



## Negative affect: effects on an evaluative measure of human pain

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### Abstract

Prior work indicates that exposure to fear-inducing shock inhibits finger-withdrawal to radiant heat in humans (hypoalgesia), whereas anxiety induced by threat of shock enhances reactivity (hyperalgesia; Pain 84 (2000) 65–75). Although finger-withdrawal latencies are thought to reflect changes in pain sensitivity, additional measures of pain are needed to determine whether pain perception is altered. The present study examined the impact of negative affect on visual analog scale (VAS) ratings of fixed duration thermal stimuli. One hundred twenty-seven male and female human subjects were randomly assigned to one of three emotion-induction conditions: (1) negative affect induced by exposure to three brief shocks; (2) negative affect elicited by the threat of shock without presentation; and (3) neutral affect, with no intervention. VAS ratings were tested before and after emotion-induction. Results suggest that both negative affect manipulations reduced pain. Manipulation checks indicated that the emotion-induction treatments induced similar levels of fear but with different arousal levels. Potential mechanisms for affect induced changes in pain are discussed.

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### 1. Introduction

Several theories predict that negative affect can modulate the experience of pain (Melzack and Wall, 1965; Beecher, 1966; Melzack and Casey, 1968). Although understanding the link between negative emotion and pain may have implications for pain management, relatively few well-controlled studies have examined this issue. The few human studies that have been conducted report mixed results, with some observing decreased pain (Bobej and Davidson, 1970; Willer et al., 1979; Malow, 1981; Pitman et al., 1990; Janssen and Arntz, 1996; Rhudy et al., 1999; Rhudy and Meagher, 2000, 2001a), while others report increased pain (Haslam, 1966; von Graffenried et al., 1978; Schumacher and Velden, 1984; Weisenberg et al., 1984; Malow et al., 1987; Cornwall and Donderi, 1988; Meagher et al., 2001a).

In contrast, animal studies have examined the impact of a variety of stressors on pain, with most reporting pain inhibition (hypoalgesia) after exposure to noxious and

non-noxious aversive stimuli (Bodnar 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). Interestingly, many of these stressors (e.g. shock, predators, cues paired with shock) also elicit behaviors indicative of fear (e.g. freezing, tachycardia, increased startle, decreased social interaction), suggesting that fear mediates stress-induced hypoalgesia (Bolles and Fanselow, 1980; Fanselow, 1984, 1986; Lichtman and Fanselow, 1990). Indeed, under some circumstances the amygdala, a neurological structure implicated in the production of fear responses, can activate descending pain modulatory pathways (Helmstetter, 1992, 1993; Helmstetter and Bellgowan, 1993; Watkins et al., 1993; Fox and Sorenson, 1994; Manning and Mayer, 1995a,b; Manning, 1998; Crown et al., 2000). Taken together, these data suggest that highly arousing negative affective states, such as fear, can inhibit pain. However, under other circumstances pain enhancement (hyperalgesia) is observed following a stressor (Vidal and Jacob, 1986; Illich et al., 1995; King et al., 1996; Meagher et al., 1998a,b, 2001b; King et al., 1999; McLemore et al., 1999).

How can these seemingly divergent findings be resolved?

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Recent animal studies suggest that the direction of a modulation may depend on the severity of the stress-inducing event (Meagher et al., 1998, 2001a,b; Sieve et al., 2001). Hyperalgesia is typically observed after exposure to less severe stressors or in situations of diffuse threat (e.g. mild shock, novelty, holding), whereas hypoalgesia occurs after exposure to severe stressors (e.g. exposure to a predator, intense shock). Differences in the severity and imminence of the stress-inducing stimulus are likely to result in differences in arousal. Therefore, we have proposed that highly arousing negative affect may cause hypoalgesia in humans, whereas low-to-moderately arousing negative affect results in hyperalgesia (Rhudy and Meagher, 2000, 2001c; Meagher et al., 2001a,b).

This hypothesis was tested in three experiments modeled after animal studies. Rhudy and Meagher (2000) demonstrated that exposure to three brief shocks produced physiological and subjective indicators of fear (negative affect, high arousal), followed by increased finger-withdrawal latencies to radiant heat (hypoalgesia). In contrast, induction of anxiety (negative affect, low arousal) by verbal threat of shock (without actual delivery) decreased withdrawal latencies (hyperalgesia). In a subsequent study, surprising bursts of white noise were substituted for shocks to demonstrate that a non-noxious fear-inducing stimulus could elicit hypoalgesia (Rhudy and Meagher, 2001a). Recently, conditioned hypoalgesia was elicited by exposure to a stimulus (CS +) that had been previously paired with shock relative to a CS – that was unpaired (Rhudy and Meagher, 2001b). Because these studies were modeled after animal studies, pain reactivity was assessed using a method similar to the tail-flick test – finger-withdrawal from radiant heat. Similar to the tail-flick test, the latency from heat onset to finger-withdrawal was used as the index of pain reactivity. To further mimic the animal paradigm, a rapid onset heat stimulus was used that ostensibly elicited a finger-withdrawal reflex rather than a supraspinally mediated, evaluative pain response. Although it was assumed that the observed effects would generalize to other indices of pain, this hypothesis requires testing. This is important because several animal studies indicate that the inhibition of a protective withdrawal reflex is not necessarily associated with a reduction in supraspinally mediated measures of pain sensitivity (Meagher et al., 1989, 2001a,b; Morgan et al., 1994; Illich et al., 1995; King et al., 1996, 1997).

