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DOI
10.1016/j.jpain.2025.105506

Publication date
2025

Document Version
Final published version

Published in
Journal of Pain

Citation (APA)
Nadinda, P. G., van Laarhoven, A. I. M., Vlaeyen, J. W. S., Peters, M. L., & Evers, A. W. M. (2025). I expect therefore I avoid? The effects of negative expectancy learning on pain and pain-related avoidance behavior. *Journal of Pain*, *35*, Article 105506. https://doi.org/10.1016/j.jpain.2025.105506

Journal of Pain 35 (2025) 105506

Contents lists available at ScienceDirect

The Journal of Pain

journal homepage: www.jpain.org

I expect therefore I avoid? The effects of negative expectancy learning on pain and pain-related avoidance behavior☆

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ARTICLE INFO

Keywords:
Hyperalgesia
Expectancy
Avoidance
Conditioning
Experimental paradigm

ABSTRACT

Expectancies and avoidance behavior are key factors influencing pain perception and its maintenance, but few empirical studies have investigated their relationship. Thus, two separate studies with a two-fold primary aim were conducted. The first part of the primary aim was to investigate whether negative expectancies lead to hyperalgesia. The second part of the primary aim was to investigate whether negative expectancies lead to more costly pain avoidance. The studies included a total of 116 and 98 participants respectively. In both studies, participants were randomly assigned to either the experimental or the control group. Pain expectancies were induced verbally and via conditioning, and avoidance was measured through a novel pain avoidance task in which participants could choose between avoiding a more painful stimulus by playing a difficult game or enduring a more painful stimulus by playing an easy game. In Study 2, adjustments were made to the conditioning procedure and the novel pain avoidance task based on the results of Study 1. Both studies demonstrated that negative expectancies led to hyperalgesia, indicating that the negative expectancy paradigm produces robust effects. However, negative expectancies did not lead to more pain avoidance suggesting that other factors may be at play in avoiding more pain. Further studies are needed to fully unravel the interplay between expectancies and avoidance in pain.

Perspective: This article found that negative expectancies can lead to hyperalgesia but not necessarily to more pain avoidance behavior in individuals without chronic pain. Findings from this article support the ample studies indicating that expectancies provide a strong target for pain treatment.

Introduction

It is well established that pain is a multidimensional somatosensory experience that is influenced by various neurobiological, psychological, and social factors.[1] Of these factors, response expectancies, or expectations in reaction to something, have been shown to play a substantial role in pain perception.[2–5] The effect of expectancies has especially been evaluated in the context of placebo and nocebo effects in which positive expectancies can lead to symptom reduction indicating a placebo effect,[6–8] whereas negative expectancies can lead to symptom worsening indicating a nocebo effect.[7,9] One prominent example of the role of expectancies in pain is hyperalgesia, which can occur as a result of expecting high pain that can further generate new negative expectancies and draw attention towards pain.[7,10,11] These expectancies can be acquired through verbal instructions, observational learning, and experiential learning.[12–14]

Negative expectancies as well as fear-related beliefs (e.g., catastrophizing) can lead to safety-seeking behaviors such as avoidance.

☆ The current work was conducted at Leiden University

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https://doi.org/10.1016/j.jpain.2025.105506
Received 21 January 2025; Received in revised form 9 July 2025; Accepted 17 July 2025
Available online 21 July 2025

Avoidance is another key mechanism in the maintenance of pain.[15–17] In fact, some have argued that the interaction between expectancies and other cognitive-affective factors (e.g., fear, catastrophizing) can predict pain, avoidance behavior, and disability.[18–20] Although avoidance behavior can be adaptive in acute pain, continuous avoidance behavior can instead be costly – especially when fear and expectancies generalize towards novel stimuli that were not previously associated with pain.[21] As a result, negative expectancies are also maintained as the cycle of avoidance impedes any opportunities to adjust expectancies based on actual pain experience.[22,23]

Despite theoretical evidence that expectancies can lead to avoidance behavior,[16,19] most empirical studies have only assessed this relationship indirectly (see e.g., [24–26]). Additionally, studies that have directly investigated the link between expectancies and avoidance behavior have yielded mixed results. While one study indicated that verbally induced pain expectations can lead to avoidance behavior in individuals with chronic low back pain,[27] another study indicated that even when expectancies are learned, healthy participants do not fully engage in avoidance behavior.[28] Thus, it is unclear whether negative pain expectancies lead to more avoidance behavior.

Considering the relationship between expectancy and avoidance, the current work had a twofold aim which was investigated in two successive studies. The first aim was to experimentally investigate whether negative expectancy learning leads to hyperalgesia. If it is determined that negative expectancy learning led to hyperalgesia, then the following aim was to test whether costly pain-related avoidance behavior was increased by negative expectancies induced through verbal suggestions and experiential learning. It was expected that those with induced negative pain expectancies would report significantly higher pain and significantly more avoidance behavior than those without induced negative pain expectancies. Additionally, the role of individual baseline factors (e.g., fear, catastrophizing) on the relationship between expectancy and avoidance were explored.

Study 1

Methods Study 1

Design

In a between-subjects design, participants were assigned to either the experimental or control condition on an alternating schedule based on the order of participation in the study. The assignment was done automatically by the experiment program (OpenSesame) based on participant number (odd vs. even). Negative expectancies regarding the electrical pain stimuli were induced experimentally via verbal suggestions and conditioning for the experimental group, and no negative expectancies were induced for the control group. Electrical pain stimuli were used in this study as the study design required multiple repeated administration of the pain stimuli as well as to provide immediate reinforcement at a controlled and distinguishable intensity to the conditioned cues, similar to previous expectancy and avoidance related studies (e.g., [11,29,30]). The experiment consisted of five phases: the calibration phase, avoidance task familiarization phase, conditioning phase, hyperalgesia test phase, and the avoidance test phase (see Figure 1). Various experimenters were involved in this study consisting of (doctoral) students (100%) and mostly women (78%). The study was approved by the Psychology Research Ethics Committee (2021–02-20-A. W.M. Evers-V1–2988) and preregistered in the Netherlands Trial Register (NL9306) prior to the start of the study. There was no public nor patient involvement in the design, conduct, or analysis of Study 1 and Study 2.

Participants

Based on G-Power calculations, a total of 116 healthy participants were required for the study assuming that a significant avoidance effect would be reached using a chi-square analysis if at least 75% (proportion p2) of participants selected the avoidance task in the experimental group while 50% (chance level, proportion p1) of participants in the control group would select the avoidance task (two-tailed, $\alpha = 0.05$, power = 0.80, allocation ratio N2/N1= 1). Participants between the ages of 18–35 were recruited via the research participation system of Leiden University (SONA Systems Ltd.), electronic advertisements, flyers, social media platforms, and via word of mouth. Any participant who met the inclusion criteria was welcome to participate in the study regardless of background (e.g., gender, education). Based on self-reports, participants were excluded if they were diagnosed with chronic pain (pain duration $>$ 3 months); had (previously diagnosed) psychiatric or neurological conditions; used recreational drugs more than three times a month; had upper body disabilities; were colorblind; used pacemakers; and were pregnant or breastfeeding. Participants were also excluded during the calibration procedure if they did not reach a pain level that took some effort to tolerate before reaching the maximum current of 8 mA, were too sensitive to the pain stimulation, and/or could not discriminate between the high and medium intensity electrical pain stimuli used in the study (see *procedure* for more details). All participants provided informed consent and were compensated via monetary reimbursement or SONA course credits.

