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Narrative Review

The effects of tea polyphenols on emotional homeostasis: Understanding dementia risk through stress, mood, attention & sleep

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SUMMARY

Decades of research provide evidence that certain phytochemicals in tea (*Camellia sinensis*) and other herbal beverages are protective against the development of sporadic types of dementia in later life. Since tea drinking is an economical and widely adopted social-cultural practice across all age groups, it is an ideal product to target in designing low-cost dietary interventions for Alzheimer's Disease (AD), the most prevalent form of dementia. In this review, we focus on the protective roles of tea-derived polyphenols and other phytochemicals on mood, the stress response, attention, and sleep, in keeping with the perspective that many early neuropathological events in AD may stem, in part, from allostatic overload. This approach aligns with the perspective that many forms of dementia, including AD, begin to take root in the brain decades prior to symptom onset, underscoring the need for early uptake of accessible and viable lifestyle interventions. The findings reviewed here suggest that consuming green and oolong tea can improve mood and reduce overall stress. However, given the caffeine content in tea and its association with stress reactivity, the effects of daily whole tea consumption on the emotional state are likely dose-dependent with an inverted-U relationship to wellbeing. Plant-based beverages that are to be consumed in high daily quantities for health purposes and which are naturally free of caffeine, such as Rooibos, may be more appropriate as a dietary supplement for managing emotional regulation over the lifetime.

1. Introduction

Dementia is a neurodegenerative syndrome involving deterioration in cognitive faculties, especially memory, and changes in mood and behaviour that significantly affect quality of life and ability to function. While older persons are more likely to be affected, symptoms of dementia are not attributable to the normal ageing process. Those affected require intensive social and medical support, placing heavy psychological, financial, and structural demands on families and communities [1]. In older populations, dementia due to Alzheimer's Disease (AD) accounts for 60–80% of all dementia cases [2]. It is one of the leading causes of dependency and disability, affecting nearly 50 million people worldwide [2]. The heterogeneity of risk factors, aetiologies, and neuropathologic processes associated with AD makes it challenging to develop new treatments that can slow disease progression, and this calls for novel approaches in addressing and understanding risk and prevention across the lifespan.

2. Aetiology

Defined as a non-communicable disease, AD is characterised by progressive neurodegeneration that has been linked to the accumulation of amyloid-beta and tangles of hyperphosphorylated tau protein in the brain. Major risk factors are diverse and overlap substantially with those associated with cardiovascular disease,

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such as atherosclerosis [3], hypertension [4], sedentary lifestyle [5]; high BMI [6], diabetes [7] and increased psychosocial stress [8,9]. Recent literature reviews have implicated many interacting pathways in the development of the disease. These studies highlight critical roles for a wide range of biological processes, including those related to normal aging [10], vascular functioning [11], immunity and inflammation [12,13], lipid [14] mitochondrial [15] and glucose metabolism [16], insulin-signalling [17], oxidative stress [18], sleep [19], endocrine function [20] and psycho-social stress [21]. Several inter-individual variables have also been established as critical risk factors, including age, genetic predisposition, traumatic brain injury, low education, and psychiatric factors [22–26]. While this research has plotted a complete picture of disease mechanisms involved in AD, the series of events that confine these pathologies to specific neuroanatomical brain regions are far less clear. Not surprisingly, current therapies have proven unsuccessful in stalling the disease progression [27], mainly because therapies that commence when symptoms first present cannot compensate for the irreversible neuronal loss that marks the final stages in a decades-long chain of neuropathological events.

Some of the earliest documented cytopathological events are observed in a brainstem nucleus called the locus coeruleus (LC) [28], which is known to be involved in attention, stress and arousal. Accumulating evidence suggests that hyperphosphorylated tau in this region, as the first detectable AD-like pathology in the brain, may be attributed largely to allostatic load [29]. This entails oxidative damage and neuroendocrine changes arising in response to chronic psychosocial stress, with significant downstream effects on the brain's inflammatory pathways and other AD markers.

2.1. Stress-related damage in the subcortex

Mechanistically, when LC neurons are stimulated by a corticotrophin-releasing factor (CRF) as part of the hypothalamic-pituitary-adrenal (HPA) axis stress response, norepinephrine (NE) is released to facilitate a state of hypervigilance [30]. While this response is adaptive in the short-term, it can lead to allostatic load, which refers to the long-term cost incurred by chronically stimulated neural or neuroendocrine responses activated to maintain short-term adaption in the face of repeated stress [31]. In neurons, excitotoxicity from overactivation of excitatory amino acid receptors can ensue, leading to neurophysiological imbalance and changes in the cytosol, mitochondria and endoplasmic reticulum [32]. Pre-clinical work has shown that tau proteins accumulate and become hyperphosphorylated in response to stress [33]. Such cellular changes occurring within the LC can have profound consequences on the overall functioning of the brain. Not only does the LC-Norepinephrine (NE) system innervate widespread parts of the brain and regulate cerebral vascular functioning [34], but it plays a central neuroprotective role by reducing neuroinflammation [35,36]. NE can down-regulate the expression of proinflammatory cytokines, such as IL-6 and TNF-α [37], by acting on β adrenergic receptors on microglia, the brain's principal immune cells. Indeed, one of the significant shifts in the research over the past decade has been a spotlight on the role of oxidative stress and inflammation in the aetiology of AD. For instance, large-scale genomic investigations have identified dysregulations in immune-related pathways as central events in the disease's pathological cascade. This evidence is corroborated by animal models and autopsies in humans [38–40]. Elevated levels of inflammatory markers are a consistent finding in post-mortem studies of AD brains [41] and other studies show that abnormal production of pro-inflammatory cytokines and reactive oxygen and nitrogen species disrupt nerve terminals leading to loss of synapses [42,43]. In fact, the APOE ε4 gene, considered the most substantial genetic risk factor in sporadic or late-life AD, has been associated with increased inflammatory cytokine response, which may explain the increased vulnerability in carriers [44].

While it is almost certain that multiple pathways are implicated in the degenerative process, the concept of allostatic load is useful for understanding these multidimensional factors within a coherent aetiological framework. Chronic exposure to stress throughout the lifespan has been the focus of many studies because of the similarities between the biological mechanisms involved in chronic stress and the pathophysiology of AD, which include dysregulation in the HPA neuroendocrine axis, chronic inflammation, abnormalities in insulin signalling, circadian rhythm imbalance, obesity, hypertension, and atherosclerosis [8,9,11–13,45];. This suggests that stress reduction should be a focus of early intervention strategies.