The present study evaluated the impact of negative affect on a pain index that requires supraspinal, evaluative processes. To do so, pain was tested before and after one of three emotion-induction conditions: (1) shock – exposure to three brief shocks intended to produce highly arousing negative affect (e.g. fear), (2) threat of shock – verbal threat of shock without delivery intended to produce moderately arousing negative affect (e.g. anxiety), and (3) neutral – no affect intervention. Pain was tested using subjective VAS ratings of a fixed duration and intensity heat stimulus. We hypothesized that the less severe threat of shock

manipulation would produce hyperalgesia while the relatively severe shock manipulation would produce hypoalgesia. Furthermore, to examine whether emotion differentially modulates threshold and suprathreshold pain, two intensities of heat were used. Half of the participants received heat at a fixed duration corresponding to their pain threshold, whereas half received heat with duration 20% longer than their pain threshold.

This study also evaluated whether the magnitude of pain modulation depends on test location by testing two other fingers (middle, ring) of the ipsilateral hand. Although several studies suggest that pain modulation may be localized (Prentice et al., 1996; Benedetti et al., 1999), others report diffuse modulation (Le Bars and Villaneuva, 1988; Villaneuva and Le Bars, 1995). If pain modulation is localized to the site of electrical stimulation (index finger), pain ratings on non-shocked fingers should be unchanged following shock exposure. Alternatively, if pain modulation is diffuse, ratings on non-shocked fingers should vary as a result of shock to the index finger.

## 2. Method

For a thorough explanation of methods, apparatus, and stimuli see the study by Rhudy and Meagher (2000).

### 2.1. Subjects

Participants were 127 undergraduate psychology students who received course credit for participation. Thirty-two were excluded due to equipment problems or failure to comply with instructions (i.e. removed finger from heat source before computer turned it off) leaving 48 women and 47 men. Of those, 87% were Caucasian, 9% Hispanic, 2% African American, and 2% Asian. Mean age was 19.01 years (SD = 1.07). Subjects were excluded if they had: circulatory, cardiovascular, or neurological problems, chronic pain, recently used tobacco, analgesics, antidepressants, or alcohol, or experienced a recent psychological trauma.

### 2.2. Apparatus and physiological recording

All data acquisition and stimulus presentation were computer-controlled. Skin conductance level (SCL) and heart rate (HR) sensors were attached to fingers of the non-dominant hand and sampled at 50 Hz. Blood pressure (BP) was measured pre- and post-experiment using a digital meter (Eckerd Drug Company-Model-E7622).

### 2.3. Electrocutaneous stimulation

Fear stimuli consisted of three, brief, 12 mA (moderately painful) shocks applied to the index finger of the dominant hand.

2.4. Radiant heat pain

To measure pain, a bottom-illuminated radiant heat device was used. Briefly, a condenser lens positioned above a slide projector bulb focused light onto the distal digit of the participants' blackened finger on the dominant hand. Initially, baseline pain threshold was assessed by having participants remove their finger as soon as the heat became painful. After a practice trial, two baseline pain threshold tests were assessed and averaged using this methodology. This average latency was used to calculate the duration for all constant heat pain tests. The constant heat test required participants to keep their finger on the heat source until it was turned off by the computer. Heat intensity varied between subjects – half received a heat stimulus equal to the duration of their average withdrawal (i.e. pain threshold) and half received a heat stimulus 20% longer than their average withdrawal (i.e. suprathreshold). The number of participants receiving each intensity was approximately equal across each affect condition (shock: thresh = 14/supra = 15, threat of shock: thresh = 16/supra = 20, neutral: thresh = 15/supra = 15). After every heat test, participants rated their pain on a 100 mm visual analog scale (VAS) ranging from 0 (no pain) to 100 (the most intense pain you can imagine). Pain was tested on three fingers of the dominant hand (index, middle and ring) to prevent sensitization and determine if pain modulation generalizes to other non-shocked fingers.

2.5. Manipulation checks

The self-efficacy to reduce pain (SE-PR) scale assessed the subject's belief that they can influence their pain (Rhudy and Meagher, 2000). The Center for Epidemiological Studies – depression scale (CES-D; Radloff, 1977) measured pre-existing emotional distress.

Participants rated their reaction to the emotion-induction procedure using the self-assessment manikin (SAM; Lang, 1980) and affective descriptors. Using the SAM,

participants rated subjective valence (1 'unhappy' to 9 'happy') and arousal (1 'calm' to 9 'excited'). Affective descriptors were 43 words (e.g. happy, fear, sad, angry) ranging from 0 (not at all) to 4 (strongly).

