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Affective associative learning modifies the sensory perception of nociceptive stimuli without participant's awareness

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Abstract

The present experiment examined the possibility to change the sensory and/or the affective perception of thermal stimuli by an emotional associative learning procedure known to operate without participants' awareness (evaluative conditioning). In a mixed design, an aversive conditioning procedure was compared between subjects to an appetitive conditioning procedure. Both groups were also compared within-subject to a control condition (neutral conditioning). The aversive conditioning was induced by associating non-painful and painful thermal stimuli – delivered on the right forearm – with unpleasant slides. The appetitive conditioning consisted in an association between thermal stimuli – also delivered on the right forearm – and pleasant slides. The control condition consisted in an association between thermal stimuli – delivered for all participants on the left forearm – and neutral slides. The effects of the conditioning procedures on the sensory and affective dimensions were evaluated with visual analogue scale (VAS)-intensity and VAS-unpleasantness. Startle reflex was used as a physiological index of emotional valence disposition. Results confirmed that no participants were aware of the conditioning procedure. After unpleasant slides (aversive conditioning), non-painful and painful thermal stimuli were judged more intense and more unpleasant than when preceded by neutral slides (control condition) or pleasant slides (appetitive conditioning). Despite a strong correlation between the intensity and the unpleasantness scales, effects were weaker for the affective scale and, became statistically non-significant when VAS-intensity was used as covariate. This experiment shows that it is possible to modify the perception of intensity of thermal stimuli by a non-conscious learning procedure based on the transfer of the valence of the unconditioned stimuli (pleasant or unpleasant slides) towards the conditioned stimuli (non-painful and painful thermal stimuli). These results plead for a conception of pain as a conscious output of complex informational processes all of which are not accessible to participants' awareness. Mechanisms by which affective input may influence sensory experience and clinical implications of the present study are discussed.

Keywords: Pain affect; Multidimensional pain experience; Evaluative conditioning; Emotion; Consciousness; Startle reflex

1. Introduction

The relation between pain and classical conditioning has almost exclusively been studied in animals, and more particularly through the conditioned stress-induced analgesia phenomenon. Hypoalgesia is observed in fearful animals as part of a more general defense reaction to danger (Bolles and Fanselow, 1980) which can be triggered by either natural or learned stressors. Typically, in conditioned stress-induced analgesia studies, a tone-signal (the conditioned stimulus or CS) acquires, through pairing with an electric shock (the unconditioned stimulus or US), the same ability as the US to elicit hypoalgesia. Recently, Flor and Grüsser (1999) have shown that classically conditioned stress-analgesia could also be obtained in humans. Nevertheless, they questioned whether not only analgesia but also hyperalgesia could be influenced by learning as observed in animals (McLemore et al., 1999; Meagher et al., 2001). As a matter of fact, clinical experience suggests that anxiety and depression often enhance pain perception rather than reduce it. It would be expedient to conclude that negative emotions should increase pain perception while positive emotions should decrease it (Vingoe, 1994).

That pain perception may be modified by emotional (or motivational) conditionings has already been suggested by animal counterconditioning experiments conducted in Pavlov's laboratory (Erofeeva, 1916, 1921, cited in Dick-

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inson and Pearce, 1977). It was shown that noxious stimuli (electrical shocks, heat) consistently followed by food, did not elicit nociceptive responses (as withdrawal reflexes) but, on the contrary, appetitive responses (as salivation, approach behaviors). Besides animal counterconditioning experiments, human studies have also shown that the aversiveness (or the pleasantness) of a stimulus may be modified by an affective conditioning procedure. Many experiments have repeatedly demonstrated that the mere contingent presentation of neutral stimuli (neutral pictures or odors) with liked or disliked stimuli (pleasant or unpleasant pictures or odors…) is sufficient to change the neutral stimulus into a stimulus with positive or negative affective value (Levey and Martin, 1975; Baeyens et al., 1990; Hamm et al., 1993; Todrank et al., 1995; Stevenson et al., 1998). Importantly, this kind of affective (or evaluative) conditioning is considered as operating without awareness since participants are unable to recall which stimuli have been paired with which others. According to Zajonc (1984) or Levey and Martin (1975), all living organisms evaluate their environment in terms of what is beneficial/harmful, pleasant/unpleasant. This evaluation triggers an immediate, irresistible reaction in terms of autonomic, motor or verbal responses. Although each organism is equipped or 'hard-wired' with the essential likes and dislikes appropriate to its probable environment, it can also acquire new 'likes' and 'dislikes' that facilitate adaptation to the actual environment. Evaluative conditioning then refers to the process by which an evaluative reaction (ER) evoked by a significant unconditional stimulus (US) is transferred to a previously neutral stimulus (CS), presented contingent to the significant stimulus.

In this perspective, the present experiment was designed to study whether prior unconscious associations between thermal stimuli (non-painful and painful) and an emotional context may subsequently modify the sensory and/or the affective perception of these thermal stimuli in an emotionally neutral context. In the majority of cases, the nociceptive stimuli may be considered a US because perception of pain is an inherent quality of life itself and because it does not require any prior experience. However, as stressed by Anand and Craig (1996), sensory experiences are also mediated by the affective impact of other positive and negative experiences that are contiguous with a nociceptive stimulus. Thus, in the present experiment, thermal stimuli will be considered the stimuli to be conditioned (CS) and the emotional contexts (pleasant or unpleasant pictures) the US.

A number of theorists (e.g. Konorski, 1967; Estes, 1969; Bindra, 1974) have suggested that the motivational properties of stimuli are mediated by two separate central systems that sustain appetitive and aversive behaviors. The strength of appetitive or aversive behaviors is seen as determined by the level of activity in the related system. Consequently, manipulations designed to increase activity in the aversive system, such as presenting an aversive CS or US, should increase the strength of defensive behavior, whereas the occurrence of an aversive inhibitor (e.g. appetitive CS or US) should result in a drop of defensive behavior (Dickinson and Pearce, 1977). Thus, we hypothesize that the association of painful stimuli with aversive emotional events reinforces the aversiveness of noxious stimuli. Furthermore, it is well-known that aversive stimuli can easily inhibit appetitive behavior, whereas it is harder to inhibit aversive behaviors with appetitive stimuli (for discussion see Dickinson and Pearce, 1977; Bouton, 1993). Consequently, we hypothesize that it is easier to increase the aversiveness of painful stimuli (aversive conditioning) than to decrease it (appetitive conditioning). Nevertheless, we expect that associations of painful stimuli with positive pictures should alleviate painful stimulus perception. The fact that motives can inhibit each other is indeed suggested by the counterconditioning experiments conducted in Pavlov's laboratory as mentioned above (Erofeeva, 1916, 1921, cited in Dickinson and Pearce, 1977).

