

# THE TEMPERATURE SENSES IN THE FROG'S SKIN

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ONE FIGURE

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## INTRODUCTION

Is a temperature sense present in the frog's skin? Can it be isolated from the chemical and tactile senses which have already been shown to be there? Is it separable into the elementary senses of heat and cold as in the human skin? If so, what is the limitation and the nature of the responses to heat and cold?

It is in common knowledge that frogs go down into the mud in the winter and come up in the spring and an expectation of March and April that they will be heard on the warm nights. Their thermic susceptibility has long been known, both in nature and in the laboratory. Brown-Séquard ('47) alluded to the possible effect of temperature upon his reflex frogs which lived longest during the months from June to September, and Kunde

('60) recorded that reflex frogs dosed with strychnia were seized with spasms in a warm room, but became quiet when placed upon ice. A series of investigations followed these early suggestions, actual experiments on the direct and indirect effects of temperature upon the central nervous system (Tarchanow, '71; Archangelsky, '73; Freusberg, '75; Wundt, '76), the sensory nerve endings (Heinzmann, '72; Foster, '73; Rosenthal, '75; Sedgwick, '82), and the general behavior of the frog under stimulation by heat and cold. Recent workers upon its responses to light, electricity, sound, chemicals, and temperature have either shown something of its thermic sensitiveness (Korányi, '92; Parker, '03; Torelle, '03; Yerkes, '06; Pearse, '10) or have suggested the presence of a temperature sense in the skin. But its exclusive presence there, its existence as a separate sense, and the nature of its responses have not been adequately shown. It was with the hope of doing this and of answering the questions already suggested that the present study was undertaken.

The problem was suggested to me by Prof. G. H. Parker, and it gives me pleasure to express my appreciation of his friendly criticism and constant help.

#### HISTORICAL

Temperature studies upon the frog have covered a wide range of attack. Information regarding the effect of temperature upon the skin has come into the literature indirectly, usually in connection with special studies of a system of organs or the behavior of the whole organism. In the hope of showing these different aspects with greater clearness, I have discussed them by topics rather than in historical sequence.

*Frogs respond to variations in temperature by visible motor reactions.* This was established experimentally by Kunde ('60), Cayrade ('64), Goltz ('69), Tarchanow ('71, '72), Archangelsky ('73), Rosenthal ('75), Freusberg ('75), and Wundt ('76). The means of stimulation were partial or complete immersion in warm or cold water, dipping in warm or cool dilute acid, and ice packs and hot sand baths. From treatment of these kinds one group of workers (Kunde, '60; Richardson, '67; Weir-Mitchell, '67;

Rosenthal, '75) maintained that cold caused a depression in reflex excitability, except in the case of ice packs, which increased it (Richardson, '67; Weir-Mitchell, '67; Wundt, '67), and another group were of the opinion that heat properly applied also caused excess excitability (Cayrade, '64; Goltz, '69; Tarchanow, '71, '72; Freusberg, '75).

*When cold or heat are applied very gradually to a frog the reactions decrease in extent and vigor.* There has been a good deal of disagreement in the literature, regarding reactions to gradually applied stimuli. The question was opened by Goltz ('69), who immersed normal and reflex frogs in water of gradually increasing temperatures. When slowly stimulated up to 30°C., the normal frog became violent, but the reflex frog remained inert. Goltz's main purpose had been to show the difference between the two conditions in the animal, and he immediately declared the lassitude of the reflex frog due to its brainless state. By the same method, Tarchanow ('71, '72) secured similar results on normal frogs. The next year Heinzmann ('72) continued similar experiments from the point of view that the sensory nerves might be affected by a stimulus increasing in intensity so slowly that destruction of the nerve would result before a reaction could occur. Normal and reflex frogs were heated with the expected results to both of them, and these were explained as due to the very gradual succession of the stimuli. In 1875 Fratscher repeated these experiments with identical results. The quiet normal frogs of Heinzmann and Fratscher were thus pitted against the violent normal frogs of Goltz and Tarchanow, but the main conclusion seems to have been that no reaction would result if stimulation were applied with sufficient gradualness.

Foster ('73) had previously questioned Goltz's statement that brainless frogs would give no reaction to stimuli to which normal frogs reacted so vigorously. He immersed reflex frogs 'locally and totally' and obtained very different results in the two cases. When large areas of the body were immersed there was no response, but when only the toes were dipped, no matter how gradually the heat was increased, they were always withdrawn at about 35°C. This peculiar result was explained by Foster

on the ground that immersion of the larger areas heated the blood, which in turn warmed the spinal cord and reduced its irritability. With the stimulation of the small area no such general warming could take place, and hence the normal irritability of the cord was retained and the vigorous response followed.

Certain puzzling phases immediately presented themselves, and Sedgwick ('82) repeated the experiments upon which this explanation was based. He suspended the reflex frogs in the manner described by Foster and at once discovered that in this upright position the heart was practically empty and could not possibly circulate the blood as stated by Foster.

From this tangle of statements the best evidence seems to show that the reflex frog will respond to heat at certain degrees, no matter how gradually it is applied, but that the extent and vigor of these responses may be reduced by the graded application of the stimulus.

*Effect of heating and cooling the spinal cord.* With the object of stimulating the spinal cord, Archangelsky ('73) suspended reflex frogs with their trunks surrounded by a jacket of hot air which produced a rise of excitability, and by a jacket of slowly heated air which produced no change. Tarchanow ('71, '72) stimulated the cord directly with an ice pack, thereby causing a depression of reflexes.

*Frogs can withstand a temperature as low as 6°C.* The body temperature of frogs was recorded by Milne-Edwards ('68) and by Rogers and Lewis in 1916. Knauthe ('91) and Müller-Erzback ('91) froze frogs in water and exposed them to temperatures of  $-4^{\circ}\text{C}.$  to  $-6^{\circ}\text{C}.$  for several hours. Maurel et Lagriffe ('00) studied the effect of temperatures from  $-4^{\circ}\text{C}.$  to  $41^{\circ}\text{C}.$  and maintained that a frog may survive a temperature of  $0^{\circ}\text{C}.$  or even  $-3^{\circ}\text{C}.$

*Respiration is quickened under stimulation by heat.* When Babák ('13) warmed the skin of a reflex frog, the speed of respiratory movements was quickened, and when he cooled it, correspondingly the speed was decreased.

*Frogs which are immersed in cold water will swim downward and will remain at the bottom a greater percentage of the time as the cold*

*is increased.* Frogs which Torelle ('03) placed in water of 10°C. immediately swam down and remained below, usually with legs stiffly outstretched. In 1918 Brooks corroborated this by a series of detailed observations on frogs which were placed in water of decreasing temperature. As the water was cooled the frogs remained for a shorter and shorter time at the surface till at 5°C. they settled to the bottom and remained there.

*The skin is sensitive to variations in the temperature of air, of water, and of acid solutions.* Comparing the sensibility of the skin and afferent nerves by treatment with warm and cool acid solutions, Tarchanow ('72) was the first to point out that the thermal end-organs must be in the skin and that the quicker response to the warmer acid solutions was due to an increased irritability in the nerve endings, agreeing in this with Archangel-sky ('73) who had used the same stimulus. This sensitiveness of the skin has been mentioned or investigated by recent workers in connection with studies of other sense organs, and Korányi ('93) and Pearse ('10) found the frog's integument responsive to both light and heat. Pearse secured responses from frogs whose feet were dipped in water at 40°C. and 45°C. and Reese ('06) obtained similar results from *Cryptobranchus*, while Parker ('03) and Yerkes ('06) both alluded to the susceptibility of the skin to changes of temperature.