2.2. Tea and the brain

Anecdotal reports link tea with stress relief, but scientific inquiries into tea and mental functioning have largely focussed on cognitive capacity. Several decades of research have provided substantial evidence that tea polyphenols protect against the development of sporadic types of dementia in later life. For example, habitual tea drinkers, those that have consumed at least 3–5 cups per day throughout their lifetime, are 28% less likely to develop sporadic AD than their non tea-drinking counterparts [46]. Tea leaves from the *Camellia sinensis* plant contain an estimated 30,000 polyphenolic compounds, one of the most important of which being flavonoids (also referred to as catechins or tannins) [47]. Flavonoids can be further broken down into subclasses: flavonols, flavones, isoflavones, and anthocyanins [48]. The most prolific of which is flavanols (flavan-3-ols). Major phytoconstituents of flavanols contain catechin (C), epicatechin (EC), epicatechin gallate (ECG), gallocatechin (GC), epigallocatechin (EGC), and epigallocatechin gallate (EGCG) [49]. EGCG is the most active and predominant constituent of this group and is extensively studied due to its abundance of antioxidants in relation to their effects on health and well-being [50]. During oxidation, flavanols are converted to theaflavins and thearubigins in black tea [51]. Tea also contains amino acids and caffeine, the main methylxanthine in tea [52]. These primarily include theanine, specifically, L-theanine, which is responsible for the distinct 'tea' taste, also known as umami [49]. *C. sinensis* is also relatively rich in minerals. This includes fluorine, manganese, arsenic, nickel, selenium, iodine, aluminium, and potassium. Due to tea's popularity across the globe and its abundance of antioxidants and minerals, it has been studied for its broad health benefits [52].

In terms of brain health, the protective effects of tea polyphenols have been attributed to their ability to counteract neuropathological changes, including oxidative damage, inflammation, insulin resistance and blood–brain barrier dysfunction. For instance, a metanalysis by [37] shows that the oxidizing of macromolecules is a predicating factor of AD. That along with its incredible antioxidant capacities, tea polyphenols have anti-amyloidogenic properties. Caffeine, in turn, protects against the degradation of the blood–brain barrier and is proposed to block the adenosine A2A receptors, which help minimise damage caused by β-amyloid. Several reviews in recent years provide evidence that these protective effects appear to support cognition over the long term. For instance [53], published a systematic review of findings on green tea and cognitive functioning, indicating that green tea positively affected cognitive functioning and minimised the presence of cognitive dysfunction. Similar systematic reviews by [54] and [55] found that there was an inverse relationship between tea consumption and cognitive impairment.

In comparison to the roles of tea in supporting cognition, very little attention has been paid to the effects of tea on mood, emotion, and stress. This is curious given that tea is one of the world's most popular drinks precisely because it is a preferred beverage, suggesting that tea has rewarding properties. In the following review, we focus our attention on the role of tea and its major polyphenolic constituents in supporting emotional homeostasis, that is, stress relief, with the view that chronic stress over the course of a lifetime may predispose genetically vulnerable individuals towards the development of AD. For purposes of limiting our scope, we focus on evidence reported to date on mood, stress physiology, attention, and sleep.

3. The effects of tea on mood, emotion and stress

In the following sections, health benefits in relation to mood and emotion, physiological stress response, attention and sleep are grouped and reviewed according to tea type and individual tea constituents.

4. Teas

4.1. Green tea

Mood and Emotion. In a cross-sectional cohort of approximately 42,000 Japanese adults over the age of 40, [56] found that a higher daily intake of green tea was associated with lower incidences of psychological distress. Similarly, [57] reported that the prevalence of depressive symptoms was 44% lower for participants aged 70 years or older who consumed ≥4 cups of green tea than those who consumed ≤1 cup/d. Notably, both studies utilised self-reports to gauge mental health experiences and daily tea intake.

Alternatively, in a Netherlands-based study that administered four grams of matcha green tea in snack bars to 23 participants using a single-blind placebo-control design, no significant changes in mood were found as measured by the Profile of Mood State [58]. Another study in Japan found that after adjusting for age, area, perceived mental stress, lifestyle and daily caffeine intake, the consumption of brewed green tea was not statistically associated with any decrease in risk of mental ill-health among either males or females (aged 20–69) as measured by the 12-item General Health Questionnaire [59]. In examining green tea constituents [60], in their investigation of a double-blind, crossover design, reported that low-caffeinated green tea (0.3/0.4 times that of control) as compared to the standard green tea resulted in significantly fewer symptoms of fatigue and stress as per self-report measures. In a Korean population analysis of 9576 participants, a 21% decrease in the prevalence of depression was revealed by frequent consumption (>3 cups/week) of green tea [61].

These findings suggest that changes in subjective feeling states due to green tea are positive yet modest. Green tea appears to have a dose-dependent relationship with mood and might only come into effect after long periods of daily intake. Some of the acute effects of tea on subjective wellbeing are probably mediated by its caffeine content, but the research is still in its nascent stages.

Stress Response. In a blind, placebo-controlled study of daily matcha consumption over eight days, reduced counts of salivary α-amylase activity (sAA), an oral cavity enzyme that denotes sympathetic system excitement, was observed by those in the experimental condition (Unno et al., 2018). In an earlier study undertaken by many of those same authors, levels of sAA decreased significantly following low-caffeinated green tea consumption as compared to standard green tea. This effect was most notable following a day's work in 19 middle-aged Japanese men and women [60]. Similarly [62], found that 250 ml of green tea suppressed salivary chromogranin A (CgA), another stress biomarker, following mental tasks over three experimental trials. Heintzpeter et al. (2011) furthermore reported that green tea inhibited the enzyme 11 b-hydroxysteroid dehydrogenase type 1 (11 b-HSD1), which aids in the conversion of cortisone to cortisol (a stress hormone) in human liver tissue. This was true even of small concentrates:1 g of green tea in 10 ml of water.