In concordance with actual multidimensional models of pain, the effects of conditioning manipulations were evaluated on both sensory (visual analogue scale (VAS)-intensity) and affective (VAS-unpleasantness) dimensions of pain. We propose to complete both scales by a biological measure of the affective dimension (startle reflex). The choice of the startle reflex is based on the fact that the affectivo-motivational dimension of pain is less well defined and operationalized than the sensory dimension. Gracely (1992) has proposed a definition of the 'immediate pain affect' dimension that is akin to the concept of valence (unpleasantness) as described in recent dimensional models of emotion (e.g. Frijda, 1986; Leventhal and Scherer, 1987; Öhman, 1987; Lang et al., 1990). Based either on the innate preference/aversion (sensorimotor level) or on learned preference/aversion (schematic level), intrinsic pleasantness evaluation (emotional valence) determines whether a stimulus event is pleasant – inducing approach tendencies, or unpleasant – inducing avoidance tendencies (Leventhal and Scherer, 1987). In case of unpleasant feelings associated with the immediate nociceptive sensation ('immediate unpleasantness') behaviors of escape and avoidance are automatically evoked, i.e. independently of conscious cognition (Gracely, 1992), as an 'action readiness' (Jensen and Karoly, 1992) or an 'urge to escape' (Crombez, 1994). Lang et al. (1990) have demonstrated that the startle reflex is a valid psychophysiological method to measure the valence disposition of an organism. Replicated in numerous studies (for a review see Lang et al., 1990), Vrana et al. (1988) showed that the amplitude of the defensive startle reflex to a sudden noise is accentuated during unpleasant emotional states (elicited by slides or films of aversive contents) and reduced during pleasant emotional states (elicited by slides of pleasant contents). In the pain field, Crombez et al. (1997) obtained potentiation of a startle reflex to a noise burst during noxious thermal stimuli in comparison with low-intensity stimuli. Considering that the vigor of the startle reflex is dependent on the ongoing emotional state, we

hypothesize that the startle reflex is enhanced during non-painful and painful stimuli previously associated with aversive stimuli and diminished when non-painful and painful stimuli have been conditioned with pleasant pictures.

2. Method

2.1. Participants

Participants were 38 undergraduate psychology students (32 women, 6 men; 18–20 years of age). They were all right-handed and free of medication. They received course credit for their participation and were informed they could withdraw from the experiment at any time without losing their course credit. The rules of the Ethics Committee of the Faculty of Psychology were observed.

2.2. Stimulus materials

USs used during the conditioning phase were a selection of color slides with various affective contents coming from the International Affective Picture System (IAPS, Center for Psychophysiological Study of Emotion and Attention, University of Florida, Gainesville, USA, 1994). The selection of slides was realized during a pre-experiment designed to validate the IAPS material on an European student population ($n = 25$) on two parameters: (1) a bipolar valence VAS (unpleasant vs. pleasant) and (2) the magnitude of the startle reflex (see Section 2.3) elicited by a startle probe when viewing the slides. Aversive USs were chosen among slides that were rated as the most unpleasant (symbolized by ☹ US), and elicited the largest startle reflexes. Reciprocally, appetitive USs were selected among slides that were judged the most pleasant (symbolized by ☺ US), and elicited the smallest startle reflexes. It was also checked that neutral slides (symbolized by 😐 US) induced scores around mid-point on the bipolar valence VAS and intermediary startle responses in our student population. Four pictures of mutilations (IAPS numbers 3010 (*mafia hit*), 3060 (*mangled face*), 3120 (*body*), 3170 (*baby with tumor*)) were used as unpleasant USs to induce the aversive conditioning. The appetitive conditioning was induced by four pictures of pleasant scenes which were partly different for female (1610 (*rabbit*), 2530 (*elderly couple*), 2540 (*mother and baby*), 4470 (*nude male*)) and male (1610 (*rabbit*), 2540 (*mother and baby*), 4250 (*erotic female*), and 4290 (*nude female*)) participants. During both types of conditioning, four neutral pictures were used as 'neutral' USs (IAPS numbers 7000 (*rolling pin*), 7080 (*fork*), 7090 (*book*), and 7150 (*umbrella*)) as a within-subject control condition. Pictures were presented two times and 16 other neutral pictures served as distractors during inter-trial intervals.

The to-be-CS were non-painful and painful thermal stimuli delivered on the volar surface of the forearm. Although the research focus mainly on the nociceptive system, non-painful stimuli were also used as conditioned stimuli in order to have – as in prototypical pavlovian conditioning studies – really neutral CSs. This kind of baseline was needed because it could not be asserted that aversive pictures (the US) would be sufficiently negative to make the already aversive painful stimuli (CSs) still more aversive. The non-painful stimulus temperature was fixed at 40°C for all participants whereas the painful stimulus temperature was adjusted to each participant's pain threshold (43–47°C). Thermal stimuli reached the maximum temperature in 10 s. which was maintained for 4 s. (i.e. the plateau temperature). Then the thermode took 15 s more to return to its baseline temperature (fixed at 37°C), participants were instructed to remove their forearm from the thermode as soon as they felt temperature falling. Judgments of intensity and unpleasantness concerned the perception during the thermal plateau. No participant realized that there were only two different plateau levels. The acoustic startle probe stimuli (110 dB white noise) were presented binaurally through headphones for 50 ms. They were delivered with a random latency during the thermal plateau (i.e. between tenth and 14th second after thermal stimulus onset). No probes were administered during the conditioning phase.

2.3. Apparatus and recording

The eyeblink component of the startle response was measured by recording electromyographic (EMG) activity over the orbicularis oculi muscle beneath the left eye using Ag/AgCl surface electrodes (Meditrace model ECE1801) connected to a Gould Universal Amplifier (Model 134615-58) with a bandpass of 0.1–1 kHz and a gain of $\times 25{,}000$. The raw EMG signal was digitized (Cambridge Electronic Design Model 1401, UK) at 4000 cps for a period of 400 ms, beginning 100 ms before the onset of the startle probe. The recordings were stored for off-line analysis with the SIGAVG V6.30 software procedures (Cambridge Electronic Design, UK). The eyeblink response was quantified by computing the mean amplitude (μV) of the full-wave rectified EMG over a time-window of 75 ms, starting 25 ms after the acoustic probe onset. For each record, a baseline correction was performed by subtracting the mean amplitude of a 75 ms pre-stimulus time-window from the eyeblink response.

Thermal stimuli were delivered via a thermode of $25 \times 50\ mm^2$ and were designed by the T-Pulse software (Somedic, Sweden). Thermal thresholds (sensory and pain thresholds) were estimated by the Senselab software (Somedic, Sweden). An electronic timer (Master-8, Israel) controlled the onset and offset of the slide projections, the inter-trial intervals, and the sequence of thermal stimuli and startle probes.

Sensory and affective dimensions of pain were assessed by VASs. Researchers consider that simple VAS measures of pain-sensation (VAS-intensity) and pain affect (VAS-

unpleasantness) may be extremely helpful in identifying these factors (Price et al., 1987). Intensity and unpleasantness ratings were expressed on 11-cm scales, with higher scores indicating that stimuli were judged more intense or more unpleasant. Visual stimuli were presented by a slide projector (Leitz Pradovit CA-2500, Germany) situated in the experimental room. The pictures were projected onto a white screen (120×100 cm^2) approximately 1.5 m in front of the participant. The size of the visible picture was 100×80 cm^2. Slides used to induce the USs were projected for 11 s starting 7 s after thermal stimulus (CS) onset. Slides used as distractor stimuli were projected for 4 s during the inter-trial interval (i.e. at the 51st second after thermal stimulus onset).

2.4. Procedure and design

After arriving at the laboratory, volunteers consented to the procedure after having received information that painful thermal stimuli and emotional pictures would be used. They were misleadingly informed that the aim of the experiment was to study how emotions and cognitions interact to modify the perception of thermal stimuli. From the outset, participants were told that they would choose themselves (based on their pain threshold) the most painful stimulus used which would never be exceeded during the experiment. Physiological sensors were then attached while the participant sat down in front of a table where the thermode was fixed. Participants were informed that occasional noises heard over headphones could occur and be ignored. Two preliminary startle probes were presented. As the session was long and complex, participants were explained that the experiment comprises four phases (i.e. sensory and pain thresholds assessment, pre-conditioning, conditioning and post-conditioning phases) and that they would progressively receive more details concerning the procedures.

