STUDY PROTOCOL:

Efficacy of Pain Neuroscience Education plus Cognition-Targeted Exercise Therapy versus usual care evidence-based physiotherapy in chronic spinal pain: Protocol of a randomized clinical trial.

Objectives

1. Effect of a modern neuroscience approach on pain compared to usual care evidence-based physiotherapy
2. Effect of a modern neuroscience approach on indices of central pain processing (i.e. pressure pain thresholds (PPTs) and conditioned pain modulation) compared to usual care evidence-based physiotherapy
3. Effect of a modern neuroscience approach on functioning compared to usual care evidence-based physiotherapy
4. Effect of a modern neuroscience approach on brain gray matter structure compared to usual care evidence-based physiotherapy
5.

Design

A 12-month multi-center, triple-blind, randomized, controlled, parallel group trial. Patients with CSP (including low back and neck pain, failed back surgery and chronic whiplash associated disorders) will be enrolled in a structured 3-month rehabilitation program organized in University Hospital Brussels and Ghent University Hospital. More specifically, therapeutic pain neuroscience education combined with cognition-targeted exercise therapy will be compared to back/neck school and general exercises.

Treatment outcomes will be assessed at baseline, after 3 treatment sessions, post-treatment (at 3 months), at 6 months and 1 year follow-up (Figure 1). Following the go/no-go principle, however, the 1-year follow-up examination will not take place in case that treatment effects are no longer present at 6 months follow-up in none of the treatment arms.

Study population

This study will include 120 CSP patients. Patients will be recruited from the hospital, from primary care practices (medical doctors) and via adverts. Inclusion criteria are: Dutch speaking male and female adult (aged 18 – 65 years) patients seeking care for non-specific CSP (at least 3 days/week) for at least 3 months, not starting new treatments or medication and continuing usual care 6 weeks prior to and during study participation (to obtain a steady state). Patients will be excluded in case of: neuropathic pain, chronic widespread pain according to the 1990 ACR criteria, a history of back or neck surgery in the past 3 years, a lifetime history of specific back or neck surgery (e.g. surgery for spinal stenosis) or osteoporotic vertebral fractures, rheumatologic diseases, concomitant therapies (i.e., rehabilitation, alternative medicine or therapies), medical conditions or contra-indications for MRI, pregnancy in the last year before enrolment, and people living or working outside a 50km radius of the treatment locations. Study participants will be asked to refrain from analgesics 48 h prior to assessments, to abstain from caffeine, alcohol and nicotine

24 h prior to assessment, and not to undertake physical exercise (>3 metabolic equivalents) in the 3 days before assessment.

Randomization

Participants will be randomized to either control or experimental group (1:1 ratio) using a stratified permuted block allocation with stratification factors being treatment center (Brussels or Ghent), gender (male or female) and dominant pain location (low back or neck) and with a block size of four. Randomization will be done by an independent investigator at the Biostatistics Unit (Ghent University) using the SAS version 9.4 package. The randomization schedule will be known only to 1 investigator who is not involved in patient recruitment.

Blinding

The randomization will be concealed from patients and the other investigators involved in patient assessments and analyses.

Outcome measures

1. Primary outcome measures
    a. A Numerical Rating Scale (NRS) for pain ranging from 0 = “no pain” to 10 = “the worst pain imaginable” (“How would you rate your spinal pain, on average, over the last three days?”)
    b. The Central Sensitization Inventory (CSI) assessing current health symptoms indicative of central sensitization in 25 statements; on a Likert scale from 0 (never) to 4 (always), resulting in a total possible score of 100; higher scores are associated with a higher degree of self-reported symptomology
    c. The Short Form Health Survey – 36 item (SF-36) will be used to assess self-reported metal and physical health.
    d. Pressure Pain Thresholds will be assessed using a digital Wagner algometer (Wagner Instruments, Greenwich, CT). at the symptomatic levels (the upper trapezius muscle midway between C7 and the tip of the acromion and 5 cm lateral of the spinous process of L3) and at remote sites (quadriceps muscle and the web between thumb and index finger). The pressure will be increased at a constant rate of 1 kg/m2/s. PPTs will be tested unilaterally at the most painful side will be assessed unless the pain is evenly distributed on both sides. Then, the dominant side will be investigated. At each of the selected measuring points, the threshold will be determined as the mean of 2 consecutive (30 s in between) measurements.
    e. Conditioned Pain Modulation will evaluate the efficacy of the descending inhibitory modulation of pain (i.e. conditioned pain modulation) using the immersion of the hand in a cold water bath (12 degrees Celsius) for 2 minutes. Before and during submersion, the pressure pain thresholds will be measured on several body sites using pressure algometry (see above). Subjects will be asked to rate the perceived pain intensity on an 11-point visual numeric rating scale.
    f. The Pain Disability Index will be used to rate perceived disability due to pain.

