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5-hydroxytryptophan, a serotonin precursor, as a novel therapy for attention-deficit hyperactivity disorder in adults

Submission date
03/11/2025

Recruitment status
No longer recruiting

Registration date
06/11/2025

Overall study status
Completed

Last Edited
04/11/2025

Condition category
Mental and Behavioural Disorders

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The aim of this project is to look at the impact of 5-Hydroxytryptophan (5-HTP) on distractibility. 5-HTP is the precursor to the neurotransmitter serotonin, a chemical that your body produces naturally following the consumption of the amino acid Tryptophan, which can be found in dietary sources such as soy products, egg whites, and pumpkin seeds and forms part of a standard diet. There is evidence that distractibility is associated with a decreased level of serotonin, a neurotransmitter also important for sleep, emotional state and aggression. This research aims to investigate whether administering 5-HTP to individuals alters their distractibility, which will form part of an initial assessment to determine whether 5-HTP could be used to support individuals with attention deficits.

Who can participate?
Healthy adult volunteers aged between 18 to 65 years who have a high or low level of distractibility, as assessed by a pre-screening survey.

What does the study involve?
The study involves first completing a pre-screening survey to make sure that participants meet the inclusion criteria for the study. This takes around 5 minutes.

Eligible participants are then invited to book a slot at the University of Sheffield, which will take around 2.5 hours. Around 36 hours before the study, participants will be sent a reminder email with a food diary to complete, as some foods might affect the amount of 5-HTP you have in your body, and other things, such as caffeine and alcohol, might affect participant responses. On the day of the study, participants are asked not to have anything containing caffeine, alcohol or nicotine, and to fast for two hours before the study so we can assess just the effect of 5-HTP.

At the university, participants will meet with the researcher and go to a quiet room with a computer, where they will fill in a consent form and do some computer tasks with distractors. These will take around 30 minutes to complete.

After completing the tasks, participants will be given two tablets to take with a glass of water and asked to wait for 90 minutes, which can be spent at leisure. No food can be consumed during this time. After the 90 minutes are finished, participants will repeat the computer tasks, and then will be allowed to leave.

What are the possible benefits and risks of participating?
- Because of the nature of the study, participants will have to fast for a period of time.
- Sitting in front of a computer may cause eye strain. Participants will be given the chance to have breaks and asked to use glasses if they need them.
- 5-HTP may cause nausea and tiredness in some individuals. We have determined a dose to try and prevent this as best as possible, but participants are asked to inform the researcher if they start to feel sick or tired during the study. We advise against using heavy machinery or driving following the experiment.

Where is the study run from?
The University of Sheffield, UK.

When is the study starting and how long is it expected to run for?
The study started recruiting in May 2024 and completed recruiting in February 2025.

Who is funding the study?
The University of Sheffield, UK.

Who is the main contact?
Eleanor Jackson, efjackson1@sheffield.ac.uk

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Assessing the impact of acute 5-hydroxytryptophan supplementation on distractibility

Study objectives
This project seeks to observe the effect of a nutritional supplement, 5-hydroxytryptophan, on measures of distractibility in individuals with varying levels of ADHD-like symptoms. 5-Hydroxytryptophan is a metabolic product produced by the body following consumption of the amino acid Tryptophan, which can be found in dietary sources such as soy products, egg whites and pumpkin seeds. 5-Hydroxytryptophan can also be obtained from the seeds of the edible plant Griffonia Simplicifolia, which have long been used in traditional medicine. Both tryptophan and 5-hydroxytryptophan are metabolic precursors to serotonin, a neurotransmitter implicated in sleep regulation, emotional state, aggressive behaviours and most relevantly for this research, in orienting overt and covert attention by inhibiting the superior colliculus. 5-hydroxytryptophan has been used in a range of therapies; unlike its precursor, the amino acid tryptophan, it is easily absorbed from the intestinal tract and bypasses the rate-limiting step of serotonin synthesis, making it an ideal nutritional supplement which could be efficacious in treating ADHD-like symptoms.

There is significant evidence which implicates the serotonergic system in ADHD; Serotonin application to the superior colliculus has been found to depress activity in the same way that well-established ADHD treatments methylphenidate and d-lisdexamfetamine do, and a significant number of the genes that are involved in the regulation of serotonin synthesis are mutated in individuals with ADHD. As such, it seems that increasing serotonin levels by using natural nutritional supplements may ameliorate ADHD symptoms. One study looking at 5-hydroxytryptophan administration in Rhesus Macaques found it increased attention in animals with a low baseline of attention, and reduced attention in animals with a high baseline. Although 5-hydroxytryptophan has been used previously in the treatment of depression, obesity, insomnia and other conditions, there is little to no research on how the supplement may be beneficial to

individuals with ADHD. Therefore, we intend to look at the impact of 5-hydroxytryptophan supplementation in groups of individuals with high and low levels of ADHD-like symptoms

