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Effect of Ambient Temperature on Human Pain and Temperature Perception

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Background: **Animal studies show reduced nociceptive responses to noxious heat stimuli and increases in endogenous β-endorphin levels in cold environments, suggesting that human pain perception may be dependent on ambient temperature. However, studies of changes in local skin temperature on human pain perception have yielded variable results. This study examines the effect of both warm and cool ambient temperature on the perception of noxious and innocuous mechanical and thermal stimuli.**

Methods: **Ten subjects (7 men and 3 women, aged 20–23 yr) used visual analog scales to rate the stimulus intensity, pain intensity, and unpleasantness of thermal (0–50°C) and mechanical (1.2–28.9 g) stimuli applied on the volar forearm with a 1-cm^2 contact thermode and von Frey filaments, respectively. Mean skin temperatures were measured throughout the experiment by infrared pyrometer. Each subject was tested in ambient temperatures of 15°C (cool), 25°C (neutral), and 35°C (warm) on separate days, after a 30-min acclimation to the environment. Studies began in the morning after an 8-h fast.**

Results: **Mean skin temperature was altered by ambient temperature (cool room: 30.1°C; neutral room: 33.4°C; warm room: 34.5°C; $P < 0.0001$). Ambient temperature affected both heat (44–50°C) and cold (25–0°C) perception ($P < 0.01$). Stimulus intensity ratings tended to be lower in the cool than in the neutral environment ($P < 0.07$) but were not different between the neutral and warm environments. Unpleasantness ratings revealed that cold stimuli were more unpleasant than hot stimuli in the cool room and that noxious heat stimuli were more unpleasant in a warm environment. Environmental temperature did not alter ratings of warm (37 and 40°C) or mechanical stimuli.**

Conclusions: **These results indicate that, in humans, a decrease in skin temperature following exposure to cool environments reduces thermal pain. Suppression of Aδ primary afferent cold fiber activity has been shown to increase cold pain produced by skin cooling. Our current findings may represent the reverse phenomenon, *i.e.*, a reduction in thermal nociceptive transmission by the activation of Aδ cutaneous cold fibers. (Key words: Cold; cool; psychophysics; warm.)**

THE sensation of pain is dependent on many factors, including the strength of the noxious stimulus, state of the organism, and environmental variables. One variable that may be important in nociceptive processing is environmental temperature. Extremely cold or hot environmental temperatures produce an opioid-mediated stress-produced analgesia (see Bodnar *et al.* for review).[1] Several studies have also shown that moderately cool environmental temperatures also produce an antinociceptive effect in animals. Tail flick and tail pinch latencies increase in rats exposed to an air temperature of 4°C,[2] and response times in the hot plate test increase when rats are exposed to the environmental temperatures of 10°C.[3] Plasma β-endorphin levels in dogs have been shown to double after a 30-min exposure to an environmental temperature of 19°C,[3] suggesting that the antinociceptive effects of moderately cool environments may be mediated by endogenous opioid activation. The effect of warm environments on nociception in animals is less clear. Schoenfeld *et al.* showed that warming the environment to 30 or 35°C decreases rat hot plate paw-lift latencies,[3] indicating a hyperalgesic effect, and that β-endorphin levels tend to concurrently decrease. Nevertheless, another study showed that, in rats, plasma β-endorphin levels increase after exposure to a temperature of 36°C,[4] suggesting the possibility of analgesia during exposure to hot environments.

These observations in animals support the hypothesis that, in humans, pain perception would be suppressed by cool ambient temperatures and may be altered by warm ambient temperatures. However, data from human psychophysical and clinical studies have thus far been inconclusive. Using localized skin cooling, some studies show cool-related analgesia,[5–7] whereas others do not find such an effect.[8,9] In one study in which skin and body temperatures were altered by submerging subjects in hot and cold water baths, heat pain threshold

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and heat pain tolerance were not affected by skin and body temperatures.[10] Given the inconsistencies among studies, the current experiment employed sensitive psychophysical techniques to compare the effect of both warm and cool ambient temperatures on human perception of noxious and innocuous mechanical and thermal stimuli in the same subjects. A preliminary version of this study has been presented in abstract form.[11]

Materials and Methods

Participants

With the approval from the Committee on Human Research of the Royal Victoria Hospital, we studied 10 healthy volunteers (7 men and 3 women). None of the subjects was obese or taking medication. Mean values for morphometric characteristics included age 21 yr (range, 20–23 yr), weight 66 kg (range, 50–100 kg), and height 178 cm (range, 160–193 cm).