*Warmth produces a positive and cold a negative response to light.* When frogs were placed in warm air or water they moved toward the light, but in the same media at 8°C. they moved away from the light (Torelle, '03). L. J. Cole ('07) secured similar results when he placed a frog in a dark box between a large and a small illuminated area at the opposite ends. When the frog was cooled to 6°C. and 10°C. it would move toward the smaller area, but when warmed it would immediately move toward the larger one. In order to compare the relative effects of light and heat, Pearse ('10) arranged a series of tubes, with a measured heat radiation upon the sides of a totally dark box. Another box contained a light whose heat output was one-half that of the pipes. Eyeless toads placed in these boxes proved to be almost totally indifferent to the heat, but were strongly phototropic, showing that light

and heat were unlike in effect and that the photoreceptors were much more easily excited than the receptors for heat. A slight difference in light, on the other hand, made no impression on frogs with which Torelle ('03) worked. They swam up and down in the jars regardless of adjustments of light and dark.

*Frogs are stereotropic in temperatures between 10°C. and 4°C.* When Torelle placed frogs in water cooled to 10°C. or below, they flattened their bodies against the bottom or crept under rocks placed on the floor of the aquarium.

*Effect of temperature on responses to electricity.* An electric current which produced tetanic movements on a warm frog showed retardation when the frog was cooled (Kunde, '60).

#### METHODS

The experiments which follow were performed upon green frogs (*Rana clamitans*) and leopard frogs (*Rana pipiens*) in a laboratory the temperature of which varied between 18°C. and 23°C. The work was done between October and January upon animals which were kept in a basement tank and brought into the laboratory at least two days before they were used for experimentation.

For all except one experiment, the front part of the head was removed by a single transverse cut made just in front of the eardrums. Through the lower jaw thus left intact a loop of silk was drawn, and by this the frog was suspended, thus avoiding the irritation caused by the repeated use of a metal hook.

Frogs were hung from an extension bar, attached to a standard; the bar could be easily raised and lowered. They were completely immersed in a bath of water at the beginning of each experiment, and at certain intervals during treatment in order to keep the temperature normal, the skin moist, and free from particles of dust. At the beginning of an experiment the temperature of the room, bath water and frog were taken, the latter being secured by putting a thermometer through the mouth and down into the stomach. Records of these temperatures have been given with each experiment recorded in this paper. The experimental frogs were easily kept in good condition and usually lived from four to five weeks.

The surface of the foot was the only area treated. Sometimes one foot was stimulated and the other kept as a check, but in most cases there was an alternate stimulation of the normal feet, or of the normal and the treated foot. Baths of water and applications of stimuli were given at definite intervals which were kept uniform through each experiment. Preliminary experiments were made with each different kind of stimulation in order to find out what reaction might be expected.

At each test a definite allowance of time was given, and if the reaction did not occur within that period the stimulus was regarded as producing no reaction and recorded as  $\infty$ . In the tables the period just described is termed the reaction allowance. The interval which actually elapsed between the application of the stimulus and the reaction was taken in seconds with a stop-watch and recorded with the description of the response. No periods less than half a second were recorded. Intervals which separated stimulations sufficiently to prevent exhaustion were also selected by experiment. These have been designated the stimulation intervals.

During the experiments the normal feet were kept in 'bath water' unless actually undergoing stimulation. In experiments made under cocaine treatment the foot was always returned to the cocaine solution after it had been immersed in the stimulant. In the preliminary part of this work a good deal of trouble was experienced by the washing out of the cocaine, so this procedure was found necessary. A solution of 1 per cent cocaine was the only anaesthetic used.

#### OBSERVATIONS

##### *Responses to heat*

The first experiments of this series were made in order to determine whether the frog's foot would regularly react to heat, and if so to what degree of heat. A typical heat response was also looked for, a position or movement which should recur in many different individuals. Both feet of the experimental frog were kept in normal condition. In the first experiments considered

(table 1) only the right foot was stimulated and the left served as a check. The right foot was first immersed in water at 30°C. and at intervals of two minutes after that in baths increasing each time by 1°C. from 30°C. to 50°C.: no responses occurred below 39°C., and in some instances none below 43°C. As the heat was increased the vigor of the response was also increased

TABLE 1

*Reaction intervals in seconds of frogs' right feet subjected to temperatures ranging at one degree intervals from 30° to 50°C. No reactions (indicated by ∞) were obtained at temperatures of 38° or lower, hence this part of the table is condensed. Feet normal. Reaction allowance, 30 seconds. Stimulation interval, 2 minutes*

Number of individual.....	2	4	6	7	13	8	9	10	11	11	3
Number of experiment .....	1	1	1	1	1	1A	1A	1	3	4	1
Temperature of room.....	24°	19°	21°	24°	22°	21°	25°	23°	21°	24°	19°
Temperature of bath water.....	21°	17°	18°	21°	18°	20°	20°	19°	18°	21°	17°
Temperature of frog.....	22°	18°	19°	22°	19°	20°	23°	20°	19°	21°	18°
Stimulated by water 30°C.											
to 38°C.....	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞
39°C.....	∞	∞	∞	∞	∞	∞	∞	∞	∞	10	∞
40°C.....	∞	24	∞	∞	∞	∞	∞	15	17	5	12
41°C.....	9	14	∞	22	∞	29	∞	22	8	6	17
42°C.....	9	11	∞	∞	∞	14	∞	15	10	4	13
43°C.....	6	10	12	15	5	8	21	3	7	3	12
44°C.....	4	6	9	12	5	7	20	4	6	2	8
45°C.....	3	4	5	9	7	8	12	5	4	4	4
46°C.....	2	3	4	8	3	5	13	5	4	2	7
47°C.....	2	4	3	5	3	6	8	4	3	2	4
48°C.....	2	3	2	3	2	2	6	4	3	2	3
49°C.....	2	1	2	4	1	3	5	3	2	2	3
50°C.....	2	1	1	2	1	3	5	2	3	2	2

and the reaction interval became shorter and shorter. The heat response was a vigorous upward jerk of the foot, so uniform that usually no attempt to describe it has been made except by the word 'jerk' and the statement of the length of the reaction interval, i.e., the time between the application of the stimulus and the reaction itself.

