A detailed approach on the health benefits of L-theanine

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(***Received: April 2019 Revised: June 2019 Accepted: August 2019)***

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ABSTRACT

Tea has been consumed for thousands of years and is an integral part of people's daily routine, as an everyday drink and a therapeutic aid for health promotion. Consumption of tea has been linked to a sense of relaxation commonly associated with the content of the non-proteinogenic amino acid theanine, which is found within the tea leaves. The aim of this review article is to outline the health benefits of L-theanine. The review includes a descriptive analysis of L-theanine in its role in improvement of immune function, cancer prevention, reduced cardiovascular risk and its cognitive potential usefulness in our bodily systems when compared with available conventional methods. This review states in detail about the health benefits and lots of various other uses of L-theanine which is meant as a relaxing agent or a template for antidepressant drugs. This systematic review is done to acknowledge all the useful and necessary uses of l-theanine and its importance to society.

Keywords: L-Theanine; non-proteinogenic; cardiovascular risk; therapeutic; cognitive.

INTRODUCTION

L-Theanine (γ-glutamylethylamide) is a unique amino acid present almost exclusively in the tea plant (*Camellia sinensis*). Theanine crosses the blood-brain barrier via the large neutral amino acid (leucine preferring) transport system (1). L-Theanine is an amino acid that is not common in the diet (not one of the essential amino acids or even one of the common nonessential amino acids) and is deemed a non-dietary amino acid similar to L-ornithine or L-citrulline. L-Theanine has structural similarity to glutamine and both neurotransmitters that are produced from it such as gamma -aminobutyric acid (GABA) and glutamate and be summed up as being a relaxing agent without sedation (relative to something like a lemon balm which relaxes but may also sedate) and is also implicated in reducing the perception of stress and slightly improving attention. While L-theanine does not appear to induce sleep, it may (quite weakly) help with sleep although its potency suggests it may not be a good first-line treatment for this. Interestingly, the relaxing and attention promoting properties of L-theanine coupled with the lack of sedation may L-theanine have its most significant supplemental role in attenuating the 'edge' of many stimulants. A combination of L-theanine with caffeine (200 mg each) is noted to be synergistic in promoting cognition and attention. L-Theanine, for the most part, is a relaxing but not sedating amino acid that is synergistic with stimulants such as caffeine as it can 'take the edge off'. It is effective by itself in the standard supplemental dosages as well, and although it can be attained via a diet high in green tea ingestion that is the only dietary source of L-theanine. There are some health benefits associated with green and black tea ingestion that are thought to be more reflective of the theanine content rather than the green tea catechins or the theaflavins, and this is thought to be related to cardiovascular health (as L-theanine positively regulates nitric oxide) and some cognitive benefits. There has been a resurgence of interest in the anxiety-relieving powers of L-theanine, an amino acid found in green tea. Discoveries over the past two years have uncovered exciting additional properties of this nutrient best known for inducing calming, tranquilizing effects while simultaneously improving alertness. In this research update, we examine how L-theanine acts in the brain and review compelling new studies on its actions that include potentially reduced risk of stroke and less brain damage if an ischemic stroke were to occur.

Benefits of L-theanine on the brain

Theanine, when reaching the brain, has been shown in rats to increase both serotonin and dopamine production. Animal studies have shown that L-theanine is able to inhibit the stimulation produced by caffeine, as evaluated by electroencephalogram (EEG; 2). It has been demonstrated previously that i.p. injection of theanine reduced the size of cerebral infarcts in middle cerebral artery (MCA) occlusion mice showing its neuroprotective activity against cerebral ischemia (3). Kimura and Murata reported that 30 min after i.p. injection of theanine, it was incorporated into the mouse brain without any metabolic change (4). In addition, Takeshima reported that theanine, when administered

orally, was transported into the brain through the blood-brain barrier (BBB), suggesting that theanine passes easily through this barrier (5). L-theanine has also been shown to inhibit the downregulation of neurotrophic factors thus preventing the SH-SY5Y neurons from PD related environmental neurotoxicants (6). Moreover, theanine exerts a neuroprotective action against cerebral ischemia when administered systemically, providing further evidence for the permeability of the BBB to theanine.

