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Treatment of complex regional pain syndrome (CRPS) with sensory-motor adaptation

Submission date	**Recruitment status**	[X] Prospectively registered
24/03/2017	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/03/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
22/10/2021	Signs and Symptoms	

Plain English summary of protocol

Background and study aims
Complex Regional Pain Syndrome (CRPS) is a distressing condition that can develop after damage to a limb. People with CRPS experience continuous pain that is disproportionate to the severity of injury, as well as swelling and movement difficulties in the affected part of the body. Patients also report abnormal perception of the size and shape of their painful limb, and recently it has been found that patients with CRPS show changes in how much attention they pay to their affected limb and surrounding space. These changes in limb perception and attention resemble symptoms that can arise after brain damage, for example due to stroke. Considering these and other findings, it has been suggested that pain and other physical symptoms of CRPS may result from errors in brain signals about the shape and location of the affected body part. If this is the case, it might be possible to treat CRPS with methods that are thought to restore normal body perception and attention. This study is looking at the effects of a new type of treatment that targets those changes, called sensory-motor adaptation. This method can reduce problems with attention in stroke patients, and initial results suggest that it also reduces pain in CRPS patients. However, sensory-motor adaptation has only been tested in small numbers of CRPS patients so far, and never in a well-controlled trial. The aim of this study is to test the efficacy of this treatment on people with CRPS.

Who can participate?
Adults who have CRPS which has been affecting an arm for at least three months, and healthy adults of the same age.

What does the study involve?
Participants with CRPS are randomly allocated to take part in two weeks of either sensory-motor adaptation treatment or control (dummy) treatment at the participant’s home. It involves performing simple movements with the affected arm while wearing goggles that distort vision. Both the sensory-motor adaptation treatment and control treatment involve goggles that distort vision in some way, therefore it isn't possible for participants to tell which treatment group they have been allocated to. Aside from undergoing sensory-motor adaptation treatment or control treatment, participants are not required to alter their treatment regimen during the study (i.e. they can continue taking their medication and/or performing physiotherapy as normal). In order to determine whether the sensory-motor adaptation relieves CRPS symptoms

more than the control treatment, participants' symptoms are examined in four research visits spread over 11 weeks. Two visits take place before the treatment period (weeks 1 and 4), and two visits take place after the treatment period (weeks 7 and 11). Research visits involve filling out questionnaires, undergoing physical assessments and completing computer-based tasks. Participants are also asked to fill out follow-up questionnaires to be sent to them and returned by mail on two further occasions after the last research visit (weeks 19 and 31).
Healthy volunteers are invited to one of the research centres for a single visit at which they complete questionnaires, undergo physical assessments and complete computer-based tasks so that the results can be compared to those with CRPS.

What are the possible benefits and risks of participating?
Participants with CRPS who receive the treatment may directly benefit from reduction in pain and other symptoms. However, it is important to note that this study aims to investigate the effectiveness of a novel treatment, and it is possible that participants might experience little or no symptoms reduction. Should the treatment prove to be effective, all participants will have an opportunity to undergo real sensory-motor adaptation after the trial is completed. In addition, all participants benefit from financial compensation for taking part. There are no notable risks involved with participating.

Where is the study run from?
1. University of Bath (UK)
2. Oxford University Hospitals NHS Foundation Trust (UK)
3. University of Oxford (UK)
4. University of Exeter (UK)
5. University of Liverpool (UK) (as of 05/10/2018)

When is study starting and how long is it expected to run for?
October 2016 to September 2019

Who is funding the study?
Reflex Sympathetic Dystrophy Syndrome Association (USA)

Who is the main contact?
1. Ms Monika Halicka (public and scientific)
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2. Dr Janet Bultitude (public and scientific)
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Pain Reduction by Inducing Sensory-Motor Adaptation in Complex Regional Pain Syndrome (CRPS): a double-blind randomized control trial

