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EFFECTS OF OLFACTORY AND GUSTATORY STIMULI ON SELF-STIMULATION OF THE BRAIN

by

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ABSTRACT

Recent studies with rats showing the enhancement of self-stimulation rate by gustatory stimulation have focussed attention on the relationship between the peripheral sensory systems and the central "reward" system. The main purpose of the present investigation was to determine whether the self-stimulation rate of rats could be facilitated by stimulating another sensory system.

Following the successful elicitation of self-stimulation from electrodes placed in the olfactory bulb, this preparation was used to test the effects of different odours on self-stimulation. The pleasant odours of both amyl acetate (banana oil) and peppermint enhanced self-stimulation at threshold intensities, and at threshold + 20%, but not at optimal intensities. These odours had no effect on self-stimulation at diencephalic sites outside the olfactory system. The procedure was repeated using the noxious odour of quinoline and the results obtained were the opposite to those obtained with a pleasant

odour. The self-stimulation rate at olfactory bulb-sites was attenuated at the two lower intensities, whereas the odour had no significant effect at control sites. These findings are very similar to those obtained with gustatory stimulation and suggest that the effects of conventional reinforcers are subserved by the areas of the brain from which self-stimulation can be obtained.

In another experiment a different paradigm was employed to test the relationship between gustatory stimuli and self-stimulation. The rats in this experiment were allowed to choose between self-stimulation of the lateral hypothalamus and solutions of different sweetness. Using both lever pressing data and time measurements, the preference for self-stimulation was shown to vary with the palatability of the alternative solution. These results contradict the idea that self-stimulation of the lateral hypothalamus, at optimal current intensities, is more reinforcing than conventional reinforcers and suggest that preference is based on the quality of these different forms of reward.

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INTRODUCTION

Reinforcement has been, and still is, a very important concept in psychology. Since the early days of experimental psychology when Thorndike (1911) demonstrated the importance of the consequences of a response in determining the frequency with which that response will be used in the future, there has been a concerted effort to provide a satisfactory analysis and explanation of what he called "a satisfying state of affairs". Important contributions were made by Hull (1943) and his colleagues, but their conception of reinforcement was based on the rather naive assumption that the reduction of a drive state or the alleviation of a biological need, was the only basis of reinforcement.

The shortcomings of this formulation soon became apparent and an extensive debate has followed. Certain sensory stimuli, such as the taste of saccharine (Sheffield and Roby, 1950; Carper and Polliard, 1953) were shown to be capable of reinforcing behavior in satiated animals, and incomplete copulation (Sheffield,

Wulff, and Backer, 1951) was also found to have reinforcing effects. These findings seemed more suited to Young's (1936) hedonic theory of "affective arousal" than a theory of reinforcement based on drive-reduction. Further difficulties for the classical theory of drive-reduction arose from the demonstration that monkeys became increasingly proficient in solving mechanical puzzles and improved their performance in the absence of food or other conventional rewards (Harlow, Harlow and Meyer, 1950). This finding led Harlow and co-workers to postulate a "manipulation drive" aroused by external stimuli, rather than by internal stimuli that accompany a bilogical need. Hebb (1955) cited other examples including the fact that chimpanzee's fear of snakes and strangers does not seem to depend upon learning in the presence of biological needs. These examples help to illustrate the difficulties in achieving a satifactory definition of reinforcement and give some idea of the impasse that had been reached by the mid 1950's.

A new source of information was needed, and Hebb (1955) provided a clue to its whereabouts when he argued for a greater reliance on physiological constructs in the development of ideas in psychology. Hebb was acutely aware that the concept of drive reduction was based on a rather simplistic biological model, and urged psychologists to become more familiar with the latest developments in

physiology and to formulate new ideas on the basis of this information. With regard to the concept of reinforcement, consideration of the neurophysiological substrates of reward would undoubtedly aid in the development of a more adequate definition, and at the same time provide additional information about brain function. It is for these reasons that the discovery, some 15 years ago of positive (Olds and Milner, 1954) and also negative (Delgado, Roberts and Miller, 1954) reinforcement, from direct electrical stimulation of the brain, generated such a great deal of interest.

This new discovery had immediate implications for the study of reinforcement, because it showed, contrary to drive-reduction theory, that the excitation of neural tissue in the absence of a primary drive state could be reinforcing. In order to learn more about this new phenomenon, researchers at first concentrated on mapping the effective sites of stimulation, examining the phenomenon in a wide variety of species and studying the effects of manipulating the various parameters of electrical stimulation. Once it was established that brain stimulation could be reliably employed as a positive reinforcer, attempts were made to understand the nature of self-stimulation by correlating it with known brain functions.

Studies of the effects of physiological deprivation (Brady, Boren, Conrad and Sidman, 1957; Olds, 1958b) on the rate of self-stimulation, and demonstrations that various types of consummatory behavior could be elicited from the same sites as self-stimulation (Margules and Olds, 1962; Caggiula and Hoebel, 1966; Mogenson and Stevenson, 1966) suggested that reinforcing brain stimulation was intimately related to the subcortical systems for homeostatic regulations. Recently, because self-stimulation rate has been shown to be influenced by peripheral reinforcers (Mogenson and Morgan, 1967), interest has focussed on the relationship between peripheral sensory systems and reinforcing brain stimulation. Studies of this sort hold a great deal of promise and will undoubtedly contribute to our understanding of the neural basis of reinforcement.

The following review will begin with a brief description of the research that preceeded the discovery of self-stimulation and go on to a more detailed discussion of some of the pertinent literature in this field. Rather than provide a general review, specific topics have been selected on the basis of their relevance for understanding reinforcement produced by direct stimulation of the brain. The anatomical basis of self-stimulation, the relationship between self-stimulation and homeostatic control systems as well as the role of sensory factors in self-stimulation

will be considered.

Experimental Developments Preceding The Discovery of Reinforcing Brain Stimulation

The methodological developments that led to the discovery of reinforcing areas in the brain can be traced directly to the application of the technique of chronic brain stimulation. Ewald in 1893 (cited by Doty, 1969) was the first to administer electrical stimulation to the brains of freely moving animals, although Fritsch and Hitzig two decades earlier had stimulated the cortex in acute experiments. Ewald's electrode assembly consisted of wires inserted into a hollow ivory button that was screwed into the skulls of dogs and by passing current from a small dry cell battery through stimulating wires running along the leash to an electrode in the cortex, he was able to elicit movements.

The study of subcortical mechanisms in behavior had to await the development of a method that permitted reliable access to specific anatomical structures. Such investigation was made possible by the introduction of the stereotaxic apparatus (Horsley & Clarke, 1908). By means of this instrument, electrodes could be placed into the brain with reference to three standard planes (a) lateral plane: a line connecting the two auditory meatuses; (b) anteroposterior plane: a line bisecting the cranium in the midline; and (c) a line connecting the

external auditory meatus with the infraorbitol ridge, providing a reference for the vertical plane (Carpenter and Whittier,1952). These standard planes were then used to prepare atlases of the brain which related the location of different brain structures to a common reference point that coincided with the point of intersection of the three standard planes (stereotaxic zero). Guided by the brain atlases and aided by the precision of the stereotaxic instrument, brain researchers were able to embark upon the exploration of subcortical regions.

Early and outstanding contributions to our knowledge of subcortical function were made by W.R. Hess. He studied the effects of localized stimulation and destruction of a variety of subcortical loci in unrestrained animals. Utilizing cats that were prepared with chronic electrodes implanted under stereotaxic control, Hess was able to observe a host of different behaviors that followed stimulation, including sleeping, licking, retching, defecation, urination, eating, flight and defence reactions. These observations which were recorded on motion picture film, were supplemented by detailed protocols containing information of the electrode dimensions, their placement, and parameters of electrical stimulation, as well as histological confirmation of electrode sites (Hess, 1954). By combining these various techniques, Hess developed an important new

methodology that is now used extensively in the field of physiological psychology.

Neural Basis of Reinforcement

The utilization of Hess' chronic stimulation technique led to the discovery of positive reinforcement areas in the brain. The discovery took place at McGill University in 1953 when according to Olds,"a rat fortuitously evidenced a neuronal rewarding effect by returning to the place on the table top where it had been when an electrical stimulus was applied to the brain via chronically implanted electrodes"(Olds,1969,p.114). This original observation was extended by employing a Skinner box in which the rats received no other reward than electrical stimulation of the brain (Olds and Milner, 1954). Rats with electrodes implanted in the septum, cingulate cortex and mammillo-thalamic tract acquired a lever pressing response in order to stimulate their brains repeatedly. One animal with a septal placement stimulated itself over 7500 times in 12 hours. Later it was observed that this level of performance could easily be reached in one hour with other placements, but the results were so striking that they led Olds and Milner to postulate a system in the brain that subserved rewarding effects on behavior.

Self-stimulation of the brain has been observed subsequently in a number of other species in cats

(Neilson, Doty and Rutledge, 1958), monkeys (Brady,1958), the guinea pigs (Valenstein, 1958), humans (Heath and Mickle, 1960), dolphins (Lilly and Miller, 1962), goldfish (Boyd and Gardener, 1962), dogs (Stark, Fazio and Boyd, 1962), goats (Persson, 1962), squirrels (Wetzel and King, 1966), pigeons (Goodman and Brown, 1966), chicks (Andrew, 1967), and rabbits (Bruner, 1967). It seems to be a phenomenon characteristic of most vertebrates. Whether or not it is limited to this level of the phylogenetic scale will have to await further investigation.

Neuroanatomy of reinforcing brain stimulation: The mapping of anatomical substrates has been most important in the study of self-stimulation. This is not only important for providing a more complete picture of the phenomenon in question, but also for understanding the way in which neural structures subserve reinforcement. There have been several studies whose purpose was to delineate the anatomical correlates of self-stimulation such as those based on the rat brain (Olds,1956; Olds and Peretz, 1960; Olds and Olds, 1963), the cat brain (Wilkinson and Peele, 1963; O'Donohue and Hagamen,1967) the monkey (Lilly, 1957) and rabbit brain (Bruner,1967). This information is continuously supplemented by the results of histological verification of electrode sites accompanying most self-stimulation studies. Yet, as

pointed out so effectively by Wetzel (1968), our knowledge of the anatomical substrates of self-stimulation is far from complete.

Although mapping is not complete, there is general agreement that the most effective sites of self-stimulation are located in the region of the medial forebrain bundle (MFB) of the lateral hypothalamus (LH). Olds and Olds (1963) have defined the MFB as beginning at the lateral reaches of the midhypothalamus, extending medially to the supramammillary area and the medial region of the adjacent tegmentum. In a later study (Olds and Olds, 1964), they emphasize that phylogenetically the system was derived from a pathway connecting the olfactory bulb to the tegmentum. Connections between the MFB and olfactory structures have been further substantiated by Powell, Cowan and Raisman (1965) particularly with the prepyriform cortex, an area from which self-stimulation can also be elicited (Olds and Olds, 1963). In fact, many of the more rostral self-stimulation sites, including the olfactory cortex (Spear, 1962), tractus olfactorius intermedius (Valenstein and Campbell, 1966), diagonal band of Broca (Olds, 1958) are connected to the olfactory system (for a more detailed description of the neuroanatomy of the olfactory system, see Appendix A).

If a similar overlap between the "reward" system and other sensory systems could be demonstrated, it would provide strong support for the idea that an inter-

action of sensory input with the "reward" system is the neural-basis of reinforcement. Although the evidence is by no means extensive, a relationship between the taste system and the self-stimulation system can also be demonstrated. Gustatory stimulation has been shown to affect neuronal activity in the LH (Mogenson and Morgan, 1967; Sharma,1967) and self-stimulation has been elicited from electrodes aimed at a subnucleus of the ventromedial thalamic nucleus (Phillips, unpublished date), which is concerned with taste (Benjamin, 1963). Self-stimulation has also been elicited from parts of the septum (Olds and Milner, 1954) a structure that appears to exert a modulatory influence on taste preference (Beatty and Schwartzbaum, 1968).

There is also a great deal of additional evidence from electrophysiological studies (Gloor, 1960; Stuart, Porter, and Adey, 1964; Campbell, Bindra, Krebs and Perenchak, 1969) showing that afferent input from visceral and somatic receptors impinge on structures in the limbic system from which self-stimulation can be elicited. Although these afferent projections undoubtedly relay information to the "reward" system, an emphasis is placed here on the olfactory and gustatory inputs, because these systems seem to be the more important for relaying the immediate effects of reinforcement to the central "reward" system.

Similarly the neural pathways for pain project to or overlap the sites at which electrical stimulation is aversive. In the midbrain, stimulation of the dorsomedial tegmentum, layers of the tectum and pretectum are aversive (Valenstein, 1966), as is stimulation of the medial and lateral lemnisci, medial and lateral geniculate bodies, spinothalamic tract, and the trigeminal nerve and its root (Olds, 1962). The lateral spinothalamic tract, and the medial lemniscus terminate in the ventral thalamic nucleus, and this system is thought to play a role in the localization of pain. The trigeminal nerve and its spinal root are also concerned with pain and thermal sensitivity (Everrett, 1965). Considering that the conscious recognition of pain occurs at the thalamic level, it is not surprising that stimulation of the ventral thalamic nucleus, and sensory pathways relaying pain, results in an aversive reaction.

Sites in the telencephalon from which aversive effects have been reported appear to border on the lateral ventricles and have been described as the periventricular system (Olds and Olds, 1963). This system passes into the diencephalon just lateral to the third ventricle. It is not known whether pain fibers project to the periventricular system,but it is tempting to speculate that negative reinforcing brain stimulation accompanies the artificial stimulation of structures normally activated by painful stimuli.

So far in our discussion of the anatomical correlates of self-stimulation we have emphasized the relationship between sensory afferents and the "reward" system, in the belief that such considerations may hold the key to understanding the neural basis of reinforcement. This is by no means the only approach, and in fact many authors have stressed the importance of the motor, or efferent side of the nervous system.

For example, Routtenberg and Malsbury (1969) have advanced the idea that reinforcing brain sites in the more caudal aspects of the brain may be best classified as belonging to the extra-pyramidal system. Specifically referred to are the basal ganglia composed of the putamen, globus pallidus, caudate nucleus, and related structures including the substantia nigra and the red nucleus a structure that, according to these authors, may play an important integrative role in positive reinforcement. Self-stimulation sites have been identified in the globus pallidus (Brady and Conrad, 1960) and certain areas of the caudate nucleus (Olds, Travis and Schwing, 1960). Stimulation of other sites in the caudate nucleus yielded neutral or strongly aversive effects (Olds and Olds, 1963). Although the evidence is somewhat tentative, the elicitation of self-stimulation from the extra-pyramidal system could be taken as support for the Glickman and Schiff (1967) hypothesis that self-stimulation accompanies facilitation

of motor responses pre-patterned in the brainstem. However, no reports of extra-pyramidal stimulation leading to any observable form of "species-specific" behavior and low rates of self-stimulation cautions against this interpretation.