The next step was to discover whether there would be different results if the heat was applied with differences of temperature

greater than 1°. It will be remembered that some of the early workers (Goltz, '69; Tarchanow, '71, '72) maintained that if heat were increased slowly enough a frog might be subjected to an extreme degree without making responding resistance. No such results were secured in this investigation even when the heat was increased very slowly. A frog's foot was placed in a beaker of water at 2°C., and a stream of warm water allowed to flow into this which brought it up to 45°C. with almost imperceptible slowness. Although care was taken to prevent the foot from

TABLE 2

*Responses in seconds to heat increasing by 5°C. at each stage of stimulation. Feet normal. Reaction allowance, 30 seconds. Stimulation interval, 2 minutes for nos. 8, 9, 10, and 5 minutes for no. 11. ∞ = no reaction*

Number of individual.....	8	8	8	8	10	10	9	9	11	11	11	11
Number of experiment.....	6A	6A	6A	6A	3	3	1B	1B	5	5	5a	5a
Foot stimulated.....	R	L	R	L	R	L	R	L	R	L	R	L
Temperature of room.....	24°	24°	24°	24°	20°	20°	25°	25°	22°	22°	25°	25°
Temperature of bath water....	20°	20°	21°	21°	18°	18°	20°	20°	22°	22°	20°	20°
Temperature of frog.....	23°	23°	22°	22°	18°	18°	23°	23°	22°	22°	23°	23°
Stimulated by water at												
30°C.....	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞
35°C.....	∞	∞	∞	15	∞	∞	∞	∞	25	29	11	12
40°C.....	7	22	4	5	19	14	12	21	7	12	4	4
45°C.....	3	3	1	2	6	18	5	12	6	8	1	1
50°C.....	2	2	1	1	3	4	4	3				

being affected by this stream, the feet were invariably lifted before the heat had reached 45°C.

Variations in the stimulation time and in the heat increments were also tried (table 2). Heat was increased by 5°C. at each stimulation and the right and left feet of the frog were dipped at one-, two-, and five-minute intervals. Of nine frogs used only four reacted at a degree lower than that to which the frogs responded which were subjected to 1°C. increases. The results showed the tendency toward the later reaction with gradually applied stimuli, but also suggested that individual idiosyncrasies

were a factor and that certain frogs were especially sensitive to heat. This opinion was further justified by a series of tests repeated over and over on particular individuals. The right foot of each of these frogs was stimulated by hot water whose temperature ranged from 25°C. to 50°C. and at intervals of 5°, the experiment being repeated seven times consecutively (table 3). This was done to find out whether each frog would preserve its individual eccentricities toward heat in successive tests and

TABLE 3  
*Responses in seconds of two frogs to hot water whose temperature was increased by 5°C. at each stimulation. Each series repeated consecutively seven times. Feet normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes. ∞ = no reaction*

Number of individual.....	11							11							14						
Number of experiment.....	1							2							1						
Foot stimulated.....	R							R							R						
Temperature of room.....	22°							22°							20°						
Temperature of bath water.....	20°							20°							18°						
Temperature of frog.....	22°							22°							21°						
Stimulated by water at																					
25°C.....	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞
30°C.....	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞
35°C.....	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	6	7	4	∞	4	3	12
40°C.....	∞	9	10	5	5	7	5	5	22	∞	19	6	15	∞	3	5	4	3	4	2	3
45°C.....	3	3	3	3	3	3	2	3	6	2	4	3	3	5	2	3	2	3	2	1	2
50°C.....	2	1	1	1	2	1	1	2	3	3	2	2	2	2	1	2	1	2	2	1	1

on different days. Two records selected (no. 11, 1; no. 11, 2) were of a frog of average susceptibility and the tests 1 and 2 were made on different days, and the third (no. 14, 1) was chosen because it showed unusual sensitiveness. Both types were fairly common and the sensitiveness or dullness persisted with repeated stimulations in nearly all the animals tested. These results indicated that the speed of applying stimuli is not the only factor present in quick or slow responses.

The heat responses were characteristically sharp upward jerks of the leg. As it was pulled upward the toes were held together

with the web folded between them, a very different position from that later observed in the response to cold. Responses increased in vigor with the increase in heat and were often followed by jerking and twisting of the whole body.

The interval between stimulation and response to heat (actual reaction time) was relatively long. Frogs which responded unfailingly at 40°C. might not do so for twenty seconds after contact with the stimulant. This also contrasted with the short reaction time of the cold response and indicated that the receptors for warmth in the frog's skin lie deep, and those for cold are superficial as in the human skin. The reaction time showed a fairly regular decrease with the increase of the heat. This was observed in all experiments with increasing temperatures. Thus far the experiments with heat show a characteristic response which occurred with clock-like regularity; with increasing heat the first responses were between 35°C. and 43°C. and the reaction time was comparatively long, but decreased as the heat increased. The range of the first type of response was only slightly modified when the stimulus was very gradually applied.

Is there a temperature sense in the skin? With regular responses thus secured in the foot, the next problem was to show that these responses were not due to stimulus of the muscles, and to prove the exclusive presence of the temperature sense in the skin.

The skin was desensitized by three different methods. A series of tests paralleling the preceding was made upon frogs with one foot normal and the other treated with a solution of 1 per cent cocaine, upon frogs with one foot normal and the other with the sciatic nerve cut, and upon frogs with one leg normal and the skin removed to the ankle from the other.

The cocaine method of desensitizing the skin has been used by L. W. Cole ('10), Crozier ('16), and others. By varying the length of treatment with the 1 per cent solution of cocaine, different senses in the skin can be affected or even eliminated. In experiments which involved only the heat sense the foot was cocained for thirty minutes immediately preceding the experiment. It was also immersed in the cocaine solution during the

intervals between stimulations. Cocained and normal feet were alternately stimulated by water increasing in heat by  $1^{\circ}$  at a time from  $30^{\circ}\text{C.}$  to  $50^{\circ}\text{C.}$  (table 4). The first reaction of the cocained foot was at  $45^{\circ}\text{C.}$  after a reaction interval of 24 seconds, but the first response of the normal one was at  $40^{\circ}\text{C.}$  after a reaction interval of 5 seconds. The average degree of first re-

TABLE 4

*Responses in seconds to heat increasing by  $1^{\circ}\text{C.}$  at each stimulation. Right foot cocained 30 minutes. Left foot normal. Reaction allowance 30 seconds.*

*Stimulation time, 2 minutes.  $\infty$  = no response*

Number of individual.....	11	11	48	48	47	47	46	46
Number of experiment.....	8	8	7	7	8	8	5	5
Foot stimulated.....	R	L	R	L	R	L	R	L
Temperature of room.....	$16^{\circ}$	$16^{\circ}$	$19^{\circ}$	$19^{\circ}$	$22^{\circ}$	$22^{\circ}$	$21^{\circ}$	$22^{\circ}$
Temperature of bath water.....	$15^{\circ}$	$15^{\circ}$	$17^{\circ}$	$17^{\circ}$	$19^{\circ}$	$19^{\circ}$	$18^{\circ}$	$18^{\circ}$
Temperature of frog.....	$15^{\circ}$	$15^{\circ}$	$18^{\circ}$	$18^{\circ}$	$20^{\circ}$	$20^{\circ}$	$19^{\circ}$	$19^{\circ}$
Stimulated by water at $38^{\circ}\text{C.}$ .....	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$
$39^{\circ}\text{C.}$ .....	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$	$\infty$
$40^{\circ}\text{C.}$ .....	$\infty$	5	$\infty$	4	$\infty$	5	$\infty$	4
$41^{\circ}\text{C.}$ .....	$\infty$	5	$\infty$	6	$\infty$	6	$\infty$	3
$42^{\circ}\text{C.}$ .....	$\infty$	4	$\infty$	5	$\infty$	4	$\infty$	4
$43^{\circ}\text{C.}$ .....	$\infty$	1	$\infty$	4	$\infty$	3	$\infty$	5
$44^{\circ}\text{C.}$ .....	$\infty$	4	$\infty$	3	$\infty$	4	$\infty$	4
$45^{\circ}\text{C.}$ .....	24	2	$\infty$	4	20	3	18	3
$46^{\circ}\text{C.}$ .....	24	2	25	3	21	3	17	2
$47^{\circ}\text{C.}$ .....	24	1	23	2	18	2	20	2
$48^{\circ}\text{C.}$ .....	28	1	22	2	24	1	22	2
$49^{\circ}\text{C.}$ .....	26	1	25	1	24	1	24	1
$50^{\circ}\text{C.}$ .....	30	1	28	1	25	1	25	1

sponse for the cocained foot was  $45^{\circ}\text{C.}$  after an average reaction time of 21.75 seconds. For the normal foot the average first response was at  $40^{\circ}\text{C.}$  after an average reaction interval of 4.5 seconds (table 4).