Study Protocol

Study Design. The experiments were conducted in January through March 1998. Studies started at approximately 8:00 AM to minimize circadian changes in body temperature. The tests were performed in a silent room with ambient temperatures of 25 ± 0.5°C corresponding to the neutral environment, 15 ± 0.5°C corresponding to the cool environment, and 35 ± 0.5°C corresponding to the warm environment on three different days. The humidity was maintained at 35–45%. There was at least a 1-week interval between the experimental days for each subject, and the order of the exposure to different room temperatures was randomized among subjects.

Volunteers fasted at least 8 h before each study day, were dressed in a hospital gown, and rested comfortably in a chair for at least 30 min prior to the experiment to adapt to the room temperature. Throughout the experiment, core temperature was recorded from the tympanic membrane using Mon-a-Therm thermocouples (Mallinckrodt Anesthesiology Products Inc., St. Louis, MO). Mean skin surface temperature was calculated using the four-points formula proposed by Ramanathan[12]:

$$°\text{skin} = 0.3(T°\text{chest} + T°\text{arm}) + 0.2(T°\text{thigh} + T°\text{calf})$$

Four skin probes were situated on the chest lateral to the left nipple, on the lateral aspect of the upper arm, on the the ventral surface of the mid-thigh, and on the lateral aspect of the mid-calf. Temperatures at these sites were recorded at 15-min intervals using an infrared pyrometer. The infrared pyrometer and the thermocouples were calibrated and accurate to 0.1°C.

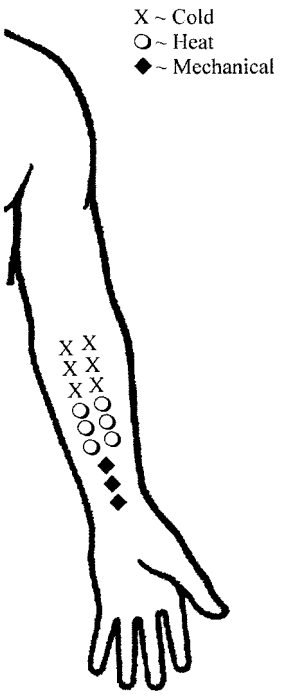

Fig. 1. Points of stimulation.

Temperature and Pressure Sensitivity. The pain threshold and perception for noxious heat, noxious cold, and mechanical stimulation were measured using a 1-cm-diameter contact thermode and von Frey filaments, respectively. After adaptation to room temperature, heat, cold, and mechanical pain sensitivity were measured using the method of constant stimuli (*i.e.*, sequences of predetermined intensities were applied in a double-blind procedure). The starting temperature was 30°C, and the rate of temperature increase or decrease was 20°C/s. Sequences were randomized among subjects.

For determination of heat pain and warm temperature sensitivity, six 5-s heat stimuli ranging from 37 to 50°C were applied one time to each of the six locations on the volar forearm, each separated by at least 1 cm and arranged in a 3-×-2 matrix (fig. 1). Similarly, for cold pain and cool temperature sensitivity determination, six 15-s cold stimuli ranging from 0 to 25°C were applied one time to each of the six locations on the volar forearm. To avoid skin sensitization, the interstimulus interval between each of the six test sites was at least 2 min.

Mechanical pain threshold and perception were measured using von Frey filaments of three randomly chosen