Studies also show that green tea has beneficial effects on hypertension, considered a biomarker of stress. Green tea extracts (208 mg of decaffeinated green tea polyphenols) taken twice daily over three months have been shown to significantly decrease diastolic and systolic blood pressure in obese, hypertensive adults [63]. Similar research designs by [5] and [64] observed decreases in diastolic blood pressure only, while [65] noticed a reduction in systolic blood pressure [66]. reported that their healthy sample experienced a sustained lowered systolic blood pressure three months following decaffeinated green tea compound capsules (200 mg green tea extracts and 100 mg L-theanine, equivalent to roughly 13 cups of green tea or 4–5 cups of black tea) taken twice daily [67]. additionally noted a decrease in resting heart rate following 12 weeks of twice-daily green tea extract consumption. However, some null findings have been reported [68,69]. found that caffeinated green tea supplementation versus placebo had no effect on blood pressure parameters in overweight females and healthy men, respectively.

Overall, findings suggest that green tea consumption can help reduce activity in the HPA axis regardless of dose. However, only decaffeinated green tea results in lowered blood pressure parameters.

Attention. In a double-blind, randomised controlled trial, 25 Japanese adults between 50 and 69 were administered 336.4 mg of decaffeinated green tea catechins. The catechin group performed better on the continuous performance task, a measure of attention, compared to the placebo but this same performance was not observed during other tests of attention. These tests included the Stroop test and a shifting attention task. There were no significant differences for the remaining cognition tests [70].

Another double-blind, placebo-controlled experiment by [71] showed that green tea extracts and L-theanine (1680 mg over 16 weeks) improved memory and selective attention scores on the Mini-Mental State Examination-K in those with mild cognitive impairment. [72,73]; and [74] observed moderate increases in attention-switching accuracy and slight increases in reaction time following acute doses of green tea derived caffeine (approximately 40 mg) and L-theanine (approximately 97 mg) [75]. observed the effects of 100 mg of L-theanine and 50 mg of caffeine, equivalent to 1 cup of green tea or 2 cups of black tea. They found that both caffeine alone and the combination of L-theanine and caffeine as found in green tea increased scores on attention-switching tasks as well as memory tasks compared to control. Importantly, doses were administered in three test sessions, separated by 7-day washout periods. Effects were observed 60 min and 90 min following administration. Using the same quantities [28], observed the modulation of alpha brain activity via EGG and improved visuo-spatial cueing following ingestion of both caffeine and L-theanine over four days [76]. suggest that these findings hint at anticipatory visual attention networks. In investigating slightly higher doses (250 mg L-theanine and 150 mg caffeine) [77], reported a positive L-theanine by caffeine interaction effect for delayed word recognition reaction time. This was observed over five study days, separated by 7-day washout periods.

These findings suggest that green tea improves attention and may even aid other areas of cognition, including memory. However, findings by [72,70,73], and [74] pose questions surrounding the role of caffeine and cognition and how much cognitive improvements

may be attributed to single tea constituents or in combination as consumed by green tea.

Sleep. In a double-blind crossover design [60], found that when comparing low-caffeine green tea and standard green tea, there was a marked improvement in sleep quality for the low-caffeine group. Sleep quality included sleep efficiency, sleep onset latency, and non-REM sleep as measured by an EEG. Furthermore, standard green tea was not correlated with total sleep time, whereas low-caffeinated green tea was positively correlated with slow-wave sleep. Another study by [78] examined the effects of standard green tea and low-caffeinated tea in an elderly sample. While non-significant effects were examined between groups with regards to sleep quality, it was discovered that sAA levels were negatively correlated with total sleep time and sleep efficiency, proposing that it was the theanine present in the green tea that suppressed the effects of caffeine on sleep disturbance that are mentioned further below in the paper.

4.2. Oolong tea

Mood and Emotion. In a sample of 3177 elderly participants, [79] observed that those who were habitual tea drinkers (equal to three or more cups of green, black or oolong tea) were at significantly lower risk of developing depression than their non-tea drinking counterparts as measured by the Geriatric Depression Scale. Similarly, in their pre-test and post-test design [80], reported a decrease in acute stress following an acute ingestion of GABA-fortified oolong tea in a healthy sample of thirty males and females.

Stress Response. In a university sample, GABA (γ-aminobutyric acid)-fortified oolong tea improved heart rate variability, an indicator of adaption to stress [80]. In a one-year, retrospective study of 1507 healthy Taiwanese adults [81,82], observed a reduced risk of hypertension in daily drinkers of half a cup of oolong or green tea. This was after adjusting for age, sex, socio-economic status, lifestyle and dietary factors, hip-to-waist-ratio, BMI, family history of hypertension, sodium intake, cigarette smoking and alcohol consumption. The study further noted a dose-dependent relationship between tea consumption and hypertension.

Attention and Sleep. To our knowledge, no studies have measured Oolong tea's impact on traditional measures of attention or sleep in human subjects.

4.3. Black tea

Mood and Emotion. In a crossover design, self-rated questionnaires revealed an increase in 'energetic arousal' and feelings of pleasure and reduced fatigue following acute consumption of both coffee (75 and 150 mg) and black tea (37.5 and 75 mg). The relationship appeared to be dependent on caffeine content and beverage strength [83]. Similarly, in a double-blind, placebo-controlled, crossover design by [72] wherein 26 healthy volunteers were administered two cups of black tea and one cup of 'placebo tea', self-rated alertness levels increased significantly during the experimental condition. However, in their investigation of black tea's effect on self-rated feelings of contentment and calmness, no significant effect was found. Alternatively, in a multivariate analysis of black tea and depression [84], found that consuming more than one cup but no more than four cups a day, protected against depression in 491 Turkish adults. Moreover, consuming 450–600 mg of caffeine appears to be more effective in reducing depression than quantities that fall outside this range.

Stress Response. Looking at cortisol levels in saliva, studies suggest that black tea has beneficial effects on stress arousal. In a double-blind parallel study design, 75 men aged 18–55 were administered either black tea (total tea extract equivalent to 1050 mg) or a placebo for six weeks. Following stress-inducing activities, cortisol levels dropped significantly at the 50-min mark for those in the tea group. However, all other measures of a stress response, including blood pressure, heart rate and subjective stress levels, did not differ between groups [85]. Nevertheless, several studies do show that black tea alleviates hypertension. In a non-crossover, randomised placebo-controlled, double-blind trial, women aged 35–75 in the experimental group consumed 3 cups of black tea daily over six months [86]. Compared with those who received a placebo, there was an observed drop in blood pressure parameters. In a crossover design of 32 adult males and females [83], observed a short-lived spike in diastolic blood pressure but a maintained increase in systolic blood pressure following acute consumption of caffeinated black tea (4.6 mmHg over baseline). Additionally, there was a temporary increase in heart rate that fell dramatically after the 10-min mark. Skin conductance rate (SRC) was also measured and revealed that, following black tea consumption, there was a significant increase in SRC as compared to 'no-drink' and 'hot water' conditions.

