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Fear and anxiety: divergent effects on human pain thresholds

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Abstract

Animal studies suggest that fear inhibits pain whereas anxiety enhances it; however it is unclear whether these effects generalize to humans. The present study examined the effects of experimentally induced fear and anxiety on radiant heat pain thresholds. Sixty male and female human subjects were randomly assigned to 1 of 3 emotion induction conditions: (1) fear, induced by exposure to three brief shocks; (2) anxiety, elicited by the threat of shock; (3) neutral, with no intervention. Pain thresholds were tested before and after emotion induction. Results suggest that findings from animal studies extend to humans: fear resulted in decreased pain reactivity, while anxiety led to increased reactivity. Pain rating data indicated that participants used consistent subjective criteria to indicate pain thresholds. Both subjective and physiological indicators (skin conductance level, heart rate) confirmed that the treatment conditions produced the targeted emotional states. These results support the view that emotional states modulate human pain reactivity. © 2000 International Association for the Study of Pain. Published by Elsevier Science B.V.

Keywords: Fear; Anxiety; Stress; Analgesia; Hyperalgesia; Pain

1. Introduction

Pain is not simply determined by the intensity of nociceptive stimulation, but also depends on psychological factors such as the emotional and motivational state of the organism. Innumerable animal studies suggest that pain reactivity is decreased by fear (e.g. Bodner et al., 1980; Bolles and Fanselow, 1980; Basbaum and Fields, 1984; Fanselow, 1984, 1986; Watkins and Mayer, 1986; Maier, 1989; Meagher et al., 1989, 1990; Lichtman and Fanselow, 1990). For example, rats exposed to a few brief shocks subsequently exhibit analgesia on standard tests of pain reactivity (e.g. inhibition of tail withdrawal from radiant heat) (Fanselow, 1984; Grau, 1984; Meagher et al., 1989, 1990; Maier, 1989). This phenomenon, known as 'stress-induced analgesia', has been linked to the release of endogenous opioids because it is attenuated by both opioid antagonists (e.g. naloxone or naltrexone) and morphine tolerance (Akil et al., 1976; Lewis et al., 1980; Terman et al., 1984; Watkins and Mayer, 1986; Meagher et al., 1989). Although this effect is thought to generalize across species, the few studies that have examined this phenomenon in humans report mixed results. In some cases decreased pain was observed (Bobey and Davidson, 1970; Malow, 1981; Willer et al., 1981; Janal et al., 1984;Bandura et al., 1988; Pitman et al., 1990; Al Absi and Rokke, 1991; Johnson and Helmstetter, 1994; Janssen and Arntz, 1996), while others report increased pain, or hyperalgesia (Haslam, 1966; Bowers, 1968; Schumacher and Velden, 1984; Weisenberg et al., 1984; Dougher et al., 1979, 1987; Cornwall and Donderi, 1988; Al Absi and Rokke, 1991). We propose that these seemingly contradictory findings were obtained, in part, because the paradigms employed produce two different psychological states: fear and anxiety.

Fear is an immediate alarm reaction to present threat, characterized by impulses to escape, and typically results in surge of sympathetic arousal (Barlow et al., 1996). Anxiety, on the other hand, is a future-oriented emotion characterized by negative affect and apprehensive anticipation of potential threats, and results in hypervigilance and somatic tension (e.g. muscle tension). Fear mobilizes the organism to take action (fight/flight response), whereas anxiety leads to increased environmental and somatic scanning that facilitates sensory receptivity. In light of these distinctions, several researchers have argued that fear and anxiety represent qualitatively distinct emotional states (for a reviews, see Maier, 1993; Barlow et al., 1996; Davis et al., 1997). Support for this view comes from recent animal studies indicating that the neural circuit which mediates fear may be distinct from the circuit involved in anxiety (Gray and

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McNaughton, 1996; Davis et al., 1997). Alternatively, the central states relevant to pain may depend on the same neural circuit which has different behavioral consequences depending on its level of activation; intense activation may induce fear and analgesia, whereas moderate activation may induce anxiety and hyperalgesia. Support for this quantitative account is provided by recent animal research demonstrating a non-monotonic relationship between shock severity and its subsequent impact on pain (Walters, 1994; King et al., 1996; Meagher et al., 1998, in review). Irrespective of whether fear and anxiety differ qualitatively or quantitatively, both accounts anticipate divergent effects on pain. Both predict that direct exposure to a noxious event should induce high levels of fear and arousal that will inhibit pain, whereas the relatively diffuse threat of a future noxious event, without actual exposure, will induce a state of anticipatory anxiety (lower levels of fear and arousal) which will enhance pain. Supporting this, clinical research indicates that victims of traumatic stress report feeling numb and insensitive to pain during the fear eliciting trauma (Burgess and Holmstrom, 1976; Suarez and Gallup, 1979). In contrast, patients with generalized anxiety are hypervigilant about their internal bodily states (Barlow et al., 1996) which should increase attention to pain, thereby amplifying its perceived intensity.

The present study examines the effect of fear and anxiety on pain reactivity in human subjects. To allow a relatively direct comparison with animal research, we used a pain reactivity test, methodology, and parameters that paralleled previous animal studies (e.g. Grau, 1984, 1987; Meagher et al., 1989, 1990). Radiant heat was chosen as the pain test stimulus because of its widespread use with rats in the tail-flick test. Pain thresholds were assessed prior to and following the induction of fear (group 1), anxiety (group 2), or neutral (group 3) emotional states. Fear was induced by exposure to three brief shocks that have been shown to elicit analgesia and conditioned fear in animal studies (Fanselow, 1984; Grau, 1984; Meagher et al., 1990). Prior human studies have also shown that exposure to shock elicits intense sympathetic arousal and subjective reports of fear (Willer et al., 1981; Greenwald et al., 1998). Anxiety was induced by the verbal threat of shock without actual exposure. Participants were told they may or may not receive shocks, which induced a state of 'anxious apprehension' regarding this potential future threat that was uncertain and unpredictable (Barlow et al., 1996). This method of generating anticipatory anxiety has been shown to be effective in several human studies even though shocks are not presented (Deane, 1961; Haslam, 1966; Al Absi and Rokke, 1991; Grillon et al., 1993; Barlow et al., 1996). Finally, a neutral state was induced in the control participants by informing them that shock would not be administered. To verify that these experimental manipulations induced different levels of arousal and negative affect, both subjective and physiological reactions were measured as manipulation checks.