2.4.1. Phase 1: sensory and pain thresholds assessment

In order to familiarize participants with thermal stimuli, they were instructed that a series of six thermal stimuli (i.e. heat ramps of +2°C/s) would be delivered on their right arm and that they should press the pushbutton as soon as they felt a rise in temperature (sensory threshold). After that, the pain threshold was measured for each participant through six similar thermal stimuli (delivered alternatively on both forearms) which were reversed (turning points in °C) by pressing the pushbutton as soon as the participant judged them as becoming painful. The pain threshold was defined as the average of the temperatures measured at the six turning points. This averaged temperature was used as the painful stimulus during the whole experimental session.

2.4.2. Phase 2: pre-conditioning

Participants were then familiarized with the evaluation of thermal stimuli. Referring to the procedure used by Harkins et al. (1989), they were explained the differential meaning of VAS-intensity and VAS-unpleasantness scales. All participants ($n = 38$) were then exposed to six non-painful and six painful thermal stimuli delivered alternatively on the right and the left forearm. Non-painful and painful temperatures were randomly distributed with the restriction that no more than two identical successive temperatures were allowed. On ten of the 12 thermal trials, acoustic startle probes were administered with a random latency but during the thermal plateau. To enhance unpredictability of the startle presentation, ten startle probes were also presented during inter-trial intervals (between the 16th and the 20th second after the thermal stimulus onset). As soon as participants felt the temperature falling, they were instructed to remove their arm from the thermode and to express immediately their judgment on the intensity and unpleasant VAS scales. This pre-conditioning phase was performed in dim light (a desk lamp was just turned on during participants' ratings) in order to mimic the context of the conditioning phase where similar lightning was imposed by slide projections.

2.4.3. Phase 3: conditioning

Participants were informed that, while still exposed to thermal stimuli on both arms, they would see a series of slides. The experimenter explained that participants should concentrate on each picture because difficult questions would be asked about it at the end of the experiment. The 38 volunteers were randomly assigned to one of the two between-subject conditions i.e. aversive or appetitive conditioning. To induce the aversive conditioning, one half of the participants ($n = 19$) were receiving thermal stimuli on their right forearm (☹ CS +) when they saw unpleasant slides (☹ USs) and on their left forearm (😐/☹ CS$^-$) when they saw neutral slides (😐 USs). Alternatively, the other half of participants ($n = 19$) were submitted to an appetitive conditioning so that thermal stimuli delivered to the right forearm (☺ CS +) were systematically associated to pleasant scenes (☺ USs) and thermal stimuli delivered to the left forearm were always associated to neutral slides (😐/☺ CS$^-$). In a within-subject design, thermal stimuli conditioned by valenced pictures (on the right arm) were considered as 'relevant conditioned stimuli' (CS +) whereas thermal stimuli conditioned by neutral pictures (on the left arm) were used as a control condition, and then considered as 'irrelevant conditioned stimuli' (CS$^-$). The USs used were four pleasant, four unpleasant and four neutral pictures which were shown two times during the conditioning procedure. The sixteen non-painful and painful thermal stimuli used were distributed in a random order with the restriction that no more than two identical successive temperatures were allowed. Valenced and neutral pictures were projected alternatively. To help participants to dismiss the vividness of pictures from their minds (particularly mutilation scenes), distractive neutral pictures and logic problems were introduced between each conditioning trial. No physiological or psychometric measures were taken during this conditioning step. Using this pretext to make a pause, the experimenter

Table 1
Description of symbols used in text and Fig. 1

Symbol	Description	Experimental design
US	*Unconditioned stimulus*	*Slides*
☹ US	Aversive unconditioned stimulus	*Aversive* slides used to induce the aversive conditioning
☺ US	Appetitive unconditioned stimulus	*Appetitive* slides used to induce the aversive conditioning
😐 US	'Neutral' unconditioned stimulus	*Neutral* slides used as control condition
CS	*Conditioned stimulus*	*Thermal stimuli*
CS +	Relevant conditioned stimulus	Thermal stimuli delivered to the right forearm which have been associated with *valenced* (aversive or appetitive) slides
CS$^{\sim}$	Irrelevant conditioned stimulus	Thermal stimuli delivered to the left forearm which have been associated with *neutral* slides
☹ CS +	Aversive relevant conditioned stimulus	Thermal stimuli delivered to the right forearm which have been associated with *aversive* slides
☺ CS +	Appetitive relevant conditioned stimulus	Thermal stimuli delivered to the right forearm which have been associated with *appetitive* slides
😐/☹ CS$^{\sim}$	Neutral-irrelevant conditioned stimulus for the group receiving aversive US	Thermal stimuli delivered to the left forearm which have been associated with *neutral* slides while thermal stimuli delivered to the right forearm were associated with *aversive* slides
😐/☺ CS$^{\sim}$	Neutral-irrelevant conditioned stimulus for the group receiving appetitive US	Thermal stimuli delivered to the left forearm which have been associated with *neutral* slides while thermal stimuli delivered to the right forearm were associated with *appetitive* slides

ended this phase by commenting, with each participant, the solutions of the logic problems.

Table 1 provides a short description of the different symbols used.

2.4.4. Phase 4: post-conditioning and awareness assessment

The post-conditioning phase was rigorously identical, for both experimental groups, to the former pre-conditioning phase (phase 2). Dependent variables (VAS scores and startle responses) were recorded during 12 thermal stimuli trials. At the end of this phase, the experimenter removed headphones and physiological sensors. Participants were then instructed to complete a recognition questionnaire to assess whether they had noticed any contingency between the CSs and the USs. A first question asked participants to identify from a list of pictures those which were associated to thermal stimuli applied to the right forearm and those which were associated to thermal stimuli applied to the left forearm. A second and a third question explicitly asked participants if they had noticed a link between (a) aversive (or appetitive) slides and the right arm and (b) the neutral slides and the left arm. Finally, participants were informed about aims and methodological details of the experiments.

2.5. Data transformation and analysis

Dependent variables (scores of intensity and unpleasantness on VAS, magnitude of eyeblink reflex) were standardized within-subjects using a z-score transformation (i.e. raw scores for each participant were subtracted from that person's mean score and divided by that person's standard deviation). In order to evaluate the effects of conditioning procedures, difference scores (post-conditioning minus pre-conditioning) were computed for each dependent measure and entered into a 2 ('group': aversive/appetitive conditioning) × 2 ('painfulness': non-painful/painful thermal stimuli) × 2 ('CS relevance': CS + /CS$^{\sim}$) analysis of variance (ANOVA) with repeated measurements of the last two variables. As the direction of our hypothesis was clearly given by previous experimental studies on conditioning (for a review see e.g. Dickinson and Pearce, 1977; Lang et al., 1990), a priori one-tailed orthogonal contrasts (Bonferroni mean comparisons) and *t*-tests were also used.