2. Secondary outcome measures
    a. Brain gray matter structure will be measured using high-resolution magnetic resonance imaging (Siemens medical solutions, Erlangen, Germany). A T1-weighted structural MRI will be acquired by using a 3D-FLASH sequence (repetition time 2250 ms, echo time 4.18 ms, flip angle 9°, field of view 256 × 256; 176 slices), acquisition time 05'14". Regional gray matter density will be assessed with voxel-based morphometry that allows for applying voxelwise statistics to detect regional differences in gray matter volumes. Preprocessing will be performed using Freesurfer and will involve spatial normalization, gray matter segmentation, and 10 mm spatial smoothing with a Gaussian kernel.
    b. Motor control:
        i. Postural steadiness will be characterized by postural sway features as measured by an AccuGait portable forceplate (50 cm × 50 cm) (Advanced Medical Technology, Inc. Watertown, MA) during bipedal standing with eyes closed on a firm surface.
        ii. For the assessment of habitual standing posture in the sagittal plane, the orientation of gross body segments with respect to the vertical will be quantified using posthoc analyses of digitized photographs of participants.
        iii. Range of motion of the cervical spine (flexion, extension, lateral flexion) will be measured in neck pain patients (seated position) using the Acumar™ digital inclinometer (Model ACU 360, Lafayette Instrument Company, Lafayette, IN) that is placed on the vertex of the head through T1.
        iv. Lumbar lateral flexion will be measured using the Acumar™ digital inclinometer (see above) placed on T12 through S1.
        v. Proprioception will be determined by evaluating the position-reposition accuracy of the spine. In neck pain patients, repositioning will be assessed by the cervicocephalic relocation test to the neutral head position with eyes closed.
        vi. Neuromuscular control will be assessed as the patients' ability to perform the skill of activation of specific, deep stabilizing muscles for which there is scientific evidence that they play a crucial role in spinal stability. In neck pain patients, the contraction of the deep neck flexors will be evaluated through the craniocervical flexion test and the lower and middle trapezius muscles will be assessed via the scapular holding test/scapula setting. In low back pain patients, multifidus and transverse abdominis contraction will be evaluated in prone and supine (drawing-in action), respectively.
    c. Muscle properties:
        i. isometric muscle strength will be measures using a hand-held dynamometer. In neck pain patients, the testing procedure will consist of seated isometric strength measures for neck flexion, extension and side bending (left and right). In patients with dominant low back pain, trunk flexor and extensor muscle strength will be evaluated.

ii. Muscle endurance will be assessed using isometric tests, i.e. patients will be instructed to maintain an imposed posture as long as possible. In neck pain patients, endurance of the neck flexors will be evaluated with the deep neck flexor endurance test. Low back pain patients will perform a trunk flexor and extensor endurance test.

d. Psychosocial correlates
    i. The Pain Catastrophizing Scale will be included to assess catastrophic thinking about pain. It consists of 13 items describing different thoughts and feelings that individuals may have when experiencing pain.
    ii. The Pain Vigilance and Awareness Questionnaire will be used to investigate patients' attention to pain.
    iii. The Tampa Scale for Kinesiophobia (TSK) is a 17-item questionnaire that will be used to measure the fear of (re) injury due to movement
    iv. The Illness Perception Questionnaire-Revised consists of 3 domains and will be used to measure patients' illness perceptions.

Interventions

Experimental intervention

Patients will participate in an initial group session (maximum 6 persons/group) of pain neuroscience education that will last about 1 hour and includes the possibility for patients to ask questions during the session. After this first session, the patient is sent home with an information leaflet as refresher and for informing the significant other. Furthermore, the patient is asked to complete the "feared activity form", a clinical tool that assesses which activities could worsen complaints and cause damage according to the patient. The next session is an online module performed at home. The content is comparable, but also the role of stress is explained. The online module consists of movies, interrupted by online questioning. The last session is a 30'-individual session addressing specific questions and translating the content to the daily life of the patient. Perceptions are questioned again, goals are discussed and therapeutic alliance is checked.