2. Method

2.1. Subjects

Participants were 30 male and 30 female introductory psychology students at Texas A&M University who received course credit toward their research requirement. They had the option to participate in other experiments or to write brief research reports. Participants were informed they may withdraw from the study at anytime without forfeiting research credit. Of those, 76.7% were Caucasian, 20% Hispanic, and 3.3% Asian. Mean age was 19.2 years (SD = 1.62). Persons were excluded for circulatory, cardiovascular, or neurological problems; chronic pain; or tobacco, analgesic, antidepressant, or recent alcohol use.

2.2. Apparatus and physiological recording

Data acquisition and stimulus presentation were computer controlled by LabVIEW software and an AT-MIO-16DL DAQ board (both by National Instruments). Physiological signals were amplified by a Grass Instruments polygraph (Model 7E; Model 7DA driver amplifiers; Model 7P8 and Model 7P1 preamplifiers). Skin conductance level (SCL) was recorded via 2 sensors (Grass F-EGSR) attached to the palmar surface of the middle segments on the index and middle fingers of the non-dominant hand. Heart rate (HR) was measured using a Grass Instruments pulse transducer (Grass PPS) attached to the distal segment of the index finger of the non-dominant hand. Both SCL and HR were sampled at 50 Hz and recorded 1 min prior to and during each radiant heat test, as well as during the treatment period. Changes in HR and tonic SCL were compared before and after treatment. In addition, discrete changes in HR during treatment were examined by breaking the data into 5 s blocks. Changes in autonomic functioning, as measured by SCL and HR, were used as a way of checking the efficacy of our emotion induction.

2.3. Electrocutaneous stimulation

Exposure to electric shock was used to induce fear, whereas anticipation of shock (without exposure) was used to induce anxiety. Electrocutaneous stimuli were presented using a Grass S88 stimulator with a transformer isolation unit (Grass SIU8T) and a constant current unit (Grass CCU1) (see Dowman, 1991, for a detailed description). Two electrodes (Ag–AgCl), filled with isotonic paste, were spaced approximately 1.5 cm apart and attached to the proximal, dorsal surface of participants' index finger of the dominant hand. To aid conduction, the skin was degreased and gently abraded. Stimulations in the fear condition consisted of three brief shocks delivered at 200 Hz, with 1 ms pulse duration, 0.75 s train duration, at 12.4 mA, and 20 s inter-train intervals.

2.4. Radiant heat pain threshold

Changes in pain reactivity were assessed using a radiant heat pain threshold test (Lee and Stitzer, 1995). A bottom-illuminated radiant heat device was constructed using a 300 W slide projector bulb. A condenser lens was positioned 2 cm above the bulb to focus the light onto 1 cm^2 of the distal digit of the participant's index finger. The finger was blackened with a marker and placed on a platform made from PVC tubing (5 inch by 1 inch) mounted above the light. Finger withdrawal was automatically detected by photoresistors embedded in the platform. Participants were instructed to remove their finger as soon as it became painful: 'Keep your finger on the platform until it becomes painful. When it becomes painful, withdraw your finger and the heat source will turn off.' Pain threshold was defined as the latency from light onset to finger withdrawal. The heat was automatically terminated after 8 s to avoid tissue damage. Similar to the rodent tail-flick test and the human finger-flick test (Lee and Stitzer, 1995), all threshold tests occurred at the same location (index finger). To avoid potential secondary effects of the test per se, subjects were given just 5 radiant heat tests (1 practice, 2 baseline, and 2 post-treatment) with long intervals between trials (5 and 6 min). To minimize cues predicting the light's onset, participants focused on a target placed on the wall and wore sound attenuating headphones. Twelve participants whose average baseline latency was less than 1 s or greater than 5 s were excluded from analyses, because their response criteria were inappropriate in reaction to the pain.

2.5. Manipulation checks

To evaluate the consistency of subjective criteria used to indicate pain threshold, participants rated the intensity and unpleasantness of each radiant heat test using visual analog scales (VAS). Each VAS consisted of a 10 cm line whose anchors ranged from 'no pain sensation' to 'the most intense pain sensation imaginable' (intensity) and 'not at all unpleasant' to 'the most unpleasant imaginable' (unpleasantness) (Price et al., 1983).

Perceived self-efficacy for pain reduction (SE-PR) was measured with a 15-item scale that assesses the subject's belief that they can influence their pain (Bandura et al., 1988). Participants indicated 'yes' or 'no' to questions asking whether they believed they could make reductions in pain (small, medium, or large) for varying intensities of pain (mild, discomforting, distressing, horrible, and excruciating). Responses of 'yes,' were rated on their certainty using a scale ranging from 0 (uncertain) to 10 (certain). The sum of the 15 items was used as an indicator of self-efficacy. The Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), a 20 item questionnaire of depression and anxiety symptoms, was administered to control for pre-existing emotional distress.

The emotional impact of the treatment condition (fear, anxiety, or neutral) was assessed by the Self-Assessment Manikin (SAM; Lang, 1980) which consists of two pictogram scales indicating various levels of valence (ranging from 'happy' to 'unhappy') and arousal ('excited' to 'calm'). Participants also rated their emotional reaction on 5-point Likert scales that ranged from 'not at all' to 'strongly' for seven affective descriptors (happy, disgusted, fear, neutral, surprised, sad, angry).