Acronym
CRPS PRISMA

Study objectives
1. There will be greater reduction in Complex Regional Pain Syndrome (CRPS) symptoms in the patients undergoing sensory-motor adaptation treatment, compared to the patients receiving control treatment
2. Baseline abnormalities in perception of and attention to the affected limb and surrounding space in patients with CRPS (as compared to the perception and attention of healthy participants) will correlate with the severity of pre-treatment clinical symptoms

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Health Service Oxfordshire Research Ethics Committee A, 11/12/2012, ref: 12/SC/0557

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Complex Regional Pain Syndrome (CRPS)

Interventions
Eligible patients will be allocated to 1 of 2 treatment groups: sensory-motor adaptation treatment group or control treatment group, by method of randomization with stratification to minimize baseline group differences. Group allocation will be blocked in three consecutive blocks of ten participants and one final block of twelve participants. The first four patients in each block will be allocated by means of a coin toss performed by a researcher who is not involved in assessing the symptoms of the participants (heads = sensory-motor adaptation treatment, tails = control treatment). Each subsequent participant in each block will be allocated using a minimization procedure, matching the two groups for gender balance, age, baseline pain, CRPS chronicity and other demographic characteristics. If a participant is allocated to a group and commences sensory-motor adaptation/control treatment, but is unable to complete the study, then the minimization procedure for future participant allocation will be adjusted to ensure equal numbers in the two groups. Additional participants who are recruited to replace such withdrawals will be treated as a new participant in the final allocation block (e.g. if one patient withdraws, the final allocation block will have 13 participants, if two patients withdraw, the final allocation block will have 14 participants, etc.).

Updated 14/07/2017: change in allocation procedure:
Instead of the minimization procedure described above, the participants will be allocated in the following way. At the time of this update, two patients have been tested for baseline data (week 1/session 1), but have not been allocated to treatment groups. They, and all subsequent patients, will be allocated according to the updated procedure below.
The final minimization procedure is as follows: Eligible patients will be allocated to 1 of 2 treatment groups: sensory-motor adaptation treatment group or control treatment group, by method of randomization with stratification to minimize baseline group differences. Group allocation will be performed using MINIM programme (available from https://www-users.york.ac.uk/~mb55/guide/minim.htm) by a researcher who is not involved in assessing the symptoms of the participants. Minimization programme automatically controls for stratification factors. The stratification factors of sex, age, dominant hand, affected limb, CRPS duration, presence of other non-CRPS pain and presence of CPRS in other body parts will receive weight = 1, while the stratifications of baseline pain intensity and CRPS severity score will receive weight = 2. If a participant is allocated to a group and commences sensory-motor adaptation/control treatment, but is unable to complete the study, their data will be removed from the minimization procedure and an additional participant will be recruited for the trial to ensure equal numbers in the two groups.

Intervention: Sensory-motor adaptation is a type of sensory-motor training, often used to study how people coordinate their movements with what they see and feel, and to treat problems with perception and attention that can follow a stroke. The form of sensory-motor adaptation

used here uses goggles fitted with lenses which distort vision, and involves a simple pointing-to-target task. Participants will perform this sensory-motor training twice-daily for two weeks in their own home in a self-guided fashion. While wearing the goggles, a pointing task to visual targets placed within reaching distance will be carried out with the affected hand. Participants will perform a total of 50 rapid pointing movements in a single training session, taking less than 5 minutes per session.

Control: The control treatment involves performing the same arm movements as the sensory-motor training while wearing goggles that distort vision but will not induce sensory-motor adaptation.

During the training sessions, participants in both groups will be wearing goggles fitted with lenses that distort vision in slightly different ways. Goggles used by the sensory-motor adaptation treatment group are thought to reduce pain by inducing sensory-motor adaptation. The goggles used by control treatment group also alter the vision but are not thought to reduce pain.

