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SKIN TEMPERATURE AND CUTANEOUS PAIN

DURING

WARM WATER IMMERSION*

BY

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ABSTRACT

Measurements of skin temperature were made during the sudden immersion of the skin of human subjects in water baths at 36-41°C and related to the reports of pain elicited during the first few seconds of immersion. Within 0.5 seconds, the skin temperature rose to bath temperature and remained at this level during the 10-15 seconds of immersion, pain was reported at 37-41°C occurring 1-5 seconds after the start of the immersion and adapting in 2-6 seconds. Calculation of the subcutaneous temperature and thermal gradients indicate maximal thermal gradients in superficial skin layers during the first 0.1 - 0.2 seconds of immersion (60°C/mm) decreasing rapidly during the first 5 seconds to 6°C/mm. Analysis of the transient pain indicated that it could be considered as the more sensitive "phasic" response of the pain ending of which the "static" unadapting response occurs at skin temperatures of 43-46°C. Several alternative explanations including subcutaneous thermal gradients, vasomotor reactions, and thermo-chemical changes in the nerve membrane were considered as possible explanations. The last most likely possibility requires a second order kinetic system with highly temperature sensitive reaction velocities to account for both the phasic and static components of the pain.

Introduction

In studies of pain sensation using thermal radiation and other methods of heating the skin, many investigators have reported the pain threshold in terms of the skin temperature reached at the time of report of minimal pain. (1,10) This threshold temperature has been variously reported to lie between 43 and 47°C and has been noted to be independent of sex, age and cultural background. On the other hand, the report of Lele et al (15) of their investigation of heat transfer and cutaneous sensibility revealed that skin temperatures as low as 36°C had produced reports o pain for some subjects. Although differences in method of application of the heat stimulus as well as site and size of area stimulated were apparent, these data brought into question the critical importance of a skin temperature near 45°C as the threshold of thermal, cutaneous pain sensation. It was also reported by Lele (15) and Neisser (17) that the sensation of thermal pain adapted in a few seconds, confirming an observation made originally by Stone and Dahlenback, (22). These observations appeared to contradict the evidence of Greene and Hardy (8) who found that subjects when asked to maintain a threshold level of pain by controllin a stimulus of thermal radiation, voluntarily maintained a skin temperature of 45°C (or slightly below) for periods of time up to 50 minutes. Thus, pain appeared not to adapt when the stimulation temperature was near or at 45°C and, indeed, the skin became more sensitive as the duration of the stimulation increased. In view of these contrary findings, the present study was undertaken in an attempt to gather further information in regard to the pain stimulated at skin temperatures in the range 36-41°C and to test the hypothesis proposed by Lele, Weddell and Williams (15) that heat pain results from subcutaneous thermal gradients.

Method

The subjects were four members of the laboratory staff, three men and one woman. Three of them had had previous experience in the study of cutaneous pain threshold. The apparatus consisted of a bath positioned in the center of the experimental room which could be filled quickly to about a 6-inch depth with hot water. The bath was stirred vigorously during the experiment and its temperature was measured by means of a mercury thermometer calibrated to 0.1°C; readings of water temperature were taken every ten seconds during the exposure of the subject. Skin temperature was measured continuously throughout the exposure time of the subject by means of an insulated fine wire copper-constantan thermocouple (#40 gauge) suspended within a lucite ring 2 cm in diameter (see Figure 1). The ring was attached with spring bronze supports held in place by adhesive tape so that the thermocouple pressed gently into the skin surface. It is known that under these conditions the thermocouple will read a temperature which corresponds to a depth somewhat below the actual skin surface (21). During these experiments, the thermocouple readings were stable in air and during water immersion read slightly below the water temperature. Experiments were also made using a thermocouple (0.001" wire) inserted into a hair follicle, but as these readings were essentially the same as those obtained with the thermocouple pressed against the skin and as the arrangement was more difficult, the latter method was used in most experiments. Thermocouple voltage after d.c. amplification (Allegheny Instrument Co.) was recorded continuously on an oscillographic recorder (Visicorder). The experimental arrangement is shown schematically in Figure 1.

Figure 1

The response of the system was tested by plunging the thermocouple into water as shown by the record at the bottom of Figure 1. It was less than 0.01 second, sufficiently rapid to follow the expected rapid rise in skin temperature to be measured during the immersion of the skin. Calibration of the thermocouple was carried out in a stirred water bath by direct comparison of thermocouple emf with the reading of a standard mercury thermometer before and after each experiment. Temperature calibrations were reproducible to $\pm$ 0.1°C.

After the thermocouple had been secured to the subject's skin in the area to be tested (usually the lower back), the subject, wearing an ordinary swim suit, sat down in the tub with water temperature 37-41°C. A short time was allowed to elapse in order to permit the initial sensations in the subject's lower extremities to subside. When it was reported that the water felt more or less neutral, the experiment began with the subject quickly leaning backward so as to immerse a portion of his back in the water and he immediately began reporting his sensations noting particularly the appearance of pain. He continued to report his sensations of pain during the period of immersion. The trial ended shortly after the subject reported that the pain had disappeared. These reports were noted on the visicorder record at the time they were made.

