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Review

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Effects of L-Theanine, a Constituent of Tea, on Cognitive Functions and Attention

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Abstract

Tea (*Camellia sinensis*) is a historically and economically important beverage for Sri Lanka; and is traditionally believed to have relaxing or calming effects. Some evidence attributes these effects to a constituent of tea leaves; L-theanine, a non-protein-forming amino acid structurally similar to glutamic acid. Over the years, research has found L-theanine to also have effects on various cognitive functions, including attention. This review focuses on the research conducted thus far on the acute effects of L-theanine on neurobehavioral, neurophysiological, and functional neuroimaging indices, cognition and attention. Despite the heterogeneity of testing paradigms across studies, experimental evidence increasingly suggests that L-theanine could improve visual selective attention. Contrary to traditional belief, the amount of L-theanine in a cup of tea (4.5-22.5mg) seems to cause no significant effects; and attentional improvement is more prominent with much higher doses (100-500mg). This makes it worth exploring the possibility of enriching tea with L-theanine, while preserving the unique flavour of the product. L-theanine has an additive effect with caffeine in enhancing attention, but unlike caffeine, L-theanine can be ingested in high doses with no risk of adverse effects, tolerance or dependence. The evidence on attentional effects of L-theanine is almost entirely based on healthy samples who have undergone laboratory-based attentional tasks that employed abstract stimuli. When translating these laboratory findings to real-life scenarios, incorporating more real-life-based stimulus paradigms (i.e., simulated driving scenarios) is warranted. The clinical relevance of L-theanine research could also be improved by exploring the effects of L-theanine in cognitively compromised groups of individuals.

Keywords: L-theanine, tea, cognitive functions, attention, caffeine

AN INTRODUCTION TO L-THEANINE AND ITS EFFECTS

Tea has been traditionally consumed as a beverage, and in contrast to coffee, it is believed that it has certain relaxing and calming effects. These effects were attributed to one of its constituents, L-theanine [1-3]. L-theanine, also known as gamma-glutamylethylamide, is a non-protein forming amino acid with a chemical structure similar to that of glutamic acid [4], and

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this happens to be the only significant dietary source of L-theanine. A cup of tea including both green and black tea, contains 4.5-22.5 mg of L-theanine [2]. Apart from its use in research, purified L-theanine is available as a nutritional supplement and a food additive [5, 6]. Certain types of supplements and beverages are now being enriched with L-theanine [7-9].

In humans, L-theanine is absorbed through the small intestine and shows a peak plasma concentration 0.8 hours after ingestion, and this concentration is dose-dependent [10, 11]. L-theanine crosses the blood brain barrier and shows EEG changes starting around 40 minutes after oral administration [12, 13]. It has a plasma elimination half-life of about 65 minutes, and is completely eliminated from plasma within 8 hours [11].

L-theanine has a structure similar to glutamic acid. It binds to subtypes of glutamate receptors, but with relatively low affinity. It has been shown to increase dopamine concentration in the rat brain in a dose-dependent manner [14, 15]. Animal studies have reported a complex range of neurochemical actions following L-theanine administration, including inhibiting glutamate reuptake [16], potentiating brain GABA [17], and striatal dopamine and glycine concentrations [15], while serotonin levels were reported to decrease globally with region-specific increases in the striatum, hippocampus and hypothalamus [14].

L-theanine is safe even in very high doses. Animal studies show that rats [18] and mice [19] fed with extremely high doses (up to 4 g per kilogram body weight) of L-theanine for 13 weeks do not develop significant adverse effects. Similarly, 8-12-year-old boys with attention deficit hyperactivity disorder (ADHD) have tolerated 400 mg of L-theanine per day for a period of 6 weeks, with no adverse effects [20]. Similarly, Sarris et al. [21], found greater sleep satisfaction on self-report among patients with generalised anxiety disorder following doses of 450-900 mg of L-theanine, but no significant adverse effects.

The effects of L-theanine alone as a relaxant were proved to a certain extent [1, 2]. Lu et al. [22] studied the subjective mood effects of L-theanine and found that 200 mg of L-theanine was able to increase 'tranquil' ratings, as measured by the 'tranquil-troubled' item of the Bond-Lader visual analogue scales [23]. However, this finding was only evident in rested participants and was not replicated when participants were under conditions of increased anxiety. Later, in 2007, it was shown that a single 200-mg dose of L-theanine reduced acute stress responses (i.e. subjective perception, heart rate and salivary IgA levels) induced by a mental arithmetic task [24]. It was further proved that a 250-mg dose slowed reaction time on a visual probe task, indicating reduced anxiety [3]. In a recent systematic review, Williams et al. [25] suggested that doses of 200-400 mg of L-theanine may exhibit certain stress-relieving effects.