Following this twelve more frogs were tested by similar methods, but with the stimulations beginning at  $15^{\circ}\text{C.}$  and continuing by  $5^{\circ}\text{C.}$  intervals to  $45^{\circ}\text{C.}$  (table 5). Since no responses were secured, the lower degrees  $15^{\circ}\text{C.}$  to  $30^{\circ}\text{C.}$  have not been

included in the table. At 40°C. the normal foot of each frog responded after an average reaction time of 10 seconds. At 45°C. the cocained foot responded after an average reaction interval of 16.75 seconds against an average of 8 seconds for the normal foot. Such results showed that when the skin was anaesthetized the temperature sense was affected—a clear proof that the heat receptor is located only in the skin.

In order to test this question further, however, the cutaneous nerve supply was cut off by severing the sciatic nerve at the thigh. In four frogs thus treated the injured and the normal leg were

TABLE 5

*Responses in seconds to heat increasing by 5°C. at each stimulation in a range of 15°C. to 45°C. Right foot cocained 30 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes. ∞ = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.				REACTIONS	
		Room	Bath water	Frog	Stimulus	Right foot	Left foot
25	2	16°	16°	15°	35°	∞	∞
25	2	16°	16°	15°	40	∞	10
25	2	16°	16°	15°	45	25	10
27	2	19°	15°	16°	35	∞	∞
27	2	19°	15°	16°	40	∞	5
27	2	19°	15°	16°	45	10	2
30	1	18°	15°	16°	35	∞	∞
30	1	18°	15°	16°	40	∞	15
30	1	18°	15°	16°	45	15	12

alternately stimulated by the same degree of heat, but not the slightest response was obtained from the denervated leg, showing that the response was in no sense purely muscular. From three other frogs the skin of one foot was removed. The feet of one were alternately immersed in water of increasing temperature, those of the other two were dipped in water at 45°C. Again there was no reaction except in the normal foot whose responses were uniform with those already secured. Hence the skin of the frog's foot is essential to these reactions. The results of these experiments show that the temperature sense is at once affected by cocaine, and that it is entirely eliminated by destruction of the cutaneous nerve supply or by removal of the skin.

*Independence of the responses to touch and heat.* In the human skin responses to tactile stimulations occur quickly, but pain and heat have a longer reaction interval. In the frog reaction times to touch and heat were first compared in the normal skin as a step toward the separation of the two senses and finally from those of cold, pain, and the chemical senses.

In these comparative experiments the heat stimulation was conducted as before. In applying the tactile stimulus a simple

TABLE 6  
*Responses in seconds to heat at 40°C. and to heat increasing by 5°C. at each stimulation in a range of 25°C. to 50°C. Left foot with skin removed. Right foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes. ∞ = no response*

Number of individual.....	8	8	8	8	9	9		13	13
Number of experiment.....	4	4	5	5	4	4		4	4
Foot stimulated.....	R	L	R	L	R	L		R	L
Temperature of room.....	22°	22°	22°	22°	24°	24°		21°	21°
Temperature of bath water.....	18°	18°	18°	18°	18°	18°		18°	18°
Temperature of frog.....	17°	17°	17°	17°	18°	18°		19°	19°
Stimulated by water at 40°C.....	3	∞	10	∞	8	∞	25°C.	∞	∞
40°C.....	6	∞	12	∞	8	∞	30°	∞	∞
40°C.....	3	∞	8	∞	8	∞	35°	20	∞
40°C.....	3	∞	6	∞	5	∞	40°	10	∞
40°C.....	3	∞	15	∞	6	∞	45°	4	∞
40°C.....	3	∞	10	∞	6	∞	50°	3	∞
40°C.....	3	∞	7	∞	7	∞			
40°C.....	3	∞	5	∞	5	∞			

device was employed by which the stimulus could be kept uniform and brought to bear on a particular area (fig. 1). This device consisted of a single iron standard from the top of which the frog was suspended by an adjustable arm. Below this were two adjustable arms also provided with clamps. Into the lower and longer one a small board was fastened by a flexible wire so that the board could be easily turned in any direction. This board served to support the frog's foot very lightly and when flooded with water there was probably little tactile stimulation from it.

The upper clamp held a large tube through which common steel shot could be easily rolled. This tube was adjustable in the clamp so that its angle of inclination could be easily changed. When a tactile stimulation was to be made the frog was suspended

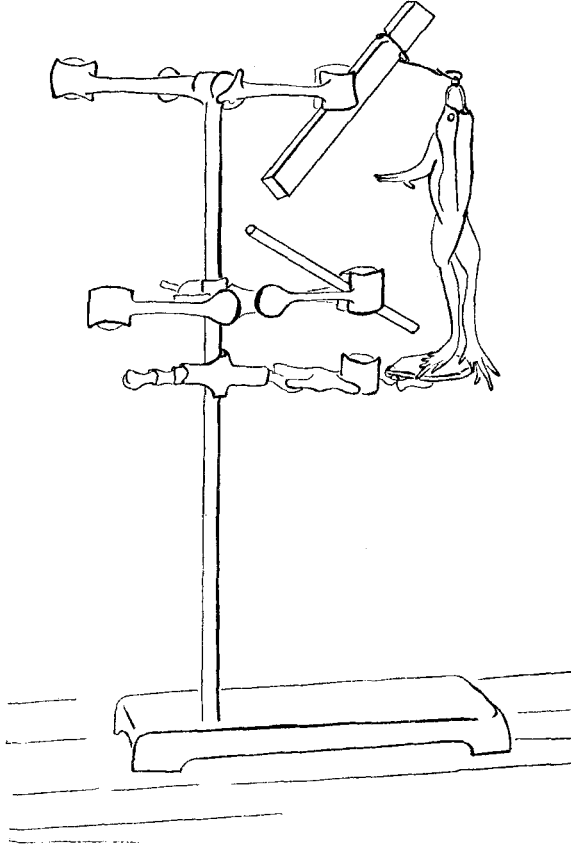


Fig. 1 Apparatus for suspending frog and for tactile stimulation by falling shot.

with its foot resting very lightly on the support, and with the glass tube trained upon the spot to be stimulated, so that when the shot was rolled through the tube it would strike the proper surface of the foot. The distance between the surface of the foot and the end of the tube, the inclination of the tube at  $45^{\circ}$ ,

and the size of the shot were kept constant, but the length of the tube was varied according to the strength of the stimulus desired. The length of the tube and one or two words descriptive of the reaction have been recorded in each table. The results secured