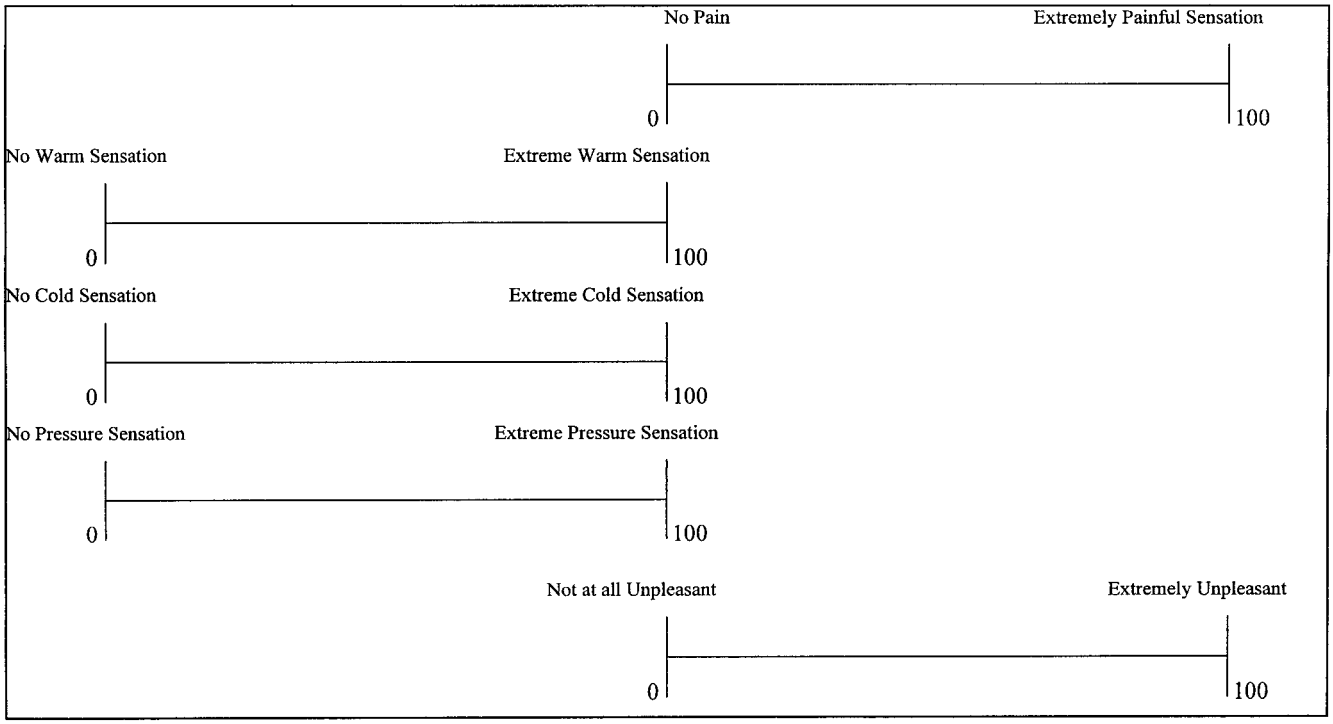

Fig. 2. Visual analog scales used to measure presented stimuli.

forces ranging from 1.2 g to 28.9 g applied one time to each of three locations on each subject's forearm. Heat, cold, and mechanical stimuli were applied in blocks to three different areas on the subject's forearm, and the order was randomized among subjects. There was at least 15 min between each block.

Response Measures

Two dimensions of the thermal and mechanical sensations were measured. The first is the perceived intensity, which corresponds to the degree of warmth, coolness, or pressure of the stimulus. The second dimension is hedonic, which corresponds to the unpleasantness of the stimulus (*i.e.*, how disagreeable is the stimulus). Consequently, subjects were asked to rate each stimulus on different visual analog scales to separate the two dimensions of the thermal and mechanical sensations. The following visual analog scales were used (fig. 2): Scale for temperature or pressure (from "no sensation" to "extreme warm, cold, pressure sensation"), scale for pain intensity (from "no pain" to "extremely painful") and scale for unpleasantness (from "not at all unpleasant" to "extremely unpleasant"). A score of 100 on the first scale corresponded to 0 on the pain intensity scale. During the analysis, these scales were combined, and 100 represented the pain threshold. Periodically, subjects were asked to rate the pleasantness or unpleasantness of the room temperature on a scale from −100 ("extremely unpleasant") to +100 ("extremely pleasant"). Zero on this scale corresponded to a neutral temperature rating.

Statistical Analysis

For statistical evaluation of the data, two-way and one-way analysis of variance (ANOVA) with repeated measures, followed by a *t* test with Bonferroni correction for multiple comparisons, was used. $P < 0.05$ was considered to represent a significant difference. Heat, cold, and mechanical pain thresholds were determined using graphic interpolation. Responses to stimuli classified as cold (0–25°C), hot (44–50°C), and warm (37–40°C) were analyzed separately based on neurophysiologic evidence that these temperatures generally activate separate populations of primary afferent fibers.[13–21] Results are expressed as mean ± SD.

