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Experimentally Induced Mood Changes Preferentially Affect Pain Unpleasantness

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Abstract: **Our group previously demonstrated that changes in mood induced by pleasant or unpleasant odors affect the perceived unpleasantness of painful heat stimuli, without significantly altering perceived pain intensity. In the present study, we examined whether changing mood by viewing emotionally laden visual stimuli also preferentially alters pain unpleasantness. Twelve female subjects immersed their right hand in hot water while observing a video showing a person experiencing the same type of pain (ie, model condition), unpleasant scenes not involving people (ie, disasters condition), or a cityscape video (ie, cityscape condition). Subjects were asked to rate pain intensity, pain unpleasantness, mood, anxiety/calmness, and video unpleasantness, and their skin conductance was measured throughout the experiment. Pain unpleasantness (but not intensity) ratings were higher during the disasters condition, which was associated with the worst mood, than during the cityscape condition; neither mood nor pain unpleasantness was altered in the model video compared with the cityscape video. Moreover, mood was significantly correlated with pain unpleasantness but not with pain intensity. Because these results are similar to those observed when odors were used to alter mood, we conclude that the effects of mood on the affective components of pain are independent of mood induction technique used.**

Perspective: ***This article provides new evidence that changes in mood affect the pain experience by preferentially modulating pain unpleasantness. This finding could potentially help health professionals to treat pain symptoms in patients with altered mood, suggesting methods of pain management aimed at easing the affective, along with the sensory, components of pain.***

Key words: *Mood, emotions, pain, psychophysics, heat, human.*

An association between mood and pain perception has been widely documented in both clinical and laboratory settings. For instance, cardiac patients with depressed mood have an earlier onset and a more prolonged duration of angina than do nondepressed patients.[15] Similarly, oncology patients who have cancer-related pain report more mood disturbance than those who are pain free.[11] In chronic pain patients, self-report of depressive symptoms and global affective distress were found to be significantly correlated with self-report of pain.[9]

Although the association between mood and pain in most clinical reports is simply correlational and could therefore be explained in terms of pain worsening mood rather than mood affecting pain, experimental studies provide evidence in favor of an effect of mood on pain. A number of laboratory studies have assessed the effect of

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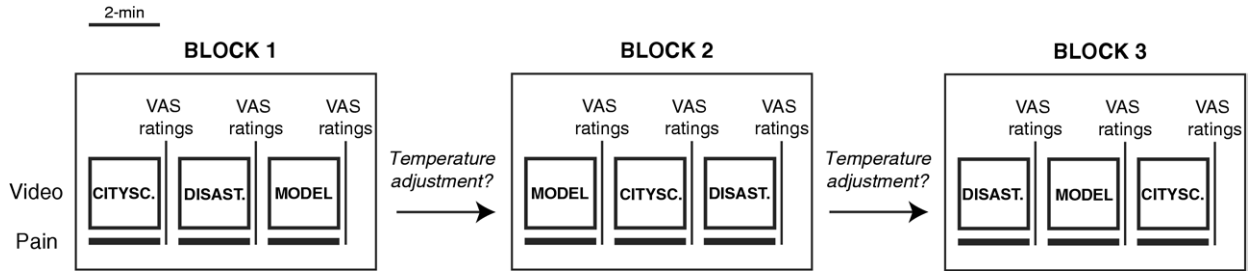

Figure 1. Schematic overview of the protocol. Example sequence for 1 subject; other subjects received other sequences, using a pseudorandomized block design. The protocol included 9 pain trials (3 blocks × 3 trials). In each trial, subjects immersed their hand in hot water while watching a 2-minute video (cityscape [CITYSC.], disasters [DISAST.], or model). At the end of the video, the painful stimulation was interrupted and subjects expressed their visual analog scale (VAS) ratings (pain intensity and unpleasantness, video unpleasantness, mood, and anxiety/calmness). The heat stimulus was adjusted between blocks, if necessary, to maintain a stable pain perception throughout the session. See Methods for more information.

different emotions on pain, using emotion-altering procedures involving odors,[31] videos,[32,37] pictures,[5,21] music,[28,34] emotionally laden statements,[36] and hypnotic induction of emotional states.[24] Although most of these studies did not directly assess mood, they show that changing emotional state influences pain sensitivity. Overall, results from these studies suggest that experimentally induced emotional shifts either enhance or dampen perceived pain, depending on whether the valence of the emotion induced is negative or positive, respectively.