2.6. Procedure

Fig. 1 illustrates the experimental procedure. After obtaining informed consent, subjects were acclimatized to the experimental context for 15 min. During this time, subjects completed 3 questionnaires (demographics, SE-PR, and CES-D) and the physiological sensors and stimulating electrodes were attached. To reduce anxiety during baseline measures, the stimulating electrodes were not connected to the stimulator. After a practice trial (baseline 1), participants received two baseline radiant heat tests (5 min ITI). Next, participants were notified of their treatment condition which was determined by random assignment. In the fear condition ($n = 20$), electrodes were plugged in and participants were told, 'You may or may not receive brief, surprising, and painful electrical shocks.' This group received three 12 mA shocks spaced 20 s apart starting 2 min from the end of the last baseline threshold

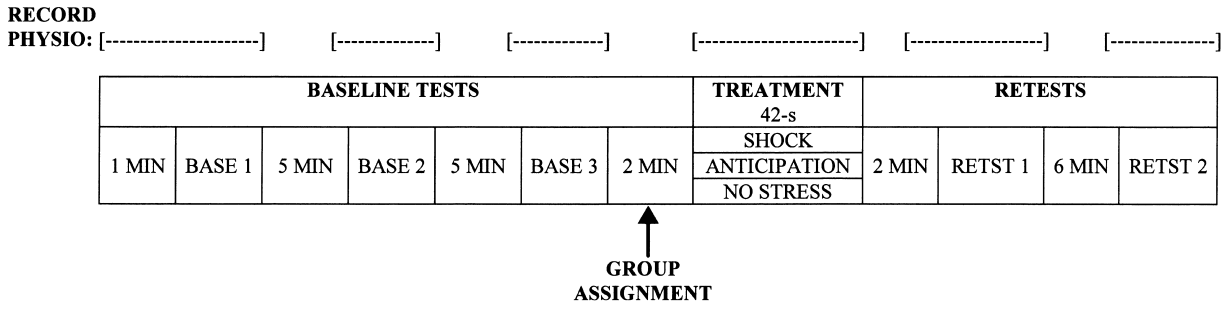

Fig. 1. Experimental procedure. Three baseline tests with 5 min inter-trial intervals (ITIs) occurred before the treatment period, followed by two retests with a 6 min ITI. Bars above the matrix indicate times that physiological data were recorded. Physiological data were recorded 1 min prior to and during every trial, as well as during treatment. The arrow indicates when the experimenter told the participant what condition s/he was assigned to and either removed or plugged in the electrodes.

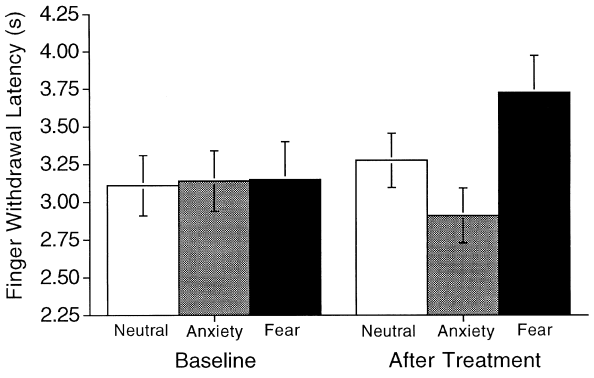

Fig. 2. The effect of fear and anxiety on finger withdrawal latencies. Means represent average baseline latency (baseline 2 and 3), and retests (at 2 and 8 min following treatment) grouped by treatment condition.

test. The procedure was the same for the anxiety group ($n = 20$), except they did not receive shock. Participants in the neutral control condition ($n = 20$) were told, 'You will not receive any surprising stimulations during this experiment' and electrodes were removed. Two additional pain threshold tests occurred 2 and 8 min following treatment. In all instances, VAS questionnaires were filled out after each radiant heat test. A total of 5 radiant heat thresholds were obtained (1 practice, 2 baseline, and 2 post-treatment) and only one heat stimulus was presented at each time point. Threshold tests were not explicitly signalled, however subjects were instructed to keep their finger on the radiant heat device through the experiment**.** The experimenter remotely monitored the participants' behavior by video monitor from a separate room and communicated with them over headphones during baseline, treatment, and retest phases. After pain testing was complete, participants rated the emotional impact of their treatment condition using the SAM and affective descriptor scales. All experimental procedures were approved by Texas A&M University's Human Subjects Committee.

3. Results

Unless otherwise noted, all statistical assumptions were met for analyses. In cases where the assumption of sphericity was not met, the Greenhouse-Geisser correction was used (epsilons, ϵ, are noted following P-values).

3.1. Pain reactivity

Fig. 2 depicts the mean finger withdrawal latencies collapsed across the 2 baseline and 2 post-treatment retests. Baseline latencies are presented on the left while retests are presented to the right. Because the second and third baselines did not differ ($t(59) = 0.78, P > 0.05$), they were averaged to provide a baseline measure of pain reactivity prior to treatment. To control for within group differences, an ANCOVA was used entering retests 1 and 2 as a repeated measure (trial), condition and gender as between-group variables, and baseline finger withdrawal latency as a covariate [self-efficacy (SE-PR) and distress (CES-D) scores were originally entered as covariates, but they were dropped because they were not correlated with the dependent variables]. First, the analysis was conducted with a Covariate × Condition interaction to test the homogeneity of regression assumption. Because this interaction was not significant (assumption met), the interaction was dropped and the analysis was conducted again. This analysis revealed that baseline latency was a significant covariate, $F(1, 51) = 111.10$, $MSE = 0.685$, $P < 0.001$. Moreover, a significant main effect for condition emerged after adjusting for the covariate ($F(2, 51) = 11.66$, $MSE = 0.685$, $P < 0.001$). Pairwise comparisons of the estimated means collapsed across trials revealed that persons in the fear condition had significantly longer latencies ($P < 0.01$) than persons in the neutral condition. This suggests that the fear condition induced analgesia. In contrast, participants in the anxiety condition had significantly shorter latencies than the neutral condition ($P < 0.05$), indicating an increased sensitivity to pain, or hyperalgesia. Fear and anxiety conditions were significantly different from one another ($P < 0.001$). The main effects for gender and trial were not significant, nor were any of the interaction terms (all $Fs < 1.34$, $P > 0.05$).