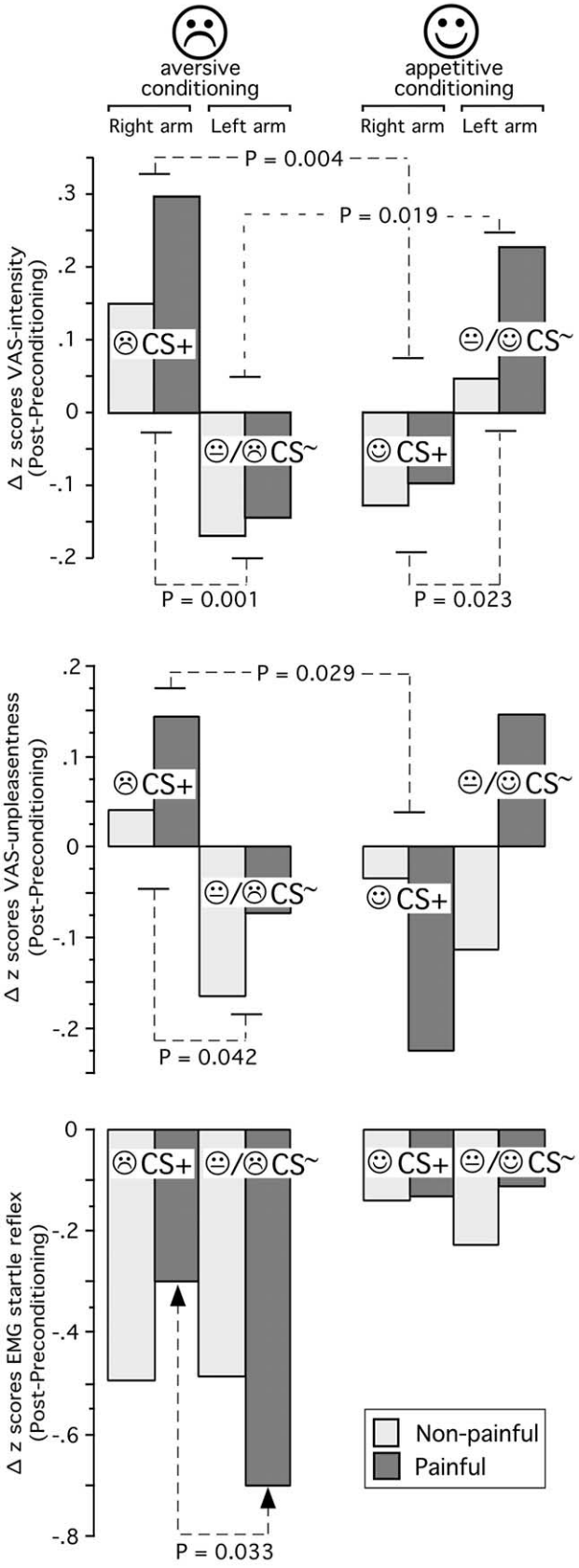
3. Results

3.1. Contingency awareness

The questionnaire concerning contingency awareness (see Section 2.4.4) revealed that no participants were aware of the contingency between the CS and the US. No participants were able to associate in more than a random fashion pain stimulus sidedness with slides valence. Furthermore, when explicitly asked, none of them had realized (a) that aversive (or appetitive) slides were always associated to thermal stimuli delivered on the right arm and (b) that neutral slides were always associated to thermal stimuli delivered on the left arm.

3.2. Pre-conditioning analysis

First analyses were conducted in order to verify both the presence of a painfulness effect and the group equivalence prior to conditioning procedures. Standardized dependent variables were entered into a 2 × 2 × 2 repeated measures



ANOVA using 'group' as a between-group factor and both 'painfulness' and 'conditioned stimulus relevance' as within-group variables. As expected, results confirmed that painful thermal stimuli were judged more intense ($F(1,36) = 481.6$, $P < 0.000$) and more unpleasant ($F(1,36) = 473.0$, $P < 0.000$) than non-painful thermal stimuli. Startle response magnitudes were marginally larger during painful stimuli than during non-painful stimuli ($F(1,36) = 3.418$, $P = 0.092$). Although this result only approaches statistical significance, our a priori hypothesis was strong enough (replicating the study of Crombez et al., 1997) to consider one-tailed probability results as significant (one-tailed $P = 0.046$). As expected, groups of participants conditioned either by an aversive or an appetitive procedure did not significantly differ (all $P > 0.05$) on VAS-intensity and VAS-unpleasantness scores, as well as on EMG amplitude, prior to learning. With regard to the within-group condition, thermal stimuli conditioned on the right arm by relevant unconditioned stimuli (CS +) and on the left arm by irrelevant unconditioned stimuli (CS¯) did not differ prior to learning on VAS-intensity and VAS-unpleasantness scores as well as on EMG amplitudes.

3.3. Post-conditioning analysis (Fig. 1)

3.3.1. VAS-intensity

In order to evaluate the effects of conditioning procedures (see Section 2), VAS-intensity was entered into a 2 ('group': aversive/appetitive conditioning) × 2 ('painfulness': non-painful/painful thermal stimuli) × 2 ('CS relevance': CS + /CS¯) ANOVA with repeated measurements for the last two variables. As expected, this ANOVA indicated an interaction between 'group' and 'conditioned stimulus relevance' ($F(1,36) = 22.111$, $P < 0.000$). A non-significant main effect of the 'painfulness' variable ($P = 0.269$) indicated that conditioning procedures have worked in the same way when painful or non-painful thermal stimuli were used. A priori one-tailed contrasts comparisons (see Fig. 1) computed on different groups of participants (i.e. aversive vs. appetitive conditioning groups), confirmed that relevant

Fig. 1. Effect of aversive and appetitive unconscious conditionings on sensory and affective perception of non-painful (light gray) and painful (dark gray) thermal stimuli. Results are expressed in z-scores as the difference between post- and pre-conditionings (Δ z-scores) for each dependent variable: VAS-intensity (upper panel), VAS-unpleasantness (middle panel) and startle reflex (lower panel). In a mixed design, an aversive conditioning procedure (☹ CS +) was compared between subjects to an appetitive conditioning procedure (☺ CS +) for thermal stimuli always delivered to the right arm. The aversive conditioning ((☹ CS +) on the right arm) was also compared within-subject to a neutral conditioning ((😐/☹ CS¯) on the left arm) used as a control condition. Furthermore, the appetitive conditioning ((☺ CS +) on the right arm) was also compared within-subject to a neutral conditioning ((😐/☺ CS¯) on the left arm). After aversive conditioning, non-painful and painful thermal stimuli were judged more intense and more unpleasant than when preceded by appetitive or neutral conditionings. Startle reflex was significantly increased only in the condition that used painful stimuli after the aversive conditioning.

conditioned thermal stimuli (CS +) were rated as significantly more intense after aversive learning than after appetitive learning (one-tailed $P = 0.004$). Theses results were also supported by within-group a priori contrasts analysis. Aversive conditioned stimuli (☹ CS +) were judged significantly more intense after aversive learning (one-tailed $P = 0.001$) when compared to neutral conditioned stimuli (😐/☹ CS¯). Inversely, appetitive conditioned stimuli (☺ CS +) were rated as less intense (one-tailed $P = 0.023$) when compared to their control condition (😐/☺ CS¯). An unexpected finding was the significant difference (one-tailed $P = 0.019$) observed between the two control groups (😐/☹ CS¯ and 😐/☺ CS¯) after learning. Neutral conditioned stimuli were perceived as less intense after the aversive learning procedure and neutral conditioned stimuli were rated as more intense after the appetitive learning procedure.

