PJ-008200 Measurements on healthy subjects to design a nociception index

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The primary objective is to measure the effect of nociceptive stimuli on features derived from ECG, ABP, PPG, EEG and facial video recordings, to be used to design an index of nociception. The index of nociception should correlate well with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Administration site reactions
Study type	Observational non invasive

Summary

ID

NL-OMON28208

Source
Nationaal Trial Register

Brief title
Measurements to design a nociception index

Condition

- Administration site reactions

Health condition
Measurements, such as vital signs, brain activity and facial expressions, are obtained from healthy subjects while they experience noxious sensations. The noxious stimuli will be created by applying a short thermal pulse or electrical pulse to the skin of the lower leg (calf). The thermal and electrical pulses will be repeated multiple times at different levels. For a more prolonged nociceptive stimulation, the subjects are asked to put their hand in a bucket of ice water for a maximum of three minutes or until they want to take it out. For a part of the study, they will receive an analgesic medication that will reduce the nociceptive experience, remifentanil. The measurements from all subjects will be combined to design a new index of nociception.

Research involving

Human

Sponsors and support

Primary sponsor: Philips
Source(s) of monetary or material Support: Philips

Intervention

- Other intervention

Explanation

Outcome measures

Primary outcome

The primary endpoint of the study is the correlation between the presence of nociception and measures of nociception (features derived from ECG, ABP, PPG (pulsations in finger), GSR (sweatproduction on hand) EEG and facial recordings)

Secondary outcome

- the effect of remifentanil on the correlation between the index of nociception and the stimulus strenghts and related NRS scores - the performance of within Philips Research erlier developed vital sign based (i.e.HRV, BP) algorithms - the index of nociception with indices on the market such as ANI - the performance of the PainCheck facial expressions algorithm for pain detection

Study description

Background summary

Pain is defined by the International Association for the Study of Pain as “an unpleasant sensory and emotional experience

associated with actual or potential tissue damage, or described in terms of such damage”. Nociception is “the neural process of

encoding noxious stimuli”.

Nociception during surgery can lead to surgically-induced neuropathic pain (SNPP). SNPP has been estimated to occur in 10-

50% of patients. To prevent SNPP, a perioperative strategy would be to continuously block nociception, and for this an objective

measure of nociception is necessary.

In clinical practice it is seldom possible to completely block activation of the nociceptive pathways. When spinal or regional

anesthesia is not possible, the one of the opioid drugs is administered to counteract the nociceptive signals. At present it is very

difficult for clinicians to judge when or if the opioid dose is adequate, and this is a problem because both inadequate and

excessive doses have adverse consequences. In adequate doses of opioids are associated with sympathetic activation and

hemodynamic instability (tachycardia and hypertension), and possibly an increased risk of SNPP. On the other hand excessive

doses are associated with adverse effects such as bradycardia and hypotension, post-operative nausea and vomiting,

generalized itching and constipation. Moreover, excessive doses may be associated with opioid tolerance and opioid-induced

hyperalgesia which can lead to increased post-operative opioid requirements, and eventually a higher incidence of SNPP.

Nociception measurement and management is a quality indicator for hospitals. Monitoring of nociception in the OR could result

in improved patient safety, higher OR throughput, and better patient outcome.

In current clinical practice, anesthesiologists primarily rely on changes in heart rate (HR) and arterial blood pressure (ABP) as a

measure of the balance between nociception and anti-nociception (i.e. the dose of analgesic drugs) during surgery. However,

with this approach some nociceptive responses may be missed.

There is a need for a continuous, objective nociception index especially for sedated unconscious patients who cannot express

their pain levels. There is an increasing number of new nociception/pain/stress indices in the market using a combination of vital

signs, using galvanic skin conductance or brain signals or using a combination of different parameters. However, none of these

technologies is currently better than BP and HR in predicting nociceptive response and there is definitely room for improvement.