These findings, therefore, suggest that caffeinated black tea does appear to influence the physiological stress response. However, the evidence is sparse, and further studies are required to establish a reliable effect of black tea on stress physiology.

Attention. In the same crossover design mentioned above [72], asked their 26 healthy participants to complete attention tasks following the ingestion of two cups of black tea in one condition and two cups of 'placebo tea' in another condition for their first study investigation. These drinks were consumed within 60 min. In total, cups contained 1040 mg of tea solids, 100 mg of caffeine, and 46 mg of theanine. In study 2, three cups of black tea were administered in one condition while three cups of 'placebo tea' were administered in another. These drinks were consumed over 90 min. In total, cups contained 1140 mg of tea solids, 90 mg of caffeine, 36 mg of theanine. 'Placebo teas' were prepared with water, tea flavourings and oak tannin. Across studies, results concluded that black tea consumption significantly improved performance accuracy on attention tasks. Another crossover design by [83] investigating the effects of caffeine derived from black tea and coffee, found that arousal increased following caffeine consumption, regardless of dosage (37.5 and 75 mg in tea, 75 and 150 mg in coffee). Furthermore, a study by [87] assessed the effects of black tea on 32 adults with a mean age of 21, by administering a battery of cognitive tests. Black tea consumption demonstrated improved alertness and attention allocation. Contrarily, participants that consumed black tea scored lower on their delayed memory recall task in comparison to the water placebo. This finding is possibly due to the high caffeine content in black tea, which is known to alter brain activity in the dorsolateral Pre-Frontal Cortex during a working memory task [88].

Sleep. To our knowledge, no study to date has investigated the effects of black tea on sleep in humans.

5. Tea constituents

5.1. L-theanine

Mood and Emotion. In a randomised, double-blind, placebo-controlled, crossover design, 30 participants were administered both 200 mg of L-theanine and a placebo each night before sleep over four-week period [89]. After each administration, participants completed various mental health and sleep questionnaires. Results suggested a reduction in anxiety and depressive symptoms following L-theanine consumption. Likewise, in a study conducted by [62]; 16 voluntary participants, over the age of 20, were administered 200 mg of L-theanine prior to completing various

mental and stressor tasks. This began by establishing a baseline which included the administration of a subjective stress assessment and attaching a skin-surface probe following a 15-min rest on arrival. Thereafter (approximately 25 min after arrival), L-theanine was administered, and physiological and psychological measurements were taken again approximately 45 min following sample ingestion. Results indicated that L-theanine reduced tension and anxiety scores during stressor tasks, as measured by the Profile of Mood States rating scale.

Similarly, in a sample of 16 volunteers, between the ages of 18 and 34 [90], utilised a double-blind, placebo-controlled design to show that intake of 200 mg of L-theanine, 1 h following baseline measurements, decreased self-reported anxiety prior to an anticipated anxiety-provoking event. This was observed 2 ½ hours and 5 h after treatment. However, L-theanine did not indicate any significant anxiety-reducing effects during conditions of heightened anxiety. Alternatively [77], in their randomized, double-blind, placebo-controlled, balanced crossover study of 24 university participants, found that there was no indicated effect on subjective mood ratings 30 min, and again, 90 min after intake of 250 mg L-theanine alone.

Looking at the effects of L-theanine on those with neurological conditions, [91]; reported that 400 mg of L-theanine supplemented with prescribed antipsychotic medication not only decreased anxiety but also helped alleviate a negative mood. This was a randomized, double-blind, placebo-controlled design wherein 60 patients (mean age 36.4 years) diagnosed with schizophrenia and schizoaffective disorder received one 200 mg L-theanine capsule or a placebo twice a day for 8 weeks. Baseline measures were established prior to treatment and measures were taken again at 2 weeks, 4 weeks, 6 weeks and at the end of the trial.

In summary, it appears that moderate-to-large quantities (200 mg–400 mg) of L-theanine reduces anxiety symptoms just before completing anxiety-inducing tasks. However, this same reduction is not present during the completion of these tasks [90]. Findings by [77] might indicate that the presence of heightened and anticipatory anxiety that allows for significant effects due to L-theanine (250 mg). The same promising effects of L-theanine on mood and emotion appear to be true for both a non-clinical and clinical population [91].

Stress Response. In a randomised, placebo-controlled, double-blind crossover design, 36 healthy participants between 18 and 40 years were administered 200 mg of L-theanine mixed in a 430 ml solution. Salivary cortisol was measured 1 h and again 3 h post-dose. Testing took place over two full days with identical procedures, including a baseline assessment and a 48-hr washout period between each day. The experimental group receiving an acute treatment of L-theanine was significantly lower than the control 3 h following ingestion on both days [92]. Furthermore, the participants in the experimental group were more relaxed when performing stressful tasks and had decreased cortisol levels in comparison to the placebo group. This finding highlights the anxiolytic effects of consuming L-theanine.

Looking at heart rate variability, in a double-blind, placebo-controlled experiment that administered 200 mg of L-theanine to a sample of 12 male students between 20 and 25 years [93], found that intake of L-theanine reduced self-reported psychological stress, as well as reduced physiological stress during an acute stressor task. An evaluation of heart rate variability suggested that L-theanine may reduce sympathetic nervous system activation, thereby minimizing the experience of stress.

Regarding blood pressure [62], observed that L-theanine (200 mg) administered over three testing days with one-week washout periods between each day significantly impeded increases in blood pressure during stressor tasks in high-stress response participants. Alternatively, in a double-blind, placebo-controlled study of 44 young adults between the ages of 18 and 34 years [74], found that an acute combination of 97 mg of L-theanine and 40 mg of caffeine, equivalent to approximately 4 cups of black tea or 12 cups of green tea, raised both systolic and diastolic blood pressure 70 min post-ingestion. This was observed in a sample of habitual caffeine drinkers.

