

Effects of L-theanine and Caffeine on Attention and Attention-related Brain Activity of Children With Attention Deficit Hyperactivity Disorder

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT03533556

Recruitment Status : Not yet recruiting

First Posted : May 23, 2018

Last Update Posted : May 23, 2018

See [Contacts and Locations](#)

Sponsor:

Texas Tech University

Collaborator:

Texas Tech University Health Sciences Center

Information provided by (Responsible Party):

Texas Tech University

• Study Details

• [Tabular View](#)

• [No Results Posted](#)

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Study Description

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Brief Summary:

L-theanine and caffeine are two natural constituents of tea. Both of these compounds are among the U.S. Food and Drug Administration's list of Generally Recognized as Safe (GRAS) substances. Results of several clinical trials the PI and his team has conducted are consistent with results of many others to indicate that oral intake of each of 2.5 mg/kg body weight of L-theanine and 2.0 mg/kg body weight of caffeine is associated with improved attention in adults. Furthermore, there is evidence to suggest that, when taken in combination, L-theanine and caffeine seem to have additive effects in improving attention in adults. However, the specific actions of these substances have not been examined in children and adolescents with attention deficit hyperactivity disorder (ADHD), who are characterized by impaired attention, hyperkinesia and impulsivity.

Therefore, we plan to study the functional activity of brains (both at rest and when performing standard tasks designed to measure attention) in children diagnosed with ADHD using functional magnetic resonance imaging, after they consume either 2.5 mg/kg of L-theanine, 2.0 mg/kg of caffeine and their combination as compared to a placebo (water). Based on our previous findings, we expect to observe improvements (speed of responding and accuracy) in standard tests of attention with intake of L-theanine, caffeine and their combination as compared to the placebo. We also expect to observe decreased functional activity in brain regions that typically show increased activity during mind wandering with intake of L-theanine, caffeine and their combination.

Condition or disease	Intervention/treatment
Attention Deficit Hyperactivity Disorder	Dietary Supplement: L-theanine Dietary Supplement: Caffeine Dietary Supplement: L-theanine and Caffeine Combination Other: Placebo

Study Design

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Study Type : Interventional (Clinical Trial)

Estimated Enrollment : 12 participants

Allocation: Randomized

Intervention Model: Crossover Assignment

Intervention Model Description: 2.5 mg/kg body weight of L-theanine, 2.0 mg/kg body weight of caffeine and their combination each dissolved in 100 ml of water (solvent) or the solvent alone (i.e. placebo) will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order.

Masking: Single (Participant)

Primary Purpose: Treatment

Official Title: Effects of L-theanine and Caffeine on Attention and Attention-related Brain Activity of Male Children and Adolescents With Attention Deficit Hyperactivity Disorder: a proof-of- Concept fMRI Study.

Estimated Study Start Date : May 14, 2018

Estimated Primary Completion Date : August 31, 2018

Estimated Study Completion Date : December 31, 2018

Resource links provided by the National Library of Medicine

[MedlinePlus](#) related topics: [Attention Deficit Hyperactivity Disorder](#) [Caffeine](#)

[Drug Information](#) available for: [Theanine](#)

[U.S. FDA Resources](#)

Arms and Interventions

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Intervention Details:

Dietary Supplement: L-theanine

Oral administration of 2.5 mg/kg body weight of L-theanine dissolved in 100 ml of water

Dietary Supplement: Caffeine

Oral administration of 2.0 mg/kg body weight of caffeine dissolved in 100 ml of water

Dietary Supplement: L-theanine-Caffeine Combination

Oral administration of a combination of 2.5 mg/kg body weight of L-theanine and 2.0 mg/kg body weight of caffeine dissolved in 100 ml of water

Other: Placebo

Oral administration of 100 ml of water

Outcome Measures

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Primary Outcome Measures :

1. Differences of fMRI blood oxygen level dependent (BOLD) responses of the brain in response to Stop Signals of an SSRT recorded following administration of each treatment and the placebo [Time Frame: 45 minutes after the administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of functional magnetic resonance imaging reactivity of the whole brain, anterior and posterior nodes of the default mode network, bilateral dorsolateral prefrontal cortex and anterior cingulate cortex in response to stop signals of a stop signal reaction time task following administration of each treatment will be compared with the placebo.