Because pain is a multidimensional experience, which includes both sensory components (eg, the intensity, quality, and spatiotemporal characteristics of the sensation) and affective-motivational components (ie, the unpleasantness and aversiveness of the sensation), it is possible to further dissect the effect of mood on pain. Using pleasant or unpleasant odors, our group previously showed that emotional state mainly affects the unpleasantness of painful heat stimuli without altering perceived pain intensity. Further, we showed that mood is a better predictor of pain unpleasantness than other emotional variables such as anxiety level or unpleasantness of the mood-inducing stimulus used.[31] The present study examines whether pain unpleasantness is more consistently modulated than pain intensity also when mood is manipulated with emotionally laden visual stimuli and whether any such modulation is related more to mood than to other emotional variables. Our main aim is therefore to determine whether the mood-related pain modulation we observed using olfactory stimuli is specific to the involvement of the olfactory system or is a general phenomenon related to mood. We chose to use video stimuli because these have been suggested to be particularly effective in inducing emotions, both negative (ie, depression) and positive (ie, elation).[10] Moreover, to evaluate the generality of the mood effect on pain unpleasantness, in this experiment we recruited middle-aged subjects, in contrast to the young adults studied by Villemure et al.[31]

Materials and Methods

Subjects

Twelve women between the ages of 45 and 55 years (mean, 51.3 ± 3.5 SD) were recruited through advertisements posted on university classified ads. Written informed consent was obtained from each subject. Exclusion criteria included chronic pain, neurological disease, serious cardiovascular disease, pregnancy or breastfeeding, and current use of analgesic drugs. Ethical approval was obtained through the McGill University Faculty of Medicine Institutional Review Board.

Procedure

Subjects were seated in an adjustable chair in a ventilated room and were asked to submerge their right hand up to the wrist in a circulating hot water bath (Neslab RTE-111; Neslab Instruments, Inc., Newington, NH) during 9, 2-minute trials (3 blocks, each composed of 3 trials; Fig 1). Subjects were encouraged to keep their hand in the water for as long as possible (up to the end of the trial) but were told that they could withdraw the hand at any time if the heat became too uncomfortable. During each trial, subjects were asked to pay attention both to the sensation in their hand and to a video that was simultaneously projected onto a large screen in front of them. The video either showed another individual (unknown to the subject) receiving the same type of pain (ie, putting 1 hand in a hot water bath; model condition), unpleasant scenes not involving people (ie, fires, explosions destroying buildings, etc; disasters' condition), or a cityscape video (ie, sidewalks, buildings; cityscape condition). The model and disasters videos were chosen as 2 different means of inducing a negative emotional state, and the cityscape video was chosen as a neutral control. During the testing session, each video was presented 3 times, once per block; the order of the presentation was block randomized, so that all 3 videos were presented in each of 3 blocks of trials. Using methods previously reported by our group,[20,31] at the end of each trial the subjects were asked to numerically rate the heat intensity and unpleasantness as well as mood, anxiety/calmness, and video pleasantness/unpleasantness, using 200-mm visual analog scales (VAS) (Fig 2 A–E, *y*-axes), as a reference (the VAS were presented to the subjects who were asked to verbally report a number indicating where they would place a mark on the VAS[20,30,31]). The heat/pain intensity scale was anchored with 0 (no heat) and 200 (most intense pain tolerable) with a mid-point of 100

