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Highlights

- Instruction to avoid a painful heat stimulus increases pain-related fear
- Avoidance behaviour maintains pain-related fear
- Avoidance behaviour maintains threat value of the pain stimulus

The opportunity to avoid pain may paradoxically increase fear

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Abstract

Fear-avoidance models propose that pain-related fear may spur avoidance behaviour leading to chronic pain disability. Pain-related fear elicits avoidance behaviour, which is typically aimed at reducing fear. We hypothesized that engaging in avoidance may (paradoxically) increase rather than decrease pain-related fear (i.e. bidirectionality hypothesis). In a between-subject design, participants (*N*=64) were randomly assigned to the avoidance group or the control group. Avoidance group participants were led to believe they could avoid full exposure to a painful heat stimulus by pressing the stop-button, while control group participants believed they were exposed to the full painful heat stimulus at all times. In reality and unknown to the participants, the intensity and duration of the heat stimulus was independent of the avoidance response, and was identical in both groups. During the test, the avoidance response (i.e. pressing the stop-button) was no longer available. As expected, pain-related fear levels were higher after avoiding the painful heat stimulus. Interestingly, in the avoidance group, pain-related fear increased after receiving instructions that avoidance would be possible, even before actually engaging in avoidance behaviour. In the control group, no significant change was observed in pain-related fear throughout the experiment. The eyeblink startle measures did not corroborate this data pattern.

Perspective: These observations provide partial support for the bidirectionality hypothesis between avoidance behaviour and fear. These findings may have clinical implications and suggest that allowing avoidance behaviours during treatment may thwart fear reduction.

Key words: pain intensity; avoidance; pain-related fear; threat; heat pain

Introduction

It is commonly accepted that pain can occur in the absence of apparent tissue damage, which is often the case in chronic pain[17]. Furthermore, beliefs and expectations can influence the experience of pain[1]. The fear-avoidance model of chronic pain provides a cognitive-behavioural explanation on how acute pain may turn into chronic pain, and how pain and disability may be maintained[34,35]. The model emphasizes how catastrophic (mis)interpretation of pain elicits pain-related fear that in turn may spur avoidance behaviour leading to chronic pain disability. Recently, it has been proposed that engaging in pain avoidance may paradoxically increase pain-related fear, suggesting that the relationship between avoidance behaviour and fear may be bidirectional[36].

Fear refers to an immediate alarm reaction to a present threatening stimulus[3]. In the Encyclopedia of Pain, pain-related fear is described as "*a general term to describe different forms of fear with respect to pain*"[15]. Avoidance behaviour can be viewed as safety-seeking behaviour, which refers to a range of actions intended to detect, avoid, escape or neutralise a feared outcome[6,7]. Although safety-seeking behaviours that actually reduce threat are essential for survival and people's well-being[10], studies have shown that anxious individuals often conservatively employ these in the absence of objective danger[5,25]. In this way, the absence of expected danger may be erroneously misattributed to the safety-seeking behaviour, which prevents the disconfirmation of dysfunctional threat beliefs[25]. Anxious individuals might conclude that their own actions (i.e. their safety-seeking behaviours) prevent feared outcomes, thereby leading them to draw invalid conclusions about the situation, i.e. behaviour as information[14]. A recent study by Engelhard, van Uijen, van Seters and Velu[13] showed that safety-seeking behaviour directed towards a stimulus that was never paired with an unpleasant outcome paradoxically increased threat expectations to that stimulus when it was

subsequently presented in the absence of the safety-seeking behaviour. These findings indeed indicate that safety-seeking behaviour itself may bear threat-inducing properties.

The current study investigated the effect of avoidance behaviour on pain-related fear. We designed a between-subject study in which the opportunity to avoid was experimentally manipulated by creating the illusion to avoid a painful stimulus in one group (avoidance group), and not in another (control) group. However, the calibrated pain stimulus intensity or duration was identical for both groups, and did not change throughout the experiment. We hypothesized that (previous) avoidance of a painful stimulus serves as a source of information that further fuels pain-related fear. More specifically, our main hypothesis was that the prior possibility to avoid the pain stimulus increases fear (self-reported and startle), threat value, and intensity/unpleasantness of subsequent pain stimuli when the option to avoid is not available anymore. As our second hypothesis, we expected that the ability to avoid would attenuate pain-related fear and pain, despite identical physical stimulus intensity.

