Exploration of the effects of high frequency stimulation induced secondary hyperalgesia on the NDT-EP method.

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The primary objective of this study is to investigate the quality and content of the MTT-EP model in response to electrocutaneous stimuli by determining stimulus-related and/or physiological-related components, before and after the occurrence of HFS...

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

Summary

ID

NL-OMON49836

Source
ToetsingOnline

Brief title
Exploration of effects of HFS on the NDT-EP method

Condition

- Other condition

Synonym
Chronic Pain

Health condition

(chronic pain), peripheral sensitization, central sensitization

Research involving
Human

Sponsors and support

Primary sponsor: University of Twente
Source(s) of monetary or material Support: NWO: TTW

Intervention

Keyword: central sensitization, Chronic pain, electroencephalography, evoked potentials, high-frequency stimulation, intra-epidermal electrical stimulation, nociceptive detection threshold, punctuate mechanical stimulation, secondary hyperalgesia

Outcome measures

Primary outcome

- NDTs Subject Response: The subject*s response to the stimulus, detected or

not detected.

- EEG Signals: Electric signals reflecting the subject*s neurophysiological

activity related to the stimulus, extracted at a fixed interval around every

stimulus.

- NRS after HFS stimulation: Scoring the intensity of pinpricks by means of

numerical rating score after inducing secondary hyperalgesia using

high-frequency stimulation.

- Punctate mechanical stimulation: Pinprick stimulation using Semmes-Weinstein

monofilaments for assessing the occurrence of secondary hyperalgesia

Secondary outcome

- Response Time: Subject*s response time.

- Participant Characteristics: Age and sex, handedness.

- Electrode-skin Impedance: To assess whether the setup of the HFS was able to

reach the required voltages for intensity 20 times higher the subject*s

detection threshold.

Study description

Background summary

Chronic pain often is results from disturbed processes in the central nervous system. Once chronic pain is established, treatment is relatively ineffective, with * at best * one patient in three or four achieving 50% pain intensity reduction. Early detection and therapeutic action would mean better treatment outcome and less clinical efforts per patient, but appropriate diagnostic tools are lacking. An increased sensitivity to noxious stimuli is widely recognized as a key factor in chronic pain development. Noxious stimuli are processed by neural mechanisms at several stages in the ascending pathway from periphery to brain, into a conscious pain experience. As a response to injury or disease, maladaptive changes in this pathway may result in an increased pain sensitivity. Clinical observation of the specific malfunctioning of peripheral and central components of this pathway is limited at present, but would permit a better understanding and early selection of interventions for treatment or prevention of chronic pain. Recently, we developed a new method for observing the properties of nociceptive processing utilizing subjective detection of electrocutaneous stimuli in combination with objective neurophysiological brain responses (NDT-EP). In this method, nociceptive afferents are activated by temporally defined current stimuli with varying number of pulses and varying inter pulse intervals. As these different temporal stimulus properties result in different excitation of nociceptive processing mechanisms of the ascending system, subsequent processing of stimulus-response pairs (SRPs) into estimated nociceptive detection thresholds (NDTs) and Evoked brain Potentials (EPs) of multiple stimulus types may provide information about the properties of these mechanisms.

A crucial step in exploring whether the above method could serve as a diagnostic tool is the assessment of the observability of changes in nociceptive function which are relevant for the development or maintenance of chronic pain. This can be achieved by measuring the effect of a well characterized and demonstrated alteration in nociceptive processing mechanisms on the NDTs and EPs. Other research groups have demonstrated that high frequency electrocutaneous stimulation (HFS) of sufficient duration and intensity can be used for prolonged activation of central sensitization mechanisms. These central sensitization effects are observed as a post-HFS secondary hyperalgesia to pin-prick stimuli and considered to play a key role in the development of chronic pain. Other results show that HFS also modulates the EPs obtained by electrocutaneous stimulation on the site of induced secondary hyperalgesia. Recently during a pilot study here at the University of Twente, we have assessed that HFS is technically feasible to implement in our lab. Therefore, the next step is to use HFS in an experiment together with the NDT-EP method.

Study objective

The primary objective of this study is to investigate the quality and content of the MTT-EP model in response to electrocutaneous stimuli by determining stimulus-related and/or physiological-related components, before and after the occurrence of HFS-induced central sensitization onto the skin of healthy subjects.

Study design

The current study is a mono-center, cross-sectional study. Each subject will undergo a single measurement session.
Each Measurement Session (155 minutes) consists of:
* Introduction (10 minutes): The subject will be provided with information about the experiment and asked for consent to participate in the experiment.

* Preparation (20 minutes): The subject will be connected to the EEG equipment and the nociceptive stimulation device.

* Familiarization (10 minutes): The subject will be familiarized with the stimuli. In this phase, the subject can get used to determining whether a stimulus exceeds the stimulation threshold, and learn how to behave during the experiment.

* 1st punctate mechanical stimulation (2 minutes): The target for the mechanical pinpricks are marked and the first mechanical stimulation is performed.

* Experiment (103 minutes): The actual experiment, in which nociceptive stimulus-response pairs will be measured for a variety of nociceptive stimuli.
- 35 minutes: first NDTs acquisition
(both arm and hand)
- +2 minutes: 2nd punctate mechanical
stimulation
- +5 minutes: HFS and assessment of
perceived pain
- +2 minutes: right after HFS for 3rd
pinprick stimulation
20
minutes break
- +2 minutes: 4th pinprick stimulation
- +35 minutes: second and final NDTs
acquisition (both arm and hand)
- +2 minutes: 5th and final punctate
mechanical stimulation

* Round-Up (10 minutes): Disconnection and debriefing of the subject.

Study burden and risks

The healthy participants will be asked to come to the Human Physiology Lab of the BSS Group at the University of Twente for one session. First, the participant is familiarized with the stimuli by stepwise application of increasing stimuli until stimulus detection. During the experiment, the participant will receive randomized stimuli around the detection threshold according to the multiple threshold tracking paradigm. Afterwards, HFS is applied to induce secondary hyperalgesia. Lastly, the subjects will receive a second series of randomized stimuli around the detection threshold according to the MTT paradigm. During the entire duration of the experimental session, cortical activity of the subject will be recorded using an EEG cap. All participants will be compensated for their participation. The participants will obtain no direct personal benefit.

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

Age between 16 and 40 years old.

Exclusion criteria

* Participant refusal during the study.
* Language problems.
* Skin problems at site of stimulation or EEG recording.
* Diabetes.
* Implanted stimulation device.
* Pregnancy.
* Usage of analgesics within 24 hours before the experiment.
* Consumption of alcohol or drugs within 24 hours before the experiment.
* Pain complaints at the time of the experiment.
* A medical history of chronic pain.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-11-2021
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	29-06-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL72937.091.20