Pain processing in PTSD - Investigating neural correlates of dissociative analgesia

Published: 16-01-2020
Last updated: 05-10-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON49599

Source
ToetsingOnline

Brief title
Pain processing in PTSD

Condition

- Other condition
- Dissociative disorders

Synonym
psychological trauma, PTSD

Health condition

Post-traumatic stress disorder

Research involving
Human

Sponsors and support

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

Intervention

Keyword: analgesia, fMRI, pain processing, PTSD

Outcome measures

Primary outcome

The main study parameters are differences in BOLD activation in response to the painful (vs. non-painful) stimulation following the traumatic (vs. neutral) script in PTSD patients (vs. controls). The regions of interest include the caudate head, thalamus, amygdala, anterior insula cortex, anterior cingulate, and periaqueductal gray. Subjective pain ratings of the thermal stimulation and pain threshold will be analyzed and compared between conditions/groups. Further parameters are associations between interview-assessed ratings of PTSD symptomatology and dissociative experiencing and task-related neural activation.

Secondary outcome

Secondary parameters consist of BOLD responses to the emotion reactivity task. Neural activity will be compared within-groups (supraliminal vs. Subliminal stimulus presentation) and between-groups (PTSD vs. TEC). The other relevant secondary parameter is the psychophysiological reactivity elicited during the functional imaging paradigms as well as during script collection (heart rate). Differences in reactivity in a) heart rate and b) skin conductance following the trauma-related task (script-driven imagery) and trauma-unrelated task

(emotion reactivity task) will be analyzed. The heart rate elicited during

script collection will be compared within-subjects (neutral script vs.

Traumatic script), and between-subjects (PTSD vs. TEC group). Furthermore, the

self-reported capacities in emotion regulation skills will be associated with

neural responses elicited during the emotion reactivity task.

Study description

Background summary

Post-traumatic stress disorder (PTSD) depicts high comorbidity with chronic pain conditions indicative of dysfunctional pain processing. Experimental pain research suggests that many PTSD patients show decreased pain perception, thus are less sensitive to painful stimuli. Most evidence points towards a model of stress-induced analgesia, in which exposure or reminders of aversive experiences leads to numbing of sensory and emotional processing, including reduced pain sensitivity and elevated levels of dissociation. It is hypothesized that the analgesic effect derives from excessive top-down inhibition of subcortical regions via the opiate-based pain modulation system as a compensatory reaction to the greater initial (emotional) distress experienced in PTSD patients. However, the neurobehavioural mechanisms underlying the maladaptive coping with acute pain have not been well-understood and imaging studies on the neural underpinnings of pain processing in PTSD are scarce. To date, only one fMRI study investigated neural markers of stress-induced analgesia in PTSD. Mickleborough et al., (2011) employed a pain processing paradigm combining script-driven imagery and thermal stimulation. Imaging data suggested that the analgesic effect is related increased activation in the caudate head and that subjective ratings of dissociation are related to inhibited amygdala activity. However, replication of the detected neural markers is strongly warranted given the scarcity and methodological limitations of the prior imaging studies.

Study objective

The current study aims to elucidate neural correlates of pain processing and dissociative analgesia in PTSD. To this end, we want to replicate the pilot study by Mickleborough et al., (2011) and test the functional pain processing protocol with sufficient statistical power. Additionally, assessment of psychophysiological reactivity, e.g. heart rate variability, and an emotional processing task will be included to gain further insight into the objective

markers of pain processing and dissociative symptoms.

Study design

The current research is a replication study of Mickleborough et al., (2011) and employs functional neuroimaging to experimentally investigate pain processing in PTSD. Within a 2-by-2-by-2 study design, participants (PTSD patients vs. trauma-exposed controls) will undergo a fMRI paradigm in which participant receive thermal stimulation (painful vs. nonpainful) after listening to autobiographical memory scripts (traumatic vs. neutral). Former research will be extended with the additional assessment of psychophysiological markers and an emotion reactivity task. The tasks tests bottom-up emotion processing by presenting fearful vs. neutral faces above (supraliminal) and below (subliminal) the perceptive threshold.