Results

Figure 2 illustrates a typical protocol with the skin temperature record before and during immersion together with notations of the time pain was first reported, when it reached a maximum and when it disappeared. Thermocouple calibrations before and after the experiment are also indicated in the figure.

Figure 2

A summary of the results on four subjects is shown in Figure 3. The skin

Figure 3

temperature in °C at the report of maximal sensation, whether pain was perceived or not, is plotted on the ordinate and the time after immersion is indicated on the abscissa. Although individual differences are apparent in the skin temperature at which the report of pain occurred as well as in the delay time of subject's report of pain, reports of pain were obtained for all subjects at 38.7°C and for one subject at 36.8°C.

Discussion

The data shown in Figure 3 confirm the report of Lele, Weddell and Williams that rapid immersion of skin areas in water 36-40°C will evoke pain. This temperature is well below the skin temperatures near 45°C consistently found by Hardy and his associates (9) as necessary to elicit a report of pain with the thermal radiation method. Also, it was noted in all cases (as illustrated in Figure 2 for one protocol) that the pain was transient, disappearing in 5 to 6 seconds, in contrast to the reported lack of adaptation of thermal pain reported by Greene and Hardy. A further finding was that a second attempt to restimulate the transient pain by re-immersion at the same bath temperature which had been originally effective (after allowing the skin to cool for one or two minutes) did not evoke the pain a second time. Although the pain sensations evoked by the water bath and the thermal radiation seemed to have the same quality, i.e. pricking pain, there were clear differences between the "transient" and steady

state pain sensations. Principal among these are: (a) the threshold pain produced by radiant heating to a skin temperature near 45°C is reproducible upon repeated stimulation whereas the pain evoked at temperatures of 37-40°C cannot be immediately re-stimulated and its threshold is thus not readily reproducible; (b) the pain evoked at 45°C does not adapt rapidly, if at all, whereas pain experienced at temperatures of 37-40°C does adapt rapidly. Although many of the properties of this low temperature pain are yet to be worked out, it is clear that cutaneous thermal pain sensation has the properties of "phasic" and "static" stimulation which are similar to those reported for other skin sensations such as warmth, cold and touch (14, 6). The thresholds for warmth and cold sensations are commonly measured in terms of the more sensitive "phasic" components of these sensations rather than the steady state sensation, whereas for thermal pain the reproducible "static" sensation has been more commonly studied and the presence of the phasic component of thermal pain has only been recently reported. The phasic character of pain and temperature senses may be associated with the initial rapid firing of cutaneous receptors described by Dodt(5) for "pain receptors" and by Hensel (14) for temperature receptors. An hypothesis of "two pains" of different origin can be used to avoid contradiction between the results of the present work and those reported by Hardy (9) as to temperature level for "static" pain stimulation and by Greene (8) as to lack of adaptation of pain. However, such an assumption does little to explain the origin of either type of pain and does not indicate how the "two pains" may be related. Based on the facts available concerning the relation of skin temperatur to both transient and steady state pain and on the assumption that the "two pains"

are evoked from the same nerve fiber endings and thus are in reality different aspects of the same type of peripheral excitation, the following analysis has been made:-

Lele, Weddell and Williams (15) who first reported eliciting heat pain at skin temperatures near 36°C, inferred that this sensation was essentially similar to warmth and resulted from the "bolometer" type action of the unencapsulated endings in the skin. That is, if heat were being put into the skin, a temperature difference would result between the unencapsulated endings and the stem fiber and this thermal gradient would give rise to action potentials which could be interpreted as warmth, heat or pain depending upon the "temporo-spatial patterns" of impulses. They inferred further that the greater the temperature difference and the greater the "rates of heat transfer" into the skin the more intense the pain. It thus seemed worthwhile to examine analytically the thermal gradients existing in the skin during these studies when pain was reported on immersion of the skin in hot water. The skin temperature measurements in this experiment are considered fairly reliable and from them an approximation of the temperature profiles in the subcutaneous layers can be made using the uni-directional heat flow theory for a semi-infinite solid. The general equation is (18):-

1. $dT = \frac{a^2 d^2 T}{dx^2}$

2. $a^2 = K/\rho c$

in which T = temperature at any depth at time t, and

a = temperature diffusivity of the tissues of the skin

x = depth below the skin surface

K = thermal conductivity

ρ = density

c = specific heat

In order to solve equation (1) analytically, it is necessary to assume that the skin is a solid with uniform thermal properties and this assumption is so restrictive from an anatomical and physiological viewpoint that an analytic solution would be of doubtful value. However, a less general but perhaps more realistic approach can be made by taking the best accepted values of K, ρ, c for each of the various skin layers from the literature (1, 9, 12), and then solving the heat flow problem by the method of finite differences. The "model" of the skin so constructed is shown in Figure 4. In this analysis eight layers were used; two dry, horny layers 50μ thick on the surface followed by two layers of wet protein-like tissue to a depth of 0.2 mm, three vascular layers 0.2 mm thick and a final fat layer 10 mm thick. The properties of the fatty layer do not have significant influence on the problem in the water bath.