L-Theanine on anxiety and stress

L-Theanine relieves anxiety in large part because it bears a close resemblance to the brain signaling chemical glutamate. L-theanine produces the opposite effect in the brain. While glutamate is the brain's most important excitatory neurotransmitter, L-theanine binds to the same brain cell receptors and blocks them to glutamate's effects. This action produces inhibitory effects (7, 8). That inhibition of brain overactivity has a calming, relaxing effect in which anxiety fades (9). In addition to blocking excitatory stimuli at glutamate receptors in the brain, L-theanine also stimulates the production of the inhibitory, relaxing neurotransmitter GABA, adding to its calming, anti-anxiety effects. Unlike prescription anti-anxiety drugs, however, some of which mimic GABA's effects, L-theanine produces its anti-anxiety effects without producing sleepiness or impairing motor behavior (10). In fact, L-theanine has been shown in human studies to moderately improve alertness and attention while exerting its anxiety-reducing effects (11). Studies show that L-theanine supplementation prevents the abrupt rise in blood pressure that some people experience under stress (7). This is so critical that many people have normal blood pressure readings at rest that spike up to dangerously high levels when subjected to stressful situations. These periods of surging blood pressure inflict massive arterial damage and are the main reason why at-home and at-office blood pressure testing are so important.

Dosage and directions for L-theanine

In general, it is recommended that users begin with the smallest suggested dose, and gradually increase until it has an effect. For sleep, stress and other uses: 100 mg to 400 mg in combination with caffeine: 12-100 mg L-theanine, 30-100 mg caffeine. Researchers are now increasingly interested in applications for L-theanine far beyond its anti-anxiety properties. Excessive glutamate stimulation of brain cells (excitotoxicity) is a factor in the development of long-term neurodegenerative disorders, stroke, and schizophrenia (12). Therefore, L-theanine's glutamate-blocking capabilities make it promising for neuroprotection and prevention in these areas. And while its deeper mechanisms are still under investigation, there is tantalizing evidence that L-theanine influences expression of genes in brain areas responsible for fear and aggression (amygdala) and memory (hippocampus), helping to balance the behavioral responses to stress, and potentially improve conditions such as mood disorders, post-traumatic stress disorder (PTSD), and substance dependence (13).

Promotion of cognitive function

There's a link between anxiety, reaction to stress, and the brain's most fundamental function, maintaining cognition. Studies over the past two years suggest a potential role for L-theanine in supporting cognitive function and preventing its loss. Stress has powerful negative effects on one's ability to think clearly and make smart decisions. This is demonstrated physiologically by animal experiments showing that stress significantly reduces animals' performance on standard tests of learning and memory, as well as by increased oxidative stress in the brain and elevated blood levels of stress-response hormones such as catecholamine and adrenaline. Treating animals with L-theanine before the stress is applied, however, results in reversal not only of cognitive impairment but also of the elevation of stress hormones and oxidative damage (14). Studies such as these demonstrate that L-theanine can specifically reduce the molecular impacts of acute stress, and the resulting excitotoxicity, on brain cells. The issue with chronic glutamate-driven excitotoxicity is profound and long-lasting cognitive dysfunction, including neurodegenerative disorders such as Alzheimer's, Parkinson's, Huntington's diseases, and amyotrophic lateral sclerosis (ALS; 15). The protective effects of L-theanine have been shown in animal models for at least the first three of these disorders, suggesting that regular L-theanine supplementation might be important in fending off these tragic conditions by opposing the destructive effects of long-term glutamate excitotoxicity (16). In a rat model study for Huntington's disease, researchers investigated the protective effects of L-theanine against 3-nitropropionic acid (3-NP). Rats exposed to 3-nitropropionic acid experienced significant reductions in body weight, oxidative defenses, and locomotor activity, as well as impaired mitochondrial enzyme activity. But when exposed to L-theanine, the behavioral, biochemical, and mitochondrial enzyme activities were significantly attenuated, leading authors to conclude that "L-theanine has neuroprotective activity against 3-nitropropionic acid-induced neurotoxicity (18). Recent studies show that L-theanine can prevent both the biochemical and structural damage to brain cells induced by aluminum, offering yet another means by which this nutrient can prevent or slow cognitive decline (19).

Impact of L theanine on stroke

A stroke is the result of a sudden blockage of blood (ischemia) to a part of the brain, resulting in massive chemical stresses, extreme excitotoxicity, and eventual death of brain cells (20). The latest studies show that L-theanine has properties that may both help to prevent strokes and to mitigate the damage caused when they do occur.

Lab studies show that L-theanine is capable of significantly improving nitric oxide production in endothelial cells (21). This has the potential to lower stroke risk because nitric oxide is a signaling molecule that endothelial cells use to communicate information about blood flow and pressure to muscles in the artery walls, telling them to constrict or relax appropriately in response and distributing blood flow appropriately. In another stroke-preventing mechanism, L-theanine has recently been shown to significantly reduce the expression of adhesion molecules to the endothelial wall by inhibiting tumor necrosis factor-alpha (TNF-a), thereby reducing the risk of an artery-blocking clot or obstruction that produces a stroke (22). L-theanine protects the body from the damage of blood reperfusion or refilling that occurs after the abrupt loss of circulation during the stroke and administration of L-theanine up to 12 hours after a stroke is induced protects brain cells and reduces the size of the damaged brain areas. Even treatment as late as 24 hours after the stroke improves neurological status (23).