Attention. An acute dose of L-theanine (250 mg diluted in 200 ml of room temperature water) has been shown to alter alpha brain activity and result in sustained attention during rest and during attention-demanding mental tasks, as observed by EEG recordings [94]. Similarly [95], reported that consuming 200 mg of L-theanine resulted in relaxation without drowsiness because of increased activity in the alpha frequency band 45, 60, 75, 90 and 105 min after ingestion. Furthermore [96], observed a decrease in background alpha levels compared to the placebo condition during mental activities suggesting that L-theanine mediated selective attention.

Similarly [74], found that a combination of L-theanine (97 mg) and caffeine (40 mg) enhanced alertness and attention, and reduced self-reported fatigue amongst participants. On the contrary [77], showed only adverse outcomes on attentional tasks and greater experience of headaches 30 min, and again 90 min, after intake of 250 mg L-theanine alone, equivalent to approximately 10 cups of black tea or 31 cups of green tea. However, such as that found by [74]; the results of a combination of 97 mg L-theanine and 40 mg caffeine were more promising, indicating increased attention and alertness, as well as fewer reports of mental fatigue, general tiredness, and headaches. These findings suggest that while L-theanine alone alters brain activity, indicating heightened alertness, this effect does not seem to improve scores on attention-orientated tasks or effect self-perceptions of alertness. However, there does appear to be a positive interaction effect between caffeine and L-theanine and attention on these same measures.

Sleep. A review by [97] concluded that L-theanine induces relaxation and not drowsiness, improving the quality of sleep. The absence of drowsiness following awakening offers an advantage over most sleep sedatives. Additionally [89], observed a decrease in sleep quality following L-theanine consumption (200 mg/day for four weeks) compared to the placebo condition. However, sleep latency and sleep disturbance reportedly decreased compared to placebo.

In a clinical sample conducted by [98]; 17 patients diagnosed with schizophrenia, according to the Diagnostic Statistical Manual of Mental Disorders 4th edition, were administered 250 mg of L-theanine daily in combination with prescribed antipsychotic medication. After 8 weeks of treatment, results showed a significant improvement in sleep quality as assessed by the Pittsburgh Sleep Quality Index (PSQI). This index comprises of 19 self-rated questions and five that are answered by a next-of-kin, monitoring their sleep. Items reveal experience around subjective sleep quality, latency, and duration, as well as sleep efficiency and sleep disturbances [99]. Significant differences were found in total scores pre- and post-treatment [98]. Results showed an inverse relationship between L-theanine consumption after 8 weeks and positive and negative symptoms associated with schizophrenia, as measured by Positive and Negative Syndrome Scale (PANSS).

Further clinical samples including boys with attention deficit hyperactivity disorder (ADHD), have been studied by [100]: In a randomised, double-blind, placebo-controlled design spanning 10 weeks, 93 boys between the ages of 8–12 were administered two 100-mg L-theanine tablets or a placebo in the morning and afternoon daily. Sleep was recorded via an actigraph sleep monitor strapped to the wrist as well as subjectively using the Paediatric Sleep Questionnaire. Results suggested that L-theanine improves

sleep quality and decreases nightly activity. However, no significant differences were found for sleep onset and total sleep duration.

5.2. EGCG

Mood and Emotion. In a double-blind, placebo-controlled, crossover study, 27 healthy adults were administered a placebo and two doses (135 and 270 mg) of EGCG. During the absorption period of 45 min, participants completed mental activities for a further 42 min, and a questionnaire that measured aspects of mood and emotion. Results concluded no significant differences across treatments [101].

Stress Response. In that same study by [101]; there was an observed significant reduction in heart rate and blood pressure following doses across treatments.

Attention and Sleep. To our knowledge, there are no existing data pertaining to the effects of EGCG on attention and sleep in human subjects.

5.3. Caffeine

Mood and Emotion. In a cross-sectional Japanese health survey study of 537 working-class men and women spanning 5 months [102], observed an inverse relationship between caffeine consumption, assuming one cup of green tea and coffee contains 20 mg and 60 mg of caffeine, respectively, per 100 ml and depressive symptoms. This relationship was present regardless of whether caffeine was derived from green tea or coffee. Depressive symptoms were assessed using the twenty-item Japanese Epidemiological Studies Depression (CES-D) scale. The same finding was reported by [103] in a prospective, longitudinal study that spanned 10 years. The sample of 50,739 US women (mean age 63) were free of depressive symptoms at baseline. During the follow up, 2607 cases of depression were identified in the sample. There was an observed decreased risk of depression with dose-dependent consumption of caffeine from various sources, including coffee, energy drinks, soft drinks, and various foods such as chocolate. The same finding was not present for decaffeinated coffee.

Similarly, a Finnish population study investigating coffee and the risk of suicide in 1972, 1977, 1982, 1987, and 1992 reported that the same inverse relationship was observed but only up to 6 or 7 cups. Thereafter, the risk of suicide increased [104]. Conversely, positively correlated findings were observed in a younger sample: In a cross-sectional study by [105] of 234 middle school students (average age 15 years) in Korea, it was found that there was a significant relationship between high caffeine content and high subjective depression and anxiety scores. Alternatively, in a study by [106,107] that investigated the effects of 30 h of caffeine withdrawal in chronic caffeine consumers, it was found that mood changes, as compared to their placebo conditions, were non-significant. Mood was measured using a compilation of self-rated items drawn from previously established measures. Another randomised, placebo-controlled study by [108] investigated the effects of caffeine (3.3 mg/kg) on 31 male medical university students, 20 of which were normotensive and 11 hypertensive, during a lecture and again during an exam. On days when participants reported to lectures, caffeine was administered approximately 5 h before the lecture and the time of post-treatment testing. On days when participants reported to exam rooms, caffeine was administered approximately 45 min prior to writing and 2 h 45 mins- 3 h 45 min prior to post-treatment testing. Via self-reports, it was found that caffeine did not influence feelings of distress in either setting. These findings suggest that the socio-demographics of a sample may moderate the effects of caffeine on mood and emotion.