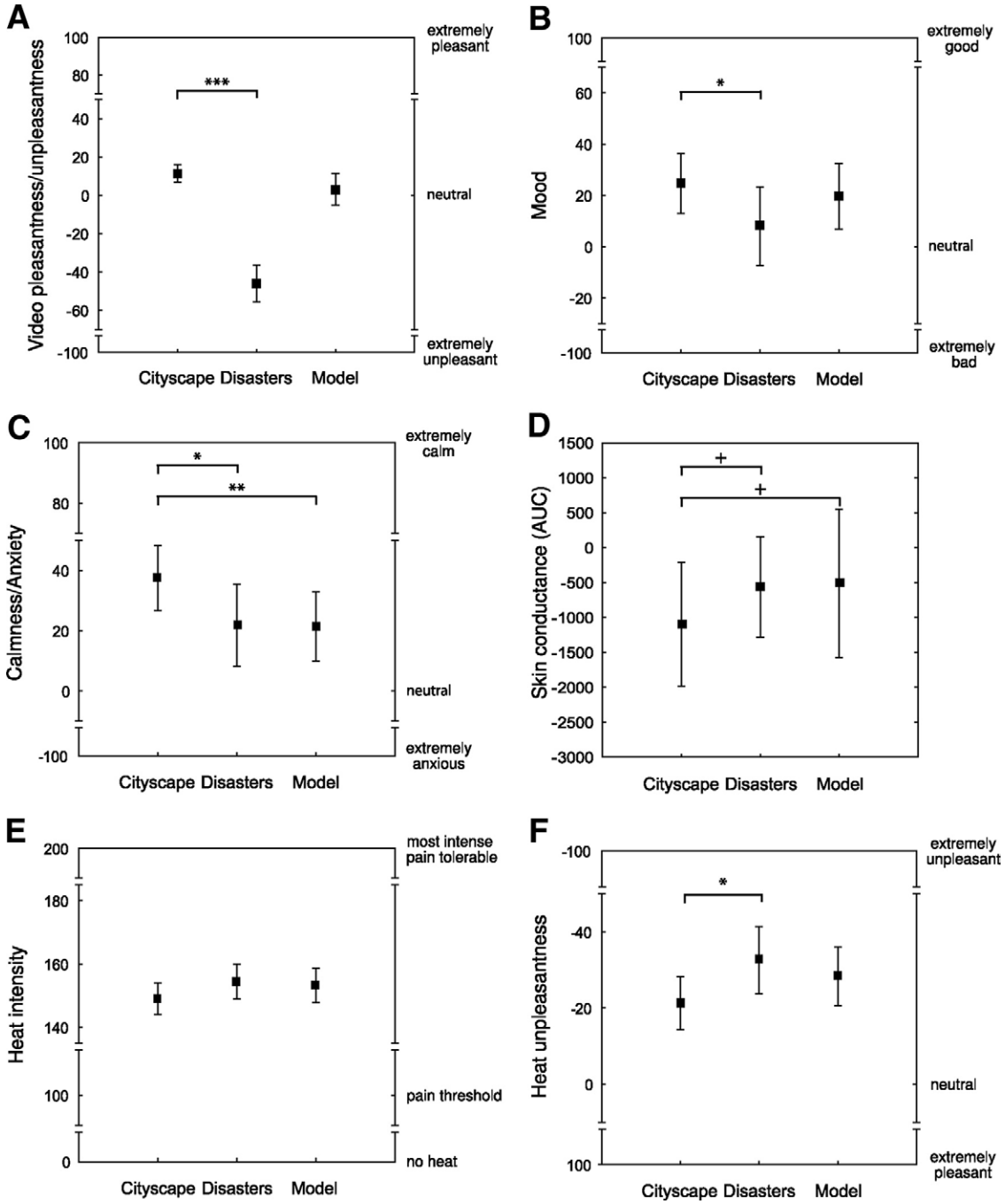

Figure 2. Video effects on visual analog scale ratings and skin conductance. During the disasters video, subjects reported worse mood, less calmness, higher ratings of video unpleasantness, and pain unpleasantness compared with the cityscape video. The model video was only associated with less calmness compared with the cityscape video. The disasters and model conditions also tended to be associated with similar increases in skin conductance, compared with the cityscape condition (P's = .051 and .084, respectively). **A, B, C, E,** and **F,** Anchors for each visual analog scale are reproduced on the right y-axes. The y-axes of the heat unpleasantness graphs in this figure and in Fig 3 are inverted, so that higher values mean worse pain. Symbols represent mean ± SEM. $+P < .1$, $*P < .05$, $**P < .01$, $***P < .001$.