Procedure

Upon registration of the study, potential participants were sent an information letter via email that contained information regarding the study procedure. As the study was conducted during the COVID-19 pandemic, participants underwent a COVID-19 screening prior to participation. Only participants without COVID-19 symptoms were invited to participate in the lab. Upon arrival in the research lab, participants were informed about the study verbally. They were told that

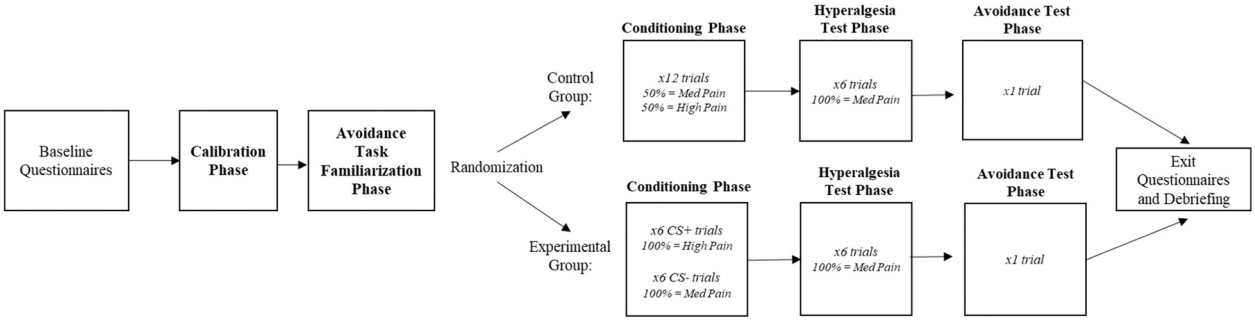

Fig. 1. Overview of Study 1 design. Participants began the experiment by answering baseline questionnaires that consisted of demographic and psychological measures. Then participants underwent a calibration phase to individually tailor the electrical pain stimuli used in the experiment. In the avoidance task familiarization phase, participants played a game called Tower of Hanoi at different levels of complexity and were subsequently randomized to one of the two groups: control and experimental group. After undergoing the last three phases of the experiment (conditioning, hyperalgesia, and avoidance test phase), participants answered a set of exit questionnaires and were debriefed.

the aim of the study was to assess how pain influences cognitive task performance and that they would play a game and experience individualized pain stimuli. Participants signed the consent form if they agreed to participate in the study.

Subsequently, participants were asked to complete a set of baseline questionnaires regarding demographics and psychological measures. After the baseline questionnaires were completed, two electrodes were attached to the participants non-dominant arm, and the calibration phase began.

Calibration phase. To determine participants' individual pain level that took some effort to tolerate, a stepwise calibration procedure was used in which the stimuli were administered for 10 s each, starting from a low intensity (0.5 mA) with 0.5 mA increments for every step, and a 30 s break between each stimulus. After each stimulus, participants were asked to rate their pain on a 0–10 numerical rating scale (NRS) with 0.5 intervals. A score of 0 indicated *"no pain"* and a 10 indicated "*worst pain imaginable*." Participants were asked to continue the step-up procedure until they reached a pain level that took some effort to tolerate as indicated by the participants – this was used as the high intensity stimulus during the study. A medium intensity stimulus was defined as the stimulus that the participants rated as medium pain (i.e., between 3 to 5.5 on the NRS) provided that the current intensity was at least 1.5 mA lower than the high intensity stimulus. If the participants did not reach a pain level that took some effort to tolerate before reaching the maximum current (8 mA), then the electrodes were readjusted, and the step-up procedure was repeated. Participants who did not reach a pain level that took some effort to tolerate after the second step-up procedure were excluded from the study.

To ensure that participants could differentiate between the two stimulus intensities, the participants were given the medium and high stimulus once each at random. They were then asked to rate the pain intensities of each of the stimulus to confirm that they could discriminate between the two stimuli, i.e., rating the high stimulus higher than the medium stimulus. Participants who could not differentiate the two stimuli were given the discrimination test again using a medium intensity stimulus that was 0.5 mA lower than the initial medium intensity current. Participants who were unable to differentiate the two stimuli after the second discrimination test were also excluded from the study.

Avoidance task familiarization phase. Once the pain intensities were calibrated, participants were asked to play *Tower of Hanoi*. This game consisted of three poles and multiple discs of different sizes with the largest disc at the bottom, and smallest at the top. The goal of the game was to move the discs one at a time from the starting pole (left-most pole) to the end pole (right-most pole) and recreate the tower in the same order. Participants were not allowed to place a smaller disc on top of a larger disc. The game was adjusted based on three difficulty levels: 4 discs, 5 discs, and 6 discs. Participants could explore each level for about two minutes each. For each level, participants were asked to rate "*How difficult did you find the game with 4 discs/5discs/6discs?*" on an NRS scale ranging between 0 and 10 (0 = *not difficult*, 10 = *difficult*). No electrical stimuli were administered in this phase.

Conditioning phase. During the conditioning phase, a third (sham) electrode was placed on the participants' arm. Participants were randomized to the control or experimental group and received separate instructions regarding the third (sham) electrode before the start of the conditioning phase.

Experimental group. In line with the conditioning procedure, participants in the experimental group were told that the electrical stimulus intensity would differ based on the activation of the third electrode. The activation of the third electrode could be identified based on the colored circles (yellow or purple) presented on the screen. One of the colors would act as the conditioned cue (CS+) where it would be paired with a high intensity stimulus, and the other would act as the control cue (CS-) where it would be paired with a medium intensity stimulus. Both colors were semi randomized in that, for half of the participants in the experimental group, the purple cue acted as the CS+, and the yellow cue acted as the CS-. For the other half of the group, the opposite was true. In reality, the third electrode did not control the intensity of the pain stimulus.

Control group. Participants in the control group were not told the purpose of the third electrode to avoid any verbal suggestions. Instead, participants were only told that the electrical stimuli would be delivered through the surface electrodes, including the third electrode. Additionally, the high and medium stimulus intensities were semi-randomized in that both color cues were paired evenly with a high and medium intensity to avoid conditioning.

The conditioning phase consisted of twelve trials. Each trial began with a question asking participants "*How much pain do you expect to feel when you see the color cue below?*" on an NRS scale of 0 *(no pain)* to 10 *(worst pain imaginable),* with 0.5 intervals to measure pain expectancies. Induced pain related fear was rated with the question "*How afraid are you of the upcoming stimulus when you see the color below?*" on a scale of 0 *(no fear)* to 10 *(worst fear imaginable)* with 0.5 intervals. No electrical stimuli were administered during these questions. Upon responding to the two questions, the color cues and the corresponding electrical pain stimulus were administered for 10 s simultaneously. After each stimulus pair, participants were asked to rate the level of pain intensity they experienced (i.e., "*How much pain did you experience?*") on a scale of 0 (*no pain*) to 10 (*worst pain imaginable*). Of the twelve trials, the purple and yellow color cues were displayed six times each in random order, with 30 s of interstimulus interval in between each trial.

Hyperalgesia test phase. The hyperalgesia test phase was identical for participants in both groups but consisted of only six trials with stimulus intensities set at a medium level for both CS+ and CS-. At the end of the conditioning phase and hyperalgesia test phase, participants were asked to rate how aversive they found the stimuli (on a scale of 0 to 10), and whether their expectation was lower, the same, or higher than expected.

