ment—if only an agreement to embrace the whole purpose of those statutes establishing the federal biomedical research institutes. That purpose, and the ultimate policy goal, has been, and will no doubt continue to be, to reduce and, if possible, to eliminate disease.

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Physiological Role of Pleasure

A stimulus can feel pleasant or unpleasant depending upon its usefulness as determined by internal signals.

Michel Cabanac

The living organism receives information about the external environment and its changes through a certain number of sensitivities. Receptors or free nerve endings act as detectors, then this information is carried to the central nervous system. In man, some of these sensitivities give rise to a phenomenon of consciousness that is referred to as sensation. A sensation will therefore bring information about the existence of a certain variable of the "milieu exterieur" and/or its modifications. The physical and chemical characteristics of the stimulus are translated into nervous impulses describing the nature and the magnitude of this stimulus, and the sensation is related to the stimulus according to a certain law. Sensation is therefore descriptive. These analytical characteristics are not the only aspect of the conscious phenomenon created by a stimulus. Sensation can also have an affective aspect, described in common language as pleasure or displeasure.

The importance of this sensory pleasure-displeasure has been pointed out as an important determinant of behavior (*1*), since in itself this factor can explain many behaviors just by the attractiveness or the repulsiveness of the stimulus. For example, sucrose stimulus is rewarding at all concentrations and quinine is aversive at all concentrations. Indeed, pleasure or displeasure could be stimulus bound. We shall now see that, in fact, this is not quite true; the pleasure or displeasure of a sensation is not stimulus bound but depends on internal signals, at least with regard to thermal, olfactive, and gustative stimulations.

Thermal Sensations

In thermal sensation, the peripheral signal is skin temperature. Skin detec-

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tors will translate this thermal signal into a nervous message describing local temperature and its changes: the skin will therefore feel "cold," "warm," or "hot" according to the stimulus. The dependence of pleasure-displeasure, given by cutaneous thermal stimulus, upon internal temperature has been obtained repeatedly in many subjects (*2–4*).

One example is given in Fig. 1. A range of peripheral stimuli was offered to a subject by dipping his hand in a container. The subject was asked to give a quantitative response describing the pleasure-displeasure of the sensation on a five-point continuous scale. Meanwhile, internal temperature was monitored and mean skin temperature was assumed to be close to the temperature of a water bath in which the subject was immersed for the duration of the experiment. The responses were different according to the thermal states of the subject. When the internal temperature was high, the cold or cool stimuli were pleasant, and warm or hot stimuli were unpleasant. The temperatures did not evoke pain; that is, they were between the pain thresholds at 15° and 45°C. The opposite response was given by the subject while he was hypothermic. To him, cold was unpleasant and warm was pleasant. Therefore, a given nonpainful thermal stimulus could be perceived as pleasant or unpleasant according to the internal thermal state of the subject. He was, however, quite able to discriminate temperatures.

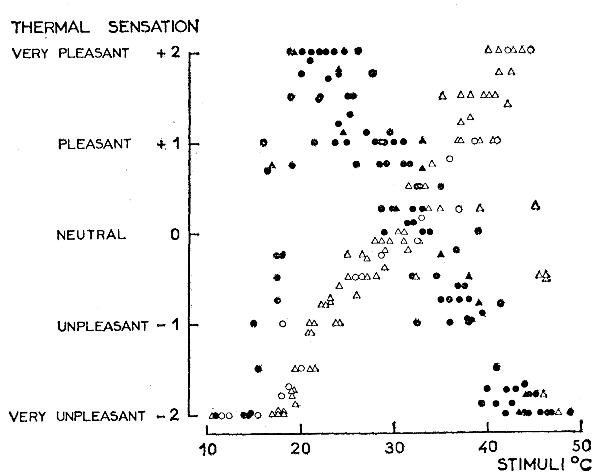
Although Ogata *et al.* and Corbit (*5*) have shown that internal hyperthermia or hypothermia did not modify temperature sensory thresholds, this question remains open. The discriminative part of sensation apparently relies only upon peripheral signals and seems independent from the affective part. Within the limits of pain the affective part of thermal sensation depends only on the internal state. This can even give some paradoxical situations at temperatures at the threshold of pain. A hypothermic subject will like a hot, although slightly burning, stimulus, and a hyperthermic subject will like a biting cold stimulus although these temperatures are slightly painful. Therefore, pleasure-displeasure seems not to be stimulus bound. Pleasure occurs whenever a sensation indicates the presence of a stimulus which helps to correct an internal trouble, cold being pleasant during hypothermia, warm during hypothermia. Conversely, displeasure occurs whenever a stimulus threatens homoiothermia, cold being unpleasant during hypothermia, warm during hyperthermia. Thus we can state about thermal sensation:

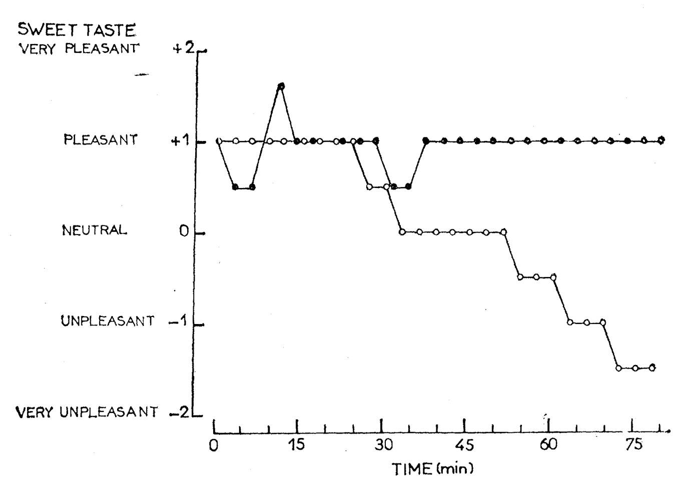
PLEASANT = USEFUL

Is it then possible to find the same phenomenon with other sensations?

Gustative and Olfactive Sensations

Fasting subjects were given a sweet stimulus and responded with positive grades on the same affective scale as in the above experiment. They expectorated the tasted sample and rinsed their mouths. They enjoyed the samples that followed throughout the entire experiment provided that they never swallowed them. After the subjects ingested a certain amount of su-





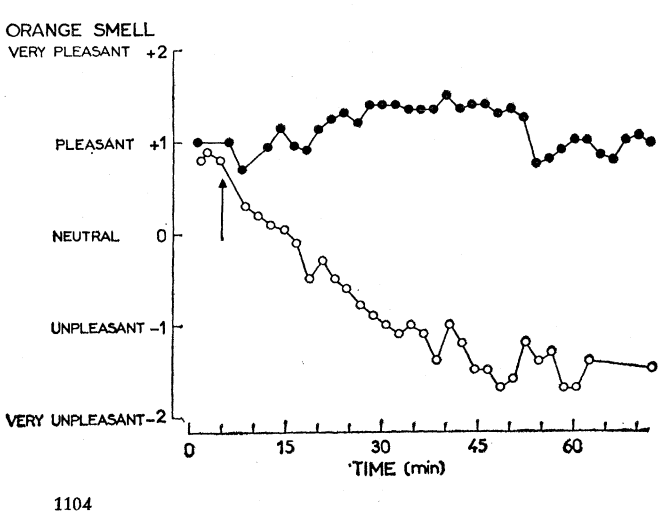


Fig. 1 (above left). Affective responses given by one subject immersed in a stirred water bath. Each point is a response given after a 30-second thermal stimulus of his left hand. Open symbols, hypothermic subject (rectal temperature from 36.3° to 36.6°C); closed symbols, hyperthermic subject (rectal temperature from 37.1° to 37.8°C) (*2*). Fig. 2 (above right). Affective responses given by one fasting subject to a sweet gustative stimulus. The same stimulus is repeated during the entire experiment. Closed circles, control; the subject expectorates the samples after tasting; open circles, the subject swallows the test samples (10 grams of sucrose in 50 milliliters. Fig. 3 (below left). Affective responses given by one fasting subject when given an olfactive stimulus related to food. The same stimulus is repeated throughout the experiment. Closed circles, control, no sugar administered; open circles, the subjects ingest 100 grams of glucose in water at the time shown by the arrow (*7*).

crose or glucose solution, or simply if they swallowed them, the sweet samples that followed became unpleasant. An example of these experiments is given in Fig. 2 (*6*). Here again, as in thermal sensation, a given stimulus can be perceived as pleasant or unpleasant according to the internal state of the subject. It is an internal consequence of the ingested solution that switches the sensation given by an identical stimulus from pleasant to unpleasant.