Neurophysiological control systems and reinforcing brain stimulation: One of the most striking anatomical findings is that the best sites for self-stimulation overlap regions of the brain concerned with physiological regulation and homeostasis. The first suggestion of this association came from observations of the effects of drive states on self-stimulation. Subsequently, more direct evidence came from studies in which consummatory behaviors were elicited from the same sites as self-stimulation. Because of the theoretical emphasis on the relationship between reinforcement and drive reduction (Hull, 1943: Miller, 1957), it is not surprising that a good deal of attention has been given to these findings (Miller,1961; Glickman and Schiff, 1967). The observation of "stimulus-bound" behavior is probably most responsible for the stress on the efferent side of the nervous system, as outlined at the end of the last secion. This section will begin with a discussion of the earlier studies concerned with the effects of deprivation on self-stimulation and then go on to the later studies in which self-stimulation

and stimulus-bound consummatory behavior were elicited from the same electrode site.

Brady, Boren, Conrad and Sidman (1957) studied the effects of food and water deprivation on self-stimulation and found that after 48 hours deprivation, the lever pressing rates for an intracranial electrical stimulation reward in rats and cats were significantly higher than those recorded after zero or one hour deprivation. Olds (1958) found similar effects for food deprivation, and also reported that at some electrode placements, castration caused a decline in the rate of response in male rats. Recovery occurred after injection of testosterone. The effects of food deprivation and castration were specific to the locus of stimulation. The effects of food deprivation have been confirmed by Hodos and Valenstein (1960), but they found no difference in the rate of self-stimulation in females during hormone induced estrous. Prescott (1966), on the other hand, has found that hypothalamic self-stimulation rates increased in rats on the night of behavioral estrous and Meyerson, Wilkins and Sawyer (1969) have reported that estrogen increased the self-stimulation rate when the electrodes were located in the anterior hypothalamus. In the latter study, the increase in self-stimulation was obtained with only two animals, so the effects of estrogen on self-stimulation may be

still open to question.

There is also some rather tenuous evidence of a relationship between the thermoregulatory system and self-stimulation. Briese (1965) has reported that stimulation at sites in the LH was accompanied by an increase in rectal temperature but an attempt to reproduce these results proved unsuccessful (Phillips, unpublished data). In a subsequent study, Briese, Echeverria, and De Quijada (1966) have presented further evidence for a specific relationship between thermoregulatory and self-stimulation systems by replicating the previous findings that a hot environmental temperature reduced hypothalamic self-stimulation (de Haan and Hamilton, 1966) whereas cold increased it (Reid and Porter, 1965).

Mogenson (1969) has reported that water deprivation did not increase the rate of self-stimulation, although as in previous experiments, there was an increase in the rate with food deprivation. He suggested that this effect on self-stimulation may not be a specific one (i.e., sensitization of neural control system for homeostatic regulation), but rather a general effect on activity and performance. There are some studies, however, in which activity effects were controlled for, (Olds, 1958, Prescott, 1966; Wilkinson and Peele, 1962)

and yet drive states appeared to have specific effects on reinforcing brain stimulation.

Several experiments have revealed anatomical overlapping of the loci that are involved in the regulation of feeding and drinking behavior and the points from which self-stimulation can be elicited. Morgane 1961a,b), Margules and Olds (1962), and Hoebel and Teitelbaum (1962) have elicited both self-stimulation and feeding from electrical stimulation of a common locus in the LH and drinking and self-stimulation accompanied stimulation of the perifornical region of the LH (Mogenson and Stevenson, 1966). Seminal discharge has also been observed to accompany self-stimulation (MacLean, Denniston and Dua 1961; Herberg, 1963; Plutchik, McFarland and Robinson, 1966) and copulatory behavior and self-stimulation have been obtained from the same electrode in the posterior hypothalamus (Caggiula and Hoebel, 1966). There is still some disagreement as to the significance of the relationship between self-stimulation and induced consummatory behaviors. It seems unlikely that the reward for self-stimulation is drive reduction, because the concurrent elicitation of consummatory behavior implies that a drive is being induced rather than reduced.

This inconsistency can be resolved by postulating that different systems subserve self-stimulation and stimulus-bound behavior (Mogenson, 1968) or that different aspects of the same system are activated. To elaborate on the latter point, the information from the various receptors monitoring the dynamic physiological state of the organism must be integrated in such a way as to initiate behavior appropriate to the maintenance of homeostasis. In addition to receptors that are sensitive to the internal mileaux, a homeostatic control system would also rely heavily on information from peripheral exteroceptors, especially when the organism is engaged in consummatory behavior. Stimulus-bound consummatory behavior could accompany the activation of either the integrating mechanism, or efferent motor pathways. Self-stimulation, on the other hand would only occur when either the sensory afferent that normally relays the consequences of consummatory behavior, or the site of interaction with the integrating mechanism, is activated. Stimulation of the integrating mechanism would result in the elicitation of both self-stimulation and stimulus-bound behavior. Given this model, the sensory systems, especially the chemosensitive systems, would appear to play a major role in reinforcement, rather than the motor systems.

Facilitation of Reinforcing Brain Stimulation: Interaction of Stimulus-Bound Consummatory Behavior And Self-Stimulation.

In contrast to the stress on the efferent side of the nervous system, which has resulted from elicited species-specific behavior (Glickman and Schiff, 1967), it has been suggested that it is not the elicited species-specific behavior per se, but the sensory consequences of this behavior that is important for the reinforcing effects which occur during self-stimulation (Mogenson and Kaplinsky, 1969). Some indirect support for this argument comes from experiments on the role of sensory stimuli in eliciting gnawing (Roberts and Carey,1965), attack (MacDonnell and Flynn,1966; Roberts and Keiss, 1966) or sexual behavior (Vaughan and Fisher, 1962) by hypothalamic stimulation, but these studies were not directly concerned with intracranial self-stimulation. More direct evidence has come from studying the effects of electrically-induced consummatory behavior on the concurrent self-stimulation rate.

Mogenson and Morgan (1967) were the first to conduct experiments of this nature, and reported that the electrically-induced drinking of water facilitated concurrent self-stimulation behavior. This finding led them to the suggestion that the inputs

and feedbacks elicited by the electrical stimulation of a drive system can enhance neural activity in the "reward" system, thereby increasing the rate of self-stimulation.

The importance of these inputs and feedbacks has been confirmed by Mendelson (1967) and by Coons and Cruce (1968) using somewhat different experimental conditions. Employing stimulus intensities that were below threshold for self-stimulation, but above threshold for "stimulus-bound" behavior, these authors were able to elicit self-stimulation if a goal object (i.e. food or water) appropriate to the behavior elicited, was available. It is important to emphasize that the parameters of electrical stimulation were kept constant in all these studies and that the effects were presumably due to the sensations accompanying feeding and drinking. The following data lend some support to this idea.

Phillips and Mogenson (1968) in replicating and extending the findings of Mogenson and Morgan (1967) enhanced the sensory stimulation by adding either quinine or saccharine to the water ingested by "stimulus-bound drinkers" and found the bitter taste of quinine attenuated the rate of self-stimulation, while saccharine increased it to a greater extent than water. Poschel (1968) obtained identical results with animals that ate when stimulated

in the hypothalamus.

These studies offer the first direct evidence of an interaction between "peripheral" and"central" reinforcers,and suggest that the same neural system subserve both types of reward. Certain tastes, which are known to reinforce behavior in the absence of a drive (Young, 1967) may do so by influencing the regions of the brain from which self-stimulation can be obtained, as several authors have indicated (Pfaffmann,1960; Valenstein,1966; Young, 1967).

Purpose Of The Present Investigation.

In the present investigation, the possible facilitative effects of odours on self-stimulation were studied. The decision to use the olfactory system was based on its accessibility for electrode implantation (especially in the periphery) and the fact that self-stimulation can be elicited from many secondary olfactory structures (see Appendix A). An attempt was also made to improve upon the earlier facilitation studies by not having the presence of the peripheral stimulus contingent upon the self-stimulation response.

In addition to these neuropsychological studies on the role of sensory factors in reinforcement, a behavioral experiment concerned with changes in preference for self-stimulation as a function of the palatability of

the alternative reward will be described. It demonstrated, using a different paradigm, the importance of sensory factors in reinforcement.

GENERAL METHODS

Subjects

The subjects (Ss) were albino rats of the Wistar strain obtained from Woodlyn Farms, Guelph, Ontario. At the time of operation, the animals ranged in age from three to five months, and weighed between 250 and 400 gm. At the completion of the experiments, they were five to nine months of age and weighed between 450 and 575 gm.

Prior to surgery, the Ss were housed in colony cages with Purina lab chow and water available ad libitum. Immediately before surgery, the Ss were transferred to individual wire mesh cages in which they were housed until the experiments terminated. They were kept in a controlled environment of 40% relative humidity at a temperature of $24^{\circ} \pm 1^{\circ}C$, and were subjected to a 12-hour light-dark cycle. Unless otherwise specified, Purina lab chow and tap water were available ad libitum.

Materials and Apparatus

Bipolar electrodes supplied by Plastic Products Company, Roanoke, Virginia (MS 303-010"; MS 303-005")

were used. These electrodes consisted of two twisted insulated nichrome wires soldered to two female connectors embedded in a Teflon pedestal. In preparation for implantation, the electrodes were cut to the desired length with sharp wire cutters exposing only the tips of the wire. The electrodes were implanted by means of a Kopf stereotaxic instrument.

The implanted electrodes were connected to a stimulator by a receiver cord of light earphone wire (Plastic Products Co., 303-018"- 303-32"). The receiver cord was suspended by means of a commutator (Scientific Prototype Corp., MC4). This arrangement permitted freedom of movement and reduced the risk of accidental extraction of the electrodes.

Two Skinner boxes (30 x 15 x 30 cm.), constructed of lucite, 3 mm. thick were used to test all animals, initially for self-stimulation. A lever, 1.9 cm. wide (Lehigh Valley Electronics, Model 1535), was located in the middle of the back wall. It extended 2 cm. into the box at a distance 4 cm. from the floor. The lever sensitivity was 10 gm. Depression of the lever activated a step-up transformer and delivered a 60 cycle sine wave stimulation to the S. The step-up transformer was operated from a 110 volt A.C. line. The stimulus

intensity (peak current) could be varied from 0-400 microamperes (μA) and the stimulus train duration was regulated by an interval timer(Hunter, Model 108C). An impulse counter (Sodeco Model TCE24E) was connected to the terminals of the Hunter timer to record lever presses. Current flow to the animal was monitored at all times by a dual beam oscilloscope (A.B. Dumont Lab, Passaic, N.J., Model 279).

The Skinner boxes were housed in separate sections of a plywood experimental chamber lined with 1.3 cm. insulated board. Each section measured 56 x 34 x 86 cm. and was illuminated by a 40-watt over-head lamp and ventilated with a small exhaust fan (Fasco, model 5075-IN) which provided a partial masking of extraneous noise. The temperature in the experimental chamber was maintained at $25^{\circ} \pm 1^{\circ}$C. A small observation window in the door permitted observation of the animal in the chamber.

Operative Procedure

After placing and straightening the electrode in the electrode holder of the stereotaxic frame, the stereotaxic zero was recorded. The animals were prepared for surgery by first anaesthetizing them with sodium pentobarbital (50 mg./kg.). The head was then

shaved and scrubbed with a solution of 85% alcohol and .001% zephiran chloride mixed in a proportion of 7:3. After the animal was placed in the stereotaxic instrument with the incisor bar 1 mm. below the level of the ear bar, an incision was made along the midline. When the electrode was aimed at the hypothalamus, the incision started at bregma and extended caudally for 1.5 cm. The skull was scraped bare with a scalpel blade and powdered norepinephrine was applied to the skull to arrest bleeding. A hole 1 mm. in diameter was trephined in the skull with a dental drill and size 722 burr. Four small holes were drilled around the burr holes and stainless steel jeweller's screws were partially screwed into these guide holes to anchor the electrode unit to the skull. The electrode was lowered the desired distance from the surface of the skull and cranioplastic cement (Plastic Products Co.) was poured around the screws and the electrode. After the cement had hardened the electrode holder was raised and the S was removed from the frame.

Testing Procedure for Self-Stimulation

Following a five to seven day post-operative recovery period, Ss were tested for self-stimulation. The experimenter shaped the Ss to lever press by delivering electrical stimulation to the brain each time the S

approached the lever. The intensity of the stimulation was varied from 0 μ A to 200 μ A with the stimulus train duration constant at 0.2 seconds. This procedure was followed for a minimum of seven days. Any Ss which did not learn to lever press were not retained for further testing.

Histology

The Ss were anaesthetized with ether. After breathing had ceased, the thoracic cavity was opened, and the right auricle of the heart perforated. Perfusion was accomplished by first injecting the left ventricle with isotonic saline, followed by 10% formalin. The brains were then removed, stored for at least a week in 10% formalin; frozen sections were cut at 50 μ and stained with cresyl violet.

EXPERIMENT I: SELF-STIMULATION OF THE OLFACTORY BULB

In the discussion of the anatomical correlates of self-stimulation above it was mentioned that moderate rates of self-stimulation (30-50 responses per min.) are obtained from structures such as the amygdala, the prepyryform cortex (Olds and Olds, 1963) and the tractus olfactorius intermedius (Valenstein and Campbell,1966). In the present experiment, electrodes were implanted into the olfactory bulb in an attempt to obtain self-stimulation.

Method

The Ss were 10 male and two female Wistar rats weighing between 250-350 gm. at the time of operation. The implantation techniques differed slightly from those outlined in the General Methods since there are no stereotaxic references for the olfactory bulbs. Estimates of the co-ordinates were made by studying skull markings and exposing the olfactory bulbs in a rat cranium positioned in the stereotaxic apparatus.

Four animals were implanted with bipolar electrodes constructed from stainless steel wire .010 in. in diameter (Plastic Products Company MS 303-018-312-010 in.) and a smaller bipolar electrode (.005 in. wire) was implanted in

each of the remaining eight Ss. Surgery was performed under sodium pentobarbital anesthesia in accordance with the procedure described previously. The stereotaxic co-ordinates employed were 16 mm. anterior to the interaural line, 0.75 mm. lateral to the midline and 3 mm. ventral to the surface of the skull. All stereotaxic implantation was performed with the mouth bar located 1.5 mm. below the interaural line.