2. Differences of fMRI blood oxygen level dependent (BOLD) responses of the brain in a Go-NoGo CPT recorded following administration of each treatment and the placebo [Time Frame: 60 minutes after the administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of functional magnetic resonance imaging reactivity of the whole brain, anterior and posterior nodes of the default mode network, bilateral dorsolateral prefrontal cortex and anterior cingulate cortex in Go-NoGo continuous performance task following administration of each treatment will be compared with the placebo.

3. Differences of resting state fMRI functional connectivity recorded following administration of each treatment and the placebo [Time Frame: 75 minutes after the administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of functional magnetic resonance imaging resting state functional connectivity of the anterior and posterior nodes of the default mode network, bilateral dorsolateral prefrontal cortex and anterior cingulate cortex and the remaining regions of the brain following administration of each treatment will be compared with the placebo.

Secondary Outcome Measures :

1. Differences of cerebral blood flow measured following administration of each treatment and the placebo [Time Frame: 80 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of cerebral blood flow estimated using arterial spin labeled echo following administration of each treatment will be compared with the placebo.

2. Differences of delay discounting following administration of each treatment and the placebo [Time Frame: 140 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of delay discounting as measured using a delay discounting task presented on a laptop computer following administration of each treatment will be compared with the placebo.

3. Differences of stop signal delay following administration of each treatment and the placebo [Time Frame: 45 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of stop signal delay of a stop signal reaction time task performed in the magnetic resonance imaging scanner following administration of each treatment will be compared with the placebo.

4. Differences of reaction times of correct Go responses in a Go-NoGo CPT following administration of each treatment and the placebo [Time Frame: 60 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of reaction times of correct Go responses in a Go-NoGo continuous performance task performed in the magnetic resonance imaging scanner following administration of each treatment will be compared with the placebo.

5. Differences of commission errors in the Go-NoGo CPT following administration of each treatment and the placebo [Time Frame: 60 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of commission errors in the Go-NoGo continuous performance task performed in the magnetic resonance imaging scanner following administration of each treatment will be compared with the placebo.

6. Differences of performance in Flanker Inhibitory Control and Attention Test following administration of each treatment and the placebo [Time Frame: 100 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of performance in Flanker Inhibitory Control and Attention Test of the NIH Toolbox Cognition Battery following administration of each treatment will be compared with the placebo.

7. Differences of performance in Dimensional Change Card Sort Test following administration of each treatment and the placebo [Time Frame: 100 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of performance in Dimensional Change Card Sort Test of the NIH Toolbox Cognition Battery following administration of each treatment will be compared with the placebo.

8. Differences of performance in Pattern Comparison Processing Speed Test following administration of each treatment and the placebo [Time Frame: 100 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of performance in Pattern Comparison Processing Speed Test of the NIH Toolbox Cognition Battery following administration of each treatment will be compared with the placebo.

9. Differences of post- vs. pre-treatment change of STAI-CH State Scale following administration of each treatment and the placebo [Time Frame: Immediately before and 90 minutes after administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of State Trait Anxiety Inventory for Children (State Questionnaire) immediately prior to and following administration of each treatment will be compared with the corresponding post- vs. pre-treatment change of placebo.

Other Outcome Measures:

1. Differences of commission errors in SSRT following administration of each treatment and the placebo [Time Frame: 45 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of commission errors of the stop signal reaction time task performed in the magnetic resonance imaging scanner following administration of each treatment will be compared with the placebo.

2. Differences of omission errors in SSRT following administration of each treatment and the placebo [Time Frame: 45 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of omission errors of the stop signal reaction time task performed in the magnetic resonance imaging scanner following administration of each treatment will be compared with the placebo.