In addition to its effects on mood, recent studies have focused on the effect of L-theanine on specific cognitive functions. The experimental studies conducted hitherto on the acute cognitive effects of L-theanine, both alone, and in combination with caffeine (another constituent of tea and coffee) are summarised in Table 1. A general trend observed in these experimental studies was that L-theanine was administered in relatively high doses (50-400 mg) given that it is safe in high doses. Later, it was also shown that the amount of L-theanine in a single cup of tea does not make significant changes to cognitive functions [26]. The participants of most of these studies were healthy young individuals between the ages of 20 and 40 years, perhaps because potential interference from confounding factors is far less in that group of participants when compared with more extreme age groups.

However, the studies were heterogeneous in two main aspects: 1) the variability in cognitive functions tested and 2) the variability in techniques used to assess these functions (Table 1). Researchers have investigated the effect of L-theanine on different cognitive domains including attention, memory encoding, working memory, judgment and evaluation, reasoning, problem solving, and decision making. For example, Kelly et al. [27], White et al. [28], Dodd et al. [29], Rogers and Smith [3] and Foxe et al. [30] experimented on the effect of L-theanine on selective attention; whereas White et al. [28] examined the effects on mathematical processing, psychomotor tracking and memory (Table 1).

Table 1. Summary of experimental studies that determined the acute effects of L-theanine on cognitive functions.

Study	Design	Participants	Treatments	Outcome measures and results	Comments
(Gomez-Ramirez et al., 2007)	Double blind, placebo-controlled, counter-balanced trial	15 healthy volunteers	1. 250 mg L-theanine in 200 ml water 2. Placebo (200 ml of water)	Reaction time in intersensory (auditory and visual) attention task: Slower after L-theanine treatment than placebo for both the unisensory – auditory and multisensory-auditory stimulus types. Alpha EEG activity: Attention related increase in anticipatory (i.e., phasic) alpha power and decrease in background (tonic) alpha power.	
(Kelly et al., 2008)	Single-blind, placebo-controlled, 4-way, crossover trial	16 healthy volunteers (5 females); age 21-40 years; with low habitual tea (3.7 cups/week) and coffee (3.8 cups/week) consumption	1. 100 mg of L-theanine 2. 50 mg of caffeine 3. L-theanine and caffeine combination 4. Placebo (100 ml distilled water)	L-theanine: In a visuospatial attention task, no improvement on hit rate, discriminability index, reaction time or EEG alpha power Caffeine: significantly improved stimulus discrimination theanine-caffeine combination: improved hit rate and stimulus discrimination	Single blinding may introduce a bias. The order effect superseded that arising from treatment.
(Rogers et al., 2008)	Randomized, double-blind placebo-controlled trial.	48 healthy volunteers divided into 4 groups; age 18-28 years	1. 200 mg of L-theanine 2. 250 mg of caffeine 3. L-theanine and caffeine combination 4. Placebo (distilled water)	Reaction time: L-theanine slowed reaction time on the visual probe task whereas caffeine had no significant effect.	

Table 1. Continued.

Study	Design	Participants	Treatments	Outcome measures and results	Comments
(Haskell et al., 2008)	Randomized, placebo-controlled, double-blind, counter-balanced, crossover study	24 healthy volunteers; age 18-34 years	1. 200 mg of L-theanine 2. 250 mg of caffeine 3. L-theanine and caffeine combination 4. Placebo (Peach Lite Lipton iced tea)	L-theanine: Improved simple reaction time. No change in choice reaction time, Digit vigilance RT, or rapid visual processing reaction time or % accuracy. Caffeine & L-theanine combination improved simple reaction time, accuracy of rapid visual information processing, numeric working memory reaction time, delayed word recognition reaction time and accuracy of sentence verification.	
(Gomez-Ramirez et al., 2009)	Double-blind, placebo-controlled, counter-balanced experiment.	13 healthy volunteers (9 females) mean age: 23.5 years (SD = 3.25 years)	1. 250 mg L-theanine in 200 ml of water 2. Placebo (200 ml of water)	Visuospatial choice reaction time: No significant difference in target-distracter discriminability. Tonic alpha band activity: Reduction over posterior regions of right hemisphere with L-theanine. Phasic EEG alpha band activity: Directing attention to the left visual field evoked significantly greater alpha band activity over the left hemisphere than directing attention to the right visual field.	
(Higashiyama et al., 2011)	Double-blind, Placebo-controlled, counter-balanced, crossover study	18 healthy male volunteers; age 18-20 years	1. 200 mg of L-theanine in 100 ml of water 2. Placebo (100 ml of water)	L-theanine caused faster auditory tone discrimination RT in high- but not low-anxiety-propensity group.	