3.2. Manipulations checks

Previous research suggests that differences in subjective pain criteria, self-efficacy, emotional distress, and emotional reactivity can influence pain. Thus, the following manipulation checks were designed to determine whether non-equivalent distribution of these factors occurred across the three treatment conditions. We established that: (1) participants used consistent subjective criteria to indicate pain thresholds (VAS), (2) groups did not differ prior to testing on measures of self-efficacy (SE-PR) and emotional distress (CES-D), and (3) both subjective and physiological indicators (SCL, HR) confirmed that the treatment conditions produced different levels of negative affect and arousal. Although minor gender differences were observed, males and females exhibited similar response profiles. In cases where males and females did not differ, gender was dropped from the analysis to simplify data presentation. Table 1 lists all means and standard deviations for SE-PR, CES-D, and emotion ratings.

3.2.1. VAS criteria

Fig. 3 depicts VAS intensity and unpleasantness scores collapsed across condition. If participants in each condition used consistent subjective criteria to indicate pain threshold across the five radiant heat tests, then intensity and unpleasantness scores should not change over trials for each condition. Supporting this, a repeated measures ANOVA entering condition and gender as between-group factors and trial as a within-subject factor failed to find a main effect of condition

Table 1
Means and standard deviations of self-report data by condition[a]

Condition		CES-D 0–60	SE-PR 0–150	Valence 1–9	Arousal 1–9	Happy 1–5	Disgust 1–5	Fear 1–5	Neutral 1–5	Suprise 1–5	Sad 1–5	Angry 1–5
Fear	M	10.25_a	35.70_a	3.70_a	7.20_a	1.58_a	2.05_a	2.90_a	2.25_a	3.85_a	1.50_a	2.55_a
	SD	7.10	25.74	2.05	1.85	0.96	1.50	1.29	1.12	1.27	0.61	1.64
Anxiety	M	7.45_a	53.10_a	5.20_b	4.95_b	1.90_a	1.15_b	2.00_b	3.70_b	1.80_b	1.10_a	1.15_b
	SD	5.04	23.57	1.15	1.93	0.91	0.49	0.86	1.45	1.15	0.31	0.49
Neutral	M	10.65_a	47.10_a	5.90_b	3.80_b	2.70_b	1.20_b	1.40_c	3.65_b	2.75_c	1.40_a	1.25_b
	SD	6.47	28.14	1.80	2.19	1.13	0.70	0.75	1.09	1.16	0.68	0.55

[a] Below each scale is the range of potential scores. CES-D is the Center for Epidemiological Study-Depression scale, SE-PR is the Self-Efficacy for Pain Reduction scale, valence and arousal are from the Self-Assessment Manikin, and the others are affective varbal descriptors. Means are in each column, below are standard deviations. Means in the same column that do not share the same subscript differ at $P < 0.05$.

(VAS-I: $F(2, 53) = 0.01$, $MSE = 986.84$, $P > 0.05$; VAS-U: $F(2, 53) = 0.26$, $MSE = 1176.36$, $P > 0.05$), gender (VAS-I: $F(1, 53) = 0.17$, $MSE = 986.84$, $P > 0.05$; VAS-U: $F(1, 53) = 0.27$, $MSE = 1176.36$, $P > 0.05$), or trial (VAS-I: $F(3.29, 174.48) = 2.27$, $MSE = 81.31$, $P > 0.05$; VAS-U: $F(2.89, 153.25) = 0.34$, $MSE = 128$, $P > 0.05$) for VAS intensity or unpleasantness, respectively. Moreover, condition did not interact with trial (VAS-I: $F(6.58, 174.48) = 0.46$, $MSE = 81.31$, $P > 0.05$; VAS-U: $F(5.78, 153.25) = 0.412$, $MSE = 128$, $P > 0.05$), and none of the remaining interaction terms reached statistical significance (VAS-I: all $F < 0.71$, $P > 0.05$; VAS-U: all $F < 2.52$, $P > 0.05$).

3.2.2. Self-efficacy and distress

An ANOVA indicated that self-efficacy scores ($F(2, 60) = 2.33$, $MSE = 670.10$, $P > 0.05$) and CES-D scores ($F(2, 60) = 1.55$, $MSE = 39.25$, $P > 0.05$) did not differ between groups. Because all groups were homogeneous on these variables, any between-group differences cannot be attributed to pre-existing differences in self-efficacy or emotional distress.

3.2.3. Emotion ratings

The emotion ratings are presented in Table 1. To assess the emotional impact of the treatment, 2 × 3 ANOVAs were conducted on SAM valence and arousal scores, entering gender and condition as between-subject variables. For valence, there was a significant effect for condition, $F(2, 60) = 8.95$, $MSE = 2.82$, $P < 0.001$. Group mean comparisons indicated that the fear condition resulted in greater unpleasant affect than anxiety ($P < 0.05$) and neutral ($P < 0.001$) conditions, which were not different from one another ($P > 0.05$). Analysis of arousal ratings indicated a significant main effect for condition ($F(2, 60) = 14.74$, $MSE = 4.06$, $P < 0.001$). Mean comparisons indicated that participants in the fear condition were more aroused than those in the anxiety ($P < 0.001$) and neutral ($P < 0.001$) conditions, which were not different from one another ($P > 0.05$), though a trend for greater arousal was present in the anxiety relative to the neutral condition. No gender differences were found for either measure.