Outcome measurements will be carried out blind to group allocation. The two primary outcome measures are current self-reported pain intensity measured using item 6 of the Brief Pain Inventory and CRPS diagnosis and symptoms severity measured using Budapest research criteria. The timepoints of primary interest are: week 4 / session 2 (1-5 days after randomization; before commencing the treatment) and week 7 / session 3 (after completing the treatment). The researcher collecting the data will be unblinded as to the group allocations of the participants once the last participant has passed the primary endpoint (week 11 / session 4), as there are no further research session in which symptoms will be assessed by this researcher. Follow-up measurements at weeks 19 and 31 will be carried out via postal questionnaires only and scored by another researcher who is blind to the group allocations. Each participant will be unblinded once they have completed the study (week 31).

Healthy volunteers are invited to one of the research centres for a single research visit lasting up to 4 hours. During this visit, they will complete analogous questionnaires (Bath CRPS Body Perception Disturbance Scale, Profile of Mood States, Edinburgh Handedness Inventory, computer-based tasks (Landmark, Greyscales, Directional hypokinesia, Hand laterality judgement, visual Temporal Order Judgement and Mental number bisection tasks) and undergo the same clinical assessment (Budapest criteria assessment, Quantitative Sensory Testing, Two-point discrimination test) as people with CRPS.

Intervention Type
Behavioural

Primary outcome(s)
1. Current self-reported pain intensity measured using item 6 of the Brief Pain Inventory (short form) at weeks 4 (immediately before the commencement of the treatment period) and 7 (immediately after the end of the treatment period)
2. CRPS diagnosis and symptoms severity measured using Budapest research criteria at weeks 4 and 7

Key secondary outcome(s))
Pain:
1. Current self-reported pain intensity in weeks 1, 11, 19 and 31
2. Worst and least pain over the last 24 hours measured using items 3 and 4 of the Brief Pain

Inventory (short form) at weeks 1, 4, 7, 11, 19 and 31
3. Neuropathic component of pain measured using Pain Detect Questionnaire at weeks 1, 4, 7, 11, 19 and 31

Physical/clinical signs:
1. CRPS diagnosis and symptoms severity measured using Budapest research criteria at weeks 1, 11, 19 and 31
2. Mechanical detection and pain thresholds and dynamic mechanical allodynia measured using selected tests from Quantitative Sensory Testing (QST) at weeks 1, 4, 7 and 11
3. Tactile discrimination threshold measured using Two-Point Discrimination test (2PD) at weeks 1, 4, 7 and 11
4. Limb temperature asymmetry (unaffected-minus-affected hand) measured using infrared thermometer at weeks 1, 4 ,7 and 11

Limb perception:
1. Presence, nature and extent of body perception disturbance measured using Bath CRPS Body Perception Disturbance scale (BPD) at weeks 1, 4, 7, 11, 19 and 31
2. Body representation disturbance measured using Hand Laterality Recognition task at weeks 1, 4, 7 and 11

Attention to the affected limb and surrounding space:
1. Visual spatial attention measured using Landmark task, Greyscales task and Temporal Order Judgement task (TOJ) at weeks 1, 4, 7 and 11
2. Motor spatial performance measured using Directional Hypokinesia task at weeks 1, 4, 7 and 11
3. Mental representation of space measured using Mental Number Bisection task at weeks 1, 4, 7 and 11

The following measures will also be recorded to check that the groups are matched on extraneous factors that are thought to influence pain, attention, and treatment effects (these measures may also be included as covariates in our analyses):
1. Mood measured using the Profile of Mood States (short form) at weeks 1, 4, 7, 11, 19 and 31
2. Levels of optimism and pessimism measured using Revised Life Orientation Test (LOTR) at week 1
3. Patient-centred expectations and criteria for success regarding treatment in chronic pain measured using Patient-Centred Outcomes Questionnaire (PCOQ) at week 1

Updated 23/10/2017: Correction to the name of one of the secondary outcome measures:
1. Mood measured using the Profile of Mood States at weeks 1, 4, 7, 11, 19 and 31

Other measures:
1. Fear of movement due to pain measured using Tampa Scale for Kinesiophobia at weeks 1, 4, 7, 11, 19 and 31
2. Patient's impression of how much their symptoms have changed as a result of treatment measured using Patient's Global Impression of Change questionnaire (PGIC) at weeks 7, 11, 19 and 31
3. Pain, range of movement and symptoms interference with daily activities measured using 0-10 Numeric Rating Scales in patient logbook, daily from week 1 to 11. These measures will allow tracking of the time-course of any change in these three measures during the four-week baseline period, treatment period, and the first four weeks of the post-treatment period.