Table 1. Continued.

Study	Design	Participants	Treatments	Outcome measures and results	Comments
(Foxe et al., 2012)	Double-blind, placebo-controlled, 4-way, crossover trial	27 healthy volunteers (8 females); age 18-40 years.	1. 100 mg L-theanine 2. 50 mg caffeine 3. L-theanine and caffeine combination 4. Placebo (200 ml water)	Sustained visual attention to response task: L-theanine significantly decreased omission errors by 36% and decreased commission errors by 23% relative to placebo. No main or interaction effects involving theanine, caffeine or the combination on reaction time.	Only post-dose recording. No pre- vs. post-dose comparison.
(Dodd et al., 2015)	Double-blind, placebo-controlled, counter-balanced, crossover study	24 healthy volunteers (10 males); age 18-35 years	1. 50 mg L-theanine 2. 75 mg of caffeine 3. L-theanine and caffeine combination 4. Placebo	L-theanine: No effect on simple or choice reaction time, or reaction time in rapid visual information processing. No effect on Stroop test performance. Caffeine decreased reaction time. L-theanine co-administration with caffeine abolished this effect.	
(White et al., 2016)	Randomized, placebo-controlled, double-blind, crossover study	36 healthy volunteers; age 18–40 years	1. L-theanine (200 mg) 2. Placebo 3. L-theanine (200 mg) 4. Placebo	Mood response to cognitive stress: Subjective stress response to a multitasking cognitive stressor, was significantly reduced one hour after administration of L-theanine. Resting state MEG alpha oscillatory activity: Significantly greater in posterior scalp sites after L-theanine compared to placebo.	Change in resting state alpha oscillatory activity did not correlate with change in subjective stress response or the cortisol response.

Table 1. Continued.

Study	Design	Participants	Treatments	Outcome measures and results	Comments
(Giles et al., 2017)	Double-blind, counter-balanced, 4-way, crossover study	36 healthy volunteers (12 males); mean age 19.3, SD = 1.7 years	1. 200 mg L-theanine 2. 200 mg caffeine 3. L-theanine and caffeine combination 4. Placebo	Hierarchical Shape Task: L-theanine accentuated local processing (higher percentage compared to placebo). Global processing increased with caffeine than placebo, no significant difference in global and local processing between combination treatment and placebo. Caffeine accentuated global processing. Visual attention: Caffeine or L-theanine didn't affect orienting or alerting.	
(Kahathuduwa et al., 2017)	Double-blind, placebo-controlled, 5-way, counter-balanced crossover study.	20 healthy males; age 21-23 years	1. L-theanine (200 mg) 2. Caffeine (160 mg) 3. L-theanine and caffeine combination 4. Black tea (150 ml) 5. Placebo (distilled water 150 ml)	Recognition visual reaction time: Significantly improved by L-theanine, caffeine and their combination but not by tea or placebo. Simple visual reaction time: Did not show significant inter-treatment difference. Auditory event-related potentials: L-theanine, caffeine and the combination elicited lager mean peak to peak N2-P300 ERP amplitude than placebo.	Auditory event-related potentials were measured only post-dose. No pre- vs. post-dose comparison.

Table 1. Continued.

