rate

To evaluation of heart rate by distribution heart rate and compared with good sample data, excessive stress state in the system.

2.5.2.5 Autonomic nervous Balance

The result of measuring data analysis will place on 9 areas for evaluation the state of stress (Good example or Excessive stress state).

2.5.2.6 Stress index

Stress index is expressed as the combination of index with Pulse diversity, measured data analysis, distribution and autonomic nervous balance.

The many studies in acute stress, changes in several autonomic parameters, such as blood pressure (BP) and heart rate pulse, have been evaluated when subjects were engaged in acute stress tasks such as the mental arithmetic, a stroop task, and a cold pressor task, the speaking in public speaking (Atanackovic, Brunner-Weinzierl, Kröger, Serke & Deter, 2002; Bosch, Berntson et al., 2003, Bachen et al., 1992; Herbert et al., 1994; Breznitz et al., 1998; Willemsen et al., 1998, 2002; Winzer et al., 1999; Bosch, de Geus et al., 2003) In this study we attempted to estimate activity in the autonomic nervous system during the task by analyzing heart rate variability (HRV). HRV describes the variations between consecutive heartbeats, and has been widely used as a quantitative marker of the autonomic nervous system (Task Force of the European Society of Cardiology, The North American Society of Pacing and Electrophysiology, 1996). The former is related to respiratory sinus arrhythmia and is exclusively attributable to parasympathetic influence reflecting vagal activity, while the latter mirrors the baroreceptor feedback loop that controls blood pressure and appears to reflect both sympathetic and parasympathetic activity. However, the relative

contribution of LF and HF power (LF/HF) was thought to reflect the sympathovagal balance. We observe the decreasing in the HF component and a remarkably increased LF/HF ratio during the task indicated that the sympathetic nervous system was prominently activated by this task. Moreover, the stress task successfully induced not only a physiological stress state, but also subjective stress feelings and state anxiety. Thus, this experimental protocol allowed us to evaluate the possibility that L-Theanine could be effect to autonomic activity and subjective stress feelings during an acute stress challenge in subjects. In the present study, we measured the mental arithmetic stress intensity, HRV as a indices of acute stress responses, and examined in each time point resting period effect of L-Theanine and Stresstab on such responses by asking participants to drink a cup of water containing L-Theanine or Stresstab before the mental arithmetic stress started.

Short term Heart Rate Variability, or HRV is determined by breathing, baroreceptor, chemoreceptor and variation of autonomic nerves' activity. The influence of autonomic nerves affects sinus node automatism changes every moment according to internal/outside environmental change. This is called Heart Rate Variability. Its clinical usefulness is shown on the ongoing researches since Hon and Lee reported in 1965 that under fetal distress status, change of interval between heart rates comes ahead of heart rate change itself. Researches on relationship with a heart have been undergone, but recently the usefulness in the department of psychiatry brought up. Determining the level of activity or balance in sympathetic and parasympathetic nerves might be used as very useful information for treatment and prognosis. These possibilities led to a clinically experimental research on various diseases recently.

Despite some controversies, HRV analysis, currently the most responsive and reproducible is thought to be widely used for diseases related to autonomic nerves. Still, with characteristics. HRV analysis, capable of evaluating changes in autonomic nerves, is the most responsive and reproducible method. Still, with stress emerging as a serious social issue recently, evaluating stress in quantitative fashion or index for diagnosis or prognosis were much needed. In this regard, it is clear that HRV is an important method to be studied.

Even if there were a few researches on clinical significance locally, they failed to clarify comparative objects and hard to determine research significance. (Park, Van

Bavel, Vasey & Thayer, 1994) Not much research is found abroad about HRV with an ordinary demographic group without a cardiac disorder (Tsuji et al., 1994). Despite the research on HRV with an ordinary demographic group, it lacks samples and has some limits. Since HRV can be used as a vital predictor for stress-related diseases including cardiovascular diseases, etc., much is needed to develop criterion data out of ordinary demographic group. Moreover, it is expected to greatly contribute to treating and determining preventive interruption, if vital factors of HRV is determined out of massive demographic groups and analysis dangerous causes of stress-related diseases and further comparison with patients' characters are conducted.

2.5.3 Arithmetic Task

The Arithmetic Task is the computerized Mental Arithmetic Task Based Human Stress Level Detection Using Physiological Signal. Objective of this study is to study the effect of L-Theanine and Stress formula vitamin by induce human stress level through computerized mental arithmetic task and was measured HRV stress index. Karthikeyan, Murugappan and Yaacob (2012), suggested that mental arithmetic task is one of the efficient stimuli to induce the stress. Consequently, the protocol was tested with normal subjects and multiple physiological signals were acquired simultaneously. The normal volunteer subjects were invited for the participation in this study. The physiological signal was analyzed using algorithm based on the characteristics of each signals for arithmetic task by using analyzed HRV stress index device. Amongst the several physiological signals, the HRV signal is frequently used as an efficient measure to identify the stress. However, HRV signal is used to study stimuli based stress measurement and used in heart related diseases such as myocardial ischemia due to stress and Coronary Artery Disease (CAD).

Stress Task Mental Arithmetic. There are two major variations:

1. Countdown task in which subject must subtract some number (e.g., 17) sequentially from a large number as fast as possible.

2. Working math problems mentally that are generated by a computer which also provides feedback on performance. In this study we used number.

All subjects and the participants will rest for 20 minutes before starting performed a mental arithmetic task for 10 min.

2.5.4 Max Pulse

The Max Pulse is a simple, user-friendly, non-invasive, FDA Class II medical screening device. The device provides measurements using Photoelectric Plethysmography, Accelerated Plethysmography, and other technologies to access overall cardiovascular and ANS wellness. System uses a finger clip, the blood's pulsewave is followed from the time it leaves the heart and travels through the blood vessels down to the finger. The pulsewave is a snapshot into the cardiovascular system and evaluates arterial elasticity (arterial stiffness), which is related to atherosclerosis. Arterial stiffness is a major cardiovascular risk factor. There is strong scientific evidence supporting the use of plethysmography as a diagnostic and prognostic tool for early warning signs of cardiovascular disease and peripheral vascular disease (including primary and secondary Raynaud's phenomenon).

Figure 2.1 Max Pulse System

2.5.4.1 Max pulse system Test Analysis.

1. Heart Rate Variability (HRV) - determines one’s overall health status and autonomic nerve system. Meta analyses of published data demonstrate that reduced cardiovascular autonomic function, as measured by heart rate variability, is strongly associated with an increased risk of silent myocardial ischemia (lack of oxygen to the heart w/o symptoms) and mortality.