2.6. Procedure

Fig. 1 illustrates the experimental procedure. After obtaining informed consent, subjects were acclimated for 15 min while they completed demographics, SE-PR, CES-D and BP measures and the physiological sensors and stimulating electrodes were attached. After baseline testing, participants were randomly assigned to one of three emotion-induction conditions. In the shock condition (n = 29), stimulating electrodes were plugged into the stimulator and participants were told, "You may or may not receive brief, surprising, and painful shocks". This group received shocks. The same procedure was used for the threat of shock group (n = 36), except they did not receive shocks. To ensure that negative affect persisted throughout the remainder of the experiment, neither group was told the amount or timing of shocks. Participants in the neutral condition (n = 30) were told, "You will not receive any electrical stimulations" and electrodes were removed. After emotion-induction, six follow-up constant heat tests were conducted. After pain testing, participants rated their reaction to the emotion-induction condition and BP was re-assessed. All procedures were approved by Texas A&M University's IRB.

3. Results

For high sphericity, the Greenhouse–Geisser correction was used where epsilons ( $\epsilon$ ) are noted. Gender, condition and heat intensity (threshold vs. suprathreshold) were between-subject factors. Trial was a within-subject variable. Unless noted, gender and heat intensity were non-significant. Change scores were generated by subtracting baseline

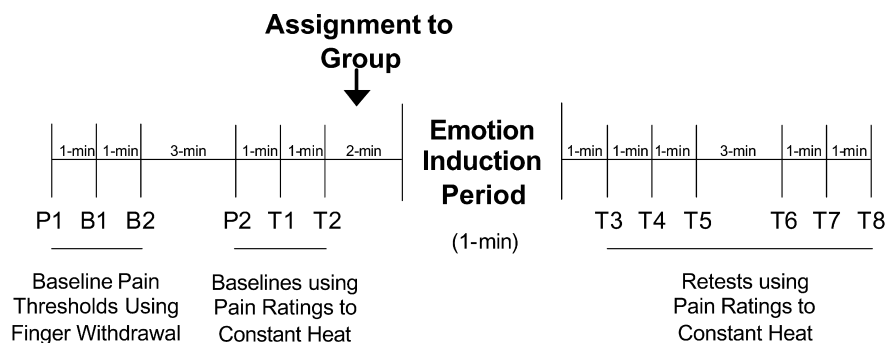


Fig. 1. Experimental procedure. After a practice trial (P1), two baseline pain thresholds (B1 and B2) were assessed at 1 min ITI using the finger-withdrawal method (rotating finger tested). The average of these baselines was used to determine the duration of future heat stimulations. Half of the participants received heat tests equal to their average withdrawal latency, while the other half received tests 20% greater than their average latency. A practice trial (P2) and two baseline pain tests (T1 and T2) were delivered using the constant heat intensity paradigm. Two minutes after T2, subjects were randomly assigned to one of three emotion-induction conditions. Pain was retested using the constant heat procedure at 1, 2, 3 and 6, 7, 8 min following emotion-induction.

Table 1  
Means and standard deviations of baseline VAS scores by heat intensity setting

		Finger-withdrawal method		Constant heat method	
		Baseline 1	Baseline 2	Baseline 1	Baseline 2
Threshold intensity setting ( $n = 45$ )	<i>M</i>	28.04	27.33	41.82	43.04
	<i>SD</i>	17.97	18.90	25.77	24.41
Suprathreshold intensity setting ( $n = 50$ )	<i>M</i>	24.68	24.39	43.16	43.50
	<i>SD</i>	16.34	17.97	22.77	20.06

Note: Means are in each column, below are standard deviations.

values from those collected during emotion-induction (SCL and HR) and post-induction (SCL, HR, pain, BP). Tukey LSD tests were used for follow-up planned comparisons ( $P$ -values are listed as follow-up tests are mentioned).

### 3.1. Participant exclusion

Several participants were excluded due to early finger removal ( $n = 27$ ), 22 were excluded due to finger removal following affect induction (neutral = 6, shock = 6, threat of shock = 10). The number of participants excluded did not vary significantly across conditions ( $\chi^2(2, n = 22) = 1.46, P = 0.48$ ). SCL data indicated increased physiological arousal following the onset of the constant heat tests, suggesting increase levels of fear. Because fear motivates avoidance behavior, it may explain the high level of non-compliance with instructions. Additionally, some subjects may have been confused because they were allowed to withdraw their finger during initial threshold testing.

### 3.2. Pain ratings

The two finger-withdrawal and two constant heat baselines were analyzed to determine if there were differences in VAS ratings. A significant trial effect [ $F(2.03, 180.93) = 71.97, P < 0.001, \epsilon = 0.68$ ] indicated that pain ratings following finger-withdrawal were lower

than ratings of the constant heat ( $P < 0.001$ ). Heat intensity did not have a significant effect on pain ratings [ $F(1, 89) = 0.05, P = 0.82$ ] (Table 1). Thus, exposure to constant heat led to pain ratings above threshold for both heat intensities, which did not differ from one another.

