Brain kinetics of neurotransmission during JWH-018 intoxication

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Primary Objective: to assess brain kinetics of glutamate, GABA and dopamine and the associated functional connectivity of the mesocorticolimbic circuit during the absorption and elimination phase of JWH-018, as compared to the control condition....

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

Summary

ID

NL-OMON53287

Source
ToetsingOnline

Brief title
Brain activity under the influence of JWH

Condition

- Other condition

Synonym
not applicable

Health condition

hersenkinetiek

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Brain kinetics, Intoxication, JWH-018, Neurotransmission

Outcome measures

Primary outcome

The main study parameter is the drug-induced change in neurotransmission of glutamate, GABA and dopamine which will be assessed by using MRS and resting state fMRI.

Secondary outcome

Secondary parameters include changes in attentional salience processing, memory, JWH-018 kinetics, metabolomics, and cytokines in blood and subjective experience of the drug effects, and drug liking and wanting.

Study description

Background summary

JWH-018 is a synthetic cannabinoid sold under different brand names as a substitute of cannabis. JWH-018 is a full agonist of central CB1 receptors and can elicit similar or stronger acute effects on neurocognitive function and consciousness compared to cannabis, which is a partial agonist of CB1. The neural mechanism underlying the acute effects of JWH-018 on human neurocognition and consciousness have not yet been assessed.

Study objective

Primary Objective: to assess brain kinetics of glutamate, GABA and dopamine and the associated functional connectivity of the mesocorticolimbic circuit during the absorption and elimination phase of JWH-018, as compared to the control condition.

Secondary Objective(s): to assess the effects of JWH-018 on memory, attention and attentional salience processing and psychotomimetic symptoms, and on brain imaging measures of neurotransmission and functional connectivity.

Study design

Acute influences of JWH-018 on neurotransmission in the limbic system will be assessed and compared to a control condition in a double-blind, randomized within-subject study in occasional cannabis users. A seven-day washout period will precede each drug condition.

Intervention

Subjects will receive a single dose of 7.5 mg of JWH-018 and control condition on separate testing days.

Study burden and risks

Participants will inhale a control and JWH-018 vapour. After administration, participants will go into the MRI scanner for 1 hour, where brain scans will be taken at rest and during the completion of an attentional salience processing task. At regular time windows, up until 3.5 hours after administration, subjects will be asked to indicate how they feel, and blood samples will be taken.
Volunteers will be enrolled for minimally three weeks, which will include three lab visits, and undergoing two treatment 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 two lab visits consist of the two acute testing days in which participants are given the drug treatment, where they will inhale control and JWH-018 vapor while lying in an fMRI scanner. Brain scans will be taken and subjects will be requested to indicate how they feel and perform cognitive tasks, during a time window of 3,5 hours after administration. Blood samples will also be taken at regular intervals. In addition, subjects will fill in questionnaires regarding their subjective drug experience. The acute drug testing days will be interspersed by 7 days, to allow for a washout period.
Over the course of the medical examination and the lab visits, participants will give a total of 143 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

* Used cannabis between 1 time a month and 2 times a week during the previous year
* Age between 18 and 40 years
* Free from psychotropic medication
* Good physical health as determined by medical examination and laboratory analysis
* Absence of any major medical, endocrine and neurological condition as determined by medical examination and laboratory analysis
* Normal weight, body mass index (weight/height2) between 18 and 28 kg/m2
* Written Informed Consent
* Good knowledge and understanding of the English language
* 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 drinks 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.

Exclusion criteria

* History of drug addiction (determined by the medical questionnaire, drug questionnaire and medical examination). * Pregnancy or lactation or pregnancy planned during study participation. * Hypertension (diastolic > 90 mmHg; systolic > 140 mmHg). * Current or history of psychiatric disorder (determined by the medical questionnaire and medical examination). * Current presence or history of psychosis 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). Furthermore, to participate in MRI scanning a few conditions need to be satisfied by the subject. In the following cases, a MRI scan is not possible: * The subject had an operation to his head or brain. * The subject has implanted electronic devices, like a pacemaker. * The subject has an insulin pump under his skin. * The subject suffers from epilepsy. * The subject suffers from claustrophobia. * The subject has cardiological irregularities. * If there is a chance that the subject might be pregnant. * If, apart from teeth fillings and connectors, there are other metal parts in the body, like: o protheses o implants o clips on blood vessels o metal parts in the eye o spiral o metal braces o other metal objects In the following cases the researcher first needs to establish, in collaboration with the participant, whether it would be possible to have an MRI scan: * Subject has a tattoo (also permanent make-up). * Subject has one or several piercings that cannot be removed. * Subject has a metal wire behind his teeth.

Study design

Design

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

Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-12-2023
Enrollment:	29
Type:	Actual

Ethics review

Approved WMO Date:	02-08-2023
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	18-12-2023
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	NL83881.068.23
Other	Not yet available

Study results

Date completed: 04-10-2024

Summary results
Trial ended prematurely