2. Differential Pulse Wave Index (DPI) - Overall cardiovascular health.

3. Eccentric Constriction (EC) - Constriction power of vessels from the left ventricle.

4. Arterial Elasticity (AE) - Overall elasticity of large, small and peripheral arteries (arterial stiffness).

5. Remaining Blood Volume (RBV) - Remaining blood in the vessels after systolic contraction of the heart.

6. Wave Type - Aging vascular health indicator.

7. Mean Heart Rate - Average beats per minute or heart rate.

8. Arteriosclerosis Progress - 7 pictorial wave types showing typical artery status.

9. Stress Score - Overall stress health compared to resistance levels.

10. Stress Levels - Mental stress, physical stress, and resistance to stress. Changes in pressure, velocity, blood volume, and other indices.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Study Design

The study was randomized, single-blind controlled study in which 20 participants were randomly allocated into two groups (L-Theanine 200 mg, and Stress formula vitamin (Stresstab 600 mg) as recommended dose for treatment. Each participant was instructed to take two tablets before stress measurement by HRV stress index. All measures were assessed at baseline, 10, 20 and 50 minutes post-treatment.

3.2 Population and Sample Size

The participants are healthy male and female participants from Bangkok with age between 25-55 years old.

The Sample size was defined by the formula as follows:

$$n = \frac{2\sigma_d^2 (Z_{\alpha/2} + Z_\beta)^2}{(\mu_1 - \mu_2)^2}$$

$$= \frac{2*25.49\ (10.49)}{52.70}$$

$$n = 10.14$$

n = Sample size

$Z_{\alpha/2}$ = Set confident interval at 95% (=1.96)

Z_β = The standard value of power of test (=1.28)

σ_d^2 = when variance value before experimental / after experimental

= $(SD_{before} + SD_{after})^2$ = $(3.86+3.28)^2 / 2$ = 25.48

$(\mu_1-\mu_2)$ = The mean differental value from before and after experiment from previous study (Haskell et al., 2008; Foxe et al., 2011; Kimura, Ozeki, Juneja & Ohira, 2007)

= $(7.26)^2$ = 52.70

A drop-out rate of 10%was expected, so in this study, the sample size was 20 healthy participants.

3.3 Participant Selection and Criteria

Volunteers were recruited, all of volunteers were provided with a trial participant consent form. After providing signed consent, the volunteers will undergo a screening evaluation to determine eligibility for an entry into the study.

A sufficient number of volunteers were screened to ensure that the required subject number is reached. Each potential volunteer must meet the following inclusion and exclusion criteria in order to quality into the study

3.3.1 Inclusion Criteria

3.3.1.1 Male/ Female gender

3.3.1.2 Age between 25-55 years old

3.3.1.3 Healthy subject

3.3.1.4 No routine medication

3.3.1.5 Abstain alcohol and caffeine beverages for 24 hours before the intervention

3.3.1.6 Not allergy to caffeine/tea

3.3.1.7 No drugs use

3.3.1.8 Agree with the consent form

3.3.2 Exclusion Criteria

3.3.2.1 Caffeine/Tea allergy

3.3.2.2 On medication

3.3.2.3 Pregnant / breastfeeding

3.3.2.4 Cardiac conditions

3.3.2.5 Uncontrolled hypertension

3.3.2.6 Unstable psychiatric disorder

3.3.2.7 Unstable medications <90 days

3.3.2.8 Allergy or sensitivity to test articles, foods or beverages provided during the study

3.3.3 Discontinue Criteria

Subjects was advised that they are free to withdrawal from the study at any time for any reason or, if necessary.

3.4 Research Protocol

Twenty participants (10 men and 10 women (M = 35.6 years, SD = 10.5 years), who were not suffering from any chronic illnesses and not taking any medication known to influence health participated in this experiment. All twenty participants received a detailed explanation of the study and gave their informed written consent to participate.

The study design is use the single dose open label crossover experimental study. Each subject will take either L-Theanine 200 mg or Stress formula vitamin 600 mg, and perform a stress task. Stress is measured by HRV machine (MaxPlus system) for baseline recording, after the task and after resting period.

3.4.1 Step of experiment

3.4.1.1 The subjects will come to the experimental room at 9.00 am, no breakfast controlled, and then they was explained about the objectives, method, benefits and adverse effect from the experiment. Then, the subjects sign the informed

consent.

3.4.1.2 Posture: A chair people place their back against and legs are used. Caution is needed so that subjects can pose same posture with their back against around 70 degree in a same chair while being examined in a work place.

3.4.1.3 Requirements:

1. Test between 8 a.m. – noon, Sympathetic nerve exacerbation is expected in afternoons so examining in mornings is desirable. Still, work places are exception.
2. No food within 2 hours prior to test

3.4.1.4 Setting

1. Maintaining bright indoor light
2. Block outside noise (No irrelevant personnel entrance or chatting)
3. Maintaining appropriate indoor temperatures (±20~25 C.)

3.4.1.5 Notice

1. Relaxed mind and posture, and breathing
2. No conversation
3. Examine keeping eyes open
4. Keep eyes on the room wall. (no attention to monitor's change)
5. Keep breathing comfortably.
6. When the examinee looks nervous, stop a test and conduct for five minutes at a time he/she is fine.

3.4.1.6 HRV was measured, as the baseline, before the subjects rest for 20 minutes.

3.4.1.7 The subjects take either L-Theanine or Stress formula vitamin, and HRV was measured before they perform stress task for 10 minutes, then it was measured again after the task.

3.4.1.8 The subjects rest for 20 minutes, and HRV was measured afterwards.

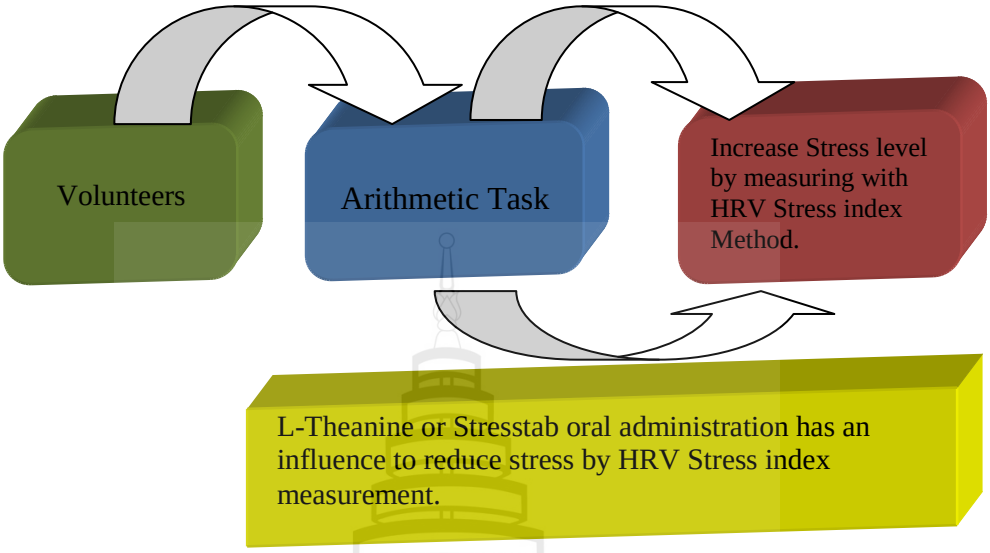

Figure 3.1 The Experimental Diagram

Twenty participants undergo two separate trials: one in which they take L-Theanine at the start of an experimental procedure, one in which they take StressTab. The experimental sessions were performed by single-blind, and the order of them was counterbalanced. The four time points of HRV were measurement by Max Plus system as the HRV stress index value.