After a seven-day postoperative recovery period, the Ss were tested for self-stimulation for 30 min. per day in the plexiglass chamber described earlier. Initially, the animals were tested under a wide range of stimulus intensities (0-200μA) and durations (0.05 sec.- 3.0 sec.) in an attempt to induce self-stimulation. Following the establishment of optimal stimulation parameters, threshold intensities were determined. The optimal stimulation intensities were reduced 5μA every 5 min. until the Ss failed to respond, at which point the intensity was raised 2μA every 5 min. until sustained pressing was re-established. This intensity was taken as threshold.

On completion of the experiments, the animals were sacrificed and the brains removed. The electrode placements were confirmed by external examination of the

olfactory bulbs for electrode tracts.

Results

Seven of the 12 animals prepared for testing became self-stimulators. Of the remaining Ss, four failed to self-stimulate after 14 days of testing, and one died before testing commenced. There was clear evidence of electrodes entering the olfactory bulb in all seven Ss that self-stimulated but no evidence in the four Ss that did not self-stimulate. On the basis of superficial examination of the olfactory bulbs, the loci which elicited the highest rates of self-stimulation (i.e., 15-25/min.) were in the middle portion of the bulb, while lower rates were obtained from the most anterior placements. Figure 1 depicts the electrode placements from three of the Ss that self-stimulated.

The parameters which proved most effective in eliciting self-stimulation were similar to those employed for self-stimulation of the LH, that is, a 60 cps sine wave at an intensity of 20-40μA for 0.2-0.5 sec. duration. The maximum rates of lever pressing averaged 502/30 min., with a range from 167-850. Threshold intensities were established between 4μand 12μA with a mean self-stimulation rate of 80/10 min. and a range of 43 to 124. Self-stimula-

FIGURE I

Three examples of olfactory bulb electrode placements.(outlined in black).

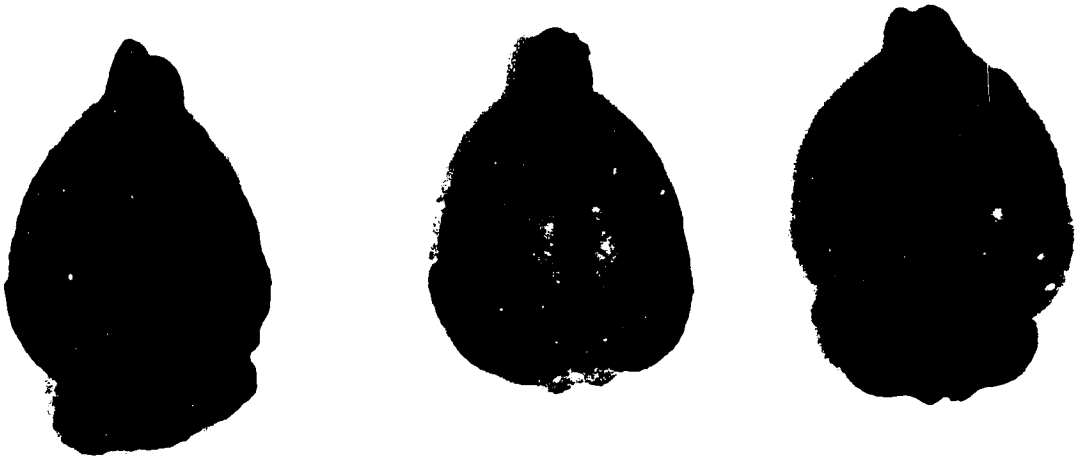


TABLE I

MINIMUM AND MAXIMUM SELF-STIMULATION RATES FROM OLFACTORY BULB ELECTRODE PLACEMENTS: EXPERIMENT I.

Subject Number	Minimum Rate/10 min.	Maximum Rate/30 min.
OB-2	43	167
OB-3	124	486
OB-7	87	362
OB-9	51	388
OB-12	67	681
OB-14	68	580
OB-15	121	850
MEAN	80	502
MEAN PRESSES PER MIN.	8/min.	17/min.

tion data for all seven Ss are presented in Table I.

Convulsions often accompanied self-stimulation at the highest current intensities. The convulsions occurred immediately after the animals had received several stimulations and lasted 20 to 30 sec. They consisted of a bilateral clonus involving the head and forelimbs which was followed by a period of heightened re-activity which lasted 1 - 3 min. If the current was too high, convulsions were displayed by all the Ss from which self-stimulation could be elicited supporting Goddard's (1967) finding that epileptic seizures can be induced by stimulation of the olfactory bulbs.

Discussion

The finding that animals will self-stimulate the olfactory bulb emphasizes that natural 'peripheral' reinforcement and 'central' reinforcement produced by electrical stimulation of the brain have a good deal in common. When self-stimulation of the olfactory bulb is considered in conjunction with recent evidence that odours can be used to maintain lever pressing in the presence or absence of a drive state (Long and Tapp, 1967,1968; Long and Stein, 1969) it suggests that these totally different forms of stimulation may be having similar effects on behavior because they both influence the same neural system.

There is anatomical and electrophysiological evidence (Ban and Zyo, 1962; Scott and Pfaffmann, 1967; Leonard and Scott, 1969) that fibers originating in the olfactory bulbs project to the MFB in the region of the LH. This is the area from which the highest rates of self-stimulation have been obtained and Olds and Olds (1964) considered this region of the brain to be a critical focus of the "reward" system, with self-stimulation occurring at other sites because of influences on this LH focus. With respect to natural stimuli, Pfaffmann (1960) has contended that "sensory stimulation per se together with its ensuing central neural events be considered as a primary determinant of reinforcement" (1960, p.254). The "ensuing central neural events" referred to in the quotation could presumably correspond to the initiation of activity in specific parts of the 'reward' system as Olds and Olds (1964) suggested. It is conceivable that a natural olfactory stimulus may provide positive reinforcement by initiating activity in olfactory pathways that relay information to the subcortical system that subserves positive affect. From the present study, it appears that artificial activation of these same pathways is reinforcing and provides the basis for olfactory bulb self-stimulation.

A point of view that has been considered for

some time by our group, was recently expressed by Stevenson (1969). It was suggested that self-stimulation may occur when positive feedback pathways to the control systems for appetitive behavior are activated. More explicitly, "positive feedbacks such as taste in feeding and drinking and tactile sensation in copulation are subjectively perceived as pleasurable in man and reinforce the behavior that activates them. Artificial stimulation of such positive feedbacks would be expected to reinforce the activity which caused such stimulation, i.e., to result in self-stimulation of the central representation of such a positive feedback system". (pp. 1082-83).

With regard to this quotation, one might question whether electrical stimulation of positive feedback pathways, (or sensory afferents) would result in a sensation that was subjectively similar to natural stimulation. Although the evidence is rather sparse, the answer appears to be affirmative. Electrical stimulation of olfactory structures in man, resulted in the subjective impression that an odour was present (Sem Jacobsen and Torkildsen, 1960). It is also known that human subjects will report sensations of pleasure and sexual feelings when self-stimulating the septal region (Heath, 1964).

One might question why an electrical stimulus should elicit a complex subjective experience. Doty (1969) has stated that whenever electrical stimulation elicits

behavior and sensations, "the neural organization responsible for such complex outcome lies remote to the neurons stimulated. The current cannot impose upon neurons the spatiotemporally coded and integrated neural events they normally achieve; it can only drive them in bizarre and nonsensical synchrony. Thus any subtle, highly integrated neural effects resulting from the stimulation must ensue only because the neural systems downstream (or, possibly, to a slight degree upstream) receiving the nonsense signal are able to transform it into an effective neural code." (p 292). With respect to self-stimulation, the "nonsense signal" initiated by stimulating a sensory afferent is presumably rewarding, because it is unravelled by the more central aspects of the "reward" system.

Self-stimulation of the olfactory bulb also lends support to the idea that projections from sensory systems, namely olfactory, gustatory and cutaneous senses, may constitute the peripheral aspects of the 'reward' system. Pfaffmann (1960) hinted at this possibility when he stated that the neural mechanisms mediating the reinforcing properties of sensory stimulation consist of "primary projection systems and their ramifications in the thalamic and old brain neural connections" (p.265). This argument will be considered in greater detail in the General Discussion.

EXPERIMENT II: ENHANCEMENT AND INHIBITION OF SELF-STIMULATION OF THE OLFACTORY BULB BY ODOURS.

Evidence of a relationship between the sensory systems that are activated by conventional reinforcers and the self-stimulation areas of the brain has come from studies showing an enhancement of self-stimulation accompanied by gustatory stimulation. (Mogenson and Morgan, 1967; Phillips and Mogenson, 1968; Poschel, 1968). This relationship would seem even more convincing if facilitation effects could also be shown using a different sensory modality. In order to provide this additional support, several experiments were designed to test the effects of pleasant and noxious odours on self-stimulation of sites in the olfactory bulb and control sites in the diencephalon.

In the experiments that showed gustatory facilitation of self-stimulation of the LH, the presentation of the sensory stimulation was always contingent upon the same behavior that delivered the brain stimulation. From this it may be argued that the increase in lever pressing, that is thought to reflect enhanced activity in the region of the stimulating electrode, is merely

due to the fact that two rewards are associated with the lever. To control for this possibility, the odours in the following experiments were presented continuously as a background stimulus throughout the test session.

Effect of Amyl Acetate on Self-Stimulation

The first odour tested was amyl acetate. This odour has been rated 'pleasant' by human observors (Yoshida, 1964) and has also been demonstrated to have reinforcing properties, as rats will press levers in order to smell this odour (Long and Tapp, 1967). Previous experiements with oral stimulation have shown that the facilitation of self-stimulation only occurs at low levels of electrical stimulation, and consequently both low and high levels of stimulation were used in this experiment. It is predicted that the pleasant odour will only affect self-stimulation at the lower intensities confirming the effects of gustatory stimulation.

Method

Subjects: The Ss were 18 male Wistar rats weighing between 250-350 gm. at the time of surgery. According to a surgical procedure that was described above, nine animals had bipolar electrodes implanted into one olfactory bulb and the remaining nine animals with electrode implants aimed at dorsal and ventral hypothalamus constituted a

control group.

Apparatus: In order to test for the effects of odor on self-stimulation, the test chamber (15 cm. x 30 cm. x 30 cm.) with a grid floor, was housed in a cabinet (45 cm. x 60 cm. x 100 cm.) that was built according to the design described by Long and Tapp (1968). A background odor could be introduced into the cabinet through 1/4" Teflon tubing by passing compressed air (1/2 lb./sq.in.) into a 1 L. Erlenmeyer flask containing cotton balls soaked in 5 ml. of amyl acetate solution (British Drug Houses Ltd., Poole, England). The flow rate was measured by a Fisher Flow-meter (11-164) and was found to be 7200 cc/min. at a temperature of $22^{\circ} \pm 1^{\circ}$C. The outlet for the odorized air was located 10 in. above the lever. At this point, the compressed air could mix with the flow of air from the air conditioning system that was used to maintain constant ventilation of the cabinet.

Procedure: Prior to the main experiments, all of the animals had exhibited self-stimulation and were tested further in order to determine the minimum and maximum stimulus intensities for eliciting self-stimulation. The minimum intensity was obtained by starting at an intensity that would maintain self-stimulation and decreasing the intensity 5 A every 2 min. until the rate of lever pressing was equal to or less than an operant

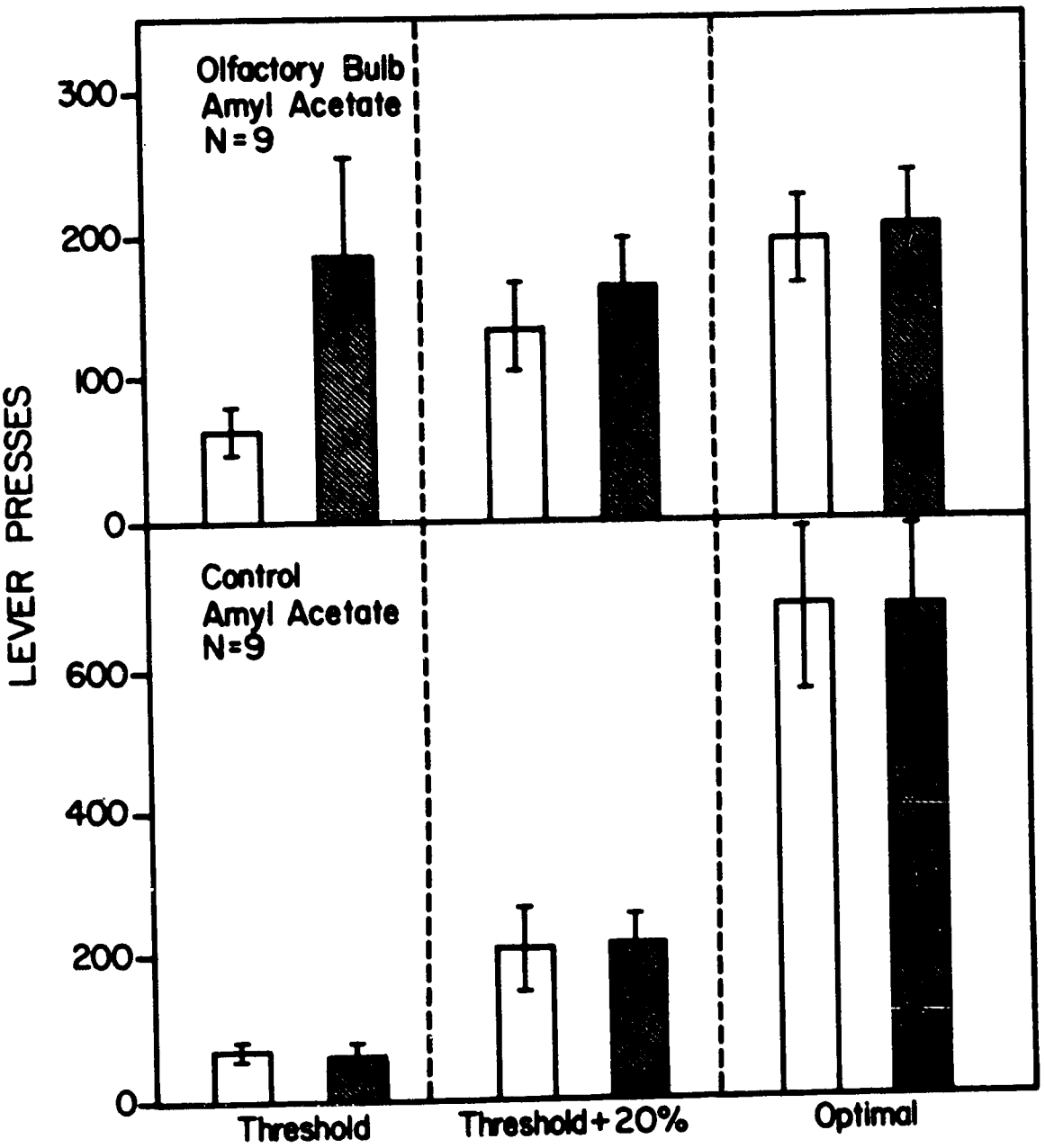
rate established at the beginning of the test session. At this point, the intensity was raised 2μA every 2 min. until sustained pressing was re-established. The optimal intensity was defined as the stimulus intensity which produced the highest rates of lever pressing and at the same time did not induce epileptic seizures.

