The effect of LSD on neural synchrony, prosocial behavior, and relationship quality

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To assess this, the effect of a single administration of LSD (50 µg) on neural synchrony, prosocial behaviour, and relationship quality, and the relationship between these variables, will be assessed between healthy, romantic partners, when given...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53689

Source
ToetsingOnline

Brief title
LSD hyperscanning

Condition

- Other condition

Synonym
not applicable

Health condition

drug effects

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Neuropsychopharmacology, Psychedelics, Social behavior

Outcome measures

Primary outcome

Quantification of neural synchrony (defined as EEG phase locked values) between couples utilizing previously validated naturalistic interaction paradigms. Specifically during the motor cooperation task, empathy giving task, and affective touch and eye contact paradigm.

Secondary outcome

Secondary endpoints will be based on providing a comprehensive assessment of the effects of LSD on (pro)social cognitive processing. Tasks which have previously shown psychedelic-induced enhancements of (pro)social cognitive behaviours will be utilized, and adapted to be performed between dyads, or expanded on in order to further elucidate the effect of LSD. The tasks will measure: empathy, self-other distinction, altruism, social influence processing, social rejection processing, creativity, sociality, and conflict resolution. Subacute secondary outcomes on (pro)social cognitive processing will determine whether LSD induces changes which outlast the acute stage.

Tertiary endpoints will include acute assessment of LSD drug concentrations in blood, and subjective drug effects. Additionally, the influence on socially

relevant hormones and cytokines in blood will be assessed. Finally, persisting changes in relationship quality, sexual function, and subsequent personal well-being will be measured.

Study description

Background summary

Psychedelic research has seen a revival in the past decades, leading to a wave of new studies investigating the effects of these substances in both clinical populations and in healthy volunteers. In regard to clinical studies, evidence is growing that psychedelic substances such as psilocybin, lysergic acid diethylamide (LSD) and ayahuasca could be a potential alternative treatment option for common and difficult to treat psychiatric conditions, such as depression, anxiety, addiction, and post-traumatic stress disorder (PTSD). One proposed mechanism that psychedelics target, which is a hallmark of seemingly all psychiatric disorders, are deficits in social cognitive abilities. It has been repeatedly found that a single ingestion of a psychedelic drug increases prosocial behavior such as enhanced empathy, willingness to disclose sensitive information about a person*s life, and (emotional) connectivity with others. That said, the neural underpinnings of psychedelic-induced alterations in prosocial behavior are currently unknown. We hypothesize psychedelics increase such prosocial behaviors by increasing neural synchrony, which is the coupling of brain-to-brain activity across two or more people; it has been found to underlie social connection and various forms of shared prosocial behavior. Hyperscanning allows for the measurement of electroencephalography (EEG) activity of multiple brains simultaneously, and thus assessment of neural synchrony in dyads.

Study objective

To assess this, the effect of a single administration of LSD (50 µg) on neural synchrony, prosocial behaviour, and relationship quality, and the relationship between these variables, will be assessed between healthy, romantic partners, when given the substance simultaneously.

Primary Objectives:

Primary objectives are to investigate the effects of one dose of LSD (50 µg) on neural synchrony, as assessed via EEG hyperscanning, between members of a

romantic couple.

Secondary Objectives:

Secondary objectives are to investigate whether LSD (50 µg) enhances (pro)social behaviour, defined by changes in empathy, self-other distinction, altruism, social influence processing, social rejection processing, creativity, sociality, and conflict resolution, between the members of the romantic couple (assessed via task batteries and questionnaires), and whether outcome measures of prosocial behaviour correlate with neural synchrony.

Tertiary Objectives:

Tertiary objectives are to investigate the effects of LSD (50 µg) on relationship quality, as assessed via subjective questionnaires measuring relationship and sexual satisfaction, at set time points after the acute dosing day. The outcome variables of relationship quality will be correlated with the outcome variables of neural synchrony and prosocial behaviour, to assess whether there is a relationship. Additionally, tertiary objectives include assessment of LSD, metabolomics, oxytocin, and cytokine concentrations in blood.

Study design

The study design will be conducted according to a double-blind, placebo-controlled, 2 way crossover design. Healthy subjects who are in a relationship will receive placebo and an oral dose of 50 µg of LSD, with both subjects receiving the same treatment on the same test day. After the initial dosing day, participants will return 2 days later to complete follow-up measures. Up to four days after the dosing day, they will complete short questionnaires asking about how they feel and about their perceived relationship quality. Between each dosing condition, there will be a minimum of 14 days washout.