3.4.2 Study Location

Mae Fah Luang University Hospital, Bangkok

3.5 Data Collection

Basic personal profile, age, weight and gender were recorded by record form in the appendix. Then determines one's overall health status and autonomic nerve system. The time point resting period divided in 4 groups as shown bellow for HRV Stress index's data recording:

1. After 20 minutes rest then start recording for Baseline (Baseline Group).

2. Take L-Theanine or Stress formula vitamin and performed a mental arithmetic task for 10 min, then recording HRV (Task Group)

3. To recording HRV again After resting 20 minutes (Rest 1 Group)

4. To recording HRV again After resting 20 minutes next from Rest 1 period (Rest 2 Group)

Totally are 4 recording.

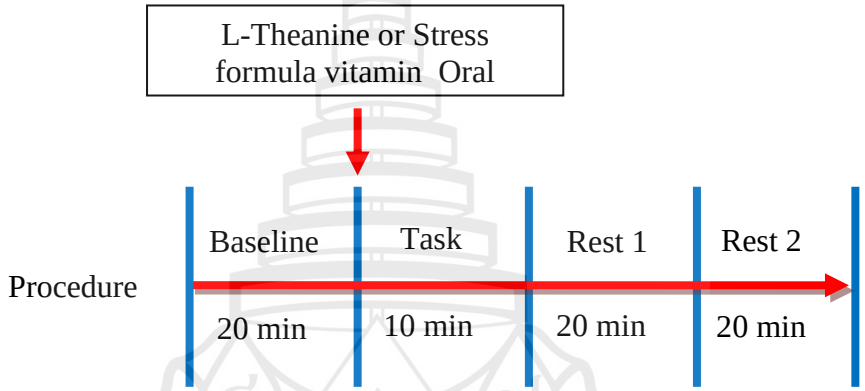

Figure 3.2 Experimental protocol of this experiment. Arrowed line indicates the time point at which participants took the water with L-Theanine or Stress formula vitamin

3.6 Data Analysis

Significance levels for all analyses were set p-value<0.05 with hypothesis with L-Theanine has an effect to stress reduction better than Stress formula vitamin.

3.6.1 Treatment Evaluation

3.6.1.1 Calculated the mean of HRV stress index from baseline scores in each time point and compared between L-Theanine and Stress formula vitamin (Baseline, Task, Rest1 1 and Rest 2 Group). The t-test statistics was used to evaluate the difference in statistics.

3.6.1.2 Compared means of HRV stress index of stress reduction at Rest 1 group (20 minutes after stress task) and Rest 2 group (40 minutes after stress task) between L-Theanine and Stress formula vitamin. The paired t-test statistics was used to evaluate the difference in statistics.

3.6.1.3 Calculated the mean of HRV stress index of change scores of Stress reduction among L-Theanine and Stress formula vitamin supplement. The paired t-test statistics was used to evaluate the difference in statistics.

3.6.2 Specific Objective Evaluation

By using parameter values received from HRV stress index measurement of each supplement in each time point period. The evaluations in this study are following below;

3.6.2.1 Evaluation means of both were compared at baseline period for similar testing of sample size between both supplements.

3.6.2.2 Evaluation means of both were compared at each time point of resting period for comparison efficacy between both supplements.

3.6.2.3 Evaluation means of different value of Task & Rest 1 and Task&Rest 2 own each supplements were compared between both supplements for efficacy to stress reduction.

3.6.2.4 Evaluation means of different value of Task & Rest 1 and Task&Rest 2 among supplement were compared for efficacy to stress reduction. (= post treatment value minus pretreatment value divided by pretreatment value multiply by 100) of each technique were to compare same as clinical score.

3.6.3 Participants Assessments

In descriptive statistics, SD assess from Twenty participants (10 men and 10 women (M = 35.6 years, SD = 10.5 years), who were not suffering from any chronic illnesses and not taking any medication known to influence health participated in this experiment.

CHAPTER 4

RESULTS

In this study, we investigated the effects of orally administered L-Theanine 200 mg or Stress formula vitamin (Stresstab 600 mg) on Mental Arithmetic Task Based Human Stress Level Detection Using Physiological Signal. Twenty participants each underwent two supplements, in which they orally took either L-theanine or Stress formula vitamin. Then all subjects are taken supplementary drug for testing again after 1 month later of first oral administration.

Stress index data during baseline recording, stress task and resting time point periods are presented in Figure 4.1 and Table 4.1. The comparison between L-theanine and Stress formula vitamin of Stress index by mental arithmetic stress task, the mean value at each time point period, including task and baseline of all supplementary were computed and used in statistical analyses. The analyses of student t test were performed using statistic analysis software. Data are expressed as means ± standard division (SD), P value < 0.05 was considered significant.

To assess the Stress index by measurement the stress index of heart rate variability test (HRV), subjects were administration first supplement and test on mental arithmetic task and test again with second supplement after 1 month later. Mean stress index of HRV stress index between L-theanine and Stress formula vitamin were shown in Table 4.1.

Table 4.1 Means (S.D) of HRV stress index from baseline scores in each time point between L-Theanine and Stress formula vitamin (n = 20/Group)

Supplements	Baseline	Task	Rest 1	Rest 2
L-Theanine	46.25 (± 11.68)	55.65 (± 11.85)	52.95 (± 12.21)	47.60 (± 12.99)
Stress formula vitamin	44.90 (± 10.37)	52.05 (± 11.48)	52.30 (± 10.96)	50.85 (± 11.04)

Note. p-value 0.14

Student t test analysis between L-theanine and Stress formula vitamin showed a significant difference between the mental arithmetic task test group (Task) and resting period at 40 min rest group (Rest 2) in HRV stress index value ($p < 0.05$). For stress index HRV value of Baseline group (Baseline), Task group (Task), Resting period at 20 minutes (Rest 1), student t test analysis showed that not significant between L-theanine and Stress formula vitamin in each time point as shown in Table 4.1 and Figure 4.1.

Baseline group compared between L-Theanine and Stress formula vitamin, HRV stress index of L-Theanine = 46.25 (± 11.68) and Stress formula vitamin = 44.90 (± 10.37), the statistically are not different at $p < 0.05$. Although baseline value in Stress formula vitamin group showed lower result than L-Theanine, However, we did not find any significant differences between L-Theanine and Stress formula vitamin in HRV stress index recording. The Task group compared between L-Theanine and Stress formula vitamin, HRV stress index of L-Theanine = 55.65 (± 11.85) and Stress formula vitamin = 52.05 (± 11.48). The change scores of the HRV stress index by mental arithmetic task compared between L-Theanine and Stress formula vitamin, in L-Theanine was significantly higher than Stress formula vitamin at ($p<0.05$). In addition, the state HRV stress index in Baseline was remarkably higher than during start test in Stress formula vitamin.

