Observing Electrical Brain Responses during Processing of Nociceptive Stimuli around the Detection Threshold combined with a Cold Pressor Test: an Explorative Study

Published: 19-12-2019
Last updated: 27-04-2024

The aim of this study is to explore the feasibility to combine measurements of the NDT and EEG recording with a cold pressor test (CPT) in a clinical environment. In this explorative study, multiple types of stimuli are delivered. The NDT and EEG...

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

Summary

ID

NL-OMON48333

Source
ToetsingOnline

Brief title
CPT-study

Condition

- Other condition

Synonym
pain

Health condition

Chronische pijn, centrale sensitisatie, perifere sensitisatie

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit van Twente
Source(s) of monetary or material Support: Vanuit het TTW Perspectief programma 14-12 NeuroCIMT project 2: Nocicept

Intervention

Keyword: cold pressor test, electrocutaneous stimulation, evoked potential, failed back surgery syndrome, nociceptive detection threshold

Outcome measures

Primary outcome

The nociceptive detection threshold

EEG signals

Secondary outcome

Current pain (NRS)

Average pain in the lasts seven days (NRS)

Questionnaire about symptoms of central sensitization: central sensitization

inventory (CSI)

Current medication intake

Patient characteristics: age, sex, BMI

Immersion time and water temperature

Neurological evaluation

FBSS duration (in months, patients only)

pQST/PPDT

Study description

Background summary

The development of treatments for chronic pain requires a more profound understanding of the physiological and psychological aspects of chronic pain. Several types of chronic pain, including FBSS, are linked to increased sensitivity of the central nervous system. Therefore, it is important to study the underlying mechanisms of this increased sensitivity. However, one major obstacle is the lack of an objective measure of peripheral and central sensitivity. Besides hampering the development of new treatments, this causes inaccuracies in chronic pain diagnoses, resulting in delayed or unnecessary treatments. Tracking detection thresholds of nociceptive specific electrocutaneous stimuli can facilitate the investigation of the underlying mechanisms of sensitization.

Recently, a subjective method was developed for tracking multiple psychophysical thresholds over time, referred to as multiple threshold tracking (MTT), which has been shown sensitive to central changes in nociception. An objective measure of nociception related activity in the central nervous system is the electroencephalographic (EEG) signal. Multiple-trial averages of this signal, referred to as evoked potentials (EPs), have been shown to reflect nociceptive sensitivity tochanges in stimulus parameters. Since MTT has been shown to be effective in measuring the effect of stimulus parameters on stimulus detection, while the EP has been shown to reflect neurophysiological activity related to stimulus processing, a combination of both techniques might provide insight into the relation between neurophysiological activity and nociceptive stimuli. We have recently investigated this relationship in healthy subjects in a study at Biomedical Signals and Systems at the University of Twente (approved by the METC Twente numbered NL62721.044.17). In this research, it was shown that components of the EP are closely related to the stimulus detection.

Furthermore, research has shown that the descending pathways seem to show an crucial role in the modulation of pain. In this study we try to activate these pathways by applying a cold pressor test to see how this test will affect the detection threshold and to what extent pain is modulated (Conditioned Pain Modulation, CPM). Results from the MTT-EP method combined with CPT are needed to validate the measurement technique in pain-free subjects. Next, it is important to explore the feasibility in chronic pain patients. Subsequently, results may contribute to provide insight into the underlying pathophysiology of chronic pain.

A similar study has been performed at the University of Twente whereby a cold pressor test was applied at one hand (see attached file K6, Doll et al.). However, this study only comprises the nociceptive detection threshold

measurements (no EEG was recorded).

Additionally, we did not yet investigate the NDT and EPs combined with CPT in patients with altered pain processing mechanisms. Measurements of NDTs and EPs in chronic pain patients could aid the diagnosis and the development of new treatments in these patients in the future. To enable this, it is necessary to understand how the NDTs and EPs in these patients behave pre-, during and post-CPT when compared to healthy subjects.

Study objective

The aim of this study is to explore the feasibility to combine measurements of the NDT and EEG recording with a cold pressor test (CPT) in a clinical environment. In this explorative study, multiple types of stimuli are delivered. The NDT and EEG are measured and analysed with respect to the stimulus parameters.

A primary objective is to explore the feasibility of CPT with the MTT-EP method in a clinical environment and to evaluate and explore NDTs and EPs pre-, during and post-CPT-induced CPM activation of healthy subjects and FBSS patients. Another primary objective is to describe how the NDTs for electrical stimuli behave pre-, during and post-CPT in healthy controls and FBSS patients using a multiple threshold tracking paradigm, and how neurophysiological responses (EPs), measured pre-, during and post-CPT, are related to the delivered electrocutaneous stimuli properties in healthy controls and FBSS patients. Lastly, a primary objective is to explore the reproducibility of the MTT-EP measurement in healthy subjects and FBSS patients by a test-retest in the St. Antonius Hospital Nieuwegein.

Secondary objective is to analyze how the NDT and EEG pre-, during and post-CPT are related to sensitization in FBSS patients. Furthermore, other secondary objectives are to see if differences in NDTs and EPs pre-, during and post-CPT can be found between FBSS patients and healthy controls and between different age groups in healthy subjects and FBSS patients.

Study design

Mono-center, cross-sectional study.

Study burden and risks

The participants are asked to come to the St. Antonius Hospital for two sessions. Participants are not allowed to consume alcohol or use drugs during the 24 hours prior to the session (they are allowed to take medication). At the start of the session, the participant fills in a questionnaire. Subsequently, 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 (MTT) paradigm at the dominant hand. The burden during the session is minor, as the electrical stimuli are expected to stay below the pain threshold* but participants will undergo the experiment for two hours in total, of which they need to be very concentrated for approximately 30 minutes. Furthermore, during the experiment the participants are asked to immerse one foot into a container filled with cold water. This could be experienced as painful, however, previous study has been performed at the University of Twente resulting in good results (see attached file K6, Doll et al.). For this, the subjects will be compensated with a voucher. The risks are expected to be neglectible.

*The pain threshold in healthy subjects lays around 2 mA for intra-epidermal stimulation, see the IMDD of the AmbuStim (D2). The pain threshold in FBSS patients might be lower. However, using the MTT paradigm, stimuli are applied around the detection threshold estimated during the experiment. Therefore, the pain threshold will not be reached unless the subject fails to respond adequately to the applied stimuli.

Contacts

Public
Universiteit van Twente

Drienerlolaan 5
Enschede 7500 AE
NL
Scientific
Universiteit van Twente

Drienerlolaan 5
Enschede 7500 AE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy subjects:
Age of 18 or above;
No history of pathological pain.

FBSS patients:
Age of 18 or above.

Exclusion criteria

Patient*s refusal during the study;
Skin problems at the site of the pain sensitivity measurement;
Communication problems or incapable of following the instructions;
Pregnancy;
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;
Unable to undergo pain sensitivity measurement;
Cardiac arrhythmias;
Heart valve defects;
Heart muscle diseases;
Open wound on the foot to be immersed;
Frequent caffeine use (>8 units/day);
Smokers (>5 cigarettes/day);
BMI > 30 kg * m-2;
Type 1 or 2 diabetes mellitus.

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):	22-01-2020
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	19-12-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL71927.100.19