Figure 4

The equations describing heat flow into and out of each of the layers have the general form as modified from equation 1,

$$3.\ \rho_n c_n \Delta X_n \frac{dT_n}{dt} = K_{(n-1/2)} [T_n - T_{(n-1)}] - K_{(n+1/2)} [T_{(n+1)} - T_n]$$

In this equation

$\rho_n c_n \Delta X_n$ is the volume heat capacity of the skin layer "n", and the left side of the equation represents the change in heat content of this layer. n is taken to increase with depth and has values from 1 to 8.

$K_{(n-1/2)}$ is the thermal conductance between the centers of layers n and n-1.

$K_{(n+1/2)}$ is the average thermal conductance between the centers of layers n and n + 1.

T_n, $T_{(n-1)}$ and $T_{(n+1)}$ are the temperatures at the midpoints of layers n, n-1, and n + 1 respectively.

Since in the above model of the skin, eight layers have been assumed, eight equations of the general form of equation 3 replace the general expression of uni-directional heat flow in a semi-infinite solid equation 1. Boundary conditions are, $t<o$, $T_s = 34°C$, and $T_8 = 37°C$ with linear gradient; at $t = 0$, $T_s = 40°$, other temperatures change passively. The problem of evaluating the temperature of any layer as a function of time is readily solved by hand, or more easily by an analog computer, as was done in this instance, for the temperature at the center of each of the layers following the immersion of the skin in 40°C water. The thermal constants are shown for K, ρ, and c in the table at the bottom of Figure 5, and on top are shown the initial thermal gradients and the calculated gradients at 0.5 and 2.0 seconds following immersion in water at 40°C. It is evident that the subcutaneous thermal gradients are maximal immediately after immersion and decrease rapidly with time.

Figure 5

The temperature changes calculated separately as a function of time after immersion for layers 1 through 7 are shown in Figure 6 for a period of 5-1/2 seconds; experimentally determined values of the skin temperature are shown in Figure 6 for comparison. The thermal insulation of the skin layers is so great that large thermal gradients are established in the subcutaneous tissues during the first few seconds of the immersion, and for this reason actual measurements of subcutaneous temperature would be most difficult to make and would be of doubtful value.

Figure 6

In Figure 7 are shown the calculated values of the temperature gradients between the most superficial layers of the skin model. The gradients between layers 2 and 3 and 3 and 4 correspond to the most likely positions of the peripheral nerve terminations and they are maximal at 32°C/mm and 17°C/mm within the first 0.1 and 0.2 seconds following immersion. Were the gradients responsible for the noxious stimulus, pain should have been consistently reported within a second following immersion if time is allowed for nerve conduction and other delay times.

Figure 7

In general, however, as shown in Figure 4 and in Figure 2, there was a variable delay in the pain perception of 1-5 seconds which would seem to make the gradient explanation somewhat doubtful, but not entirely impossible for the transient pain stimulation. However, an even more difficult problem for the gradient theory is posed by the inability to explain why the pain cannot be stimulated after a period of cooling. Also, thermal gradients are very small when the skin has been heated slowly for several minutes with radiant heat and maintained near 45°C; yet in this situation, pain persists as shown by Greene and Hardy. These facts seem to rule out thermal gradients as the explanation of the pain whether transient or steady state. There are two other theories of heat pain which have been widely quoted; one theory attributes pain to vasomotor activity and the second to inactivation of cellular proteins by heat. These theories will be considered in the light of the present experiments.

Nafe and Wagoner (16) have proposed that cutaneous sensations of heat and cold as well as pain result from contraction and relaxation of the smooth muscle, probably located around blood vessels of the skin. It is possible.

that such contractions may give rise to sensations of pain....particularly during strong transient conditions as occur during rapid temperature and pressure changes, strong emotional states, etc. However, neither maximal cutaneous vasodilitation nor constriction are necessarily associated with pain in the steady state and indeed chemical agents, which upon local application, evoke strong vasodilitation or constriction generally do not cause pain. Thus, although the transient vasomotor changes associated with immersion of the skin in hot water could possibly be the source of the pain observed in these experiments, they would not be expected to be the cause of thermal pain in the steady state or in situations in which the skin temperature is changed slowly.

An hypothesis proposed by Hardy some years ago (9) attempts to account for thermal noxious stimulation as being due to thermo-chemical changes possibly related to inactivation of the proteins of the pain fiber ending. This theory was based upon the following: (a) the thresholds for continuous thermal pain and thermal injury are roughly the same (45° $\pm$ 1.5°C), (b) thermal pain, unlike thermal injury, depends upon temperature level rather than the temperature-time integral for temperatures above 45°C, and (c) the psychophysical scale for pain intensity appears roughly proportional to the logarithm of the protein inactivation rate for temperatures above 45°C. As originally conceived, this hypothesis held that the depolarization of the pain fiber ending by heat resulted from the breaking of molecular bonds due to thermal agitation and the reconstitution of the membrane by some metabolic process. The pain threshold and injury threshold were identified by rates of molecular degradation more rapid than the metabolic rates of resynthesis. The two reactions envisioned were of the form

$$4. \quad P \xrightarrow{k_d} P^* \quad \text{and}$$

$$P^* \xrightarrow{k_r} P,$$

in which P and P* are the relative concentrations of some natural and "inactivated" protein complex respectively and k_d and k_r are the rates of thermal inactivation and metabolic repair. The general form of the reaction rates can be written as (7):

