Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

L-Theanine

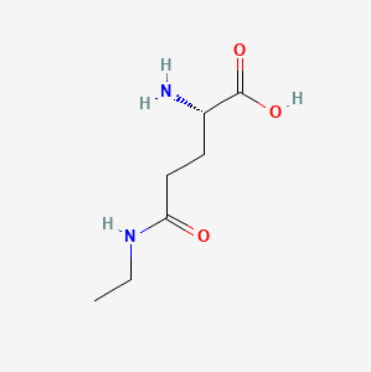
Evidence Summary

L-theanine appears to have short-term effects on attention and relaxation but it does not appear to improve cognitive function long-term. It is generally well tolerated.

Neuroprotective Benefit: While L-theanine administered acutely has led to some positive short-term effects on attention and relaxation in healthy adults, studies of chronic dosing have not shown improved cognitive function.

Aging and related health concerns: -theanine improves some measures of sleep. Laboratory studies have shown that L-theanine extends lifespan in worms and mice under stressful conditions and suppresses tumor growth in mice.

Safety: L-theanine treatment in clinical trials has generally been well tolerated, with headache, migraine, and gastrointestinal disorders being the most frequently reported adverse events.

Availability: OTC	**Dose**: not established; in clinical trials, 200 mg daily, orally, has been the most commonly tested dose	**Chemical formula**: $C_7H_{14}N_2O_3$ **MW**: 174.20  Source: PubChem
Half-life: ~65 minutes	**BBB**: penetrant	
Clinical trials: The largest meta-analysis of randomized controlled trials testing L-theanine have included a total of 897 participants.	**Observational studies**: No observational studies have examined L-theanine intake specifically. Numerous large observational studies have examined green tea and green tea extract intake.	

What is it?

Green tea (including sencha, matcha, and gyokuro), black tea, and oolong tea are all derived from the same plant, *Camellia sinensis*, a perennial evergreen shrub. L-theanine is an amino acid analogue structurally similar to glutamate and acts as a weak agonist of glutamate receptors. L-theanine is contained in green, black, and oolong tea, comprising about 1-3% of the dry weight of tea leaves [1]. A single cup of liquid tea contains 5-85 mg of L-theanine, depending on the type, quality, and preparation of the tea. L-theanine readily crosses the blood-brain-barrier [2] and is traditionally used as a relaxation-promoting agent [3]. Animal studies have shown that L-theanine inhibits glutamate receptors while increasing dopamine release, gamma-aminobutyric acid (GABA) concentrations, and serotonin levels in the brain [2; 4; 5; 6].

Neuroprotective Benefit: While L-theanine administered acutely has led to some positive short-term effects on attention and relaxation in healthy adults, studies of chronic dosing have not shown improved cognitive function.

Types of evidence:

- 3 systematic reviews or meta-analyses of clinical trials testing L-theanine
- 15 randomized controlled trials

- 1 open-label study in people with major depressive disorder
- 1 review
- 6 laboratory studies

***Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function*:**

Studies of chronic dosing: In a double-blind randomized controlled trial of 69 people aged 50-69 years old, L-theanine treatment (100.6 mg/day, orally after breakfast; Suntheanine, Taiyo Kagaku Co., Japan) for 12 weeks did not significantly affect the primary end points, which were cognitive functions measured by MMSE-J and Cognitrax [7]. After a single dose of L-theanine, improved reaction time, correct answers, and omission errors were seen in attention tasks (Stroop test), though these findings were not corrected for multiple comparisons. L-theanine treatment (acute or chronic) had no effect on memory tasks, facial expression recognition task, visual information processing tasks, or motor function.