Methods

Participants

A total of 64 healthy, pain-free volunteers participated in the study (40 females; mean (range) ± SD age = 26.11 (18-59) ± 9.78 years). Participants were recruited at the KU Leuven, using social media and distribution of flyers around the campus. Psychology students received course credits for participation; other participants received a monetary compensation of €8,-. Participants were excluded if they reported to suffer from any cardiovascular disease, chronic pain conditions, pain at the non-dominant forearm, psychiatric disorders (current or in the past), neurological conditions or were pregnant. The Social and Societal Ethics Committee of KU Leuven approved the experimental protocol (registration number: G-2015 12 430). All participants provided a written informed consent, which stated that they were allowed to decline participation at any time during the experiment without any consequences.

Participants were randomly assigned to one of two experimental groups: the avoidance group (n=32, 22 females) or the control group (n=32, 18 females).

Apparatus

Phasic painful heat stimuli were generated by a Peltier element-based computer controlled thermal stimulation device (Medoc, TSA, RAMA Yishau, Israel), and delivered through a thermode surface of 30 x 30 mm^2 attached to the non-dominant medial forearm. Acoustic startle probes (white noise delivered at 102 dBA with instantaneous rise time 50 ms) were presented binaurally using headphones (Hoher, Stereo headphones, HF92) to evoke the eyeblink startle responses to measure pain-related fear[4].

Study protocol

Heat stimulus intensity was set at individual pain threshold using a calibration procedure based on a temperature protocol provided with Medoc software (previous studies have used a similar procedure[26,27]). During this individual calibration, a series of five heat stimuli were administered, starting at a temperature of 36 °C ramping up at a rate of 0.5 °C/s with a maximum temperature of 49 °C. To avoid temporal summation we used an intertrial interval of 30-35 s during calibration and the experiment, as well as a 2-minute break between the different experimental phases. Participants were instructed to stop the heat stimulus by pressing a stop-button, i.e. clicking the left computer mouse button, at the moment the stimulus became painful. The mean temperature of the last three trials of the calibration procedure was set as the pain threshold (PTH). After calibration, participants received a heat stimulus that was 1 °C higher than the pain threshold (PTH+1°C), and they were told that this was the maximum stimulus intensity they would receive during the remainder of the experiment. The heat stimulus always started at a baseline temperature of 10 °C below the

maximum intensity and ramped up with a rate of 0.5 °C/s to the individually determined maximum temperature and remained at that temperature level for 5 s. During each heat stimulus presentation, we provided visual feedback on the computer screen about the progress of the rising temperature of the heat stimulus, consisting of a vertical bar with the labels "baseline" at the bottom of the bar, and "maximum" at the top of the bar (see Figure 1 for an overview of the experimental design and trial structure). While the temperature was rising, the bar grew upwards and gradually coloured red. Depending on group allocation, we manipulated the visual feedback that was provided to the participant. During the *experiential learning phase*, all participants received two trials, during which the heat stimulus reached the maximum PTH+1°C temperature and the visual feedback displayed that the maximum temperature was reached. Next, two trials followed where the heat intensity reached the PTH temperature and the visual feedback stopped before it reached its maximum. This phase was included so participants experienced that the visual feedback on the screen corresponded to the experienced temperature on the arm. During the *full intensity phase*, all participants received three trials, during which the heat stimulus and visual feedback concurrently stopped at maximum intensity and thus at the top of the feedback bar. At the onset of the crucial *intervention phase*, participants in the avoidance group (n=32) were led to believe that they successfully could avoid the pain stimulus peak, and received the following instructions: "*As soon as you see the stop-cue on the screen, press the stop-button immediately to stop the heat stimulation"*. This cue was a stop sign presented next to the visual feedback bar on the screen. Next, three trials followed during which the visual feedback stopped before it reached its maximum when the avoidance response was triggered (i.e. stop-button press). In reality however, the participants in the avoidance group still received the maximum intensity heat stimulus, similar to the control group. Participants in the control group received no stop-cue or any instructions at the start of the intervention phase; they received three trials during

which the visual feedback again stopped at its maximum. Finally, during the *test phase*, three additional heat stimulations occurred where participants in the avoidance group were told: "*The stop-cue will no longer be presented, you cannot stop the stimulation anymore"*. Participants in the control group received no instructions during the test phase. Throughout the experimental phases, startle probes were presented during each trial (trial duration: 26.5 s): two during the painful heat stimulus (one in the beginning, between 2-8 s, and one towards the end of the stimulation, between 18-24 s), and one startle probe was presented randomly during the intertrial interval (ITI: 30-35 s, between 10 and 20 s).