$$5. \quad k = (e^{\Delta S/R}) \ (e^{-E/RT})$$

in which, k is the reaction velocity; ΔS = entropy change; ΔE - activation energy; R = gas constant; and T = absolute temperature. Approximate values of ΔE near 100,000 gm cal/mol have been obtained for various proteins (20), and for burning the skin ΔE has a value in the neighborhood of 150,000 gm cal/mol (11). For many enzymatic reactions ΔE lies in the range of 20,000 gm cal/mol. Values of ΔS are similarly different being of the order of 300-400 for protein inactivation and 10-20 for enzyme reactions. As noted by Chick and Martin (3), the great sensitivity of k_d to temperature and the relative insensitivity of k_r to temperature ensures that k_d will exceed k_r at some temperature for every protein. Without implying that a single master reaction, in the Crozier sense (4), is responsible for the changes in the pain nerve ending, it can be valuable to explore the concept that a highly sensitive thermal reaction (i.e. inactivation of protein by heat) results in the accumulation of some critical amount of P*, "inactive" protein, which brings about the permeability changes responsible for the generator potential at the pain ending, the firing of the neuron, the sensation of pain and its adaptation. Hensel (13) and Sand (19) have proposed similar concepts of "excitor" and "inhibitor" substances at the nerve ending to account for the stimulation of cold fiber endings in the cat's tongue and in the sensory organs of the Ampullae of Lorenzini of the ray but without any specification as to the nature of the substances or the reactions producing them. In the present case, we initially specify only that reactions, with relative reaction rates such as can be calculated from equation 5 using activation energies of 100,000 and 20,000 gm cal/mol for k_d and k_r respectively, are involved; that is:

6. $P \rightleftarrows P^*$

However, in this case there can be no transient maximum value of P* even for the situation involving a step function increase in temperature and thus the phasic pain cannot be accounted for by equation 6 if the concentration of P* is the only determinant for the pain excitation. This model must be discarded if the transient adapting pain is to be accounted for. Thus, in addition to the specifications concerning relative reaction velocities, we will assume the following:-

a. initially the cell has a large amount of natural protein P and very little P*, the excitor substance;

b. the rate of formation of P* is proportional to the concentration of P;

c. k_r is assumed to decrease rapidly at temperatures greater than 42°C, whereas k_d increases rapidly with temperature;

d. since the transient pain implies some second order effect, we have assumed that P* must be further reduced to a form P_n before the repair process can begin and the rate of formation of P_n is proportional to the concentration of P*; that is, the reaction is

7. $$\begin{tikzcd} P \arrow[r, "k_d"] & P^* \arrow[r, "k_r"] & P_n \arrow[ll, bend left, "k_n"] \end{tikzcd}$$

The problem is then to adjust k_n so that the following conditions are met (k_d is chosen equal to k_r at 44°C):

1) the generation of P* to some transient critical level in layer 4 of the skin (0.175 mm depth) in 1-3 seconds following immersion of the skin in water at 40°C followed by a decrease in P* to a new equilibrium value above its initial value;

2) upon re-immersion of the skin after 1-2 minutes in air at 25°C, P* will not show the initial overshoot - thus accounting for the inability to re-stimulate the transient pain;

3) upon raising the skin temperature more slowly as by heat radiation, P* reaches the critical steady state value for pain excitation and remains at this level. The three differential equations for the assumptions a,b,c,d made above are:

$$8.\ v\frac{dP}{dt} = k_n P_n - k_d P$$

$$9.\ v\frac{dP^*}{dt} = k_d P - k_r P^*$$

$$10.\ v\frac{dP_n}{dt} = k_r P^* - k_n (P_n - P_{n_o})$$

in which v is the volume of tissue concerned and the concentrations and reaction velocity constants are as defined above. It is assumed that at any temperature there will be some degradation of P and therefore some small pool of P_{n_o} will always be present to provide a replacement of P. The solution of the three first order equations can then be accomplished by using the values of temperature in layer 4 as shown in Figure 6 to calculate the instantaneous values of k_d and k_r (k_n is assumed to have a negligible dependence on temperature although a modest dependence, $Q_{10} = 2$, would not affect the solution), from equation 5 using $\Delta E = 100,000$ and $\Delta E_r = 20,000$ between 30°C and 40°C. For temperatures above 40° kd is assumed to decrease in a manner similar to the O_2 consumption of cortex tissue exposed to high temperature (2). An analogue computer can be used for this purpose, particularly as the model for developing the time function of temperature is available from the bath study and function generators for k_d, k_r, and k_n can be used as shown in Figure 8 for the temperature dependent reaction velocities.