The content, format and pictures of the educational sessions are based on the book 'Explain Pain' and 'Pijneducatie een praktische handleiding voor (para)medici'. We will present the educational information verbally (explanation by the therapist) and visually (summaries, pictures, metaphors and diagrams on computer and paper). A more detailed description on the organization of the education is also provided in our masterclass guideline.

The education covers the physiology of the nervous system in general and of the pain system in particular.

Topics addressed during the educational sessions will include the characteristics of acute versus chronic pain; how pain becomes chronic (plasticity of the nervous system, modulation, modification, central sensitization, etc.); potential sustaining factors of central sensitization like emotions, stress, pain cognitions, and pain behaviour; etc. Level A evidence supports the use of pain neuroscience education for chronic musculoskeletal disorders in reducing pain and improving patient knowledge of pain, improving function and lowering disability, reducing psychosocial factors, enhancing movement, and minimizing healthcare utilization.

Once adaptive beliefs are acquired regarding CSP a further time-contingent, cognition-targeted approach to daily (physical) activity and exercise therapy.
Cognition-targeted exercise therapy comprises two main phases: cognition-targeted motor control training and cognition-targeted dynamic and functional exercises.
Important is the time-contingent approach, the continuous targeting of cognitions and perceptions about their problems and the outcome of each exercise and the gradual progression to more feared movements and activities. The specific content of the exercises is tailored based on the "feared activity form".

PHASE A: COGNITION-TARGETED MOTOR CONTROL TRAINING
This phase consists of a proprioception, coordination, and sensorimotor control training program based on the principles and ideas of researchers and clinicians such as, Sahrmann, Comerford and Mottram, and Richardson and Jull, adapted to comply with modern pain neuroscience and thus providing the CSP patient a cognition-targeted approach. In neck pain patients, this phase of the exercise will involve retraining of the deep cervical flexors/extensors and scapular muscles, whereas retraining of the deep muscles surrounding the lumbopelvic region (e.g., multifidus, transversus abdominis, psoas, pelvic floor muscles) will be performed in patients with low back pain.
Crucial again is the method of delivering these types of exercises to the patient within the modern neuroscience framework, which will be mostly depending on communication techniques that should be aligned with the content of the pain neuroscience education: exercise as brain therapy rather than a modality to correct biomechanical deficits.

PHASE B: COGNITION-TARGETED DYNAMIC AND FUNCTIONAL EXERCISES
The purpose of this phase is to confront the patient with movements and activities that are feared, avoided and/or painful. During the physiotherapy sessions, home exercises and in daily life it is crucial to avoid all 'safety behaviour' and to focus on normal and functional movements. This phase involves increasing the complexity of exercises. Progression is targeted and developed towards those movements and activities the patient is fearful of (e.g. bending forward in chronic low back pain, or neck extension in chronic neck pain patients).
All exercises, movements and activities used in the cognition-targeted exercise training can be implemented in the home program. Throughout the cognition-targeted motor control training program, patients' cognitions and perceptions about their problem and about exercises will be addressed.

Control intervention
The control group will receive traditional back/ neck school, including back care education and general exercises. Back care education will cover anatomy and biomechanics of the spine, common causes of spinal pain, the load-tolerance model, nociceptive pain processing, and ergonomic counseling based on the inherent postural strain associated with various postures and daily activities (including standing, sitting, and lifting). As such, the education sessions will prepare the patients for a symptom-contingent, biomedical approach to daily (physical) activity and exercise therapy. In session 4, the general exercise therapy will be started with specific emphasis on treating dysfunctional muscles and joints. Different therapeutic goals will be pursued (e.g. microcirculation, mobility, endurance, strength) depending on what emerges from the clinical reasoning as the most dominant peripheral

dysfunction. The program will also involve aerobic fitness improving exercises. The progressive exercise program will mainly entail an increase in exercise intensity, and an evolution towards functional activities and more physically demanding tasks while keeping the spine in physiological neutral positions to minimize strain imposed upon the spinal structures. All exercises will be performed in a symptom-contingent way.

Sample size calculation

Sample size was calculated using G*Power software based on partial eta squared = 0.02, alpha = .05 and a power of 0.80; and accounted for F tests and 30% loss to follow-up after 1 year, resulting in a total ample size of 117 individuals.

Ethics

This trial will be conducted in compliance with the Declaration of Helsinki (1964 and amendments) and Good Clinical Practices. Patients will give their written informed consent prior to the start of any study-related procedure. Approval to conduct this study was granted by the Ethics Committee of the Ghent University Hospital and the University Hospital Brussels.