- Insert FIGURE 1 about here -

Outcome measures

Dependent variables were self-reports assessing 1) pain-related fear, 2) threat value of the heat stimulus, 3) pain intensity, and 4) pain unpleasantness on a numerical scale (NRS) from 0 to 100. At the start of each of the three phases, all participants were asked to report how afraid they were of the next heat stimulation on a scale from 0 to 100, with the labels 0 = "not afraid at all" and 100 = "extremely afraid". Participants rated the threat value of the painful heat stimuli twice, i.e. before the experimental phases started (pre), and at the end of the experiment after the last painful heat stimulus (post). The questions assessing threat value were respectively: 1) "*To what extent do you think the heat stimuli will be harmful to the skin?"*, and 2) "*How harmful to the skin did you think the heat stimuli were?"*. On a trial-by-trial basis, participants rated pain intensity and unpleasantness before and after each heat stimulation (i.e. prospective/retrospective ratings). In addition to the self-reports, a psychophysiological correlate of pain-related fear (i.e. the eyeblink startle response) was measured (for an overview of psychophysiological correlates of pain-related fear see[18]). The

startle reflex, which is triggered by startle-evoking stimuli (in this case an acoustic probe), is a cross-species, full-body reflex involved in defensive response mobilisation. The eyeblink response is one component of the startle response. In human fear conditioning research, eyeblink startle responses are generally measured by recording the surface electromyography (EMG) activity on the M. orbicularis oculi beneath the left eye. An increase in startle response occurs during fear states elicited by the anticipation of an aversive stimulus, and is thought to be an index of fear learning[37]. Electrodes were attached according to the site specifications described by Blumenthal and colleagues (2005). The raw signal was amplified by a Coulbourn isolated bioamplifier with a bandpass filter (LabLinc v75-04). The recording bandwidth of the EMG signal was between 90 Hz and 1 kHz. The signal was rectified online and smoothed by a Coulbourn multifunction integrator (LabLinc v763-23A) with a time constant of 20 ms. The EMG signal was digitized at 1000 Hz from 500 ms before the onset of the auditory startle probe until 1000 ms after probe onset.

Questionnaires

For descriptive purposes, participants completed several questionnaires upon completion of the experiment: the trait version of the State-Trait Anxiety Inventory[30] (STAI); the Fear of Pain Questionnaire[32] (FPQ-III NL); and the trait version of the Positive Affectivity and Negative Affectivity Scale[12] (PANAS).

Manipulation check

At the end of the experiment one question about the perceived control over the heat stimulus was asked as manipulation check in the avoidance group on a 101-NRS ("*When it was possible, to what extend did you feel you could influence the duration and thus also the intensity of the heat stimulus?*").

Data analysis strategy

First, descriptive statistics were computed to describe the sample, and to test for group differences. To test our primary hypothesis that avoidance behaviour increases pain-related fear for subsequent painful stimulations, we performed a Group (2: avoidance/control) x Phase (3: full intensity/intervention/test) RM ANOVA on the pain-related fear measure. Next, planned comparisons were performed to identify expected differences. We primarily expected that avoidance behaviour would lead to increased pain-related fear in the test phase compared to the full-intensity phase. For the threat value measures, a Group (2: avoidance/control) x Time (2: pre/post) RM ANOVA was performed. We primarily expected that avoidance behaviour would lead to increased threat value of pain in the test phase compared to the full-intensity phase. We expected a similar pattern in the startle data, for which we performed a Group (2: avoidance/control) x Probe (2: during stimulation/ITI) x Phase (3: full intensity/intervention/test) RM ANOVA.