The animals were tested four times at each of the following current intensities; minimal current intensity, 20% above minimal, and optimal intensity. During half of the trials, a background odour was produced by passing the compressed air over cotton balls soaked in 5 ml. of amyl acetate solution. On the remaining trials, the air passed through an uncontaminated flask.

The daily order of testing was varied randomly among Ss with respect to stimulus intensity and presence or absence of odour. Each day half of the animals were tested with odour present, while the remainder were tested without the background odour. Each animal with an olfactory bulb electrode was paired with a control animal, and this pair was tested consecutively. The odour was always presented during the last half of the daily testing, allowing 18 hrs. of ventilation prior to the next day of testing. A daily trial consisted of a 10 min. self-stimulation session, during which the number of lever presses was recorded.

FIGURE 2

Comparison of self-stimulation rates at sites in the olfactory bulb (upper panel) and control sites in the diencephalon (lower panel), with odour of amyl acetate present (shaded column) and absent (open column).


Olfactory Bulb
Amyl Acetate
N=9
Control
Amyl Acetate
N=9
LEVER PRESSES
300
200
100
0
600
400
200
0
Threshold
Threshold+20%
Optimal

Results

As illustrated in Figure 2, exposure to air odourized by amyl acetate resulted in an increase in self-stimulation of the olfactory bulb at minimal and minimal + 20% current intensity levels but not at optimal intensities. The odour had no effect on self-stimulation at control sites at all intensity levels.

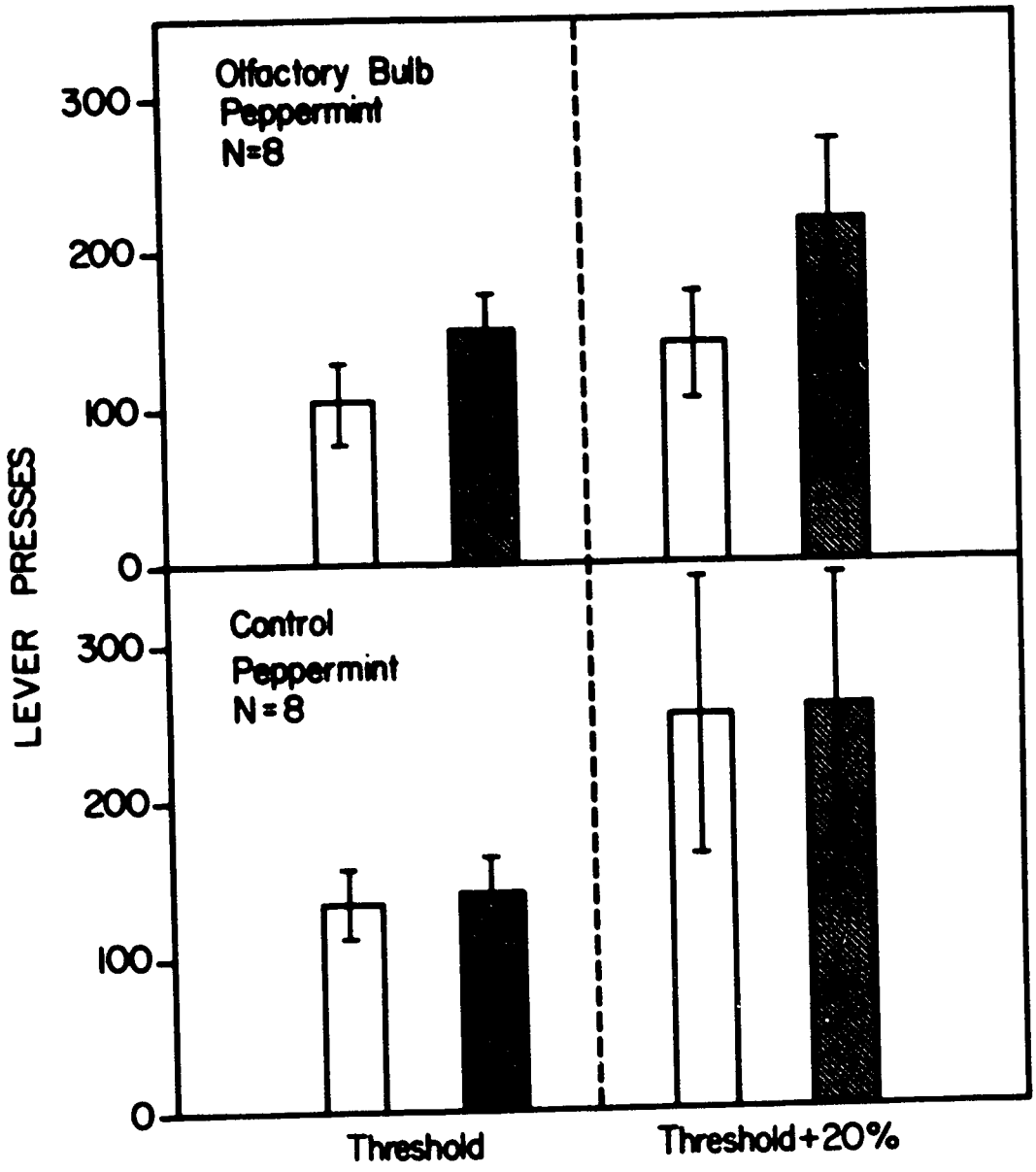
When these data were analysed by a Type 3 Analysis of Variance (Winer, p.319), a groups by odour interaction revealed a probability level of .10 ($F = 3.53, df. = 1/16$), but as this trend was in the predicted direction, it warranted further examination of the contributing means. A-posteriori t tests (one-tailed) revealed a significant increase in self-stimulation of the olfactory bulb at the minimal intensity ($t = 1.94$, $p < .05$) and at 20% above minimal intensity ($t = 2.70$, $p < .025$) but no significant difference was found at the optimal intensity; nor were any significant differences found in self-stimulation rates at control sites at all intensity levels.

Effect Of Peppermint On Self-Stimulation.

This experiment was undertaken to see whether another "pleasant" odour would also facilitate self-stimulation of the olfactory bulb. Peppermint was selected since it has been classified as pleasant by human

FIGURE 3

Comparison of self-stimulation rates at sites in the olfactory bulb (upper panel) and control sites in the diencephalon (lower panel), with odour of peppermint present (shaded column) and absent (open column).


Olfactory Bulb
Peppermint
N=8
Control
Peppermint
N=8
LEVER PRESSES
300
200
100
0
300
200
100
0
Threshold
Threshold+20%

subjects (Yoshida,1964).

The two lower intensities of electrical stimulation were used because, from the results of the previous experiment, it was expected enhancement of self-stimulation would occur with these current levels.

Method

The Ss were 16 of the 18 rats employed in the previous experiment. Rat number OB-44 had a damaged electrode assembly and was subsequently dropped from the experiment along with its control. The procedure was similar to that used in the previous experiment with the exception that the two lower current intensities were used. The cotton balls were soaked in 5 c.c. of peppermint solution that was I part of oil of peppermint (Bush Co., Montreal) and 50 parts Sherriff Pure Peppermint Extract (Salada Foods Ltd., Toronto).

Results

The effects of the odour of peppermint on self-stimulation were similar to those produced by amyl acetate (see Figure 3). The data were analyzed by a Type 3 analysis of variance (Winer, p.319) and the group by odour interaction was significant ($F=5.79$, df 1/14, $p<.05$). A-posteriori t tests (one-tailed) showed that self-stimulation rates were significantly increased in the

presence of the odour at both minimal current intensity ($t = 2.89$, $p < .025$) and 20% above minimal current intensity ($t = 2.54$, $p < .025$). As in the previous experiment, the odour had no effect on self-stimulation at control sites.

Effect Of Quinoline On Self-Stimulation

Unpleasant gustatory stimuli have been shown to attenuate the rate of self-stimulation at lateral hypothalamic sites from which drinking and feeding are elicited (Phillips and Mogenson, 1968; Poschel, 1968), and therefore an experiment was designed to determine the effects of a malodourous substance on self-stimulation of the olfactory bulb. The decision to use the odour of quinoline (Fisher Scientific Co., Fair Lawn N.J.) in this experiment was based on its experimental classification as an offensive odour by human subjects (Kniep, Morgan, Young, 1931; Yoshida, 1964).

Method

Testing was conducted at three intensities of electrical stimulation in accordance with the experimental procedure described above. The Ss were the 16 rats used in the previous experiment. Following the completion of this experiment the animals were sacrificed and the brains examined to determine the electrode placements.

FIGURE 4

Comparison of self-stimulation rates at sites in the olfactory bulb (upper panel) and control sites in the diencephalon (lower panel), with odour of quinoline present (shaded column) and absent (open column).

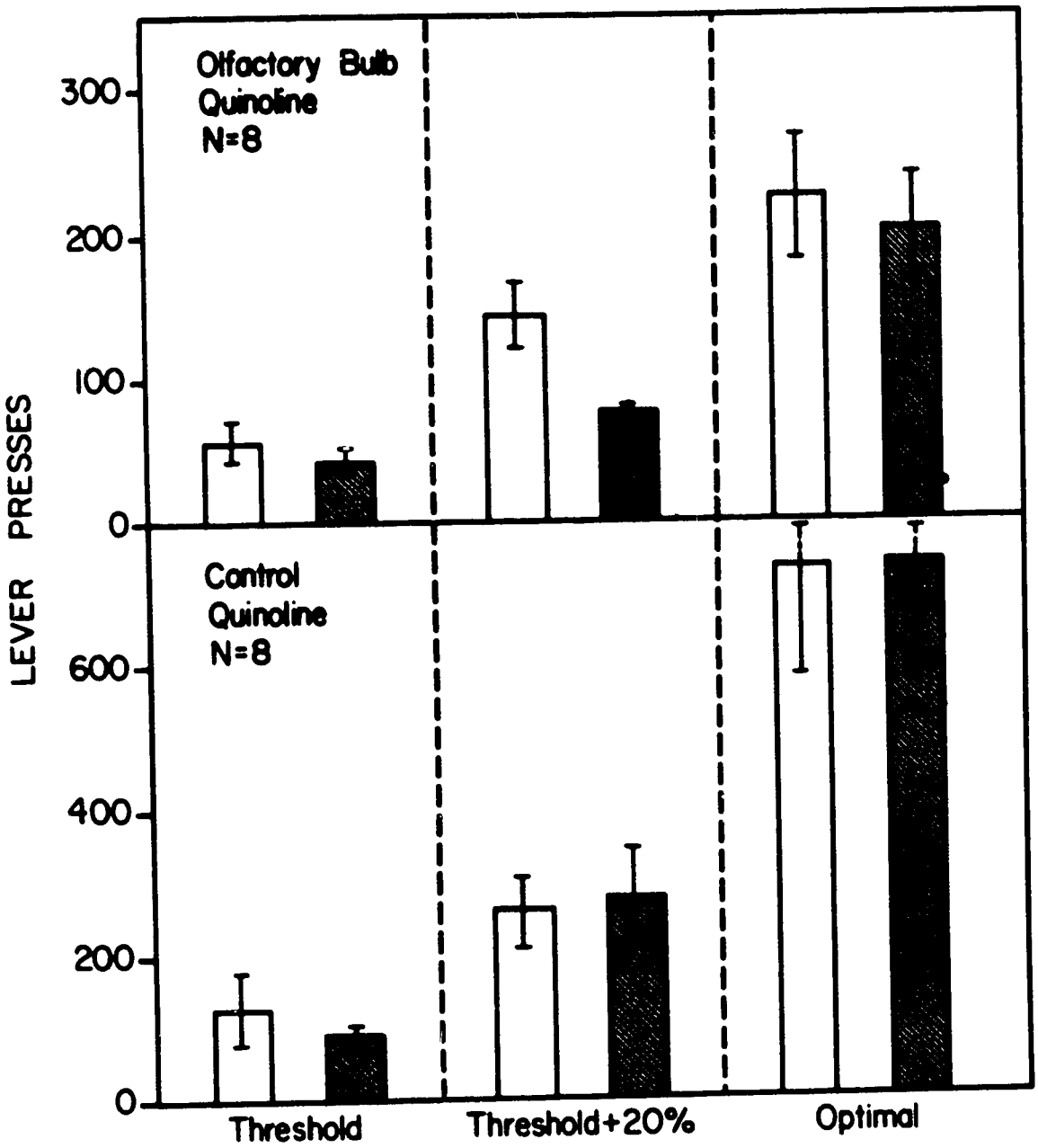

Olfactory Bulb
Quinoline
N=8
Control
Quinoline
N=8
LEVER PRESSES
300
200
100
0
600
400
200
0
Threshold
Threshold+20%
Optimal

FIGURE 5

Two examples of electrode tracts in the olfactory bulb, as shown by sectioning the brain in the saggital plane.