Results

Core Body and Skin Temperature

Skin temperature was monitored throughout the experiment for all subjects, and core temperature was

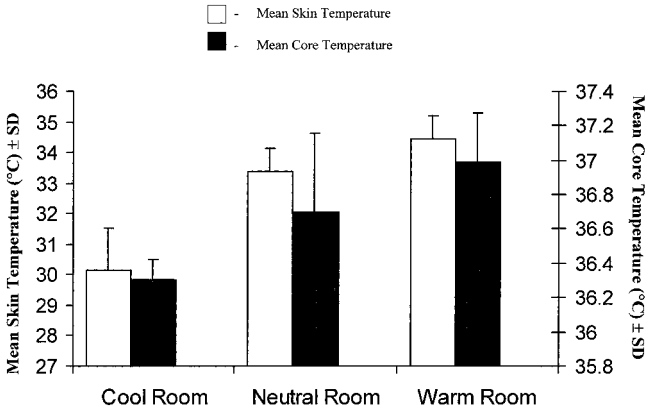

Fig. 3. Mean skin and core body temperatures in cool (15°C), neutral (25°C), and warm (35°C) environments. There was a significant effect of ambient temperature on mean skin temperature in all subjects ($P < 0.0001$, repeated measures analysis of variance [ANOVA] followed by paired t test, n = 10). Similarly, there was a significant effect of ambient temperature on mean core body temperature measured in four subjects ($P < 0.05$, repeated measures ANOVA followed by paired t test, n = 4). Error bars represent SD.

monitored for four subjects. Mean skin temperatures of 34.5 ± 0.7°C, 33.4 ± 0.8°C, and 30.1 ± 1.3°C were obtained in the warm, neutral, and cool environments, respectively. Skin temperature was significantly lower during exposure to the cold environment than in the neutral and warm environments ($P < 0.0001$, 2-ANOVA, n = 10) There was also a significant difference in skin temperature between the neutral and warm environments ($P = 0.008$; fig. 3).

Core body temperature data are shown in figure 3. Mean core body temperatures were 36.9 ± 0.3°C, 36.7 ± 0.5°C, and 36.3 ± 0.12°C in the warm, neutral, and cool environments, respectively. There was a significant effect of environmental temperature on core body temperature ($P < 0.05$, 2-ANOVA, n = 4). However, because core temperature only measured in four subjects, *post hoc* tests did not show a significant difference between the core body temperatures in warm compared with neutral ($P = 0.33$) and in cool compared with neutral ($P = 0.35$) environments (paired samples t test, n = 4). There was a slight but significant decrease in core body temperature in the cool compared with the warm environment ($P < 0.05$).

Thermal Sensitivity

Perceived intensity of both cold (0–25°C) and heat (44–50°C) stimuli were reduced in the cool ambient temperature. Intensity ratings of cold stimuli (fig. 4A) were lower in the cool compared with warm ($P = 0.009$) and neutral ($P = 0.05$) environments (2-ANOVA; factors, room temperature, stimulus intensity). The warm environment had no suppressive effect on the subjects' ratings of cold (0–25°C) stimuli, because there was no change in temperature sensitivity in the warm compared with the neutral environment ($P = 0.95$). The average cold pain threshold in the neutral environment was estimated to be just above 0°C, whereas in both the cool and warm environments, on average, none of the cold stimuli were rated as painful.

Intensity ratings for hot stimuli are shown in figure 4B. There was an overall significant effect of room temperature on intensity ratings ($P = 0.03$). Intensity ratings of hot stimuli were lower in the cool compared with the warm environment ($P = 0.01$), with a similar tendency in the neutral environment ($P = 0.07$; 2-ANOVA; factors, room temperature, stimulus intensity). As was observed for ratings of cold stimuli, the warm ambient temperature did not have a suppressive effect on the intensity ratings of hot stimuli (44–50°C), because there was no difference in temperature sensitivity in the warm compared with the neutral environment ($P = 0.39$). Average heat pain thresholds in cool, neutral, and warm environments were estimated to be 48.5, 47.5, and 47.0°C, respectively. Graphic interpolation of individual responses to heat stimuli (44–50°C) resulted in significantly higher heat pain thresholds in the cool compared with the warm environment ($P = 0.006$).

Figure 4C demonstrates intensity ratings for warm stimuli (37–40°C). There was no overall effect of ambient temperature on the perception of warm stimuli ($P = 0.99$). Neither the cool nor the warm environment affected thermal sensitivity to innocuous warm stimuli.