In order to test our second hypothesis, that the avoidance group to report less fear and pain during the intervention phase, a Group (2: avoidance/control) x Phase (3: full intensity/intervention/test) RM ANOVA was performed on pain-related fear and pain intensity/unpleasantness ratings. Planned comparisons between the full-intensity phase and the intervention phase, as well as between the intervention phase and the test phase were performed within each group. For each significant RM ANOVA effect, η_g^2 is reported as the recommended effect size statistic for repeated measures designs[2]. In case of violation of sphericity, Greenhouse-Geisser corrections were applied. All statistical tests are considered significant at $p < .05$. Holm-Bonferroni corrections were applied to correct for multiple comparison testing. See online supplementary material for the tables of means, and standard errors of all measures.

Results

Descriptive statistics

Groups did not differ on self-reported pain intensity or temperature (PTH+1 °C) of the stimulation during calibration (on a scale from 0 to 100; $M_{\text{avoidance}}$ = 72.22, $SD_{\text{avoidance}}$ = 17.72, $M_{control}$ = 72.38, SD_{control} = 15.42; $t(61) = -0.04$, $p = 0.97$; temperature: $M_{\text{avoidance}}$ = 43.48 °C, $SD_{\text{avoidance}}$ = 1.73 , $M_{control}$ = 43.65 °C, SD_{control} = 1.89), indicating that the heat stimuli were perceived similar across groups at the onset of the experiment. There were no significant differences in trait anxiety (STAI), fear of pain (FPQ-III-NL), and positive and negative affect (PANAS) between groups. The mean score for STAI was 49.32 (SD = 4.41). The mean FPQ-III-NL score was 65.9 (SD = 14.88), with 37.15 (SD = 5.64) on the positive affectivity scale and 19.02 (SD = 6.86) on the negative affectivity scale of PANAS. The avoidance group indicated to feel in control of the intensity of the heat stimulus (M = 74.72, SD = 23.58)

Self-reported pain-related fear

Figure 2 displays the mean pain-related fear ratings per group measured before each phase. Testing our first hypothesis, the RM ANOVA on the pain-related fear ratings revealed a main effect of Group, $F(1, 62) = 4.10$, $p < .05$, $\eta_g^2 = .05$, indicating that the avoidance group reported more fear than the control group across all phases. There was a significant main effect of phase, $F(2, 124) = 8.28$, $p < .001$, $\eta_g^2 = .02$, indicating that fear ratings changed during the different experimental phases. Most importantly, the Group x Phase interaction effect was significant, $F(2, 124) = 4.73$, $p < .05$, $\eta_g^2 = .01$, suggesting that fear ratings across the phases of the experiment evolved differently for the avoidance group and the control group. The planned contrast evaluating the change in fear from the full intensity phase to the test phase between groups reached significance, $t(124) = 3.61$, $p < .001$. For the test of our second hypothesis, the planned contrast evaluating the change in fear from the full intensity phase to the intervention phase also reached significance, $t(124)=3.44$, $p < .01$, but not in the expected direction. Participants in the avoidance group paradoxically reported more pain-

related fear after they received the instruction to avoid but prior to their actual avoidance behaviour, instead of the expected decrease in pain-related fear. Based on this unexpected finding of the pain-related fear ratings, an additional post-hoc comparison was made to test whether pain-related fear increased from the intervention phase to the test phase, which did not reach statistical significance ($t(124) = .17$, $p = .87$).

-Insert FIGURE 2 about here-

Eyeblink startle measures

We calculated the peak amplitudes using Psychophysiological Analysis[8] (PSPHA). Every peak amplitude was defined as the maximum of the response curve within 21-175 ms after probe onset and was scored by subtracting its baseline score (averaged EMG level between 1 and 20 ms after probe onset). The raw scores were transformed to T-scores to account for inter-individual differences in physiological reactivity. All startle waveforms were visually inspected for technical abnormalities and artifacts. All startle data was included during the analysis, because it did not yield different results.

