Central sensitisation in patients with chronic low back pain radiating to the leg

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To determine the presence or absence of central sensitisation in patients with CLBPr and to determine the effect of segmental nerve interventions on central sensitisation.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)
Study type	Observational invasive

Summary

ID

NL-OMON50666

Source
ToetsingOnline

Brief title
CLaSSICO

Condition

- Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)
- Spinal cord and nerve root disorders

Synonym
Chronic low back pain radiating to the leg, Chronic lumbosacral radicular syndrome

Research involving
Human

Sponsors and support

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

Intervention

Keyword: central sensitisation, chronic, low back pain, radiating pain

Outcome measures

Primary outcome

* QST (Quantitative Sensory Testing)

* BSE (Bed Side Examination)

* CSI (Central Sensitization Inventory)

Secondary outcome

Other measurements (mostly part of the standardised care or CaU) are: Pain Catastrophising Scale (PCS), Pain Vigilance and Awareness Questionnaire (PVAQ), 36-Item Short Form Health Survey (SF-36), Pain Disability Index (PDI), Work Ability Index (WAI), STarT Back Screening Tool (SBST), Numeric Rating Scale for Pain (NRS) and drawing in standard leg images

Other study parameters

Demographic descriptive items: age, gender, weight, height, co-morbidities, medication and ethnic background.

Study description

Background summary

There is growing evidence for sensitisation in patients with chronic pain. Continuing nociceptive inputs can induce a reduction in threshold and an increase in responsiveness of peripheral nociceptors, i.e. peripheral sensitisation, which on itself may lead to a prolonged increase in excitability and synaptic efficacy of neurons in central nociceptive pathways, i.e. central sensitisation. Several methods are advocated to measure central sensitisation.

For example, quantitative sensory testing (QST) is a psychophysical method that objectively measures responses to calibrated graded innocuous or noxious stimuli and represents, in most respects, an extension of the routine standardised sensory measurements. Furthermore, central sensitisation can be assessed with the Central Sensitisation Inventory (CSI). For treatment of severe cases of chronic low back pain, patients are referred to multidisciplinary pain clinics for further assessment. If the diagnosis in patients with chronic low back pain radiating to the leg (CLBPr) is not clear despite extensive physical, neurological, orthopaedic and radiological examination, a precision diagnosis, such as diagnostic segmental nerve root block (dSNRB), has been advocated. After a positive dSNRB, possible interventions are therapeutic SNRB (tSNRB) or pulsed radiofrequency (pRF). The extent of central sensitisation in patients with CLBPr, its role in chronification and its interaction with diagnostic and therapeutical interventions are unknown up to now.
Therefore, the main questions of this study are: can we find signs of central sensitisation in patients with CLBPr? Can we quantify it? Do the interventions (tSNRB and pRF) normally applied in care as usual affect central sensitisation?

Study objective

To determine the presence or absence of central sensitisation in patients with CLBPr and to determine the effect of segmental nerve interventions on central sensitisation.

Study design

Study design
Observational study in 50 patients with chronic low back pain radiating to the leg (CLBPr) and 50 sex- and age-matched healthy control subjects.
Patients will be screened for this study at the Spine Center Groningen or at the UMCG Anesthesiology Pain Center (APC). Leg pain must be higher than back pain in those patients.
Patients will receive care as usual. Diagnostic and therapeutic SNRBs, as well as pRF, will be performed according to the standard procedures of the APC (see appendix 1 - Wortelblokkades: diagnostische, therapeutische en radiofrequente behandelingen op cervical, lag thoracaal, lumbaal en sacral niveau)
Healthy control subjects (colleagues, friends and friends of the patients) will also be screened for this study at the Spine Center Groningen or at the APC, but will not receive any diagnostic or therapeutic nerve block. They will undergo all the measurements (BSE, QST and questionnaires as described below).
Patients and healthy control subjects who fill the inclusion criteria will be given written information about the study. After a few days, a member of the research team will call the participant to ask whether they have any questions and want to participate. If they agree in joining the study, they will be asked to return the informed consent. Upon arrival of the informed consent,

