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Original experimental

Unpredictable pain timings lead to greater pain when people are highly intolerant of uncertainty

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HIGHLIGHTS

- Intolerance of uncertainty influenced pain perception.
- High intolerance predicted higher pain scores when stimulations became unpredictable.
- This relationship was observed only when the cued delay was long.

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ABSTRACT

Background and purpose: Many psychological factors are known to influence pain perception. Among them, intolerance of uncertainty (IU) may play a key modulating role in situations where uncertainty prevails, especially uncertainty regarding the timing of painful events. The objective of this study was to explore the impact of individual differences in IU on pain perception during predictable and unpredictable stimulation timings. We hypothesized that people with high IU, as opposed to those with low IU, would perceive more pain when the timing of painful stimulations cannot be predicted, as compared to when they can.
Methods: Twenty (20) healthy adults, aged between 18 and 35 years old, were recruited. Painful sensations were provoked using transcutaneous electrical stimulations of the right sural nerve. By measuring IU (Intolerance of Uncertainty Scale) and subjective pain (verbal numerical rating scale), it was possible to test the relationship between IU and pain perception, by simulating predictable and unpredictable painful experiences. This was done through cued shock interval (CSI) blocks, with either variable timing or fixed timings (long or short time frame). Self-administered questionnaires were also used to measure pain hypervigilance, pain catastrophizing, state anxiety, and trait anxiety.
Results: Pearson correlations confirmed the presence of an association ($r = 0.63$) between IU and the change in pain intensity provoked by unpredictable stimulation timings. Importantly, this association was significant only for stimulations provided at long CSIs, indicating that higher IU scores predicted higher pain intensity scores when stimulation timings became unpredictable, and when the cued delay was long. No association was found between pain scores and other psychological variables.
Conclusions: Our results show that IU moderately correlates to the change in pain intensity provoked by unpredictable stimulation timings. High IU scores were associated with a worsening of the subjective pain experience, especially during long delays in an unpredictable situation. These observations suggest that IU could be considered as a psychological variable that is able to influence pain perception in certain situations.
Implications: Assessing and addressing IU could be an added value in pain-related therapy, especially in chronic pain.

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1. Introduction

Many factors, including psychological ones, influence pain perception [1–4]. Anxiety, hypervigilance to pain, and pain catastrophizing have been proven to influence pain perception [5–9]. Another psychological factor that may play a role in pain perception is intolerance of uncertainty (IU). This psychological construct can be defined as the tendency to respond to uncertain situations or events with negative emotional, cognitive, and behavioural reactions [10]. The absence of literature linking pain perception and intolerance of uncertainty shows that IU is a putative pain-related psychological factor which remains poorly studied. Previous studies have demonstrated that subjects who are intolerant of uncertainty are both more anxious [11] and more attentive to potentially dangerous situations [12], two predispositions which are known to heighten the subjective experience of pain [5,13]. IU, therefore, may be an important factor in explaining why humans differ so much in their response to pain. Specifically, IU may play a modulating role in situations where uncertainty prevails, especially when uncertainty regarding the timing of painful events abounds [14,15]. To indicate the time of onset of the stimulation, and its predictability or non-predictability, many types of cueing designs can be used, such as sound cueing and visual cueing [11,14,16]. Both variations (predictability and length of the delay before the shock) have shown their influence on pain perception [14,15,17]. Indeed, recent studies confirm that when the timing of pain cannot be fully predicted, some react quite poorly and report increased pain [14,15]. To this day, there is no consensus on the best way to create an unpredictable environment in experimental settings.

Understanding why some of us react so poorly to unpredictable pain, while others do not, may require that we pay closer attention to innate predispositions regarding IU. The objective of this study was to explore the impact of individual differences in IU on pain perception, during predictable and unpredictable stimulation timings. We hypothesized that people with high IU, as opposed to those with low IU, would perceive more pain when the timing of painful stimulations cannot be predicted, as compared to when they can.