Each affective descriptor was entered into a 2 × 3 ANOVA using gender and condition as between-group variables. Significant main effects for condition were found for: anger, fear, surprise, happy, disgust, and neutral ratings, $F(2, 60) = 10.83$, 11.19, 15.66, 6.78, 4.90, and 9.92, respectively, $P < 0.05$. Subjects in the fear condition reported feeling more anger and disgust, and less neutral, than persons in either the neutral or anxiety conditions. Ratings of fear were greatest for the fear condition, followed by the anxiety condition, and least for the neutral condition. Happiness ratings were higher in the neutral condition compared to the fear or anxiety conditions. Participants reported being most surprised by the fear condition, less surprised by neutral affect, and least surprised by the anxiety condition. The only effect for gender was found for neutral affect ($F(1, 60) = 7.02$, $MSE = 1.37$, $P < 0.05$), with men having higher ratings than women.

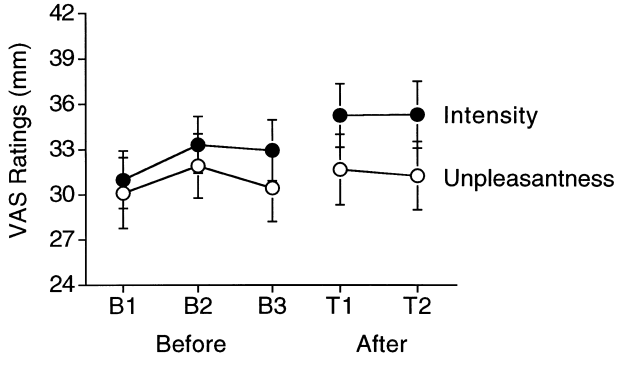

Fig. 3. Mean (SEM) visual analog scale (VAS) ratings (mm) of radiant heat intensity and unpleasantness collapsed across treatment conditions. B1–B3 occurred before treatment, whereas T1–T2 occurred after.

3.2.4. Skin conductance level

Fig. 4 illustrates the effects of treatment on SCL. It is apparent that subjects in the fear and anxiety conditions showed a marked increase in SCLs during and following treatment, verifying that both conditions produced auto-

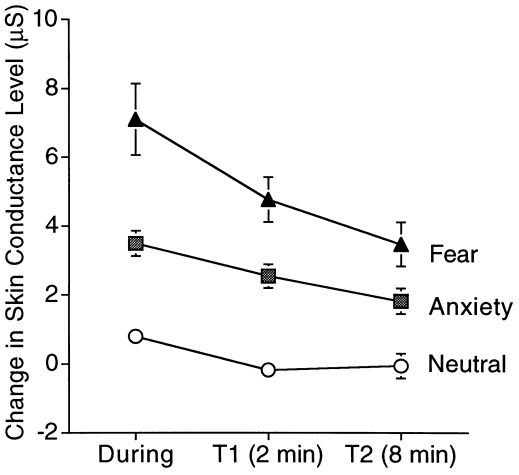

Fig. 4. Mean (SEM) change in tonic skin conductance levels (SCL; S) during treatment and after retests (2 and 8 min) by treatment condition.

nomic arousal. To analyze the effects of treatment on tonic SCL, change scores were calculated by subtracting the mean baseline SCL from treatment, retest 1, and retest 2 tonic SCLs (Dawson et al., 1990). Three change scores resulted and were analyzed using a mixed ANOVA, with each change score (trial) used as a within-subject variable and condition and gender as between-group variables. Significant main effects for trial and condition emerged. However, these were qualified by a significant Trial × Condition interaction ($F(3.06, 78.06) = 5.34$, $MSE = 2.61$, $P < 0.01$, $\epsilon = 0.765$). Bonferroni mean comparisons indicated that during treatment, SCL was greatest for fear, followed by the anxiety condition, and then the neutral condition ($P < 0.01$), with the same results at retest 1 ($P < 0.01$). At retest 2, fear and anxiety were marginally different from one another ($P = 0.07$), but both were different from neutral ($P < 0.01$). No gender differences were found, although when the analysis was conducted without using change scores a significant main effect for gender was found, with men having a higher overall SCL.

3.2.5. Heart rate

Similar to SCL, HR changed as a function of treatment. As described earlier, heart rate was analyzed using two procedures. First, global changes in HR were examined by analyzing 1 min intervals taken prior to and during each radiant heat test, as well as during the treatment period. Second, discrete changes in HR during treatment were analyzed by breaking the treatment period into 12 5 s intervals.

Fig. 5 illustrates global HR results as beats-per-minute (BPM) scores. A mixed ANOVA was used entering the six 1 min HR samples as the within-subject variable (trial) and gender and condition as between-group variables. There was a significant main effect of Trial, a significant Trial × Gender interaction, and a significant Trial × Condition interaction, but these were qualified by a significant Trial × Gender × Condition interaction ($F(2.37, 5.09) = 2.37$, $MSE = 36.35$, $P < 0.05$, $\epsilon = 0.509$). To examine the Trial × Gender × Condition interaction, men and women's heart rate data were analyzed separately using mixed ANOVAs. For men, no significant results were found, but women had a significant Trial × Condition interaction ($F(3.55,44.38) = 3.75$, $MSE = 65.41$, $P < 0.05$, $\epsilon = 0.355$). Bonferroni mean comparisons revealed that women's heart rates were higher during treatment when exposed to shock than when made anxious (marginally significant, $P = 0.06$).