TABLE 7

*Responses in seconds to touch and heat. Shot rolled through tube striking upon the surface of the foot. Feet normal. Reaction allowance 30 seconds. Stimulation time, 2 minutes.  $\infty$  = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.			STIMULATED BY		REACTIONS	
		Room	Bath water	Frog	Shot; length of tube used for shot	Water	Right foot	Left foot
					<i>inches</i>			
12	6	20°	19°	20°	2		1 lifted	1 lifted
12	6	20°	19°	20°	2		1 lifted	1 lifted
12	6	20°	19°	20°	2		1 lifted	1 lifted
12	6	20°	19°	20°		45°C.	6 jerked	3 jerked
13	5	16°	16°	15°	2		1 lifted	1 lifted
13	5	16°	16°	15°	2		1 lifted	$\infty$
13	5	16°	16°	15°	2		1 lifted	$\infty$
13	5	16°	16°	15°		45°C.	6 lifted	3 lifted
15	3	19°	11°	11°	2		1 jerked	1 jerked
15	3	19°	11°	11°	2		1 jerked	1 jerked
15	3	19°	11°	11°	2		$\infty$	1 lifted
15	3	19°	11°	11°		45°C.	6 jerked	5 jerked
16	1	23°	19°	18°	2		$\infty$	$\infty$
16	1	23°	19°	18°	2		1 jerked	1 jerked
16	1	23°	19°	18°	2		1 lifted	1 jerked
16	1	23°	19°	18°	2		1 lifted	1 lifted
16	1	23°	19°	18°		45°C.	14 lifted	9 lifted
13	3	22°	19°	18°	2		1 jerked	1 lifted
13	3	22°	19°	18°	2		1 jerked	1 lifted
13	3	22°	19°	18°	2		$\infty$	$\infty$
13	3	22°	19°	18°		45°C.	5 jerked	5 jerked

by stimulating the normal feet by the stroke of the shot, also by heat, are shown in table 7. Twelve experiments were made and the records of five were selected because these showed the early exhaustion of the tactile sense and the persistent presence of the heat response, the shorter reaction time and gentler response to touch contrasted against the abrupt reaction of heat following a long reaction time.

If the receptors for heat lie deeper than those for touch and cold, as is true in the human skin, it seemed that it would be possible to affect them sooner by a solution of cocaine and thus demonstrate the independence of the two senses. This was attempted by stimulating a normal and a cocained foot with the falling shot and with heat. Some difficulty was experienced in

TABLE 8

*Responses in seconds to touch and heat. Touch stimulation shot, rolled through tube striking upon surface of the foot. Right foot cocained 10 to 20 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes. ∞ = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.			STIMULATED BY WATER	STIMULATED BY SHOT; LENGTH OF TUBE	COCAINE TREATMENT	REACTIONS	
		Room	Bath water	Frog				Right foot	Left foot
						<i>inches</i>	<i>minutes</i>		
13	4	22°	18°	19°		2	20	∞	1 lifted
13	4	22°	18°	19°		2	20	∞	1 jerked
13	4	22°	18°	19°	45°C.		20	11 jerked	1 jerked
15	4	18°	19°	17°		2	20	∞	1 lifted
15	4	18°	19°	17°		2	20	∞	1 lifted
15	4	18°	19°	17°	45°C.		20	8 jerked	4 lifted
15	7	19°	19°	18°		5	15	∞	1 lifted
15	7	19°	19°	18°		5	15	∞	1 lifted
15	7	19°	19°	18°	45°C.		15	8 jerked	4 lifted
13	6	16°	16°	16°		2	10	∞	1 lifted
13	6	16°	16°	16°		2	10	∞	1 con- tracted
13	6	16°	16°	16°	45°C.		10	8 jerked	4 jerked
12	7	23°	19°	20°		2	20	∞	1 lifted
12	7	23°	19°	20°		2	20	∞	1 lifted
12	7	23°	19°	20°	45°C.		20	4 jerked	2 jerked

keeping the skin from being exhausted by tactile stimulation before the cocaine treatment was finished. Frogs which struggled had to be repeatedly adjusted, and this could hardly be accomplished without touching the frog somewhere. It was necessary, therefore, to perform a good many experiments and to select quiet frogs. Fifteen such frogs were used, and from their records the five in table 8 were selected. In these fifteen frogs

the normal foot never failed to react to touch except in two cases, clearly caused by a faulty technique. The cocained foot failed to react to the strike of the falling shot at any time (table 8), but both the normal and cocained foot reacted regularly and with the same retardation which had been affected by the cocaine in previous experiments (tables 4, 5). The conclusion is that independent heat receptors are present in the foot of the frog and that a complete separation of the touch and the heat sense had been affected.

TABLE 9

*Responses in seconds to pain and heat. Pain stimulation by pricking outer side of fifth toe. Feet normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.			STIMULATED BY NEEDLE	STIMULATED BY WATER	REACTIONS	
		Room	Bath water	Frog			Right foot	Left foot
10	10	20°	19°	18°	Pricking		1 jerked	1 jerked
10	10	20°	19°	18°	Pricking		1 jerked	1 jerked
10	10	20°	19°	18°		40°C.	6 jerked	7 jerked
50	1	21°	20°	19°	Pricking		1 jerked	1 jerked
50	1	21°	20°	19°	Pricking		1 jerked	1 jerked
50	1	21°	20°	19°		40°C.	6 jerked	7 jerked

*Independence of the responses to pain and heat.* The method used in this separation was dipping the foot in water at 40°C. and pricking the skin on the outer side of the fifth toe. No degree of heat higher than 40°C. was used, because of the possibility that the higher degrees of heat might be painful and the two responses thus confused. Pricking the web between the third and fourth toes was first tried, the particular web being quite arbitrarily selected for stimulation. In some cases the foot would react to pricking done anywhere on this web, in other cases it would react to it in certain areas only, and in still other cases the foot would fail or almost fail to give any reaction at all to pricking anywhere on this web. Other webs were afterward tried with much the same result. When the skin on the

side of the toe was pricked, the normal foot never failed to react, though care was taken that the needle did not pass through underlying tissue.

TABLE 10

*Responses in seconds to pain and heat. Pain stimulations by pricking the side of the fifth toe. Right foot cocained 50 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes. ∞ = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.			STIMULATED BY NEEDLE	STIMULATED BY WATER	REACTIONS	
		Room	Bath water	Frog			Right foot	Left foot
47	1	18°	16°	16°	Pricking	40°C.	∞	1 jerked
47	1	18°	16°	16°			1 jerked	1 jerked
47	1	18°	16°	16°	Pricking	40°	∞	8 jerked
47	1	18°	16°	16°			1 jerked	1 jerked
47	1	18°	16°	16°	Pricking	40°	∞	15 jerked
48	1	21°	18°	16°		40°	∞	6 jerked
48	1	21°	18°	16°	Pricking		1 jerked	1 jerked
48	1	21°	18°	16°		40°	∞	5 jerked
48	1	21°	18°	16°	Pricking		1 jerked	1 jerked
48	1	21°	18°	16°		40°	∞	10 jerked
49	1	21°	17°	16°	Pricking	40°	∞	9 jerked
49	1	21°	17°	16°			1 jerked	1 jerked
49	1	21°	17°	16°	Pricking	40°	28 jerked	12 jerked
49	1	21°	17°	16°			1 jerked	1 jerked
49	1	21°	17°	16°	Pricking	40°	29 lifted	12 jumped
47	2	20°	17°	16°		40°	∞	7 jerked
47	2	20°	17°	16°	Pricking		1 jerked	1 jerked
47	2	20°	17°	16°		40°	25 lifted	6 jerked
47	2	20°	17°	16°	Pricking		1 jerked	1 jerked
47	2	20°	17°	16°		40°	∞	15 jumped
47	3	16°	12°	12°	Pricking	40°	∞	12 jerked
47	3	16°	12°	12°			1 lifted	1 lifted
47	3	16°	12°	12°	Pricking	40°	25 lifted	5 lifted
47	3	16°	12°	12°			1 lifted	1 lifted
47	3	16°	12°	12°	Pricking	40°	∞	25 lifted