In a double-blind randomized controlled trial of 30 people (mean age, 48.3 years old), L-theanine treatment (200 mg/day, Suntheanine, Taiyo Kagaku Ko., Japan) for 4 weeks significantly improved verbal fluency and executive function scores compared to baseline (p=0.001 and 0.031, respectively) and decreased stress-related symptoms measured by Self-rating Depression Scale, State-Trait Anxiety Inventory-trait, and Pittsburgh Sleep Quality Index scores (p=0.019, 0.006, and 0.013, respectively)[8]. However, when change from baseline were compared between L-theanine and placebo administrations, no significant differences were found for any of the 12 cognitive outcomes.

In a double-blind randomized controlled trial in 91 patients with MCI, the combination of green tea extract and L-theanine (1680 mg of the supplement LGNC-07, which contained 240 mg of L-theanine) for 16 weeks did not significantly affect memory or attention at the end of the trial but marginal improvement in memory was observed at the 8-week time point [9]. However, in a subgroup who had relatively severe baseline impairment (MMSE scores of 21-23), significant improvements in memory and attention were observed. Brain theta waves were increased in the temporal, frontal, parietal, and occipital cortex after 3 hours, suggestive of cognitive alertness.

In a double-blind randomized controlled trial of 99 older adults with subjective cognitive decline or mild cognitive impairment, 2 grams of matcha daily (containing 170 mg of catechins and 48 mg of theanine) for 12 months significantly improved the social acuity score (p=0.028), as evaluated by the perception of facial emotions [10]. There was also a trend toward improvement in sleep quality (measured by change

from baseline on the Pittsburgh Sleep Quality Index scores) with the matcha intervention compared to placebo (p=0.088). However, the primary outcomes, Montreal Cognitive Assessment (MoCA) or Alzheimer's Disease Cooperative Study Activity of Daily Living (ADCS-ADL) scores showed no significant changes with the matcha intervention compared to placebo. There were also no significant differences between matcha and placebo groups for reaction time, complex attention, cognitive flexibility, executive function, simple attention, ADCS-MCI-ADL, MMSE, ADAS-J cog, or Repeatable Battery for Assessment of Neuropsychological Status (RBANS).

In a systematic review of 11 randomized controlled trials in people with mental disorders (e.g., ADHD, OCD, MDD, sleep disorders, GAD, Tourette syndrome), L-theanine treatment for 8-10 weeks when used as an adjunct to standard treatment reduced psychiatric symptoms more effectively than control (standard treatment alone) in people with schizophrenia, anxiety disorders, and ADHD [11]. However, the authors noted limitations in the existing evidence, including the scarcity of studies, potential publication bias, and lack of standardized dosages.

Studies of acute dosing: In a double-blind randomized controlled crossover study of 32 healthy young adults, a single administration of L-theanine (100, 200, and 400 mg) significantly improved reaction time in a visual reaction time task (RTI, at the 100 and 200 mg doses; p=0.009 for both) compared to baseline and compared to placebo [12]. L-theanine treatment also improved reaction time on the Rapid Visual Information Processing task (RVP, at the 200 and 400 mg doses) compared to baseline, but change from baseline was not statistically significant compared to placebo. L-theanine treatment did not improve the more complex sustained attention tasks (stop-signal task) or executive control tasks.

In a double-blind randomized crossover study of 24 healthy volunteers who were sleep-deprived overnight, L-theanine administration (200 mg dose in 150 mL of distilled water) improved visual attention in a traffic scene-based attention task [13]. L-theanine significantly reduced false alarms (responses to safe scenes) (p=0.014) and increased target-distractor discriminability (p=0.009), whereas placebo did not (p>0.05). L-theanine treatment also reduced hit reaction time by 38.65 msec (p=0.007), and placebo by 19.08 msec (p=0.016), however reaction time changes from baseline were not significantly different between treatments (p>0.05).

A single-blind randomized placebo-controlled trial of 80 men and women (average age, 21) examined the effects of L-theanine (200 mg; Bulk Supplements, Hard Eight Nutrition, NV; n=25) and L-tyrosine (2000 mg; Bulk Supplements; n=28) on markers of stress and cognitive performance in response to a virtual reality active shooter drill and cognitive challenge [14]. The active shooter drill significantly

increased heart rate, State-Anxiety Inventory score, and salivary markers of stress, including α-amylase and secretory immunoglobulin A. L-theanine (or L-tyrosine) taken prior to the stress did not affect markers of stress. L-theanine also did not affect cognitive function measured by Stroop challenge and mental arithmetic.