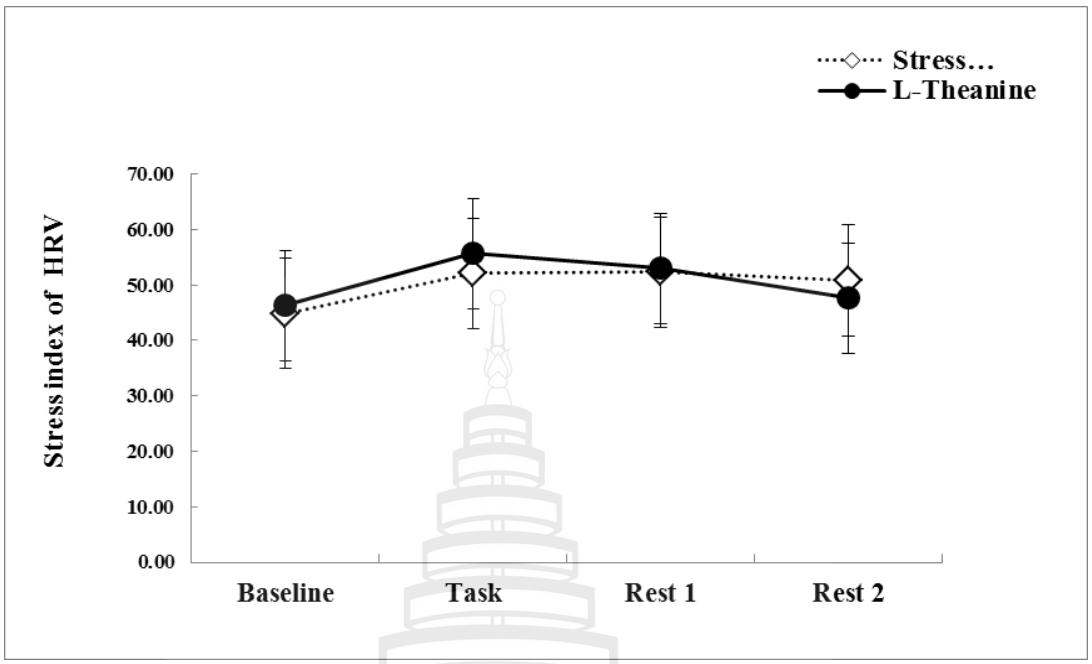

Figure 4.1 The stress index of heart rate viability changing compared between L-Theanine and Stress formula vitamin from baseline at each time point in the mental arithmetic task. Error bars indicate standard deviations, (*) indicate the significant different at $p < 0.05$

Figure 4.1 showed the comparison between L-Theanine and Stress formula vitamin at each time points. In addition, the mean L-Theanine (Figure 4.1), HRV stress index value in L-Theanine was decreased continuously in each time point period from Task = 55.65 (± 11.85), Rest 1 = 52.95 (± 12.21) and Rest 2 = 47.6 (± 12.99) as shown in table 4.1. Student t-test showed a significant difference in mental arithmetic task testing (Task) group and Rest 2 group at ($p < 0.05$) as shown in figure 4.1

The mean value ± SD of Stress formula vitamin (Figure 4.1), Stress formula vitamin, showed that stress index reduction in Rest 2 = 50.85 (± 11.04). However Stress formula vitamin, stress index in Rest 1 = 52.30 (± 10.96), the value is higher than Task Group and not significant in student t test analysis, and HRV stress index is reduced in Rest 2 Group when compared with Task Group of which show significantly at $p < 0.05$, which show significantly at $p < 0.05$ as shown in Table 4.1 and Figure 4.1. The reason of these results, it might be from the absorption time of

Stress formula vitamin has an influent with time dependent reduces in stress index reduction.

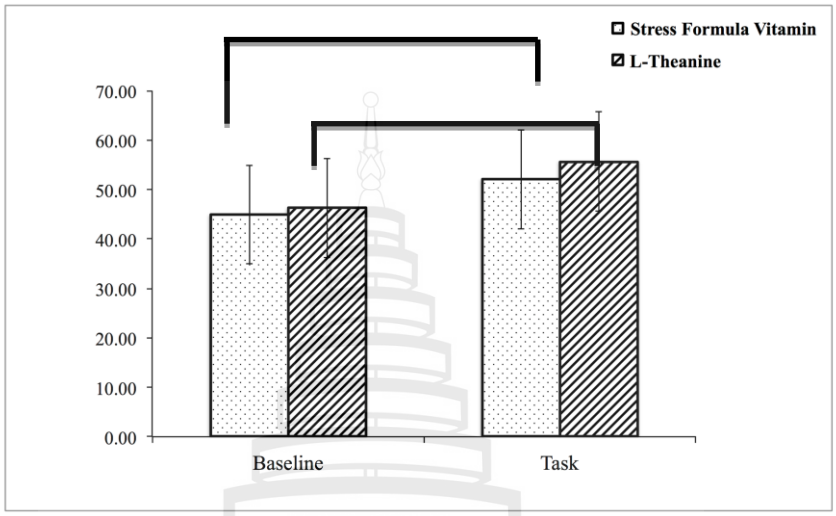

Figure 4.2 HRV stress index compared between Baseline and Task group of both supplements (L-Theanine and Stress formula vitamin). Error bars indicate standard deviations, (*) indicate the significant different at $p < 0.05$

The Task group compared to Baseline group showed significantly different between L-Theanine = 55.65 (± 11.85) and Stress formula vitamin = 52.05 (± 11.48). The comparison clarified that the mental arithmetic task stress test in this study, especially during the task period and in each time point resting period able to induce stress to subjects which showed a higher value than Baseline group at $p < 0.05$.

The mental arithmetic task and stress reduction among L-Theanine and Stress formula vitamin are presented in Table 4.2 and Table 4.3

Table 4.2 Means different change scores (S.D) of Stress reduction different of among L-Theanine (n = 20/Group)

Group	HRV stress index different		t	df	p-value
	Mean	SD			
Rest 1 -Task	- 2.70	2.99	-8.08	19	0.001
Rest 2 -Task	- 8.05	4.31			

In L-Theanine, Paired sample t-test revealed significant interactions between Rest 1 Group and Rest 2 Group. The comparisons by rest time point period (Rest 1, Rest 2 Group) clarified that the Then the L-Theanine able to reduce the stress by mental arithmetic task in each rest time point periods (Rest 1 -Task) = - 2.70 (± 2.99), $p < 0.05$) and (Rest 2 -Task) = - 8.05 (± 4.31), $p < 0.05$) as shown in Table 4.2.

Table 4.3 Means different change scores (S.D) of Stress reduction among Stress formula vitamin (n = 20/Group)

Group	HRV stress index different		t	df	p-value
	Mean	SD			
Rest 1 -Task	0.25	3.10	-2.59	19	0.018
Rest 2 -Task	- 1.20	1.70			

In Stress formula vitamin, Paired sample t test revealed significant interactions between Rest 1 Group and Rest 2 Group. The comparisons by rest time point period (Rest 1, Rest 2 Group) clarified that the Then the Stresstab able to reduce the stress by mental arithmetic task in each rest time point periods (Rest 1 -Task) = 0.25 (± 3.10), $p < 0.05$) and (Rest 2 -Task) = - 1.20 (± 1.70), $p < 0.05$) as shown in Table 4.3.