Avoidance test phase. The avoidance test phase consisted of one trial. First, participants were asked again how much they expected to feel pain, and their level of stimulus related fear towards each of the color cues. Then they were asked to choose one of the Tower of Hanoi game levels to play. The choices were presented on a computer monitor where two colored circles (i.e., the CS+ and CS-) were displayed side by side. The middle of the colored circles contained a text of the Tower of Hanoi

Fig. 2. Display of game selection in the avoidance test phase. The game selection display was the same in both groups, however, the pairing of the color cue and the games depended on the condition that participants were assigned to. In Study 1, the text [Easy Game] was replaced with the game level that participants rated as easiest (e.g., "4 discs") and [Hard Game] was replaced with game level rated as most difficult (e.g., "6 discs"). In Study 2, the text [Easy Game] was replaced with "Open Game" and [Hard Game] was replaced with "In Box Game.".

game level (see Figure 2). Both groups were asked to select either the easy game or the difficult game. The current study tried to replicate the ecological setting as much as possible by including a cost to performing the avoidance behavior. Prior to the start of the project, the game was pilot tested alongside different pain intensities to validate that the expectation of a high intensity stimulus could lead to avoidance behavior, even when performing the avoidance behavior was associated with a cost (time and task difficulty). The pairing between the stimulus intensity, color cue, and game difficulty differed between the experimental and control group.

Experimental group. For this group, the easy game text was presented in the middle of the CS+ colored circle, whereas the difficult game text was presented in the middle of the CS- colored circle. Thus, based on previous associations between the color cues and the electrical stimulus, participants had a choice between selecting the easy game and receiving the high pain stimulus or avoiding the high pain stimulus by playing the difficult game and receiving the medium pain stimulus.

Control group. The game text, color cues, and stimulus intensities were semi-randomized between participants on an alternating schedule, in that for some participants the difficult game text was paired with the yellow circle and the easy game text was paired with the purple circle, whereas for others, the game text and colors were reversed. Thus, each participant had a 50/50 chance of receiving the high stimulus, no matter which choice they selected.

Participants were informed that upon selecting the game, they would receive an electrical pain stimulus and were asked to complete the game they selected. The electrical stimulation began immediately for a duration of 10 s after a selection was made. Once the game was finished, the participants were asked to complete an exit questionnaire which consisted of questions regarding the experiment, how enjoyable they found the Tower of Hanoi game, and the level of pain at which participants generally engaged in avoidance behavior (using an NRS). At the end of the exit questionnaires, participants were debriefed both verbally, and via a debriefing letter shown on the screen.

Materials and measures

Demographic measures. Demographics for each participant were collected as part of the baseline questionnaires. Participants were asked to indicate their age, gender, handedness, and education level.

Psychological measures. The psychological measures were included as part of the baseline questionnaires to assess the correlations between psychological states, the pain ratings, and avoidance behavior. It included a set of questions measuring pain catastrophizing, state anxiety, fear of pain, and pain vigilance.

Pain catastrophizing. The Pain Catastrophizing Scale (PCS) was used to measure the level of pain catastrophizing. It consists of 13 statements to describe thoughts associated with pain e.g., "*I feel like I can't go on*"; "*I anxiously want the pain to go away*." Participants were asked to indicate to what degree they experience these thoughts on a scale of 0 indicating *none at all* to 4 indicating *all the time*. A total score of the PCS was obtained by summing the scores on each response. Higher scores indicate higher catastrophizing.[31]

State anxiety. The state component of the State-Trait Anxiety Inventory (STAI-S) was used to measure state anxiety. It consists of 20 statements such as "*I am tense*", "*I feel secure*", "*I feel nervous*." Participants were asked to indicate how they felt when reading these statements on a Likert scale from *almost never, sometimes, often,* to *almost always*. A total score of the STAI-S was obtained by assigning a score and summing each of the responses. Higher scores on the STAI indicate high anxiety.[32]

Fear of pain. The Fear of Pain Questionnaire (FPQ-III) was used to measure fear of pain, and it consists of three subscales: dental pain, minor pain, and severe pain. This study only used the minor pain questionnaire which consists of 10 statements that describe painful experiences such as "*burning your fingers with a match*", "*having muscle cramp*", and "*biting your tongue while eating*." Participants were asked to indicate how fearful they were of these experiences on a scale from *not at all, a little, fair amount, very much,* to *extreme*. Each response was given a score and summed to calculate a final subscale score in which higher FPQ-III scores indicated higher fear of minor pain.[33]

Pain vigilance. The Pain Vigilance and Awareness Questionnaire (PVAQ) was used to measure pain vigilance. It consists of 16 statements such as "*I am very sensitive to pain*", "*I find it easy to ignore pain*" and "*I know immediately when pain starts or increases*." Participants were asked to indicate how frequently the statements reflect their behavior on a scale of 0 to 5 with 0 indicating *never*, and 5 indicating *always*. Scores of each individual response were summed to result in a total final score. In this case, higher scores indicate higher pain vigilance and awareness.[34]

Pain stimulus. Electrical stimuli were administered through two surface electrodes using a Digitimer DS5 constant current stimulator (Digitimer Ltd., Welwyn Garden City, UK). The two surface electrodes by VCM Medical (2×10 mm diameter) were placed about 0.5 cm apart at the center of the dorsal side of the non-dominant arm. A different (sham) third electrode (2 cm diameter) was placed on the dorsal side of the participants' arm about 2 cm distal to the stimulus electrodes. The stimuli were administered for 10 s at a 0.4 ms pulse duration and 50 Hz frequency,[35] with 30 s between each stimulus.

The participants received a total of 19 pain stimuli: 12 in the conditioning phase, 6 in the hyperalgesia test phase, and 1 in the avoidance test phase. Medium and high stimulus intensities were determined based on the individual calibration (see *Calibration Phase*). The maximum current of the electrical stimuli was set at 8 mA.

Software and hardware. The experiment was programmed in Python using OpenSesame version 3.3.10,[36] which controlled the visual and electrical stimuli through a Signal Generator (created by the Lab Support team at Leiden University) that connected to the Digitimer DS5. The calibrated stimulus intensity was entered manually for each phase. The questionnaires were displayed via an electronic survey tool (Qualtrics, Provo, UT, USA) on a Dell intel core i3 desktop computer monitor.

Statistical analysis

All analyses were performed using SPSS version 24.0 for Windows (SPSS Inc. Chicago, USA). To test for baseline differences between two groups, chi-square tests and independent sample t-tests were performed on demographics data (age, gender, and education level). Means of NRS scores for pain, expectancy, and induced fear in the conditioning and hyperalgesia test phases were calculated and prepared using R (R Core Team, Vienna, Austria). All variables included in the analyses were checked for outliers, missing values, normality, and sphericity. Assumptions for each analysis were met unless indicated otherwise. All analyses were tested two-sided with $p < 0.05$ set as the level of statistical significance.

To assess whether negative expectancy learning led to expectancy induced hyperalgesia, a repeated measures analysis of variance (RM-ANOVA) was performed with "group" (experimental vs. control) as the between subjects' factor and "color-cue" (average pain expectancy ratings of the CS+ vs. CS- during the conditioning phase) as the within-subjects factor to check the effectiveness of the verbal suggestions and conditioning procedure. Then, the same RM-ANOVA procedure was performed with the average pain ratings associated with each color cue in the hyperalgesia test phase as the within-subjects factor.

To test whether the experimental group indeed showed higher avoidance behavior compared to the control group, a chi-square test was used to measure the proportion of participants that selected the easy game and the hard game between groups.

In line with the preregistration, exploratory analyses were also

conducted for those in the experimental group where it was first explored whether individual factors (i.e., PCS, PVAQ, FPQ-III, and STAI-S) moderated the relationship between negative expectancy and hyperalgesia, and negative expectancy and avoidance behavior by performing separate moderation analyses using PROCESS model 1.[37] Additionally, this study explored whether induced fear mediated the relationship between negative expectancy and hyperalgesia, and whether negative expectancy mediated the relationship between group and avoidance behavior. Mediation analyses were performed using PROCESS model 4.[37] The first mediation analysis was done with negative expectancy as the predictor, hyperalgesia as the outcome, and induced fear ratings as the mediator. The second mediation analysis was conducted with group assignment (experimental vs. control) as the predictor, avoidance behavior as the outcome, and negative expectancy as the mediator.