Figure 3 depicts the mean fear potentiated startle amplitudes for both groups separately for the three phases. The RM ANOVA revealed a significant main effect of Phase, $F(2, 124) = 4.58$, $p < .05$, $\eta_g^2 = .03$. Also, a significant main effect of Probe (during stimulation or ITI) was observed, $F(1, 62) = 34.42$, $p < .001$, $\eta_g^2 = .09$. As expected, the startle amplitudes elicited during stimulation, were higher than the startle amplitudes during ITI, suggesting that participants were more fearfully aroused during heat stimulation than in absence of the stimulation. There was no significant main effect of Group. The Probe x Phase interaction was significant, $F(2, 124) = 4.42$, $p < .05$, $\eta_g^2 = .02$. To test our main hypothesis whether pain-related fear would increase after avoidance behaviour, planned contrasts were

performed evaluating the changes from the full intensity to the test phase. This comparison did not reveal any significant effects. However, after visual inspection of the data, we noticed an increase in startle amplitudes during the intervention phase for the avoidance group only. In order to test our second hypothesis, we further analysed the startle amplitudes with post-hoc contrasts and found that the startle amplitudes during stimulation were significantly potentiated in the avoidance group during the intervention phase in comparison with the full intensity phase, $t(247) = -2.75$, $p < .01$, and test phase, $t(247) = 4.17$, $p < .001$. There was no such change in startle amplitudes in the control group, $t(247) = -0.37$, $p = .71$; $t(247) = .98$, $p = .32$. In sum, the eyeblink startle responses do not seem to corroborate the self-reported increase in pain-related fear during the test phase (after performing the avoidance response). Although there is an initial increase in the mean eyeblink startle response of the avoidance group during the intervention phase, this increase is not maintained during the test phase.

-Insert FIGURE 3 about here-

Threat value: perceived harmfulness of the painful heat stimulus

The RM ANOVA on threat value ratings revealed significant Group x Time interaction, $F(1, 62) = 7.46$, $p < .001$, $\eta_g^2 = .02$. Mean comparisons indicated that control group participants reported the heat stimulus as less threatening at the end of the experiment, $t(62) = 2.85$, $p < .01$, while no changes were reported in the avoidance group, $t(62) = -1.01$, $p = .32$.

Pain intensity and unpleasantness

The trial-by-trial pain intensity and unpleasantness ratings were merged across the three full intensity, three intervention and three test trials. The RM ANOVA only showed a significant main effect of prospective pain intensity for Phase, $F(2,124) = 8.05$, $p < .001$, $\eta_g^2 = .01$.

Participants expected the heat stimulus to be more painful at the end of the experiment compared to the beginning of the experiment, full intensity *vs.* test: $t(124) = -4.03$, $p < .001$. The RM ANOVA for the prospective unpleasantness also only revealed a significant main effect for Phase, $F(2,124) = 4.41$, $p < .05$, $\eta_g^2 = .007$. Participants expected the heat stimulus to be more unpleasant at the end of the experiment compared to the beginning of the experiment, full intensity *vs.* test: $t(124) = -2.96$, $p < .05$. For the retrospective pain intensity ratings, a significant Group x Phase interaction was found, $F(2,124) = 7.36$, $p < .001$, $\eta_g^2 = .006$. We also tested our second hypothesis. Participants in the avoidance group rated an identical heat stimulus as less painful when they thought they were avoiding the maximum stimulus intensity, full intensity *vs.* intervention: $t(124) = 3.74$, $p < .001$, and more painful when they could not avoid the maximum stimulus intensity, intervention *vs.* test: $t(124) = -2.67$, $p < .05$. This was not the case for the control group. The RM ANOVA for retrospective unpleasantness ratings did not reveal any significant effects. For the figure of pain intensity and unpleasantness ratings see online supplementary material.

Discussion

The present study tested the fear < - > avoidance bidirectionality hypothesis. Although avoidance of a painful stimulus is mainly intended to reduce the accompanying anticipatory fear, it increases pain-related fear when previous avoidance behaviour is no longer available. In line with our expectations, the results showed that self-reported pain-related fear was higher after performing an avoidance response (pressing the stop-button), despite equal intensities and duration of the heat stimulus as in the control condition. The observed increase of pain-related fear as a result of avoidance behaviour is in line with previous research, which was mainly conducted in the field of anxiety disorders, and proposes a bidirectional relationship between fear and avoidance[7,14,22]. For example, anxious patients might conclude

that their own actions (i.e. their safety-seeking behaviours) prevent feared outcomes, thereby leading them to draw invalid conclusions about the situation (behaviour as information), even in the absence of information about objective danger. This tendency to infer danger on the basis of safety-seeking behaviours may start a vicious circle: safety-seeking behaviour increased threat perception in turn increasing safety-seeking behaviour, and so on.