2. Materials and methods

2.1. Participants

Twenty (20) healthy adults between the ages of 18 and 35, including 10 men (mean age 22.5 ± 2.4 years) took part in this study. All participants provided written, informed consent, and the research protocol was approved by the ethics committee of the Centre hospitalier universitaire de Sherbrooke (CHUS).

2.2. Subjective pain intensity

Pain intensity was assessed using a verbal numerical rating scale (NRS). The scale ranged from 0 to 100, where 0 was defined as "no pain" and 100 was defined as "intolerable pain intensity". Numerical rating scales have excellent psychometric properties, and are very sensitive to minimally experienced changes in subjective pain [18].

2.3. Sural nerve stimulation

Painful sensations were provoked using transcutaneous electrical stimulations of the right sural nerve. The sural nerve was stimulated over its retromalleolar path. Stimulations of the sural nerve consisted in 10 electrical impulses with a wavelength of 1 ms and a frequency of 240 Hz. Prior to testing, a pre-experimental session was carried out to help participants become familiar with all electrical stimulations, to determine their pain threshold level, and to identify the stimulation intensity required to provoke a sensation of 30/100 pain (i.e., suprathreshold pain sensitivity). During the testing phase of the experiment, electrical stimulations of the sural nerve were always cued ahead of time, using a visual cue (red light) which signaled the presence of an upcoming shock. Subjects were seated 100 cm from the visual cue (home-made stimulus box containing a red light-emitting diode placed behind a translucent circular screen, 2 degrees in diameter). The visual cue was turned off one second after stimulus onset, and remained turned off until the next trial, which occurred 6 s later. Participants were asked to provide their pain ratings during this 6 s cue-off interval. A depiction of the cueing design is presented in Fig. 1. Shocks were administered in 3 separate testing blocks: 2 fixed blocks and 1 variable block. Each fixed block contained 8 sural nerve stimulations. In fixed blocks, shocks were always presented after a fixed delay following cue onset. The cue shock interval (CSI) was always the same length in a given fixed block, either 6 or 15 s, depending on the block. In the variable block, shocks were presented after a variable delay following cue onset. The CSI in the variable block varied between 6, 9, 12 and 15 s. In this block, 4 sural nerve shocks per CSI were presented, for a total of 16 stimulations. CSIs within the variable block were always presented using the same, pre-established, random sequence. Participants were told that shocks would always be cued ahead of time, and that the CSI would remain fixed within the fixed blocks, and variable within the variable block. Regardless of block type, CSI length was never directly specified. Participants were also never told that the stimulation intensity would be kept constant throughout testing (at a stimulation intensity value required to provoke 30/100 pain). To ensure homogeneity between the group receiving variable shocks first, and the group receiving the fixed block first, the participants in these groups were matched for sex and IU score.

It is important to point out that psychological variables other than IU, such as anxiety, hypervigilance to pain, and pain catastrophizing, may further contribute to the pain enhancing effects of unpredictable timing; see for instance Ruscheweyh et al. who demonstrate the enhancing effect of pain catastrophizing on pain perception [9]. To properly identify the unique contribution of each of these variables to the putative pain enhancing effects of unpredictable timing, and because these variables may explain pain enhancement as well as (or better than) IU, we included them as predictor variables in the present study.

2.4. Questionnaires

2.4.1. Intolerance of uncertainty

IU was measured using the Intolerance of Uncertainty Scale (IUS) [19]. The IUS was developed to assess emotional, cognitive, and behavioural reactions to ambiguous situations, implications of being uncertain, and attempts to control the future [20]. It shows excellent internal consistency and good test-retest reliability [19,20]. The IUS is a 27-item questionnaire scored on a 5-point Likert scale. The IUS score varies from 27 to 135 points, where high scores represent higher levels of uncertainty.

2.4.2. Anxiety

The State-Trait Anxiety Inventory (STAI) was used to measure anxiety. The STAI consists in two 20-item questionnaires scored using a 4-point Likert scale. The STAI measures a standard index of situational (state = STAI-S) and dispositional (trait = STAIT-T) anxiety. The STAI has excellent psychometric properties [5,21] and is frequently used in pain research [22–24]. High scores on the STAI (state or trait) indicate elevated levels of anxiety.