Unpleasantness ratings of thermal stimuli are shown in figure 5. The only stimulus rated as more than mildly unpleasant was 50°C. There was an effect of ambient temperature on the stimulus unpleasantness ratings to hot stimuli (44–50°C; $P = 0.01$), which was probably due to significantly higher unpleasantness ratings of the 50°C stimulus in the warm compared with the neutral environment ($P = 0.03$). A small overall effect of ambient temperature on the unpleasantness ratings of cold stimuli (0–25°C) was observed ($P = 0.02$), which was due to significantly lower unpleasantness ratings of these stimuli in the warm compared with the cool environment ($P = 0.02$). There was no effect of ambient temperature on the unpleasantness ratings to warm stimuli (37–40°C; $P = 0.4$).

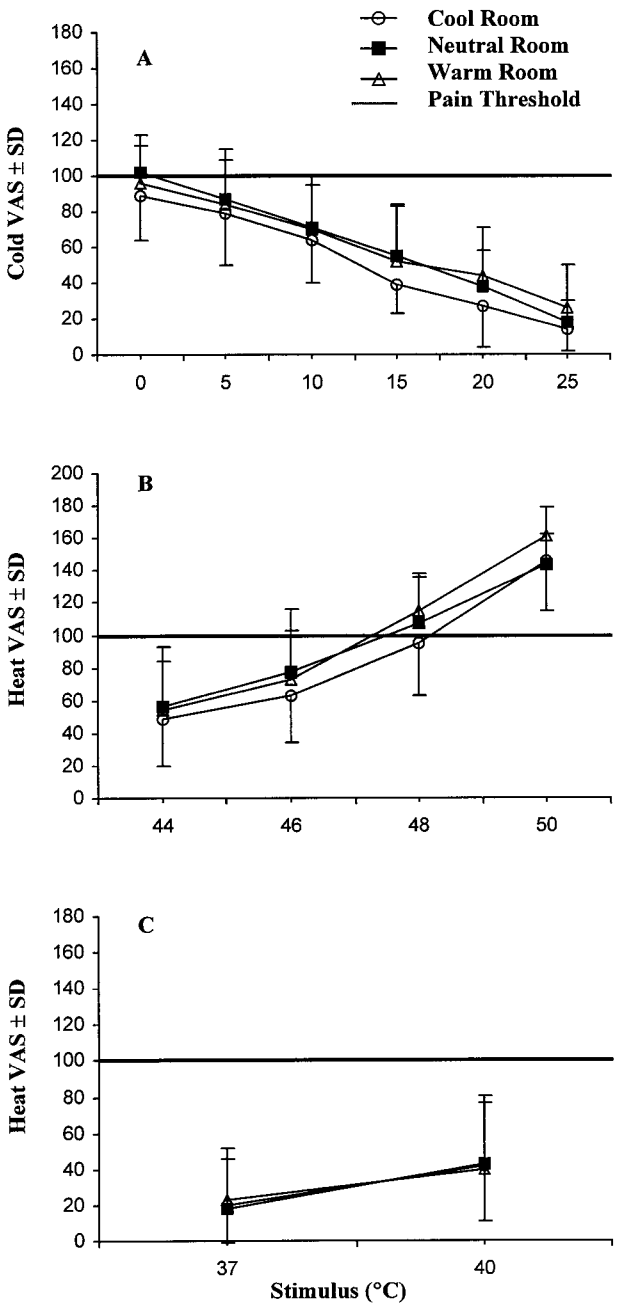

Fig. 4. (*A*) Intensity ratings to cold stimuli (0–25°C) were lower in the cool than in the warm ($P = 0.009$) and neutral ($P = 0.005$) environments. (*B*) Intensity ratings to heat (44–50°C) stimuli were lower in the cool compared with the warm ($P = 0.01$) and neutral ($P = 0.07$) environments. (*C*) Intensity ratings to warm (37 and 40°C) stimuli were not affected by the environmental temperature ($P = 1.0$; repeated measures analysis of variance [ANOVA], n = 10). Error bars represent SD.