Neural mechanisms of L-theanine

Theanine has been found to cross the blood-brain barrier, as systemic injections and oral intake (24) and can increase brain concentrations of the compound which appears to be mediated via the leucine-preferring transport (25) system (the neutral amino acid transport). The concentrations reaching the brain at this oral dose are around 2µM/g and serum concentrations in this study peaked at above 12.5µM/mL within an hour and were reduced to similar concentrations as the brain at 16 hours. Specific brain organs that have been shown to have increased in theanine concentration following oral intake include the hippocampus (19). Orally administered L-theanine supplementation can cross the blood-brain barrier. L-Theanine supplementation in the standard dosages (50-250mg) has been repeatedly noted to increase α-waves in otherwise healthy persons. This may only occur in persons with somewhat higher baseline anxiety or under periods of stress positive (4) and negative results (22) but has been noted to occur during closed eye rest (5) as well as during visuospatial tasks (16) around 30-45 minutes after ingestion (4,5). It appears that only the α-1 wave (8-10Hz) is affected, with no influence on α-2 wave (11-13Hz) (4). α-waves (8-12Hz) are known to be associated with a state of relaxation (23). These altered wave functions are said to be evidence that theanine has 'relaxing and attention promoting' properties. One study has reported increased theta wave function, but with a combination supplement of both theanine (60 mg) and green tea extract (360mg) taken thrice daily over 16 weeks (15). Theanine supplementation appears to cause an increase in alpha-1 wave production within 30-45 minutes following the oral ingestion of standard supplemental doses. This increase in alpha-1 production is highly associated with the most common benefits of Theanine supplementation (relaxation and attention).

How L-theanine works

L-theanine promotes relaxation and facilitates sleep by contributing to a number of changes in the brain:

Boosts levels of GABA and other calming brain chemicals

L-theanine elevates levels of GABA, as well as serotonin and dopamine. These chemicals are known as neurotransmitters, and they work in the brain to regulate emotions, mood, concentration, alertness, and sleep, as well as appetite, energy, and other cognitive skills. Increasing levels of these calming brain chemicals promote relaxation and can help with sleep.

Lowers levels of "excitatory" brain chemicals

At the same time, it is increasing chemicals that promote feelings of calm, L-theanine also reduces levels of chemicals in the brain that are linked to stress and anxiety. This may also be a way that L-theanine can protect brain cells against stress and age-related damage.

Enhances alpha brain waves

Alpha brain waves are associated with a state of "wakeful relaxation." That's the state of mind you experience when meditating, being creative, or letting your mind wander in daydreaming. Alpha waves are also present during REM sleep. L-theanine appears to trigger the release of alpha-waves, which enhances relaxation, focus, and creativity. One of the appealing aspects of L-theanine is that it works to relax without sedating. That can make L-theanine a good choice for people who are looking to enhance their "wakeful relaxation," without worrying about becoming sleepy and fatigued during the day.

Benefits of L-theanine improving sleep

With its ability to increase relaxation and lower stress, L-theanine can help in sleep in several ways. L-theanine may help people fall asleep more quickly and easily at bedtime, thanks to the relaxation boost it delivers. Research also shows L-theanine can improve the quality of sleep not by acting as a sedative, but by lowering anxiety and promoting relaxation. There's evidence that L-theanine may help improve sleep quality

in children with attention deficit hyperactivity disorder (ADHD). A study examined the effects on the sleep of boys ages 8-12 and found that the supplement worked safely and effectively to improve the quality of their sleep, helping them to sleep more soundly.

Reducing stress and anxiety

L-theanine is what's known as an anxiolytic it works to reduce anxiety. Some anxiolytics, such as valerian and hops, have sedative effects. L-theanine, on the other hand, promotes relaxation and stress reduction without sedating. L-theanine can help foster a state of calm, attentive wakefulness. L-theanine has positive effects on both the mental and physical symptoms of stress, including lowering heart rate and blood pressure. Research suggests that L-theanine can help reduce anxiety in people with schizophrenia and schizo-affective disorder.

Enhancing attention, focus, memory and learning

Under stress, the body increases the production of certain hormones, including cortisol and corticosterone. These hormone changes inhibit some brain activity, including memory formation and spatial learning. L-Theanine helps to lower levels of the stress hormone corticosterone and avoid interference with memory and learning. L-Theanine may help boost other cognitive skills. Research shows L-theanine can increase attention span and reaction time in people who are prone to anxiety. It may help improve accuracy; one study shows that taking L-theanine reduced the number of errors made in a test of attention. Sometimes, L-theanine is used with caffeine to enhance cognitive skills. Studies show that combinations of L-theanine and caffeine can improve attention span, enhance the ability to process visual information, and increase accuracy when switching from one task to another.