Initially, calculation was made of the steady state concentrations as a function of tissue temperature as shown at the bottom of Figure 9. As the system is assumed to be closed, the equilibrium values of the relative concentrations of P, P*, and P_n

Figure 8

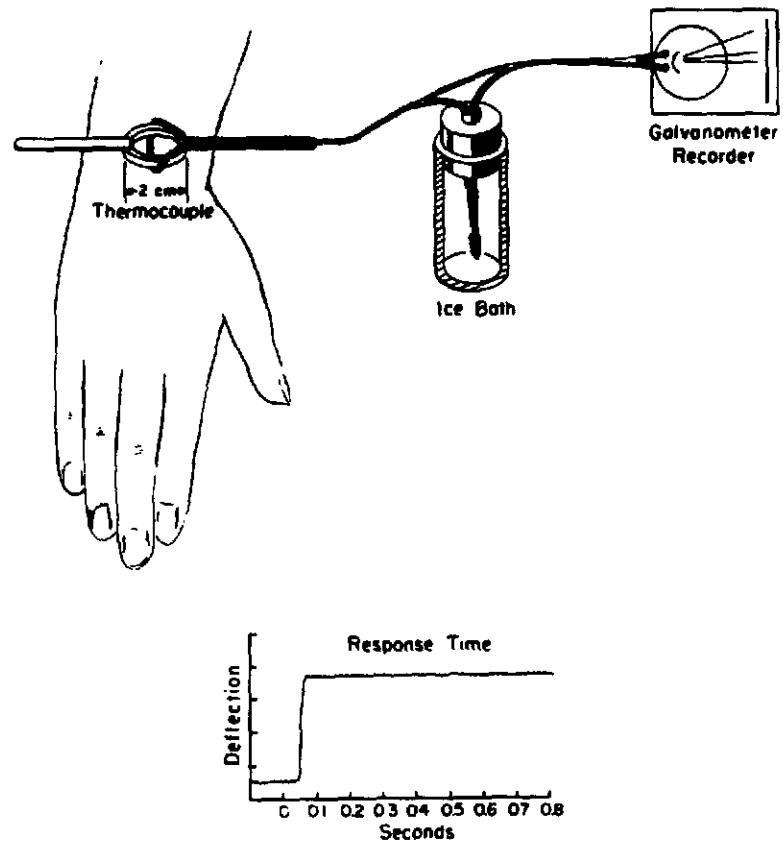
will depend upon the relative reaction velocities k_d and k_r as functions of temperature since k_n is not assumed to vary appreciably over this range. For the sudden increase in skin temperature to 40°C, the relative concentration of P* reaches a value of more than 20% in two peaks as shown at the top of Figure 9; the first peak occurs about 1 second after immersion and the second peak 3 seconds later. This long and double peaked transient would be in keeping with the variable delays in pain report noted in Figure 3. Also, it had long been noted in experiments with thermal radiation using short exposures on the forehead that there occasionally occurred a first pain preceding the more clear cut pain used to denote threshold. A sudden increase in temperature to 38°C also develops a concentration of P* above the pain threshold as shown. Skin temperature elevations to levels lower than 36°C have relatively little affect on P*. It was found impractical to plot the re-immersion experiment on the same time scale as that shown in Figure 9, but calculation shows that immersion of the skin at 40°C for 10 seconds followed by an immersion at 34° for 10 seconds and a re-immersion at 40°C is not associated with a transient increase in P*.

In view of the paucity of data on the actual changes in the nerve membrane associated with transient temperature elevations, it did not seem useful to push the calculations further. However, as the presence of the transient pain at tissue temperature within the 37-41° C range forced a considerable modification of the

hypothesis relating pain to tissue damage by heat as originally proposed, the treatment given above to modify the hypothesis seemed justified. It may be worth noting the three compartment system as suggested above may be arranged also to account for the strength-duration curve for pain threshold, using the thermal radiation stimulus, and for the psychophysical curve of pain intensity as a function of temperature above 45°C.

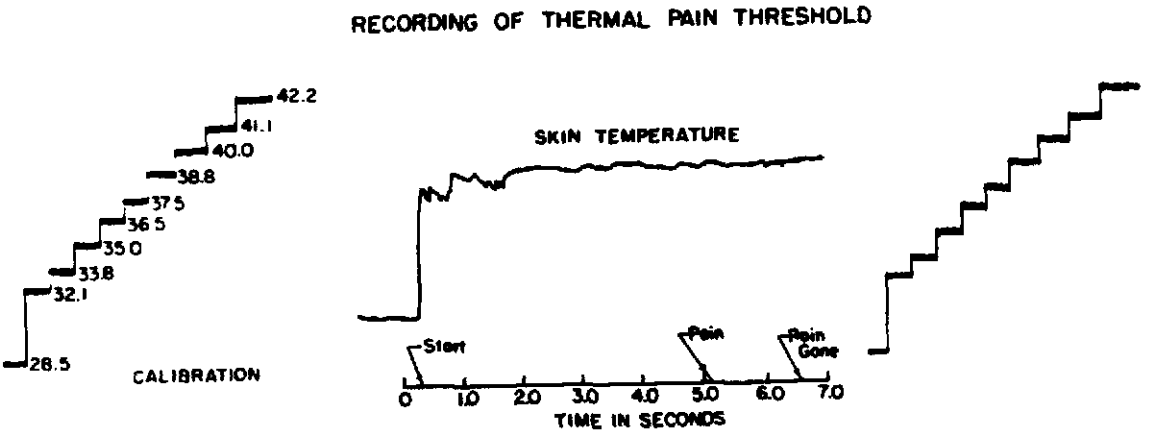
The conceptual hypothesis outlined above is thus quantitatively compatible with a variety of observations on thermally induced pain. We have shown that, using plausible temperature coefficients for rates of protein destruction and repair, it can make predictions of pain in time and in intensity and that it makes compatible seemingly conflicting observations on thermal pain. Thus, it meets the requirement of a working hypothesis which could usefully be taken into account in further studie of pain, and perhaps of other thermal sensations.