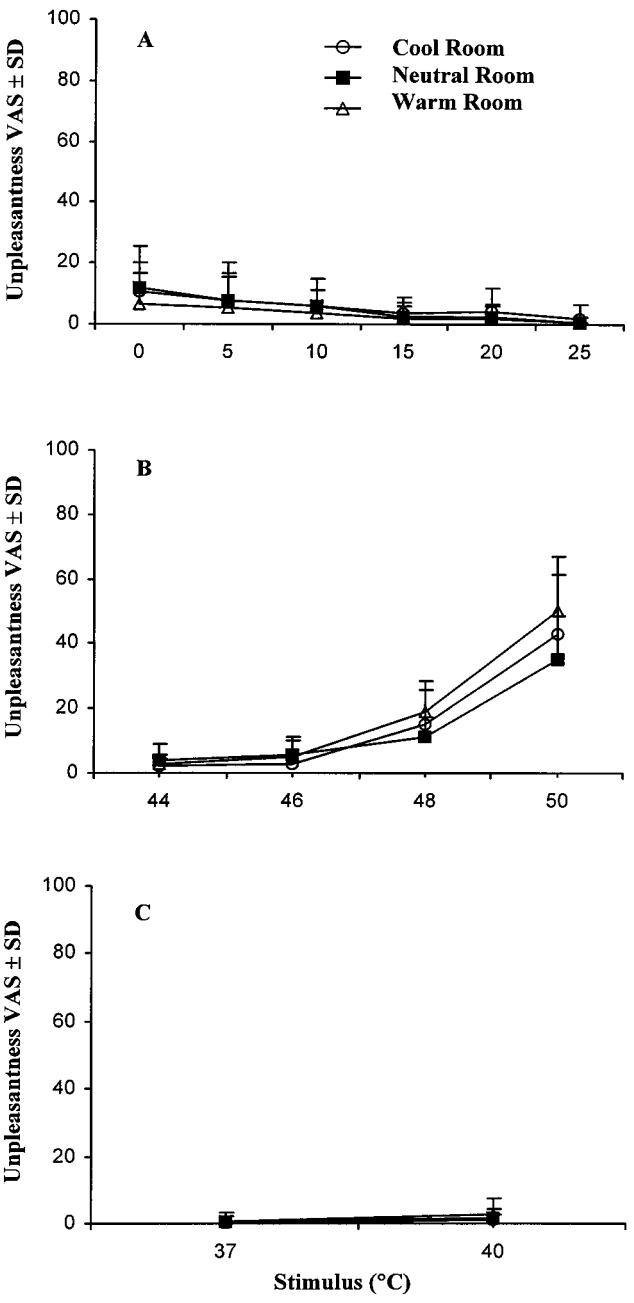

Fig. 5. (*A*) Unpleasantness ratings to cold stimuli (0–25°C) were higher in the cool than in the warm ($P = 0.025$) environment but were not different from the neutral environment ($P = 1.0$). (*B*) Unpleasantness ratings to heat (44–50°C) stimuli were higher in the warm compared with the neutral ($P = 0.03$) and cool ($P = 0.08$) environments (*C*) Unpleasantness ratings to warm (37 and 40°C) stimuli were not affected by the environmental temperature ($P = 0.4$; repeated measures analysis of variance [ANOVA], n = 10). Error bars represent SD.