defined as the pain threshold. The video pleasantness/unpleasantness scale was anchored with −100 (extremely unpleasant) and +100 (extremely pleasant), with a mid-point of 0 labeled neutral. Similarly, the mood and anxiety/calmness scales were anchored with −100 (extremely bad/anxious) and +100 (extremely good/calm), with a mid-point of 0 labeled as neutral. We have used these scales previously and found them to be reliable and sensitive to psychological manipulations such as state empathy and odor-evoked changes in mood.[20,30,31]

To allow subjects to distinguish sensory and affective components of pain, we stressed the differences between stimulus intensity and pleasantness/unpleasant-

ness by using explanations similar to those adopted by Price et al.[23] Subjects were allowed as much time as they needed to express their ratings so that they could calmly and judiciously evaluate various aspects of the sensations evoked by the pain and video stimuli attended; this was especially important to allow them to carefully distinguish between pain intensity and unpleasantness. Before the actual experimental session, subjects participated in a preliminary "stimulus search" session: In the absence of a video presentation, a series of 2-minute pain stimuli (starting at 46°C) was delivered to the subjects to identify a temperature that elicited ratings of moderate pain (ie, ratings between 120 and 160 on the intensity scale; *y*-axes in Fig 2E). In the experimental session, which immediately followed the preliminary session, the temperature of the water was initially set at the level identified in the stimulus search session; however, depending on each subject's individual ratings, it could be adjusted after each block of trials to maintain a stable pain perception throughout the experimental session. If a subject rated the pain as very intense (≥180 on the intensity scale) or was unable to tolerate the full 2 minutes in at least 1 of the 3 trials of a given block, for the following block the temperature was reduced by up to 0.5°C, depending on the reported pain values or withdrawal latency. If, conversely, within a certain block a subject rated her pain as less than moderate (≤120 on the intensity scale) at least once, then the water temperature for the subsequent block of trials was increased by up to 0.5°C, depending on the pain rating. Importantly, to examine the effect of each video on pain ratings, the temperature was kept constant within each block, so that the temperature subjects received while viewing each video was the same.

Skin conductance, a commonly used measure of sympathetic arousal in pain studies,[2,3,16,32,33] was measured throughout the experiment to examine whether differences in arousal were sufficient to explain differences in pain perception in our study. Skin conductance was recorded in microSiemens (μS; sampling rate, 32 Hz) both during the preliminary and the experimental sessions, using 2 circular Ag/AgCl electrodes (1 cm diameter) positioned on the distal phalanx of the index and middle finger of the left hand (PROCOMP+ system; Thought Technology, Montreal, Canada).

Statistical Analysis

Statistical analyses were performed with Statistica 6.0 (StatSoft, Inc., Tulsa, OK), using a significance level of $P < .05$ for all analyses. First, single-sample *t* tests were performed on the video pleasantness/unpleasantness ratings against the reference value of 0 (neutral) to determine whether each video was considered unpleasant, neutral, or pleasant. Planned comparisons (within-subject) were performed between each experimental condition (disasters and model) and the control condition (cityscape) for the dependent variables of pain intensity, pain unpleasantness, mood, anxiety/calmness, video unpleasantness, and skin conductance. For each subject, the VAS ratings of pain intensity, pain unpleasantness, mood, anxiety/calmness, and video unpleasantness were averaged across trials for each experimental condition. Skin conductance was quantified by calculating the area under the curve (AUC) in each trial; the AUCs for all trials of each experimental condition were then averaged and subtracted from the baseline AUC (ie, the skin conductance recorded during the last stimulus delivered during the preliminary session). Because we had specific a priori hypotheses concerning the direction of the effects (ie, cityscape video rated as less unpleasant, and associated with better mood, less anxiety, less arousal, and less pain unpleasantness but equal pain intensity), we used 1-tailed tests. Pearson correlations were used to address the relationship between the different relevant dependent variables; these correlations were computed both independently for each experimental condition (eg, mood versus heat intensity in the cityscape condition), and after collapsing the different conditions (ie, after averaging the values obtained in all 3 conditions). Differences in the relationship between mood and pain intensity and between mood and pain unpleasantness were assessed by using Williams' T2 formula,[35] which tests for the equality of 2 dependent correlations (ie, obtained from the same sample of subjects) having an index in common[29] (ie, mood, in our case).

