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# REPORT

## Brain Benefits of L-Theanine

By Angela Sanford

There's been a resurgence of interest in the anxiety-relieving powers of **L-theanine**, an amino acid found in green tea.<sup>1</sup>

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.

### How L-Theanine Works in the Brain to Block 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.<sup>1,2</sup> That inhibition to brain overactivity has a calming, relaxing effect in which anxiety fades.<sup>3</sup>

In addition to blocking excitatory stimuli at glutamate receptors in the brain, L-theanine also stimulates production of the inhibitory, relaxing neurotransmitter GABA, adding to its calming, anti-anxiety effects.<sup>2</sup>

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.<sup>4</sup> In fact, L-theanine has been shown in human studies to moderately improve alertness and attention while exerting its anxiety-reducing effects.<sup>5</sup>

Of particular interest are studies showing that **L-theanine** supplementation prevents the **abrupt** rise in **blood pressure** that some people experience under stress.<sup>1</sup> The reason this is so critical is 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.

### New Directions for L-Theanine

Scientists 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 development of long-term neurodegenerative disorders, stroke, and schizophrenia.<sup>6,7</sup> 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.<sup>8</sup>

### L-Theanine Protects Brain Cells and Promotes 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.<sup>9</sup>

Studies such as these demonstrate that L-theanine can specifically reduce the molecular impacts of acute stress, and the resulting excitotoxicity, on brain cells.<sup>10,11</sup> 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).<sup>12</sup>

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.<sup>13-16</sup>

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.**"<sup>17</sup>

Exposure to toxic chemicals is another known risk factor for many of the neurodegenerative disorders, with the metal aluminum being a major culprit.<sup>18,19</sup> Recent studies show that L-theanine is capable of preventing 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.<sup>20</sup>

### Taste the Relaxation

The molecular similarity of L-theanine with glutamic acid can be experienced simply by tasting it. L-theanine provides the *umami* flavor that gives green tea its richness.<sup>31</sup> One of the more common molecules that delivers umami taste is glutamic acid, and studies show that glutamate and L-theanine both stimulate the same receptors on our tongues, in a vivid demonstration of molecular mimicry.<sup>32,33</sup>

In the brain, of course, the similarity is only close enough for L-theanine to bind to brain glutamate receptors but without stimulating them, which is why L-theanine produces relaxing, as opposed to stimulating, effects.

## L-Theanine Reduces Stroke Impact

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.<sup>21</sup> 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 (artery-lining) cells.<sup>22</sup> 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- $\alpha$ ), thereby reducing the risk of an artery-blocking clot or obstruction that produces a stroke.<sup>23</sup>

L-theanine protects the body from the damage of blood reperfusion, or refilling that occurs after the abrupt loss of circulation during the stroke.<sup>24</sup>

This *ischemia-reperfusion* injury results in massive release of glutamate and produces deadly excitotoxicity.<sup>25</sup>

Animal studies show that 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.<sup>24</sup>

## L-Theanine May Play a Role in Ameliorating Schizophrenia

Schizophrenia, literally a "split mind" in which sufferers experience a cut-off from reality, is one of the most tragic and misunderstood disorders known. People with schizophrenia may experience *positive symptoms* such as hallucinations, delusions, and paranoid thinking, as well as negative *symptoms* including loss of ability to experience pleasure, blunted emotions, and diminished speech capacity.<sup>26</sup>

Perhaps because schizophrenia may involve excitotoxic damage to brain cells, L-theanine has recently been the focus of human studies in patients with this disease.<sup>27</sup>

In one study of 40 patients with schizophrenia, subjects were given placebo or **400 mg** L-theanine along with their regular medications for an eight-week trial. The supplemented patients demonstrated significant reductions in their anxiety and general symptoms of psychopathology.<sup>28</sup>

A **250 mg** per day dose of L-theanine significantly improved, in a different study scores on positive symptoms, as well as in sleep quality.<sup>29</sup> And the combination of L-theanine (**400 mg** per day) with the hormone pregnenolone (**50 mg** per day) was capable of reversing not only anxiety, but also negative symptoms.<sup>30</sup>

## Summary

L-theanine, an amino acid found in green tea, reduces anxiety by blocking excitatory stimuli at glutamate receptors in the brain while stimulating production of the inhibitory, relaxing neurotransmitter GABA. But unlike prescription anti-anxiety drugs, L-theanine relieves stress without causing drowsiness or impairing motor behavior. 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.

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