

# Efficacy of systolic extinction training (set) in fibromyalgia

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<b>Registration date</b> 22/06/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 25/10/2022	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Plain English summary under review

## Study website

<http://www.setmarburg.com/>

## Contact information

### Type(s)

Scientific

### Contact name

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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 sham 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 sham 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 orbitofrontal 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 sham 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 Finapres 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 calculation 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 (systolic 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?
<a href="#">Protocol article</a>	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
<a href="#">Results article</a>	analysis	01/05/2019	06/01/2020	Yes	No