Exploration of the effects of HFS-induced secondary hyperalgesia on the NDT-EP method with paired probing stimuli

Published: 14-01-2025
Last updated: 07-06-2025

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

Summary

ID

NL-OMON57266

Source
ToetsingOnline

Brief title
Effects of HFS on the NDT-EP method with paired probing

Condition

- Other condition

Synonym
central sensitization, Chronic pain

Health condition

chronic pain

Research involving
Human

Sponsors and support

Primary sponsor: Research Group Biomedical Signal and Systems (BSS), University of Twente
Source(s) of monetary or material Support: TKH-HTSM Connecting Industries subsidie

Intervention

Keyword: evoked potentials, high-frequency stimulation (HFS), intra-epidermal electrical stimulation, secondary hyperalgesia

Outcome measures

Primary outcome

NDTs, EPs, and subjective ratings (NRS) of the perceived strength of mechanical

punctuate stimuli will be collected from a testing (HFS) and a control site,

before and 20 minutes after induction of secondary hyperalgesia using HFS.

Secondary outcome

Response Time: Subject*s response time.

Participant Characteristics: Age and sex, handedness.

Study description

Background summary

In Europe, pain is considered the major cause of disability and disease burden affecting 20.27% of the population over 18 years of age. A class of syndromes characterized by a persistent pain lasting over normal healing times is defined as Chronic Pain Syndromes. Central sensitivity is a phenomenon associated to chronic pain and is defined by the occurrence of unpleasant sensations in response to normally-innocuous stimuli. The increased sensitivity over an injured area is known as primary hyperalgesia, whereas the spreading of sensitization to an uninjured, adjacent region is called secondary hyperalgesia. The underlying mechanism of secondary hyperalgesia is also addressed as central sensitization, since sensitized neurons are located in the central nervous system (i.e. dorsal horn of the spinal cord) and contribute to neurogenic hyperalgesia. Thus, investigating the alteration of nociceptive processing might yield to an understanding of the mechanisms generated by

central sensitization and resulting in secondary hyperalgesia. However, further investigation of underlying mechanisms occurring in central sensitization has been challenging due to the lack of an objective measure of peripheral and central sensitivity.

In general it is difficult to measure how much pain one is experiencing as numerical scores are dependent on personal experiences and thus subjective. Over the past few years, the BSS group of University of Twente has developed the NDT-EP a new method for combined observation of Nociceptive Detection Thresholds (NDT) and Evoked Potentials (EP) to investigate brain activation in response to nociceptive stimuli via intra-epidermal electrocutaneous stimulation (IES). Several studies with the NDT-EP methods have demonstrated differences between patients and pain-free subjects and treatment effects. A next step is to link these findings to well-known mechanisms underlying changes in the nociceptive function, like central sensitization, which can be studied using experimentally induced secondary hyperalgesia. The High Frequency Stimulation (HFS) paradigm is an established and well characterized experimental model for induction of secondary hyperalgesia. Therefore, the goal of this study is to explore HFS induced changes in NDT-EP measurement results in pain-free subjects. For this purpose, the NDT-EP method is extended with a paired probing feature to also capture the coding of well-defined suprathreshold stimuli simultaneously in the evoked potentials.

Study objective

The primary objectives are to describe NDTs from double pulse IES stimuli before and 20 minutes after HFS induced secondary hyperalgesia, as verified by responses to mechanical pinprick stimuli, and describe EPs of detected double pulse IES stimuli and of paired quadruple pulse IES stimuli of equal amplitude.

The secondary objective is to evaluate the effects of HFS on nociceptive gating (threshold) and coding (EP) by comparing pre- and post-HFS NDT and EPs, and EPs from double and quadruple pulse stimuli.

Study design

Mono-center, cross-sectional study

Study burden and risks

All participants will be asked to come to the Human Physiology Lab of the BSS Group at the University of Twente for one session that is split up in two parts. In the first part, the participant is familiarized with the stimuli of the IES electrode during the NDT-EP measurement by stepwise application of increasing stimuli until the sensation is clearly felt and with one train of HFS. HFS trains induce a painful but short sensation and are generally

experienced as the most unpleasant part of the experiment. After the first part of the experiment, the subject is invited to proceed with the second part of the experiment.

In the second part of the NDT-EP method will be performed. The participant will receive randomized stimuli around the detection threshold and suprathreshold according to the paired probing paradigm. The sensations of these stimuli are best described as brief pinpricks. Next five trains of HFS are administered after which a second series of the NDT-EP and paired probing stimuli are given. During the entire duration of the experimental session cortical activity of the subject will be recorded using an EEG cap. The participants will obtain no direct personal benefit for their personal health but will be compensated for their participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age between 18 and 40 years old

Exclusion criteria

- Participant refusal during the study
- Language problems
- Skin problems at site of stimulation or EEG recording
- Diabetes
- Small fiber neuropathy
- 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
- Having a position of dependency on one or more of the researchers (i.e. being directly supervised and graded by one of the researchers).

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-02-2025
Enrollment:	20
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	14-01-2025
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	NL88051.091.24