Results

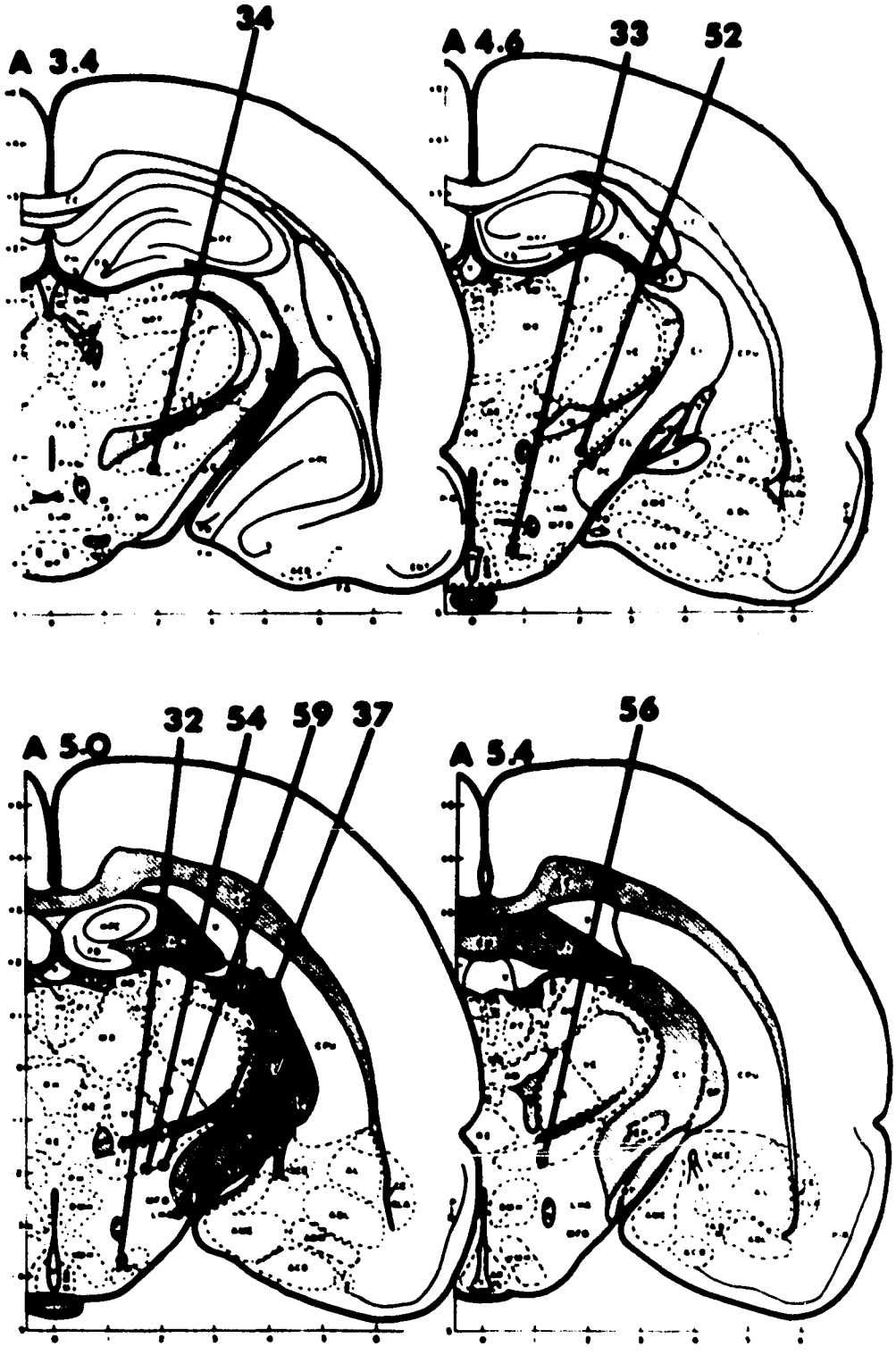
The rates of self-stimulation of the olfactory bulb were reduced by the odour of quinoline at the two lower current intensities. Using a Type 3 analysis of variance (Winer, p.319) a significant odour effect was demonstrated ($F=6.825$, df 1/14, $p < .05$) and a-posteriori t tests revealed significant effects of the odour on olfactory bulb self-stimulation with the minimal current intensity ($t= 2.13$, $p<.05$) and with 20% above the minimal intensity ($t = 2.48$, $p<.025$). No significant change occurred at the optimal current intensity ($t = 1.14$, $p>.05$). Although a large mean decrease in self-stimulation at control sites accompanied the presence of quinoline at the minimal intensity, the difference in means was not significant ($t = 0.90$, $p>.05$) as most of the decrease was accounted for by one S (LH-56.). The odour also had no significant effect on self-stimulation at control sites, at the higher intensity levels.

Histology

Examination of the brains of animals with olfactory bulb electrode implants confirmed that in all cases the electrode had penetrated the bulb. Saggital sections of the brains of two of the Ss (OB-44, OB-48) showing the electrode tracts in the olfactory bulb are presented Figure 5.

FIGURE 6

Schematic presentation of location of electrode tips at control sites in the diencephalon, after de Groot (1959). Experiment 2.


A 3.4
34
A 4.6
33
52
A 5.0
32
54
59
37
A 5.4
56

55

In the nine control animals, six of the electrodes terminated in the ventral region of the zona incerta, two were located in the nucleus premammilaris ventralis and the tip of the remaining electrode was found to be in the far lateral hypothalamus on the edge of the cerebral peduncle. These placements are shown in Figure 6.

Discussion

The augmentation and attenuation of self-stimulation of the olfactory bulb by different odors suggests that the neural structures activated by both odorous substances and electrical stimulation are interrelated. Odors play an important role in initiating, directing and maintaining many important aspects of behavior such as nutrition (Harris, Clay, Hargreaves and Ward, 1931), drinking (Novakova and Diouka, 1960) possibly via osmoreception (Sundsten and Sawyer, 1959; Vance, 1967), and sexual behavior in both male (Beach, 1942; Heimer and Larsson, 1967; Bermant and Taylor, 1969) and female (Whitten, 1956; Bruce, 1960). Certain odors also have intrinsic reinforcing properties that will maintain lever pressing (Long and Tapp, 1967, 1968; Long and Stein, 1969) possibly by activating the same system that has been activated electrically to produce self-stimulation.

One possible explanation of the facilitation effect,

especially with gustatory stimulation is that two rewards become associated with the lever, resulting in higher rates of lever pressing. It is clear, however, that in the present investigation the increase in response rate was not a simple result of the addition of a reinforcing odour. In the first place, the presentation of the odour was not response dependent, and secondly, the increase was evident only with olfactory bulb self-stimulation.

As stated previously, Scott and Pfaffmann (1967) have reported that electrical and natural stimulation of olfactory structures in the rat, produced activity in neurones located in the lateral ventral portion of the MFB. All of the diencephalic placements in the present study were located some distance from this site and were presumably uninfluenced by activity in the olfactory system. Electrodes located in this region would be expected to elicit self-stimulation, and consequently odours would be expected to influence self-stimulation although the parameters of the electrical stimulation remained constant.

One might question whether the continuous presence of a strong odour produces habituation or fatigue of sensory receptors, thus influencing the results. Contrary to popular opinion, the olfactory receptor has been

shown to adapt relatively slowly. Adrian (1950) has presented evidence that the activity in the mitral cells of the rabbit olfactory bulb show little change in their firing rate after more than one hour of stimulation. This finding has received additional support from the work of Ottoson (1956) who showed that recordings of the receptor response of the sensory mucosa exhibited a decline from its initial peak to a level that remained constant for the rest of the stimulation. The exposure time of 10 min. used in the present experiments lies well within these limits and eliminates receptor fatigue as source of artifact.

Although no attempt was made in these experiments to measure the physiological changes that accompanied the presentation of the different odours, there is electrophysiological evidence that odours, including amyl acetate and peppermint, can increase the level of neuronal activity in the olfactory bulbs (Adrian, 1950; Mozell, 1958). This increased activity could render the electrical stimulus more effective by enabling it to activate a greater number of neurones. The effect would be equivalent to that produced by an increase in current. This would only be expected at less than optimal current settings since at an optimal current intensity level the self-stimulation rate should plateau and a further

increase in neuronal activity would not be expected to produce an increment in rate.

In regard to the decrease in self-stimulation rate produced by malodorous substances, there is evidence of a centrifugal system that exerts an inhibitory effect on both spontaneous activity in the bulb and its responses to olfactory stimuli (Kerr and Hagbarth, 1955; Dennis and Kerr, 1968). If a decrease in olfactory bulb activity accompanies the presence of quinoline (it must be emphasized that at present, there is no evidence for this), ther an electrical stimulus would be expected to be less effective and consequently produce a lowering of self-stimulation rate. The fact that malodorous substances do not produce a significant decrease in self-stimulation rate at the highest intensity is likely to be related to the relatively low sensitivity at this region of the response rate-stimulus intensity curve.

It is also known that bulbar activity may be affected by activation of the trigeminal nerve (Beidler, 1965; Tucker, 1963) especially when the odor is highly noxious (Parker and Stabler, 1913). Stone, Williams and Carragal (1968) have shown that blocking the trigeminal nerve significantly increases the frequency and amplitude of olfactory bulb activity and claim that the trigeminal nerve plays an important role in central regulatory

control of olfactory afferent inputs. In light of this evidence, possible trigeminal influences on olfactory bulb self-stimulation cannot be ruled out.

EXPERIMENT III: CHANGES IN SELF-STIMULATION PREFERENCE AS A FUNCTION OF THE INCENTIVE VALUE OF ALTERNATIVE REWARDS.

Although it may be argued from the results of the preceeding experiments that conventional reinforcers and reinforcing brain stimulation are subserved by the same neural pathways, the finding that brain stimulation is preferred to natural rewards (Routtenberg and Lindy, 1965; Spies,1965) suggests a qualitative difference between them. Perhaps this difference reflects the ease with which the incentive value of reinforcing brain stimulation can be changed, as compared to natural rewards. Once the electrode is in the appropriate location, this can be accomplished simply by manipulating the parameters of electrical stimulation. With natural reinforcers the procedure is more difficult and may involve the manipulation of more than one dimension such as quantity, quality, or delay in presentation.

Electrical stimulation of the LH, using currents of optimal intensity is preferred to conventional peripheral rewards such as food (Routtenberg and Lindy,1965; Spies, 1965) or water (Falk, 1961; Morgan and Mogenson, 1966) even after extended periods of food or water

deprivation. It must be emphasized that the parameters of electrical stimulation used in those studies were carefully selected to ensure very high lever pressing rates, whereas the alternative reinforcements were simply dry pellets and plain tap water with presumably less incentive value than the brain stimulation.

The present experiment was concerned with the question of whether animals would still prefer self-stimulation of the LH when the peripheral reinforcer was made more palatable. Rats deprived of food and water had as the alternative to hypothalamic stimulation, water, saccharine solution, sucrose solution, or a solution of saccharine mixed with glucose.

Method

Subjects: The Ss were 24 male Wistar rats weighing between 250-375 gm.

Apparatus: The Ss were tested for their preference between self-stimulation and liquid reinforcers, in a Plexiglass chamber (50 cm.x 50 cm.x 30 cm.) with two levers (Lehigh Valley Electronics Model 1535) located 6 in. apart, protruding through the back wall. The levers could be wired to deliver either reward. Pressing one lever activated a constant current stimulator operated from a 110 ac line, which delivered 60 cps sine wave stimulation to the S. Stimulus train duration was regulated

by an interval timer (Hunter Manufacturing Co., Model 100C) and the number of lever presses was recorded by an impulse counter (Sodeco, Model TCe24E) connected to the terminals of the Hunter timer. Depression of the other lever activated a liquid pump (Davis Scientific Instruments, Model LR-131) which was calibrated to deliver .01 ml. of liquid into a Plexiglass dish located beside the lever. The number of times the liquid pump was activated was also recorded by an impulse counter.

Provision was also made for recording the amount of time spent at each lever. A 6 volt light was located in a wooden tower (5 cm. x 5 cm. x 50 cm.) attached to the back wall, midway between the two levers. A small hole in the tower 1.5 cm. from the back wall, and 5 cm. above the floor, passed a beam of light which was intercepted by two photocells (Hunter, Model 31) located in the side walls of the chamber. The photo cells were connected to photo contact relays (Hunter, model 330) which in turn activated two Hunter Klock Kounters (Model 120A), recording the total amount of time that the photobeams were broken.

Solutions: The three solutions employed in these experiments were prepared every second day in the following manner. Four gm. of sodium saccharine were added to 996 ml. of distilled water, to provide a 0.4% saccharine

solution. The 32% sucrose solution was prepared by adding 320 gm. of sucrose to 680 ml. of hot distilled water, and the mixture was stirred until all the sucrose had dissolved. Each 100 ml. of saccharine-glucose mixture consisted of 0.25 gm. of sodium saccharine and 3 gm. of glucose. All solutions were stored in a refrigerator in air tight bottles.

Surgery: Animals under sodium pentobarbital anaesthesia (50 mg./kg.) had bi-polar electrodes implanted into the LH under stereotaxic control (de Groot: A=5.0-5.5, L = 1.75, V = 2.5) according to the procedure outlined in the General Methods section.

Testing for self-stimulation: Following a seven-day post-operative recovery period, the Ss were tested for self-stimulation in a Plexiglass Skinner box (see General Methods). Each lever press delivered a 0.2 sec. train of stimulation from the constant-current stimulator. Testing for self-stimulation continued for 15 min. per day for seven days until the Ss attained a rate of 20 presses/min. The six Ss which had not reached this criterion after seven days of testing were not retained for further testing. Those Ss which had attained this level were given continued testing to establish the

stimulation intensities that would elicit maximum rates of lever pressing ($\bar{X}$ = 102/min.).

The following procedure was then employed to determine the intensity of electrical stimulation yielding the maximum rate of self-stimulation for each S. On the first day, each S received the stimulus intensity employed during the previous seven days of testing. The intensity was advanced 5μA per day until the self-stimulation rate reached an asymptote, or declined. The current level (40-70μA) giving the maximum response rate was bracketed by 5μA intervals, and then by 2μA intervals to pinpoint the optimal current.

Procedure: One week prior to the beginning of testing, 10 Ss were placed on a 22 hr. food and water deprivation schedule. A divider partitioned the test chamber into two testing areas, and the Ss were trained to lever press for water at each lever. Following the establishment of lever pressing for water, the Ss were permitted to press 10 min. per day for self-stimulation or one of the liquid rewards. According to this schedule, each S was given three days experience pressing for (a) water, (b) a 0.4% saccharine solution, (c) a 32% sucrose solution, and (d) self-stimulation at optimal intensity.

The daily ordering of the different rewards was randomized across the 12 days. To facilitate the identification of the reward delivered by a particular lever,

half of the Ss had a black clue associated with self-stimulation and a white clue with liquid, while the opposite was used with the remaining Ss. This was accomplished by placing black or white bristleboard on the side wall nearest the lever, and on the half of the back wall from which the lever protruded. As the reward delivered by a particular lever changed, so did the colour associated with it. Position bias was controlled by delivering each liquid on the right for two trials, and on the left for the other two trials.