The same phenomenon can be found with an olfactive stimulus (*7*). Sniffing orange syrup was pleasant to fasting subjects and remained pleasant when repeated. After ingestion of a glucose load this olfactive stimulus turned unpleasant. An example is given in Fig. 3. There again, a given stimulus related to food intake can be perceived as pleasant or unpleasant depending on a modification of the internal state following ingestion of glucose by the subject.

It is likely that this phenomenon with gustative and olfactive stimulations is part of satiety and one sees immediately how food intake will be limited by the displeasure caused by peripheral stimuli. Therefore, here again pleasure is a signal of usefulness and displeasure is a signal of the absence of any need.

Alliesthesia

This relationship between pleasure and usefulness leads one to think that pleasure-displeasure is a determinant of an adapted behavior. A subject will seek all pleasant stimuli and try to avoid all unpleasant stimuli. Since pleasure is an indication of need or at least of usefulness as described above, this is a way that behavior can be adapted to its physiological aim. Indeed, it has been known for a long time that animal behavior, such as food or water intake, can be triggered by internal signals related to the "milieu interieur." In order to avoid using a whole sentence saying that a given external stimulus can be perceived either as pleasant or unpleasant depending upon signals coming from inside the body, it may be useful to use a single word to describe this phenomenon. I hereby propose the word *alliesthesia* (*8*) coming from esthesia (meaning sensation) and allios (meaning changed). This word will be used in the remainder of this article.

Internal Signals

Alliesthesia depends upon internal signals. In the three cases reported above, these internal signals were temperature, with regard to thermal sensation, and a yet unidentified signal after ingestion of glucose or sucrose with regard to "orange odor" and sweet taste (*3*).

Is it then possible to go a step further in the analysis of these internal signals? Let us consider temperature regulation and fever. We have seen that (Fig. 1) a stimulus is pleasant when it facilitates the return of internal temperature to its normal value or prevents any further internal change. Actually, in temperature regulation the internal signal activating panting, sweating, shivering, and other thermoregulatory reactions is not simply internal temperature. It is the difference between the real core temperature and a set value. This set temperature depends upon the species and is about 37°C in man. Fever is a state where the set value of the regulated body temperature is higher than it is in the healthy state. Let us look at thermal sensation during fever (Figs. 4 and 5). In feverish subjects, alliesthesia was adapted to the higher set temperature. For example, a warm stimulus is normally unpleasant to a subject whose temperature is 37.5°C since his set temperature is 37°C. He is hyperthermic compared to his set temperature. However, during fever if his set temperature is 38°C, a 37.5°C core temperature is below his set value and he will describe a warm skin stimulus as pleasant. Therefore, if we look at thermal sensation, we find that alliesthesia depends upon the same complex internal signal as do thermoregulatory reactions such as shivering, namely the difference between actual core temperature and set temperature. This similarity will allow us to use the same experimental approach with alliesthesia as with thermoregulation. Usually, it is possible to gain some information about the set point of internal temperature just by observing shivering or sweating. This set point should be found by the observation of an alliesthetic shift in thermal sensation.

In temperature regulation, the set temperature is always an assumption. It is assumed that core temperature in man is regulated at 37°C. A behavioral approach using alliesthesia as an indication of the value of set temperature can be used in controversial circumstances: muscular work and the menstrual cycle. In muscular work the internal temperature has been supposed to be reset at a higher value since core temperature plateaus at values independent of ambient temperature (*4*). An opposite theory has been proposed, according to which internal temperature was set at a lower value during exercise which triggered more intense reactions in order to protect the body against overheating (*9*). In man, the study of thermal preference showed no alliesthesia, neither at the onset nor at the end of exercise. A shift of preference from warm to cold did occur but