Stress Response. In a correlational, longitudinal study, running between 2008 and 2010 [109], observed a very weak, non-significant association between caffeine consumption and heart rate variability in approximately 15,000 Brazilian citizens (aged 35–74). In a study by [62]; 14 voluntary participants, over the age of 20, were administered 100 mg of caffeine 45 min prior to completing various mental and stressor tasks. Results indicated that caffeine produced an inhibitory effect on blood pressure during stressor tasks in high-stress response participants, which was comparable, but less significant, to the effects of L-theanine (200 mg). This finding contrasts those found by [74] who observed a rise in blood pressure parameters following a combination of both L-theanine (97 mg) and caffeine (40 mg).

In a double-blind, randomised, placebo-controlled study of 30 university students [110], found that caffeine concentrate (98 mg) resulted in increased systolic and diastolic blood pressure compared to placebo, while the comparative naturally sourced caffeinated herbal drink (approximately 85 mg) resulted in a less dramatic increase in systolic blood pressure. In a similar cohort [108], administered 3.3 mg/kg of caffeine or a placebo before two lectures and two exam periods. Cortisol saliva levels and blood pressure was monitored throughout these four sessions. Caffeine consumption and the exam condition increased cortisol saliva secretion. For both hyper- and normo-tensive participants, blood pressure was raised following caffeine consumption in combination with added stress of the exam condition, pointing to additive effects of caffeine. Similar findings by [111] revealed that in both experimental groups, consuming 200 mg and 400 mg of caffeine, respectively, and attending to 20 min of mental arithmetic, sAA levels increased dramatically. The same effect was not found for the control group who only completed the psychological stressor. Moreover [111], observed a dose-dependent relationship between caffeine and sAA levels.

[112] furthermore demonstrated the increase of adrenocorticotropic hormone levels and cortisol in plasma of both normo- and hypertensive young men following 3.3 mg/kg of caffeine. This increase was reported following caffeine consumption alone as well as in combination with completing mental and psychomotor tasks. Replicating the same dose and research design [113], affirmed these findings in strictly normotensive men: caffeine increased blood pressure parameters and decreased heart rate at rest as compared to placebo. In a smaller sample of 10 healthy men and women who ingested an acute dose of caffeine (4 mg kg-1), a crossover design observed an immediate decrease in heart rate when participants were asked to stand up from their chairs following caffeine consumption. However, their heart rates soon evened out. Moreover, changes in blood pressure following caffeine ingestion were non-significant [114].

Looking closer at the effects of caffeine just before exercising on healthy individuals [115], found an increase in both diastolic and systolic blood pressure as well as a decrease in heart rate following 3.3 mg/kg of caffeine as compared to placebo. These effects lasted throughout the 1-h exercise session. Similar findings have been reported by studies that include washout periods wherein participants are asked to abstain from caffeine for an amount of time prior to, during, or after a study trial: In a between-subjects design, 54 volunteers were categorised as 'heavy caffeine users', 'heavy smokers' and 'non-smokers and non-caffeine users' were asked to abstain from caffeine for 24 h. Afterwards, subjects were administered coffee containing 2.2 mg/kg of caffeine. Across groups, there was an observed elevation in blood pressure parameters, and there were no significant differences between groups. There was, however, a longer half-life for those intolerant of smoking and caffeine [116].

In investigating higher doses of caffeine over a longer period [117], designed a double-blind, placebo-controlled, crossover,

counterbalanced design which involved four experimental conditions wherein 36 healthy men and women ingested either caffeine or a placebo three times a day for the first six days which was then followed by an extra day of either caffeine or a placebo. At the end of the trial, there was an observed elevation in blood pressure immediately following caffeine ingestion which levelled out or even decreased after a period of caffeine withdrawal [118]. affirmed the same finding by, comparing those drinking boiled or filter coffee, to those who abstained completely from caffeine for nine weeks experienced a slight but insignificant decrease in heart rate as well as in blood pressure parameters. Overall, there were no significant differences between those assigned boiled coffee and those assigned filtered coffee in a healthy sample.

These findings suggest that caffeine mediates the physiological stress response. There appears to be a more substantial effect of caffeine on blood pressure parameters compared to heart rate variability for both normo- and hyper-tensive participants. Moreover [117], suggests that these effects may be reversed following a period of caffeine abstinence.

Attention. [74] furthermore found that a combination of small quantities of L-theanine (97 mg) and caffeine (40 mg) enhanced alertness and attention, and reduced self-reported fatigue amongst participants. This was observed within 70 min of ingestion. Similarly, in a randomized, double-blind, placebo-controlled, balanced crossover study of 24 university undergraduate students, there was an observed improvement on several attentional measures and a reduced experience of mental fatigue among participants after intake of 150 mg of caffeine alone, equivalent to approximately 2 cups of black tea or 3–4 cups of green tea. Additionally, the results of a combination of 250 mg of L-theanine and 150 mg of caffeine resulted in increased attention and alertness, as well as fewer reports of mental fatigue, general tiredness, and headaches over the five study days [77].

In another double-blind, placebo-controlled crossover study, 17 daily caffeine consumers (approximately 350 mg/d) were asked to either abstain from caffeine for a 30-h period or adhere to regular caffeine consumption before being administered a placebo or 250 mg of caffeine [106]. In the abstained condition, caffeine had a greater effect on choice reaction time as compared to the normal adherence group, but caffeine was found to positively influence selective attention in both conditions compared to placebo. In another study in which caffeine withdrawal effects were observed [107], administered 250 ml drinks of 37.5 g glucose, 75 mg caffeine and flavourings or a placebo to 14 undergraduate males and females who had fasted and abstained from caffeine overnight. The results demonstrated that compared to placebo, the caffeinated drink improved simple, choice and digit vigilance reaction time. Both studies that investigated the effects of caffeine withdrawal also noted the improvements of memory as compared to placebo. No other cognitive outcomes were significant.

[108] furthermore reported that following caffeine consumption (3.3 mg/kg), students experienced greater feelings of 'activation' than the placebo as per self-reports. Greater activation was also noted for exam days as compared to lecture days. Participants furthermore reported greater activation when caffeine was paired with an exam day as compared to caffeine paired with a lecture day. Based on this literature, both caffeine alone as well as in combination with L-theanine positively influences attention and alleviates feelings of fatigue. Moreover, the effects of caffeine on attention appear more prominent following caffeine withdrawal than following normal caffeine adherence. Findings furthermore suggest that these effects are present in quantities as little as a single dose of 75 mg, equivalent to 1–2 cups of black tea or 1 cup of green tea.