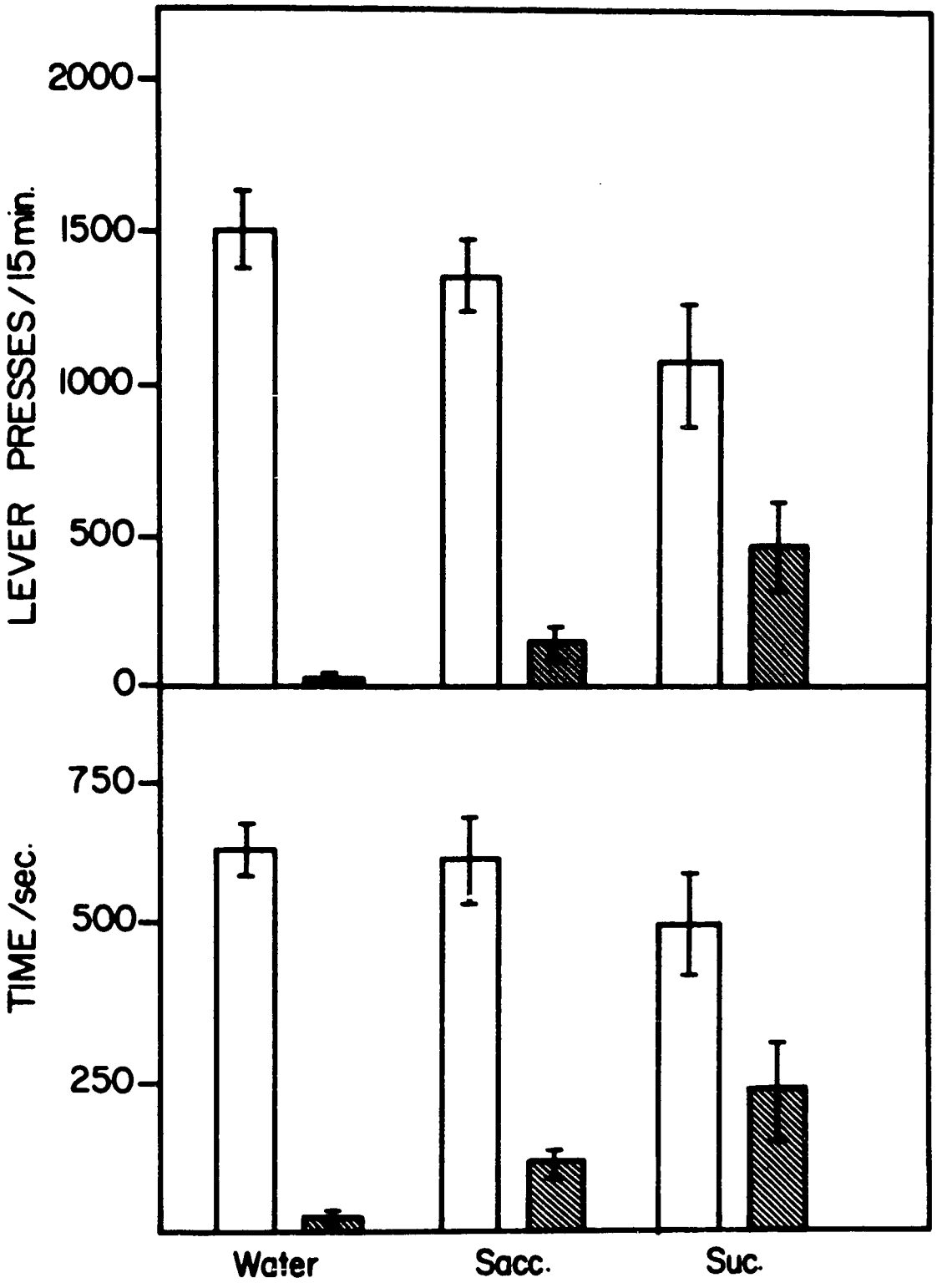
During the next 12 days, the Ss were given the opportunity to choose between self-stimulation and the liquid rewards for 15 min. daily. Each liquid was paired with self-stimulation on four occasions according to a random schedule of presentations.

At the beginning of each daily session, the S was given separate 30 sec. 'priming' periods with each reward. The two 'priming' periods were followed by a 30 sec. rest period during which the divider between the levers was removed. The S was placed into the test chamber again and the number of lever presses for both self-stimulation and liquid was recorded as was the amount of time spent at each lever.

A second group of 8 Ss was tested in exactly the same manner. Following replication of this procedure, these Ss were tested for four days with self-stimulation

FIGURE 7

Comparison of lever presses (upper panel) for self-stimulation (open column) and water, saccharine and sucrose solutions (shaded columns) and the amount of time spent at each lever (lower panel): Experiment 3, Series I.


2000
1500
1000
500
0
LEVER PRESSES/15min.
750
500
250
TIME/sec.
Water
Sacc.
Suc.

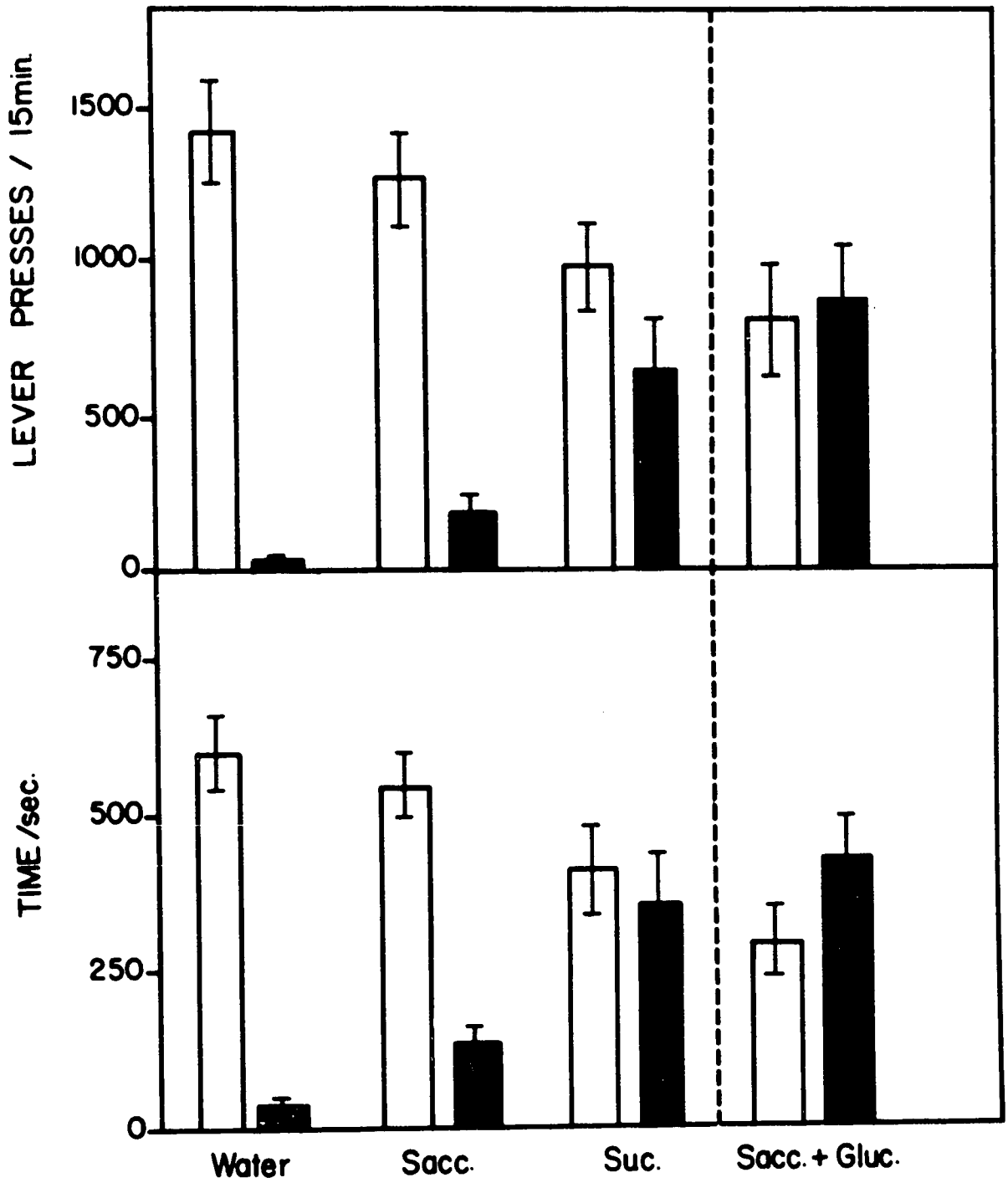
in competition with a very palatable solution of saccharine (.25%) + Glucose (3%) which Valenstein, Cox and Kakolewski (1967) have shown to greatly increase the daily liquid intake in rats.

Results

Series I: The results presented in Figure 7 were analyzed by means of a Type 3 analysis of variance (Winer, p 319) and a significant interaction effect was revealed. More specifically, the type of solution available had a significant effect on the self-stimulation rate ($F=10.62$, $df = 2/18$, $p < .01$). When water and self-stimulation were in competition, the first group of Ss showed a strong preference for self-stimulation, pressing very few times for water ($t = 13.01$, $p < .01$). When saccharine was the alternative there was a slight reduction in the mean self-stimulation rate from 1523 presses in 15 min. with water available, to 1376, but this difference was not significant when tested with an a-posteriori t test ($t = 1.15$, $p > .05$). However, with sucrose solution as the alternative, the mean number of lever presses for self-stimulation was significantly reduced to 1189 ($t = 2.12$, $p < .05$) while the mean number of lever presses for the liquid was significantly increased from 14 presses for water to 441 for sucrose ($t = 3.68$, $p < .01$). In terms of preference

FIGURE 8

Comparison of lever presses (upper panel) for self-stimulation (open column) and water, saccharine, sucrose, and saccharine + glucose solutions (shaded columns) and the amount of time spent at each lever (lower panel): Experiment 3, Series II.


LEVER PRESSES / 15min.
1500
1000
500
0
TIME /sec.
750
500
250
0
Water
Sacc.
Suc.
Sacc. + Gluc.

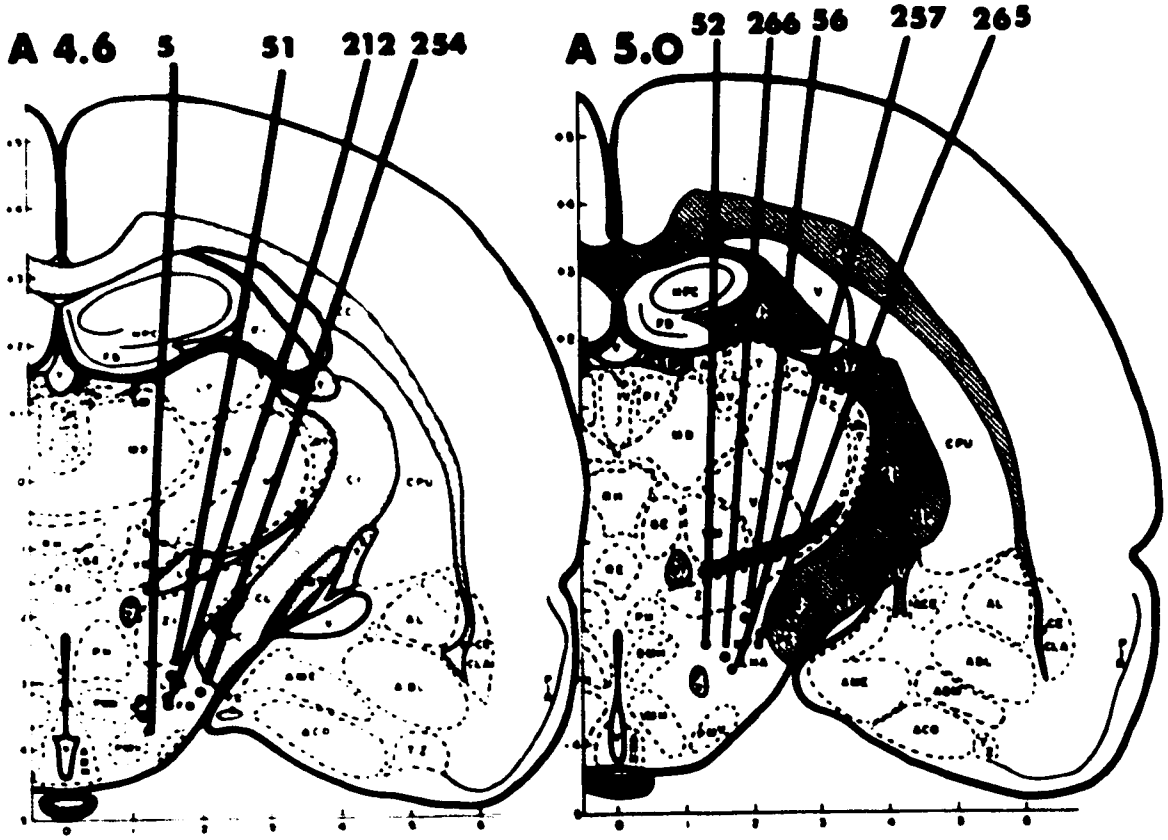
these Ss still pressed significantly more for self-stimulation than for the sucrose solution (t = 6.44, $p < .05$). An analysis of variance and a-posteriori t tests of the time measurements outlined in the lower panel of Figure 7 support the lever pressing data (F = 7.97, df 2/18, $p < .01$).

