Optimization of the Conditioned Pain Modulation Protocol using the Q-sense

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In the current study, we will 1) evaluate the usefulness and reliability of this new device, and 2) evaluate whether the anatomic site used will impact the measured CPM effect.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON42364

Source
ToetsingOnline

Brief title
CPMQ study

Condition

- Other condition

Synonym
healthy volunteers, pain measurements

Health condition

endogene pijnstilling

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: endogenous pain modulation, sensory testing

Outcome measures

Primary outcome

The aim of this study is to assess the usefulness of the Q-sense CPM device for CPM studies. The end-point is defined as: reproducible and significant pain relief of the test stimulus when combined with the appropriate conditioning stimulus.

Secondary outcome

Furthermore, we will evaluate whether the anatomic site used will impact the measured CPM effect.

Study description

Background summary

Activation of nociceptors (pain sensors) at peripheral sites leads to trafficking of afferent sensory information to the brain where pain is perceived as an unpleasant sensation or feeling. The afferent sensory information undergoes complex modulation at various points of its trajectory, both at the spinal cord and at higher brain centers. Central modulation of pain responses occurs via descending pathways originating at higher centers in the CNS including the prefrontal cortex, rostral anterior cingulate cortex (rACC) and insula, which project to the periaqueductal gray (PAG), and rostral ventromedial medulla (RVM) in the brainstem and modulate nociceptive input at the level of the dorsal horn [2,9,10]. Expressions of the endogenous pain modulation system are placebo- and stress-induced analgesia and conditioning pain modulation (CPM) [6,7].
In experimental CPM studies, central inhibition of a focal pain stimulus is induced by applying a noxious stimulus at a remote area, thereby reducing the perception of the focal pain stimulus. Recently published guidelines on the experimental set-up of CPM experiments report the need for standardization [8]. However, the studies on which these guidelines were based, used different methodology to study endogenous pain modulation pathways in patients [1,3-5].

These discrepancies include different test stimuli (noxious heat, pressure pain, electrical pain), different conditioning stimuli (hot water, cold water), and different test locations (hands, feet, contralateral and ipsilateral sites). The impact of these differences on assessment of CPM effects has never been systematically evaluated.
The development of the guidelines has resulted in the development of an easy-to-use CPM device (Q-sense, Medoc). This device uses two experimental heat stimuli to evaluate the CPM effect.

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[2] Derbyshire SW, Osborn J. Offset analgesia is mediated by activation in the region of the periaqueductal grey and rostral ventromedial medulla. NeuroImage 2009;47(3):1002-1006.
[3] Grosen K, Vase L, Pilegaard HK, Pfeiffer-Jensen M, Drewes AM. Conditioned pain modulation and situational pain catastrophizing as preoperative predictors of pain following chest wall surgery: a prospective observational cohort study. PLoS One 2014;9(2):e90185.
[4] Treede RD, Meyer RA, Campbell JN. Myelinated mechanically insensitive afferents from monkey hairy skin: heat-response properties. Journal of Neurophysiology 1998;80(3):1082-1093.
[5] Wilder-Smith OH, Schreyer T, Scheffer GJ, Arendt-Nielsen L. Patients with chronic pain after abdominal surgery show less preoperative endogenous pain inhibition and more postoperative hyperalgesia: a pilot study. J Pain Palliat Care Pharmacother 2010;24(2):119-128.
[6] Yarnitsky D. Conditioned pain modulation (the diffuse noxious inhibitory control-like effect): its relevance for acute and chronic pain states. Curr Opin Anaesthesiol 2010;23(5):611-615.
[7] Yarnitsky D, Arendt-Nielsen L, Bouhassira D, Edwards RR, Fillingim RB, Granot M, Hansson P, Lautenbacher S, Marchand S, Wilder-Smith O. Recommendations on terminology and practice of psychophysical DNIC testing. Eur J Pain 2010;14(4):339.
[8] Yarnitsky D, Bouhassira D, Drewes AM, Fillingim RB, Granot M, Hansson P, Landau R, Marchand S, Matre D, Nilsen KB, Stubhaug A, Treede RD, Wilder-Smith OH. Recommendations on practice of conditioned pain modulation (CPM) testing. Eur J Pain 2014.
[9] Yelle MD, Oshiro Y, Kraft RA, Coghill RC. Temporal filtering of nociceptive information by dynamic activation of endogenous pain modulatory systems. Journal of Neuroscience 2009;29(33):10264-10271.
[10] Yelle MD, Rogers JM, Coghill RC. Offset analgesia: a temporal contrast mechanism for nociceptive information. Pain 2008;134(1-2):174-186.