Interactions with caffeine: A combination of L-theanine and caffeine was reported to improve alertness and attentional switching accuracy in a meta-analysis of 10 acute randomized controlled trials in healthy adults [15]. However, the majority of the attention-enhancing effects were attributed to caffeine. L-theanine may interact with caffeine, improving attention and ability to ignore distractions, and together, enhance performance on cognitively demanding tasks [16]. In a randomized controlled trial of 16 healthy adults, L-theanine alone did not affect attentional focus, but L-theanine (100 mg) combined with caffeine (50 mg) showed improvement in target detection and discrimination [17].

A double-blind randomized controlled crossover study of 22 elite curling athletes examined the effects of theanine (6 mg/kg), caffeine (6 mg/kg), its combination, or placebo (400 mg maltodextrin) on shooting and cognitive performance and found that the caffeine+theanine combination led to superior shooting and cognitive performance [18]. The caffeine+theanine combination led to superior performance in guard, draw, and take-out compared to the placebo condition ($p<0.001$ for all). On the Stroop test during the neutral reaction task, caffeine+theanine condition showed significantly lower reaction times compared to caffeine alone, theanine alone, or placebo. Reaction times for congruent reaction and incongruent reaction were superior for caffeine+theanine combination compared to the placebo condition. The caffeine+theanine combination also led to improved neutral error rates compared to caffeine alone, theanine alone, or placebo. The caffeine+theanine condition also achieved significantly lower congruent error rate and incongruent error rate compared to the placebo condition.

In a double-blind randomized controlled crossover trial of 9 healthy adult men, a single administration of L-theanine (200 mg; Powder City Inc., York, PA) or L-theanine+caffeine combination (200 mg and 160 mg, respectively; Powder City Inc.) resulted in faster reaction times to the target stimuli on the visual color stimulus discrimination task compared to placebo (-27.8 msec, $p=0.018$ for L-theanine; -26.7 msec, $p=0.037$ for combination)[19]. The doses for L-theanine and caffeine are equivalent to doses found in 8 cups of green tea. L-theanine treatment was associated with decreased functional MRI responses to distractor stimuli in brain regions that regulate visual attention, suggesting that L-theanine may decrease neural resource allocation to process distractors, thus promoting attention to targets. Factorial analysis suggested that L-theanine and caffeine appear to have a synergistic action in decreasing mind wandering.

It is possible that L-theanine may have effects independently of caffeine. In a randomized controlled crossover study of 20 healthy adult males, recognition visual reaction time significantly improved with L-theanine (200 mg), caffeine (160 mg), or a theanine-caffeine combination, but not with a single cup of tea or placebo [20].

While these studies suggest modest benefit, some others report mixed effects. In a double-blind randomized controlled trial crossover study, L-theanine partly attenuated the beneficial effects of caffeine on cognition and mood [21]. For example, the caffeine group had a higher number of responses and faster reaction times on the Stroop test compared to the placebo group; these benefits were not seen in the L-theanine group. However, errors on the Stroop test were significantly lower in the L-theanine group compared to the theanine-caffeine combination group. Thus the calming effects of L-theanine may improve accuracy at the expense of speed.

Brain wave activity: Several EEG studies have shown that L-theanine increases alpha activity, indicative of a state of wakeful relaxation [3; 22; 23]. L-theanine increases attention-related anticipatory alpha activity while decreasing background alpha activity, potentially improving focus [22]. A double-blind randomized controlled trial of 34 healthy adults under cognitive stress (multitasking) showed that an L-theanine-based nutrient drink (containing 200 mg of L-theanine, 25 mg of alpha GPC, 1 mg of phosphatidylserine, and 10 mg of chamomile) also increased alpha activity while decreasing stress [24]. However, changes in alpha activity were not correlated with subjective stress or cortisol levels. The functional relevance of alpha activity changes is not yet clear.