Pain ratings were analyzed in two ways. First, change scores were analyzed over time following emotion-induction (Fig. 2). Second, to examine whether pain modulation generalized to non-shocked fingers, trials corresponding to the shocked finger (index) were omitted and the remaining scores were averaged (1–3, 5–8 min) and change scores were created (Fig. 3).

In the first analysis, a significant condition effect [ $F(2, 83) = 3.55, P = 0.03$ ] suggested that shock decreased pain ratings compared to the neutral condition ( $P_s = 0.01$ ). This finding was qualified by a marginal trial  $\times$  condition interaction [ $F(7.22, 299.55) = 1.97, P < 0.06, \epsilon = 0.72$ ] suggesting that shock led to a decrease in pain compared to controls at 1, 2 and 3 min ( $P_s < 0.02$ ) and a marginally significant decrease at 6 min ( $P = 0.06$ ). Threat of shock also led to marginally significant decreases in pain at 1, 2 and 3 min ( $P_s < 0.07$ ) compared to controls. The difference between threat of shock and shock was only significant at 1 min. In sum, both the shock and threat of shock conditions induced hypoalgesia, but the threat of shock effect was smaller.

In the second analysis, a main effect for condition

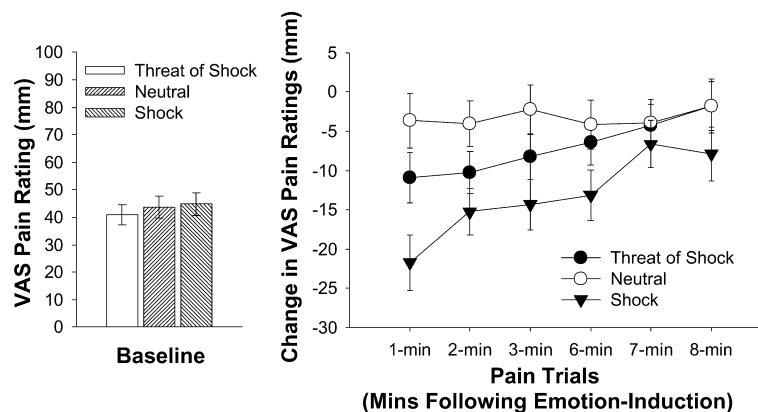


Fig. 2. The effects of emotion-induction on pain ratings to a fixed, constant radiant heat source. The left panel presents baseline VAS ratings to constant heat across all conditions. The right panel presents the mean change from baseline score ( $\pm$  SEM) for each condition at each pain retest.

Table 2  
Means and standard deviations of self-report data by condition

Condition		CES-D (0-60)	SE-PR (0-150)	SAM valence (1-9)	SAM arousal (1-9)	Scores on components of affective descriptors				
						Fear–anxiety	Anger	Humor	Happiness	Fatigue
Shock	<i>M</i>	9.72 <sub>a</sub>	43.03 <sub>a</sub>	4.14 <sub>a</sub>	6.62 <sub>a</sub>	0.27 <sub>a</sub>	0.53 <sub>a</sub>	−0.49 <sub>a</sub>	−0.45 <sub>a</sub>	−0.30 <sub>a</sub>
	<i>SD</i>	6.16	22.82	1.96	2.24	1.08	1.72	0.61	1.29	0.83
Threat of shock	<i>M</i>	11.00 <sub>a</sub>	45.31 <sub>a</sub>	4.53 <sub>a</sub>	5.17 <sub>b</sub>	0.17 <sub>a</sub>	−0.30 <sub>b</sub>	−0.34 <sub>a</sub>	0.28 <sub>b</sub>	0.24 <sub>a</sub>
	<i>SD</i>	8.76	30.28	1.86	2.37	1.13	0.42	0.67	0.69	1.07
Neutral	<i>M</i>	9.23 <sub>a</sub>	41.63 <sub>a</sub>	6.63 <sub>b</sub>	3.37 <sub>c</sub>	−0.64 <sub>b</sub>	−0.11 <sub>b</sub>	0.90 <sub>b</sub>	−0.04 <sub>a,b</sub>	0.14 <sub>a</sub>
	<i>SD</i>	5.62	25.47	2.01	1.79	0.37	0.43	1.05	1.10	0.96

Note: Each scale is followed by the range of potential scores. CES-D, Center for Epidemiological Study – depression scale; SE-PR, self-efficacy for pain reduction scale, valence and arousal are from the SAM, and the others are affective verbal descriptors. Means are in each column, below are standard deviations. <sub>a,b,c</sub> Means in the same column that do not share the same subscript differ at  $P < 0.05$ .

emerged [ $F(2, 82) = 3.52$ ,  $P = 0.03$ ]. Shocks decreased pain ratings compared to neutral and threat of shock ( $P < 0.05$ ). The trial  $\times$  condition interaction [ $F(2, 82) = 4.07$ ,  $P = 0.02$ ], indicated that shock led to decreased pain at 1–3 min ( $P < 0.05$ ), but not at 6–8 min ( $P > 0.05$ ). These data suggest that negative affect inducing shocks caused hypoalgesia that generalized to non-shocked fingers.

