Serotonergic modulation of population receptive fields

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON54157

Source
ToetsingOnline

Brief title
Sm-pRF

Condition

- Other condition

Synonym
There is no specific disease being investigated

Health condition

There is no specific disease being investigated

Research involving
Human

Sponsors and support

Primary sponsor: Spinoza Centre for Neuroimaging
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Computational modelling, Functional magnetic resonance imaging, Human visual cortex, Serotonergic neurotransmission

Outcome measures

Primary outcome

* Changes in population receptive field parameters exerted by psilocybin

administration.

* Relation with computational aspects of Divisive Normalization pRF model.

Secondary outcome

* Relation of pRF parameter changes with psychophysical measures of low-and

high level visual and somatosensory perception.

* Relation of pRF parameter changes with questionnaire on subjective experience.

* Relation of pRF parameter changes with 5-HT receptor maps.

* Changes in location, extent and connectivity profile of category-specific

regions in higher-level visual cortex

* Changes in somatotopic maps: location, extent and overlap between cortical

activations relating to stimulation of individual digits

Study description

Background summary

The population receptive field (pRF) is the region of visual and somatosensory space that elicits a response from a specific population of neurons [1]. FMRI

measurements at ultra-high field enable the sampling of these populations of neurons over large scales in the living human brain, and allow the investigation of neural computations with high sensitivity and specificity [2]. Like our cognitive processes, PRFs are not static but dynamic: an important open question concerns the degree and mechanisms underlying flexibility of pRFs [3]. Multiple lines of evidence implicate the serotonergic system in the modulation of brain responses to visual and tactile stimuli [4,5]; however, analysis of the effects of serotonergic manipulation on human visual and somatosensory cortex pRF responses
is lacking. We hypothesise that neuropharmacological manipulation of the serotonergic system will alter pRF properties in a systematic and robust way, and have developed a computational model that allows us to investigate these changes. The aim of the proposed study is to provide evidence for this hypothesis, and hence for the first time provide evidence in humans of the role of the serotonergic system in visuospatial and somatosensory pRF computations.

References

[1] Dumoulin, Serge O., and Brian A. Wandell. "Population receptive field estimates in human visual cortex." Neuroimage 39.2 (2008): 647-660.
[2] Dumoulin, Serge O., et al. "Ultra-high field MRI: Advancing systems neuroscience towards mesoscopic human brain function." Neuroimage 168 (2018): 345-357.
[3] Dumoulin, Serge O., and Tomas Knapen. "How visual cortical organization is altered by ophthalmologic and neurologic disorders." Annual Review of Vision Science 4 (2018): 357-379.
[4] Kometer, Michael, and Franz X. Vollenweider. "Serotonergic hallucinogen-induced visual perceptual alterations." Behavioral neurobiology of psychedelic drugs (2016): 257-282.
[5] Azimi, Zohre, et al. "Separable gain control of ongoing and evoked activity in the visual cortex by serotonergic input." Elife 9 (2020): e53552.

Study objective

The primary objective is to determine the effects of serotonergic stimulation, via the administration of psilocybin, on population receptive fields in different modalities and to relate these effect to specific computational aspects of the divisive normalization pRF model. The secondary objective is to draw relations between these changes and low-level visual and somatosensory perceptual processes (measured with psychometry) and subjective experience (measured with questionnaires).

Study design

The proposed study consists two study parts. Both will have a

within-participant double-blind placebo-controlled randomised crossover design, and will consist of one preliminary data collection session and three experimental sessions. For each study part, twenty healthy male and female English and/or Dutch speaking participants between 21-55 years old will be recruited. Participants will visit the laboratory site four times. During the first visit, informed consent will be collected, as well as preliminary data (structural MRI). During the three experimental sessions, participants will receive either placebo, or a low dose of psilocybin (5mg), or a medium dose of psilocybin (10mg). After the administration, each experimental session encompasses an fMRI scan in a 7T Philips scanner, and behavioural psychophysics tests of visual perception (study part 1) or visual and somatosensory perception (study part 2).

Study burden and risks

Participants will visit the laboratory site 4 times. The first time informed consent and preliminary data will be collected (anatomical MRI). On each of the following visit, participant will receive placebo or a dose of psilocybin orally, before an fMRI scan and psychometric tests. In the week before experimental sessions all participants will have to adhere to some simple restrictions regarding medication, alcohol and drug intake, as this may affect the response to neuropharmacological manipulation. The most common adverse effects of psilocybin include uncomfortable feelings of cognitive impairment, anxiety, fear, nausea [6]. Adverse effects are strongly dose-dependent, and subside within at most few hours from administration (see Figures 3-4 in Document C1, section 12.1). We also remark that our highest dose is approximately one third of the highest dose used in previous neuroimaging studies involving psilocybin administration [8]. Considering the relatively low doses involved in our study, exclusion criteria, screening procedure and constant monitoring of the participants, no serious side effects are expected. MRI is a safe method with no long-term side effects. Though the participants of this study will have no direct benefits from participating, the results contribute to new insights into the highly promising field of neuropharmacological modulation of information encoding in the human brain. The overall nature and extent of the added risk associated with participation in the current study is to be classified as negligible and the burden can be considered minimal. References [6] Studerus, Erich, et al. "Acute, subacute and long-term subjective effects of psilocybin in healthy humans: a pooled analysis of experimental studies." Journal of psychopharmacology 25.11 (2011): 1434-1452. [7] Brown, Randall T., et al. "Pharmacokinetics of escalating doses of oral psilocybin in healthy adults." Clinical pharmacokinetics 56.12 (2017): 1543-1554. [8] Dos Santos, Rafael G., et al. "Classical hallucinogens and neuroimaging: A systematic review of human studies: Hallucinogens and neuroimaging." Neuroscience & Biobehavioral Reviews 71 (2016): 715-728.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy english-speaking volunteers between 21 and 55 years old;
Male or female;
At least one previous experience with a hallucinogenic substance, but not in the 4 weeks prior to the beginning of the study.

Exclusion criteria

Personal, or first-degree relative with, diagnose of psychiatric conditions (schizophrenia, bipolar disorders).
History of neurological disorders (including stroke, convulsion, epilepsy) as well as concussion with loss of consciousness.
Used psychotropic drugs or medications over a period of 1 week prior to each

test session.
Currently using substances interacting with the metabolism of psilocybin or the serotonergic system (e.g. monoamine oxidase inhibitors, SSRIs).
Contraindications for 7T MRI (e.g. claustrophobia, osteosynthetic material, pacemaker, artificial cardiac valves, pregnancy, tinnitus).
Significant previous adverse response to a psychotropic substance.
Significant previous adverse response to fMRI scanning.
Participant does not speak English.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2023
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	05-11-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Not approved Date:	21-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	03-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL77985.018.21