Stress/Mood: L-theanine may have a role in regulating anxiety due to its effects on the serotonin and GABA systems [2; 5].

In a systematic review of 9 randomized controlled studies including a total of 270 people, L-theanine treatment (most studies tested a single dose of 200 mg) was associated with reductions in stress and anxiety-like symptoms under conditions of acute stress [25]. Because most studies examined acute administration of L-theanine, randomized controlled trials that are longer in duration and with a larger number of people are needed to determine L-theanine's effects on chronic stress and/or anxiety.

In an open-label uncontrolled study in patients with major depressive disorder, L-theanine administration improved mood, verbal memory, and executive function [26], but a placebo-controlled study is required to confirm these effects.

Human research to suggest benefits to patients with dementia:

No studies have tested the effects of L-theanine treatment in dementia patients.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Preclinical data suggest that L-theanine acts on the central nervous system by potentiating GABA, dopamine, and serotonin responses. Neuroprotective effects may be mediated by its antagonistic effects on glutamate receptors (AMPA, kainite, NMDA, and group 1 metabotropic glutamate receptors) [4; 5]. For example, theanine has been shown to inhibit neuronal death from exposure to glutamate and this effect was abolished by blocking the group I metabotropic glutamate receptors (mGluRs) [27].

Models of Alzheimer's disease: In rats, L-theanine attenuated Aβ42-induced memory impairment, reduced neuronal death in the cortex and hippocampus, and inhibited the Aβ42-induced activation of ERK, p38 MAPK, and NFkB [28]. L-theanine also reduced oxidative damage to proteins and lipids while elevating glutathione levels in the brain. L-theanine-treated rats have 20% lower oxidation levels in the cortex compared to untreated controls [29]. These changes were accompanied by increased levels of PLC-β1 and PLC-γ1 in the cortex. In cell culture, rotenone- and dieldrin-induced apoptosis and DNA fragmentation are partially prevented with L-theanine treatment [30]. L-theanine appeared to exert its neuroprotective effects by suppressing heme oxygenase-1 and restoring ERK1/2 phosphorylation, BDNF production, and GDNF production.

Stress models: Positive effects of L-theanine on cognitive functions have been observed in a rodent model of stress [31]. Restraint stress for 3 weeks significantly impaired cognitive performance in mice while increasing corticosterone levels. L-theanine reversed the cognitive impairments and oxidative damage while restoring healthy levels of corticosterone and catecholamines in the brain and serum.

Ischemia models: In a mouse ischemia model, L-theanine treatment reduced cerebral infarct size and this neuroprotective effect was prevented by a GABA-A receptor antagonist, suggesting that neuroprotective effects of theanine is partly mediated by GABA-A receptors [32].

APOE4 interactions*:* It is unknown whether L-theanine has different effects in ApoE4 carriers versus non-carriers. Some studies have examined the interactions between ApoE status and caffeine intake from tea or coffee [33], which have produced inconclusive results.

Aging and related health concerns: L-theanine improves some measures of sleep. Laboratory studies have shown that L-theanine extends lifespan in worms and mice under stressful conditions and suppresses tumor growth in mice.

Types of evidence:

- 1 meta-analysis of randomized controlled trials examining the effects of L-theanine on sleep
- 3 randomized controlled trials
- 1 open-label study on sleep quality in patients with major depressive disorder
- Numerous laboratory studies

Lifespan: MIXED FINDINGS

In *C. elegans*, L-theanine (at 100 nM, 1 µM, and 10 µM) promotes resistance from paraquat toxicity and extends lifespan by up to 4.4% [34]. In a mouse model of psychosocial stress, L-theanine consumption (20 µg/ml, 5-6 mg/kg) prevented the shortening of lifespan, cerebral atrophy, learning impairment, and oxidative damage of cerebral DNA [35]. However, no effect of L-theanine on lifespan was observed in control mice that were not exposed to psychosocial stress. Both of these studies show that L-theanine has lifespan-extending properties when the organism is under harmful insults. L-theanine does not appear to be as beneficial in healthy animals.