Statistical analysis plan of the study 'A Randomized Trial of Pain Neuroscience Education Combined With Cognition-targeted Motor Control Training'

A. Original statistical analysis:

1. Data Source:

Data are derived from people with chronic spinal pain that participated in this randomized controlled trial. Participants were evaluated at baseline, and after 3, 6 and 12 months. Outcome measures were related to pain, disability, brain gray matter morphology, pain cognitions, and motor control. All participants received 18 sessions of physiotherapy (either the modern neuroscience approach or usual care physiotherapy)

2. Analysis objectives

To investigate the effectiveness of the modern neuroscience approach compared to usual care physiotherapy regarding the above-mentioned outcome measures

3. Population

People with chronic spinal pain

4. Endpoints

We are interested to see the change in the outcome measures from baseline to each follow-up measurement point (3 months, 6 months and 12 months)

5. Covariates

In these analyses, treatment center, dominant pain location and gender will be entered as covariates.

6. Handling of missing data

Intention-to-treat analysis using first-observation-carried-forward

7. Statistical methodology

7.1 Statistical procedures

Baseline data will be analyzed in order to determine descriptive statistics for the different outcome measures for the complete CSP group. Comparability of the groups before the intervention will be studied with the Fisher exact test and independent samples t test. Possible changes in the outcome measures in response to the intervention will be examined between the two groups by using repeated measures analysis of variance with intervention serving as the between-subjects factor and time as the within-subjects factor.

7.2 Measures to adjust for confounders, heterogeneity, etc.

The assumption of homogeneity and sphericity will be checked by Levene's and Mauchly's test respectively. When the assumption of sphericity is violated, Greenhouse-Geisser corrections will be used. Treatment center, dominant pain location and gender will be entered as covariates.

B. Actual statistical analysis: (changes compared to the original statistical analysis are highlighted in red)

1. Data Source:

Data are derived from people with chronic spinal pain that participated in this randomized controlled trial. Participants were evaluated at baseline, and after 3, 6 and 12 months. Outcome measures were related to pain, disability, brain gray matter

morphology, pain cognitions, and motor control. All participants received 18 sessions of physiotherapy (either the modern neuroscience approach or usual care physiotherapy)

2. Analysis objectives

To investigate the effectiveness of the modern neuroscience approach compared to usual ware physiotherapy regarding the above-mentioned outcome measures

3. Population

People with chronic spinal pain

4. Endpoints

We are interested to see the change in the outcome measures from baseline to each follow-up measurement point (3 months, 6 months and 12 months)

5. Covariates

In the final design of the study, a stratified randomization was performed, based on treatment center, dominant pain location, gender. Therefore, no covariates were entered in the final analysis.

6. Handling of missing data

The final analysis was carried out using linear mixed models. Linear mixed models can make use of all the available data in the estimation of model parameters due to a flexible handling of the time predictor. For instance, data of a subject with only a baseline assessment can be included in an analysis and contribute to the estimation of model parameters.

7. Statistical methodology

7.1 Statistical procedures

All data were analysed using SPSS 24.0. Measurements of PPT and CPM at the primary body site (lower back and trapezius muscle) were taken together using body site as a covariate in the model. For each variable, the percentage of change compared to baseline was calculated. Effect sizes of the mean group differences were calculated as Cohen's D. To assess the difference between groups in response to treatment, a random-intercept linear mixed models analysis, using Bonferroni Post-hoc analyses, was applied using an unstructured covariance matrix. The model included treatment, time, and treatment*time as fixed effects together with a random intercept for each patient.

7.2 Measures to adjust for confounders, heterogeneity, etc.

Covariates were not used in the final analyses, since a stratified randomization was performed.

<u>C. Explanation for the changes made to the original statistical analysis:</u>

By stratifying based on treatment location, dominant pain location, and gender, we were able to conduct an analysis without including covariates. Linear mixed models was used as a final analysis method for its handling of missing data. Using this method, we did not have to manipulate the data prior to the analysis, which provided a better way of handling these longitudinal data.

Universitair Ziekenhuis Brussel
Vrije Universiteit Brussel

UNIVERSITEIT GENT

REQUEST FOR ADVICE OF THE ETHICS COMMITTEE

REGARDING A PROJECT FOR AN EXPERIMENT IN HUMANS

INTERVENTIONAL STUDY

Please fill out

Head researcher:

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Head of the department :

Prof. Dr. Peter Vaes (VUB)

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Jo Nijs

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0496462572

TITLE OF THE STUDY PROTOCOL :

A modern neuroscience approach to chronic spinal pain:

Pain Neuroscience education combined cognitive motor control training

PROTOCOL NUMBER : **Date Protocol :** 13-12-2013

EUDRACTNR (if applicable) : Not applicable

1. General data

- Is this a sponsored study?
  - ☐ Yes
    Who is the sponsor?
  - ☒ NO
- Is this an academical study?