Finally, this study explored whether individual factors correlated with hyperalgesia, negative expectancy, and avoidance behavior. Pearson correlation coefficients were calculated for those in the experimental group between individual factors, negative expectancy, and hyperalgesia. Additionally, point biserial correlations were calculated between individual factors and avoidance behavior as the avoidance outcome was binary. For all exploratory analyses, the variables negative expectancy, hyperalgesia, avoidance behavior, and induced fear, were all calculated by computing a difference score in which the average CS+ responses were subtracted by the CS- responses for each variable in the hyperalgesia test phase.

Results Study 1

Participant characteristics

A total of 148 participants were recruited for the current study. Of those, 21 were excluded due to not reaching a pain level that took some effort to tolerate, 3 were excluded due to high sensitivity to the electrical stimulus, 3 were excluded because they were unable to discriminate between the two electrical stimuli, and 5 were excluded due to technical/experimenter error. The final sample consisted of 116 participants as planned based on sample size calculations. A description of these participants can be seen in Table 1. The differences between group means at baseline were not statistically significant.

Electrical stimulation ratings

On average the current used for the high stimuli was 5.7 mA, and the current used for the medium stimulus was 3.5 mA. On average participants rated the high stimulus as a 7 on the NRS, and the medium stimulus as a 4.6 on the NRS. Average pain, expectancy, and induced fear ratings for each stimulus can be found in Table 2.

Table 1
Individual characteristics of participants in Study 1.

	Experimental (N = 58)	**Control** (N = 58)
Age (M(SD))	21.3(2.7)	21.2(3.2)
Gender female[a] **(N(%))**	45(77.6)	52(89.7)
Education Level (N(%))		
Primary Education	-	-
Secondary Education	10(17.2)	8(13.8)
Tertiary Education	45(77.6)	49(84.5)
Missing	*3(5.2)*	*1(1.7)*
FPQ-III score (M(SD))	23.1(5.1)	23.1(6.1)
PVAQ score (M(SD))	32.6(10.1)	32.3(10.9)
STAI-S score (M(SD))	33.9(8.3)	39.2(8.1)
PCS score (M(SD))	16.7(8.9)	17.8(8.9)

Note. M = Mean; SD = Standard Deviation; N = Number of Participants; FPQ-III = Fear of Pain Questionnaire (scale ranges from 10 to 50); PVAQ = Pain Vigilance and Awareness Questionnaire (scale ranges from 0 to 80); STAI-S = State subscale of the State Trait Anxiety Inventory (scale ranges from 20 to 80); PCS = Pain Catastrophizing Scale (scale ranges from 0 to 42).

[a] One non-binary participant in the control group.

Table 2
Descriptive statistics of the pain, expectancy, and induced fear variables for Study 1.

	Experimental (N = 58)				**Control** (N = 58)			
Conditioning Phase	*Pain*		*Induced Fear*		*Pain*		*Induced Fear*	
	CS+	*CS-*	*CS+*	*CS-*	*"CS+"*	*"CS-"*	*"CS+"*	*"CS-"*
Mean	6.5	3.4	4.8	2.6	5.1	5.3	3.7	3.9
SD	1.3	1.9	2.2	1.9	1.4	1.2	1.9	1.9
Hyperalgesia Test Phase	*Expectancy*		*Induced Fear*		*Expectancy*		*Induced Fear*	
	CS+	*CS-*	*CS+*	*CS-*	*"CS+"*	*"CS-"*	*"CS+"*	*"CS-"*
Mean	6.2	3.4	4.2	2.3	5.1	5.4	3.7	4.0
SD	1.4	2.0	2.4	2.0	1.5	2.0	2.2	2.4

Note. SD = Standard Deviation. All outcomes are between a scale of 0 – 10 with higher numbers indicating higher pain, expectancy, and induced fear.

Expectancy manipulation check

Results of the RM-ANOVA indicated a significant interaction between color cue type and group in the conditioning phase ($F(1,114) = 90.82$, $p < 0.001$, $\eta_p^2 = 0.44$). Participants in the experimental group had higher negative pain expectancies associated with the CS+ (M = 6.4; SD = 1.2) than the CS- (M = 3.6; SD = 1.7), whereas participants in the control group had similar levels of pain expectancy between the "CS+" (M = 4.7; SD = 1.4) and "CS-" (M = 5.1; SD = 1.5). A paired sample t-test showed a significant difference in the pain expectancy associated with each color cue in the experimental group [$t(57) = 10.88$, $p < 0.001$], but not for the control group [$t(57) = -1.68$, $p = 0.10$], suggesting that the expectancy manipulation was successful in the conditioning phase.

Main results

Hyperalgesia test. Results of the RM-ANOVA indicated a significant interaction between color cue type and group in the hyperalgesia test phase ($F(1,114) = 34.08$, $p < 0.001$, $\eta_p^2 = 0.23$). Participants in the experimental group rated the pain stimuli associated with the CS+ (M = 4.5; SD = 1.9) higher than the CS- (M = 3.4; SD = 2.0), whereas participants in the control group had similar levels of pain for the "CS+" (M = 4.1; SD = 1.8) and "CS-" (M = 4.2; SD = 2.0). A paired sample t-test showed a significant difference in the pain ratings associated with each color cue in the experimental group [$t(57) = 6.01$, $p < 0.001$], but not in the control group [$t(57) = -1.21$, $p = 0.23$], suggesting that hyperalgesia was only present in the experimental group.

To follow up, a post-hoc analysis was conducted to see whether negative expectancies predicted hyperalgesia for those in the experimental group. Results of a linear regression indicated that negative expectancies did indeed predict hyperalgesia for those in the experimental group ($p < 0.001$).

Avoidance effect. In total, 25 participants selected the difficult game. Of those, 9 (16%) were in the control group and 16 (28%) were in the experimental group. Based on the chi-square test of independence, results indicated there was no significant effect on the relation between experimental condition and game selection $X^2(1, N = 116) = 2.50$, $p = 0.11$. Those in the experimental group were not more likely to choose the difficult game than the easy game as opposed to the control group.

Exploratory analyses

Moderation analyses. Results of the moderation analyses indicated that none of the individual baseline factors moderated the relationship between negative expectancy and hyperalgesia (all $p > 0.05$). Similarly, none of the individual baseline factors moderated the relationship between negative expectancy and avoidance behavior (all $p > 0.05$).

Mediation analyses. Results indicated a significant indirect effect of negative expectancy on hyperalgesia through fear $b = 0.19$, BCa CI[0.01, 0.32], indicating that induced fear mediated the relationship between negative expectancies and hyperalgesia (Figure 3). As there was no significant main effect on avoidance behavior, mediation analyses were not conducted to test whether there was an indirect effect of group on avoidance behavior through negative expectancies.

Correlation analyses. Exploratory correlations between individual characteristics (i.e., baseline fear of pain, pain catastrophizing, pain vigilance, and state anxiety), hyperalgesia, avoidance behavior, and negative pain expectancies can be seen in *Supplementary File* Table S1. Overall, there was no significant correlation between these variables. However, there was a significant weak positive correlation between pain catastrophizing and avoidance behavior.