### 3.3. Confound and manipulation checks

#### 3.3.1. Self-efficacy and distress

Table 2 presents self-efficacy and distress data. Self-efficacy scores did not differ between conditions [ $F(5, 89) = 0.16$ ,  $P = 0.85$ ]; however, a significant gender effect [ $F(1, 89) = 6.04$ ,  $P = 0.02$ ] suggested that men scored higher than women ( $M = 50.00$  vs. 36.77). Although CES-D scores did not differ between conditions [ $F(2, 89) = 0.72$ ,  $P = 0.49$ ], a significant gender effect [ $F(1, 89) = 16.79$ ,  $P < 0.001$ ] indicated that women reported more distress than men ( $M = 12.83$  vs. 7.21). A gender  $\times$  condition interaction [ $F(2, 89) = 4.54$ ,  $P = 0.01$ ]

indicated that men's CES-D scores did not differ between groups, but women in the threat of shock condition scored higher than those in the neutral group ( $M = 6.00$  vs. 9.53;  $P = 0.02$ ). Because only gender differences were found, differences found for condition on other variables cannot be attributed to pre-existing differences in self-efficacy or emotional distress.

#### 3.3.2. Emotion ratings

Table 2 presents data for emotion ratings. For valence ratings, a significant condition effect [ $F(2, 89) = 15.15$ ,  $P < 0.001$ ] suggested that shock and threat conditions were more unpleasant than neutral ( $P_s < 0.001$ ). This was qualified by a gender  $\times$  condition interaction [ $F(2, 89) = 3.42$ ,  $P = 0.04$ ]. For women, the pattern was the same, but men only rated the shock condition as more unpleasant than the neutral. For arousal ratings, a condition effect was also found [ $F(2, 89) = 16.58$ ,  $P < 0.001$ ] and all conditions differed (shock  $>$  threat of shock  $>$  neutral;  $P < 0.01$ ). Thus, both the shock and threat of shock manipulations were rated as unpleasant and arousing, but shock was more arousing.

The number of affective descriptor variables was reduced by a principal components analysis (PCA) with Varimax rotation (Guadagnoli and Velicer, 1988). The scree plot suggested five components<sup>1</sup> should be extracted that accounted for 69% of the variance: (1) fear–anxiety, (2) anger, (3) happiness, (4) humor, and (5) fatigue. Factor scores for each component were analyzed. Groups

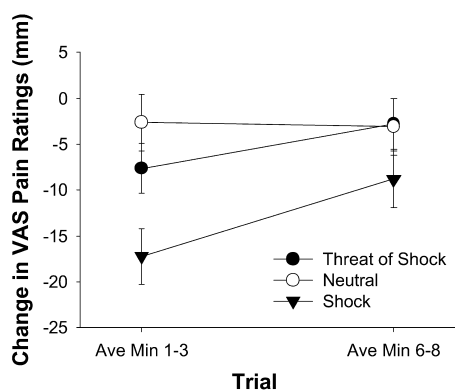


Fig. 3. The effects of emotion-induction on pain ratings of non-shocked fingers of the ipsilateral hand. Scores represent mean change from baseline scores ( $\pm$  SEM) for each condition that are averaged across 1–3 and 6–8 min to accommodate omitting shocked finger.

<sup>1</sup> To obtain the complete table of loadings from the PCA of affective descriptors, contact the authors. To briefly summarize, the following descriptors loaded on the fear–anxiety component: worried, scared, afraid, fear, nervous, frightened, dread, tense, panicky, uneasy, on edge, restless, helpless, jumpy, anxious, apprehensive, relaxed (negatively), nauseated (mean loading = 0.77). The anger component: spiteful, furious, desperate, hostile, annoyed, ready to fight, resentful, revolting, irritated, angry, disgusted (mean loading = 0.76). The humor component: funny, humorous, hilarious, lively, energetic, invigorated (mean loading = 0.75). The happiness component: pleased, cheerful, happy, joyous, elated, jovial, comforting (mean loading = 0.73). The fatigue component: bored, tired, fatigued (mean loading = 0.71).

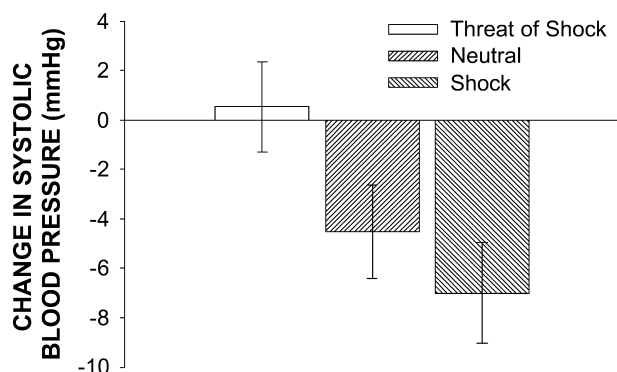


Fig. 4. The effects of emotion-induction on SBP. Means ( $\pm$  SEM) represent changes in SBP for each emotion condition measured at the beginning and end of the experiment.

