nature portfolio

Corresponding author(s): Prof. Serge Rudaz

Last updated by author(s): Sep 8, 2025

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	*Provide a description of all commercial, open source and custom code used to collect the data in this study, specifying the version used OR state that no software was used.*
Data analysis	*Provide a description of all commercial, open source and custom code used to analyse the data in this study, specifying the version used OR state that no software was used.*

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available because of privacy or ethical restrictions.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	This study reports data on male participants only. It was designed to investigate endocrine alterations and reproductive health in male.
Reporting on race, ethnicity, or other socially relevant groupings	No socially relevant categorization was performed in this study. Participants were only stratified according to their consumption of cannabis, which was both self-declared and confirmed with the quantification of phytocannabinoids in urine.
Population characteristics	All participants aged 18-23 at the time of sampling.
Recruitment	Over 97% of all young Swiss men, aged between 18 and 22 years, are asked to attend a mandatory 2–3-day military camp prior to their potential enrollment into the army. Six recruitment centers distributed among the main Swiss cantons (states) are located in Lausanne (Vaud), Windisch (Aargau), Monteceneri (Ticino), Ruti (Z€urich), Sumiswald (Bern), and Mels (St-Gallen). These centers were involved sequentially in the sampling process over a period spanning from September 2005 to June 2017. For each canton, the number of required participants was calculated proportionally to the resident male population (16–60 years). All enlisted conscripts of a given center received a detailed description of the study, a consent form, and two questionnaires— one for themselves and one for their parents. Volunteers were given an appointment to undergo a physical examination and provide a semen sample in a nearby andrology laboratory. No exclusion criteria were applied during data collection.
Ethics oversight	Ethical approval was obtained according to the requirements in the cantons of Vaud (17-01-2005, 01/02), Zurich (EK-StV-Nr. 27-2006), Ticino (Rif.CE 1886) and Geneva (2016-01674).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No sample size calculation was performed prior to the study. 47 participants were included in each group for a total of 94 samples analyzed, according to the experience of the lab in case-control studies and to the technical feasability of analyzing such a high number of samples.
Data exclusions	No data were excluded from the analyses.
Replication	Quality Control samples (QCs) were prepared by pooling all experimental samples of this study. Ten of these QCs were injected all along the LC-MS sequence. It was verified that peak areas of all the steroid compounds included in the analysis had a CV lower than 30% to confirm the technical reproducibility.
Randomization	Samples were not randomly allocated to any group. The distinction of groups relied on cannabis usage. The potential confounders of steroid metabolism analysis that were previously identified were tobacco smoking and Body Mass Index. They were respectively declared and measured for each participant. Statistical analyses presented in the Supplementary Information demonstrate no significant effect of these potential confounders. Randomization was relevant during LC-MS data acquisition, where the injection order of exeperimental samples was randomized, so that there could be no effect of instrumental drift that would affect only one of both groups.
Blinding	There was no blinding of samples, as it was necessary to ensure randomization of samples along the LC-MS sequence. The investigator had to verify that 'THC-positive' and 'THC-negative' samples were correctly alternated throughout the sequence. Blinding was not necessary, as it is impossible to bias the outcome of the study in manual steps of data acquisition and data processing, with a data matrix comprising as many as 70 compounds and 94 samples.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.