Completion date

30/09/2019

Eligibility

Key inclusion criteria
Healthy volunteers:
1. Willing and able to give informed consent for participation in the study
2. Aged 18-80
3. Healthy and without current pain

Patients:
1. Willing and able to give informed consent for participation in the study
2. Aged 18-80
3. Diagnosed with CRPS type I of minimum three months chronicity, primarily affecting one upper limb, based on Budapest research criteria that will be assessed on the first research visit
4. Reporting current pain intensity ≥2 on a 0-10 Numeric Rating Scale on the first and second research visit (as of 05/10/2018)

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Total final enrolment
76

Key exclusion criteria
All participants:
1. A history of neurological disorder (e.g. a stroke, neurodegenerative disease, traumatic brain injury)
2. Classified as legally blind
3. Lacking sufficient English language ability to provide informed consent

Patients:
1. CRPS affecting both sides of the body, or confirmed presence of nerve damage
2. Dystonia or any other physical limitation that is severe enough to prevent movement of the affected limb

Decisions whether or not to exclude a participant suffering from a psychiatric disorder will be made on a case-by-case basis, as patients with CRPS often present with co-morbid depression and anxiety.

Date of first enrolment
31/03/2017

Date of final enrolment
01/03/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Bath
Claverton Down Road
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Study participating centre
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Sponsor information

Organisation
University of Bath

ROR
https://ror.org/002h8g185

Funder(s)

Funder type
Charity

Funder Name
Reflex Sympathetic Dystrophy Syndrome Association

Alternative Name(s)
RSDSA

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

Current IPD sharing statement as of 05/10/2018:
Participant level data will be stored using the Open Science Framework repository. Digital quantitative data generated from questionnaires, clinical assessments and computer-based tasks will be anonymised and access to the data will be granted upon request. Access shall be requested by contacting Ms Monika Halicka or Dr Janet Bultitude via email, using addresses supplied within contact information. Description of the data and specific instructions for gaining access will be listed in a publicly-available format in the repository and, where possible, in any journal articles that result from the study. The data will be made available at the time that the paper describing the trial outcome is published, upon the completion of Ms Monika Halicka's PhD programme, or two years after the end of the trial (whichever comes first). The consent form for the trial includes an item specifically asking the participant if they agree for their anonymised data collected in the study to be given to researchers, including those working outside of the EU, to be used in other research studies. There are no ethical or legal restrictions in sharing the data.

Previous IPD Sharing plan:
Participant level data will be stored using the University of Bath Research Data Archive (http://researchdata.bath.ac.uk/). Digital quantitative data generated from questionnaires, clinical assessments and computer-based tasks will be anonymised and access to the data will be granted upon request. Access shall be requested by contacting Ms Monika Halicka or Dr Janet Bultitude via email, using addresses supplied within contact information. Description of the data and specific instructions for gaining access will be listed in a publicly-available format in the repository and, where possible, in any journal articles that result from the study. The data will be made available at the time that the paper describing the trial outcome is published, upon the completion of Ms Monika Halicka's PhD programme, or two years after the end of the trial (whichever comes first). The consent form for the trial includes an item specifically asking the participant if they agree for their anonymised data collected in the study to be given to researchers, including those working outside of the EU, to be used in other research studies. There are no ethical or legal restrictions in sharing the data.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2021	27/08/2020	Yes	No
Protocol article	protocol	19/02/2020	24/02/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes