The development of electrophysiological readouts for migraine attack prediction

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

Summary

ID

NL-OMON55696

Source
ToetsingOnline

Brief title
Electrophysiological prediction of migraine attacks

Condition

- Headaches

Synonym
Migraine; headache

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO

Intervention

Keyword: EEG, Migraine, Prediction, Visual Evoked Potential

Outcome measures

Primary outcome

AC-EEG: For the AC-EEG recordings we will use eight to 128 leads, which we will use to measure fluctuations. Our interpretation is that changes in fluctuations will become slower, resulting in e.g. increased autocorrelation and variance. Phase and amplitude correlations between electrodes will be used as measure of cortical excitability.

VEP: Visual evoked potentials (VEPs) are electrical potential differences recorded from the scalp in response to visual stimuli. They represent a mass response of cortical and possibly subcortical visual areas. In this study we will use unpatterned flash stimuli because this is a simple and robust way of visual stimulation that will perturb the visual system. We aim to measure the dynamics from the VEP responses (e.g. timing, amplitude of frequency) to assess the recovery phase of the visual system after perturbation to its original state. We expect that the time the visual system needs to recover to its original state is a measure of resilience of the system.

Secondary outcome

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Study description

Background summary

Self-propagating, centrifugally-expanding waves of cerebral neuronal firing, known as spreading depolarizations (SD), are believed to be the starting point of attacks of migraine. We hypothesize that the start of a SD corresponds to a critical transition that occurs when the dynamical brain system approaches a tipping point. Migraine may thus strike when a combination of genetic predisposition and modulating factors such as hormonal fluctuations and other endogenous and exogenous changes have raised the neuronal excitability to a level where even minor perturbations can trigger spreading depolarization. As the vicinity of a tipping point is associated with the universal phenomenon of *critical slowing down* in dynamical systems, we expect that, in the brain, this phenomenon will be reflected in electrophysiological characteristics which may serve as early warning signals to impending migraine attack. Identifying such a new class of early warning signals may open up new avenues for dissecting triggering mechanisms of migraine attacks and developing measures to prevent impending attacks.

Study objective

The overall objective of this study is to combine a conceptual model with empirical evidence to demonstrate that the start of a migraine attack corresponds to a critical transition that occurs when the dynamical brain system approaches a tipping point.
1. To develop an experimental paradigm to objectively measure parameters indicating the approach of a critical transition as a landmark in the dynamic alterations in brain excitability and thereby predict the tipping point in migraine patients.
2. To show that this experimental paradigm is able to predict an impending migraine attack in migraine patients.

Study design

Part 1: AC-EEG measurements and newly designed Visual Evoked Potential (VEP) paradigms will be performed on volunteers for up to 6 consecutive days. Several types of signal processing and signal analysis will be used to develop a new experimental paradigm that enables us to measure changes in cortical excitability. For the development of useful visual stimuli, measurements can take place on just one occasion or on several days for repeatability and reproducibility measures with a maximum of 6 days. Using high-density EEG the brain topographical response to visual stimulation and functional connectivity is studied. As part of this development stage we will also try to validate a new questionnaire on subjective visual aversion and sensitivity which we will also use in part 2.

Part 2: Migraine patients with a predictable component to their attacks (like

women with menstrual migraine), and a matching group of healthy controls will come for a period of three to six measurments (maximum of 1 measurement per day), prior to their predicted attack onset, to the department of neurophysiology of the LUMC or at the particpant' home. Each day, they will fill in some questionnaires, undertake pattern glare and photosensitivity testing, and AC-EEG measurements will be done. This will take a maximum of 1 hour per day.

Study burden and risks

EEG recordings: none
LED-bril offering light flases: none
Pattern glare test: none
Photosensitivity test: increasing light intensity can cause discomfort, at that light level the test will end.

Burden: there is no direct health gain for participating patients. Duration of participation (max 1 hour per day with a maximum of 6 days) is moderate. After careful consideration, we think possible side effects/risks are outweight by the expected gain in pathophysiologic knowledge, with hopefully therapeutical consequences in the future. In order to relieve some of the burden a fraction of the participants will be offered to have the EEG recordings at home.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Migraine with/ without aura or chronic migraine according to IHS / ICHD-III-beta criteria
- Patients have to experience active migraine, which is defined for this study as at least one migraine attack per month on average in the past 6 months.
- Age 18 years or older

Exclusion criteria

General exclusion criteria for episodic migraine patients and healthy controls: i) Severe depression and/or panic disorders and/or schizophrenia and/or psychiatric disorders; ii) Epileptic disorders (epilepsy); iii) Severe visual impairment; iv) Only for part 1: use of chronic medication (other than oral contraceptives) in the four weeks preceding the investigation; v) Malignancy in medical history; vi) only for part 2: use of (oral) contraceptives., Episodic migraine patient specific: i) Only for part 1: use of prophylactic medication for migraine in the four weeks preceding the investigation; ii) Inability to differentiate between migraine and other variants of headache;
iii) Use of acute migraine or headache drugs on more than 6 days per month., Healthy control specific: i) Suffering from periodic pain attacks or a brain disorder;
ii) Personal of family history in first-degree relatives of migraine or trigeminal autonomic cephalgia (TAC); iii) More than one tension-type headache in 3 months., Exclusion criteria for chronic migraine patients: i) Severe depression and/or panic disorders and/or schizophrenia and/or psychiatric disorders; ii) Epileptic disorders (epilepsy); iii) Severe visual impairment;
iv) Malignancy in medical history.

Study design

Design

Study type:	Observational non 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):	29-08-2014
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO

Date:	14-04-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	10-03-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	20-04-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-06-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-05-2021
Application type:	Amendment
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	NL47008.058.13