Sleep. In a randomised, double-blind, placebo-controlled trial, it was found that 400 mg of caffeinated pills taken 0, 3 and/or 6 h prior to sleep, significantly disrupted the sleep of 16 healthy daytime workers, as measured by EEG and sleep diaries [119]. In a double-blind, crossover study of both a young adult group and a middle-aged adult group, 200 mg of caffeinated pills produced an increase in sleep latency, decreased sleep duration and reduced sleep efficiency in both age groups [120]. Similarly, in a cross-sectional study in Thailand, university students that reported drinking caffeinated drinks had significantly longer sleep latency and reported greater difficulty functioning during the days than those who did not. This finding is further supported by [121] who, in a randomised, double-blind, longitudinal study, administered 49 healthy participants with either decaffeinated or caffeinated coffee. This involved a five-day washout period, a five-day treatment period, and another five-day washout period following treatment. Results demonstrated that there were no significant changes in sleep quality or quantity for those who received decaffeinated coffee. However, for the caffeinated group, there was a significant decrease in overall sleep during the treatment period. Further self-reports suggested that caffeine affected time spent awake and therefore the circadian rhythm and homeostatic balances related to sleeping.

This finding was furthermore true for studies that administered caffeine derived from green tea: In a double-blind crossover experiment by [60,78]; 20 middle-aged individuals were administered both standard caffeinated green tea and decaffeinated green tea in their investigation of stress and sleep. Results concluded that following low-caffeinated consumption, individuals experienced significantly better sleep quality as per EEG recordings and fewer accounts of fatigue as per self-reports as compared to measures following consumption of the cup of standard green tea.

Alternatively, in a cross-sectional US national survey, researchers observed a non-significant relationship between caffeine consumption and insomnia. However, there was an observed interaction effect between higher caffeine consumption and lower habitual sleep with a higher risk of non-restorative sleep [122].

5.4. Quercetin

Mood and Emotion, Attention and Sleep. To the best of our knowledge, there is no available data on the effects of quercetin on mood and emotion on human subjects. However, the neuroprotective effects of quercetin are attributed to its ability to cross the blood–brain barrier and is identifiable in the brain numerous hours after administration [123]. The anxiolytic effects of quercetin have been demonstrated by ischemic brain injury inhibition *in vivo* [124]. Furthermore [125], highlight preclinical studies of depressive-like behaviour models, treated with quercetin doses between 10 and 100 mg/kg, which together with its glycosides provide potential anti-depressive effects.

Stress Response. In a randomised, controlled, crossover design by [126]; 15 healthy participants attended five testing sessions where they were administered either 0, 50, 100, 200 or 400 mg of quercetin. Between each testing session, participants entered a week-long washout period. Blood pressure was measured an hour before and after administration. Whilst a dose-dependent relationship was observed for quercetin consumption and quercetin plasma levels, no effect on blood pressure was found between treatments.

Likewise, in a double-blind, placebo-controlled crossover design, five normotensive and 12 stage 1 hypertensive men were administered 1095 mg of quercetin and corn starch placebo [127]. Treatments occurred in single sessions and were separated by a one-week washout period. As compared to the placebo, a single dose of quercetin lowered blood pressure parameters in hypertensive men but not normotensive men. This finding furthermore

affirms the lack of dose-dependency of quercetin and blood pressure levels as observed by [126]. Investigating a slightly lower dose [22], observed the effects of 730 mg of quercetin daily for 28 days on blood pressure and oxidative stress in 41 stage 1 hypertensive and prehypertensive males and females. There were no significant changes in blood pressure in those prehypertensive following quercetin ingestion. There was however a decrease in blood pressure parameters for stage 1 hypertension.

In a similar research design by [128]; ninety-three overweight and obese participants between the ages of 25 and 65 were administered 150 mg of quercetin daily for six weeks. Five-week washout periods took place between treatments. Compared to the placebo, quercetin reduced systolic blood pressure in both those overweight and obese. The difference in levels of c-reactive protein, a biomarker of stress, between groups and treatments were non-significant.

Alternatively, in their investigation of 50 women between the ages of 19 and 70 with rheumatoid arthritis, 500 mg of quercetin daily for 8 weeks as compared to placebo did not result in changes to blood pressure parameters, oxidative stress, or inflammatory biomarkers [129]. A similar finding was observed by [130] who investigated the effect of 1000 mg of quercetin or a placebo daily on eight male endurance runners. Following the trial there were no changes in heart rate variability.

6. Discussion

Research accumulated over the last thirty years suggests that polyphenols in tea may have an important role to play in slowing or preventing dementia due to neurodegeneration. While there have been many reviews of the effects of tea on cognitive capacities [53,131,132]), far fewer studies have considered emotion and stress. This gap is pertinent since the field of Alzheimer's disease has begun to appreciate the strong links between chronic stress over the lifetime and elevated risk for developing neurodegenerative disorders in later life [8,9]. To address this gap, here we have provided an overview of the literature on the role of *C. sinensis* in supporting emotional homeostasis by reviewing studies on the effects of tea on emotion and mood, stress biomarkers, attention, and sleep. In doing so, we aimed to comment on the potential role of lifelong tea drinking in reducing risk factors for Alzheimer's Disease (AD) related to chronic stress and allostatic overload.

Overall, there is a modest but encouraging body of evidence indicating that different types of tea (green, black and oolong) and the various tea constituents (L-theanine, caffeine, quercetin and EGCG) support psychological wellbeing and improve stress reactivity, sleep, and attention in humans. There has been far greater research into the effects of one specific type of tea, that is, green tea, and one specific tea constituent – caffeine – over other varietals and polyphenols on physical and psychological health. Of note, research concerning rutin, a bioflavonoid with known antioxidant capacities [133], and its effects on the various variables investigated is extremely underdeveloped and was consequently excluded from the review. As some of the studies included in this review did not control the tea constituents under investigation, it is difficult to conclude whether the overall effects reported are attributed to a combination effect or a sole constituent.

