The influence of female sex hormones on the subjective and cognitive response to cannabis

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Primary Objective: To assess the acute subjective drug effects (good/bad drug effect, drug liking/wanting, anxiety), cognition (attention, working memory, information processing speed, verbal memory, verbal fluency, motor inhibition), and...

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

Summary

ID

NL-OMON57351

Source
ToetsingOnline

Brief title
Sex hormones impact on cannabis response

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: Stichting Edmond Hustinx

Intervention

Keyword: Cannabis, Neuropsychopharmacology, Sex hormones

Outcome measures

Primary outcome

The main study parameter is the drug-induced change in subjective state, cognition, and pharmacokinetics across the menstrual cycle, when comparing cannabis to placebo.

Secondary outcome

Secondary parameters include changes in interoception and pain. Tertiary parameters include changes in inflammatory cytokine expression.

Study description

Background summary

Cannabis consumption is increasing globally due to legalization and therapeutic use, prompting concerns about its impact on daily functioning and long-term effects. While research has explored cannabis' risks, the heightened vulnerability of females to its adverse effects has been overlooked. Women experience stronger acute negative reactions and progress to cannabis use disorder faster than men. This gender disparity is likely due to sex hormone (SH) fluctuations related to menstrual cycles, emphasizing the need to study cannabis' differential impact on females to address gender-specific risks and inform treatment approaches. This study is the first to systematically determine whether the cannabis response in human females is related to SH fluctuations throughout the menstrual cycle.

Study objective

Primary Objective: To assess the acute subjective drug effects (good/bad drug

effect, drug liking/wanting, anxiety), cognition (attention, working memory, information processing speed, verbal memory, verbal fluency, motor inhibition), and pharmacokinetics of cannabis in females across 3 different phases of the menstrual cycle, compared to a placebo condition.

Secondary Objective(s): to assess the acute effects of cannabis on interoception and pain, in females across 3 different phases of the menstrual cycle, compared to a placebo condition.

Tertiary Objective(s): to assess the acute effects of cannabis on metacognition and expression of inflammatory markers in females across 3 different phases of the menstrual cycle, compared to a placebo condition.

Study design

Acute influences of cannabis on subjective state and cognition will be assessed at three different stages of the menstrual cycle, and compared to a placebo condition in a double-blind, randomized, within-subject study in occasional cannabis using biological females. A seven-day washout period will precede each drug condition.

Intervention

Participants will receive three doses of cannabis (300 µg THC/kg bodyweight), and three doses of placebo on separate testing days, during specific phases of their menstrual cycle.

Study burden and risks

Volunteers will be enrolled for minimally nine weeks, which will include seven lab visits consisting of a medical screening, six treatment administrations, and undergoing two different 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 six lab visits consist of the official testing days, which will be six acute testing days in which they are given the drug treatment. In order to plan these testing days within the specific phase of the menstrual cycle, participants will be asked to report when their menstrual cycle starts and finishes to the researchers, and to track levels of luteinizing hormone in their urine at home for a maximum of 7 days in their cycle.

During each testing day, participants will inhale a placebo or cannabis vapor. Up until 3.5 hours after administration, participants will be requested to indicate how they feel and perform cognitive tasks. Blood samples will also be taken at regular intervals. In addition, participants 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 397 ml of blood. The maximum they will give per visit is 64 ml. 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

To be eligible to participate in this study, a participant must meet all the following criteria:
* Biological female
* 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
* Free from hormonal birth control
* A regular menstrual cycle (last 3 cycles a duration between 21 and 35 days).
* 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

A potential subject who meets any of the following criteria will be excluded from participation in this study:
* 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,*)
* Tobacco smoking (>20 per day)
* Excessive drinking (>20 alcoholic consumptions per week)

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):	01-03-2025
Enrollment:	21
Type:	Anticipated

Ethics review

Approved WMO

Date:	14-03-2025
Application type:	First submission
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	NL87464.068.24