3.3.2. VAS-unpleasantness

As earlier, repeated measures ANOVA indicated a strong interaction effect between 'group' and 'conditioned stimulus relevance' ($F(1, 36) = 9.590$, $P = 0.004$). A non-significant main effect of the 'painfulness' variable ($P = 0.423$) indicated that conditioning procedures have operated in a similar way for painful and non-painful thermal stimuli. Contrasts (see Fig. 1) confirmed that thermal stimuli conditioned by an aversive learning (☹ CS +) received higher scores of unpleasantness (one-tailed $P = 0.029$) than thermal stimuli conditioned by an appetitive learning (☺ CS +). In the same way, within-group contrasts confirmed that aversive conditioned stimuli (☹ CS +) were judged significantly more unpleasant after aversive learning (one-tailed $P = 0.042$) than neutral conditioned stimuli (😐/☹ CS¯). On the other hand, contrasts did not confirm the expected effect of the appetitive learning procedure since appetitive conditioned stimuli (☺ CS +) were not significantly (one-tailed $P = 0.12$) judged different than neutral conditioned stimuli (😐/☺ CS¯).

3.3.3. Startle reflex

Eyeblink responses were unavailable for four participants because of equipment failure. EMG decreased in a monotonic fashion from the first to the last measures over the experiment because of the well-known habituation effect of the startle reflex. As for former variables, standardized EMG difference scores (post-conditioning minus pre-conditioning) were entered into a $2 \times 2 \times 2$ repeated measures ANOVA using 'group' as a between-group factor and both 'painfulness' and 'conditioned stimulus relevance' as within-group variables. This analysis did not evidence the expected interaction between 'group' and 'conditioned stimulus relevance' ($P = 0.512$). The only significant result was a main effect of the between-subjects 'group' variable ($F(1, 36) = 8.561$, $P = 0.004$). As our a priori hypothesis was stronger for the group which was exposed to an aversive conditioning, we were still interested in a priori contrasts for this former type of conditioning. Both contrast (see Fig. 1) and *t*-test for repeated measures revealed a significant effect of aversive learning (one-tailed $P = 0.033$) when compared to neutral conditioned stimuli (😐/☹ CS¯) but only for painful stimuli. Moreover, it appeared that the habituation effect was still uniformly present during the post-conditioning phase for painful stimuli conditioned by the appetitive procedure ($F(2, 16) = 3.418$, $P = 0.045$) but disappeared for painful stimuli conditioned by the aversive procedure ($P = 0.751$). Aversive conditioning seems to have slowed down startle reflex habituation.

3.3.4. Relationship between sensory and affective judgments

Analyses of covariance (ANCOVA) were used in order to study the specific contribution brought by sensory and affective judgments. To control for an exaggerated high number of observations due to our mixed design, that used simultaneously within- and between-group variables, we transformed our data. Firstly, as experimental manipulations worked similarly for non-painful and painful conditions, we calculated, for each participant, new VAS-intensity and VAS-unpleasantness scores by taking the average on these two conditions. Secondly, information obtained for both conditions of the 'CS relevance' variable (i.e. CS + and CS¯) were reduced to difference scores for each participant and for each dependent variables (i.e. VAS-intensity and VAS-unpleasantness). The VAS scores (which are themselves the difference scores between post- and pre-conditioning scores) obtained for the 'irrelevant CS' condition were subtracted from the VAS scores obtained for the 'relevant condition' (CS + minus CS¯). Our hypothesis and our former results predict that the difference between CS + and CS¯ should be positive for the aversive conditioning procedure and should be negative for the appetitive conditioning procedure. After these data transformations, the parametric correlation analyses revealed a quite significant correlation between pain intensity and pain unpleasantness ratings ($r = 0.68$, $P < 0.0001$). An ANCOVA with VAS-intensity ratings as the main factor and VAS-unpleasantness ratings as the co-variate was then performed to evaluate the residual effect of the conditioning procedure (aversive or appetitive) on pain intensity after accounting for pain-unpleasantness related variance. Comparison of residual pain intensity in the aversive and appetitive conditionings confirmed a highly significant difference between these two procedures independent of changes in pain unpleasantness ($F(1, 34) = 9,544$, $P < 0.004$). In contrast, when residual VAS-unpleasantness was computed by removing the variance shared with VAS-intensity ratings in a linear regression model, the difference between the two kinds of conditioning procedures was not significant any more ($F(1, 34) = 0.176$, $P = 0.678$).

4. Discussion

In accordance with our hypotheses, results showed a

robust and coherent effect of the unconscious aversive conditioning – within and between subjects – on all dependent variables (VAS-intensity, VAS-unpleasantness and startle reflex with painful stimuli). Further, as expected, a weaker effect was observed with appetitive conditioning. The levels of statistical significance for this second type of conditioning were smaller (VAS-intensity) or non-significant (VAS-unpleasantness, startle reflex) in the within-group comparisons (i.e. appetitive vs. neutral conditioning). These results are akin to Dickinson and Pearce's (1977) conclusions that the inhibitory effect of appetitive stimuli on negative motivation is less well supported by the literature than the inhibitory effect of aversive stimuli on appetitive motivation. More recently, it was found that aversive CSs (i.e. pictures of fear-related objects such as snakes, threatening faces) yield more robust shock conditioning than do neutral CSs (Öhman et al., 1976; Cook et al., 1986; Öhman, 1986). In concordance with the 'preparedness' hypothesis (Garcia et al., 1972; Seligman, 1971), it has been proposed (Cook et al., 1986; Öhman, 1986; Hamm et al., 1989) that the associability of CS and US is genetically facilitated when both stimuli belong to the same affective category. From this perspective, the conditioning of a painful CS, given an aversive picture US, ought to be facilitated by an a priori affective association (i.e. both stimuli are unpleasant and arousing). Startle reflex is also seen as being mediated by a match between the central state generated by fear conditioning and the protective (aversive) nature of the startle reflex (Lang et al., 1990). Such synergy fails to occur if the participant is not in an aversively motivated state. This could explain why univariate analyses showed a significant increase of the startle reflex (i.e. revealed by a reduction in habituation) only in the condition that used painful stimuli after the aversive conditioning. It is in those conditions that the matching between the defensive reflex and the emotional state (fear conditioning + current painful stimuli) was the greatest.

Statistical analysis revealed an unexpected difference for VAS-intensity between the two control groups – i.e. those groups receiving thermal stimuli on the left forearm associated with neutral slides during the aversive or the appetitive conditioning. Indeed, neutral CSs were perceived as less intense after the aversive learning procedure, whereas neutral CSs were rated as more intense after the appetitive learning procedure. These results may suggest that participants relied on relative rather than on absolute judgments when using VAS-scales. This phenomenon is well-known in psychometry and could furthermore have been reinforced by our instructions which insisted more on the comparison between each stimuli than on the 'true' anchorage point.