Discussion Study 1

Study 1 investigated whether negative expectancies can increase pain, resulting in hyperalgesia, and whether these negative expectancies led to avoidance behavior. The results indicated that negative expectancies did indeed lead to hyperalgesia, however, it did not lead to more avoidance behavior. This may be due to a few factors. First, although participants in the experimental group had higher negative expectancies regarding the CS+ compared to the CS- in the avoidance test phase, the level of expectancy was not as high as it was during the conditioning phase, indicating that extinction may have occurred throughout the experiment. Second, as the visual stimuli were presented in a new context during the avoidance test phase, it could be that participants were not consciously aware of what the combination between the color cues and game levels entailed, especially given that the avoidance test phase only consisted of one trial. Having additional trials in the avoidance test phase would allow participants to learn the association between game, color cue, and pain stimulus in a new context. Finally, based on exit interviews, some participants expressed that even if they knew that the CS+ would lead to higher pain, they would rather endure more pain for 10 s, than finish the difficult game as they found the game too difficult. On the other hand, some participants expressed that they selected the difficult game because they found the challenge of completing the game more enjoyable. These reasons indicated that there may have been an imbalance between the cost of the high pain stimulus and the cost of playing the difficult game. Therefore, the current avoidance paradigm may not have been optimal to assess pain avoidance behavior.

Study 2

Overview Study 2

Given the limitations of Study 1, Study 2 aimed to improve the avoidance paradigm to further understand the relationship between negative expectancies, pain, and avoidance behavior. To address the first limitation, the conditioning procedure was changed from a continuous reinforcement schedule to a partial reinforcement schedule as there has been evidence demonstrating that a partial reinforcement schedule may be less susceptible to extinction effects.[38,39] Additionally, to further prevent the risk of extinction, reacquisition trials were added after the hyperalgesia test phase and throughout the avoidance test phase. The number of avoidance trials were also increased to allow the participants to experience the association between the game and the color cues in a new context. Finally, the avoidance task was adapted so that both tasks had the same difficulty level (4 discs), but one task was made more aversive than the other by playing it in a different manner. This was done to adjust the balance between the cost of the pain stimuli and the game.

As many participants were excluded in Study 1 due to lack of sensitivity to the pain stimulation, minor adjustments were also made to increase the inclusion rate by adapting the calibration procedure, increasing the maximum mA, decreasing the duration of electrical stimulation, and changing the location of the electrodes.

Finally, as there were indications on the role of fear in the relationship between negative expectancy and hyperalgesia in Study 1, the role of fear was further explored in Study 2 by adapting the exploratory aims. More specifically, in addition to the primary aims, this study explored whether the same individual factors as in Study 1 also correlated with induced levels of fear. Another aim was to explore whether individual baseline factors moderated the relationship between negative expectancy and avoidance behavior, as well as the relationship between induced fear and avoidance behavior. Finally, this study explored whether induced fear and negative expectancy mediated the relationship between group and pain (i.e., hyperalgesia), and group and avoidance behavior.

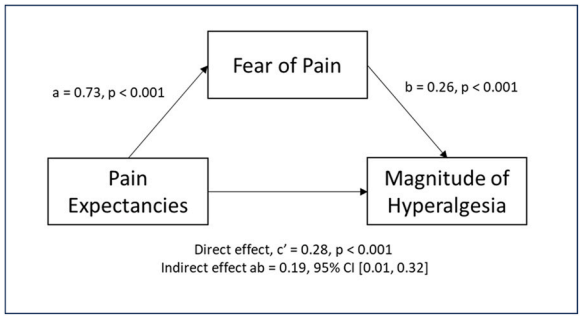

Fig. 3. Mediation model of pain expectancies on hyperalgesia through fear of pain.

Methods Study 2

Design

Like Study 1, this study used a between-subjects design with two conditions (experimental vs. control). Randomization was done in the same way as Study 1, and the experiment consisted of the same five phases as Study 1 (see Figure 4). As opposed to Study 1, the conditioning phase consisted of 24 trials as the current study employs a partial reinforcement procedure, thus requiring additional trials to ensure learning. Furthermore, the avoidance test phase consisted of 12 trials. The duration of the pain stimuli in this study was 2 s as opposed to 10 s to reduce habituation. The order of the questions between trials and the duration of the interstimulus interval was the same as in Study 1. Different experimenters were involved in this study that consisted of (doctoral) students (100%) and mostly women (92%). This study was approved by the psychology research ethics committee (2024–04-24- A. W.M. Evers-V1–5459). The preregistration was published prior to the start of this study and can be found on Open Science Framework (https://doi.org/10.17605/OSF.IO/6NEK9).

Participants

In this study, power calculations using G-Power indicated that a total of 128 participants were required for the study to reach a significant medium sized avoidance effect for a Kruskal-Wallis test. A Kruskal-Wallis test was selected as the avoidance measure consisted of ordinal data. The power calculations were conducted in G-power using the parametric equivalent of the Kruskal-Wallis test, i.e., a one-way ANOVA ($d = 0.25$, $\alpha = 0.05$, power $= 0.80$, number of groups $= 2$). The recruitment and inclusion criteria of this study were the same as in Study 1.

Procedure

Contrary to Study 1, participants in this study did not have to

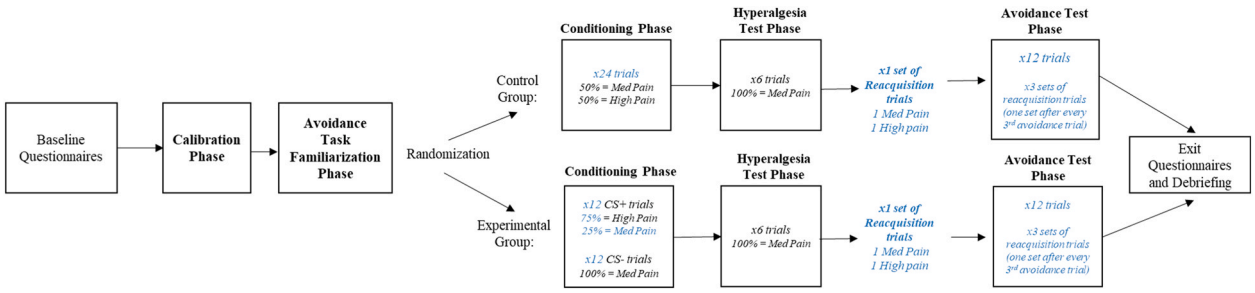

Fig. 4. Overview of Study 2 Design. Blue texts denote changes made from Study 1. Contrary to Study 1, a partial reinforcement schedule was used in the conditioning phase. Additionally, reacquisition trials were included between the hyperalgesia test phase and the avoidance test phase.

undergo a COVID-19 screening upon arrival. The remaining part of the baseline phase was identical to Study 1. Changes were made to improve the calibration phase, avoidance task familiarization phase, conditioning phase, and avoidance phase.

Calibration phase. The calibration phase consisted of a stepwise calibration procedure. However, in this study, the stimulus intensity increased in 0.5 mA increments every step until 5 mA, after which the stimulus intensity increased by 1 mA increments to a maximum of 15 mA. Participants were asked to rate each stimulus on a scale of 0 to 10 after each stimulus, as in Study 1.

Once participants reached a pain level that took some effort to tolerate, the stepwise procedure was repeated starting from the first current in which participants rated as a medium pain (between 3–5.5 on the NRS). The stepwise procedure continued until the participants reached a new level that took some effort to tolerate. This current was used as the high pain stimulus for the rest of the calibration phase. This procedure was done to minimize the effect of habituation to the pain stimulus during the main experiment.

Once the medium and high pain stimulus intensities were determined, participants underwent the same discrimination task as in Study 1 in two rounds. In the second round, 0.5 mA was added or removed from either the medium and/or high stimuli in case participants gave significantly higher or lower ratings than in the first discrimination task round. The remaining calibration procedure was the same as in Study 1.