This comparison of pain and heat was first tried upon the normal feet with a regular, sudden, and vigorous response to the pricking and the characteristic jerk and extended reaction time after heat stimulation. The response to heat was eliminated or greatly retarded by the fifty minutes' treatment with cocaine

given to the right foot, but the normal left foot showed either a normal reaction time or one slightly longer than usual. Pricking produced immediate and vigorous response in both the cocained and normal foot even after a long period.

*Independence of the responses to acid solution and heat.* The existence of the common chemical sense in the frog's skin was clearly shown by L. W. Cole ('10) and by Crozier ('16). Cole treated the skin with cocaine and found it sensitive to ammonium chloride after response to pain had wholly disappeared, and by

TABLE 11

*Responses in seconds to acid solution and to heat. Acid stimulation by 0.5 per cent HCl solution. Right foot cocained 45 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation interval, 2 minutes. ∞ = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.			STIMULATED BY WATER	STIMULATED BY HCl	REACTIONS	
		Room	Bath water	Frog			Right foot	Left foot
						<i>per cent</i>		
47	4	16°	12°	12°	40°		∞	25 lifted
47	4	16°	12°	12°		0.5	1 lifted	1 lifted
48	2	19°	16°	18°	40°		∞	12 lifted
48	2	19°	16°	18°		0.5		1 jerked
49	2	19°	15°	13°	40°		∞	25 lifted
49	2	19°	15°	13°		0.5	1 lifted	1 lifted
47	5	19°	15°	14°	40°		∞	5 lifted
47	5	19°	15°	14°		0.5	1 lifted	1 jerked
46	6	19°	15°	13°	40°		∞	7 lifted
46	6	19°	15°	13°		0.5	7 lifted	3 lifted

similar treatment Crozier secured responses to N/20 formic acid after response to pinching had altogether ceased.

In the separation of chemical and temperature senses the previous method of comparison was repeated. Water at 40°C. and a solution of one-half of 1 per cent hydrochloric acid were used as stimulants. After forty-five minutes of the cocaine treatment there was no response to heat by the right foot, although its reaction to the acid solution was as prompt and vigorous as in the left. These facts are quite in accord with those observed by Crozier.

*Responses to cold*

Normal frogs respond promptly and definitely when they are placed in water sufficiently cold. Such behavior was observed by both Torelle ('03) and Brooks ('18), who recorded that frogs immersed in water of 5°C. swam downward, attempted to regain the surface a couple of times, but finally sank to the bottom and remained there.

In studying the effect of cold, experiments such as had been made by Torelle and by Brooks were repeated in the reflex frogs so as to compare their behavior with that of normal frogs.

The temperature of the frog was taken before and after the experiment. Four gallons of water at a temperature of 4°C. to 5°C. was kept in an aquarium jar in the laboratory and frogs were placed in this water for periods of two minutes. Short records of observations were made by fifteen-second intervals (table 12). The first responses were uniformly either a spasmodic jump or a 'set' of the whole body like the 'freeze' of a rabbit, followed by a series of jumps, then a gradual sinking in which the body fell rigidly backward or forward and finally rested stiffly on the bottom of the jar with the legs extended. These responses were generally very uniform, but when there were individual peculiarities they were persistent. For example, frog no. 16 was tested on different days, but its immediate response to cold was always a sudden 'set' in which the legs were tightly flexed to the body, the toes extended, with the web tightly stretched and the soles out. In this position the frog would sink to the bottom without a contraction; it did not, however, lose its rigidity even when it was turned from side to side with a rod.

A few similar observations were made upon normal frogs to compare their behavior with reflex frogs. The two records presented in table 13 are typical of a half-dozen. Normal frogs floated longer at the surface than reflex frogs did, but in other respects the behavior of the two kinds was essentially the same.

Alternate dipping of the feet in water at 2°C. resulted in much the same response as did total immersion. The characteristic

TABLE 12

*Responses of reflex frogs to total immersion in water at 4°C. to 5°C. Entire skin normal. Observation period of 2 minutes divided into 8 sections of 15 seconds each*

NUM- BER OF INDI- VIDUAL	NUMBER OF EXPERI- MENT	TEMPERATURES IN DEGREES C.			15 SECONDS	15 SECONDS	15 SECONDS	15 SECONDS	15 SECONDS	15 SECONDS
		Cold bath	Frog							
			Before bath	After bath						
10	10	4°	17°	9°	Body sets	Rigid	At bottom	Bottom	Rigid	Bottom
13	10	4	17	9	Rigor jump	Jumps	Sinks	Rigid	Rigid	Rigid
15	6	5	16	11	Swims up	Swims up	Sinks	Prone	Rigid	Rigid
15	10	4	17	10	Swims up	Sinks	Sinks	Sinks	Prone	Prone
16	6	4	16	9	Body sets	Body sets	Sinks	Bottom	Bottom	Bottom
17	2	4	17	9	Swims	Rigid	Extended	Jumps	Swims	Rigid
16	6	4	15	9	Body sets	Kicking	Sinks	Bottom	Prone	Prone
17	2	4	15	12	Swims up	Swims up	Swims up	Sinks	Prone	Prone

TABLE 13

*Responses of normal frogs to total immersion in water 4°C. to 5°C. Entire skin normal. Observation period of 2 minutes divided into 8 sections of 15 seconds each*

NUMBER OF INDIVIDUAL EXPERIMENT	NUMBER OF NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.			15 SECONDS	15 SECONDS	15 SECONDS	15 SECONDS	15 SECONDS	15 SECONDS	15 SECONDS
		Cold bath	Frog								
			Before bath	After bath							
18	1	4°	18°	10°	Swims	Floats	Floats	Floats	Sinks	Bottom	Bottom
19	1	4	18	9	Swims	Floats	Floats	Floats	Floats	Sinks	Bottom

one was the same extension of the toes, and stretching of the web accompanied in some frogs by a spasmodic upward jerk of the leg as soon as the tip (table 14) of the toe touched the water (no. 23, exp. 2, table 15). Two frogs had persistently long reaction periods of two and eight seconds, but a very short interval was typical of the cold response.