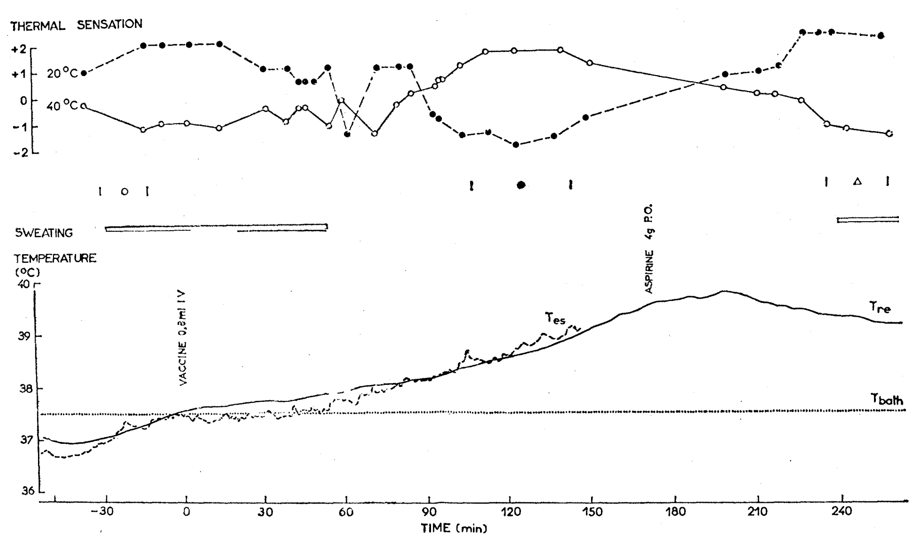


Fig. 4. Experimental acute fever in one human subject. Two upper curves, affective responses to 20°C and 40°C stimulations given repeatedly to the left hand. The affective scale is identical as in Figs. 1, 2, and 3. The subject is immersed in a constant, well-stirred water bath. At time zero, he receives an intravenous dose of vaccine. At time 170, aspirin is administered orally (*2*).

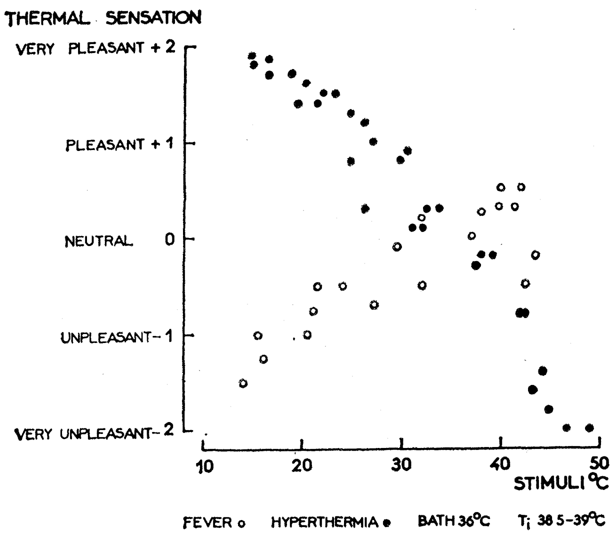


Fig. 5. Affective responses given on different days by one subject in exactly the same conditions. Same internal temperature (38.5° to 39°C). Same bath temperature (36°C). The difference between closed and open circles is a different thermoregulatory set point. Closed circles, control; open circles, acute fever due to influenza; T_i internal temperature (*2*).