Intervention

A blocked fMRI paradigm will be employed to test brain activity in response to the thermal stimulation after listening to an autobiographical script.
The paradigm begins with a 60 second baseline measurement in which participants are asked to focus on their breathing. Then, participants will listen to a 30-second pre-recorded script of a personal event via in-ear headphones and are asked to concentrate on the feelings and sensations elicited by the memory. They are asked to remember olfactory, auditory, somatosensory, and visual sensations associated with the autobiographical memory and continue doing so for another 30 seconds after the tape has ended, so 60 seconds in total. Participants will listen to the neutral script six times (Block 1) followed by listening to the traumatic script six times. It is crucial that the neutral script precedes the traumatic script because the reverse could lead to carry-over effects of the distress resulting from the trauma-recall. Each tape listening is followed by a 25 second thermal stimulation, three painful (warm) and three non-painful (hot) presented in a pseudorandomized order. Stimulation will be counterbalanced across groups to avoid anticipation potentially affecting the pain intensity ratings. After the stimulation has ended, participants rate the pain intensity and unpleasantness and how strong they experienced dissociative symptoms. After each scan, participants are given 120 seconds to relax and concentrate on their breathing before the beginning of the next script. The participants* well-being will be repeatedly assessed throughout the experiment, and participants can stop their participation at any timepoint.

Study burden and risks

Study participation consists of two main components. Firstly, participants undergo a clinical interview session (90 minutes) to determine their PTSD symptom severity, and collect autobiographical scripts required for the

functional paradigm. At the end of the session, participants are given and asked to fill out a questionnaire booklet (30 minutes). Secondly, participants will follow a fMRI scanning session (125 min) in which they undergo two tasks (pain processing paradigm and emotional reactivity task). During scanning, the participants* psychophysiological data (heart rate and skin conductance reactivity) will be recorded. Total duration is 5 hours.
Concerning the fMRI scanner, participants will be exposed to a field strength of 3 Tesla and scanner noise. Thus far, there is no evidence to suggest that exposing humans to a magnetic field of this strength has a negative influence on health. With regard to the noise, earplugs will be provided. To minimize the risk of claustrophobic sensations in the scanner, patients will be screened for a history of claustrophobia and will be offered to lay in a mock scanner to estimate their comfort level inside an MRI scanner. No disadvantages of the heart rate and skin conductance measures are known or expected. The thermal heat stimulation leading to temporary pain sensations will be carefully adjusted to the subjective pain thresholds, and to our knowledge no major risks have been associated with the procedure. The study is not intended to benefit the participants directly, but they will receive a compensation of ¤ 50,- for their participation.

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

PTSD group
1) Participants must be full of age (18 years or older).
2) Participants must be female.
3) Participants must be capable of giving consent.
4) Participants must have experienced a criterion A traumatic experience.
5) Meet the criteria for a PTSD diagnosis.
6) Must be enrolled in treatment.

Control group
1) Participants must be full of age (18 years or older).
2) Participants must be female.
3) Participants must be capable of giving consent.
4) Participants must have experienced a criterion A traumatic experience.

Exclusion criteria

Both groups

1) Presence of metallic devices, e.g. metal implants or cardiac pacemaker
2) Meet criteria for pain disorder
3) Meet criteria for bipolar disorder
4) A current diagnosis of a neurological disorder
5) Alcohol or drug abuse in the last 6 months
6) Refusal that general practitioner will be informed when structural brain abnormalities could be detected during experiment
7) Claustrophobia
8) Pregnancy (or high risk of a potential pregnancy)
9) Current medication intake of medication affecting the pain modulation system.

Additional exclusion criteria for the control group
10) developed PTSD in their lifetime

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-11-2020
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	16-01-2020
Application type:	First submission
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	NL70840.042.19