After a dependable cold response had been shown to occur, further steps were necessary to prove that the cold receptors

TABLE 14

*Response of foot to water at 2°C. Feet normal. Reaction allowance, 30 seconds.  
Stimulation period, 2 minutes*

NUM- BER OF INDI- VIDUAL	NUM- BER OF EXPERI- MENT	TEMPERATURES IN DEGREES C.			STIMU- LATED BY WATER	REACTIONS	
		Room	Bath water	Frog		Right foot	Left foot
15	13	25°	14°	13°	2°C.	Stretched, rigid, kicked	Stretched, web spread, kicked
15	13	25°	14°	13°	2°C.	Rigid, stretched, flexed	Rigid, stretched, flexed
17	5	25°	14°	14°	2°C.	Stretched, raised	Stretched, web spread
17	5	25°	14°	14°	2°C.	Stretched, raised	Stretched, web spread
20	2	18°	20°	18°	2°C.	Jerked as toe touched	Jerked as toe touched
20	2	18°	20°	18°	2°C.	Stretched, rigid, web spread	Stretched, web spread

were in the skin. Their location in its superficial layers had already been suggested by the short reaction interval. In experiments recorded in table 15 responses to cold were invariably eliminated by a half-hour cocaine treatment, whereas this only retarded the heat reaction. The records of the alternate stimulation of the normal foot and the cocained foot by water at 2°C. showed a clock-like regularity in the response of the normal foot.

At what temperature does the skin become responsive? A definite beginning point (39° to 43°) has already been established for the heat response, but investigations of the cold limitations have not yet been mentioned.

By previous tests the skin had been unresponsive to 25°C. Tests with decreasing cold were begun at this degree therefore and the temperature was decreased with intervals of 5° down to 1°C. The right feet were desensitized in order to further demonstrate the possibility of eliminating the cold sense from the skin. The right and left foot were alternately stimulated but, except

TABLE 15

*Responses of foot to water at 2°C. Right foot cocained 30 minutes. Reaction allowance, 30 seconds. Stimulation time, 2 minutes*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.			STIMULATED BY WATER	REACTIONS	
		Room	Bath water	Frog		Right foot	Left foot
13	15	17°	16°	14°	2°C.	None	Toe stretched, web spread
13	15	17°	16°	14°	2°C.	None	Stretched, body twisted
13	15	17°	16°	14°	2°C.	None	Stretched feebly, fatigued
15	15	15°	15°	14°	2°C.	None	Stretched, web spread
15	15	15°	15°	14°	2°C.	None	Leg stretched
15	15	15°	15°	14°	2°C.	None	Leg stretched, fatigue
17	7	19°	17°	14°	2°C.	None	Leg stretched, web spread
17	7	19°	17°	14°	2°C.	None	Leg stretched, web spread
17	7	19°	17°	14°	2°C.	None	Leg jerked
17	7	19°	17°	14°	2°C.	None	Leg stretched, web spread
17	7	19°	17°	14°	2°C.	None	Leg stretched, jerked
17	7	19°	17°	14°	2°C.	None	Leg stretched, fatigue
23	2	20°	18°	16°	2°C.	None	Jerked, web spread
23	2	20°	18°	16°	2°C.	None	Jerked, web spread
23	2	20°	18°	16°	2°C.	None	Jerked, jumped

in one case, there was no response till the temperature was reduced to 10°C. (table 16).

Between 35°C. to 43°C. and 10°C. to 15°C. there was a range of temperature to which the frog's skin did not respond. This range was limited on one side by the threshold stimulus for heat and on the other by that for cold. The cold as well as the heat receptors have been proved to lie in the skin. The response to cold has its own peculiar characteristics, also a shorter reaction time and an earlier exhaustion point.

*Independence of the responses of cold and heat.* Cold and heat sensation are separable by exhaustion of the cold receptors and by treatment with cocaine. The right foot was each time immersed for twenty minutes in the solution of cocaine and the right and left feet were then stimulated by water at 2°C. and

TABLE 16

*Responses in seconds of the foot to decreasing temperatures. Right foot cocained 30 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes. ∞ = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.				REACTIONS	
		Room	Bath water	Frog	Stimulus water	Right foot	Left foot
28	2	20°	15°	15°	15°	∞	∞
28	2	20°	15°	15°	10°	∞	1 toes extended, web spread
28	2	20°	15°	15°	5°	∞	1 web spread feebly
28	2	20°	15°	15°	1°	∞	1 toes extended, web spread
31	1	22°	15°	15°	15°	∞	∞
31	1	22°	15°	15°	10°	∞	∞
31	1	22°	15°	15°	5°	∞	1 jerked as toe touched water
31	1	22°	15°	15°	1°	∞	1 jerked as toe touched water
17	11	20°	15°	16°	15°	∞	∞
17	11	20°	15°	16°	10°	∞	11 foot lifted, web spread
17	11	20°	15°	16°	5°	∞	18 foot lifted, web spread
17	11	20°	15°	16°	1°	∞	∞
17	12	21°	25°	14°	15°	∞	∞
17	12	21°	25°	14°	10°	∞	1 toes extended, web spread
17	12	21°	25°	14°	5°	∞	1 jerked
17	12	21°	25°	14°	1°	∞	1 toes extended, web spread

45°C. (table 17). Responses to cold entirely ceased; those to heat remained vigorous with a lengthened reaction time.

*Independence of responses to touch and cold.* The case with which the sense of touch disappears from the skin has already been mentioned in connection with touch and heat.

In that case responses to touch failed after the foot was immersed in cocaine 10, 15, 20 and 25 minutes, but reaction to water at 45°C. remained retarded but vigorous. In the same

manner as with touch and cold, touch was very easily eliminated, and by reducing the cocaine treatment the cold sense could be preserved (table 18) in a very effective condition.

*Independence of responses to acid and cold.* The sensation of cold was separated from the chemical sense in the skins of twelve different frogs. After thirty minutes of treatment with cocaine on the right foot the feet were alternately stimulated as usual.

TABLE 17

*Responses of the foot to heat and cold. Right foot cocained 20 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes.  $\infty$  = no response*

NUM- BER OF INDI- VIDUAL	NUM- BER OF EXPERI- MENT	TEMPERATURES IN DEGREES C.				REACTIONS	
		Room	Bath water	Frog	Stimu- lus water	Right foot	Left foot
5	15	15°	15°	14°	2°	$\infty$	1 toes stretched
5	15	15°	15°	14°	45°	13 jerked	13 jerked
17	6	19°	19°	19°	2°	$\infty$	1 toes stretched, webspread
17	6	19°	19°	19°	40°	25 jerked	5 jerked
17	6	19°	19°	19°	45°	10 jerked	6 jerked
17	6	19°	19°	19°	2°	$\infty$	1 stretched, web spread
17	6	19°	19°	19°	40°	20 jerked	17 jerked
21	5	19°	16°	16°	2°	$\infty$	1 web spread
21	5	19°	16°	16°	40°	17 jerked	10 quiver, jerked
24	6	20°	16°	16°	2°	$\infty$	3 stretched
24	6	20°	16°	16°	40°	9 jerked	6 jerked

The cold response was easily obliterated by the cocaine, but the acid caused a sharp upward jerk at long or irregular reaction intervals. This response itself seemed to differ little from that of the normal foot.