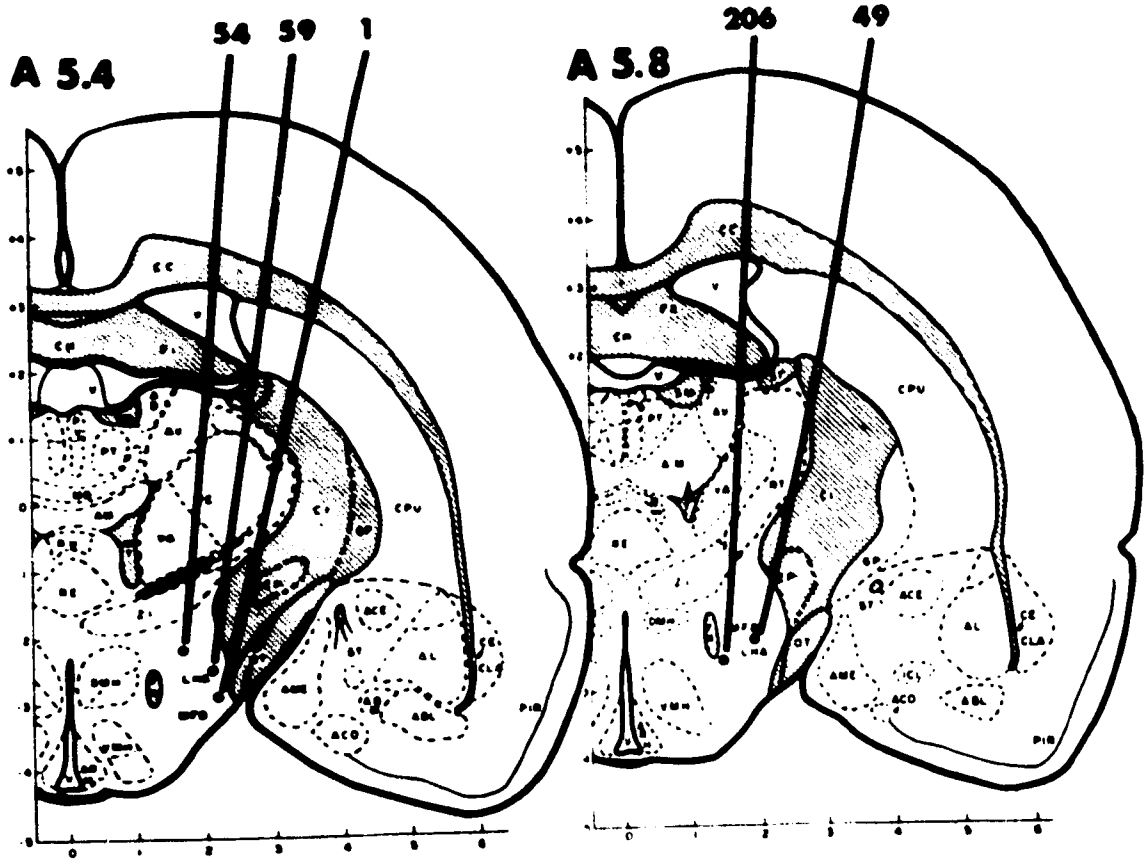
Series II: Almost identical results were observed with the second group of Ss (see Figure 8). A type 3 analysis of variance again revealed a significant interaction effect (F = 18.39, df = 2/14, $p < .01$). A-posteriori t tests detected a significant reduction in self-stimulation when the alternative liquid changed from water to a sucrose solution (t = 3.28, $p < .01$). Saccharine failed to produce a significant reduction in self-stimulation (t = 1.10, $p > .05$). An analysis of the time measurements (F = 18.84, df = 2/14, $p < .01$) and an a-posteriori t test supported the findings that the availability of sucrose produced a significant reduction in self-stimulation (t = 3.10, $p < .05$). In addition, the more sensitive time measurements showed no significant difference between the amount of time spent at the self-stimulation lever and that spent at the sucrose lever (t = 0.81, $p > .05$), revealing an equal preference for self-stimulation and 32% sucrose solution.

The second group of Ss also showed an equal

FIGURE 9

Schematic presentation of location of electrode tips, after de Groot (1959). Experiment 3.


A 4.6
5
51
212
254
A 5.0
52
266
56
257
265


A 5.4
54
59
1
A 5.8
206
49

preference for both brain stimulation and the saccharine + glucose solution ($\underline{t}$ = 1.27, $p > .05$) as determined by the lever pressing data (see Figure 8). There was also no significant difference ($\underline{t}$ = 1.00, $p > .05$) between the amount of time spent at each lever. One S, No. 257, averaged 122 presses/min. for the solution. When this S was subsequently tested for a 60 min. period of lever pressing for saccharine + glucose reinforcement, it made 9833 lever presses, ingesting over 98 ml. of the liquid, further emphasizing the potent reward value of this solution.

Histology

Histological verification of electrode placements was conducted independently by three observers. The brains of four of the Ss were damaged and consequently the sites of stimulation remained undetermined. As seen in Figure 9, the remaining 14 electrodes terminated in the region of the MFB of the LH, between anterior planes 4.6-5.6 according to DeGroot (1959). Two Ss which could be induced to drink by electrical stimulation had electrodes located at the level of the fornix, A- 4.8-5.2, L-1.5, V-8.6 (de Groot,1959) in the LH.

Discussion

As in previous studies comparing the preference for self-stimulation of the LH and natural reinforcements such as food or water (Routtenberg and Lindy, 1965; Spies,

1965; Morgan and Mogenson, 1966), the Ss in the present experiment preferred self-stimulation when water was the alternative, virtually ignoring water during a 15 min. session. When a more reinforcing solution (sucrose or saccharine + glucose) was made available, however, the Ss in Series 1 spent a great deal of time at the sucrose lever and the Ss in Series 2 showed an equal affinity for both self-stimulation and the liquid alternative. These results suggest that statements about a deprived rat's preference for self-stimulation of the LH even to the detriment of its health, must be qualified in terms of the alternatives available.

It has been suggested by Spies (1965) that rewarding stimulation may act as a food or water equivalent by simultaneously mimicking neural feedback such as gustatory and masticatory sensations, gastrointestinal cues, and increased in blood glucose levels that are normally associated with consummatory responses. As compared to food, the ingestion of water, should be accompanied by relatively few consummatory cues, and hence should compete poorly with artificial brain stimulation. Sucrose and the saccharine + glucose solutions should produce many more consummatory cues from activation of taste receptors, glucoreceptors and possibly by way of a direct pathway from the oropharyngeal cavity to the brain (Maller, Kare,

Welt and Behrman, 1967; Kare, Schechter, Grossman and Roth, 1969). It is perhaps for this reason that these solutions are preferred as much as brain stimulation in the competition test.

It is also interesting to note the high rates of lever pressing for the sucrose and the saccharine + glucose solutions. Locating the Plexiglass dish next to the lever permitted simultaneous lever pressing and drinking and as a consequence lever pressing rates of well over 100 presses/min. were obtained. These rates are comparable to the highest rates reported for self-stimulation and are many times higher than the maximum rate of 17/min. of pressing for glucose solution reported by Guttman (1953).

This finding supports the work of Gibson, Reid, Sakai and Porter (1965) who compared the reward of brain stimulation with sugar-water reinforcement. In their experiment, the Ss had to lick a dipper to receive brain stimulation, and thus made the same response for self-stimulation as they did for the solution. When the response requirements for the two rewards were equated, no difference in response rate was reported. In the present series of experiments, the Ss had to press a lever to receive both reinforcements which were delivered instantaneously. As stated above, the proximity of the

dish to the lever in combination with small reinforcements enabled the Ss to press and drink simultaneously. This equated the response for the conventional reinforcement with that normally made for intracranial reinforcement and produced nearly identical response rates for both the palatable saccharine + glucose solution and self-stimulation. Gibson et al (1965) suggested that the reputed difference between intracranial reinforcement and conventional reinforcements are artifacts. Our results would tend to support this conclusion.

Before accepting this view, however, other objections against equating reinforcing brain stimulation and conventional reinforcers, must be considered. These objections are based on differences between the behavior maintained by brain stimulation and extrinsic reinforcers and include: the rapid extinction of lever pressing that follows the termination of the electrical stimulus (Olds, 1955; Seward, Uyeda, and Olds, 1959); the necessity to initiate self-stimulation by delivering several intracranial stimulations at the start of a test session (priming) (Lilly,1958; Olds, 1958c); the difficulty in maintaining self-stimulation when the stimuli are delivered according to long variable interval and high ratio schedules (Gallistel, 1964); a decrement in performance when the first trial of a session is compared to the last trial of the

previous session (Olds,1956); and, the inability to establish secondary reinforcement (Seward, Uyeda and Olds, 1959). On the basis of this list of differences, attempts to argue for similarities between reinforcing brain stimulation and conventional reinforcers seems unwarranted, but a careful survey of the literature reveals that most of these differences can be accounted for.

With respect to the question of rapid extinction, several authors have shown that the rate of extinction for intracranial reinforcement is very similar to extinction of lever pressing for food and water, providing that methodological variables are equated (Herberg,1962, 1963a; Pliskoff, Wright and Hawkins, 1965; Gibson, Reid, Sakai and Porter, 1965). The inability of certain authors to establish secondary reinforcement with subcortical stimulation (Seward, Uyeda and Olds, 1959; Mogenson, 1965) also appears to be due to differences in methodology as others have been successful in this regard (Knott and Clayton, 1966; Gibson, et al, 1965).

Trowill, Panksepp and Gandelman (1969) feel that the most important variable to control in studies comparing behavior maintained by reinforcing brain stimulation and food, is the drive level. They point out that in contrast to experiments using conventional reinforcers, the majority of brain stimulation studies

employ animals maintained with food and water available ad libitum. Di Cara's (1966) finding that secondary reinforcement can be established using brain stimulation as a reward, providing that an appropriate drive level is present, supports the argument of Trowill et al, as do the findings of the present experiment.

A close examination of the literature also reveals that the necessity of "priming" an animal at the start of a test session, and the intersession performance decrement, while well established, applies only in a limited number of cases. The critical variable in this regard appears to be the locus of stimulation. Animals with electrodes terminating in the MFB do not show a performance decrement (Scott, 1965).

Finally, we must consider the evidence that self-stimulation cannot be elicited when the electrical stimulation is delivered on an intermittent schedule of reinforcement. In the first such study, Sidman, Brady, Conrad and Schulman (1955) maintained self-stimulation with a variable interval of 16 sec. and a fixed ratio (FR) of 7:1. According to Gallistel (1964) the largest FR in the literature was reported by Brodie, Moreno, Malis and Boren (1960) who used a very high current to maintain lever pressing at a rate of 150 responses per reinforcement. Even this animal appeared to be an

exception, as four of the eight Ss refused to respond when the FR exceeded 20:1.

This evidence appears quite convincing, but as with the other supposed anomalies, the picture is far from complete. Guinea pigs will work on an FR schedule of 1000:1 and fixed interval schedules of 10 min. (Wolfe, 1966). This behavior compares quite favorably with responses made for "peripheral" reinforcers and supports the findings of Pliskoff, Wright and Hawkins (1965) that rats pressing a lever for access to a self-stimulation lever will maintain lever pressing when the fixed interval is as long as 10 min. and the fixed ratio requiring hundreds of presses.

We may conclude from this and previous evidence that self-stimulation behavior is not markedly different from behavior maintained by extrinsic reinforcement and that it is quite justifiable to conceptualize reinforcing brain stimulation as acting in the same way as conventional reinforcing stimuli. This conclusion is strengthened by additional recent reports of similarities between "central" and 'peripheral' reinforcers. Positive and negative contrast effects have been obtained with hypothalamic reward (Panskepp and Trowill, 1969) and withholding reinforcing brain stimulation produced

frustration as measured by an increase in the rate of responding following non-reinforcement (Merrill,Bromley and Porter, 1969).

GENERAL DISCUSSION

The results of the experiments reported above indicate the importance of sensory input in the process of reinforcement. This view will be given further consideration in the following discussion.

The motor system is probably also involved in reinforcement, although the role of motor events or behavioral responses may not be the exclusive one suggested by Glickman and Schiff (1967). It is not my intention to debate the relative importance of sensory or motor aspects. Rather reinforcement is considered to be subserved by integrative processes with which both sensory and motor systems interact.

Olds (1962), in discussing the possible relationship between reinforcement from brain stimulation and reinforcement from the natural stimulation of peripheral receptors, stated that: "It is by no means clear what actual physiological pathways mediate the effects of primary rewarding stimuli on the self-stimulation area. It is not even proven that these pathways exist..... Therefore a next step should involve physiological and

behavioral studies aimed at finding and defining these pathways." (p.597).

Investigators have been slow to take this step and it is only recently that evidence has been reported which suggests a tentative solution.

Certain stimuli appear to have intrinsic reinforcing properties. For instance, rats perform instrumental responses to obtain non-nutritive substances such as saccharine (Sheffield and Roby, 1950). It has been suggested that the reinforcing effects of such stimuli are mediated via afferent projections from sensory receptors to sub-cortical self-stimulation or reward systems. (Pfaffmann, 1960; Valenstein, 1966). Indirect evidence in support of this proposal has come from experiments in which the induced drinking of a saccharine solution produced a greater enhancement of the rate of self-stimulation of the lateral hypothalamus, (Phillips and Mogenson, 1968; Poschel, 1968) than the induced drinking of tap water (Mogenson and Morgan, 1967).

It has been shown that odours can also be used to reinforce instrumental behavior; rats press a lever to deliver odorized air into a chamber in which they are housed (Long and Tapp, 1967; 1968). Does this occur because nerve impulses are conducted from the olfactory receptors to the reinforcement system that

is activated by electrical stimulation of the LH? Furthermore, does self-stimulation of the olfactory bulb, as reported in Experiment I, occur because the electrical stimulation initiates nerve impulses which also reach the reinforcement system of the forebrain? There is some evidence to suggest that this is, in fact, the case but more definitive experiments remain to be carried out.

Scott and Pfaffmann (1967) identified, in the MFB of the LH of the rat, units responsive to odours and to electrical stimulation of the olfactory bulb. Subsequently Leonard and Scott (1969) demonstrated degeneration of a collection of fibers in the basolateral aspect of the MFB when lesions were made in the olfactory cortex. Perhaps this is the pathway by which the effects of olfactory bulb stimulation, as shown in Experiments I and II, influence the subcortical structures that subserve reinforcement.

According to this view, stimulation of the olfactory bulb is reinforcing because it leads to activity in a general "reward" system that subserves all forms of positive reinforcement. If this were the case, odours should facilitate self-stimulation at all sites in the system. However, the results of Experiment II have shown that odours do not facilitate self-stimulation at diencephalic sites that have no known olfactory function.

Therefore some differentiation appears to exist between sites of self-stimulation.

An alternative to the concept of general "reward" system is the hypothesis that self-stimulation occurs whenever there is activation of a sensory afferent that normally relays the consequences of consummatory behavior, or the site at which this information is integrated with a homeostatic control system. According to this hypothesis, olfactory stimulation is reinforcing because it interacts with an appropriate drive system such as for sexual behavior in the anterior hypothalamus or for food and water intake in the LH. Stimulation of other sensory systems presumably interacts with different drive systems, although it is possible that several sensory systems could interact with a particular drive system to produce reinforcement.

The finding that self-stimulation can be elicited from the periphery of the olfactory system supports this hypothesis. The fact that odours will facilitate self-stimulation of the olfactory bulb, and not of extra-olfactory structures in the diencephalon is also consistent this point of view.

Although not specifically concerned with self-stimulation Bindra's (1968a,b) treatment of reinforce-

ment is similar to that described above. Bindra (1968a) has proposed that "Reinforcing effects arise not from drive reduction or drive induction, but from the interaction of sensory inputs arising from reinforcing (incentive) stimulus objects (e.g. food, water, sexual partner) and the corresponding drive state" (p.72). The facilitation of self-stimulation by taste (Phillips and Mogenson,1968) and odour (Experiment II) clearly supports this point of view.

This emphasis on the role of sensory stimuli in reinforcement parallels the recent trend to describe the behavioral effects of self-stimulation in terms of incentive motivation. Incentive motivation may be defined as the motivational effects brought about by the anticipation of reinforcement based on previous experience of the quality, quantity and delay in presentation of the reward (Bolles, 1967).