Table 4.4 Means different value (S.D) of stress index of stress reduction at Rest 1 group (Rest 1- task) compared between L-Theanine and Stress formula vitamin (n = 20/Group)

Group	HRV stress index different		t	df	p-value
	Mean	SD			
L-Theanine	- 2.70	2.99	3.05	38	0.004
Stress formula vitamin	0.25	3.10			

The stress index of stress reduction at Rest 1-Task group (resting time point at 20 minuets after task) compared between L-Theanine and Stress formula vitamin, HRV stress index Rest 1-Task group of L-Theanine = - 2.70 (± 2.99) and Stress formula vitamin = 0.25 (± 3.10). Furthermore, the HRV stress index of the mental arithmetic task in Rest 1-Task Group between L-Theanine and Stress formula vitamin showed significant different at $p < 0.05$.

Table 4.5 Means different value (S.D) of stress index of stress reduction at Rest 2 group (Rest 2- task) compared between L-Theanine and Stress formula vitamin (n = 20/Group)

Group	HRV stress index different		t	df	p-value
	Mean	SD			
L-Theanine	-8.05	4.31	6.61	24.80	0.001
Stress formula vitamin	-1.20	1.70			

The mental arithmetic task and rest time point periods at Rest 2-Task group (resting time point at 40 minuets after task) presented in Table 4.5. The stress index of

stress reduction at Rest 2-Task group compared between L-Theanine and Stress formula vitamin, HRV stress index Rest 2-Task of L-Theanine = - 8.05 (± 4.31) and Stress formula vitamin of Rest 2-Task = -1.20 (± 1.70). The HRV stress index of the mental arithmetic task in Rest 2-Task Group between L-Theanine and Stress formula vitamin showed significant different at $p < 0.05$.

CHAPTER 5

CONCLUSION AND DISSCUSSION

5.1 Conclusion

The comparison mental arithmetic task and stress reduction among Stress formula vitamin are concluding followed below;

5.1.1 L-Theanine 200 mg. Oral Supplement is an effective on stress reduction

5.1.2 In this study we found that L-Theanine able to reduce the stress after took about 30 minutes as reported by Kimura et al. (2005), Kobayashi et al., (1998) and L-Theanine is effect to dopamine release (Yokogoshi, Mochizuki et al., 1998; Yokogoshi, Mochizuki et al. 1998) in rats.

5.1.3 Stress formula vitamin (Stresstab 600 mg) is able to reduce the stress from mental athematic stress task as same as the L-Theanine but the effect is slower. It might be from the different ingredient of both supplement have an effect on different absorption time.

5.1.4 The present study suggested the possibility that L-Theanine can buffer such sympathetic activity during an acute stressor was aligned with several reports. Kakuda et al. (2002) reported that L-Theanine could block thebinding of L-Glutamic acid to the glutamate receptors in cortical neurons. The functional role of L-Theanine, such as a neuroprotective effect in cortical neurons via the antagonistic role with glutamate receptors (Kakuda et al., 2002; Nagasawa et al., 2004). Furthermore, it has been suggested that another mechanism, such as an effect on the glutamate transporter, might play a role in the modulation of L-Glutamic acid in the brain (Kakuda et al., 2002).

5.1.5 The result suggested the possibility that L-Theanine and Stresstab can act as the sympathetic activity during acute stressor induced by mental arithmetic stress task and L-Theanine can reduces psychological and physiological stress responses

(Kimura, Isowa, Ohira & Murashima, 2005).

5.1.6 The mean compared between L-Theanine and Stress formula vitamin are concluding followed below

L-Theanine (γ-glutamylethylamide) is a unique non-protein amino acid that is naturally found in tea plants. Stresstab is known as stress formula vitamin supplement and works by providing extra vitamins to the body. In addition, they have been proved to have many beneficial physiological effects, especially promoting relaxation, improving concentration of learning ability and anti-stress (antagonistic role of L-Theanine against glutamic acid receptors) effects. A lot of literatures have indicated that chronic stress formula vitamin supplementation can benefit to improve cognition (Grima et al., 2012) and mood (Long & Benton, 2013). Based on these promising advantages, L-Theanine and stress formula vitamins have been commercially developed as a valuable ingredient for use in food and beverages to improve and/or maintain human health.

5.2 Discussion

Both L-Theanine and Stress formula vitamin able to reduce stress response, although L-Theanine can acting better than Stress formula vitamins. The main findings in this study were acute stress responses elicited by the mental arithmetic task were reduced by the oral administration of L-Theanine and Stress formula vitamins. Moreover, The effect of L-Theanine and stress formula vitamins were consistently observed not only in subjective perception of stress by mental arithmetic stress as in this study but also effect in physiological stress responses such as HR and s-IgA (Kimura et al., 2005). Although the task group compared to Baseline group showed significantly different between L-Theanine = 55.65 (± 11.85) and Stress formula vitamins = 52.05 (± 11.48). The comparison clarified that the mental arithmetic task stress test in this study, especially during the task period and in each time point resting period able to induce stress to subjects which showed a higher value than Baseline group at $p < 0.05$. HRV stress index value indices under baseline group compared to that in task group clearly certified that the task used in this study elicited

temporal elevations of physiological responses, and suggested that the task adequately functioned as an acute stressor. Corresponding to previous findings on acute stress responses by mental arithmetic task (Kimura et al., 2005; Willemsen, Ring et al., 1998, Willemsen, 2000, Willemsen, 2002; Isowa, Ohira & Murashima, 2004). Although there is a possibility that the buffering effect was induced by a drug effect (this study used stress formula vitamins as control), as is often seen in clinical trials of medicine, we prevented the drug effect by employing a single-blind method. And in remembrance, after finished of the experimental sessions, no volunteers could identify whether they drank water with stress formula vitamins tablet or water containing L-Theanine tablet. Our study showed that L-Theanine could reduce the HRV stress index at the end of experiment, which is in good affect it with the stress formula vitamins. When compared the difference of HRV stress index at Rest 1 and Rest 2 of both group, this study showed L-Theanine group gave a higher of difference of HRV at Rest and Rest 2 than stress formula vitamins (8.05 and 1.2, $p<0.05$), significantly. These results may indicate the property of L-Theanine that it can moderate sympathetic activation better than stress formula vitamins.