Figure 1



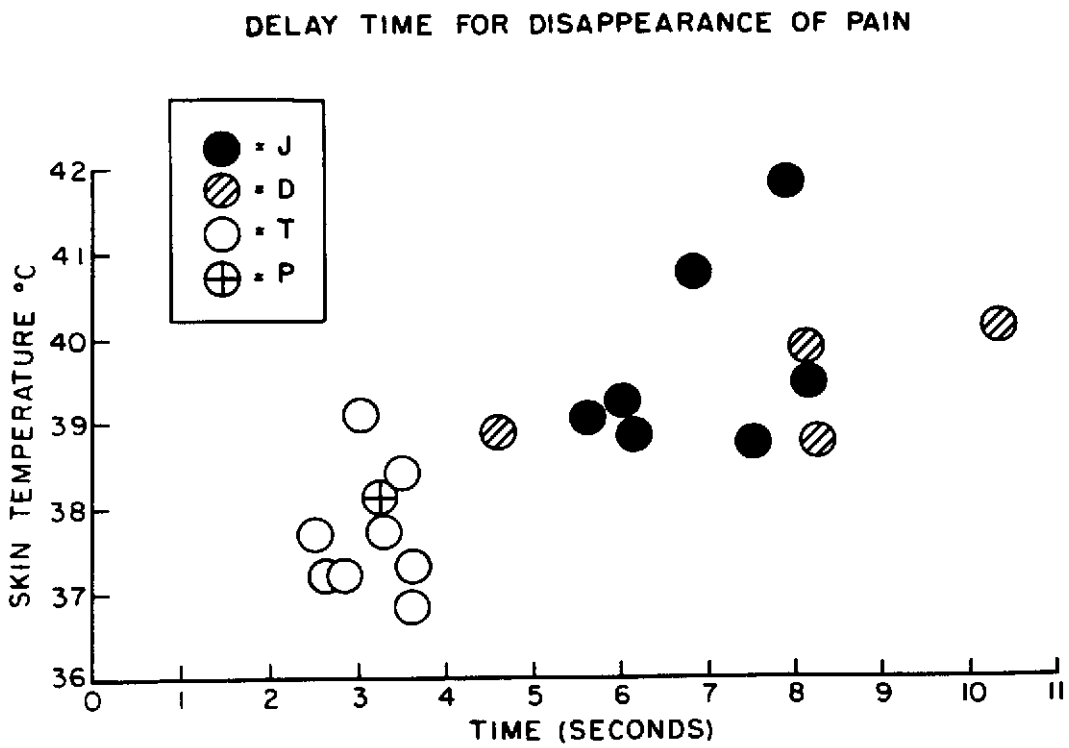
Top: Schematic arrangement for recording skin temperature changes during water immersion. Bottom: Response time of thermocouple - galvanometer system tested by thrusting unattached thermocouple into a water bath.

Figure 2



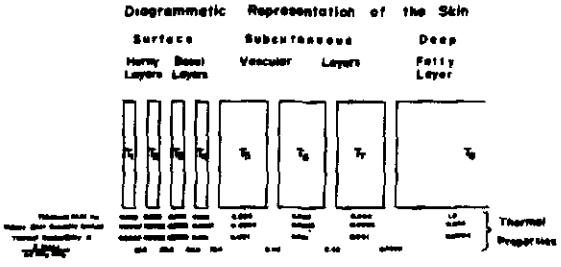
Experimental record of skin temperature showing times of onset and disappearance of pain. Calibration of thermocouple recording system at beginning and end of observation.

Figure 3



Summary of sensory reports following immersion at different bath temperatures.

Figure 4



Division of skin layers used for calculating subcutaneous temperatures and corresponding thermal properties.

Figure 5
Subcutaneous temperatures calculated for times of 0.5 and 2 seconds following immersion in 40°C water bath.