3. Differences of omission errors in Go-NoGo CPT following administration of each treatment and the placebo [Time Frame: 60 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of omission errors of the Go-NoGo continuous performance task performed in the magnetic resonance imaging scanner following administration of each treatment will be compared with the placebo.

4. Differences of performance in Picture Sequence Memory Test following administration of each treatment and the placebo [Time Frame: 100 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of performance in Picture Sequence Memory Test of the NIH Toolbox Cognition Battery following administration of each treatment will be compared with the placebo.

5. Differences of performance in List Sorting Working Memory Test following administration of each treatment and the placebo [Time Frame: 100 minutes following administration of each treatment / placebo]

L-theanine, caffeine, L-theanine-caffeine combination and placebo will be administered on 4 separate days (at least 5 days apart) in a random counter-balanced order. Differences of performance in List Sorting Working Memory Test of the NIH Toolbox Cognition Battery following administration of each treatment will be compared with the placebo.

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, [Learn About Clinical Studies](#).

Ages Eligible for Study:	8 Years to 17 Years (Child)
Sexes Eligible for Study:	Male
Gender Based Eligibility:	Yes
Gender Eligibility Description:	Participant eligibility is based on self-representation of gender identity
Accepts Healthy Volunteers:	Yes

Criteria

Inclusion Criteria:

1. Children and adolescents (age 8-17 years)
2. Male
3. Diagnosed with ADHD by a clinician (a psychiatrist or a pediatrician)
4. Responded to stimulants (i.e. the symptoms of ADHD have improved in the past with a prescription of stimulants)

Exclusion Criteria:

1. Gross impairment of vision or hearing that would prevent the participants from performing neuropsychological tasks
2. Inability to read and follow written instructions
3. WISC-V IQ score of < 80
4. Physical, neurological or concurrent psychiatric impairments (except ADHD) that could affect cognitive and motor functions
5. Regular intake of medication that could alter visual, auditory, cognitive or motor functions (except stimulants)
6. History of head injury that resulted in loss of consciousness / history of brain surgery

7. Intake of drugs containing caffeine, other phosphodiesterase inhibitors or adenosine receptor blockers within the past 3 months
8. Intake of medications which are known to have pharmacological interactions with caffeine within the past 3 months
9. Current / past diagnosis of tics or other forms of dyskinesia
10. History of development of headache, drowsiness, anxiety, insomnia or nausea following intake of caffeine or caffeine containing beverages
11. Current / past history of smoking and / or alcohol or drug abuse
12. Absolute contraindications to undergo MRI
13. Unwillingness or inability to entirely refrain from use of electronic devices during study visits
14. Unwillingness or inability to refrain from intake of L-theanine and caffeine containing food or beverages within the 24 hours prior to each study visit
15. Unwillingness or inability to follow written, on-screen and verbal instructions given by the study team

Contacts and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

*Please refer to this study by its ClinicalTrials.gov identifier (NCT number): **NCT03533556***

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Locations

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Not yet recruiting

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Sponsors and Collaborators

Texas Tech University

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Responsible Party: Texas Tech University

ClinicalTrials.gov Identifier: [NCT03533556](#) [History of Changes](#)

Other Study ID Numbers: IRB2017-767

First Posted: May 23, 2018 [Key Record Dates](#)
Last Update Posted: May 23, 2018
Last Verified: May 2018

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Undecided

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No
Product Manufactured in and Exported from the U.S.: No

Additional relevant MeSH terms:

Disease	Caffeine
Attention Deficit Disorder with Hyperactivity	Central Nervous System Stimulants
Hyperkinesia	Physiological Effects of Drugs
Pathologic Processes	Phosphodiesterase Inhibitors
Attention Deficit and Disruptive Behavior Disorders	Enzyme Inhibitors
Neurodevelopmental Disorders	Molecular Mechanisms of Pharmacological Action
Mental Disorders	Purinergic P1 Receptor Antagonists
Dyskinesias	Purinergic Antagonists
Neurologic Manifestations	Purinergic Agents
Nervous System Diseases	Neurotransmitter Agents
Signs and Symptoms	