The present study suggested the possibility that L-Theanine and Stress formula vitamin can buffer the kind of sympathetic activity during an acute stressor. L-Theanine, it is the main component responsible for the flavor and taste of green tea, has been a focus of attention due to its physical characteristics. Tea, the most famous of natural products which is used in the treatment of chronic conditions including cancer, Alzheimer, Parkinsonism, diabetes, aging, stress (Afzal, Safer & Menon, 2015). It is well known that tea is beneficial to health, because tea contains numerous naturally beneficial compounds, including polyphenols, alkaloids, catechins, L-theanine, γ-aminobutyric acid, vitamins, and mineral elements (Yamane et al., 1991; Cooper et al., 2005; Bansal, Bansal, Mithal, Kher & Marwaha, 2012). A biochemical characteristic of L-Theanine reported by Yokogoshi, Kobayashi et al. (1998) found that L-Theanine has a blood-brain permeability property, and after administration, it increased in serum, liver, and brain within 1 hour, thereafter decreasing in the serum and liver but only beginning to decrease in the brain 5 hours. In addition, L-Theanine could moderate the function of neurotransmitters in the central nervous system after oral administration at 30 min (Terashima et al., 1999). L-Theanine can bind to the

glutamate receptor subtypes (AMPA, kainate, and NMDA receptors) and blocks the binding of L-glutamic acid to the glutamate receptors in cortical neurons (Kakuda et al., 2002). Although the affinity of L-Theanine with the glutamate receptors was remarkably lower than the L-Glutamic one (about 80-30,000 fold less), there have been several reports indicating the functional role of L-Theanine, such as a neuroprotective effect in cortical neurons via the antagonistic role with glutamate receptors (Kakuda et al., 2002; Nagasawa et al., 2004). In addition, it has been suggested that another mechanism, an effect on the glutamate transporter, might play a role in the modulation of L-Glutamic acid in the brain (Kakuda et al., 2002). Since there are so many neurons activated by glutamic acid in the limbic system of the brain, and because these neurons could modulate the activation of the autonomic nervous system, it is possible that the results in the present study were induced by the antagonistic role of L-Theanine to excitation of the glutamatergic phenotype. However, many studies have reported that the oral administration of L-Theanine controlled the secretion of neurotransmitters, such as serotonin or dopamine (Kimura & Murata, 1986; Yokogoshi, Kobayashi et al., 1998; Yokogoshi, Mochizuki, et al.,1998), that mean L-Theanine not only acts as the antagonistic of glutamatergic receptors but also to other neurotransmitter systems. For example, the intra cerebral microinjection of L-Theanine increased dopamine release from the corpus striatum at a dose-dependent. Morever, L-Theanine activate the increasing of serotonin in several brain regions such as the hippocampus and hypothalamus (Yokogoshi, Kobayashi et al., 1998; Yokogoshi, Mochizuki, et al.,1998). Although, there are no studies which reveal the relative affinity of L-Theanine with receptors of these neurotransmitters and the underlying mechanisms systemically, it should be taken into account as another possible mechanism because changes in these neurotransmitters generally modulates physiological and psychological states. Study of Kobayashi and co-workers (1998) showed that after 30 min of administration, L-Theanine moderates important parameters such as the α band component of EEGs in humans (Kobayashi et al., 1998) and dopamine release (Yokogoshi, Kobayashi et al., 1998; Yokogoshi, Mochizuki, et al.,1998) in rats. This result inspires us to reconsider the time-lagged effect of this substance. However, previous studies focused on a modification or function of L-Theanine during resting situations, while the present study examined the

effect during the acute stress situation. This point of difference should be recognized. Because not only the neural activities in the central nervous system, but also the peripheral nervous system activities such as ingestion, absorption, and hemodynamics.

In this study we evaluated the effect of L-Theanine compared with stress formula vitamins to reduce of the stress response. The stress reduction effect compared between L-Theanine and stress formula vitamins during task and each time point period showed a significant difference of HRV Stress index at Resting period at 40 minutes (Rest 2) Group ($P < 0.05$). Baseline group compared between L-Theanine and Stresstab, HRV stress index of L-Theanine = 46.25 (± 11.68) and Stresstab = 44.90 (± 10.37), the statistically are not different at $p < 0.05$. Although baseline value in Stresstab group showed lower result than L-Theanine, However, we did not find any significant differences between L-Theanine and Stresstab in HRV recording. As we use the same group of subjects, it is possible resulted from the familiarity with the task, and then they are less excited with the second experimental. To compare stress reduction effect between L-Theanine and Stress formula vitamins at each time points. In addition, the mean L-Theanine, HRV stress index value in L-Theanine was decreased continuously in each time point period from Task = 55.65 (± 11.85), Rest 1 = 52.95 (± 12.21) and Rest 2 = 47.6 (± 12.99) as shown in table 4.1. Student t- test showed a significant difference in mental arithmetic task testing (Task) group and Rest 2 group at ($P<0.05$). The mean value ± SD of Stress formula vitamins (Figure 4.1), Stress formula vitamins, showed that stress index reduction in Rest 2 = 50.85 (± 11.04). However Stress formula vitamins, stress index in Rest 1 = 52.30 (± 10.96), the value is higher than Task Group and not significant in student t test analysis, and HRV stress index is reduced in Rest 2 Group when compared with Task Group of which show significantly at $P<0.05$, which show significantly at $P<0.05$ as shown in Table 4.1 and Figure 4.1. The reason of these results, it might be from the absorption time of Stress formula vitamins has an influent with time dependent reduces in stress index reduction. Stress formula vitamins supplements increase the nutrients and vitamins that body quickly absorbs during a stress response. Stress formula vitamins are high-potency B-complex vitamin formulas that help to replenish nutrients lost during periods of stress. Green vegetables, berries and Fresh fruits, contain a rich source of vitamins A, C and E. Vitamins and minerals are commonly found in stress

formula vitamin formulas, suggesting that stress formula vitamin supplementation may be able to improve mood and these food sources contain dietary antioxidants that can prevent, inhibit or repair damage caused by oxidative stress (Ames, 1983; Bourre, 2006). Oxidative stress is an imbalance or disruption in the redox state (oxidation/ reduction reactions) within cells causing impaired signaling and regulation, resulting in impaired functioning (Sohal and Orr, 2012). The maintenance of redox homeostasis is essential for healthy cellular function. Antioxidant vitamin C levels are particularly high in the brain and are needed for the transformation of dopamine into noradrenalin as well as the production of some neurotransmitters. Vitamin E is a lipid soluble antioxidant, which has neuroprotective effects against free radical damage, preventing cellular injuries to the brain related to oxidative stress (Cantuti-Castelvetri et al., 2000). Vitamins E and A protect against lipid peroxidation, a damaging process affecting the permeability of cell membranes (Mariani et al., 2005). Vitamin C works synergistically with B group vitamins and is vital for the metabolism and utilization of folate/folic acid (Huskisson et al., 2007). This study we found that stress formula vitamins able to reduce the stress from mental athematic stress task as same as the L-Theanine but the effect is slow than L-Theanine. It might be that the ingredient of both supplement have an effect to absorption time different. The result suggested the possibility that L-Theanine and stress formula vitamins can act as the sympathetic activity during acute stressor by inducing with mental athematic stress task and L-Theanine can reduces psychological and physiological stress responses (Kimura et al., 2005). Many study reported L-Theanine could block the binding of L-glutamic acid to the glutamate receptors in cortical neurons. Although the affinity of L-Theanine with the glutamate receptors was remarkably lower than the L-glutamic one (about 80–30,000 fold less), there have been several reports indicating the functional role of L-Theanine, such as a neuroprotective effect in cortical neurons via the antagonistic role with glutamate receptors (Kakuda et al., 2002; Nagasawa et al., 2004). In this study we found that L-Theanine able to reduce the stress after took about 30 minutes as reported by Kimura et al., 2005, Kobayashi et al., 1998) and L-Theanine is effect to dopamine release (Yokogoshi, Hagiwara et al., 1998; Yokogoshi, Mochizuki et al. 1998) in rats.