Cancer: SUPPRESSED BASED ON PRECLINICAL STUDIES

Theanine and theanine derivatives were shown in two studies to suppress growth of cervical tumors, lung cancer, and leukemia in cell culture systems as well as in tumor-bearing mice [36; 37]. Both of these studies showed that suppression of cancer growth with L-theanine and its derivatives (TBrC, TFC, and TNC) occurred without toxicity to the mice. TFC and TNC suppress cancer growth by targeting the EGFR/VEGFR-Akt/NF-kB pathways [37].

Blood pressure: DECREASED

A double-blind randomized controlled trial of 48 adults tested the acute effects of L-theanine (200 mg), caffeine (250 mg), and the combination, and found that while caffeine increased blood pressure and alertness, theanine attenuated this increase in blood pressure without affecting caffeine's positive effects on alertness [38]. A smaller randomized controlled trial of 14 adults showed a similar effect of L-

theanine on blood pressure, though the effect was limited to high stress-response adults [39]. Preclinical studies have shown that L-theanine activates ERK and endothelial nitric oxide synthase (eNOS), resulting in enhanced NO production and dilation of arteries [40].

Sleep: POTENTIAL IMPROVEMENT

In a meta-analysis of 18 randomized controlled trials, L-theanine treatment (dose range, 15 mg to 1000 mg, with many studies using 200 mg dose) significantly improved subjective sleep onset latency (standardized mean difference [SMD]=0.15; 95% CI, 0.01 to 0.29, p=0.04), subjective daytime dysfunction (SMD=0.33; 95% CI, 0.16 to 0.49; p<0.001), and overall subjective sleep quality score (SMD=0.43; 95% CI, 0.04 to 0.83)[41]. This meta-analysis included people of all ages and health conditions. It is worth noting that 11 studies included compounds other than L-theanine while 8 studies tested L-theanine alone. The duration of the intervention ranged from once (at night) and up to 8 weeks. No significant effects of L-theanine were observed for objective sleep onset latency, subjective sleep efficiency, objective sleep efficiency, subjective sleep disturbance, objective sleep disturbance, subjective sleep duration, and objective sleep duration.

In a double-blind randomized controlled trial of 93 boys diagnosed with attention deficit hyperactivity disorder (ADHD), L-theanine treatment (400 mg/day, Suntheanine®) for 6 weeks was associated with higher sleep efficiency (% of night spent sleeping restfully) and fewer bouts of nocturnal motor activity compared to placebo [42]. The L-theanine group had on average ~5% greater sleep efficiency and ~10% fewer nocturnal motor activities compared to controls. Sleep quality was also improved with L-theanine (250 mg/d) in patients with major depressive disorder, but it was an open-label study and placebo-controlled studies are required to confirm these effects [26].

Safety: L-theanine treatment in clinical trials has generally been well tolerated, with headache, migraine, and gastrointestinal disorders being the most frequently reported adverse events.

Types of evidence:

- 1 meta-analysis of randomized controlled trials examining the effects of L-theanine on sleep
- 2 Cochrane meta-analyses based on 14 and 11 randomized controlled trials examining the effects of green tea (not L-theanine specifically) on weight loss and cardiovascular disease prevention, respectively
- 3 randomized controlled trials examining the effects of L-theanine

- 3 rodent studies (1 toxicity/toxicokinetics study and 2 cancer studies)

In a meta-analysis of 18 randomized controlled trials, L-theanine treatment (dose range, 15 mg to 1000 mg, with many studies using 200 mg dose) was well tolerated with headache, migraine, and gastrointestinal disorders being the most frequently reported symptoms [41].