Avoidance task familiarization phase. Similar to Study 1, participants were asked to play the *Tower of Hanoi*. However, for this study, only two versions of the same Tower of Hanoi game (4 discs) were used. In one version, the game contained 4 discs with noticeably different sizes, to allow for easy differentiation of the discs. For the remainder of this procedure, this version will be referred to as the "Open" game. In another version, the game also contained 4 discs, but the size of the discs was harder to differentiate. In addition, this game was set up inside a box in front of a monitor. This version is referred to as the "In Box" game. For this version, participants were only able to see the game through a computer monitor. In the monitor, the display was reversed, meaning that any action performed was the opposite. For example, if the participant moved the piece to the left, then the monitor displayed that they moved the piece to the right. The In Box game was pilot tested to ensure that game could be solved in the same way as the Open game but was made more aversive through the reversed action.

No stimuli were administered in the Avoidance Task Familiarization phase. Participants were allowed to explore the task for a duration of 3 min for each version. If the participants finished before 3 min, they were instructed to start the game again until the 3 min had finished.

Conditioning phase. The participants were assigned to either the control or the experimental group in the same way as in Study 1, and they received verbal instructions before starting the conditioning phase.

Experimental group. The same color cues as in Study 1 were used in this study. However, in this study, a conditioning procedure with partial reinforcement was used to minimize extinction effects. Participants were told that the third electrode would increase the pain intensity *most of the time* if turned on. The participants were told that the third electrode could turn on when the CS+ color (yellow or purple) was displayed on the screen, thus the participants might feel a high intensity of pain. Contrary to Study 1, the CS+ was only reinforced with higher pain in 75% of the trials (i.e., 9 out of 12 trials), while the other 25% of the CS+ trials (3 out of 12 trials) were reinforced with medium pain. The participants were also told that when the CS- was displayed, the third electrode had been turned off. Here the CS- was reinforced with medium pain in 100% of the trials. In truth, the third electrode was always off and did not control the intensity of the pain stimulus.

Control group. The procedure for the control group was the same as in Study 1.

Hyperalgesia test phase. The hyperalgesia test phase was identical to Study 1. At the end of the hyperalgesia test phase, two reacquisition trials were administered, in which participants were shown the CS+ again while receiving a high stimulus, and the CS- again while receiving a medium stimulus. The pairing between the color cue and the pain stimuli was semi-randomized for participants in the control group (i.e., both color cues were paired evenly with a high and medium intensity).

Avoidance test phase. As opposed to Study 1, the avoidance phase consisted of 12 trials. In this phase, participants were asked to make a choice between the same two choices as in Study 1, with the exception that instead of the Tower of Hanoi levels, the texts displayed inside the color cues were "Open Game" (reflecting the easy game) or "In Box Game" (reflecting the difficult game). Participants were told "*we will ask you to play the game that you select at several different times, however you will not know at which times this will happen*" but in reality, participants were only asked to play the game that they have selected two times out of the 12 trials. Participants played the Open Game once at a random time and the In Box Game once as soon as it was selected, provided that the participant chose each version of the game at least once within the 12 trials. In case participants selected only one version of the game, then participants would play the same game twice within 12 trials. Upon making a selection, participants received the medium pain stimulus for 2 s, regardless of the choice that they made. After receiving the pain stimulus, a new trial began, and participants were asked to make another selection. After the first selection, participants were asked to respond to an open-ended question asking, "*Why did you decide to select that choice?*".

After every third trial (i.e., after trial 3, trial 6, and trial 9) two reacquisition trials (one for each color cue) were administered. During these trials, participants in the experimental group were shown the CS+ again while receiving a high pain stimulus, and the CS- while receiving a medium pain stimulus. No game selection was made during reacquisition trials. For participants in the control group, the pairing between the pain stimulus and the color cues were equally randomized

each time to avoid any conditioning.

Materials and measures

The same demographic measures, psychological measures, software, and hardware were used in this study as in Study 1. The same settings were used for the pain stimuli, except that in this study, the electrodes were placed on the ventral side of the non-dominant arm. Additionally, a different electrode brand (Digitimer Ltd.) was used in this study with the same specifications as the electrodes in Study 1. All electrical stimuli were administered for 2 s, and the maximum current of the electrical stimuli were set at 15 mA.

Statistical analysis

All analyses were performed using SPSS version 29.0 for Windows (SPSS Inc. Chicago, USA) according to the preregistration protocol. The same analyses were used as in Study 1 with the addition that a Kruskal-Wallis test was computed to assess whether the experimental group indeed showed higher avoidance behavior compared to the control group. In this analysis, the variable "group" was used as the independent variable and avoidance behavior, defined as the number of times the difficult game (In Box), was selected as the dependent variable. A chi-square analysis was also conducted as a comparison analysis to the first study in which avoidance behavior was defined as the game selected on the first trial of the avoidance test phase. As the intended number of participants was not reached by the end of the project, Bayesian analyses were conducted post-hoc to supplement the main findings of the results to assess whether the results are more in favor of the null or alternative hypothesis. Bayes factors were reported alongside frequentist results. BF_{10} indicates that there is evidence in favor of the alternative hypothesis as opposed to the null hypothesis – BF_{10} was reported in case frequentist results showed a significant effect. Meanwhile, BF_{01} indicates that there is evidence in favor of the null hypothesis as opposed to the alternative hypothesis – BF_{01} was reported in case frequentist results showed a non-significant effect.

As exploratory findings revealed that negative expectancy predicted hyperalgesia in the first study, this relationship was also investigated as a secondary aim of this study using the same linear regression model as in Study 1.

In line with the preregistration, PROCESS Model 1 was again used to perform separate moderation analyses in this study.[37] The data was taken from those who were assigned to the experimental group. The baseline variables were calculated the same way as in Study 1, however, in this study, different predictors and outcome variables were used. The first predictor variable was negative expectancy, the second predictor variable was induced fear, and the outcome variable used was level of avoidance behavior.

PROCESS Model 4 was again used to perform separate mediation analyses in this study following the preregistration.[37] Negative expectancy and induced fear were used as the mediating variables, while group was used as the predictor variable and hyperalgesia was used as the first outcome variable, and avoidance behavior was used as the second outcome variable.

The same correlation analyses were performed as in Study 1, with the addition of induced fear. Additionally, Spearman's rank correlation was performed to assess the relationship between baseline variables and avoidance behavior. The variables negative expectancy, induced fear, and hyperalgesia used in the exploratory analyses were all calculated by computing a difference score of the average CS+ and CS- responses for each variable in the hyperalgesia test phase.

Results Study 2

Participant characteristics

A total of 128 individuals were recruited for this study. Of those individuals, 29 were excluded after the calibration phase due to inability to discriminate the high and medium stimulus ($N = 7$), having too high sensitivity to the electrical stimulation ($N = 15$), and low sensitivity to the electrical stimulation ($N = 7$). Additionally, one individual was excluded as they had participated in a different study with a similar design to the current one (the study advertisements indicated the prohibition of participating in both studies). Thus, the final sample size consisted of 98 participants. The participant characteristics for this sample can be seen in Table 3.

Electrical stimulation

On average, participants rated the high stimulus as a 7.0 on the NRS and the medium stimulus as a 3.8 on the NRS. On average, the current for the high stimulus used was 7.5 mA and the current for the medium stimulus used was 4.3 mA. Average pain, expectancy, and induced fear ratings for each color cue can be found in Table 4.

Expectancy manipulation check

Results of the RM-ANOVA revealed a significant interaction between color cue type and group in the conditioning phase ($F(1,96) = 117.28$, $p < 0.001$, $\eta_p^2 = 0.55$). Consequently, a paired sample t-test was performed to investigate whether there were significant differences in pain expectancies associated with the color cues between the groups. Results of the paired sample t-test showed a significant difference between expectancy ratings between the CS+ ($M = 6.6$; $SD = 1.2$) and the CS- ($M = 3.6$; $SD = 1.3$) for those in the experimental group [$t(48) = 15.52$, $p < 0.001$]. Furthermore, there was no significant difference in pain expectancy ratings between the "CS+" ($M = 5.2$; $SD = 1.5$) and the "CS-" ($M = 5.3$; $SD = 1.3$) for those in the control group [$t(48) = -0.35$, $p = 0.73$]. These results demonstrate that the conditioning expectancy manipulation with partial reinforcement was indeed successful, in line with the findings of Study 1.