The study will be conducted in two parts. A pre-screen survey to determine eligibility. AIM = to determine the amount of ADHD-like behaviours participants present with, and determine if they are eligible for participation.
An in-person study at the University of Sheffield, where participants are given either a dose of 5-Hydroxytryptophan or a placebo, and an assessment of their distractibility will be conducted pre- and post-administration. AIM = to determine the impact of 5-HTP administration on distractibility compared to baseline measures and placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 04/03/2024, University of Sheffield Research Ethics Committee (Western Bank, Sheffield, S10 2TN, United Kingdom; +44 (0)114 222 2000; psy-ethics@sheffield.ac.uk), ref: 058170

Study design
Single-centre interventional double-blinded randomized controlled trial

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Distractibility in attention deficit hyperactivity disorder

Interventions
This is a single-centre, interventional, double-blinded, randomised controlled trial with a 2 (group: High ASRS vs Low ASRS) x2 (Intervention vs placebo) x2 (pre and 90 minutes post) design, and a 1:1 allocation to both group and intervention.

Randomisation:
Using a random number generator, randomisation was stratified by group (high ADHD traits and low ADHD traits) with a 1:1 allocation to intervention and placebo conditions, recorded as A and B. Randomisation was completed and implemented by the lead investigator. All randomisation was produced using the web applications available at http://random.org.

To blind investigators enrolling, assigning and delivering the protocol, an assistant extraneous to the trial placed doses of placebo and 5-hydroxytryptophan tablets in A or B envelopes. The contents of A and B were then written down and sealed in an envelope to be opened after the trial. Participants were also blind as to what intervention they received. Interventions were both tablets in the same quantity, with 5-hydroxytryptophan tablets being slightly larger and darker in colour than the placebo tablets; thus, they were concealed from the investigator with the use of sealed envelopes.

Participants in the intervention group are given an acute 200mg dose of 5-hydroxytryptophan, provided by 2 tablets of Nature's Best supplement containing 3982mg of Griffonia seed extract, providing 100mg of 5-hydroxytryptophan each, along with calcium carbonate, anti-caking agents (silicon dioxide, stearic acid and magnesium stearate), and tablet coating (hydroxypropyl methylcellulose, glycerol).

Participants assigned to the placebo are given 2 sucrose-lactose tablets obtained from Ainsworth's homeopathic remedies.

Intervention Type
Supplement

Primary outcome(s)
Distractibility, measured using reaction time and accuracy in a task-relevant and task-irrelevant distractor task, before administration and at 90 minutes post administration

Key secondary outcome(s))
The prevalence of ADHD symptom types was measured using the extended ADHD self-report scale (ASRS) v1.1 questionnaire during the pre-screening of participants

Completion date
27/02/2025

Eligibility

Key inclusion criteria
1. For control participants, a score of 1 or less on the Adult ADHD self-report screener (ASRS v1.1, items 1-6)
2. For high ASRS participants, a score of 4 or greater on the Adult ADHD self-report screener (ASRS v1.1, items 1-6)
3. Normal or corrected-to-normal vision

Participant type(s)
Healthy volunteer, Learner/student

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 months

Sex
All

Total final enrolment
115

Key exclusion criteria
1. Users of psychostimulant medication
2. Users of serotonin-affecting medication, e.g., SSRIs
3. Smokers/Vapers
4. Pregnant and breastfeeding people
5. Lactose-intolerant people
6. Vegans
7. Dyslexia

Date of first enrolment
01/05/2024

Date of final enrolment
27/02/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Sheffield
Western Bank
Sheffield
United Kingdom
S10 2TN

Sponsor information

Organisation
University of Sheffield

ROR
https://ror.org/05krs5044

Funder(s)

Funder type

University/education

Funder Name
University of Sheffield

Alternative Name(s)
The University of Sheffield, Sheffield University, sheffielduni, University of Sheffield UK, theuniversityofsheffield, University of Sheffield in United Kingdom, University of Sheffield, UK

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publicly available repository at https://doi.org/10.15131/shef.data.29183702.

The data shared has been anonymised and de-identified, providing demographic information, ASRS scores, intervention assignment, reaction time and accuracy in the tasks and information on experiences of side effects. The anonymised data is open access.

Data was analysed using a 2x2x2 (group x intervention x time) ANOVA in SPSS, looking at reaction time and accuracy as measures of distractibility.

Informed, written consent was obtained from each participant at two timepoints: once prior to completion of the pre-screening survey, and once prior to the completion of in-person testing.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			04/11/2025	No	Yes
Protocol file			04/11/2025	No	No