Intervention

50 micrograms LSD dissolved in ethanol, resulting in a 1 mL solution, placebo (1mL of ethanol) per oral

Study burden and risks

Volunteers will be enrolled for minimally four weeks, which will include five

lab visits, and undergoing two drug conditions in total. During the first lab visit, participants will independently undergo a full medical screening (medical history review, laboratory exam, electrocardiogram, and blood and urine samples will be taken) by a licensed physician ensuring their safety. The following four lab visits consist of the official testing days, two acute testing days in which participants are given the drug treatment, and two short follow-up visits which take place 2 days after each drug treatment. Furthermore, participants will be asked to respond to short questionnaires up to 4 days post treatment administration, from home. Each testing day will be conducted with both partners simultaneously.

The acute testing day consists of both partners taking the treatment (50 mcg LSD or placebo). Safety concerns regarding LSD are primarily psychological, i.e. transient anxiety, which is common at the beginning of the onset of the drug effect. At the doses of LSD used in the present study, subjects are expected to retain most of their thought control and in contrast to psychotic patients, subjects will remain aware of the transient state of the drug-induced experience. Negative experiences (bad trips) and flashback phenomena may occur under LSD, generally in uncontrolled conditions, and at much higher doses than used in this study. In the case of any psychiatric complications after the study session and also if the participants want to discuss negative experiences in association with the study they can contact the study physician who will offer further assistance beyond the testing days. Physiological effects are limited and include sympathomimetic effects such as an increase in systolic blood pressure, body temperature and pupil size when under the influence of the drug.

During the acute testing day, blood samples, urine sample, an EEG scan, computer tasks, a video recorded talking task, and questionnaires will also be completed. The urine sample and the first blood sample shall be taken before treatment administration. The remaining five blood samples will be used to determine LSD, metabolomics, oxytocin, and cytokine concentrations at set time-points after drug administration. Two days after the drug treatment, participants will return to give a follow-up blood sample for cytokine assessment, and complete short tasks assessing prosocial behaviour, and complete a video recorded talking task. Up to four days after the drug treatments, participants will be asked to answer short questionnaires about relationship quality and sexual functioning. The acute drug testing days will be interspersed by 14 days, to allow for a washout period. Over the course of the medical examination and the lab visits, participants will give a total of 203 ml of blood. In case they experience complaints, the medical supervisor will be contacted. The total discomfort experienced by the volunteer is minimal when all precautions are taken into account.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Written Informed Consent

Understanding the procedures and the risks associated with the study.

Age between 18 and 40 years old.

Being in a steady relationship for at least 6 months.

Proficient knowledge of the English language

Previous experience with at least one psychedelic drug (psilocybin, LSD, mescaline, Ayahuasca, DMT, 5-MeO-DMT), but not within the past 3 months

Absence of any major medical condition as determined by medical examination and laboratory analysis

Absence of any major psychological condition as determined by medical examination

Free from psychotropic medication

Participants must be willing to refrain from taking illicit psychoactive substances during the study.

Participants must be willing to drink only alcohol-free liquids and no coffee, black or green tea, or energy drink after midnight of the evening before the study session, as well as during the study day.

Participants must be willing not to drive a traffic vehicle or to operate machines within 24 h after substance administration.

Normal weight, body mass index (weight/height2) between 18 and 28 kg/m2

Exclusion criteria

History of drug addiction (determined by the medical questionnaire, drug questionnaire and medical examination)

Previous experience of serious side effects to psychedelic drugs (anxiety or panic attacks)

Pregnancy or lactation

Hypertension (diastolic > 90 mmHg; systolic > 140 mmHg)

Current or history of psychiatric disorder (determined by the medical questionnaire and medical examination)

Psychotic disorder in first-degree relatives

Any chronic or acute medical condition

History of cardiac dysfunctions (arrhythmia, ischemic heart disease,*)

For women: no use of a reliable contraceptive

Tobacco smoking (>20 per day)

Excessive drinking (>20 alcoholic consumptions per week)

Experience with a full dose of a psychedelic within the last three months

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2022
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO Date:	13-09-2022
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-08-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL80435.068.22