Main results

Hyperalgesia test. Results of the RM-ANOVA revealed a significant interaction between color cue and group in the hyperalgesia test phase ($F(1,96) = 35.26$, $p < 0.001$, $\eta_p^2 = 0.27$, $BF_{10} = 217777.29$). Paired sample t-tests revealed that for those in the experimental group, there was a significant difference between pain ratings of the CS+ ($M = 4.5$; $SD = 1.8$) and the CS- ($M = 3.3$; $SD = 1.7$), [$t(48) = 7.45$, $p < 0.001$]. Furthermore, the experiment failed to show significant difference in pain ratings for those in the control group between the "CS+" ($M = 4.5$; $SD = 1.7$) and the "CS-" ($M = 4.4$; $SD = 1.7$), [$t(48) = 1.10$, $p = 0.28$]. The results demonstrate that participants in the experimental group did indeed experience hyperalgesia compared to those in the control group.

Table 3
Individual characteristics of participants in Study 2.

	Experimental (N = 49)	**Control** (N = 49)
Age (M(SD))	21.4(3.1)	20.9(2.9)
Gender female[a] **(N(%))**	41(83.7)	36(73.5)
Education Level (N(%))		
Primary Education	-	-
Secondary Education	6(12.2)	7(14.3)
Tertiary Education	43(87.8)	42(85.7)
Missing		
FPQ-III (M(SD))	22.4(6.5)	24.0(5.9)
PVAQ score (M(SD))	32.9(12.2)	34.9(8.6)
STAI-S score (M(SD))	35.0(8.7)	34.4(9.8)
PCS score (M(SD))	19.4(9.0)	20.4(8.8)

Note. M = Mean; SD = Standard Deviation; N = Number of Participants; FPQ-III = Fear of Pain Questionnaire (scale ranges from 10 to 50); PVAQ = Pain Vigilance and Awareness Questionnaire (scale ranges from 0 to 80); STAI-S = State subscale of the State Trait Anxiety Inventory (scale ranges from 20 to 80); PCS = Pain Catastrophizing Scale (scale ranges from 0 to 42).

[a] One non-binary participant in the control group and one preferred not to say in the experimental group.

Table 4
Descriptive statistics of pain, expectancy, and induced fear variables in Study 2.

	Experimental (N = 49)				**Control** (N = 49)			
Conditioning Phase								
	Pain		*Induced Fear*		*Pain*		*Induced Fear*	
	CS+	*CS-*	*CS+*	*CS-*	*"CS+"*	*"CS-"*	*"CS+"*	*"CS-"*
Mean	6.2	3.4	4.4	2.2	5.3	5.3	4.6	4.7
SD	1.2	1.5	2.1	1.5	1.1	1.1	2.1	2.0
Hyperalgesia Test Phase								
	Expectancy		*Fear*		*Expectancy*		*Induced Fear*	
	CS+	*CS-*	*CS+*	*CS-*	*"CS+"*	*"CS-"*	*"CS+"*	*"CS-"*
Mean	6.3	3.2	4.0	2.0	5.5	5.4	4.5	4.7
SD	1.6	1.6	2.5	1.6	1.8	1.6	2.5	2.4

Note. SD = Standard Deviation. All outcomes are between a scale of 0 – 10 with higher numbers indicating higher pain, expectancy, and induced fear.

Avoidance effect. A Kruskal-Wallis test indicated that there was no significant difference in avoidance behavior between those in the experimental group and those in the control group ($\chi^2(1) = 0.60$, $p = 0.44$, $BF_{01} = 2.981$). This finding was supported by Bayesian analyses which suggest that there is inconclusive evidence for an avoidance effect and weak to moderate evidence in support of the null hypothesis. On average, the participants in the control group selected the In Box game 4 times out of 12 trials, with 12 people selecting this game more than 6 times out of 12 trials (chance level). Those in the experimental group selected the difficult game on average 5 times out of 12 trials, with 17 individuals who selected the In Box game more than 6 times out of 12 trials (chance level). This was in line with the results of the chi-square test of independence which also showed no significant effect of avoidance behavior between the two groups ($X^2(1, N = 98) = 0.20$, $p = 0.65$). In total, there were 28 individuals who selected the difficult game during the first trial. Of these people, 15 (31%) were from the control group and 13 (27%) were from the experimental group. The open ended question that was administered after the first trial of the avoidance test phase asking participants why they made that selection revealed that participants made their selection based on the pain associated with a certain color cue (12%), the game difficulty/enjoyment (58%), a combination of the pain and the game (21%), and other reasons, e.g., curiosity, distance to cursor, random choice (8%).

Secondary aim analysis

Results of the linear regression showed a statistically significant model ($F(1, 47) = 10.80$, $p = 0.002$) with an adjusted R^2 of 0.17. This model indicates that expectations significantly predicted hyperalgesia ($t = 3.29$, $p = 0.002$). However, as the data violated the assumption of homoscedasticity, the results were analyzed again using a spearman rank correlation as a sensitivity check. Results of the spearman rank correlation also demonstrated a significant correlation between negative expectancies and hyperalgesia (*Spearman's Rho* = 0.45, $p = 0.001$).

Exploratory analyses

Moderation analyses. Results of the moderation analyses indicated that none of the individual baseline factors moderated the relationship between negative expectancy and avoidance behavior ($p > 0.05$). Similarly, none of the individual baseline factors moderated the relationship between induced fear and avoidance behavior ($p > 0.05$).

Mediation analyses. Results indicated a significant indirect effect of induced fear, indicating that fear mediated the relationship between group and hyperalgesia (Figure 5A). Additionally, results also indicated a significant indirect effect of negative expectancies, indicating that expectancies also mediate the relationship between group and hyperalgesia (see also Figure 5B). As there was no main effect of avoidance behavior, mediation analyses were not conducted to assess the indirect effect of group on avoidance behavior through induced fear and negative expectancies.

Correlation analyses. Exploratory correlation analyses showed no significant relationship between baseline factors (i.e., fear of pain, pain catastrophizing, pain vigilance, and state anxiety) and avoidance behavior nor negative expectancies (all $p > 0.05$). However, there was a weak positive correlation between baseline fear of pain and hyperalgesia ($p = 0.04$), a moderate positive correlation between baseline fear of pain and induced fear of pain during the hyperalgesia test phase ($p < 0.001$), and a weak positive correlation between pain catastrophizing at baseline and induced fear of pain ($p = 0.047$). For the complete results of the correlation analyses, see *Supplementary File* Table S2.

Discussion Study 2

Study 2 aimed to replicate the goals and design of Study 1 with improvements to the novel pain avoidance paradigm. Contrary to the hypothesis, although the novel pain avoidance task had been adjusted in this study, participants in the experimental group still did not perform more avoidance behavior than participants in the control group which may indicate that avoidance behavior is influenced by different factors. The implications of the findings from Study 1 and Study 2 are further discussed in the general discussion.