☒ Yes (IWT-TBM) ☐ NO

Is this a master thesis?

☐ YES ☒ NO

Name of the student?

- Is this study
  - ☐ monocentric
  - ☒ multicentric
- Will minors participate in this study?
  - ☐ YES ☒ NO
- Will only Dutch speaking persons participate?
  - ☒ YES ☐ NO, other :
- Do you have an insurance for this experiment?
  - ☒ YES
  - ☐ NO

    If not, why not?
- Which is the planned start and end date? Februari 2014 tot November 2017

2. Committee of Medical Ethics (CME)

- Is the CME of the University Hospital Brussels and the Vrije Universiteit the CENTRAL CME?
  - ☒ YES

    If so, are there locale CME's involved? Which? YES

    CME University Hospital Ghent

    De Pintelaan 185, 9000 Gent

    Ethisch.comite@ugent.be

    Tel: +32 9 332 33 36 / +32 9 332 68 54 / +32 9 332 26 88
  - ☐ NO

    If not, which is the central CME?
- Was the study protocol already approved by this CME?
  - ☐ YES

    If so, please provide a copy of this approval.
  - ☒ NO

3. Nature of the study

- Will additional (medical) actions be performed specifically for this study?
  - ☒ YES

☐ NO

If not, please use the questionnaire for non-interventional studies

- What is the nature of the experiment?

☐ Fase 1	☐ Bioequivalence or pharmacokinetics
☐ Fase 2	☐ Farmaco-economy
☐ Fase 3	☐ Farmaco-vigilance
☐ Fase 4	
☒ Other: Therapeutic	

- Aim of the experiment (in some sentences):

  The main scientific aim of this study is to investigate the effectiveness of a modern neuroscience approach in patients with chronic spinal pain (experimental group) compared to traditional, evidence-based physiotherapy. The primary outcome measures include pain (NRS, CSI, PPTs) and disability (PDI and SF36).

- Summary of the project (in some sentences):

  120 Dutch-speaking patients with chronic spinal pain (CSP) will be recruted through firstline healthcare, the department of medical supervision at the VUB and the UGent, companies near Ghent and Brussels, and the media. These patients will be randomised into the experimental and control group. The study design entails a randomised, trippleblind controlled trial.

  Short description of the outcome measures:

  - **Baseline evaluation of 120 CSP patients: online questionnaires on pain (inclusive of symptoms of central sensitization), the impact of pain on daily functioning, and painrelated psychological variables (pain catastrophizing, pain attention, fear of movement, illness perceptions. Also, pressure pain thresholds and conditioned pain modulation will be determined using pressure algometry (combined with a cold water bath for conditioned pain modulation measurement). Body position will be evaluated using 2D digital photography with post-hoc angel measurements on the photos. Balance will be determined using the accugait and muscle properties and motor control will be evaluated using clinical tests. Last, MRI will be used to evaluate gray matter volume and the white matter integrity.**

    Filling out the online questionnaires will take about 30 minutes. During a first test moment, all other outcome measures will be tested (duration: max 1h), except for the MRI, which will be done during a second test moment (duration: max 1.5h). After three therapy sessions, these will be a small re-evaluation: PCS, PVAQ, TSK, IPR and PDI (online questionnaires). Also, the Neurophysiology of pain questionnaire will be filled out online: duration 30 min.

- In the month after the last therapy session (i.e. session 18, 3 months after baseline assessment) the short-term treatment effects will be studied: all baseline tests are repeated.
  6 months after baseline: all online questionnaires are filled out again
- 1 year after baseline treatment effects at long-term are investigated: all tests are re-evaluated.

All experimental tests are performed at the University Hospital of Ghent, except for the online questionnaires.

Short description of the interventions:

Control intervention (60 patients): 18 physiotherapy sessions: usual, evidence-based physiotherapy for chronic spinal pain, including beck/neck school and general exercises.

Experimental group (60 patients): 18 physiotherapy sessions: combination of pain neuroscience education and cognition-targeted motor control training.

Therapy sessions will take place in the University Hospitals of Ghent or Brussels, depending on the preference of the patient. All sessions will be deliverend within three months.

