Visual Snow: Studying the visual snow phenotype and shared mechanisms with migraine pathophysiology

Published: 17-11-2017
Last updated: 12-04-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Vision disorders
Study type	Observational invasive

Summary

ID

NL-OMON45361

Source
ToetsingOnline

Brief title
SNOW Study

Condition

- Vision disorders
- Headaches

Synonym
visual snow; visual tv static

Research involving
Human

Sponsors and support

Primary sponsor: Neurologie
Source(s) of monetary or material Support: oa. Spinozapremie prof. dr. M.D. Ferrari

(2009)

Intervention

Keyword: clinical description, cortical hyperexcitability, migraine, visual snow

Outcome measures

Primary outcome

1. Detailed clinical information on different visual symptoms, non-visual symptoms, triggers, (psychiatric and neurological) comorbidities and psychological well-being; including data from prospective follow-up.

2. Quantitative data on visual sensitivity and EEG and VEP profiles with specific parameters (amplitude of the posterior dominant rhythm, photic drive response); including diagnostic test characteristics.

3. Concentrations of multiple metabolites both in vivo (MRS) and ex vivo (blood, urine).

Secondary outcome

Not applicable

Study description

Background summary

Visual snow is a relatively unknown but disabling disorder characterized by the continuous presence of countless small dots moving in the entire visual field, resembling *floating snow* or *tv static*. It was originally postulated that these patients had persistent visual migraine auras, because visual snow patients often have a history of migraine aura. Unfortunately, the phenotype has not been extensively investigated and there are no objective diagnostic tests. Patients often report to be poorly understood by healthcare professionals and a subgroup of patients has psychiatric comorbidities (anxiety disorders, depression). Conventional migraine prophylaxes have small to no effect on the visual snow. In some patients the onset of visual snow occurs

after intoxication with drugs and they are diagnosed with *Hallucinogen Persisting Perception Disorder* (HPPD). Recently, it was discovered that visual snow patients have additional visual symptoms (i.e. sensitivity to light, palinopsia) besides the visual snow and it was proposed that visual snow is a clinical syndrome that is distinct from persistent migraine aura and consists of multiple visual symptoms. Interestingly, migraine patients also have increased visual sensitivity and palinopsia outside their migraine attack.

Study objective

The relationship with migraine is highly interesting and the main rationale for us to study the clinical characteristics of visual snow and its pathophysiology. Our hypothesis is that visual snow and migraine with aura are both disorders of cortical hyperexcitability and are therefore part of a spectrum. To test this hypothesis we aim to apply the techniques that provided valuable information on cortical hyperexcitability in migraine research: i) visual sensitivity tests, ii) electro-encephalograms (EEG) with specific visual evoked potentials (VEPs) and iii) proton magnetic resonance spectroscopy (1H-MRS) combined with biochemical analyses of blood and urine.

Objectives:
1. To describe the clinical characteristics (visual symptoms, non-visual symptoms, time course, triggers, neurological and psychiatric comorbidities) of visual snow.
2. To investigate whether patients with visual snow have hyperexcitability of the visual cortex resulting in visual sensitivity and specific EEG and VEP profiles (such as increased amplitude of the posterior dominant rhythm or increased photic drive response).
3. To investigate the biochemical profile of visual snow using in vivo 1H-MRS and ex vivo biochemical analysis and compare this profile with migraine (focus on neuro-excitatory and *inhibitory molecules such as glutamate and GABA).
4. To investigate the correlation between these techniques focused on hyperexcitability (EEG/VEP, in vivo 1H-MRS and ex vivo biochemical analysis)

Study design

First we will clinically characterize patients with visual snow, both patients with no clear relation with drug use (true visual snow syndrome) and patients with onset after drug use (often diagnosed as HPPD). For clinical characterization we aim to include all patients from our outpatient clinic with visual snow (current estimate of n=50) and strive for a similar sample size of patients with visual snow onset after drug use (HPPD). As control groups we include n=50 migraine patients with frequent auras to compare visual symptoms and comorbidities, n=50 tinnitus patients to compare (psychological) impact of the persistent symptoms and comorbidities, and n=50 healthy controls as reference to the healthy general population. This part will include a

structured interview on potential visual symptoms, non-visual symptoms, triggers, disease history and comorbidities and, when indicated, a neurological examination. Additionally participants are asked to fill in electronic questionnaires on severity of the symptoms, impact on daily life, psychological well-being, possible psychiatric comorbidity and on comorbid headaches and tinnitus. Patients with visual snow and HPPD will be included in prospective follow-up, where routine clinical data will be combined with questionnaires.