We have to consider also the possibility that the asymmetry observed between both kinds of conditioning procedures (aversive vs. appetitive) could have resulted from a methodological difficulty inherent to the selection of our emotions eliciting material. In our pilot study – designed to select affective pictures in function of their capacity to evoke a startle reflex, we had difficulties to find positive pictures which were as much pleasant as the aversive stimuli were unpleasant. If all participants agreed to find the unpleasant pictures particularly aversive (even more unpleasant than the noxious thermal stimuli), we obtained weaker consensus for the appetitive pictures. Actually, the difficulty to find sufficiently strong appetitive stimuli was especially true for female participants who were much less interested in arousing erotic scenes than male participants. In an experiment conducted to study the impact of affective pictures during a cold pressor tolerance test, de Wied and Verbaten (2001) resolved this problem in using highly arousing affective pictures (sports and erotic scenes) only with male participants. In that condition, they obtained: (1) valence ratings for the pleasant pictures even stronger than for unpleasant pictures and (2) a greater impact of pleasant pictures on pain tolerance compared with unpleasant pictures.

Regarding psychometric measures of pain, the present study indicated that only the sensory-discriminative dimension (VAS-intensity) was modulated by unconscious affective learning. Indeed the effect of emotional learning on the affective-motivational dimension (VAS-unpleasantness) was not confirmed when VAS-intensity was taken as covariate. This was unexpected as, according to multidimensional models of pain, it is postulated that affective responses related to pain should be more influenced by psychological and contextual manipulations than are sensory responses (Price et al., 1980). For instance, Rainville et al. (1999a) reported that alteration of the unpleasantness of noxious stimuli by selective hypnotic suggestion persisted even when the variance related to VAS-intensity was removed by a covariance analysis. However, other studies using various psychological manipulations did not succeed in differentiating highly correlated VAS-intensity and VAS-unpleasantness scores, but unfortunately did not use, for instance, analysis of covariance to assess the contribution of each dimension to the perception of pain (e.g. Miron et al., 1989; Kiernan et al., 1995; Montgomery and Kirsch, 1997; Price et al., 1999; Petrovic et al., 2000). By using an unconscious procedure which minimize suggestion effects (contrary to former studies which rely on hypnotic or placebo suggestions), it is also possible that our participants were not sufficiently guided to discriminate both scales (although they received the standard consigns used by Harkins et al., 1989). A second possibility could be that the 'sensory' experience is more sensitive or finely tuned than the 'affective' experience to pick up environmental influences. In this case, the VAS-unpleasantness scale should not be necessarily more sensitive and more valid than the VAS-intensity scale to capture contextual influences.

4.1. Unconscious affective learning

Questionnaires and post-hoc interview revealed that none

of our participants have been aware of the conditioning procedures. They all erroneously believed that we were interested in a slide effect during the conditioning step. This result makes an additional case in favor of unconscious affective conditioning, i.e. without awareness of the CS–US contingency. Levey and Martin (1975) consider that evaluative conditioning, is a purely automatic, pre-attentive process, without necessitating awareness of the crucial CS–US contingency. The organism does not learn an 'if-then' relationship, as in signal-learning, but experiences a shift in the hedonic value of the CS, explained by a fusion of the CS–US representations (Martin and Levey, 1994). Two kinds of arguments support this theory. Firstly, it has been shown that, unlike signal-learning, affective-evaluative learning is not subject to extinction (Baeyens et al., 1988, 1995); supporting then the idea that the CS 'hedonic shift' becomes intrinsic to the CS representation and thus persists even without US presentations. Secondly, in a series of studies (Öhman and Soares, 1993; Soares and Öhman, 1993; Esteves et al., 1994), Öhman and coworkers confirmed that fear conditioning can be achieved without conscious awareness of the CS, or of the relation between the CS and US. In a typical classical conditioning procedure (e.g. Öhman and Soares, 1993), a CS was presented contingently with a US. After this learning phase, the CS was presented subliminally and nevertheless was still producing the autonomic responses of the previously learned contingency.

4.2. Clinical implications

Possible mechanisms by which affective conditioning may influence the sensory experience of pain without participants awareness begin only to be understood. A study by Lenz et al. (1995) suggests that the association between sensory and affective dimensions may be encoded in the central nervous system as the results of past learning. It was observed that pains with a strong affective dimension were reproduced by stimulation in the human somatosensory thalamus only in patients who previously experienced such pain. To explain these results, the authors had to postulate connections between the sensory thalamus and the corticolimbic areas or, as suggested by animal studies (Ledoux, 1997), direct connections between posterior thalamus and the amygdala without cortical relay. In showing that fear learning in animals can be mediated by a direct thalamo-amygdala pathway that bypass the neocortex, Ledoux (reviewed in Ledoux, 1999) gave, once more, evidences that emotional learning can occur without the involvement of the higher processing systems of the brain. As being the heart and the soul of the conditioning fear system, amygdala may contribute to analgesia when activated by acute stress. Through descending projections, the amygdala controls both spinal and trigeminal dorsal horn nociceptive transmission (Fields, 2000). As suggested by Price (1999), this kind of top–down processes inhibits nociceptive transmission at the first synapse in pain-related ascending pathways where sensory and affective dimensions of pain are not differentially represented. Dubner et al. (1981) have moreover demonstrated unambiguously that associative learning may occur at the first synaptic relay of nociceptive pathways. The spinal dorsal horn cells of trained monkeys respond not only to stimulation of their cutaneous receptive field ('unconditioned stimulus') but also to a visual alerting stimulus ('conditioned stimulus'). Beside those top–down influences, Kawarada et al. (1999) has recently shown that central amygdaloid nucleus also inhibits ascending nociceptive information to the S1. Other evidences of emotional or cognitive top–top influences on the sensory dimensions of pain has been amassed during the last few years at the lateral thalamus (e.g. Lenz et al., 1995), the somatosensory cortex (e.g. for a review see Bushnell et al., 1999; Petrovic et al., 2000; Hofbauer et al., 2001), and the experiential levels (e.g. Montgomery and Kirsch, 1997; Price et al., 1999).

What could be the clinical implications of an unconscious, and probably an indelible form of affective learning, on pain perception? Firstly, when describing their pain experience, patients are often not aware of the unconscious processing of stimuli implicated either because the stimuli themselves have been unnoticed or because their implications (e.g. associative learning) were unnoticed. Therefore, it would be extremely difficult for them, as well for their physicians, to determinate which parts of their pain experience are modulated by sensory or affective inputs. They experience a conscious final output of complex informational processes that are not all accessible to consciousness. Secondly, pain is, in all likelihood, not only associated with emotional contiguous external stimuli but also with contiguous interoceptives sensations. The aversive nature of these sensations (nausea, neurovegetative and musculoskeletal reactions) could be merged with pain (the US), in a way that could durably enhance pain adversity and then participate in the chronification process. Thirdly, the best way to cope with unknown and ineffaceable learning could be to substitute former aversive learning by new learning through counter-conditioning procedures. That is what we have tried to do with the appetitive conditioning procedure. The fact that experimental and clinical pain can be powerfully reduced by pleasant emotions has been confirmed in numerous studies using pleasant pictures (de Wied and Verbaten, 2001), humorous film (e.g. Weisenberg et al., 1995, 1998), positive cognition and expectation (e.g. Zelman et al., 1991; Zillmann et al., 1996) and sexual stimulation (Whipple and Komisaruk, 1985).