L-Theanine and relaxation

Numerous studies have examined the effects of L-theanine supplements on people's state of mind. Researchers have found that L-theanine has a powerful relaxing effect on most people. Studies have compared L-theanine supplements to some commonly prescribed relaxing agents and found that L-theanine may be more effective and promoting a relaxed state (26).

Furthermore, researchers in Korea have found that L-theanine supplements alter your brain waves. After taking L-theanine tablets, participants in a study were seen to have increased alpha brain wave activity, especially those with high baseline anxiety, Alpha brain waves are associated with increased creativity, relaxation, and improved mood (27).

L-Theanine is known to promote relaxation through its effects on receptors in your brain. Specifically, L-Theanine activates the GABA receptors. GABA receptors are involved in several functions in your body and are best known as the relaxing receptors. Substances that activate GABA receptors are referred to as depressants not because they make you feel depressed, but because they depress signals from your central nervous system (28). L-Theanine can, therefore, be considered as a depressant supplement – one that helps to reduce signals from the central nervous system and promotes relaxation.

L-Theanine and mood

Many people think of L-theanine as a great supplement to improve mood. L-theanine is known to activate GABA receptors and promote relaxation, but its effects on mood are not quite as well understood. People who suffer from anxiety often experience low moods as a result of their consistent worrying. As a result, many people are searching for the L-theanine anxiety connection. Unfortunately, there have not yet been any conclusive studies on the direct link between L-theanine and mood. One important thing to consider is that Researchers have found solid evidence of L-theanine's remarkable ability to reduce stress. Stress is an important aspect of a bad mood. Studies have consistently linked stress to a low mood. Since stress is such an important feature of our daily lives, managing it is key to maintaining a healthy mood (29). Lastly, as we mentioned above, researchers have linked L-theanine supplements to increased activity of alpha brain waves. Even at low dosages of around 50mg, L-theanine exerts an effect on your brain that increases the alpha brain waves (8). Alpha brain waves are associated with a relaxed and alert state of mind. Alpha brain waves are also prominent during periods of meditation and are highly prevalent in EEG scans of deep meditators. These data indicate that alpha brain waves are linked to improved mood. (23). Researchers have found that L-theanine is an effective supplement for improving your mood.

L-Theanine and caffeine

One of the most important benefits of L-theanine is its synergistic relationship with caffeine. Multiple studies have shown that L-theanine and caffeine work well together to boost mental alertness and focus. Importantly, L-theanine is able to reduce many of the negative effects associated with caffeine (30). On the one hand, researchers have found that caffeine is associated with increased feelings of anxiety and jitteriness. This is especially relevant for people with anxiety disorders, data shows that the negative effects of caffeine are more pronounced in people who suffer from anxiety. L-Theanine and caffeine have been showed to have a good synergistic relationship. The combination of the two substances improves reaction time, working memory time, and sentence verification accuracy. Not

only this, but the combination of L-theanine and caffeine promote a reduction in headaches and tiredness when compared to either of the supplements taken alone.

CONCLUSION

L-theanine, an amino acid found in green tea, reduces anxiety by blocking excitatory stimuli at glutamate receptors in the brain while stimulating the production of the inhibitory, relaxing neurotransmitter GABA. But, unlike standard anti-anxiety drugs, L-theanine relieves stress without altering other CNS levels. In fact, studies show it improves alertness and attention. Researchers are now examining L-theanine's applications beyond its anti-anxiety effects. Studies suggest a role for L-theanine in supporting cognitive function and preventing cognitive loss by protecting brain cells and preventing strokes and reducing the damaging effects if a stroke has occurred. Lastly, L-theanine is the subject of human studies in patients with schizophrenia. In summary, L-theanine helps to promote it as a powerful supplement with Nootropic effects. Studies have shown that L-theanine affects GABA receptors and promotes relaxation. Research has also pointed to L-theanine's ability to improve sleep quality and to reduce feelings of stress. While these are all symptoms of interest to people who are interested in an L-theanine anxiety connection, they do not necessarily show that L-theanine has any relevant anxiolytic effects. L-Theanine has a synergistic relationship with caffeine. When taken together, the two supplements help to improve mental alertness and focus. L-Theanine is also able to help reduce some of the negative effects of caffeine like headaches and elevated blood pressure. Research into the relationship between L-theanine and anxiety has produced conflicting results. In the past, people used L-theanine as a powerful supplement to reduce feelings of stress. Today, L-theanine can be purchased as a dietary supplement to promote relaxation, healthy sleep, a calm mood, and as a synergist for caffeine.

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