Any way this study strongly indicated that L-Theanine and stress formula vitamins has anti-stress effects but the several limitations have to acknowledge. First, we examined only male and female 20 participants, whereas the previous study by Willemsen et al. (2002) reported sex differences in some immune responses to acute stressor. Thus, the results of the present findings must be further tested using a larger sample composed of both sexes. Second, relatively few parameters were measured in the present study. Because we did not measure HR, blood pressure, vascular resistance, noradrenaline, and adrenaline, we do only the activation and reduction of the sympathetic nervous system on the basis of the, HRV. Third, we concluded that the reduction of acute stress responses by mental athematic stress task able to mediated the stress and study the role of L-Theanine and stress formula vitamin to reduce the stress. However, we did not directly evaluate any parameters reflecting such functions and the effect of neurotransmitter of both supplements. Further studies investigating such neural mechanisms are needed. Green vegetables, berries and Fresh fruits, contain a rich source of vitamins A, C and E. Vitamins and minerals are commonly found in stress formula vitamin formulas, suggesting that stress formula vitamin supplementation may be able to improve mood and these food sources contain dietary antioxidants that can prevent, inhibit or repair damage caused by oxidative stress (Ames, 1983; Bourre, 2006). Oxidative stress is an imbalance or disruption in the redox state (oxidation/reduction reactions) within cells causing impaired signaling and regulation, resulting in impaired functioning (Cantuti & Orr, 2012). The maintenance of redox homeostasis is essential for healthy cellular function. Antioxidant vitamin C levels are particularly high in the brain and are needed for the transformation of dopamine into noradrenalin as well as the production of some neurotransmitters. Vitamin E is a lipid soluble antioxidant, which has neuroprotective effects against free radical damage, preventing cellular injuries to the brain related to oxidative stress (Cantuti-Castelvetri et al., 2000). Vitamins E and A protect against lipid peroxidation, a damaging process affecting the permeability of cell membranes (Mariani et al., 2005). Vitamin C works synergistically with B group vitamins and is vital for the metabolism and utilization of folate/folic acid (Huskisson et al., 2007). The study of vitamin C on prevention or reduction of anxiety and heart rate variability (HRV) was elucidated by de Oliveira IJ and co-workers. They

examined the effects of oral vitamin C supplements in 42 high school students, in a randomized, double-blind, placebo-controlled trial. The students were given either vitamin C (500 mg/day) or placebo. Plasma concentrations of vitamin C and blood pressure were measured before the intervention and then one day after the intervention. Anxiety levels were evaluated for each student before and after 14 days following supplementation with the Beck Anxiety Inventory. Results showed that vitamin C reduced anxiety levels and led to higher plasma vitamin C concentration compared to the placebo. The mean heart rates were significantly different between vitamin C group and placebo control group. This study not only provides evidence that vitamin C plays an important therapeutic role for anxiety but also point a possible use for the prevention or reduction of anxiety. This suggests that a diet in vitamin C may reduce anxiety (De Oliveira, de Souza, Motta & Da-Silva, 2015).

Stress is the result of an imbalance between the assessment of environmental demands and an individual's resources and skills. Although the widespread use of vitamins to compensate for the busy lifestyle, there are few controlled trials directly investigating the relationship between stress formula vitamins and stress. Two studies using a stress formula vitamins formula observed a reduction in stress symptoms after supplementation. Schlebusch et al. (2000) found that after 30 days of supplementation, with the stress formula vitamin reducing the level of anxiety and stress and improving psychological well-being (Schlebusch et al., 2000). Carroll and co-workers found that after eighty male participants were supplemented over 28 days, the result showed significant reductions in anxiety and perceived stress in the stress formula vitamin group in comparison to the placebo group (Carroll, Ring, Suter & Willemsen, 2000)

5.3 Suggestions

5.3.1 The time point period of the study should increase for more evaluation to see clearly results from completely time dependent dose of both supplements.

5.3.2 The Further study should have placebo controlled, to clarify the stress reduction effected by L-Theanine and stress formula vitamins were not from placebo effected.

5.3.3 The subjects would be nearby in age group and same type of occupation that will affect which their behavior mental stress, to clarify their mental stress and illness not be effect with the mental athematic task test.

5.3.4 It should have more study with the measurement the neurotransmitter changing during took both supplements and should be measure the blood pressure, HR too.

5.3.5 The experiment should do double-blind treatment and separate subjects half of group for treated with first supplement and the less treated with second supplement in the first round of the experiment to eliminate bias of study.

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APPENDICES

APPENDIX A

INFORMED CONSENT FORM

หนังสือยินยอมเข้าร่วมโครงการวิจัย (Informed Consent Form)

วันที่.....เดือน..... พ.ศ.....

ข้าพเจ้า (นาย/นาง/นางสาว).....นามสกุล..... อายุ.....ปี อยู่บ้านเลขที่..... หมู่ที่.....ถนน.....ตำบล/แขวง..... อำเภอ/เขต….....จังหวัด..... รหัสไปรษณีย์..... เบอร์โทรศัพท์…… อีเมล์…….

ขอทำหนังสือแสดงความยินยอมเข้าร่วมโครงการวิจัยเพื่อเป็นหลักฐานแสดงว่า

1. ข้าพเจ้ายินยอมเข้าร่วมโครงการวิจัยของ นางวิภรณ์ มงคลศรีตระกูล

เรื่อง การศึกษาเปรียบเทียบประสิทธิผลของ ธีเอนิน กับ สเตรสแทป ในการลดความเครียด (THE COMPARATIVES STUDY EFFECT OF ORAL SUPPLEMENTATION THEANIME VS STRESSTABS ON THE STRESS REDUCTION) ด้วยความสมัครใจ โดยมิได้มีการบังคับ หลอกลวงแต่ประการใด และพร้อมจะให้ความร่วมมือ ในการวิจัย

2. ข้าพเจ้าได้รับการอธิบายและตอบข้อสงสัยจากผู้วิจัยเกี่ยวกับวัตถุประสงค์การวิจัย วิธีการวิจัย ความปลอดภัย อาการหรือ อันตรายที่อาจเกิดขึ้นรวมทั้งประโยชน์ที่จะได้รับ จากการวิจัยโดยละเอียดแล้วตามเอกสารชี้แจงผู้เข้าร่วมการวิจัยแนบท้าย

3. ข้าพเจ้าได้รับการรับรองจากผู้วิจัยว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ จะเปิดเผยได้เฉพาะในรูปแบบของการสรุปผลการวิจัยเท่านั้น

4. ข้าพเจ้าได้รับทราบจากผู้วิจัยแล้วว่า หากเกิดอันตรายใด ๆ จากการวิจัย ผู้วิจัยจะรับผิดชอบค่ารักษาพยาบาลที่เป็นผลสืบเนื่องจากการวิจัยนี้

5. ข้าพเจ้าได้รับทราบว่า ข้าพเจ้ามีสิทธิที่จะถอนตัวออกจากการวิจัยครั้งนี้เมื่อใดก็ได้ โดยไม่มีผลกระทบใด ๆ ต่อการรักษาพยาบาลตามสิทธิ์ที่ข้าพเจ้าควรได้รับ

6. ข้าพเจ้าได้อ่านและเข้าใจข้อความตามหนังสือนี้แล้ว จึงได้ลงลายมือชื่อไว้เป็นสำคัญพร้อมกับหัวหน้าโครงการวิจัยและพยาน

ลงชื่อ..... ผู้ยินยอม/ผู้ปกครอง

(.....)