Fig. 6 depicts the discrete HR data collected during treatment divided into 12, 5-s intervals. A mixed ANOVA was conducted entering 5-s intervals (trial) as the within-subject variable and condition and gender as between-group variables. There was a significant Trial × Condition interaction ($F(16.22, 429.71) = 3.00$, $MSE = 80.82$, $P < 0.001$, $\epsilon = 0.733$) and a significant main effect for gender ($F(1, 53) = 4.24$, $MSE = 1689.93$, $P < 0.05$). Following up the interaction, Bonferroni multiple comparisons showed that, at the 3rd (15 s) and 6th (30 s) intervals, subjects in the fear condition had a significantly higher heart rate than

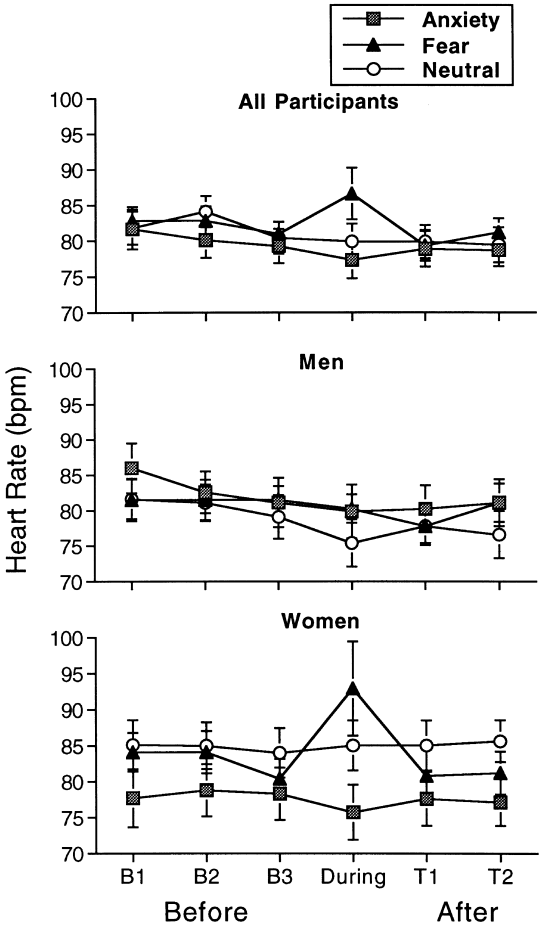

Fig. 5. Mean (SEM) heart rate (bpm) by condition before (B1–B3), during, and after (T1–T2) treatment. The top panel presents all participants, men are depicted in the middle, and women are shown at the bottom.

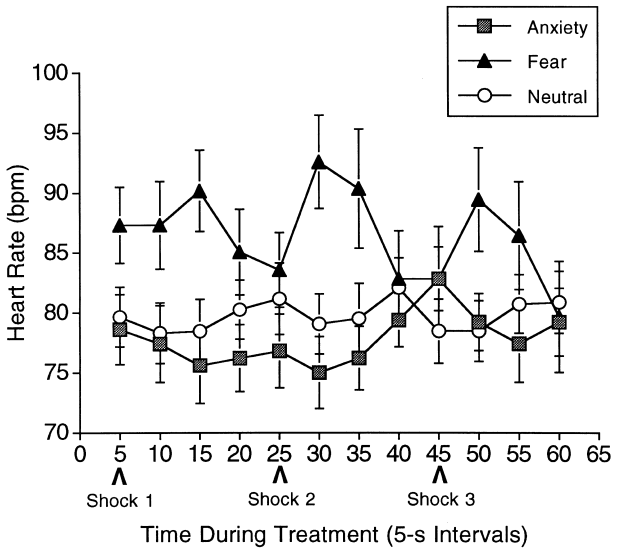

Fig. 6. Mean (SEM) heart rate (bpm) by condition sampled in 5 s intervals during treatment. Units on the horizontal axis are the last seconds contained in the interval (e.g. 5 = 0–5 s). Arrows indicate the intervals when shocks were presented.

subjects in the neutral or anxiety groups, but fear was only different from anxiety at interval 7 (35 s). At interval 10 (50 s), fear was different from neutral ($P < 0.05$). Because participants in the fear condition were exposed to shocks at 2 s, 22.75 s, and 43.55 s (corresponding to intervals 1, 5, and 9, respectively), this suggests that HR briefly accelerated following shocks, but quickly returned to baseline. Inspection of heart rate means after collapsing across trial and condition indicated that women's heart rates were higher than men's during the treatment phase.

4. Discussion

The present study shows that fear and anxiety have divergent effects on pain thresholds in humans. Specifically, fear established by the presentation of moderate shock increased finger withdrawal thresholds to radiant heat, whereas anxiety elicited by anticipation of shock (without actual exposure) decreased pain thresholds. Furthermore, visual analog scale ratings indicated that participants used consistent subjective criteria to indicate pain thresholds across the five radiant heat trials. Our manipulation checks confirmed that the fear condition received the highest ratings for fear, unpleasantness, and arousal, followed by the anxiety condition which was rated higher than the control condition. The fear condition also evoked greater increases in SCL than the anxiety condition which was greater than the control condition. Although women exhibited more pronounced changes in HR, both genders showed HR accelerations in response to shock. Taken together, these results suggest that our experimental manipulations elicited fear and anxiety and that these emotional states have opposite effects on pain reactivity.