*Independence of responses to pain and cold.* Pain responses were produced by pricking the skin of the frog on the side of the fifth toe—a procedure that produced more regular results than when the web was similarly stimulated. Care was always taken that the needle did not go into the deeper tissues. The foot was

TABLE 18

*Responses in seconds of the foot to touch and cold. Right foot cocained 10 to 25 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes.  $\infty$  = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.				LENGTH OF TUBE USED FOR SHOT	CO-CAINE TREATMENT	REACTIONS	
		Room	Bath water	Frog	Stimulus water			Right foot	Left foot
						<i>inches</i>	<i>minutes</i>		
23	18	22°	18°	17°		5	25	$\infty$	1 lifted
23	18	22°	18°	17°	2°		25	6 lifted	2 lifted
38	20	21°	16°	17°		5	15	$\infty$	1 lifted
38	20	21°	16°	17°		5	15	$\infty$	1 lifted
38	20	21°	16°	17°	2°		15	1 lifted	10 lifted
39	32	21°	17°	18°		5	25	$\infty$	1 jerked
39	32	21°	17°	18°	2°		25	1 stretched	1 jerked
40	1	20°	17°	19°		5	15	$\infty$	1 lifted
40	1	20°	17°	19°	2°		15	1 shiver	1 lifted
41	1	22°	18°	19°		5	10	$\infty$	1 jiggle
41	1	22°	18°	19°	2°		10	1 web spread	1 jerked

TABLE 19

*Responses in seconds of the foot to acid and to cold. Right foot cocained 30 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes.  $\infty$  = no response*

NUMBER OF INDIVIDUAL	NUMBER OF EXPERIMENT	TEMPERATURES IN DEGREES C.				ACID STIMULUS HCl	REACTION	
		Room	Bath water	Frog	Stimulus water		Right foot	Left foot
						<i>per cent</i>		
24	7	23°	16°	18°	2°		$\infty$	3 body twisted
24	7	23°	16°	18°		0.5	15 jerked	2 jerked
24	8	18°	15°	16°	2°		$\infty$	1 toes extended
24	8	18°	15°	16°		0.5	1 jerked	1 jerked
28	3	19°	16°	16°	2°		$\infty$	1 web spread
28	3	19°	16°	16°		0.5	20 jerked	1 jerked
32	1	22°	15°	15°	2°		$\infty$	1 web spread
32	1	22°	15°	15°		0.5	15 jerked	3 jerked

supported when being pricked and by putting the needle only through the side surface it was thought that this was avoided. Twelve frogs were stimulated by pricking and by water at 2°C. Reaction to cold was eliminated by cocaine treatment in as short a time as ten minutes. No effect upon the pain response or its reaction could be discerned.

TABLE 20

*Responses in seconds of the foot to pain and cold. Right foot cocained 10 to 30 minutes. Left foot normal. Reaction allowance, 30 seconds. Stimulation time, 2 minutes.  $\infty$  = no response*

NUM- BER OF INDI- VIDUAL	NUM- BER OF EXPERI- MENT	TEMPERATURES IN DEGREES C.				STIMULATED BY NEEDLE	COCAINE TREAT- MENT	REACTIONS	
		Room	Bath water	Frog	Stim- ulus water			Right foot	Left foot
23	1	20°	17°	18°	2°		minutes 30	$\infty$	1 spread, lifted
23	1	20°	17°	18°		Pricking	30	1 jerked	1 jerked
43	1	21°	15°	14°	2°		20	$\infty$	1 web spread
43	1	21°	15°	14°		Pricking	20	1 jerked	1 jerked
23	2	20°	18°	17°	2°		20	$\infty$	1 web spread
23	2	20°	18°	17°		Pricking	20	1 jerked	1 jerked
44	1	21°	15°	16°	2°		20	$\infty$	$\infty$
44	1	21°	15°	16°		Pricking	20	1 jerked	1 jerked
23	1	20°	15°	16°	2°		15	$\infty$	1 web spread
23	1	20°	15°	16°		Pricking	15	1 jerked	1 jerked
17	1	21°	16°	17°	2°		10	$\infty$	1 stretched
17	1	21°	16°	17°		Pricking	10	1 jerked	1 jerked

## DISCUSSION AND RESULTS

A temperature sense is easily demonstrable in the frog's skin. There is a response to heat characteristic in form and reaction time. The lowest degrees of heat which stimulate the skin lie somewhere between 35°C. and 41°C. If the skin be stimulated by water increasing in heat by 5°C. at each stimulation from 30°C. to 50°C., the first response may be expected at 35°C. If the same series is followed except that the heat be increased by 1°, the first response may occur at 40°C. or 41°C. The skin responds to the higher degrees of heat with great regularity. As the heat is increased from 35°C. to 50°C. the reaction time decreases with more or less regularity from long intervals (25, 15, 12 seconds) to short ones (2, 1 second).

It will be remembered that some of the early workers maintained (Goltz, '69; Heinzmann, '72) that if reflex frogs were stimulated gradually enough with increasing heat they could be subjected to considerable warming without resistance. My investigations show only a slight agreement with them which has been mentioned. It has not been possible to stimulate the foot with increasing heat beyond 43°C. without response, even when the frog's foot was suspended in a beaker of water at 20°C. and the heat almost imperceptibly increased by an inflow of warm water. The long reaction time of the heat response agrees with v. Frey's contention that the heat receptors are in the deeper and the cold receptors in the more superficial layers of the skin.

It has been possible to isolate the temperature sense from the tactile and chemical. This has been done by treatments with 1 per cent solution of cocaine. Crozier ('16) used this method in separating the tactile and chemical senses, and by it Cole ('10) eliminated response to pain, but preserved sensitiveness to taste. The separation of temperature from other senses gave the following results. Response to acid (0.5 per cent hydrochloric) persisted beyond response to heat. Pain persisted beyond heat; heat and cold beyond touch. With the thermal and chemical stimulations care has been taken to immerse the same amount of surface. It has of course not been possible to make any

equivalence between chemical and tactile stimuli or degrees of heat and cold. Granting this necessary inaccuracy, 45°C. heat and 2°C. cold were selected as sufficient extremes to be set against each other.

There is a definite cold sense present in the frog's skin. When the foot was immersed in water of decreasing temperatures, the first responses occurred at 10°C. Contrasted with that of heat, the interval between stimulation and response was an inconsiderable period and could not be accurately taken with a stop-watch. The responses to cold were of two types, a sudden rigidity of the muscles of the leg, with a spreading of the toes and web, or an upward jerk instantly following the contact of the toes with the water. The latter action was less frequent and usually occurred after stimulation by severe cold or in unusually sensitive frogs. Such responses differed from heat responses only in the length of the reaction time.

The sense of cold may be wholly eliminated by cutting the nerve, removing the skin, or by cocaine treatment. It can be shown to be independent of heat, and the tactile and chemical senses by the same treatment. In such comparisons sensation to cold disappears, acid remains; cold disappears and heat and pain remain, but cold remains while touch is eliminated.

The frog's skin is indifferent to temperature of 10°C. or 15°C. to 35°C., whether the stimulation be made by gradual increases or whether it be given suddenly at one selected degree.

#### SUMMARY

The skin of the frog contains well-defined receptors for heat and for cold. The heat receptors have a comparatively long reaction time. The heat receptors are stimulated by 39°C. to 43°C.; the cold receptors at 10°C. This response is immediate and becomes more vigorous as the cold is increased. The typical response to heat is an upward jerk of the leg. The typical response for cold is a rigidity and tenseness of the muscles, but there may be an upward jerk similar to that of the heat response. Responses to heat and cold may be separated from each other and from the tactile and chemical senses.

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