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Efficacy of systolic extinction training (set) in fibromyalgia

Submission date	Recruitment status	[_] Prospectively registered
06/06/2015	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/06/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
25/10/2022	Nervous System Diseases	

Plain English summary of protocol
Plain English summary under review

Study website
http://www.setmarburg.com/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Psychological pain treatment in fibromyalgia: Systolic Extinction Training (set) restores baroreflex sensitivity, reduces pain sensitivity and clinical pain report

Acronym
SET

Study objectives
1. We assume that SET consisting of the highly effective operant-behavioral pain therapy (OBT) and baroreceptor training will reach pain freedom immediately after the 5 weeks treatment with long-lasting effects in more than 80% of fibromyalgia patients compared with OBT that is combined with a sham stimulation and in comparison to cardiovascular training combined with baroreceptor stimulation.
2. The baroreflex sensitivity (BRS) is diminished in fibromyalgia patients in contrast to healthy individuals. We assume that SET will increase significantly BRS in comparison to OBT combined with shame stimulation and in comparison to cardiovascular training combined with baroreceptor stimulation.
3. We hypothesize that SET will increase heart rate variability, in particular the high frequency band (HF) in comparison to OBT combined with shame stimulation and in comparison to cardiovascular training combined with baroreceptor stimulation.
4. The activity of the early EEG components such as N50 and N150 located at the primary somatosensory cortex (SSI) and orbitofronatal cortex were diminished while the later components (P260, P390) were higher active in Fibromyalgia patients compared to healthy individuals We hypothesize that SET will increase the activity of N50 and N150 and decrease the activity of P260 and P390 in comparison to OBT combined with sham stimulation and in comparison to cardiovascular training combined with baroreceptor stimulation.
5. We propose that long-lasting pain inhibition is related to the activation of the Nucleus Tractus Solitarii reflex (NTS-) arcs that goes along with the activation of BRS that relay their action potentials to the NTS as the head of the nervus vagus and increases the parasympathetic activity. Additionally, OBT shows a bilateral activation in pain-evoked activity in the posterior insula, the ipsilateral caudate nucleus/striatum, the contralateral lenticular nucleus, the left thalamus and the primary somatosensory cortex contralateral to the stimulated side. We hypothesize that the connectivity between the mentioned brain areas is increased after SET and associated with pain freedom in comparison to OBT combined with shame stimulation and in comparison to cardiovascular training combined with baroreceptor stimulation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical School at Philipps-University Marburg, Germany, 29/11/2011, ref: 160/11

Study design
Interventional, mechanism-oriented tailored, RCT-study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Fibromyalgia

Interventions
1. The Systolic Extinction Training - SET - consists of the operant-behavioral pain therapy (OBT) and the baroreceptor stimulation as a cardiac gated, electrical, individual adjusted stimulation. Pain-free and pain stimuli (50% and 75% of the individual pain tolerance) with duration of 125ms are delivered immediately after the systolic and the diastolic peak each 5 sec for 8 minutes. Before and after the baroreceptor stimulation, sensory and pain threshold as well as pain tolerance will be determined by stimuli that are constantly increasing by 200 microAmp. The determination is performed twice. The mean value of the pain tolerance will be used for the calculation of the 50% and 75% pain stimuli used for the 8 minutes stimulation.
2. The control condition 1 consists of OBT and a sham stimulation that delivers the same stimuli comparable to the baroreceptor stimulation but independent on cardiac cycle.
3. The control condition 2 consists of cardiovascular training and the baroreceptor stimulation. The patients will sit relaxed in a comfortable chair, will be instructed to focus their attention on a relaxing situation and will be informed about their thresholds. That feedback allows the patients to recognize their increasing pain tolerance and has an operant reinforcing impact on the central desensitization.

Intervention Type
Behavioural

Primary outcome measure
1. Clinical pain. Clinical Pain will be measured before, after, 6 and 12 months after therapy using two methods:
1.1. using the visual analogue score (VAS) before and after psychophysiological experiment that we provide before, after, 6 and 12 months after therapy
1.2. using the standardized questionnaire 'West Haven-Yale Multidimensional Pain Inventory" (MPI) before, after, 6 and 12 months after therapy.
2. Physical impairment. Physical impairment / interference will be measured by using the standardized questionnaire 'West Haven-Yale Multidimensional Pain Inventory" (MPI) before, therapy and then 6 and 12 months after therapy.
3. Affective distress (according to IMMPACT guidelines). Affective distress will be measured by using the standardized questionnaire 'West Haven-Yale Multidimensional Pain Inventory" (MPI) before, after, 6 and 12 months after therapy.

Secondary outcome measures

1. Baroreflex Sensitivity (BRS): BRS will be measured using Finapress for blood pressure and heart rate recording necessary for 3 different calculation procedures to receive the BRS in an psychophysiological experiment before therapy (T1), immediately after (T2), 6 (T3) and 12 months (T4) after therapy
2. Heart rate variability (HRV): HRV will be measured using 3 channel ECG and the Acq-knowledge software program (Biopac) for calcualtion the HRV components before therapy (T1), in an psychophysiological experiment immediately after (T2), 6 (T3) and 12 months (T4) after therapy
3. Evoked potentials: Evoked potentials (ep) will be measured using a 128 channel EEG that measures the ep's in regard to 6 different markers defined by stimuli intensities (pain-free, 50% and 75% of pain tolerance) and cardiac cycle 9sysytolic and diastolic peak) in an psychophysiological experiment immediately after (T2), 6 (T3) and 12 months (T4) after therapy

Overall study start date
01/04/2015

Completion date
30/06/2020

Eligibility

Key inclusion criteria
The inclusion criteria consist of:
1. Meeting ACR (American College of Rheumatology) criteria of FM
2. Pain for a period of at least 6 months
3. Married
4. Willingness of the spouse to participate
5. Ability to complete the questionnaires and understand the treatment components.

Further essential inclusion criteria for the proposed tailored study are:
6. Cardiac hypertensive stress reactivity
7. High level of pain behaviors
8. Catastrophizing
9. Solicitous spouse responses

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
76

Key exclusion criteria
The exclusion criteria consisted of:
1. Inflammatory rheumatologic diseases and any concurrent major disease such as cancer,

diabetes, or kidney failure
2. Intake of beta-blocker (systematic), opioids, anti-depressants)

Date of first enrolment
01/04/2015

Date of final enrolment
01/07/2019

Locations

Countries of recruitment
Germany

Study participating centre
Department of Medical Psychology, Philipps-University Marburg
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Sponsor information

Organisation
University Hospital Giessen - Marburg

Sponsor details
Rudolf-Buchheim-Str. 8
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/032nzv584

Funder(s)

Funder type
University/education

Funder Name
University Hospital Giessen - Marburg (Germany)

Results and Publications

Publication and dissemination plan

Intention to publish date
28/02/2016

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	Thieme K, Malinowski R, Monbureau O, Gracely RH. Method of electrical stimulation triggered by cardiac cycle to facilitate the treatment of fibromyalgia and other chronic diseases - Systolic Extinction Training (SET) protocol. General Med 3: 6.	25/02/2015		Yes	No
Results article	analysis	01/05/2019	06/01/2020	Yes	No