participants will be invited to the hospital and receive the questionnaires that are relevant for the first visit (healthy controls will not receive the drawing pain area). They are asked to fill in these questionnaires before they come to their appointment in the hospital. Before each next visit, relevant questionnaires will be sent and participants are asked to fill them in the day before the appointment.
The intervention provided in this study is the same as the standard intervention provided at the APC and follows the guideline for segmental nerve root block (see appendix 1 for the detailed procedure). This treatment/intervention is routinely applied at the APC and is part of the Medisch Handboek Afdeling Anesthesiologie of the UMCG.
QST, CSI, PCS and PVAQ are not part of CaU, they are specifically included in this protocol for the purposes of this study. Together, these items take about 25-30 minutes to be performed.

Visit 1 = t1
At their first visit (t1), patients will undergo dSNRB. This procedure is part of CaU and will not be compensated. Healthy control subjects will not undergo dSNRB, but will pass through the measurements; they will be compensated (see item 11.6 - Incentives).
Before the block, we will assess: QST 1 and BSE. Relevant questionnaires that are assesed the day before are: CSI, NRS, PCS, PVAQ, DPA, SBST SF-36, PDI and WAI. During the block, we will assess: voltages of sensory and motor electrical nerve stimulation and mapping paresthesias (see local protocol for wortelblokkades - appendix 2). Within 2 hours after the dSNRB, we will apply the NRS back and NRS leg.
Some patients may undergo more than one dSNRB at various spinal levels, which will be performed about one week apart of each other (3 dSNRBs are the maximum). In case another diagnostic block is indicated, this t1 procedure will be repeated (and called t1a, t1b). Relevant questionnaires for these visits are the CSI and NRS scores.

In case of a pain reduction >= 50%, the patient is considered a *positive* and goes to the therapeutic intervention, about one week after the last dSNRB. The responsible physician will decide which intervention this patient will receive (part of CaU).
In case of a pain reduction < 50%, the patient is considered a *negative* and excluded from the study. This patient also goes to the therapeutic intervention, about one week after the last dSNRB. The responsible physician will decide which intervention this patient will receive (part of CaU).

Visit 2 = t2
One week after the dSNRB, the second visit takes place (t2). During this visit, patients will receive one intervention: tSNRB or pRF.
This procedure is part of CaU and patients will not be compensated.
Before the intervention, we will perform the following measurements: QST and

BSE. Relevant questionnaires that are assesed the day before are: CSI and NRS.

Visit 3 = t3
About four weeks after the intervention, the last visit will take place (t3).
The following measurements will be performed: QST, BSE, CSI, PCS, PVAQ, SBST, VAS back/leg, drawing pain area (for patients), SF-36, PDI and WAI.
QST, CSI and BSE will be measured 4 weeks later, because we are not interested in the acute pharmacologic nerve block agent effects, but in the late effects of CS.
This last visit is not part of CaU and the patients will be compensated if the appointment cannot be scheduled together with a regular visit (see item 11.6 - Incentives).
For a summary of the study design, see flowchart on page 17. The grey items are additional to care as usual.

Duration
Depending on the amount of dSNRBs performed, the duration of this study for the patient will take between 5 to 7 weeks.
Data collection will take 1 year.

Setting
UMCG Anaesthesiology Pain Centre, at Beatrixoord, in Haren.

Study burden and risks

QST and BSE are worldwide applied and considered safe techniques. Since one of the applied stimuli measures pain threshold and pain tolerance, a short-lasting experience of pain might be felt. Risk that a SAE will occur is negligible.
Benefit: for patients, participation may be considered more advantageous since the schedule of procedures planning is faster than normal.

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

Presence of chronic low back pain (> 3 months) with radiation to the leg
Leg pain > back pain
Physician must consider a minimum of 1 dSNRB, tSNRB or pRF as an appropriate treatment intervention;
Written informed consent
Age: 18 years or older

Exclusion criteria

Exclusion criteria for segmental nerve blocks (see our local protocols - appendix 2)
No or not sufficient understanding of Dutch language
Incapacity to follow instructions
Mental incompetence to provide informed consent
Pain in one (or more) sites where BSE and QST will be applied (except for the most painful point in the painful dermatome).

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-06-2018
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	20-11-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-02-2020

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL60439.042.17