Trowill, Panksepp and Gandelman (1969) have shown that if experimental conditions such as deprivation state, amount, quality, and delivery of reward are similar, the behavior displayed is the same, regardless of the type of reward used. The finding that rats will display an equal preference for self-stimulation and a highly palatable solution, as shown in Experiment III, is particularly relevant to this point of view. This suggests that a choice is made in terms of the sensory qualities of the

alternative rewards, as would be predicted from a theory of incentive motivation. Evidence that the neural basis of reinforcement involves the interaction of sensory information with the integrating circuits for appetitive behavior, also supports a theoretical concept of reinforcement based on incentive motivation.

SUMMARY AND CONCLUSIONS

The experiments described in the present investigation were designed to test the effects of sensory stimuli on self-stimulation of the brain. This was accomplished in two ways. The first involved the direct facilitation and inhibition of olfactory bulb self-stimulation by odours. The second method was more inferential in that the effects of sensory stimuli were tested by comparing the preference for self-stimulation to solutions that varied in palatability.

It was first shown that self-stimulation could be elicited from the olfactory bulbs, in the periphery of the olfactory system. The effects of pleasant and noxious odours on self-stimulation at sites in the olfactory bulb, and at control sites in the diencephalon were then tested.

The odour of amyl acetate significantly increased self-stimulation of the olfactory bulb from an average of 69/10 min. at threshold current intensities, with no odour, to 188/10 min. An increase also occurred at intensities set at 20% above threshold. i.e., 135/10 min. to 167/10 min. No increase occurred at optimal intensi-

ties and the odor had no effect at control sites.

The odor of peppermint was shown to have similar effects on self-stimulation of the olfactory bulb, and at control sites outside the olfactory system. At threshold, the olfactory bulb self-stimulation rate increased from 109 to 151 and at intensities 20% above threshold,it increased from 141 to 220.

Malodorous quinoline had the opposite effects on olfactory bulb self-stimulation, but no effects at control sites. The rate decreased from a mean of 58/10 min. to 41, at threshold and from 136 to 77 at 20% above threshold. No effect occurred at the optimal intensity.

These results suggest that pleasant olfactory stimuli are capable of enhancing the neuronal activity in the region of the stimulating electrode. From this it may be implied that self-stimulation of the olfactory bulb accompanies the activation pathways normally excited by reinforcing odors.

In the preference experiment, two series of food and water deprived rats were tested with self-stimulation in competition with water, saccharine and sucrose solutions. The second series was also tested with a highly palatable solution of saccharine + glucose. The number of lever presses for each reward, and the amount

of time spent at each lever were measured.

When water was in competition with self-stimulation, the rats in the second series pressed only 145 times for water as opposed to a mean of 1412 for brain stimulation. As the palatability of the alternative solution increased so did the amount of pressing for the solution. When saccharine + glucose solution was the alternative to self-stimulation, the rats displayed an equal preference for both rewards.

As a result of this experiment, it appears as though choice is based on the sensory qualities of the alternative rewards. This data also supports the idea that reinforcing brain stimulation can have the same effects on behavior as conventional reinforcers, providing that methodological variables are equated.

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APPENDIX A

NEUROANATOMY OF THE OLFACTORY SYSTEM

The olfactory bulb consists of seven layers concentrically arranged around the olfactory ventricle. The incoming fibers from the olfactory mucosa form a complex network over the surface of the bulb. They then turn inward and synapse with the dendrites of the tufted and mitral cells of layers three and four respectively. A spherical structure known as a glomerulus is formed by the numerous incoming nerve endings encroaching on the dendrites of the secondary cells. There is a 1000/1 convergence of olfactory nerve fibers on single olfactory bulb elements at this level as illustrated by Allison and Warwicks (1949) estimation of 25,000 axons entering a given glomerulus as opposed to the dendrites of only 24 mitral and 68 tufted cells, that leave it. As Wenzel and Sieck (1966) point out, this arrangement is similar in all vertebrates and varies little from one phylogenetic class to another.

The axons of the mitral and the tufted cells pass deeper into the bulb where they become myelinated and turn in an antero-posterior plane. Collaterals are given off in the deeper layers of the olfactory formation. It was generally accepted in the literature that the axons to the mitral cells were the main contributors to the lateral olfactory tract, but until recently the connections of the tufted cells were open to specu-

lation. In a recent study, Lohman and Mentink (1969) have concluded that both cell types send their axons into the lateral olfactory tract.

The other main efferent pathway from the bulb is the medial olfactory tract whose main function is in relating the two bulbs by way of the anterior commisure. This influence is mediated indirectly via contributions of the medial olfactory tract to the anterior portion of the olfactory peduncle, which in turn sends fibers to the anterior commisure (Lohman and Lamers, 1961; White,1965). It has been established that this pathway forms the basis for the inhibitory influence of one bulb on the other (Kerr and Hagbarth, 1955).

The main area of distribution of the lateral olfactory tract is the prepyriform and periamygdaloid cortex. Fibers also terminate in the anterior olfactory nucleus, the anterolateral quadrant of the olfactory tubercle, the anterior amygdaloid area and the nucleus of the lateral olfactory tract (Lohman and Lammers, 1963). White (1965) has emphasized that although olfactory input influences the entire olfactory cortex, it appears to effect the rostral portion more than the caudal portion in an "avalanche-like sequence," (p.473). In the same study, evidence was given for projection to the ventral

portion of the lateral entorhinal area.

It is quite difficult to specify the subcortical connections of the olfactory system but in addition to amygdaloid projections, there is evidence that the habenula and the hypothalamus are involved. Powell, Cowan, and Raisman (1965) have demonstrated that lesions in the pre-pyriform cortex led to degeneration in the olfactory tubercle and caudally into the anterior hypothalamus, specifically the lateral preoptic area and the MFB, and also into the lateral amygdala. More recent evidence of olfactory projections to the MFB has been provided by Leonard and Scott (1969). In a degeneration study, they found a compact long axon pathway running from the olfactory peduncle through the LH to the rostral midbrain. It is in these secondary olfactory centers that self-stimulation can be obtained.

APPENDIX B

SUMMARY TABLES OF TYPE 3 ANALYSES OF VARIANCE ON THE EFFECTS OF ODOURS ON SELF-STIMULATION OF OLFACTORY BULB AND CONTROL SITES.

TABLE I

SUMMARY TABLE OF " TYPE 3" ANALYSIS OF VARIANCE ON THE EFFECTS OF AMYL ACETATE ON SELF-STIMULATION OF OLFACTORY BULB AND CONTROL SITES.

SOURCE	SUM OF SQUARES	DF	MEAN SQUARES	F
Between Subjects	2491305.6875	17.		
A = Groups	726684.0781	1.	726684.0781	6.589
Subjects within Groups	1764621.6250	16.	110288.8516	
Within Subjects	5340298.1250	90.		
B = Intensity	2310037.9063	2.	1155018.9531	28.590
AB	1421683.7188	2.	710841.8594	17.596
BX Subjects	1292759.0313	32.	40398.7197	
C = Odour	13940.0833	1.	13940.0833	2.813
AC	17505.7869	1.	17505.7869	3.533
CX - Subjects	79276.9629	16.	4954.8102	
BC	10761.7222	2.	5380.8611	0.967
ABC	16279.2407	2.	8139.6204	1.463
BCX Subjects	178053.7031	32.	5564.1784	
Total	7831603.8750	107.		

TABLE II

SUMMARY TABLE OF "TYPE 3" ANALYSIS OF VARIANCE ON THE EFFECTS OF PEPPERMINT ON SELF-STIMULATION OF OLFACTORY BULB AND CONTROL SITES.

SOURCE	SUM OF SQUARES	DF	MEAN SQUARES	F
Between Subjects	1031328.4844	15.		
A = Groups	27101.3906	1.	27101.3906	0.378
Subjects within Groups	1004227.0938	14.	71730.5057	
Within Subjects	655793.2500	48.		
B = Intensity	116536.8906	1.	116536.8906	3.711
AB	19705.1406	1.	19705.1406	0.628
BX Subjects	439614.7188	14.	31401.0513	
C = Odour	17589.3906	1.	17589.3906	8.756
AC	11637.0156	1.	11637.0156	5.793
CX Subjects	28123.3438	14.	2008.8103	
BC	1181. 6406	1.	1181.6406	0.834
ABC	1570.1406	1.	1461.7835	
BCX Subjects	19834.9688	14.		
Total	1687121.7344	63.		

TABLE III

SUMMARY TABLE OF "TYPE" 3 ANALYSIS OF VARIANCE ON THE EFFECTS OF QUINOLINE ON SELF-STIMULATION OF OLFACTORY BULB AND CONTROL SITES.

SOURCE	SUM OF SQUARES	DF	MEAN SQUARES	F
Between Subjects	3834700.6250	15.		
A = Groups	1527121.5000	1.	1527121.5000	9.265
Subjects within Groups	2307579.1250	14.	164827.0801	
Within Subjects	5686560.0000	80.		
B = Intensity	2719444.0000	2.	1359722.0000	20.164
AB	958959.7500	2.	479479.8750	7.110
BX Subjects	1888136.2500	28.	67433.4375	
C = Odour	9560.0416	1.	9560.0416	6.825
AC	3800.1667	1.	3800.1667	2.713
CX Subjects	19609.7915	14.	1400.6994	
BC	1223.0833	2.	611.5417	0.223
ABC	8889.0833	2.	4444.5416	1.618
BC Subjects	76937.8330	28.	2747.7798	
Total	9521260.6250	95.		

APPENDIX C

SUMMARY TABLES OF TYPE 3 ANALYSIS OF VARIANCE OF LEVER PRESSING DATA, AND TIME MEASUREMENT DATA FROM EXPERIMENT III.

TABLE I

SUMMARY TABLES OF ANALYSIS OF VARIANCE SERIES I: EXPERIMENT III.

(A) LEVER PRESSES (B) TIME MEASUREMENTS

SOURCE	SUM OF SQUARES	DF	MEAN SQUARES	F
(A)				
Between Subjects	1998469.0000	9.		
Within Subjects	29920675.2500	50.		
B = Alternatives	20144579.2500	1.	20144579.2500	26.520
BX Subjects	6836503.3750	9.	759611.4844	
C = Solutions	38641.6330	2.	19320.8167	1.445
CX Subjects	240595.6992	18.	13366.4277	
BC	1440105.6250	2.	720052.8125	10.622
BCX Subjects	1220249.6875	18.	67791.6494	
Total	31919144.2500	59.		
(B)				
Between Subjects	53393.8145	8.		
Within Subjects	4417387.6250	45.		
B = Alternatives	2919502.5000	1.	2919502.5000	21.302
BX Subjects	1096399.8125	8.	137049.9766	
C = Solutions	22483.8147	2.	11241.9073	9.169
CX Subjects	19617.8518	16.	1226.1157	
BC	279631.3672	2.	139815.6836	7.997
BCX Subjects	279752.2930	16.	17484.5183	
Total	4670781.4375	53.		

TABLE II

SUMMARY TABLES OF ANALYSIS OF VARIANCE SERIES 2: EXPERIMENT III.

(A) LEVER PRESSES (B) TIME MEASUREMENTS

SOURCE	SUM OF SQUARES	DF	MEAN SQUARES	F
(A)				
Between Subjects	1435226.3281	7.		
Within Subjects	18424480.2500	40.		
B = Alternatives	10757920.2500	1.	10757920.2500	18.158
BX Subjects	4147218.6563	7.	592459.8047	
C = Solutions	115638.5410	2.	57819.2705	2.530
CX Subjects	320001.7891	14.	22857.2708	
BC	2233596.7813	2.	1116789.3906	18.392
BCX Subjects	850104.2031	14.	60721.7290	
Total	19859706.5000	47.		
(B)				
Between Subjects	53991.3330	7.		
Within Subjects	2972424.6563	40.		
B=Alternatives	1414533.3281	1.	1414533.3281	13.000
BX Subjects	761694.0000	7.	108813.4277	
C=Solutions	37107.8750	2.	18533.9375	8.228
CX Subjects	31569.7915	14.	2254.9851	
BC	530476.0391	2.	265238.0195	18.845
BCX Subjects	197043.6250	14.	14074.5446	
Total	3026416.0000	47.		

APPENDIX D

ABSOLUTE VALUES OF DATA PRESENTED IN FIGURES 2,3,4,7,8

TABLE I

ABSOLUTE VALUES OF DATA PRESENTED IN FIGURES 2,3,4.

Electrode Placement	Current Intensity	Self-Stimulation Rate No Odour	Odour
Figure 2. Amyl Acetate			
Olfactory Bulb	Threshold	69 ± 15.2	188 ± 67.0
	Threshold + 20%	135 ± 31.8	167 ± 35.7
	Optimal	198 ± 37.1	203 ± 39.6
Control	Threshold	78 ± 16.6	68 ± 19.8
	Threshold + 20%	210 ± 60.0	214 ± 45.6
	Optimal	684 ±118.4	681 ±124.4
Figure 3 Peppermint			
Olfactory Bulb	Threshold	109 ± 26.0	151 ± 23.9
	Threshold + 20%	141 ± 34.2	220 ± 54.2
	Optimal		
Control	Threshold	133 ± 22.1	140 ± 21.0
	Threshold + 20%	255 ± 91.7	259 ± 96.4
	Optimal		
Figure 4 Quinoline			
Olfactory Bulb	Threshold	58 ± 13.0	41 ± 10.0
	Threshold + 20%	136 ± 22.8	77 ± 18.2
	Optimal	226 ± 41.0	203 ± 38.5
Control	Threshold	132 ± 50.7	94 ± 18.5
	Threshold + 20%	263 ± 75.0	278 ± 94.2
	Optimal	743 ±153.5	744 ±151.7

TABLE 2

ABSOLUTE VALUES OF DATA PRESENTED IN FIGURES 7 and 8.

Series 1

	Lever Presses $\bar{X}$	Sem	Time $\bar{X}$	Sem
Self-stimulation	1523	± 157	644	± 39
vs				
Water	13	± 8	18	± 8
Self-stimulation	1377	± 143	611	± 63
vs				
Saccharine	145	± 43	118	± 47
Self-stimulation	1189	± 210	518	± 80
vs	441	± 130		
Sucrose			242	± 77

Series 2

Self-stimulation	1412	± 142	601	± 50
vs				
Water	32	± 15	43	± 15
Self-stimulation	1285	± 145	553	± 55
vs				
Saccharine	195	± 60	140	± 37
Self-stimulation	1017	± 146	418	± 73
vs				
Sucrose	656	± 170	360	± 79
Self-stimulation	839	± 185	298	± 29
vs				
Saccharine + Glucose	889	± 179	433	± 34