Results

Video Pleasantness/Unpleasantness

As shown in Fig 2A, subjects rated the disasters video as moderately unpleasant [single-sample *t* test against the reference value of 0, corresponding to the "neutral" anchor on the video unpleasantness scale, $t(11) = -4.79$, $P = .0003$, whereas they rated the cityscape video as slightly pleasant, $t(11) = 2.49$, $P = .015$, and the model video as emotionally neutral, $t(11) = 0.38$, $P = .36$]. Planned comparisons revealed that the disasters video was rated as significantly more unpleasant than the cityscape video [$t(11) = -7.85$, $P < .00001$]. There was no statistical difference between the ratings of the model and the cityscape videos despite the fact that the model was exhibiting pain-related facial expressions [$t(11) = -0.93$, $P = .19$].

Effects of Videos on Mood, Anxiety State, and Arousal

Figs 2B and 2C show that both mood and anxiety state differed between video conditions, as revealed by planned comparisons. Although subjects were on average in a good mood throughout the experiment, their mood was significantly less good during the disasters video than during the cityscape video [$t(11) = -2.56$, $P = .013$]. The difference in mood between the model video and the cityscape video only trended toward significance [$t(11) = -1.3$, $P = .11$]. Subjects also described themselves on average as calm throughout the experiment, but planned comparisons indicated that they were significantly less calm when watching the disasters video [$t(11) = -2.5$, $P = .015$] and the model video [$t(11) =$

-2.97, $P = .007$] than when watching the cityscape video. Accordingly, during the cityscape condition, skin conductance tended to be lower than in the disasters [$t(11) = -1.79$, $P = .051$] and model [$t(11) = -1.47$, $P = .084$] conditions; however, the 2 latter conditions did not differ in terms of skin conductance (Fig 2D).

Effects of Video on Ratings of Pain Intensity and Unpleasantness

As Fig 2E shows, planned comparisons did not reveal differences between cityscape and the 2 other conditions in terms of pain intensity [disasters: $t(11) = 1.02$, $P = .164$; model: $t(11) = 1.33$, $P = .105$]. In contrast, subjects rated pain unpleasantness higher during the disasters video than during the cityscape video [$t(11) = 1.956$, $P = .038$] (Fig 2F). However, consistent with the less significant mood differences between the model video and the cityscape video, the difference in pain unpleasantness ratings between these conditions only trended toward significance [$t(11) = 1.59$, $P = .07$].

Correlations

Collapsing all conditions, we observed that mood ratings significantly correlated with pain unpleasantness ($r = -.63$, $P = .027$) but not with pain intensity, in which case a weak (nonsignificant) trend in the opposite direction was observed ($r = .40$, $P = .195$). Furthermore, the test for the equality of 2 dependent correlations revealed that the correlation between mood and pain unpleasantness is significantly different from the correlation between mood and pain intensity [$t(9) = 7.79$, $P < .0001$] (Fig 3A). Anxiety/calmness ratings tended to correlate with pain unpleasantness ($r = -.57$, $P = .053$) but did not significantly correlate with pain intensity ($r = .33$, $P = .29$). Video unpleasantness ratings did not significantly correlate with either pain intensity or unpleasantness ratings (r's $= .07$ and $-.21$, P's $> .50$). Notably, pain intensity and pain unpleasantness ratings did not significantly correlate ($r = .38$, $P = .22$), confirming that subjects were able to differentiate these scales.