ลงชื่อ..... หัวหน้าโครงการ

(นาง วิภรณ์ มงคลศรีตระกูล)

ลงชื่อ..... พยาน

(.....)

APPENDIX B

INFORMATION SHEET

เอกสารคำอธิบาย/คำชี้แจง โครงการวิจัยแก่ผู้เข้าร่วมโครงการ

(Information Sheet)

1. ชื่อโครงการวิจัย

การศึกษาเปรียบเทียบประสิทธิผลของ ธีเอนิน กับสเตรสแทป ในการลดความเครียด

2. วัตถุประสงค์และวิธีการวิจัย

2.1 วัตถุประสงค์

เพื่อเปรียบเทียบประสิทธิผลในการลดความเครียดระหว่างธีเอนินซึ่งเป็นสารที่พบ ได้ในชาเขียว แล สเตรสแททป ซึ่งเป็นสารที่ใช้แพร่หลายในการลดความเครียด

2.2 วิธีการวิจัย

เป็นการศึกษาทดลองในมนุษย์ ชนิดการวิจัยเชิงทดลอง

3. ความเป็นมาของโครงการ ที่ทำให้ต้องศึกษาเรื่องนี้

ความเครียดเป็นสิ่งที่พบในชีวิตประจำวัน ซึ่งมีผลต่อร่างกายทั้งทางด้านร่างกายและจิตใจ การศึกษา นี้เพื่อเปรียบเทียบสารธีเอนิน ซึ่งพบได้ในชาเขียว และสเตรสแทป ซึ่งเป็นสารที่ได้รับการยอมรับ แพร่หลายในการใช้ลดความเครียด หากประสิทธิผลทัดเทียมกันก็จะเป็นอีกหนึ่งทางเลือกของ ผู้บริโภคในการเลือกสารลดความเครียด

4. สถานที่และระยะเวลาที่ต้องทำการวิจัยกับอาสาสมัคร

โรงพยาบาลมหาวิทยาลัยแม่ฟ้าหลวง กรุงเทพมหานคร ระยะเวลาเข้าร่วมโครงการ 1 เดือน (เข้าร่วม 2 ครั้ง ห่างกัน 1 เดือน)

5. รายละเอียดที่จะปฏิบัติต่ออาสาสมัคร

มีอาสาสมัครเข้าร่วมวิจัย 20 คน เมื่อถึงสถานที่ทดสอบจะให้เวลาพัก 20 นาที แล้ววัดความเครียดจากเครื่องวัดที่ปลายนิ้ว หลังจากนั้นให้รับประทาน ธีเอนิน แล้วทำการทดสอบด้วยปัญหาทางคณิตศาสตร์ 10 นาที หลังจากนั้นวัดระดับความเครียดทันที และ วัดอีก 2 ครั้งหลังพัก 20 นาที และ 40 นาที อาสาสมัครพัก 1 เดือนก่อนเข้าทำการทดสอบอีกครั้งโดยเปลี่ยนเป็นรับประทานสเตรสแทป ในขั้นตอนการทดลองเดียวกันกับการทดสอบครั้งแรก

6. ประโยชน์ที่คาดว่าจะเกิดขึ้นกับอาสาสมัครและผู้อื่น

ท่านจะได้รับการวัดระดับความเครียดก่อนและหลังการทดสอบ โดยไม่เสียค่าใช้จ่ายใด ๆ

7. ความเสี่ยงหรือผลข้างเคียงที่จะเกิดขึ้นต่ออาสาสมัคร พร้อมทั้งระบุมาตรการหรือวิธีแก้ไขที่ผู้วิจัยเตรียมไว้

ไม่มีผลข้างเคียงเนื่องจากสารที่ให้รับประทานเป็นสารจำพวกวิตามินและเครื่องที่ใช้วัดเป็นเครื่องวัดปลายนิ้วเท่านั้น

ในกรณีมีข้อสงสัยอาสาสมัครสามารถติดต่อได้ที่ นางวิภรณ์ มงคลศรีตระกูล E-mail: wiporn_m@yahoo.com

8. ขอบเขตการดูแลรักษาความลับของข้อมูลต่างๆ ของอาสาสมัคร

ข้อมูลของท่านจะเป็นความลับส่วนบุคคลในรายงานหรือผลงานการตีพิมพ์จะเปิดเผยเฉพาะใน รูปแบบของการสรุปผลการวิจัยเท่านั้น ผู้กำกับดูแลงานวิจัยจะได้รับอนุญาตให้ตรวจสอบเวช ระเบียนต้นฉบับของท่านโดยตรง เพื่อตรวจสอบความถูกต้องของวิธีการดำเนินงานวิจัยทางคลินิก หรือ ข้อมูลอื่น ๆ โดยไม่ละเมิดสิทธิของท่านในการรักษาความลับเกินขอบเขตที่กฎหมายอนุญาตไว้ โดยท่านได้ลงนามในเอกสารใบยินยอมให้บุคคลต่าง ๆ ข้างต้น มีสิทธิตรวจสอบเวชระเบียนของ ท่านโดยตรง

9. การดูแลรักษาที่ผู้วิจัยจัดให้

ท่านจะได้รับการดูแลอย่างใกล้ชิดจากแพทย์ผู้วิจัย หากมีอาการข้างเคียง แพทย์จะให้การรักษา จนหายโดยไม่คิดค่าใช้จ่ายใด ๆ

10. ค่าตอบแทนอาสาสมัคร ค่ารักษาพยาบาล และค่าชดเชย กรณีเกิดอันตรายหรือผล ที่ไม่พึงประสงค์จากการวิจัยแก่อาสาสมัคร

หากมีอาการข้างเคียง แพทย์จะให้การรักษาจนหายโดยไม่คิดค่าใช้จ่ายใด ๆ

11. สิทธิของอาสาสมัครที่สามารถถอนตัวจากโครงการวิจัยได้ทุกเมื่อโดยไม่กระทบต่อการดูแลรักษาที่พึงได้รับตามปกติ

ท่านสามารถถอนตัวได้ตลอดเวลา โดยไม่กระทบต่อการดูแลรักษาที่พึงได้รับตามปกติ

12. ชื่อ ที่อยู่ เบอร์โทรศัพท์ ของหัวหน้าโครงการวิจัยหรือแพทย์ที่ผู้วิจัยกำหนด โดยสามารถติดต่อ ได้ทุกเวลา กรณีมีเหตุจำเป็นหรือฉุกเฉิน

นางวิภรณ์ มงคลศรีตระกูล
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