differed on fear–anxiety, anger, humor and happiness [ $F(2, 80) > 3.87$ ,  $P_s < 0.04$ ], but not on fatigue [ $F(2, 80) = 2.54$ ,  $P > 0.05$ ]. Table 2 summarizes follow-up comparisons. Further, a gender effect was found for fear–anxiety and happiness ratings [ $F(1, 80) > 6.16$ ,  $P < 0.03$ ]. Women reported greater fear–anxiety ( $M = 0.22$  vs.  $-0.37$ ), and greater happiness ( $M = 0.20$  vs.  $-0.32$ ). Together, these data suggest that shock and threat of shock manipulations increased negative affect (fear–anxiety) and decreased positive affect (humor). Anger (shock  $>$  threat of shock) and happiness (shock  $<$  threat of shock) distinguished shock from threat of shock conditions.

### 3.3.3. Blood pressure (BP)

A condition effect was found for systolic BP (SBP) [ $F(5, 77) = 4.06$ ,  $P = 0.001$ ], but not for diastolic BP [ $F(5, 77) = 0.57$ ,  $P = 0.57$ ; Fig. 4]. Compared to controls, SBP in the group receiving threat of shock was moderately increased ( $P = 0.06$ ), whereas shocks did not lead to a significant change ( $P = 0.38$ ). However, SBP was significantly lower in the shock group than the threat of shock group ( $P = 0.007$ ). The shock induced decrease in BP

reflects an opponent parasympathetic response that occurs following fear-induced increases in BP.

### 3.3.4. Skin conductance level (SCL)

The emotion-induction conditions produced differential levels of SCL [ $F(2, 77) > 39.91$ ,  $P < 0.001$ ; shock  $>$  threat of shock  $>$  neutral;  $P_s < 0.01$ ; Fig. 5]. A significant trial effect was qualified by trial  $\times$  condition and trial  $\times$  gender interactions [ $F > 4.00$ ,  $P < 0.05$ ,  $\epsilon = 0.36$ ]. Shock and threat of shock groups were always higher than control ( $P_s < 0.001$ ), but the shock condition was only higher than threat of shock during emotion-induction and at 1, 2 and 6 min ( $P_s < 0.02$ ). In addition, men were lower than women at 6 min following emotion-induction ( $P = 0.03$ ). Thus, both the shock and threat of shock manipulations caused long-lasting increases in autonomic arousal, with shock having the greatest effect.

### 3.3.5. Heart rate (HR)

Although a significant effect for trial was found, this was qualified by a marginally significant trial  $\times$  condition interaction [ $F(6.76, 243.17) = 1.90$ ,  $P = 0.07$ ,  $\epsilon = 0.56$ ; Fig. 6]. Shock caused HR acceleration during emotion-induction compared to threat of shock ( $P < 0.04$ ) and controls ( $P < 0.05$ ). Threat of shock produced a moderate but persistent increase in HR compared to controls at 3, 6 and 7 min following affect induction, but these differences were only marginally significant ( $P_s \leq 0.08$ ). These data suggest that shock caused an immediate HR acceleration that quickly returned to baseline, but threat of shock caused a small increase in HR that persisted for 7 min.

## 4. Discussion

This study examined the influence of negative affect on pain ratings of a fixed duration suprathreshold heat stimulus applied before and after emotion-induction. Results indicated that fear-inducing shocks resulted in pain inhibition.



Fig. 5. The effect of emotion-induction on tonic SCL. Means represent change from baseline scores ( $\pm$  SEM) for SCL recorded during emotion-induction and 1 min prior to each pain retest.

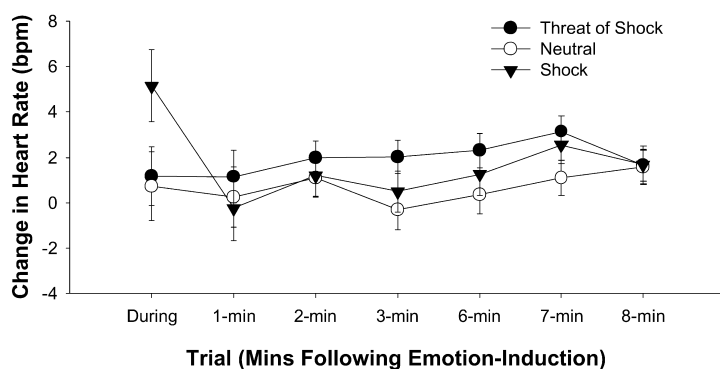


Fig. 6. The effect of emotion-induction on HR. Means represent change from baseline scores ( $\pm$  SEM) for HR recorded during emotion-induction and 1 min prior to each pain retest.

Furthermore, this hypoalgesia generalized to non-shocked fingers of the ipsilateral hand, suggesting that the effect was not specific to the shocked finger. In contrast to previously noted anxiety-induced hyperalgesia (Rhudy and Meagher, 2000), the threat of shock manipulation also resulted in hypoalgesia. Although this outcome was not predicted, manipulation checks suggest that methodological differences across studies may have altered the impact of our emotion-induction procedures. This issue will be returned to later in this discussion.