In a randomized controlled trial, L-theanine treatment (400 mg/day) for 6 weeks was well-tolerated with no significant adverse events in 98 boys diagnosed with ADHD [42]. In another double-blind randomized controlled trial, L-theanine (400 mg/day) with oral pregnenolone (50 mg/day) for 8 weeks was well-tolerated in patients with schizophrenia [43]. However, L-theanine was not tested by itself and the full text of this article was unavailable, so the rates and types of adverse events could not be evaluated.

In a double-blind randomized crossover study of 10 healthy adults, no adverse events were observed with a single dose of 400 mg L-theanine (Nootropics Depot, AZ)[44].

Two Cochrane meta-analyses of green tea consumption (beverage or extract for at least 3 months), one in overweight adults and another in healthy adults, have reported that side effects from green tea are mild [45; 46]. No significant differences in adverse events were observed between green tea and placebo groups.

In a rat toxicity and toxicokinetic study, L-theanine was administered at 0, 1500, 3000, and 4000 mg/kg/day for 13 weeks [47]. No consistent statistically significant treatment-related adverse effects were found on behavior, morbidity, mortality, pathology, body weight, food consumption, clinical chemistry, hematology, or urinalysis. The no-observed-adverse-effect-level was 4000 mg/kg/day, the highest dose tested.

Drug interactions: Interactions with drugs have not been well-studied. Because of its blood pressure-lowering properties, theoretically, concomitant use of blood pressure medications may be dangerous. Clinical data suggest that L-theanine inhibits the stimulant effects produced by caffeine [38; 39].

Sources and dosing:

Clinical trials examining the effects of L-theanine on cognitive function, blood pressure, and sleep have used doses ranging from 12-400 mg/d, with the majority of studies using 200 mg/d [15; 20; 24]. In a rat

toxicity study, the no-observed-adverse-effect-level was 4000 mg/kg/d, the highest dose tested [47]--the human equivalent dose based on body surface area is 645 mg/kg/d.

A single cup (200 ml) of liquid tea can contain 5 to 85 mg of L-theanine depending on the type of tea. Matcha is powdered Japanese green tea, where the tea powder is mixed with hot water and contains ~36 mg of L-theanine per serving (80 ml). Gyokuro is a type of green tea that is produced from shading the tea leaves, increasing theanine and caffeine production while inhibiting catechin levels, and contains 85 mg of L-theanine per cup. Sencha, the most common type of green tea in Japan (and the US), contains 8~25 mg in a cup. Black tea contains about 10~35 mg per cup [48]. The amount of L-theanine varies, with higher levels typically found in higher quality tea.

L-theanine is more bioavailable than its optical isomer D-theanine [49]. In an analysis of commercially available products labeled as L-theanine, 5 out of 6 contained significant amounts of D-theanine. Only Suntheanine® contained pure (>99%) L-theanine enantiomer [50].

Research underway:

There are several ongoing clinical trials testing L-theanine based on ClinicalTrials.gov.

A double-blind randomized placebo-controlled study is evaluating the effects of L-theanine for stress relief in 104 people who report occasional moderate to high levels of stress (NCT05854017). The primary outcomes are measures of stress (PSS-14) and anxiety (STAI). This trial is enrolling participants as of April 2025.

A randomized controlled trial is testing the effects of a combination product that includes L-theanine on stress and sleep in 115 healthy adults (NCT06889584). The combination product includes Ashwagandha, Rhodiola rosea, magnesium threonate, apigenin, and L-theanine. Primary outcomes include measures of stress, mood, and sleep. This trial is enrolling participants as of April 2025.

Search terms:

Pubmed, Google: Green tea, L-theanine, matcha

- + cognitive, + memory, *+ dementia*, + meta-analysis, + systematic review, + clinical trial, + ApoE4, + cancer, + cardiovascular, + lifespan, + safety

Clinicaltrials.gov: Green tea, L-theanine, matcha

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