Nocebo hyperalgesia induced by social observational learning

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ARTICLE INFO

Article history:
Received 15 February 2013
Received in revised form 28 March 2013
Accepted 23 April 2013

Keywords:
Nocebo response
Social observational learning
Pressure pain
Pain catastrophizing
Verbal suggestion
Nocebo hyperalgesia

ABSTRACT

Nocebo effects can be acquired by verbal suggestion, but it is unknown whether they can be induced through observational learning and whether they are influenced by factors known to influence pain perception, such as pain anxiety or pain catastrophizing. Eighty-five female students (aged 22.5 ± 4.4 years) were randomly assigned to one of three conditions. Participants in the control condition (CC) received information that an ointment had no effect on pain perception. Participants in the verbal suggestion condition (VSC) received information that it increased pain sensitivity. Participants in the social observational learning condition (OLC) watched a video in which a model displayed more pain when ointment was applied. Subsequently, all participants received three pressure pain stimuli (60 seconds) on each hand. On one hand, the ointment was applied prior to the stimulation. Numerical pain ratings were collected at 20-second intervals during pain stimulation. The participants filled in questionnaires regarding pain-related attitudes (Pain Anxiety Symptoms Scale, Pain Catastrophizing Scale, and Somatosensory Amplification Scale). Participants in the OLC showed higher pain ratings with than without ointment. Pain ratings within the CC and the VSC were at the same level with and without ointment. In the VSC, the pain ratings were higher than in the CC with and without ointment. The nocebo response correlated with pain catastrophizing but not with pain anxiety or somatosensory amplification. A nocebo response to pressure pain was induced by observational learning but not by verbal suggestion. This finding highlights the importance of investigating the influence of observational learning on nocebo hyperalgesia.

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1. Introduction

The expectation that a treatment may cause certain symptoms can lead to the occurrence or worsening of those symptoms. This phenomenon is called the nocebo effect [4]. Nocebo effects have been shown to occur in a number of contexts, such as chronic illness [24,46,47,49], motor performance in Parkinson patients [6], the effects of opioids and sedatives in postoperative pain [5], the subjective experience during invasive procedures [45], and the occurrence of mass psychogenic illness [25].

In an experimental setting, nocebo effects on pain were observed with various pain stimuli like ischemic pain [6], electric stimulation [10,11,44], mechanical stimuli, or the application of histamine [44]. No empirical study was found in which nocebo effects on pressure pain were investigated.

Little is known of the possible routes by which nocebo responses are acquired. They can be induced by conditioning or verbal suggestion alone [11,44].

Observing others might be one way in which pain-related beliefs and attitudes are acquired [19]. A mother’s modelling had an impact on her child’s pain behaviour [18]. In the same way, the pain expression of adults was influenced by the observation of models [12,13]. It is unknown whether a nocebo response can be induced in this way. One study showed that placebo analgesia could be induced by social observational learning [9] and that the effect was associated with empathy. Mass psychogenic symptoms can be caused by observing another person demonstrating symptoms [25]. No study was found in which socially induced nocebo effects on pain were investigated.

Studies concerning factors influencing the nocebo response are rare. Women demonstrated more nocebo nausea after a conditioning procedure than after verbal suggestion alone, whereas men showed stronger responses to the verbal suggestion than to the conditioning procedure [22]. Studies of placebo analgesia showed that it may be linked to factors like sex and stress [2], fear of pain [26,27] and pain catastrophizing [40]. So far, the results are inconsistent [2] and the exact impact of these factors is unknown [15].

The aim of our study was to investigate whether a nocebo response can be induced by verbal suggestion as well as by social observational learning. We expected a positive correlation between the strength of the nocebo response and fear of pain and...
pain catastrophizing. For participants in the social observational learning group, we also expected a positive correlation between the nocebo response and empathy.

2. Materials and methods

2.1. Participants

Participants were recruited via advertisements on university billboards. A total of 85 female right-handed students participated in the study. Four participants were excluded because of chronic pain, chronic bladder infection, lupus, and arthritis, respectively. One participant discontinued the experiment because she found the stimulation too painful. The remaining 80 participants (mean age 22.5 ± 4.4 years) were assigned randomly to the 3 experimental conditions. The groups did not differ with regard to age (Table 1).

2.2. Design

A 3 × 2 repeated-measures design with the between-factor “condition” (verbal suggestion, social observational learning, control) and within-factor “ointment application” (yes, no) was used. Before the pain induction, the participants were randomly assigned to one of the three conditions. All participants received pressure pain stimuli on the ring, middle, and index finger of each hand. The order of the stimulation, the ointment application, and the nocebo side was fully randomized. The dependent measure was subjective pain intensity.