Outcome assessors will be blinded for the randomization sequence. Other researchers will deliver the treatment. The participants will not be aware of the treatment group that they are in. The statistical analyses will be performed by a statistician blinded for the randomization sequence.

- Will a chemical or biologically active substance be administered?
  - ☐ YES
    If so, how?
    Name and origin of the substance:
  - ☒ NO
- Will radioisotopes be used?
  - ☐ YES
    If so, which?
    Please calculate and mention the radiation risk.
  - ☒ NO
- Will radiographic images be taken?
  - ☐ YES
    Please calculate and mention the radiation risk.
  - ☒ NO
- If a new or rare substance is used, did the investigator taken knowledge on the toxicological and pharmacological file of the substance?
  - ☐ YES

Provide references – copies – prints

☒ NO

- Will genetic research be performed in this study?
  - ☐ YES
  - ☒ NO

4. Participants

- Choice of participants:
  - Does it involve health participants?
    - ☐ YES
    - ☒ NO
  - Sick participants? ?
    - ☒ YES

      If so, which condition? **Chronic spinal pain, i.e. chronic low back pain, chronic whiplash associated disorders, chronic non-traumatic neck pain, and nonspecific failed back surgery**
    - ☐ NO
  - Amoun of participants : **120**

    Age : **18-65**

    Sex : **men and women**

- In case of healthy participants:
  - Recrutement? Where?

    /
  - Will their legally required written permission be obtained after clear and objective information of the aims of the experiment?

    ☐ YES

    Please provide a copy of the informed consent.

    ☐ NO

    If not, why?

- In case of sick participants:
  - Recrutement? Where?

    ☐ University Hospital Brussels

    ☒ Others: **through firstline healthcare, the department of medical supervision at the VUB and the UGent, companies near Ghent and Brussels, and the media.**

- Will their legally required written permission be obtained after clear and objective information of the aims of the experiment?

  ☒ YES

  Please provide a copy of the informed consent.

  ☐ NO

  If not, why?

In case of minors or incapacitated adults:

- Recrutement? Where? /

  ☐ University Hospital Brussels

  ☐ Others

- Will their legally required written permission be obtained from their legal representative after clear and objective information of the aims of the experiment?

  ☐ YES

  Please provide a copy of the informed consent.

  ☐ NO

  If not, why?

- Will a legally required written permission be obtained from the minor after clear and objective information of the aims of the experiment?

  ☐ YES

  Please provide a copy of the informed consent.

  ☐ NO

  If not, why?

- Will the participtants receive a remuneration?

  ☐ YES

  If so, which?

  ☒ NO

- Where will the experiment take place?

  University Hospitals of Brussels and Ghent

- Will the participants be under constant medical supervision during the experiment?

  ☐ YES

  ☒ NO

  - Will this supervision, if necessary, be ensured during the subsequent hours?

    ☐ YES

    ☒ NO

- When the participant returns to his/her home in the hours after the experiment, can he/she contact the researcher or a doctor if necessary?

  ☒ YES, the researcher

  ☐ NO

- Is this experiment part of a diagnostic or therapeutic framework with results that can be used in other patients soon?

  ☒ YES

  ☐ NO

- Is the experiment part of research of which the diagnostic or therapeutic implications are not directly visible, but of which results will later lead to diagnostic or therapeutic implications of a better knowledge of physiological mechanisms?

  ☐ YES

  ☒ NO

- Has such a study been conducted before?

  ☐ Either in its entirety:

  ☒ Either partly:

  1 case study and 2 small monocentric RCTs support the clinical effecitveness of the modern neuroscience approach for chronic spinal pain (Moseley GL, 2002, 2003, 2005). However, these 3 pilot studies are all from one and the same Australian research group and were conducted in the same centre. Only 30 patients with chronic low back pain were treated and one year follow-up results were present for less than 20 patients.

  The current study is a multicentric, large RCT focussing on CSP patients and not only on low back pain patients.

- Do you expect any complications or adverse effects in this experiment?

  ☐ YES

  If so, which?

  ☒ NO

WE STATE NOT TO USE ANY RIZIV-SUPPLIES TO FINANCIALY SUPPORT THIS EXPERIMENT. WE ACCOUNT FOR FULL RESPONSBILITY OF THE EPERIMENT THAT IS DESCRIBED ABOVE AND WE CONFIRM THAT THE PROVIDED INFORMATION IS TRUTHFUL, TAKING INTO ACCOUNT THE CURENT KNOWLEDGE.

RESEARCHER(S)
Seen and approved,

Title, name and given name

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Prof. Dr. Lieven DANNEELS
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