Sensory testing of the skin using heat stimulation In healthy volunteers and neuropathic Pain Patients

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

Summary

ID

NL-OMON37526

Source
ToetsingOnline

Brief title
STIPP study

Condition

- Other condition

Synonym
neuropathic pain, pain

Health condition

chronische pijn

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: adaptation, endogenous modulation of pain, Sensory system

Outcome measures

Primary outcome

Pain scores in response to a heat stimulus

Secondary outcome

None

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 centers. Modulation at spinal sites is related to the intrinsic response properties of primary afferent neurons within the dorsal horn. For example, the response of warm fibers during a 39 oC stimulus is completely suppressed by cooling pulses greater than 1 oC below 39 oC [1]. Another example is that upon noxious heat stimulation nociceptive fibers (C- and type IIA-fibers) demonstrate a similar response with an early peak frequency of discharge at the beginning of the stimulus followed by a slow adapting response towards low frequency rates at 5 seconds after the onset of the stimulus [2,3]. 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 periaquaductal gray, and rostral ventromedial medulla in the brainstem and modulate nociceptive input at the level of the dorsal horn [4-6]. The neurotransmitter involved in this process is noradrenaline that activate the postsynaptic α2 adrenergic receptor in the dorsal horn. Activation of this receptor causes profound analgesic responses. Expressions of endogenously modulated pain responses are placebo- and stress-induced analgesia and

conditioning pain modulation (CPM) [7,8].

We previously tested the paradigm of offset analgesia where a disproportional large amount of analgesia becomes apparent upon a slight decrease in noxious heat stimulation, in both healthy volunteers and neuropathic pain patients [9,10]. This test was abnormal or absent in neuropathic pain patients and suggests a malfunction of the modulatory process in pain perception, at spinal or supraspinal sites. Offset analgesia (see below, Fig 2A) is a very short test that gives valuable information but that does not allow discrimination between peripheral or central sites. Furthermore, due to its short temporal profile, no information is obtained of longer stimulation of sensory neurons.

Study objective

In the current protocol we will perform a variety of sensory tests of the skin and measure the pain response of patients and healthy volunteers. The aim of the study is (1) observational, i.e., to assess and describe the responses of patients and volunteers to a variety of different stimulation paradigms; (2) diagnostic, i.e., to assess whether specific tests are possibly diagnostic for specific pain syndromes; (3) mechanistic, i.e., whether the results of the test may give us valuable information on the site of modulation (central or peripheral). The latter is possible by applying specific pharmacological agents and observed possible changes in the response to the pain stimuli.

The following populations will be studied:
1. Healthy volunteers;
2. Neuropathic pain patients due to (a) Complex Regional Pain Syndrome, (b) Diabetic neuropathy, (c) Sarcoidosis, (d) Ischemic events in spinal cord or brain; (e) Fibromyalgia.

Study design

Open

Study burden and risks

None

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

Patient inclusion criteria. (i) Patients diagnosed with CRPS-1, small-fiber neuropathy, central neuropathic pain or fibromyalgia, according to the guidelines of the IASP or other professional pain societies (eg., Netherlands Society of Anesthesiologists); (ii) a pain score of 5 or higher; (iii) age between 18 and 75 years; (iv) being able to give written informed consent.;Volunteer inclusion criteria. Healthy volunteers in the age range 18-75 years of either sex.

Exclusion criteria

Patient and volunteer exclusion criteria. (i) Unable to give written informed consent; (ii) medical disease such as renal, liver, cardiac, vascular (incl. hypertension) infectious disease; (iii) increased intracranial pressure; (iv) epilepsy; (v) psychosis; (vi) glaucoma; (vii) a history of cerebro-vascular accident < 1 year; (viii) pregnancy; and (ix) obesity (BMI > 30).

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2012
Enrollment:	84
Type:	Anticipated

Ethics review

Approved WMO

Date:	20-04-2012
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
CCMO	NL39757.058.12