The increase in pain-related fear as a result of the mere instruction of being able to avoid, is an unexpected but interesting result. We would only have anticipated such an increase in pain-related fear after the participants had actually performed the avoidance behaviour. This early increase in pain-related fear warrants caution in interpreting the results within the context of our main hypothesis, namely that previous avoidance increases pain-related fear when the option to avoid is not available anymore. Since the increase in pain-related fear already happened before engaging in avoidance behaviour, we cannot rule out that the elevated levels of pain-related fear during the test phase might have been due to the instruction of avoidance, instead of the actual engagement of avoidance. Why would the instruction to avoid increase pain-related fear? One possibility is that the instruction to avoid increases attention towards feared stimuli[16]. Increased attention towards pain in turn may have led individuals to view themselves more at risk, leading to an increase in pain-related fear. This explanation is consistent with observations of Powers, Smits and Telch[23]. These researchers found that the availability of a safety aid already had disruptive effects on fear reduction. Our findings add to these observations by showing that the availability of an avoidance response increases pain-related fear. Since we only measured the pain-related fear before each phase, we have no data to determine if the pain-related fear remained high directly after avoiding. Therefore, the maintained increased levels of pain-related fear during test phase cannot solely be ascribed to the engagement in avoidance behaviour, but could also be a consequence of the instruction of avoidance. We can conclude that pain-related fear is at

least "maintained" through engagement in avoidance behaviour. As a result, our main hypothesis is only partially supported.

The psychophysiological data from the eyeblink startle responses are not completely in line with the self-reported increase in pain-related fear during the intervention phase (instruction to perform the avoidance response) and test phase (after performing the avoidance response). Although there is an initial increase in eyeblink startle responses of the avoidance group during the intervention phase, this increase is not maintained during the test phase. Eyeblink startle measures may not be well-suited in this paradigm, because responses may have been influenced by preparing to execute an avoidance response (motor preparation) or changes in the attentional processes in the avoidance group[29]. In addition, startle probes were delivered *during* instead of in *anticipation* of the aversive heat stimulation, as is common practice in classical fear conditioning paradigms using fear-potentiated startle measures. This procedural detail may also have rendered the startle measurement less effective/sensitive. Yet, startle responses were higher during stimulation compared to no stimulation for both groups, indicating that participants were more afraid during painful heat stimulation.

Some other observations should be highlighted. The decrease of threat value in the control group is consistent with results of exposure studies[9,28]. Indeed, we expected that avoidance of a painful stimulus would increase the threat values, which then would serve as a source of information to further fuel pain-related fear[13]. Another remarkable observation is the reduction in perceived pain intensity that was achieved by engaging in avoidance behaviour. The data suggests that our experimental manipulation worked, and that avoidance behaviour might indeed have created the expectation that participants avoided the maximum heat intensity (e.g. [24]).

This study had various strengths and limitations. An innovative and methodological strength of this study was that we employed an experimental design by creating the illusion