Study	Design	Participants	Treatments	Outcome measures and results	Comments
(Kahathuduwa et al., 2018)	Double-blind, placebo controlled, repeated-measures, counter-balanced, 4-way crossover trial	9 adult males volunteers; age 18-60 years	1. L-theanine (200 mg) 2. Caffeine (160 mg) 3. L-theanine (200 mg) and caffeine (160 mg) 4. Placebo (200 ml of distilled water)	L-theanine and the combination caused faster visual colour stimulus discrimination reaction times. L-theanine improved hit rate in go/no-go task. No significant effect on false alarms or reaction time. Functional MRI activity: L-theanine decreased fMRI responses to distractor stimuli in brain regions that regulate visual attention (i.e., decreased neural resource allocation for distractors) L-theanine and L-theanine-caffeine combination decreased fMRI responses to targets compared to distractors in brain areas involved in mind wandering.	
(Dassanayake et al., 2020)	Double-blind, placebo-controlled, 4-way crossover study	28 healthy young adults (17 males); age range: 24-37 years	1. 100 mg L-theanine 2. 200 mg L-theanine 3. 400 mg L-theanine 4. Placebo (150 ml of distilled water)	Behavioural measures: None of the doses significantly improved mean reaction time to target tones compared to the placebo. ERP measures: All doses of L-theanine reduced mean P3b latency linearly, but a significant effect only with 400 mg (i.e., L-theanine in high doses enhanced attentional processing in a dose-dependent manner.) Latencies & amplitudes of pre- or early attentive processing components: N1 latency at CZ scalp site was delayed with 100 mg of L-theanine but not with higher doses. Subjective self-assessment of level of alertness not affected by any of the doses.	Authors suggest that the task demands of the auditory two-tone attention task was relatively low leading to a “ceiling effect” behaviourally.

Table 1. Continued.

Study	Design	Participants	Treatments	Outcome measures and results	Comments
(Kahathuduwa et al., 2020a)	Randomized, placebo-controlled four-way repeated measures crossover trial.	6 male children with ADHD; age 8-17 years	1. L-theanine: 2.5 mg/kg body weight 2. Caffeine: 2.0 mg/kg body weight of 3. Combination: L-theanine 2.5 mg/kg body weight + caffeine 2.0 mg/kg body weight 4. Placebo (100 ml distilled water)	L-theanine improved hit rate in a selective attention task. No significant effect on false alarms or reaction time. No significant change on stop-signal reaction time (inhibitory control) task. Functional MRI: L-theanine and caffeine associated with task-related decrease in reactivity of default mode network, associated with mind wandering. Inhibitory control: Caffeine worsened and L-theanine had a trend of worsening inhibitory control (increased stop signal reaction time). L-theanine and caffeine combination showed a trend of improvement of inhibitory control. Overall cognition (NIH Toolbox): L-theanine and theanine-caffeine combination improved total cognition.	
(Baba et al., 2021)	Randomized, placebo-controlled double-blind parallel group study	52 healthy adults (26 in the L-theanine group, 24 in the placebo group)	1. 100.6 mg of L-theanine as capsules 2. Placebo: capsule of the same consistency	L-theanine: Improved simple rection time. No difference in reaction time or accuracy in continuous performance tasks that measured selective and sustained attention. No significant change in the Stroop task that measures inhibitory control.	Participants were non-demented, middle-aged and elderly individuals who self-reported a cognitive decline.

EFFECTS OF L-THEANINE ON SELECTIVE ATTENTION

The literature reviewed hitherto indicates that–among different cognitive domains–selective attention is the most extensively studied. Selective attention is the ability to direct attention to the task-relevant stimulus while ignoring the distractors in an environment with competing stimuli [40]. For example, in day-to-day life, at a traffic intersection, the driver should pay attention to the flashing traffic lights ahead while ignoring the flashing neon lights of billboards in the vicinity and operate the vehicle under time constraints. In this instance, selective attention is pertinent for smooth driving performance and traffic safety.

Alpha EEG rhythm is sensitive to overall attentional states of the brain. When focusing attention selectively to a certain task, anticipatory (i.e., phasic) alpha power increases and background (tonic) alpha power decreases. Gomez-Ramirez et al. [32] found that, in an inter-sensory attention task, parieto-occipital alpha power is increased more for visual stimuli than for auditory stimuli by a 250-mg dose of L-theanine. Corroborating these findings in a functional MRI study, Kahathuduwa et al. [36] also found that a similar dose of L-theanine improves visual processing in visual association areas of the brain, while decreasing the activation of some brain areas that constitute the default mode network that is associated with mind wandering. A more recent study conducted by the same authors replicated these findings in a group of children with ADHD who received L-theanine [37]. The study further went on to show that compared to a placebo, L-theanine significantly improved total cognition composite and attention in these children. Some recent electrophysiological evidence suggests that auditory attentional processing is enhanced by high doses (100-400 mg) of L-theanine in a dose-dependent manner in healthy young adults [35].