Finally and in contrast with conditioning stress-induced analgesia studies, we observed that negative emotion enhanced pain perception rather than diminished it. Other experiments have also reported hyperalgesia in human stress-induced analgesia studies (e.g. Cornwall and Donderi, 1988; Al Absi and Rokke, 1991). Rudy and Meagher (2000) have proposed that these seemingly contradictory findings with classical studies come from a confusion between fear

and anxiety. They favor the idea that anxiety induces hyperalgesia rather than analgesia if anxiety is seen as a hypervigilance state which leads to increased environmental and somatic scanning that facilitates sensory receptivity. On the other hand, fear can be seen as an alarm reaction which mobilizes the organism to take action (fight/flight response) with a high sympathetic arousal (Barlow, 1988) and an hypoalgesia (Walters, 1994). Alternatively, it has been proposed that the difference between fear and anxiety is more a question of degree; intense activation of the neural circuit may induce fear and analgesia, whereas moderate activation may induce anxiety and hyperalgesia. Support for this quantitative account is provided by recent animal research suggesting that brief-moderate shock enhances the affective impact of aversive stimuli, whereas severe shocks attenuate pain (Walters, 1994; McLemore et al., 1999; Meagher et al., 2001). It is likely that our aversive conditioning was not fearful enough to induce a conditioned stress-induced analgesia phenomenon but sufficient to induce a conditioned (non-conscious) hypervigilance which facilitate sensory receptivity. This interpretation is in accordance with an attentional theory of pain (McCaul and Malott, 1984; Arntz et al., 1991; Janssen and Arntz, 1996) stating that moderate levels of fear/anxiety enhance attention to salient events such as pain, thereby augmenting pain, whereas high level of fear may become more salient than pain, in which case fear attenuates pain.

5. Conclusions

The present experiment showed, firstly, that it was possible to modify the 'sensory perception' of thermal stimuli by an unconscious affective learning procedure based on the transfer of the valence of the unconditioned stimulus (pleasant or unpleasant slides) toward the conditioned stimulus (non-painful and painful thermal stimuli). This phenomenon appeared more robust with the aversive conditioning as compared to the appetitive conditioning. Concerning the dependent variables, more work is needed to confirm the usefulness of startle reflex in pain studies. Secondly, it was shown that affective conditioning of non-painful and painful thermal stimuli was possible without awareness of the affective learning procedure. These results are the first evidences that affective conditioning may modulate the perception of somatosensory stimuli (painful and non-painful) as it was already shown for visual and olfactory stimuli. That form of primitive learning is probably a component of ontogenetic adaptation for survival that is a fundamental property of the brain's operations sustaining all sensory modalities. This is in line with numerous other psychological and physiological investigations which have now demonstrated that (1°) conditioning can be automatic, can occur without awareness and in some cases against our will (e.g. Walker, 1987; Lieberman, 1993; Ledoux, 1999), (2°) affective processing can occur without conscious awareness (e.g. Ledoux, 1999; Kunst-Wilson and Zajonc; Shevrin et al., 1992; Wong et al., 1997) and (3°) stimulus processing that does not reach awareness in the form of conscious content but can nevertheless be stored implicitly or unconsciously and have important influences on perception, cognitions and behavior at some later time (Lewicki, 1986; Marshall and Halligan, 1988; Kihlstrom, 1996).

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References

Al Absi M, Rokke PD. Can anxiety help us tolerate pain? Pain 1991;46:43–51.

Anand KJ, Craig KD. New perspectives on the definition of pain. Pain 1996;67:3–6.

Arntz A, Dreessen L, Merckelbach H. Attention, not anxiety influences pain. Behav Res Ther 1991;29:41–50.

Baeyens F, Crombez G, Van den Bergh O, Eelen P. Once in contact always in contact: evaluative conditioning is resistant to extinction. Adv Behav Res Ther 1988;10:179–199.

Baeyens F, Eelen P, Van den Bergh O. Contingency awareness in evaluative conditioning: a case for unaware affective-evaluative learning. Cognit Emotion 1990;4:3–18.

Baeyens F, Eelen P, Crombez G. Pavovian associations are forever: on classical conditioning and extinction. J Psychophysiol 1995;9:127–141.

Barlow DH. Anxiety and its disorders. The nature and treatment of anxiety and panic, New York, NY: Guilford Press, 1988.

Bindra D. A motivational view of learning, performance, and behavior modification. Psychol Rev 1974;81:199–213.

Bolles RC, Fanselow MS. A perceptual-defensive-recuperative model of fear and pain. Behav Brain Sci 1980;3:291–323.

Bouton ME. Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. Psychol Bull 1993;114:80–99.

Bushnell MC, Duncan GH, Hofbauer RK, Ha B, Chen J-I, Carrier B. Pain perception: is there a role for primary somatosensory cortex? Proc Natl Acad Sci USA 1999;96:7705–7709.

Cook EW, Hodes RL, Lang PJ. Preparedness and phobia: effects of stimulus content on human visceral conditioning. J Abnorm Psychol 1986;95:195–207.

Cornwall A, Donderi DC. The effect of experimentally induced anxiety on the experience of pressure pain. Pain 1988;35:105–113.

Crombez G. Sensory and temporal information about impending pain: an experimental investigation. Paper presented at the Annual Conference of the British Psychology Society, March 1994.

Crombez G, Baeyens F, Vansteenwegen D, Eelen P. Startle intensification during painful heat. Eur J Pain 1997;1:87–94.

de Wied M, Verbaten MN. Affective pictures processing, attention, and pain tolerance. Pain 2001;90:163–172.

Dickinson A, Pearce JM. Inhibitory interaction between appetitive and aversive stimuli. Psychol Bull 1977;84:690–711.

Dubner R, Hoffman DS, Hayes RL. Neuronal activity in medullary dorsal horn of awake monkeys trained in a thermal discrimination task. III. Task-related responses and their functional role. J Neurophysiol 1981;46:444–464.

Estes WK. New perspectives on some old issues in associating theory. In: Mackintosh NJ, Honig WK, editors. Fundamental issues in associative learning, Halifax, Nova Scotia: Dalhousie University Press, 1969.

Esteves F, Parra C, Dimberg U, Öhman A. Nonconscious associative learning: Pavlovian conditioning of skin conductance responses to masked fear-relevant facial stimuli. Psychophysiology 1994;31:375–385.

Fields HL. Pain modulation: expectation, opioid analgesia and virtual pain. Prog Brain Res 2000;122:245–253.

Flor H, Grüsser M. Conditioned stress-induced analgesia in humans. Eur J Pain 1999;3:317–324.

Frijda NH. The emotions. Cambridge, MA: Cambridge University Press, 1986.

Garcia J, McGowan BK, Green KF. Biological constraints in conditioning. In: Seligman MEP, Hager JL, editors. Biological boundaries of learning, New York, NY: Appleton-Century-Crofts, 1972. pp. 21–43.

Gracely RH. Affective dimensions of pain: how many and how measured? Am Phytopathol Soc J 1992;1:243–247.

Hamm AO, Greenwald MK, Bradley MM, Lang PJ. Emotional learning, hedonic change, and the startle probe. J Abnorm Psychol 1993;102:453–465.

Hamm AO, Vaitl D, Lang PJ. Fear conditioning, meaning, and belongingness: a selective association analysis. J Abnorm Psychol 1989;98:395–406.

Harkins SW, Price DD, Braith J. Effects of extraversion and neuroticism on experimental pain, clinical pain, and illness behavior. Pain 1989;36:209–218.

Hofbauer RK, Rainville P, Duncan GH, Bushnell MC. Cortical representation of the sensory dimension of pain. J Neurophysiol 2001;86:402–411.

Janssen SA, Arntz A. Anxiety and pain: attentional and endorphinergic influences. Pain 1996;6:145–150.

Jensen MP, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Turk DC, Melzack R, editors. Handbook of pain assessment, New York, NY: Guilford Press, 1992. pp. 135–151.

