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Altered cerebral response to noxious heat stimulation in patients with somatoform pain disorder

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Abstract

Idiopathic chronic pain conditions with a mismatch between anatomical abnormalities and symptoms can be categorized as somatoform pain disorder according to the DSM-IV criteria. A dysfunction of pain processing circuits has been suggested as one underlying pathophysiological factor. There is accumulating evidence for a crucial role of affect regulating brain structures such as the medial frontal cortex in this context. We investigated the cerebral processing of noxious heat stimuli as objective marker for pain sensation in 12 right handed women with somatoform pain disorder fulfilling DSM-IV criteria and 13 age-matched healthy volunteers using functional MRI. The average ratings for experimentally induced pain were not significantly different between controls and patients concerning pain intensity and pain unpleasantness. Comparing patients with controls a pain related hypoactive state of the ventromedial prefrontal/orbitofrontal cortex (BA 10/11) and a hyperactive state of the parahippocampal gyrus, amygdala and anterior insula were found in the patient group. Our findings of an altered cerebral processing of experimentally induced pain in patients with somatoform pain disorder support the hypothesis of dysfunctional pain processing, especially in affect regulating regions.

Keywords: Somatoform pain disorder; fMRI; Neuroimaging; Ventromedial prefrontal cortex; Orbitofrontal cortex; Amygdala; Idiopathic chronic pain; Emotional dysregulation

1. Introduction

Somatization disorders constitute a large, clinically important, and costly health care issue that urgently need better pathophysiological understanding and improved management [54]. Somatoform pain disorder assessed with DSM-IV criteria has a lifetime prevalence of 12.2%, thus accounting for the vast majority of the total 12.9% somatoform disorder prevalence rates in the German general population [33].

This disorder is regularly linked to emotional dysregulation [53]. Recently, the powerful effects of the emotional context on the perceptual, emotional and brain response to an innocuous stimulus have been clearly demonstrated [32]. One aspect of emotional dysregulation in somatoform disorder is associated with a high affective description of individual pain. The amount of affective words used in the description of pain also correlates with pain catastrophizing [9,27]. This construct has recently been found to be positively related to the

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activity of brain regions associated with the affective aspects of pain, such as the insula, and to be negatively correlated to the activity within areas associated with top-down pain control, such as the prefrontal cortex [44]. We here hypothesized that patients fulfilling DSM-IV criteria for somatoform pain disorder would also show an increased activation in brain structures mediating the affective dimension of the pain experience.

2. Methods

2.1. Subjects

Twelve right-handed female patients fulfilling DSM-IV criteria (American Psychiatric Association, 1994) [56] for somatoform pain disorder (medium age 47.4 years, range 29–59) were selected from a consecutive sample of patients scheduled for a visit in the psychosomatic outpatient department of the Klinikum rechts der Isar, Technische Universität München. The study was approved by the local Ethics Committee of the Technische Universität München and written informed consent was obtained from all participants.

Inclusion criteria were female gender, right-hand preference according to the Edinburgh Handedness Inventory [8], range of age between 20 and 65, duration of clinical pain of at least 2 years and diagnosis of somatoform pain disorder according to the DSM-IV criteria.

2.1.1. Pain perception scale (PPS)

A major inclusion criterion was the report of a high affective dimension of the clinical pain syndrome as measured by the pain perception scale (*PPS*) [13]. This 24-item questionnaire describes the sensory and the affective qualities of pain in a "global affective score" and a "global sensory score". It has been proved to be a reliable and valid tool to measure the affective and sensory component of pain in various studies and is an essential part of the pain questionnaire of the German IASP chapter (DGSS). Thereby, the cut-off value for the inclusion of patients into the study was set at a minimum of 40 points out of 56.

The clinical pain intensity was assessed using an 11 point numerical rating scale (NRS 0–10, 0 = no pain and 10 = worst pain imaginable).

Physical and technical examinations of the patients were performed by a neurologist and orthopaedic surgeon to exclude any somatic cause of the pain syndrome.

We excluded patients with the diagnosis of fibromyalgia as characterized by chronic widespread pain (involving all 4 quadrants of the body as well as the axial skeleton) and diffuse tenderness [57]. Patients receiving any long-term medication were also excluded.

In addition, 13 healthy controls (medium age: 47.3 years, range 28–59) were matched for age, gender and handedness. These volunteers did not fulfil criteria for any psychiatric diagnosis according to DSM-IV criteria.

2.2. Psychometric evaluation

Psychometric evaluation with various questionnaires was performed to optimally characterize the recruited patients and controls.

2.2.1. Screening for somatoform symptoms (SOMS)

The screening for somatoform symptoms (SOMS) was completed with the SOMS-2 questionnaire [43]. It asks for the presence of 53 physical complaints lacking an organic disease during the previous two years and verifies further classification criteria with another 15 questions to be answered by the patient. The questionnaire includes all 33 physical complaints of the DSM-IV somatization disorder symptom list, the symptoms of ICD-10 somatization disorder, and the ICD-10 somatoform autonomic dysfunction symptom list. Therefore the SOMS-2 is suitable to screen for the presence of somatoform disorders. This scale shows high internal consistency ($\alpha = 0.92$) and is a reliable and valid instrument. The DSM-IV somatization index is a central outcome sum score recruited by the single 33 DSM-IV items of the SOMS-2. In our study, only female patients with a baseline DSM-IV somatization index score $\geqslant 6$ were included. This criterion was introduced by Escobar et al. to identify somatization syndromes of clinical relevance beyond DSM diagnosis [10].

2.2.2. Global assessment of functioning (GAF)

The Global Assessment of Functioning scale (GAF) was completed by all study participants. The GAF scale [48] is a numeric scale (0 through 100) used by mental health clinicians to rate the individual's overall (social, occupational and psychological) level of functioning in the daily life.

2.2.3. Structured psychiatric interview (SCID)

The occurrence of psychiatric disorders was assessed during a structured psychiatric interview (SCID-I, German version) [56] by a consultant psychiatrist according to DSM-IV criteria (APA, 1994). The SCID assesses current (last 4 weeks before interview) and lifetime psychiatric status for major Axis I psychiatric disorders using criteria which are in accordance with the DSM-IV.

2.2.4. Beck Depression Inventory (BDI)

The BDI is a 21-item self-report instrument measuring cognitive and endogenous aspects of depression on a four-point scale that ranges from 0 to 3. This questionnaire has undergone extensive reliability and validation studies [4].

2.3. Experimental painful stimulation protocol

2.3.1. Assessment of individual pain threshold

Before the fMRI scanning, the individual heat pain threshold was assessed using a steps protocol. The noxious heat stimulation was applied to the inner side of the left forearm with a 30×30 mm sized probe (thermode) using the MEDOC TSA-2001 (Israel) thermal stimulator. From a baseline temperature of 35 °C the temperature was increased (slope 4 °C/s) to a target temperature, for example 41 °C, which was maintained for 40 s. Subjects were blind to the applied target temperature of the thermode. If the subject did not report moderate pain sensation (numerical rating between 5 and 7/10) during the 40 s of stimulation, the procedure beginning from baseline temperature was repeated, but the target temperature was increased by 0.5 °C. This procedure was repeated until a moderate pain sensation was reached.