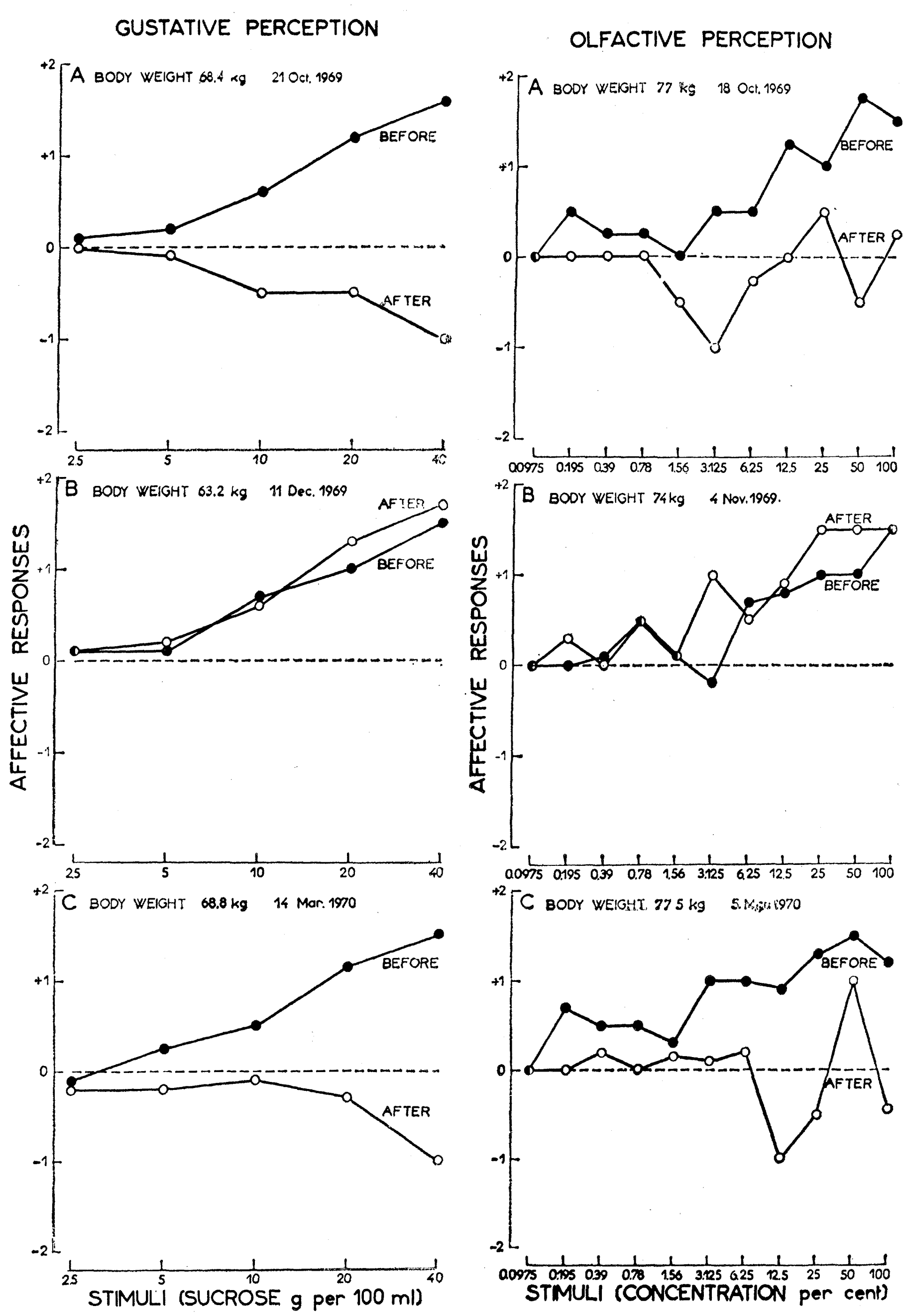


Fig. 6. Affective responses given by one subject to sweet-tasting stimuli (left) and to orange-smelling stimuli (right). Closed circles, fasting; open circles, 1 hour after ingestion of 50 grams of glucose in water. From top to bottom: (A) control experiment at normal body weight, (B) after losing 5 kg (left) or 3 kg (right), (C) after return to control body weight (*13*).

was simultaneous with a definite rise in internal temperature due to the intense heat production in muscular exercise. Alliesthesia depended not upon exercise but upon hyperthermia. This approach led to the conclusion that no reset of the internal thermostat occurs in man during muscular exercise (*10*).

The opposite situation was found during the menstrual cycle. Before ovulation, body temperature at rest is slightly lower than after the ovulation. This is the well-known "temperature curve." Is this shift in core temperature a regulated phenomenon corresponding to a resetting of the thermostat or is it a passive heat deficit before and a passive heat load after ovulation? The alliesthesic approach showed that women in the preovulatory period responded as if they were regulating their core temperature 0.4 to 0.5 of a degree lower than during their postovulatory phase (*11*).

Body Weight

It seems therefore likely, in observing thermoregulation, that alliesthesia depends upon a complex internal signal —the difference between the actual regulated variable and its set value. It is therefore tempting to look at it the opposite way and to suspect the existence of a regulation whenever we observe alliesthesia. Since alliesthesia occurs with gustative and olfactive stimuli during satiety, we may suspect the existence of some regulated variable analogous to temperature regulation and temperature sensation. Hervey has pointed out the remarkable constancy of body weight (*12*). We have therefore hypothesized the possible relation of the internal signals, inducing alliesthesia with olfactive and gustative alimentary sensations, to body weight (*13*).