General discussion

In two successive studies, the current work investigated whether negative expectancies resulted in hyperalgesia as well as increased pain avoidance behavior. It was hypothesized that those with induced negative pain expectancies would report significantly higher pain and significantly more avoidance behavior than those without induced

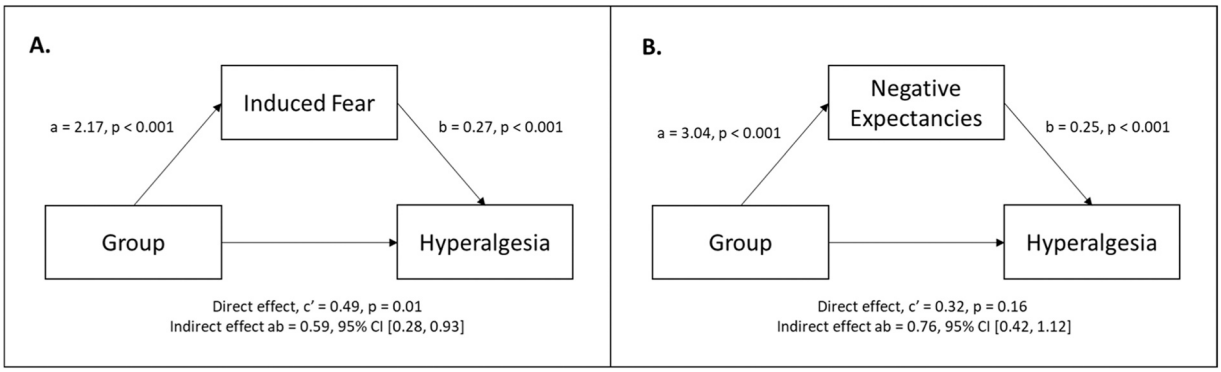

Fig. 5. Mediation model of group on pain through induced fear and negative expectancies.

negative pain expectancies. In line with the first hypothesis, results from both studies indicated that negative expectancies did indeed lead to hyperalgesia. However, contrary to the second hypothesis, both studies failed to show evidence that negative expectancies led to significantly more pain avoidance behavior. These results suggest that other factors may be at play in avoiding more pain in the pain avoidance paradigm.

The finding that negative expectancies led to hyperalgesia in both studies is in line with previous studies in the field of nocebo effects (e.g., [40–42]) demonstrating that the negative expectancy conditioning paradigm with both continuous and partial reinforcement produces robust results. These results indicate that negative expectation is a key factor in pain perception.[2,5]

Furthermore, the finding that negative expectancies did not lead to avoidance of more pain could indicate that under certain circumstances, negative expectancies may not necessarily be the main driver of avoidance behavior. One reason for the lack of avoidance behavior may be due to the cover story given to the participants. As participants were informed that the aim of the study was to assess the influence of pain on task performance, it could have led them to choose a game that they were more likely to succeed in even when it led to more pain. Another reason may be that in the novel pain avoidance task, participants had to endure pain (albeit one pain stimulus was higher than the other) regardless of the choice that they made. In other words, performing the avoidance behavior would not have led to the complete prevention of pain as participants still received medium pain, which may have been seen as a double cost with the decision to avoid. Kubanek and colleagues[43] have shown that a behavior is more likely to be performed with more rewards, but avoidance behavior is performed regardless of the magnitude of the costs. As both options in the avoidance paradigm led to a cost, perhaps instead of weighing the costs, participants made the decision based on the option that would lead to the most reward. Some evidence of this can be seen upon analyzing the reason why participants chose the difficult game over the easy game. Many answers were framed in view of the gains of making a certain choice (having less pain or playing a more enjoyable game), as opposed to the losses of making a decision (avoiding pain or avoiding a difficult game). Relatedly, as Study 2 utilized a conditioning procedure with partial reinforcement, participants in the experimental group may have been less certain of their expectations. Certainty has been shown to influence pain perception and behavior.[44–46] If participants were less certain of the outcomes of the color cues, then it could explain why participants would make a choice based on the games they preferred (in which the consequences were certain), rather than the pain that they may possibly receive.

Another related factor that may have influenced the results is the potential role of fear and catastrophizing. Overall, participants in both studies did not report high levels of induced fear in both conditioning and test phases. As participants were tested in a controlled environment and were repeatedly told that the stimuli they would be receiving were safe (albeit painful), it was likely that participants did not consider the painful stimuli to be harmful. Meanwhile, studies show that individuals tend to avoid certain stimuli due to perceived threat.[47,48] Thus, stimuli with higher threat value and induces more fear may be more likely to cause different levels of avoidance behavior. In line with previous studies,[29,42,49] some evidence on the potential importance of fear can already be seen in the mediation findings as fear was shown to be mediator between negative expectancies and hyperalgesia.

As this was one of the first studies to directly investigate the relationship between negative expectancies and avoidance behavior in pain, some limitations of the study should be discussed. First, as only individuals without chronic pain were included, it is still unclear whether the results can be generalized to a group of individuals with chronic pain. Additionally, the electrical stimulus used in this study was not comparable to clinical pain. Thus, the avoidance outcome could have been different if participants received a pain stimulus that was more comparable to clinical pain, such as pressure pain. Furthermore, despite the study being open to the public regardless of background (e.g., gender, education level), the sample was not representative of the general population as the study consisted mainly of young adults with a higher education background. Therefore, future studies could investigate the expectancy-avoidance relationship in a more heterogenous sample, including individuals with chronic pain using ecologically valid avoidance measures, for example by utilizing sensor data.[50,51] Relatedly, future studies should also consider controlling for experimenter effects as studies have shown that (professional) status, sex/gender, and non-verbal cues could influence pain outcomes (see review by Daniali and Flaten[52] for an overview). Finally, as Study 2 ended before the required sample size was reached, the results of Study 2 were limited in power. However, and despite the limited sample size, Bayesian analysis demonstrated that there was strong evidence in favor of the alternative hypothesis regarding hyperalgesia, and weak evidence in favor of the null hypothesis regarding avoidance behavior.

All in all, the current studies give insights into the relationship between two key mechanisms, namely expectancies and avoidance behavior, in pain perception and its maintenance. It shows that negative expectancies can be acquired through instructional and experiential learning, which can increase pain perception, but may not necessarily lead to more avoidance behavior. The results demonstrate that other factors may be a stronger predictor of pain avoidance behavior in participants without chronic pain. These findings illustrate the complex relationship between expectancies and avoidance behavior and the challenges of measuring costly avoidance behavior in the laboratory setting. Although a novel pain avoidance paradigm was used that approached the ecological setting as much as possible, it could not capture the many related factors including goals and motivations,[53–55] certainty,[44–46] and high levels of fear [42,56] that may play a role in the relationship between expectancies and avoidance behavior. These related factors should be considered in future studies that assess the relationship between expectancy and avoidance behavior to disentangle the interplay between expectancy and avoidance behavior in pain as a target in chronic pain treatment.

CRediT authorship contribution statement

Conceptualization: All authors; Methodology: All authors; Software: N/A; Validation: PGN & AIMvL; Formal Analysis: PGN; Investigation: PGN; Resources: AWME, JWSV, MLP, AIMvL; Data Curation: PGN & AIMvL; Writing – Original Draft: PGN; Writing – Review & Editing: All authors; Visualization: PGN; Supervision: AWME, AIMvL, MLP, JWSV; Project Administration: All authors; Funding Acquisition: AWME, JWSV, MLP, AIMvL.

Acknowledgments

We would like to thank all the LIBC interns, bachelor students, and master students involved in this project for their help in the data collection of both studies. Special thanks to Madelief Medema for her assistance in overseeing and training students involved in data collection.

Disclosure

This study is part of the project 'New Science of Mental Disorders' (www.nsmd.eu), supported by the Dutch Research Council and the Dutch Ministry of Education, Culture and Science (NWO gravitation grant number 024.004.016). The authors declare no conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2025.105506.

Data availability statement

Data collected for this work will be made available through a complete publication package in the DataverseNL repository at https://dataverse.nl/. The complete publication package includes datasets, codes and syntaxes used in the analysis, and other materials used in this paper. These datasets, codes, and materials can then be accessed by the public upon request.

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