Kawarada K, Kamata KI, Matsumoto N. Effects of conditioning stimulation of the central amygdaloid nucleus on tooth pulp-driven neurons in the cat somatosensory cortex (SI). Jpn J Physiol 1999;49:485–497.

Kiernan BD, Dane JR, Phillips LH, Price DD. Hypnotic analgesia reduces R-III nociceptive reflex: further evidence concerning the multifactorial nature of hypnotic analgesia. Pain 1995;60:39–47.

Kihlstrom JF. Perception without awareness of what is perceived, learning without awareness of what is learned. In: Velmans M, editor. The science of consciousness, London: Routledge, 1996.

Konorski J. Integrative activity of the brain: an interdisciplinary approach, . Chicago, IL: University of Chicago Press, 1967.

Kunst-Wilson W, Zajonc R. Affective discrimination of stimuli that cannot be recognized. Science 1980;207:557–558.

Lang PJ, Bradley MM, Cuthbert BN. Emotion, attention, and the startle reflex. Psychol Rev 1990;97:377–395.

Ledoux J. Emotion, memory, and pain. Commentary. Pain Forum 1997;6:36–37.

Ledoux J. The emotional brain. London: Phoenix Paperback, 1999.

Lenz FA, Gracely RH, Romanoski AJ, Hope EJ, Rowland LH, Dougherty PM. Stimulation in the human somatosensory thalamus can reproduce both the affective and sensory dimensions of previously experienced pain. Nat Med 1995;1:910–913.

Leventhal H, Scherer K. The relationship of emotion to cognition: a functional approach to a semantic controversy. Cognit Emotion 1987;1:3–28.

Levey AB, Martin I. Classical conditioning of human evaluative response. Behav Res Ther 1975;13:221–226.

Lewicki P. Processing information about covariations that cannot be articulated. J Exp Psychol (Learning, memory and cognition) 1986;12:135–146.

Lieberman DA. Learning: behavior and cognition. 2nd ed. Pacific Grove, CA: Brooks-Cole, 1993.

Marshall JC, Halligan W. Blindsight and insight in visuo-spacial neglect. Nature 1988;336:766–767.

Martin I, Levey AB. The evaluative response: primitive but necessary. Behav Res Ther 1994;32:301–305.

McCaul K, Malott J. Distraction and coping with pain. Psychol Bull 1984;95:516–533.

McLemore S, Crown ED, Meagher MW, Grau JW. Shock-induced hyperalgesia: II. Role of the dorsolateral periaqueductal gray. Behav Neurosci 1999;113:539–549.

Meagher MW, Ferguson AR, Crown ED, McLemore S, King TE, Sieve AN, Grau JW. Shock-induced hyperalgesia IV. Generality. J Exp Psychol Anim Behav Process 2001;27:219–238.

Miron D, Duncan GH, Bushnell MC. Effects of attention on the intensity and unpleasantness of thermal pain. Pain 1989;39:345–352.

Montgomery GH, Kirsch I. Classical conditioning and the placebo effect. Pain 1997;72:107–113.

Öhman A. Face the beast and fear the face: animal and social fears as prototypes for evolutionary analyses of emotion. Psychophysiology 1986;23:123–145.

Öhman A. The psychophysiology of emotion: an evolutionary-cognitive perspective. Adv Psychophysiol 1987;2:79–127.

Öhman A, Soares JJ. On the automatic nature of phobic fear: conditioned electrodermal responses to masked fear-relevant stimuli. J Abnorm Psychol 1993;102:121–132.

Öhman A, Fredrikson M, Hugdahl K, Rimmö PA. The premise of equipotentiality in human classical conditioning: conditioned electrodermal responses to potentially phobic stimuli. J Exp Psychol (Gen) 1976;105:313–337.

Petrovic P, Petersson KM, Ghatan PH, Stone-Elander S, Ingvar M. Pain-related cerebral activation is altered by a distracting cognitive task. Pain 2000;85:19–30.

Price DD. Psychological mechanisms of pain and analgesia, Progress in pain research and management, vol. 15. Seattle, WA: IASP Press, 1999.

Price DD, Barrell JJ, Gracely RH. A psychophysical analysis of experiential factors that selectively influence the affective dimension of pain. Pain 1980;8:137–149.

Price DD, Harkins SW, Baker C. Sensory-affective relationships among different types of clinical and experimental pain. Pain 1987;28:297–307.

Price DD, Milling LS, Kirsch I, Duff A, Montgomery GH, Nicholls SS. An analysis of factors that contribute to the magnitude of placebo analgesia in an experimental paradigm. Pain 1999;83:147–156.

Rainville P, Carrier B, Hofbauer RK, Bushnell MC, Duncan GH. Dissociation of sensory and affective dimensions of pain using hypnotic modulation. Pain 1999;82:159–171.

Rudy JL, Meagher MW. Fear and anxiety: divergent effects on human pain thresholds. Pain 2000;84:65–75.

Seligman MEP. Phobias and preparedness. Behav Ther 1971;2:307–321.

Shevrin H, Williams WJ, Marshall RE, Hertel RK, Bond JA, Brakel LA. Event-related potential indicators of the dynamic unconscious. Conscious Cognit 1992;1:340–366.

Soares JJ, Öhman A. Backward masking and skin conductance responses after conditioning to nonfeared but fear-relevant stimuli in fearful subjects. Psychophysiology 1993;30:460–466.

Stevenson RJ, Boakes RA, Prescott J. Changes in odor sweetness resulting from implicit learning of a simultaneous odor-sweetness association: an example of learned synesthesia. Learn Motiv 1998;29:113–132.

Todrank J, Byrnes D, Wrzesniewski A, Rozin P. Odors can change preferences for people in photographs: a cross-modal evaluative conditioning study with olfactory USs and visual CSs. Learn Motiv 1995;26:116–140.

Vingoe FJ. Anxiety and pain: terrible twins or supportive siblings? In: Gibson HB, editor. Psychology, pain and anesthesia, London: Chapman & Hall, 1994. pp. 282–307.

Vrana SR, Spence EL, Lang PJ. The startle-probe response: a new measure of emotion? J Abnorm Psychol 1988;97:487–491.

Walker S. Animal learning: an introduction. London: Routledge & Kegan Paul, 1987.

Walters ET. Injury related behavior and neuronal plasticity: an evolutionary perspective on sensitization, hyperalgesia, and analgesia. Int Rev Neurobiol 1994;36:325–426.

Weisenberg M, Tepper I, Schwarzwald J. Humor as a cognitive technique for increasing pain tolerance. Pain 1995;63:207–212.

Weisenberg M, Raz T, Hener T. The influence of film-induced mood on pain perception. Pain 1998;76:365–375.

Whipple B, Komisaruk B. Elevation of pain threshold by vaginal stimulation in women. Pain 1985;21:357–367.

Wong PS, Bernat E, Bunce SC, Shevrin H. Brain indices of nonconscious associative learning. Conscious Cognit 1997;6:519–544.

Zajonc RB. On the primacy of affect. Am Psychol 1984;39:117–123.

Zelman DC, Howland EW, Nichols SN, Cleeland CS. The effects of induced mood on laboratory pain. Pain 1991;46:105–111.

Zillmann D, de Wied M, King-Jablonski C, Jenzowsky S. Drama-induced affect an pain sensitivity. Psychosom Med 1996;58:333–341.