Nevertheless, findings suggest that green tea, especially in higher quantities and possibly with reduced caffeine content, improves mood and emotional wellbeing. Even in small doses, green tea reduces stress-induced physiological responses including cortisol secretion and blood pressure [68,134,60,62]; and its unique constituents appear to support attention and mental focus too. Despite its caffeine content, green tea also seems to improve sleep, which is more significant when its caffeine content is reduced [78]. Findings regarding black tea are sparse but what was found suggests that black tea's effect on mood and emotion is mediated by its caffeine content as well as its L-theanine content, as noted by [72]. This might explain why in some studies, black tea was positively correlated with positive mood, but in other studies no effect was found. There was however consensus that black tea consumption increased subjective feelings of alertness as compared to placebo, regardless of caffeine content. However, findings regarding the effect of black tea on stress management are mixed. In some cases, black tea was found to exacerbate stress-induced physiological responses with regards to skin conductance rate and blood pressure, while in others, black tea reduced salivary cortisol levels, a stress response, and had no effect on blood pressure and heart rate variability [86,83].

The literature reviewed here suggests that many of the stress-reducing effects of tea can be attributed to L-theanine, which has been found to alleviate negative mood and anxiety in some cases [77,90,62]. Much less is known about the effects of EGCG, quercetin and rutin on mood and stress. Caffeine in combination with L-theanine also appears to enhance attention-related performance during mental tasks [74]. However, while L-theanine alone alters brain activity, suggesting a positive attention-enhancing effect, it does not seem to affect performance on attention-related tasks [96,94]. Whilst findings concerning L-theanine on sleep were sparse and mixed, it appears that L-theanine decreases nightly disturbances during rest and might improve overall sleep quality for both neurotypical and neuro-atypical persons [98]. Literature investigating caffeine, however, was far more plentiful: Caffeine, overall, was found to positively affect mood and emotion for adult samples [103,102]. This effect was dose dependent. Negative outcomes were only associated with a younger cohort which might prompt questions pertaining to how caffeine and mood might be mediated by age [105]. Caffeine was further found to exacerbate the stress response by increasing blood pressure parameters and cortisol salivary levels while also decreasing heart rate variability in both hyper and normotensive participants [110,109,74,111,108]. Caffeine was also found to enhance overall attention and this effect was greatest following a period of caffeine withdrawal. With regards to sleep, caffeine consumption results in sleep difficulties and an overall decrease in sleep quality [119,120].

The findings reviewed here suggest that consuming green and oolong tea appears to improve mood and reduce overall stress. This appears to be true of even relatively low habitual intakes in which even 1–2 cups of daily tea intake produced beneficial effects [84,72,73,74,56,66,75,83]. However, given the caffeine content in tea and its association with stress reactivity, effects of daily whole tea consumption on emotional state are likely to be dose-dependent with an inverted-U relationship to wellbeing. Plant-based beverages consumed in high daily quantities that are naturally free of caffeine may be more appropriate as a dietary supplement for managing emotional regulation over the lifetime.

In this regard, scientific interest has steadily developed around Rooibos herbal tea (*Aspalathus linearis*), a plant endemic to South Africa [135], which is free of caffeine and has a high content of flavonoids and isoflavonoids, known for their anti-inflammatory and antioxidant capacities [136,137]). Rooibos contains dihydrochalcones (aspalathin and nothofagin), flavones (luteolin, orientin, isovitexin, vitexin) and flavonols (quercetin), but does not contain significant catechins, like teas derived from *C. sinensis*. An impressive body of literature shows that Rooibos extracts possess antioxidant, anti-inflammatory, anti-diabetic, hepatoprotective, prebiotic and, cancer–preventive properties [138–142]. In terms of supporting emotional wellbeing, the research in human subjects is underdeveloped, but studies show that Rooibos can inhibit angiotensin-converting enzyme *in vitro* and *in vivo*, mimicking the

effect of first line treatments for hypertension [143]. A study in rats has corroborated these findings showing that green/unfermented rooibos was able to significantly reduce blood pressure [144]. Rooibos also appears to have potential for reducing stress hormones. [145] demonstrated the inhibitory capacity of rooibos on adrenal steroidogenic enzyme activities and steroid hormone levels using an invitro model. In a more recent report by the same group, rats receiving Rooibos had lower plasma levels of corticosterone and its precursor metabolite, deoxycorticosterone when compared to the control group [145]. There have been no formal investigations into the effects of Rooibos on mood, cognition, or sleep, but a study by [146] found that a blend of Rooibos and dandelion extract elevated testosterone levels in male mice and improved quality of life in men. While there is a scarcity of empirical evidence, anecdotal reports from traditional Rooibos use suggest that it may help to alleviate symptoms of anxiety and insomnia, which are ailments closely linked to stress and the endocrine system. These preliminary findings are encouraging and suggest that Rooibos may prove to be an important dietary component for individuals at risk for neurodegeneration and cognitive decline.

7. Conclusion

New medicinal plants are an important potential source of multipotent therapeutic agents for neurodegenerative diseases such as Alzheimer's disease, due to their complex and varied chemical composition and generally lower toxicity. Nevertheless, at present there are no recognised pharmacotherapies for stalling the progression of dementia due to Alzheimer's disease [27]. It is believed that this in large part because treatments commence at the point of neuronal loss, which follows from a cascade of neuropathological events beginning several decades before symptom onset. While few will dispute that multiple complex pathways are implicated in the degenerative process, chronic exposure to stress throughout the lifespan has been the focus of many recent studies because of the parallels between the biological disturbances resulting from chronic stress and the pathophysiology of AD, which include dysregulation in the HPA neuroendocrine axis, chronic inflammation, abnormalities in insulin signalling, circadian rhythm imbalance, obesity, hypertension, and atherosclerosis. The concept of allostatic load due to sustained exposure to stress is therefore a useful one for understanding the multidimensional aetiological framework underpinning AD. Medicinal plants and their active compounds that target the stress response and promote emotional homeostasis represent an attractive avenue toward the prevention of the disease. The findings reviewed here support anecdotal reports that consuming tea does appear to promote relaxation. *C. sinensis* has modest but significant effects on the reduction of stress and as a mood enhancer. In large quantities, however, the relatively high content of caffeine in tea appears to attenuate this effect, and therefore caffeine-free alternatives may prove more efficacious as an everyday dietary supplement for supporting emotional health. Plant species such as Rooibos, that can be easily incorporated into the daily diet from an early age are likely to be a sustainable health-promoting option, given the large literature on the many issues surrounding medication compliance [147].

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