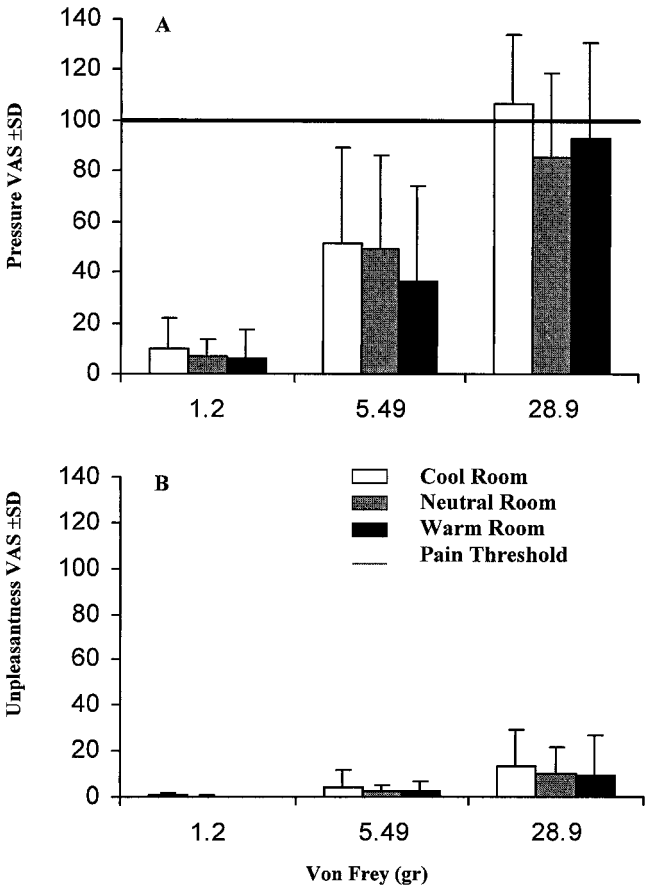

Fig. 6. (*A*) Stimulus intensity ratings and (*B*) stimulus unpleasantness ratings to pressure stimuli were not affected by the environmental temperature. Error bars represent SD.

Mechanical Sensitivity

Intensity and unpleasantness ratings of mechanical stimulation are displayed in figures 6A and 6B, respectively. Environmental temperature did not alter the intensity ($P = 0.07$) or the unpleasantness ($P = 0.4$) ratings of mechanical stimuli.

Room Unpleasantness

Table 1 shows the subjects' ratings of the pleasantness/unpleasantness of the ambient room temperature. Subjects reported the cool and warm environments to be equally unpleasant ($P = 0.99$), whereas they rated the 25°C room as neither pleasant nor unpleasant.

Discussion

This study examined whether environmental temperature alters thermal and mechanical perception in humans. As predicted, there was a small but significant effect of ambient temperature on heat and cold sensitivity and pain thresholds in normal volunteers. Compared with a neutral environmental temperature, the cool environment produced lower intensity ratings of hot and cold cutaneous stimuli and higher pain thresholds. Conversely, the warm environment had no effect on thermal perception. Environmental temperature did not affect perception of noxious or innocuous mechanical stimuli or mildly warm stimuli.

Our findings of a suppressive effect of a cool environment on thermal pain thresholds is consistent with animal studies showing that cool ambient temperatures lead to increased reaction times and nociceptive thresholds to noxious heat stimuli.[2,3] However, our findings are discrepant from those of Croze *et al.*, who observed that, in humans, heat pain threshold and tolerance are independent of skin and body temperature.[10] The differences in our results may be due to the more sensitive psychophysical methods used in the current study, which allow for the detection of small but significant differences in thermal perception. Our study extends the findings of previous animal and human studies to show that cool ambient temperatures alter cold pain thresholds as well as heat pain thresholds. This finding suggests that the modulation of the heat pain threshold is not caused by an effect of the cool environment on heat transfer from the thermode. It is more likely explained by a central nervous system modulatory influence. Furthermore, although skin cooling can alter primary afferent conduction velocity, this effect has only been reported when skin temperature is cooled to less than 10°C.[22]

We observed that a cool ambient temperature does not only alter the perception of painful stimuli but also influences innocuous hot and cold perception. Nevertheless, the perception of innocuous warm stimuli and of tactile stimuli was not altered in the cool environment. The absence of an effect of ambient temperature on innocuous warmth perception may appear to be contrary to findings in humans and animals that cool and warm thresholds and sensitivity are influenced by adapt-

Table 1. Subjects' Ratings of Ambient Room Temperature

Room Temperature	Room Unpleasantness (mean VAS)
Cool room (15°C)	−40.25
Neutral room (25°C)	5.5
Warm room (35°C)	−39.9

VAS = visual analog scale.

ing skin temperatures.[23–29] However, in our study, although the average cutaneous temperature varied significantly among environmental temperatures, the skin under the thermode was always adapted to the same temperature of 30°C. Thus, our study did not examine the effects of adapting temperature on thermal thresholds.

The differential influence of the cool environment on noxious and innocuous thermal and mechanical stimuli may be due to the response characteristics of neurons transmitting thermal and nociceptive information in the spinal cord dorsal horn and thalamus. Many neurons that are activated by noxious heat are also activated by cold stimuli less than or equal to 25°C as well as by hot stimuli greater than or equal to 44°C.[30–32] These nociceptive cells are not activated by warm temperatures (*e.g.,* 37 or 40°C), nor are they activated by moderate mechanical pressures. Other nociceptive neurons, termed wide dynamic range neurons, respond to a range of mechanical and noxious heat stimuli.[30,33] Our finding that environmental temperature did not alter the perception of noxious mechanical stimuli suggests that ambient temperatures in the range studied may not affect activity of wide dynamic range neurons. Thus, the cold environment may selectively alter activity in a subset of thermal nociceptive pathways.