Study objective

In the current study, we will 1) evaluate the usefulness and reliability of this new device, and 2) evaluate whether the anatomic site used will impact the

measured CPM effect.

Study design

This is a randomized, cross-over study in 30 healthy volunteers.
Pain measurements. Thermal stimuli will be applied on the volar side of the forearm or the front lower leg using the thermal test probe (a 3 × 3 cm thermode) and a conditioning probe (a 3 × 3 cm thermode) of the Medoc CPM Q-sense system (Medoc Ltd, Ramat Yishai, Israel). This is a computer-controlled device with two thermodes capable of generating highly reproducible thermal stimuli. The Visual Analogue Scale (VAS) will be used to quantify pain intensity in response to a thermal stimulus. VAS will be measured electronically (eVAS) using a slide potentiometer (length = 100 mm) that can be moved from the left (0 mm or no pain) to the right (100 mm or most intense pain imaginable). Using a hand the subject can move the slide during the heat stimulator test. The eVAS is recorded and collected on disk for further analyses.
In order to assess the temperature at which the subject has a specific eVAS score, various short (5 s) test stimuli will be applied in the range from 42 to 51 °C. The study will be performed with the lowest stimulus strength (in °C) which causes a specific eVAS value.
CPM paradigms. We will evaluate several CPM paradigms using the Q-sense CPM system. First, the VAS response to a heat pain stimulus (5 seconds with an intended VAS of 30 [conditioning] or 60 [test] out of 100) on the lower, non-dominant forearm will be assessed with 3-min intervals (baseline testing). Cold and hot water temperatures will be tested to assess the corresponding temperatures to the conditioning VAS of 30 mm. Next, we will test 6 different conditions in a random order, with 15-minute rest period in between (see below).
1. Test stimulus non-dominant arm, conditioning stimulus contralateral arm (ARM-ARM)
2. Test stimulus leg ipsilateral to non-dominant arm, conditioning stimulus contralateral leg (LEG-LEG)
3. Test stimulus non-dominant arm, conditioning stimulus contralateral leg (ARM-LEG)
4. Test stimulus non-dominant arm, conditioning stimulus ipsilateral leg (ARM-LEG)
5. Test stimulus leg ipsilateral to non-dominant arm, conditioning stimulus ipsilateral arm (LEG-ARM)
6. Test stimulus leg ipsilateral to dominant arm, conditioning stimulus ipsilateral arm (LEG-ARM)
The test stimulus will never be applied on the dominant arm, as this arm is used to control the eVAS slider.
The type of conditioning stimulus will either be the Q-sense CPM conditioning thermode, a cold-water bath or a hot-water bath. The size of the conditioning stimulus will be standardized at a pain score of 30 mm (of 100 mm).

Intervention

Pain measurements

Study burden and risks

Minimal risks and burden. We have ample experience with thermal stimuli testing. Heat pain testing may give a short-lasting red coloration of the skin due to vasodilatation. Subjects will undergo testing of thermal pain at VAS scores between 0 and 100, however no temperatures will be reached that have a risk of damage to the skin or any other structures.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy volunteers, aged 18 to 35 years, right-handed.

Exclusion criteria

- Unable to understand study information or give oral and written informed consent;
- Obesity (BMI > 30 kg/m2);
- History of chronic alcohol or illicit drug use;
- History of illness, condition or medication use that, in the opinion of the investigator, might interfere with optimal participation, or could confound the results of the study;
- Pregnancy / lactation

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2015
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	25-08-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO Date:	08-12-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 20926
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL53726.058.15
OMON	NL-OMON20926