Consistent with prior work, manipulation checks indicated that our shock condition evoked greater increases in SCL during the affect induction phase than the threat of shock condition that was greater than the control condition. Shock also caused HR to accelerate during the emotion-induction period, but it returned to baseline within a minute. Furthermore, shock induced a compensatory decrease in SBP pre- vs. post-experiment compared to the threat of shock condition. In contrast, the threat of shock manipulation did not result in increased HR during the emotion-induction period; however, unlike our prior study a slight acceleration was observed post-induction at the 3, 6 and 7 min time points. Emotion ratings suggested that both the shock and threat of shock conditions led to increased reports of fear, anxiety, arousal and unpleasantness relative to the control condition. In contrast to the study by Rhudy and Meagher (2000), ratings of fear–anxiety and unpleasantness did not differ between the shock and threat of shock conditions. However, the shock condition resulted in higher ratings of arousal, anger and less happiness compared to the threat of shock manipulation. Groups did not differ on self-efficacy for pain reduction, psychological distress, or fatigue; therefore, differences between conditions cannot be attributed to these variables. Together, these data suggest that fear-induced hypoalgesia.

#### 4.1. Fear-induced hypoalgesia

The hypoalgesic effects of fear are consistent with previous animal and human studies (Bolles and Fanselow, 1980; Fanselow, 1984; Rhudy and Meagher, 2000, 2001a).

Furthermore, it extends this work by providing evidence that fear-induced hypoalgesia can be observed on an evaluative, supraspinal pain index (pain ratings). More recently, we have observed that conditioned fear induces hypoalgesia on finger-withdrawal and pain rating tests after exposure to a conditioned stimulus (CS +) that had been previously paired with shock relative to a CS – that was unpaired (Rhudy and Meagher, 2001b). These findings are consistent with other laboratories examining the effects of highly arousing negative affect on human pain. For example, Pitman et al. (1990) found that exposure to a combat-related video elicited a naloxone reversible hypoalgesia in veterans suffering from post-traumatic stress disorder (PTSD). In addition, several studies by Willer et al. (Willer, 1980; Willer and Ernst, 1986a,b) have demonstrated that conditioned fear leads to an opioid mediated decrease in pain ratings and increased RIII thresholds (Willer, 1980; Willer and Albe-Fessard, 1980; Willer et al., 1981; Willer and Ernst, 1986a,b). Additionally, Janssen and Arntz (1996) elicited an opioid mediated hypoalgesia by exposing spider phobics to spiders. And finally, in an unpublished account, Janssen and Arntz (as described in Janssen and Arntz, 1999) found that fear resulting from a first time parachute jump resulted in an opioid mediated hypoalgesia. Taken together, these data suggest that highly arousing negative affect inhibits pain.

The present study found that shock induced fear caused hypoalgesia that generalized to non-shocked fingers of the ipsilateral hand. This suggests that pain modulation generalizes to other areas of the hand that are at, or distal, to the shocked site. This is consistent with animal studies by Prentice et al. (1996) who found hypoalgesia to be greatest at or near the location of shock or at distal regions of other extremities. Although our experimental design did not address whether pain modulation generalizes to other extremities, recent work in our lab suggests that fear-induced hypoalgesia generalizes to the contralateral hand (Rhudy and Meagher, 2002).

Although the present study does not examine underlying physiological mechanisms, the brief shocks used to induce fear have been shown to elicit a forebrain mediated

hypoalgesia in rats (Meagher et al., 1989, 1990). Because our methodology was modeled after these studies, it is plausible that the same fear circuits mediate the hypoalgesia. Both animal and human studies have implicated the amygdala in the perception of environmental threat and production of fear responses (Adolph et al., 1995; LeDoux, 1996; Davis, 1997; Davidson and Irwin, 1999; Fendt and Fanselow, 1999). Additionally, the amygdala has been shown to play a role in descending pain modulation (Helmstetter, 1992; Helmstetter and Bellgowan, 1993; Watkins et al., 1993; Manning and Mayer, 1995a,b; Fields and Basbaum, 1999; Crown et al., 2000). Thus, it is likely that our fear-inducing shocks caused amygdala activation of descending pain inhibitory systems that regulate the flow of incoming nociceptive signals. Additionally, fear-induced activation of the amygdala may directly modulate the affective experience of pain within the brain.

#### 4.2. Anxiety-induced hypoalgesia?

In contrast to the hyperreactivity observed using finger-withdrawal as an index of pain (Rhudy and Meagher, 2000), the threat of shock condition decreased pain when a supraspinally mediated, evaluative measure was employed. Although anxiety-induced hypoalgesia was not predicted, there are several potential explanations for this effect.

First, anxious participants may have withdrawn their fingers prematurely in our previous study (Rhudy and Meagher, 2000) because they were engaged in avoidance responding, leading to an incorrect inference of hyperalgesia. If so, these participants should have reported less pain at the point of finger-withdrawal because heat exposure would have been reduced due to premature finger-withdrawal (i.e. before pain threshold). However, analyses of VAS pain ratings at the point of finger-withdrawal suggested that all participants used the same criteria to indicate their pain threshold (Rhudy and Meagher, 2000).