Before consuming or prescribing L-theanine as a nutritional supplement, it is important to identify which types of attentional tasks are significantly improved and which are not improved by L-theanine. Previous studies based on auditory attention tasks have shown 200 mg of L-theanine to show either a delay [32] or no change [35, 38] in reaction time.

Visual selective attention paradigms have been used more often than auditory paradigms in previous studies. Even within the visual modality, the experimental paradigms are heterogenous and the findings vary. In this regard, Kahathuduwa et al. [26, 36, 37] have consistently shown improvement of colour-based visual recognition reaction time, while no improvements have been observed in object-based [29] or visuospatial reaction time tasks [3, 27, 32]. In combination, these findings suggest that the effects of L-theanine on response speed may be at least partly attributable to the sensory modalities, favouring enhancement of visual selective attention. The body of evidence, however, is too limited to infer as to why a significant improvement with L-theanine was observed in some paradigms but not in others.

PRACTICAL IMPLICATIONS AND FUTURE DIRECTIONS

Based on the evidence reviewed in this paper, we observe a number of practical implications and future directions for further exploration.

The overwhelming majority of the studies used abstract visual stimuli rather than scenes from real-life in their experimental paradigms–an inherent feature of laboratory experimentation. However, when translating the laboratory findings to real-life scenarios, incorporating more real-life-based stimulus paradigms (i.e., simulated driving scenarios) is warranted in the assessment of the effects of L-theanine on cognitive functions. This will improve the ecological validity of L-theanine research on cognition.

Even though effects of L-theanine on attention have been tested widely in healthy adults under normal conditions, only limited research has been carried out on more compromised groups of individuals. Sarris et al. [21] investigated the effects of L-theanine as an adjunctive treatment administered over few weeks in patients with generalized anxiety disorder, whereas Kahathuduwa et al. [37] tested the acute effects of L-theanine on a group of children with ADHD.

Future exploration on healthy individuals in compromised conditions, such as those who are acutely sleep-deprived may be of interest, especially as it is well-known that fatigue related to sleep-deprivation is a common cause of road traffic accidents [41].

Albeit limited, the research evidence hitherto suggests combination of L-theanine with caffeine producing additive or synergistic effects [26, 27, 32, 34, 36]. Hence, we believe that incorporating a caffeine arm to future studies may build upon and bring forth further evidence on the combined effects of L-theanine and caffeine. Therefore, future research on long-term effects of L-theanine appears to be a promising avenue, especially as it is readily available in the market as a nutritional supplement, unlike caffeine which is largely restricted from sale due to tolerance, dependance, and other adverse effects. In this regard, L-theanine was not found to have serious adverse effects, tolerence or dependance even after repeated administration [21]. Future studies with L-theanine-caffeine combination may thus be a workaround to minimize the unwanted effects, perhaps by using the synergistic effects of the combination to minimize the dose of caffeine required to achieve attentional benefits.

Only few studies hitherto have examined the effects of L-theanine on cognition in clinical populations [21, 42-44]. Given that high doses of L-theanine are proven to be safe for long-term administration, potential benefits of L-theanine as a nutritional supplement in neuropsychiatric illnesses are worth exploring further.

The content of L-theanine varies in different preparations of tea leaves [2, 45]. Brewing time is also a major factor which could influence the amount of L-theanine extracted from a cup of tea [46], however, the maximum extraction does not seem to exceed 25 mg [2]. This dose, in a single cup of tea, was not found to show significant cognitive benefits [26]. Most studies conducted hitherto demonstrate significant attentional effects only with higher doses ranging from 100 to 500 mg of L-theanine. Therefore–as L-theanine is both safe in high doses and tasteless in nature–enriching tea with L-theanine may enhance the beneficial effects of tea, and thus be a value addition to Sri Lankan tea exports. However, professional tea tasting is essential to ensure that the unique flavour of tea is preserved, before L-theanine enrichment is pursued on a commercial scale.

In the contemporary society, commercial preparations of L-theanine are already being promoted with claims of beneficial effects on cognition and performance; and L-theanine also appears as a constituent of many supplements [7, 8]. Because these supplements can be used by athletes to improve their reaction time, a degree of caution should be exercised, since the interaction of L-theanine with other constituents has not been adequately studied. This presents yet another avenue for future exploration.

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