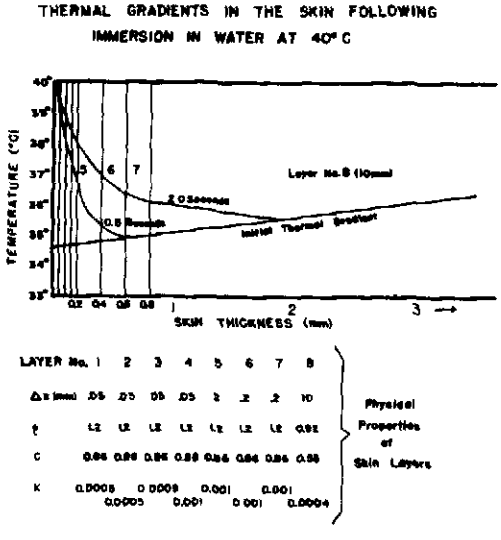
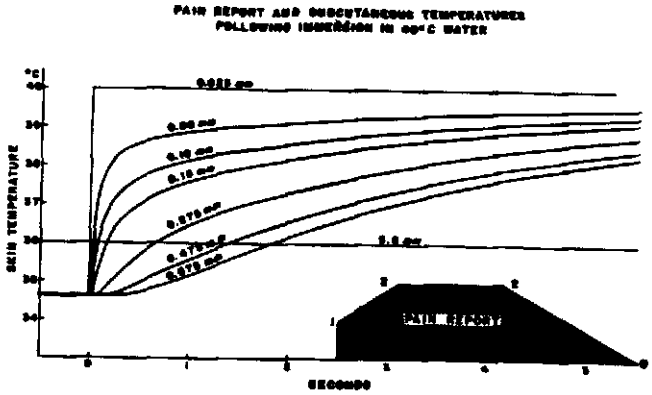


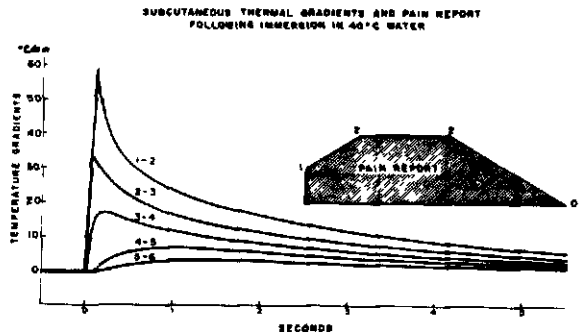
Figure 5

Figure 6



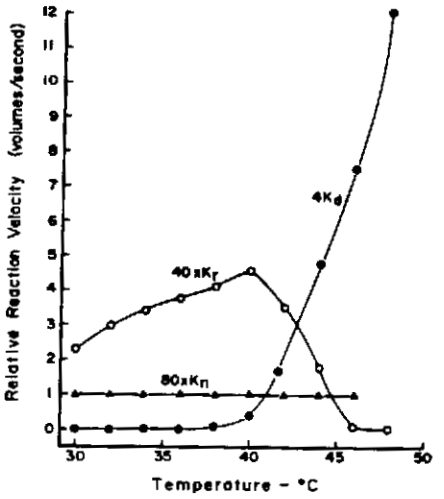
Measured (closed triangles) and calculated (solid lines) values of skin temperature and calculated temperatures for layers 2, 3, 4, 5, 6, and 7 for a 5-1/2 second immersion in 40°C water.

Figure 7



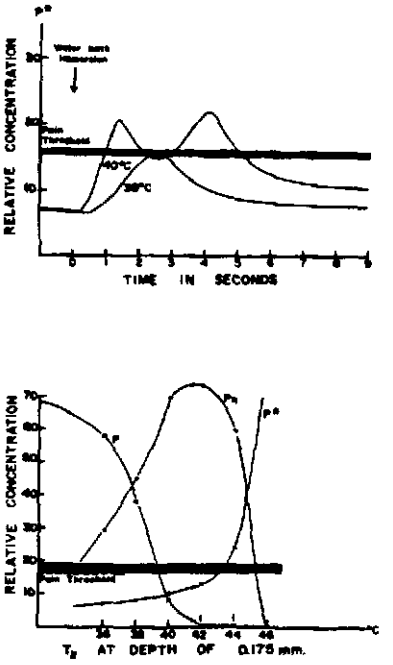
Thermal gradients (°C/mm) calculated between adjacent layers of skin as a function of time during a 5-1/2 second immersion in water at 40°C.

Figure 8



Hypothetical reaction velocities of protein inactivation kd and repair reactions, kd and kn as affected by temperature.

Figure 9



Top: Relative concentrations of P* following sudden increase in skin temperature by immersion in a water bath at 38° and 40°C. Pain threshold is the steady state concentration of P* required to excite pain ending.

Bottom: Relative concentration of P, P*, and P_n in steady state at different tissue temperatures "Pain Threshold" refers to the relative concentration of P* for steady non-adapting pain.

FIGURES

Figure 1 Top: Schematic arrangement for recording skin temperature changes during water immersion. Bottom: Response time of thermocouple - galvanometer system tested by thrusting unattached thermocouple into a water bath.

Figure 2 Experimental record of skin temperature showing times of onset and disappearance of pain. Calibration of thermocouple recording system at beginning and end of observation.

Figure 3 Summary of sensory reports following immersion at different bath temperatures.

Figure 4 Division of skin layers used for calculating subcutaneous temperature and corresponding thermal properties.

Figure 5 Subcutaneous temperatures calculated for times of 0.5 and 2 seconds following immersion in 40°C water bath.

Figure 6 Measured (closed triangles) and calculated (solid lines) values of skin temperature and calculated temperatures for layers 2, 3, 4, 5, 6 and 7 for a 5-1/2 second immersion in 40°C water.

Figure 7 Thermal gradients (°C/mm) calculated between adjacent layers of skin as a function of time during a 5-1/2 second immersion in water at 40°C.

Figure 8 Hypothetical reaction velocities of protein inactivation, kd and repair reactions, kd and kn, as affected by temperature.