When examining the 3 conditions separately (Fig 3B), mood ratings significantly correlated with pain unpleasantness ratings within each video condition ($r = -.58$, $-.63$, and $-.61$ for the cityscape, disasters, and model conditions, respectively; all P's $< .05$). However, mood ratings did not correlate significantly with pain intensity ratings in any of the video conditions ($.18 \leq r$'s $\leq .45$, P's $\geq .14$). The correlation between anxiety/calmness and pain unpleasantness scores was significant during the cityscape condition ($r = -.64$, $P = .026$) and tended toward significance in the 2 other conditions (r's $= -.53$ and $-.50$, P's $= .075$ and $.095$). Video unpleasantness ratings did not correlate significantly with either pain intensity or pain unpleasantness during any of the video conditions (P's $\geq .15$). No significant correlations were observed between skin conductance and any of the variables examined, either with conditions collapsed or not (P's $\geq .12$).

Discussion

The present findings confirm, using dynamic visual cues to alter mood, that pain unpleasantness is affected by mood, whereas perceived pain intensity is not altered. Mood worsened and pain unpleasantness was rated higher during the disasters condition than during the cityscape condition, whereas mood and pain unpleasantness were less significantly altered by the model video compared with the cityscape video. However, during all 3 experimental conditions, we observed significant correlations between mood ratings and pain unpleasantness ratings, with ratings of worse mood being associated with higher ratings of pain affect. An examination of individual subject data adds further support to the strength of the relationship between mood and pain unpleasantness; the 2 subjects who expressed the most positive mood ratings possible (ie, 100/100; Fig 3A and B) also rated the heat stimuli as just slightly unpleasant or not unpleasant at all, despite rating their pain intensity as moderately high ($\geq$163.3/200). Although it is certainly possible to interpret these correlations in terms of the effect of pain affect on emotional state, rather than vice versa, when taken together with the group effects showing higher average pain unpleasantness ratings during the disasters video than during the cityscape video, the correlations provide supportive evidence that manipulations of mood affect pain unpleasantness. Notably, whereas mood was significantly less good during the disasters condition, it was still within the positive range (ie, the videos did not induce a negative mood). This observation suggests that mood manipulations are capable of inducing changes in pain perception, even if they do not lead to a negative emotional state per se.

The experimental manipulation of mood did not significantly alter perceived pain intensity but appeared to preferentially affect the unpleasantness dimension of pain. Although pain intensity and unpleasantness frequently covary in that the more intense a pain sensation, the more unpleasant is the experience, the relationship between pain intensity and unpleasantness differs among types of pain,[27] and experimental procedures such as hypnosis can selectively alter one or the other dimension.[14,25,26] In the current study, pain intensity and unpleasantness were dissociated in that these variables did not significantly correlate, nor were they affected in the same manner by mood state.

In principle, the preferential effects of video-induced mood changes on pain unpleasantness could be an artifact of the format difference between the heat intensity scale (ie, unipolar) and heat pleasantness/unpleasantness and mood scales (ie, bipolar). However, other data obtained with these scales suggest that the unipolar intensity scale is as sensitive to changes in psychological factors as are the bipolar scales. Using the same scales, Villemure et al[31] showed, using odors to manipulate mood, that direction of attention preferentially altered pain intensity (measured by the unipolar scale), whereas mood preferentially altered pain unpleasantness (bipolar scale), thus showing that both scales are sensitive to

