The anxiolytic and cognitive effects of L-theanine

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Primary Objective: The primary objective is to show that L-theanine has beneficial anxiolytic in healthy individuals. With the current experiment setup that entails the following effects of L-theanine compared to placebo:• Reduced startle effect on...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON47787

Source
ToetsingOnline

Brief title
The anxiolytic and cognitive effects of L-theanine

Condition

- Anxiety disorders and symptoms

Synonym
Anxiety, Stress

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,AOV orthomoleculaire voedingssupplementen, Almere

Intervention

Keyword: Anxiety, Fear potentiated startle, L-theanine, Trait anxiety

Outcome measures

Primary outcome

Study 1 and 2:

Fear-potentiated startle, defined as the increase in startle reflex magnitude evoked during the threat state as opposed to startle reflex magnitude during the safe state. The STAI state is used to assess the anxiety induced by the elements of the test battery.

Secondary outcome

Study 1:

Increases in skin conductance, salivary alpha amylase, blood pressure and heart rate during FPS, Trier, Stroop, Lorist and Higashiyama tasks.

Performance on Trier, Stroop, Lorist and Higashiyama tasks.

EEG alpha band power.

For study 2 (amendment on 11-02-2019) the research is repeated with only one secondary parameter:

EEG alpha band power.

Study description

Background summary

Although there have been a number of studies investigating the anxiolytic effects, there have rarely been significant effects of L-theanine in isolation beyond increases in calmness and relaxation on self-report measures. However, none of the studies so far has looked at physiological anxiety responses directly. The Fear-Potentiated Startle (FPS) with threat of shock is a robust way of inducing and measuring a fear state in almost every individual, allowing a direct test of anxiolytic effects (Klumpers et al., 2010; METC protocol #07-165). We will test the hypothesis that L-theanine administration will provide anxiolytic effects based on reduced FPS and subjective anxiety during the FPS test and other anxiety test battery scores when compared to a placebo condition.

A secondary hypothesis is that participants with a higher score on trait anxiety will show greater improvements when compared to participants with a lower score. People with a higher level of trait anxiety have more room to improve and there are indications from previous research that this group receives stronger beneficial effects of L-theanine (Higashiyama, Htay, Ozeki, Juneja, & Kapoor, 2011; Kobayashi et al., 1998; Unno et al., 2013). An interesting result is the study by Higashiyama et al. (2011), where participants were divided into two groups based on their trait anxiety, as measured by the Manifest Anxiety Scale scores. Results showed that only participants with high levels of anxiety received beneficial cognitive effects of the L-theanine administration based on reaction time and accuracy of a mental arithmetic task. Given that high levels of anxiety are often detrimental to cognitive performance, the increased performance is thought to be due to reduced anxiety.

Study objective

Primary Objective: The primary objective is to show that L-theanine has beneficial anxiolytic in healthy individuals. With the current experiment setup that entails the following effects of L-theanine compared to placebo:
• Reduced startle effect on Fear-Potentiated Startle
• Reduced levels of anxiety after FPS, Trier social stress test and Stroop, as measured by the STAI state and Bond & Lader Visual Analogue Scale
• Increased levels of calmness as measured by the STAI state and Bond & Lader Visual Analogue Scale
• Increased alpha band activity during EEG resting state
• Decreased blood pressure, heart rate and alpha amylase levels after FPS, Trier mental arithmetic test and Stroop

Secondary Objective(s): The secondary objective is to show that for participants with high levels of trait anxiety, L-theanine can also provide beneficial cognitive effects due to decreased anxiety. With the current experiment setup that entails the following effects of L-theanine compared to placebo for the high anxiety group:
• Increased attentional and reaction time performance on Higashiyama replication task.
• Increased interference performance on the Stroop
• Increased performance on the Trier mental arithmetic test

Study design

This study follows a within subjects, double blind, placebo controlled crossover design.

Intervention

Subjects will be administered 200 mg of nutritional supplement L-theanine 30 minutes before start of the test battery. This dosage is in line with previous research. The product will be obtained from the Dutch company AOV, which specializes in vitamin and nutritional supplements. Their supplier, Taiyo, is the only producer of Suntheanine, a synthetically produced form of L-Theanine. AOV capsules are made from tullulan and contain 200 mg Suntheanin. The additional material in the capsule is the additive substance hydroxypropylmethylcellulose (HPMC), used in a variety of food and medicinal products. The placebo will be an identical looking capsule, also supplied by AOV.

Study burden and risks

The burden and risk involved in participating in this study is negligible in our opinion. Previous research has not found any side effects of L-theanine and it is regarded safe as a food additive and supplement in the United States. Additionally, the intensity of the electric shocks is determined on an individual level, and is well tolerated. Participation is voluntary, and participants can withdraw from the study at any time, this will be clearly explained to participants.

The decrease of the number of secondary outcome parameters in study 2 reduces the burden for the subjects considerably.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must the following criteria:;- Subject is a legally competent adult, aged 18 years and older
- Subject agrees to participate in the study by giving written informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:;- Subject is currently taking (prescribed or non-prescribed) psychoactive medication
- Subject is mentally incapacitated, has significant emotional problems at the time of the study, or has a history of any significant psychiatric disorder (as per self-report).
- Subject has a history of any cardiac disorder or neurological disease.
- Reduced startle reactivity, defined as no discernible response in at least 3 out of the 12 startle stimuli.
- Female subjects who may be pregnant or unwilling to commit to using reliable

contraception at the time of the study.
-Subject fails to comply with study procedures (e.g., drank a caffeinated beverage shortly before the test)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-11-2016
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	10-06-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	20-03-2019
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL57087.041.16