2.2.1. Conditions

White odourless ointment served as nocebo. It was presented in a neutral container like those used by dispensing chemists. The ointment was hypoallergenic and contained no fragrances, preservatives, dyes, or potentially irritating agents, but only the following ingredients: aqua, caprylic/capric triglyceride, glycerin, pentylene glycol, cocos nucifera, hydrogenated lecithin, Butyrospermum parkii, hydroxyethylcellulose, squalane, sodium carbomer, xanthan gum, carbomer, and ceramide 3. In every condition the ointment was applied to one hand. The conditions differed regarding the information that the ointment was designed to intensify the skin. Participants in the verbal suggestion condition (VSC) read the information that possible ways of standardizing pressure pain application were being investigated. The ointment would have no effect on pain experience, but only on the moistness and elasticity of the skin. Participants in the social observation condition (OLC) were informed that the influence of a nonverbal instruction on the experimental procedure was being tested. To this end they would be asked to watch a video in which the procedure was demonstrated. The participants in this group received no further written information. To focus their attention on the video they received 5 questions about the video prior to watching it. They were told that they would have to answer the questions after the video.

2.2.2. Pain ratings and nocebo response

Participants were asked to indicate pain intensity verbally during the application of a pressure pain stimulus every 20 seconds on an 11-point numerical rating scale with 0 indicating “no pain at all” and 10 indicating the “worst pain imaginable.” The investigators wrote down the answers.

The nocebo response was defined as the difference in pain ratings between the pressure applications with and without ointment. Higher values indicated a stronger nocebo response.

2.2.3. Pain induction

Pain was induced by a stationary pressure pain algometer, which delivers constant pressure over a fixed period of time. The main part of the algometer consists of a lever with a weight. At its end, a plunger with a surface area of 3 mm² is located. When a button is pushed, the lever with the plunger is lowered onto the finger. It rises automatically after a predetermined period of time. As a safety measure, the procedure can be stopped immediately by the pushing of a button.

A weight of 300 g set at 8 cm was used, resulting in a total pressure of 0.92 MPa, which was applied for 60 seconds. This stimulation intensity was chosen because it was below the pressure intensities used in other studies [16,17] but above the pressure pain threshold found in other studies [7,31]. We tested the chosen intensity in a pilot study in order to ascertain that the pain was tolerable for 60 seconds for all participants.

2.2.4. Video

The video was taken in the same room in which the experiment took place. It showed a seated female model and the hands of a female experimenter. The video was taken from an angle behind the model so that the model’s face was only partially visible (for a still picture, see Fig. 1). The video lasted 10.22 minutes and the sequence was as follows: the experimenter told the model that pressure pain stimuli would be applied and explained the rating scale. The pressure application started with the right hand without ointment. The model rated the pain intensity verbally on the 11-point scale (see above). The model’s ratings for the hand with without ointment ranged from 2 to 3. After all three fingers of that hand had been stimulated, the ointment was applied to the model’s left hand and allowed to take effect for 60 seconds. Then the application of pressure pain resumed. The model’s ratings for the hand with ointment ranged from 5 to 7.

Table 1

Mean test scores of participants in the three conditions and results of the one-way ANOVAs.

<table>
<thead>
<tr>
<th></th>
<th>Verbal suggestion (n = 27)</th>
<th>Social observation (n = 26)</th>
<th>Control (n = 27)</th>
<th>F(2,77)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>STAI-S</td>
<td>36.6</td>
<td>7.0</td>
<td>36.2</td>
<td>8.0</td>
<td>36.3</td>
</tr>
<tr>
<td>STAI-T</td>
<td>40.1</td>
<td>8.7</td>
<td>41.2</td>
<td>8.3</td>
<td>41.6</td>
</tr>
<tr>
<td>CES-D</td>
<td>10.1</td>
<td>5.6</td>
<td>11.9</td>
<td>6.3</td>
<td>11.1</td>
</tr>
<tr>
<td>PCS</td>
<td>22.4</td>
<td>7.8</td>
<td>22.2</td>
<td>7.6</td>
<td>25.0</td>
</tr>
<tr>
<td>PASS</td>
<td>69.3</td>
<td>19.5</td>
<td>73.2</td>
<td>24.9</td>
<td>76.1</td>
</tr>
<tr>
<td>SSAS</td>
<td>27.1</td>
<td>4.7</td>
<td>27.0</td>
<td>6.0</td>
<td>27.7</td>
</tr>
<tr>
<td>Stress</td>
<td>3.1</td>
<td>1.9</td>
<td>3.4</td>
<td>1.9</td>
<td>3.0</td>
</tr>
</tbody>
</table>

ANOVA, analysis of variance; STAI-S, State-Trait Anxiety Inventory, state version; STAI-T, State-Trait Anxiety Inventory, trait version; CES-D, Center for Epidemiological Studies Depression Scale; PCS, Pain Catastrophizing Scale; PASS, Pain Anxiety Symptoms Scale; SSAS, Somatosensory Amplification Scale.
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