The influence of a cool environment on thermal sensitivity might be explained by a phenomenon in which activity in cool-sensitive neural pathways inhibits that in thermal nociceptive systems.[32,34,35] Normally, cold-specific messages, mediated by Aδ afferent activity, gate nociceptive messages mediated by C-fiber nociceptive input. Reducing Aδ activity by inducing ischemia[35] or a specific pressure block[34] results in thermal allodynia, whereby normally nonpainful stimuli produce a burning pain sensation. In our study, the cool ambient temperature, which significantly decreased the mean skin temperature in all subjects, probably activated cool-sensitive neural pathways mediated by Aδ-fiber activity. This activation could lead to centrally mediated inhibition of thermal nociceptive activity and a subsequent reduction in perceived intensity of thermal stimuli. Similarly, it has been observed that local cooling of the skin by ether evaporation results in suppressed pain perception in human subjects.[7]

The absence of a suppressive effect of the warm environmental temperature on thermal sensitivity is generally consistent with findings from animal studies. Studies of thermal nociception in rats exposed to environmental temperatures of 30 or 35°C reveal a mild hyperalgesic effect of the warm environment.[3] Similarly, our subjects rated the 50°C stimulus as more intense in the warm environment than in the neutral or cool environment. These findings contrast somewhat with those of Deeter and Mueller, who found that rats exposed to a 36°C room for an extended period have elevated plasma β-endorphin levels, suggesting the possibility of a stress-related analgesic effect.[4] The increase in plasma β-endorphin levels has been observed in humans following brief exposure to temperatures of 47 and 90°C.[36,37] However, there is no evidence suggesting an increase in endogenous opioids by mild elevations in the environmental temperature. Thus, a warm environment probably only reduces pain perception when the intensity or duration of the heat is sufficient to produce physiologic stress in the organism.

Our results show that the ambient temperature has a different effect on the unpleasantness ratings than on the intensity ratings of thermal stimuli. The perceived intensity of both hot and cold stimuli was reduced in a cool environment. However, cold stimuli were perceived as more unpleasant in the cool than in the warm environment, whereas extremely hot stimuli (50°C) were perceived as more unpleasant in the warm environment. Previous studies have shown that the hedonic quality of thermal sensation is influenced by internal body temperature.[38] The four subjects for whom we measured core temperature showed small but significant changes related to ambient temperature. Nevertheless, the difference in subject core temperature between the warm and cool environments was only 0.6°C, indicating that the subjects were never hyperthermic or hypothermic. Skin temperature was more influenced by ambient temperature in our study, with more than a 4°C difference between the warm and cool rooms. Thus, our data suggest that the hedonic value of thermal stimuli is altered by environmental temperatures in situations that do not produce hyperthermia or hypothermia.

Cold therapy has been widely used in postoperative management of pain. Several studies have found an analgesic effect of local cooling following episiotomies, orthopedic, lumbar spine, and other surgeries.[39–42] Thus far, no study has investigated the effect of environmental cooling on postoperative or incisional pain. However, it has recently been confirmed that a 2°C decrease in core body temperature (34.8 ± 0.6°C *vs.* 36.7 ± 0.6°C) prolongs patients' postoperative recovery by at least 40 min.[43] In other words, too much cooling has a disadvantageous effect. In our study, the core body temperature did not decrease significantly in the cool com-

pared with neutral environment (36.3 ± 0.12°C *vs.* 36.7 ± 0.5°C); however, thermal sensitivity was suppressed. Therefore, it would be interesting to investigate the possibility that moderate decreases in environmental temperatures that do not produce hypothermia have beneficial effects on patients' postoperative recovery or chronic pain. Such a conclusion cannot be drawn from the current study but awaits investigation in the clinic.

We found that, in humans, a cool environment suppresses pain and temperature perception of thermal stimuli but does not affect the perception of mechanical stimuli. Further experiments are necessary to determine both the clinical implications and the mechanisms of thermal suppression by cold environments in humans, including the possible role of endogenous opioid systems.

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