The effects of three low morning and evening doses of LSD on mood, biological and psychological measures of sleep, neuroplasticity, and well-being

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To understand the effect of microdosing on mood, sleep and neuroplasticity, the effect of three repeated low doses of LSD in the morning and evening in healthy volunteers will be compared to placebo on measures of mood, sleep and neuroplasticity (...

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

Summary

ID

NL-OMON52249

Source
ToetsingOnline

Brief title
Microdosing, mood and sleep

Condition

- Other condition

Synonym
sleep and mood

Health condition

neuroplasticiteit, slaap en gemoedstoestand

Research involving

Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Mind Medicine Inc.,Mind Medicine Inc.;US

Intervention

Keyword: Lysergic acid diethylamide, microdosing, mood, sleep

Outcome measures

Primary outcome

Primary objective is to investigate the effects of three repeated morning vs evening doses of LSD (20 µg) on mood (self-rated).

Secondary outcome

Secondary objectives are to investigate the effects of three repeated morning vs evening doses of LSD (20 µg) on [1] neuroplasticity (BDNF levels in blood samples), [2] sleep parameters, [3] cognitive performance measures of different memory types, [4] emotional attention, [5] emotion regulation [6] markers of well-being (cytokines in blood samples and self-rated questionnaire). Tertiary objectives are to investigate the effects of three repeated morning vs evening doses of LSD (20 µg) on [1] cortisol levels (blood samples), and [2] endocannabinoid concentrations (blood samples).

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 psychedelic substances in clinical populations as well as in healthy volunteers. Psychedelics, such as psilocybin

and LSD, have shown to be a potential alternative treatment option for psychiatric conditions, such as stress-related disorders and addiction. Also in healthy volunteers, a psychedelic acutely induced positive effects on mood and participants described it as being among the most personally meaningful experiences of their lives. Recently, the practice of repeatedly using small doses of a psychedelic has received increasing scientific interest and is better known as *microdosing*. Both healthy and clinical populations who microdose do this to enhance cognitive performance and mood.
To understand the full potential of microdosing, knowledge about the underlying neurobiological mechanism of the positive effects on mood and behavior are pivotal. A potential mechanism underlying these positive effects that has not been investigated yet is the effect of microdosing on sleep. Nearly all of the successful treatments for mood disorders seem to affect circadian rhythms (sleep) and enhance neuroplasticity (brain-derived neurotrophic factor, BDNF), the present project seeks to investigate the effect of small doses of a psychedelic (LSD, 20 µg) on these parameters in healthy volunteers.
Studies have suggested the involvement of serotonin 1A and 2C receptors in the normalization of the circadian rhythm, and LSD is a potent agonist of these receptors, it is therefore expected that LSD affects sleep. Additionally, a recent study from our lab showed that low doses of LSD, positively influenced mood and enhance BDNF levels, a marker of neuroplasticity. We hypothesize that the aforementioned effects on sleep and BDNF underlie the positive effects of LSD on mood and well-being.
Another finding is that psychedelics* effects on sleep are dependent on the time of administration. To understand the effect of the timing of LSD administration on mood, sleep and neuroplasticity, the effect of three repeated small morning and evening doses of LSD will be compared in healthy volunteers on assessments of mood, sleep and neuroplasticity.

Study objective

To understand the effect of microdosing on mood, sleep and neuroplasticity, the effect of three repeated low doses of LSD in the morning and evening in healthy volunteers will be compared to placebo on measures of mood, sleep and neuroplasticity (BDNF). Secondly, the effects of daytime and evening low-dose LSD administration will be examined on cognitive performance, emotion regulation, well-being and immune system response.

Study design

The study follows a 2 (LSD vs placebo) by 2 (morning doses vs evening doses) double-blind, randomized, placebo-controlled, within-subject design.

Intervention

All participants will undergo four conditions. Each condition includes three

occasions of administering LSD (20 µg) or placebo in the morning, or in the evening. The three dosing days within one condition will be interspersed with one day. Between the conditions, there will be a washout period of minimal five days. All participants will go through all four conditions.

Study burden and risks

Volunteers will be enrolled for minimally eight weeks, undergoing four conditions in total. Before starting in one of the conditions, participants will undergo a full medical screening (blood and urine samples will be taken) by a licensed physician ensuring their safety and a short training session will be held to familiarize them with the testing procedures. Each condition will include four lab visits, of which three include drug administration (LSD or placebo) in the morning or evening and cognitive testing. The remaining lab visit only includes collecting a blood sample. Every day during the four conditions, participants keep a diary assessing their sleep and mood. Dosing days are interspersed by one day and between each condition, a washout of at least five days is included. On the first and last test day of each condition, four blood samples will be taken. The first blood sample will be taken just before treatment administration, the remaining three blood samples will be taken every hour after treatment administration. The blood samples will serve to determine markers of neuroplasticity, well-being (i.e. cytokines), LSD concentration, cortisol and endocannabinoid concentrations. Other blood samples will be taken 24 hours and 48 hours after the first treatment administration. Over the course of the medical examination and the lab visits, participants will give a total of 492ml 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.
• At least 18 years of age
• 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.
• Participants are asked to not make any substantial changes in their diet.
• Participants must be willing to comply with guidelines regarding their bedtime.
• 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:	Recruiting
Start date (anticipated):	15-12-2021
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	22-10-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	11-10-2022
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	NL76249.068.21