In fact, alliesthesia was present in the three experimenters acting as subjects at the beginning of the experiment (Fig. 6). Sweet-tasting sucrose solutions and orange syrup were pleasant at all the concentrations offered to the fasting subjects. After ingestion of 200 milliliters of a 25 percent aqueous solution of glucose, these stimuli became unpleasant. This was the control experiment on normal subjects. Next, the three subjects reduced their food intake to 500 or 800 kilocalories per day until they reduced their body weight by 10 percent. They kept their body weight stable for several weeks then returned to their control weight. Alliesthesia disappeared during this reduction of body weight. During this period of time, ingestion of 50 grams of glucose was insufficient to render the stimuli unpleasant. The return to control body weight restored alliesthesia. In other words, ingestion of 50 grams of glucose transformed the pleasant sensations in the fasting subjects into unpleasant sensations as in the control period.

It is therefore tempting to conclude that there exists a regulatory system controlling body weight, or some correlate of body weight. The regulated variable has to be related to body weight and probably not to food intake. This concept of a "ponderostat" implies that the regulated variable, whatever it may be, is compared to its set value. The difference between the two will judge the internal input after food intake and in turn, through alliesthesia, will control food intake. There is, of course, still a large amount of speculation in this theory, but examination of the responses given by obese subjects is encouraging (*14*). Obese subjects gave responses identical to those of the three normal subjects in the above experiment during their "lean" period. This would suggest that obesity is a resetting of the ponderostat at a higher body weight. If the obese person, for health or social reasons, combats his obesity, he will lower his body weight below the set "obese" level, alliesthesia will disappear and satiety will be impaired. This hypothetical ponderostat resetting could explain the great difficulty in preventing a relapse into obesity. If the obese person lets his body weight drift up, he will most likely reach his set point and alliesthesia will reappear.

Summary and Conclusions

A given stimulus can induce a pleasant or unpleasant sensation depending on the subject's internal state. The word alliesthesia is proposed to describe this phenomenon. It is, in itself, an adequate motivation for behavior such as food intake or thermoregulation. Therefore, negative regulatory feedback systems, based upon oropharingeal or cutaneous thermal signals are peripheral only in appearance, since the motivational component of the sensation is of internal origin. The internal signals seem to be complex and related to the set points of some regulated variables of the "milieu interieur," like set internal temperature in the case of thermal sensation (*15*). Alliesthesia can therefore explain the adaptation of these behaviors to their goals. Only three sensations have been studied—thermal, gustatory, and olfactory, but it is probable that alliesthesia also exists in such simple ways as in bringing a signal, usually ignored, to the subject's attention. For example, gastric contractions, not normally perceived, are felt in the state of hunger (*16*). Since alliesthesia relies on an internal input, it is possible that alliesthesia exists only with sensations related to some constants of the "milieu interieur" and therefore would not exist in visual or auditory sensations. As a matter of fact, luminous or auditory stimuli can be pleasing or displeasing in themselves, but there seems to be little variation of pleasure in these sensations, that is, no alliesthesia. There may be some esthetic value linked to these stimuli but it is a striking coincidence that they are in themselves rather neutral and that it is difficult to imagine a constant of the "milieu interieur" which could be possibly modified by a visual or an auditive stimulus—such as light of a certain wavelength or sound of a given frequency.

In the light of this theory, it is possible to reconsider the nature of the whole conscious experience. The existence of alliesthesia implies the presence of internal signals modifying the concious sensations aroused from peripheral receptors. It is therefore necessary to question the existence of sensations aroused by direct stimulation of central receptors, such as hypothalamic temperature detectors, osmoreceptors, and others. Does their excitation arouse sensations of their own, or does the sensation have to pass through peripheral senses? Only human experimentation could answer this question. In the same way, it is possible that self-stimulation of the brain is pleasant, not by giving a sensation in itself, but because the electrical stimulus (*17*), renders peripheral stimuli pleasant.

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17. Even Corbit's beautiful experiments (*15*) where rats stimulate their hypothalamus with heat, a specific stimulus, have to be considered in this light.