Next we will perform observational measurements in a case-control design with n=30 visual snow patients, n=30 migraine with frequent aura patients and n=30 healthy controls (sample sizes indicate successful measurements; see 4.5 for power calculation). Participants do not have to participate in all study parts; there will be separate informed consents. The following measurements will be performed: visual sensitivity tests, EEG and VEP recordings, blood and urine collection for ex vivo biochemical analyses and 1H MRS for in vivo biochemical analyses.

Study burden and risks

The burden of the clinical characterization part is minimal. Although some questionnaires might be confronting for patients we strongly believe this is outweighed by the advantages. It is directly relevant for clinical practice to know the involved psychological factors, especially for burdensome disorders which medical professionals cannot (yet) explain and cannot (yet) effectively treat. Furthermore, it is important for the interpretation of study outcomes and for future research.

The measurements are non-invasive (visual sensitivity testing, EEG and VEP profiling, MRS). We expect that the results of this study will lead to valuable clinical information that GPs, neurologists, ophthalmologist, addiction specialists and psychiatrists can use in their clinical diagnosis of visual disturbances. Hopefully it will also lead to objective diagnostic tests. The pathophysiological knowledge and understanding should benefit both visual snow research and migraine research. Therefore, we believe the burdens and risks are acceptable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

General
* Age *18 years (and <50 for those participating in MRS)
* Ability and willingness to provide written informed consent;Visual snow syndrome
* Visual disturbances suggestive of visual snow (for detailed clinical description)
* Clinical diagnosis of the visual snow syndrome (for case-control measurements);HPPD
* Continuous visual disturbances that started after drug intoxication (for detailed clinical description)
* Clinical diagnosis of visual snow starting after drug use (for case-control measurements)
;Migraine patients with frequent auras
* Meeting diagnostic criteria for migraine with aura (ICHD-III beta)
* At least one visual migraine aura per month (average of the past 6 months)
* For clinical description patients with atypical visual auras (visual symptoms mimicking visual snow description, visual auras longer than 1 hour) can also be included. For case-control measurement we aim for a homogenous study group and atypical auras are therefore excluded.;Tinnitus
* Daily complaints of tinnitus;Healthy controls
* See exclusion criteria

Exclusion criteria

General exclusion criteria for those willing to participate in case-control measurements
* Subjects who do not want to be informed about unexpected findings that are considered serious and have prognostic or therapeutic consequences
* Schizophrenia, bipolar disorder, other psychotic disorders in medical history or current clinical suspicion of psychosis (delusions)
* Malignancy in medical history
* Central nervous system disease in medical history (other than migraine)
* For those participating in MRS: Pacemaker or ICD, Metal implants which cannot be removed, Pregnancy, Claustrophobia;Visual snow
* Underlying neurological disorder or ophthalmological disorder explaining symptoms (for case-control measurements only (3.2), not an exclusion criterion for clinical description (3.1)) ;HPPD
* Underlying neurological disorder or ophthalmological disorder explaining symptoms (for case-control measurements only (3.2), not an exclusion criterion for clinical description (3.1))
* Clinical suspicion that visual symptoms are part of psychosis, delirium, neurodegenerative disease or hypnopompic hallucinations ;Migraine patients with frequent auras
* Meeting criteria for any other (comorbid) headache disorder except for tension type headache
* Clinical suspicion that patient has Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL; often presents with frequent auras) or any other hereditary cerebral amyloid angiopathy
* (History of) ophthalmological disease other than refraction error
* (History of) chronic tinnitus;Tinnitus patients
* Any symptoms of migraine, cluster headache, chronic tension type headache or medication overuse headache
* (History of) ophthalmological disease other than refraction error;Healthy controls
* Any symptoms of migraine, cluster headache, chronic tension type headache or medication overuse headache
* (History of) ophthalmological disease other than refraction error
* (History of) chronic tinnitus

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-03-2018
Enrollment:	250
Type:	Actual

Ethics review

Approved WMO

Date:	17-11-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL60333.058.17