Figure 9 Top: Relative concentrations of P* following sudden increase in skin temperature by immersion in a water bath at 38° and 40°C. Pain threshold is the steady state concentration of P* required to excite pain ending.

Figure 9 (continued)

Bottom: Relative concentrations of P, P*, and P_n in steady state at different tissue temperatures. "Pain threshold" refers to the relative concentration of P* for steady non-adapting pain.

REFERENCES

1. Buettner, K. "Surface Temperature, Pain and Heat Conductivity Experiments with Radiant Heat", J. Applied Physiol. 3, 703-713, 1951.
2. Burger, F.J. and F. A. Fuhrman, "Evidence of Injury to Tissue after Hyperthermia". Am. Journal Physiol. 206; 1062-1064, 1964 .
3. Chick, H. and C. J. Martin, "On the Heat Coagulation of Protein", Jour. Physiol. 40, 404-424, 1910 .
4. Crozier, W.J., "On the Critical Thermal Increment for Locomotion of a Diplopod, "Jour. Gen. Physiol. 7, 123-136, 1924.
5. Dodt, E., "Schmerzimpulse bee Temperaturereizen", Acta Physiol. Scand. 31, 83-96, 1954.
6. Dodt, E. and Y. Zotterman, "Mode of Action of Warm Receptors", Acta Physiol. Scand. 26, 345-357, 1952 .
7. Glasttone, S., Laidler, K.J. and Eyring, H., "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., 1941 .
8. Greene, L.C. and J. D. Hardy, "Adaptation to Thermal Pain in the Skin", Jour. Applied Physiol. 17, 693-696, 1962.
9. Hardy, J.D., "Thresholds of Pain and Reflex Contraction as Related to Noxious Stimulation", Jour. Applied Physiol. 5, 725-739, 1953.
10. Hardy, J.D., H. G. Wolff, and H. Goodell, "Pain Sensations and Reactions", 1952, Williams and Wilkins Co., Baltimore, pp. 87-122.
11. Henriques, F. C., Jr., "Studies in Thermal Injuy V.: The Predictability and the Significance of Thermally Induced Rate Processes Leading to Irreversible Epidermal Injury", Am. J. Pathology, 23, 489-502, 1947

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12. Henriques, F.D., Jr. and A. R. Moritz, "Studies in Thermal Injury I: The Conduction of Heat To and Through the Skin and the Temperatures Therein. A Theoretical and Experimental Study," Am. J. Pathology, 23, 531-549, 1947.

13. Hensel, H., "The Time Factor in Thermoreception or Excitation", Acta Physiol. Scand. 29, 109-116, 1953.

14. Hensel, H. and K. A. Bowman, "Afferent Impulses in Cutaneous Sensory Nerves in Human Subjects", J. Neurophysiol. 23, 564-578, 1960.

15. Lele, P.P., G. Weddell, and C. M. Williams, "Relationship between Heat Transfer, Skin Temperature, and Cutaneous Sensibility", J. Physiol. 126, 204-234, 1954.

16. Nafe, J. P. and K. S. Wagoner, "The Experiences of Warmth, Cold and Heat", Jour. of Psychology 3, 421-439, 1936.

17. Neisser, U., "Temperature Thresholds for Cutaneous Pain", J. Applied Physiol. 14, 368-372, 1959.

18. McAdams, W. H., "Heat Transmission", McGraw Hill Co., New York 1942, pg. 42.

19. Sand, A., "The Function of the Ampullae of Lorenzini with Some Observations on the Effect of Temperature on Sensory-Rhythms:, Proc. Royal Soc. B. 125, 524-553, 1938.

20. Sizer, I.W., "Effects of Temperature on Enzyme Kinetics, "Advances in Enzymology, vol. 3; pp. 35-62, 1943

REFERENCES

21. Stoll, A.M. and J. D. Hardy, "Thermocouples as Skin Thermometers", Jour. Applied Physiol. 2, 531-543, 1950.

22. Stone, L.J. and K. M. Dallenback, "Adaptation to the Pain of Radiant Heat", Am. J. Psychol. 66, 229-242, 1934.

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Measurements of skin temperature were made during the sudden immersion of the skin of human subjects in water baths at 36-41°C and related to the reports of pain elicited during the first few seconds of immersion. Within 0.5 seconds, the skin temperature rose to bath temperature and remained at this level during the 10-15 seconds of immersion, pain was reported at 37-41°C occurring 1-5 seconds after the start of the immersion and adapting in 2-6 seconds. Calculation of the subcutaneous temperature and thermal gradients indicate maximal thermal gradients in superficial skin layers during the first 0.1 - 0.2 seconds of immersion (60°C/mm) decreasing rapidly during the first 5 seconds to 6°C/mm. Analysis of the transient pain indicated that it could be considered as the more sensitive "phasic" response of the pain ending of which the "static" unadapting response occurs at skin temperatures of 43-46°C. Several alternative explanations including subcutaneous thermal gradients, vasomotor reactions, and thermo-chemical changes in the nerve membrane were considered as possible explanations. The last most likely possibility requires a second order kinetic system with highly temperature sensitive reaction velocities to account for both the phasic and static components of the pain.

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