that participants could avoid the maximum pain stimulus, such that both received comparable (calibrated) pain intensities throughout the experiment. Therefore, any changes in perceived pain-related fear can be ascribed to the perception of having been able to avoid the maximum heat stimulus intensity. On one side, this is a clear strength of the study, because pressing the stop-button created the perception for the participants in the avoidance group that they were actually able to avoid a painful stimulus. On the other side, this can also be seen as a limitation, because one may argue that simply pressing a stop-button with no associated cost is not ecologically valid. For example, for chronic pain patients, avoidance behaviour usually comes with a cost of limitations in daily functioning, and those patients have more to lose than to win with their avoidant behavioural patterns. In real-life however, one can argue that avoidance behaviours of chronic pain patients pertain to a combination of low- and high-cost responses. For example, avoiding certain simple movements could be a low-cost response, while not participating in valued life activities to prevent an increase of pain could be considered a high-cost response. Despite the low-cost action of the avoidance response (pressing the stop-button), the study showed effects of the perceived avoidance behaviour on the level of pain-related fear, i.e. the avoidance behaviour induced an increase in pain-related fear. In a similar way, low-cost avoidance behaviours like carrying pills, just in case pain would increase, could create the perception that this specific behaviour effectively prevented serious problems and could likewise increase threat beliefs[33]. Avoidance precludes the individual the opportunity to experience the feared situation in the absence of pain, and thereby increases fear and may lead to overgeneralisation of avoidance responses[31]. Studies have demonstrated that chronic pain patients overgeneralise pain expectancy and fear to safe situations[19,20,21]. Because of the bidirectional relationship of fear and avoidance, one could speculate that initial low-cost avoidance behaviour could develop into high-cost avoidance response via overgeneralisation of avoidance behaviour, and thereby contributing to the

development of chronic pain[11]. For example, when an individual experiences pain while lifting a box, (s)he will avoid to lift this particular box (low-cost avoidance). However, through stimulus generalisation, this person may also become afraid to experience pain while lifting his/her baby and therefore will avoid holding his/her baby (high-cost avoidance). Future research should focus on potential detrimental effects of avoidance generalisation.

The potential negative effects of pain-related avoidance behaviour may be most prominent in chronic pain patients. Hence, before generalising the findings of the study to patients with chronic pain, future studies need to validate these findings using clinical samples. A better understanding of the dynamics between avoidance behaviour and pain-related fear, including the bidirectionality, could lead to new insights regarding the complexity associated with the development and maintenance of chronic pains.

To address the outstanding issues, future research should include measures of pain-related fear directly after having performed avoidance behaviour, so that further insights of the direct effects of avoidance behaviour on pain-related fear can be obtained. Also, the effects of avoidance behaviours on fear perception using both low- and high-cost responses, including validation in a clinical population await further research.

To conclude, the results of this study do indicate that avoidance behaviour can lead to increased and maintained self-reported pain-related fear, and provide partial support for the hypothesis of a bidirectional relationship between fear and avoidance. This is an important finding, suggesting that avoidance behaviour in itself may play a role in increasing fear, rather than resulting in the intended fear reduction. Interestingly, self-reported pain-related fear in the avoidance group already increased after receiving the instructions that avoidance would be possible, but before actually engaging in avoidance behaviour. Additionally, these findings suggest that allowing avoidance behaviours in clinical therapy may be detrimental for fear reduction and this should be taken into account when providing clinical recommendations.

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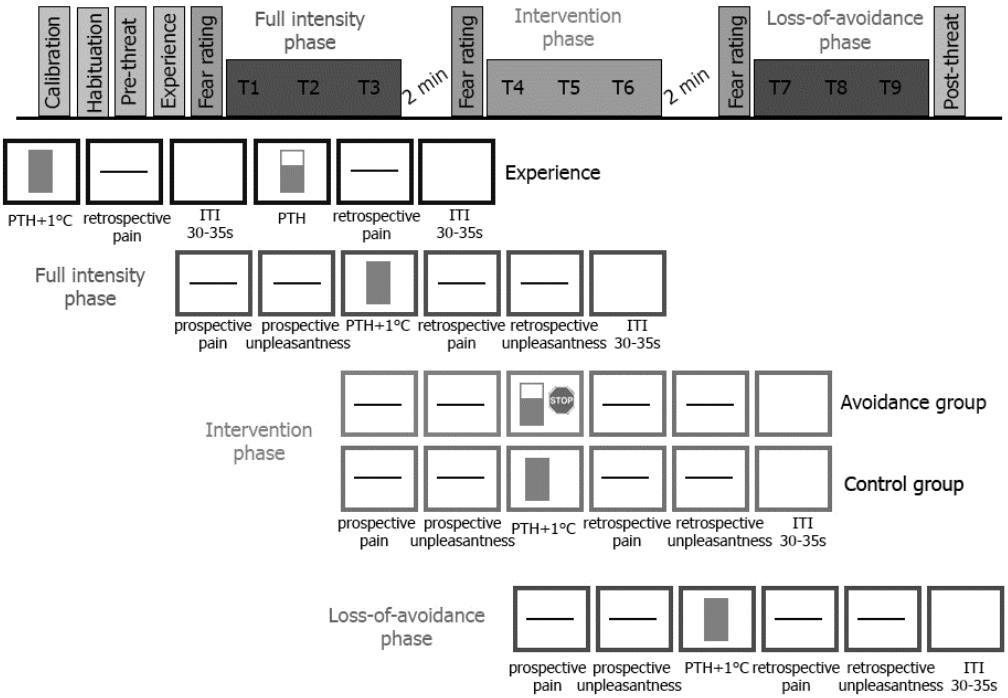
Figure 1. Overview of the experimental design and exemplary trial structure. Legend: PTH = individual pain threshold temperature; PTH+1°C = maximum temperature; ITI = intertrial interval; Calibration = determine individual pain threshold level (C); Habituation = presentation of 10 startle probes; Experience = experiential learning phase; pre-threat and post-threat = measurement times of the threat value.