Second, the radiant heat stimulus may have activated different pain fibers in the two studies, leading to differential patterns of modulation. Although both studies used a stimulus previously shown to activate A $\delta$  fibers (Yeomans et al., 1996; Yeomans and Proudfit, 1996), the present study asked participants to leave their finger on the stimulus until the computer turned it off, resulting in suprathreshold stimulation that may have activated C-fibers. Supporting this, VAS ratings of baseline finger-withdrawal tests were lower than ratings of the fixed, constant heat in both the low and high intensity groups. Thus, it is possible that the threat of shock manipulation differentially modulated A $\delta$  and C-fibers via central (Chiang et al., 1995; Wang et al., 1996) or peripheral (Morton et al., 1997) mechanisms.

Third, the threat of shock manipulation in the current experiment may have elicited greater negative affect and arousal than in Rhudy and Meagher (2000). Consistent with this view, manipulation check data indicates that the threat of shock condition resulted in higher levels of self-reported

fear–anxiety, unpleasantness and HR than the previous study. In contrast, Rhudy and Meagher (2000) observed a small non-significant HR deceleration during threat of shock. Across studies, HR acceleration appears to be linked to pain inhibition and deceleration to pain enhancement (Rhudy and Meagher, 2000, 2001a). Indeed, we have previously noted that hyperalgesia and HR deceleration occurred following non-noxious noise bursts in men (Rhudy and Meagher, 2001a). In the present study, changing the radiant heat test from a subject-controlled pain threshold measure to a computer-controlled suprathreshold pain rating test may have inadvertently altered the participant's emotional state. Exposure to uncontrollable suprathreshold pain during baseline testing alone may have led the participants to fear upcoming constant heat pain tests. Because fear motivates avoidance behavior, this may explain why many subjects were non-compliant with instructions to keep their finger on the radiant heat device during the constant heat pain tests. This interpretation is consistent with our hypothesis that negative affect with high arousal should lead to hypoalgesia, with hyperalgesia resulting from negative affect with low-moderate arousal (Rhudy and Meagher, 2000, 2001c; Meagher et al., 2001). To examine this issue, additional analyses were conducted to determine if SCL or HR increased as a result of suprathreshold testing. Indeed, SCL, but not HR, increased following the onset of constant heat tests [trial effect,  $F(2, 154) = 41.36, P < 0.001$ ]. Although this was unanticipated, it highlights the importance of using manipulation checks to determine the nature of the affective state elicited because variables other than the emotion-induction procedure may alter affect.

#### 4.3. The potential role of attention

Our findings appear consistent with prior attentional accounts (Villemure and Bushnell, 2002; Mandler, 1984; Malow et al., 1987; Cornwall and Donderi, 1988; Arntz and De Jong, 1993; Janssen and Arntz, 1996). These theories suggest that moderate levels of fear/anxiety enhance attention to salient events such as pain, thereby augmenting its perceived intensity. In contrast, high levels of fear may become more salient than pain, in which case fear would attenuate pain. While the present study was not designed to test these accounts, it could be argued that exposure to shock, or the threat of shock, induced a more extreme state of fear which diverted attentional resources away from the heat test resulting in lower thermal pain ratings. Future studies are needed to assess the effects of our shock and threat of shock manipulations on attention. It should be noted, however, that changes in attentional focus might inherently covary with changes in emotional state in our studies. Shifts in attention may be viewed as manifestations of emotional state changes that determine perceptual processing priorities. To resolve this issue, changes in emotion must be dissociated from changes in attention.

Related to this issue, a recent study independently manipulated the subject's attentional focus and the hedonic value of an odor distractor, finding that attention and odor valence independently altered pain perception (Villemure and Bushnell, 2002).

The present findings are consistent with adaptation level theory (Rollman, 1979), that suggests the perceived intensity of a painful stimulus is evaluated within the context of other concurrent or remembered experiences. In the present study, subjects exposed to the shocks, or the threat of shock, use this experience to anchor their ratings of the thermal stimulus. Because the shocks are more intense, or are imagined as more intense, thermal pain ratings were lower. Although we do not have pain ratings for shock, our SCL data suggest that the shock and threat of shock resulted in greater levels of arousal than did our thermal pain stimuli during the baseline period. This would suggest that they were experienced as more aversive.

#### 4.4. Summary

In sum, the present study found that fear-inducing shocks caused pain inhibition when an evaluative pain measure was used. Furthermore, this effect was observed on non-shocked fingers of the ipsilateral hand, suggesting that inhibition generalized beyond the site of stimulation. This hypoalgesia may reflect the actions of a descending pain inhibition circuit activated by the amygdala, a key neurological structure in the processing of fear. In contrast to previous reports, threat of shock also led to hypoalgesia, although the effect was weaker and potentially attributable to fear induced by suprathreshold pain testing.

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