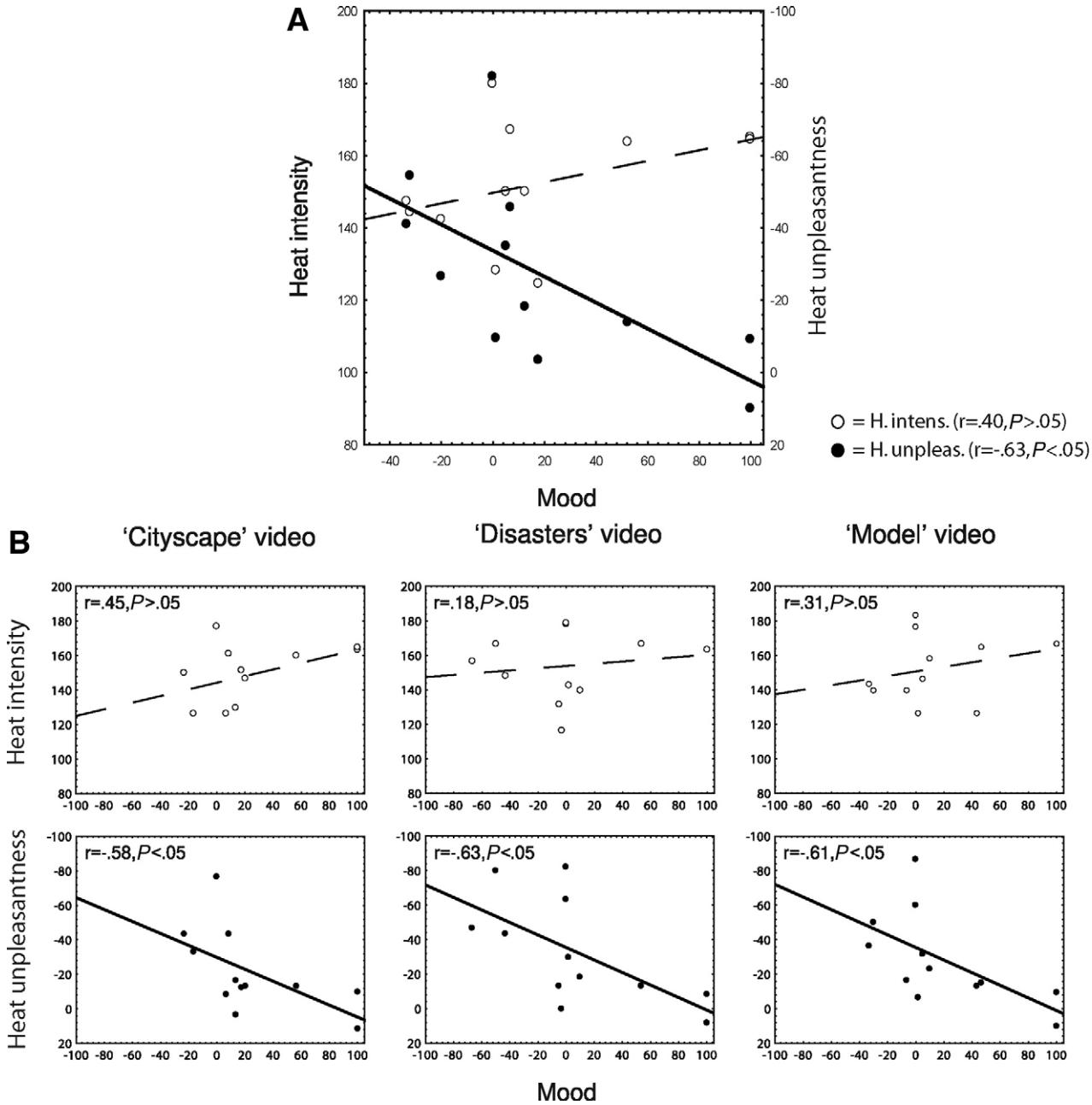

Figure 3. Correlations between mood and pain intensity or unpleasantness. **A,** Collapsing all conditions, we observed that mood ratings significantly correlated with pain unpleasantness but not with pain intensity. The difference between these 2 correlations was statistically significant ($P < .0001$). **B,** When considering each condition independently, mood ratings negatively correlated with ratings of pain unpleasantness but did not correlate with ratings of pain intensity in each of the 3 conditions. Continuous lines represent significant correlations ($P < .05$); dashed lines represent nonsignificant correlations ($P > .05$). For a description of the visual analog scales, refer to Fig 2.

psychological manipulations. Further suggesting that our findings are not an artifact of the measurement scales, Villemure and Bushnell (submitted) replicated the differential effects of attention and odor-induced mood changes by using unipolar scales for both dimensions.

Although anxiety state and unpleasantness of the video could in principle contribute to the differences in pain unpleasantness ratings among video conditions, differences in mood appear to fully explain our results. Subjects expressed a similar reduction in calmness and displayed a comparable increase in skin conductance during both the disasters and model videos. On the other hand, only the mood-worsening disasters video was associated with significantly higher ratings of pain unpleasantness, suggesting that mood has effects on pain unpleasantness which are dissociable from those possibly induced by the anxiety state and arousal levels. Moreover, the anxiety state ratings significantly correlated with pain unpleasantness ratings only during one condition (cityscape video) but not in the 2 other conditions, and no significant correlations were observed between video unpleasantness or skin conductance and pain ratings.