Figure 2. Self-reported pain-related fear ratings during the experimental phases for the avoidance and control group separately.

Figure 3. Mean startle amplitudes for the Avoidance group (left panel) and the Control group (right panel) during the full intensity, intervention and test phases during stimulation and during the intertrial interval (ITI). The raw scores from the startle measure were converted to z-scores to account for inter-individual differences. For better visualization of the data, the z-scores were transformed to T-scores, to avoid negative values on the Y-axis. The weighted average of eyeblink startle amplitudes was then calculated for each experimental phase.

Figure S-1. Self-reported pain intensity and unpleasantness ratings during the experimental phases for the avoidance and control group separately.

Figure 1.



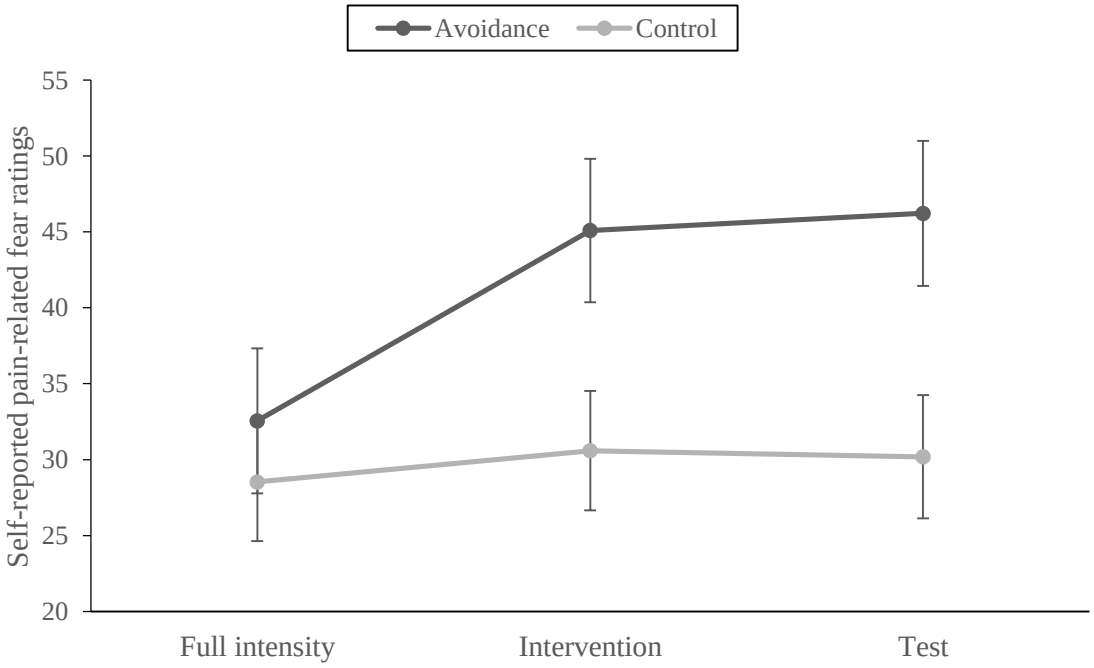


Figure 2.

Figure 3.