In our current study, we aim to use a novel combination of parameters to design a unique nociception index.

Heart rate variability (HRV) is a widely used measure of alterations in sympathetic and parasympathetic autonomic nervous

system activity. HRV has been associated with nociceptive stimuli since many years. More recent studies have underpinned the

potential value of HRV in nociception measurement.

Another physiological response to nociceptive events is an increase in blood pressure. This has been shown for tonic

nociceptive stimuli, as well as short nociceptive stimuli.

Photoplethysmography (PPG) measures local blood volume changes, e.g. at the fingertip. The pre-processing of a patient

monitor removes some of the information in a PPG waveform, which is why we chose a recording method that avoids this. The

PPG waveform consists of a DC component (i.e. low-frequency variations) and an AC component (higher frequency variations).

The AC component has been shown to be relevant for measuring nociception. Various parameters can be derived from the PPG

waveform, such as amplitude, area under the curve, and rising slope.

Galvanic skin response is a measure that is used to measure stress, and has also been linked to noci

Study objective

The primary objective is to measure the effect of nociceptive stimuli on features derived from

ECG, ABP, PPG, EEG and facial

video recordings, to be used to design an index of nociception. The index of nociception should correlate well with strength of

nociceptive stimulus and subjective NRS score.

The secondary objectives are to:

- Analyse the effect of remifentanil on the correlation between the index of nociception and the stimulus strengths and related

subjective NRS scores (remifentanil is standard in surgery care, is fast acting, and often used in other studies that research

nociception).

- Evaluate the performance of within Philips Research earlier developed vital sign based (i.e. HRV, BP) algorithms.

- Benchmark the index of nociception with indices on the market such as ANI (Analgesia Nociception

Evaluate the performance of the PainChek facial expressions algorithm for pain detection

Study design
This clinical investigation is designed as an observational pilot study, because a unique dataset needs to be obtained to design

an index of nociception

Intervention

Patient will receive a standardized pain protocol with and without administration of remifentanil. The pain protocol consists of electrical and thermical pain stimuli and the ice bucket water test.

Contacts

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Eligibility criteria

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

Inclusion criteria

1) Age between 18 and 65 years old 2) ASA I Healthy subjects 3) BMI < 35 4) Females should be using contraception

Exclusion criteria

1) Pregnancy (pregnancy test before start protocol, if female, with the exception of post menstrual women) 2) Smoking 3) Alcohol abuse 4) Medication that influeunces the central or peripheral nervous system, or the cardiovascular system 5) Drug use (drug test before start protocol) 6) Raynaud's disease (poor blood circulation) 7) Scleroderma, Dupuytren’s Contracture, or other Rheumatology issues 8) Depression and/or anxiety (the Hospital Anxiety and Depression Scale (HADS) questionnaire is given before the start of the protocol. Subjects with a score greater than or equal to 11 are excluded) 9) Food eaten in the 6 hours before the test 10) Fluid intake within less than 2 hours of the planned start of experimentation 11) Use of caffeinated beverages in the 12 hours before the test 12) Use of caffeinated food (e.g. chocolate) in the 6 hours before the test COVID-19 additional Exclusion criteria: 13) Currently displaying COVID-19-related symptoms, namely a fever, cough and/or difficulty breathing 14) Having been positively tested as infected with COVID-19 in the past 14 days 15) Travelled to or from high risk COVID-19 areas in the past 14 days 16) Been in contact with a (suspected) COVID-infected person in the past 14 days

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2021
Enrollment:	40
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Approved WMO

Date:	03-02-2022
Application type:	First submission
Review commission:	Medical Research Ethics Committees United (MEC-U) Postbus 2500 3430 EM Nieuwegein 088 320 8784 info@mec-u.nl

Study registrations

Followed up by the following (possibly more current) registration

ID: 54413
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL9366
CCMO	NL77088.100.21
OMON	NL-OMON54413

Study results