The present study confirms and extends the findings of Villemure et al,[31] who showed that exposure to pleasant and unpleasant odors altered the subjects' mood, which in turn altered the perceived unpleasantness but not intensity of experimental heat stimuli. Similar to our findings, these investigators observed that mood but not anxiety or emotional valence of the odor stimulus predicted pain unpleasantness ratings. Strikingly, the strength of the mood-pain unpleasantness correlation in these 2 studies is almost identical ($r = -.63$ in the present study vs $r = -.64$ in the study by Villemure et al). Not only does the present study show that the effects of mood on the affective component of pain are independent of mood induction technique used, it also suggests that these effects are age-independent: Villemure et al studied young male and female subjects (mean age, 24 years), whereas we studied middle-aged women (mean age, 51 years), thus further confirming the generality of the mood effect on pain unpleasantness.

At least 2 other studies have suggested that altering some aspect of emotional state more consistently modulates pain unpleasantness than pain intensity. Rainville et al[24] showed that hypnotically evoked negative emotional states such as anger or sadness produced more robust increases in pain unpleasantness than pain intensity. Moreover, a study in which subjects read a series of depressive, elating, or emotionally neutral sentences showed that pain tolerance—a measure thought to reflect mainly the motivational-affective dimension of pain—was affected by the mood manipulation, whereas the reported pain intensity was not affected.[36]

In contrast, however, 2 other studies that manipulated subjects' emotions found that both pain intensity and unpleasantness are modulated by emotional state. Meagher et al[21] induced fear and disgust by exposure to affectively charged pictures and found that subjects reported increases in both intensity and unpleasantness of pain. Similarly, Roy et al[28] found that pleasant music altered both dimensions of pain perception. Thus, it is possible that although we found a preferential effect of mood on pain unpleasantness, a more powerful mood manipulation could also modulate pain intensity. However, other differences between studies could contribute to the findings. First, distinguishing between pain intensity and unpleasantness requires a certain mental effort on the part of the subjects. Roy et al point out that they may not have allowed their subjects enough time to adequately rate the 2 separate aspects of pain. A similar argument could be made for the study by Meagher et al, in which subjects had to rate the 2 dimensions of pain by simultaneously adjusting online 2 sliding scales. In our study as well as in the 2 other studies that reported selective changes in pain unpleasantness,[24,31] subjects had unlimited time to contemplate and express their ratings. Second, in the study by Meagher et al,[21] arousal and empathy could have contributed to their findings. Highly arousing stimuli were used in both their "fear" and "disgust" conditions (eg, snakes, violent assault scenes, brutal mutilations), and arousal has been shown to influence pain perception.[19] Furthermore, as noted by the authors, the slides used in their disgust condition portrayed mutilated bodies, which "have been shown to evoke feelings of pity, which promote an approach disposition to help others."[17] Because feelings of empathy induce increases in both pain intensity and unpleasantness,[20] this factor could also have contributed to the findings Meagher et al.

The finding that emotional state alters pain unpleasantness is consistent with data from neuroimaging studies[6,13,18] that have shown that experiencing negative emotional states, such as sadness and social exclusion, activates limbic regions such as the anterior cingulate (ACC) and insular (IC) cortices. These regions are thought to code the affective component of pain perception, as indicated by both neuropsychological and functional activation studies (review in Apkarian et al[1]). For example, patients with cingulate or insular lesions show a reduction in pain-related emotional responses,[4,7,8,12] whereas patients with lesions of the primary and secondary somatosensory cortices experience "pain affect without pain sensation" in response to noxious stimulation.[22] Moreover, hypnotically induced manipulations of pain unpleasantness selectively modulate the activity of ACC.[26] We therefore propose that the exposure to emotionally negative videos increases the unpleasantness of pain perception by sensitizing the cortical areas involved in affective components of central pain processing. In confirmation of this idea, Villemure and Bushnell (submitted) showed that altering mood using odors preferentially altered pain-evoked activity in ACC.

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