4.1. Relation to prior empirical accounts

The analgesic effects of fear are in agreement with previous stress-induced analgesia studies conducted in animals (e.g. Bodner et al., 1980; Bolles and Fanselow, 1980; Fanselow, 1984; Grau, 1984, 1987; Watkins and Mayer, 1986; Maier, 1989; Meagher et al., 1989, 1990) and humans (e.g. Bobey and Davidson, 1970; Willer et al., 1981; Malow, 1981; Janal et al., 1984; Bandura et al., 1988; Pitman et al., 1990; Johnson and Helmstetter, 1994; Janssen and Arntz, 1996). For example, several animal studies have shown that exposure to a few moderately intense shocks can induce an opioid-mediated analgesia on the tail-flick and formalin tests (e.g. Fanselow, 1984; Grau, 1984; Meagher, 1989, 1990). A few human studies have also reported analgesia after exposure to discrete conditioned fear stimuli (Willer et al., 1981; Johnson and Helmstetter, 1986; Pitman et al., 1990). Willer et al. (1981) found that repeated exposure to a signal (CS) which predicted an extremely intense (70 mA) footshock (US) inhibited a nociceptive reflex in humans. What differentiates the present study is that we used moderate shock (12 mA) that presumably conditioned fear to the *context*. Although this method is frequently used in animal studies, it has received less attention in the human literature.

Our results support the view that anxiety induces hyperalgesia rather than analgesia (Melzack, 1961; Sternbach, 1968; Gracely et al., 1978; Chapman and Feather, 1983; Dellemijn and Fields, 1994). Although only a few studies have examined the effects of experimentally induced anxiety, the majority report enhanced pain. For example, Haslam (1966) showed that the threat of shock (without actual presentation) reduced radiant heat pain thresholds in humans. Likewise, several laboratories have shown that hyperalgesia is elicited by anticipation of a stressful interview, lack of control or predictability over shock, or a threatening description of the pain test itself (Bowers, 1968; Staub et al., 1971; Dougher et al., 1979, 1987; Schumacher and Velden, 1984; Cornwall and Donderi, 1988; Al Absi and Rokke, 1991). Although our results appear to conflict with Malow (1981), who reported that anticipation of shock produced analgesia, 'anxiety' was induced by exposing subjects to a 'sample' shock 1 min before pain sensitivity was tested. Rather than induce anxiety, this manipulation would be expected to condition fear to the context (Fanselow, 1984, 1986; Grau, 1987). Thus, Malow's findings provide further evidence that conditioned fear inhibits pain. The present results are also consistent with correlational studies indicating that anxiety is related to increased pain reports in clinical settings (e.g. Passchier et al., 1992; Palermo and Drotar, 1996) and in high trait anxious subjects (Staub et al., 1971; Dougher, 1979; Malow et al., 1987). Previously, these findings could not be interpreted in light

of empirical and theoretical accounts of stress-induced analgesia. However, the present study suggests that two mechanisms are at work: fear-induced analgesia and anxiety-induced hyperalgesia.

4.2. Underlying psychological mechanisms

Although the notion that there are two mechanisms is not new, theories of pain based on animal studies have emphasized the role of fear over anxiety. For example, the perceptual-defensive-recuperative (PDR) model proposes that fear inhibits pain because pain-related behaviors (i.e. nociceptive reflexes) interfere with other defensive responses, such as escape and avoidance. Although Bolles and Fanselow (1980) briefly acknowledge human studies indicating that anxiety may have a sensitizing effect, they suggest that it occurs less frequently and in situations where the state of fear was of 'the prolonged-duration, ill-defined variety usually called anxiety' (p. 299). In contrast, Walters (1994) general adaptive model of injury related behavior elaborates on the role of anxiety. This model suggests that when there is a high probability of injury, a fear state (active defensive response) is elicited that inhibits pain. In contrast, when the probability of injury is low, an anxiety state (a passive defensive response) and hyperalgesia result. Supporting this, we have recently shown that thermal pain reactivity is inhibited in rats after exposure to very severe shock, whereas hyperalgesia is observed after low to moderate intensity shock (Meagher et al., 1998, in review).

Several psychological theories suggest that attributional and attentional factors mediate the influence of fear and anxiety on pain in humans (Malow, 1981; McCaul and Malott, 1984; Weisenberg et al., 1984; Cornwall and Donderi, 1988; Al Absi and Rokke, 1991; Arntz et al., 1991, 1994; Janssen and Arntz, 1996). Unlike the present study, these models use the terms fear and anxiety interchangeably. Attribution theory suggests that pain inhibition occurs when fear/anxiety is unrelated to the pain-inducing event, whereas pain is enhanced when the anxiety/fear is related to the pain itself (Weisenberg et al., 1984; Al Absi and Rokke, 1991). From this perspective, the particular emotional state (fear versus anxiety) does not determine whether pain is enhanced or diminished, rather it is whether the emotion is perceived as relevant or irrelevant to the pain. The present findings do not support this view because both the fear and anxiety conditions were irrelevant to the pain test but produced opposite effects on pain reactivity.

In contrast, our findings appear consistent with attentional accounts (e.g. Malow, 1981; Mandler, 1984; McCaul and Malott, 1984; Malow et al., 1987; Cornwall and Donderi, 1988; Arntz et al., 1991, 1994; Janssen and Arntz, 1996, Janssen et al., 1998) which suggest that moderate levels of fear/anxiety will increase pain, whereas more intense fear/anxiety attenuates pain. According to this view, moderate levels of fear/anxiety enhance attention to salient events such as pain, thereby augmenting its perceived intensity. Conversely, high levels of fear may become more salient than pain, in which case fear would attenuate pain. Interestingly, Wall (1979) makes a similar prediction regarding the effects of arousal on pain but is silent regarding the role of attention. Although the present study was not designed to test these accounts, it could be argued that exposure to shock induced an extreme state of fear which diverted attentional resources away from the radiant heat test resulting in higher pain thresholds. In contrast, the moderate level of anxiety induced by the threat of shock increased attention to the most salient stimulus in the environment, the radiant heat, and hence lowered pain thresholds. It is important to note, however, that it is equally plausible that the anxiety condition diverted attention from pain processing. If so, then the hyperalgesic effect observed may be attributed to the anxiety state itself rather than attentional focus. To resolve this issue, future studies will need to assess the effects of our fear and anxiety manipulations on attentional processing. Such studies may reveal that changes in attentional focus inherently covary with changes in emotional states. Indeed, shifts in attention may be viewed as manifestations of emotional state changes which determine perceptual processing priorities.

Adaptation-level theory can also account for the effects of shock on thermal pain reactivity (Rollman, 1979). This theory suggests that the perceived intensity of a painful stimulus is judged within the context of other concurrent or remembered experiences. In the present case, subjects exposed to the suprathreshold shocks use this experience to anchor their judgements about the subsequent thermal stimulus. Because the shocks are more intense than the radiant heat, thermal pain reactivity is decreased.

In the present study, our experimental manipulations led to an increase in negative affect and arousal, with shock producing higher levels of fear and arousal than anticipatory anxiety. Because affective valence (unpleasantness) and arousal covaried, further work is needed to disentangle the relative contribution of these two factors. It is possible that these dimensions may have opposite effects (e.g. negative valence may induce hyperalgesia; arousal may elicit analgesia). Alternatively, these dimensions may interact to produce different outcomes depending on their product (e.g. low products yielding hyperalgesia; high products yielding analgesia). Support for the latter perspective comes from theoretical and empirical accounts suggesting that differential levels of valence and arousal may determine whether an aversive event induces hyperalgesia or analgesia (Wall, 1979; Walters, 1994; Meagher et al., 1998, in review). Additional research will be needed to determine whether these emotional states alter the sensory and/or affective dimensions of pain (Gracely et al., 1978), as well as their influence on response bias.

4.3. Underlying biological mechanisms

Multiple antinociceptive systems have been identified

which modulate nociception at different levels of the neural axis (Basbaum and Fields, 1984; Watkins and Mayer, 1986; Le Bars and Villanueva, 1988; Meagher et al., 1989, 1990, 1993). These mechanisms are influenced by fear and defensive systems which function to inhibit pain when an organism's safety is threatened. Supporting this, exposure to threatening stimuli has been shown to elicit a forebrain mediated analgesia through fear circuits in the amygdala which in turn activate descending pain inhibitory systems in the brainstem (Meagher et al., 1989, 1990; Helmstetter and Bellgowan, 1993; Fanselow, 1994). However, it is also clear that afferent stimulation can directly activate antinociceptive systems at the level of the spinal cord and brainstem (Watkins and Mayer, 1986; Meagher et al., 1993). Which system is engaged depends upon the duration and intensity of the aversive stimulus (Terman et al. 1984; Watkins and Mayer, 1986; Meagher et al., 1993), as well as the predictability and controllability of the event (Maier, 1989).

The present study showed that fear, associated with strong negative affect and intense arousal, can inhibit pain. The brief shocks used to induce fear had a surprising, sudden onset and have been shown to elicit a forebrain mediated analgesia in rats (Meagher et al., 1989, 1990). Because our methodology was modeled after these studies, it seems likely that the same fear circuits underlie the analgesia observed in our human subjects. However, it is also clear that pain can be inhibited by directly activating lower level analgesic mechanisms. For example, transcutaneous electrical nerve stimulation (TENS) which involves prolonged stimulations (20–30 min) that are gradually incremented, predictable, and controllable, ostensibly activates lower level antinociceptive mechanisms (e.g. Eriksson et al., 1985; Pomeranz, 1986, 1987; Chan and Tsang, 1987). Indeed, TENS procedures are designed to minimize induction of fear and arousal, which again suggests that TENS-induced analgesia depends on different (non-emotional) mechanisms.

The inhibition of thermal pain reactivity observed after shock may be linked to a phenomenon known as diffuse noxious inhibitory control (DNIC). Le Bars and colleagues have shown that the application of a noxious stimulus to any part of the body can produce a diffuse inhibition of nociresponsive neurons in the spinal dorsal horn in rats (Le Bars and Villanueva, 1988; Villanueva and Le Bars, 1995). DNIC is mediated by ascending spinal projections which trigger descending bulbo-spinal projections which in turn inhibit convergent neurons in the dorsal horn. Human studies have also shown that painful stimuli can inhibit both nociceptive reflexes and subjective pain elicited by sural nerve stimulation (Villanueva and Le Bars, 1995). This inhibitory effect is observed during the painful conditioning stimulus, but decays within 6–8 min following stimulus offset. Furthermore, the degree of inhibition observed increases with the intensity of the conditioning stimulus. Le Bars et al. have argued that the emotional/stressful properties of the painful conditioning stimuli are not responsible for this inhibitory effect because they do not use intolerable conditioning stimuli and do not observe changes in heart and respiration rates during the conditioning procedure (Le Bars et al., 1992). [In contrast, they suggest that emotional/stress reactions elicited by repeated exposure to intolerable pain may contribute to the inhibition reported by Willer et al. (1981).] However, it would be surprising if such painful stimuli had no effect on emotion, and hence, it remains possible that fear may contribute to the activation of descending pain inhibitory systems.

4.4. Summary

In conclusion, our findings indicate that fear and anxiety have divergent effects on pain reactivity in humans: fear reduces pain, whereas anxiety has a sensitizing effect. These data suggest that previous conflicting reports of the effects of anxiety on human pain were due to a failure to properly distinguish between the emotional states of fear and anxiety. Our use of parallel human and animal paradigms may prove especially useful for investigating the pain modulatory effects of conditioned and unconditioned emotional states, pharmacological treatments which alter affective states, and the neural circuits underlying fear and anxiety. From a clinical perspective, these data suggest that a patient anticipating an unpredictable threatening event will experience enhanced pain. In contrast, a patient that has been exposed to a threatening event will experience a fear state that inhibits pain processing

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