Brain Stimulation
and the Motivation of Behavior

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INTRODUCTION: REWARD AND ATTENTION PROCESSES
IN LEARNING

Twenty-five years ago when I entered psychology, American learning theorists were polarized about an argument that was at the crux of things. The question was: "how do motives work?". Why does the animal "come back for more"? Stimulus-response theory, exemplified in the writings of Hull (1943), said that reward "stamped in" a connection between stimuli and responses at the time of its original occurrence. Later the animal came back for more because it couldn't help it; the stamped-in connections forced him to do so. Cognitive theory as expressed by its champion, Tolman (1949), put more emphasis on the information processing that went on subsequently, at the time the animal was deciding whether or not to go back. On the first occurrence, during learning, the animal learned where things were and how they "tasted". These events were recorded; to me it seemed they were taken down as if on a tape recorder. Later, the animal played back its tapes, vicariously at first. If it found something it liked on one of the tapes, it would play it back a second time "for real". Thus, for Tolman, remembered reward did the main job, and it worked by triggering behaviors under specific conditions. For Hull, on the other hand, reward was a connector.

For Tolman, reward was not a connector but of course there was still the problem of connecting. In Hull's model, reward caused connecting of stimuli and responses. In Tolman's model, everything that happened caused the stimuli involved to be connected in some way to a "memory" and this memory to become connected to responses (so it could reproduce them). Did happenings by itself cause the connecting? Tolman and his disciples had some misgivings about the idea that happening by itself was enough. Only things that were "attended to" got remembered. This was either by planned, careful, advance attention, or, by looking back after a surprise (a person could recover some of the immediate past out of a temporary store which it had got into even without attention, and could then promote it to be an object of attention). Only events that had some special salience caused by attention, and maybe only some special subset of these, became connected to longer-lasting memories. Thus,
reward was displaced from the role of connector, and attention was introduced to perform that task.

After being displaced, however, reward was still not completely disentangled from the problem of learning. This was because a reward had to be attended to, and it had to become connected in order to be an effective reward. Because the animal could not learn without attention, it also could not be rewarded without attention. This made the connector a sine qua non of reward, and thus in one sense a part of the reward, even though the reward was not a part of the connector. The animal could attend and learn without being rewarded, although of course it could not be rewarded without attending. This clarified a way in which features and aspects not identified with reward itself could be essential ingredients of it. For this reason, in electrophysiological recording experiments many candidates for "reward neuron" status had to be inspected carefully, lest they performed this closely correlated and prerequisite function, but were really only related in a tangential fashion to the reward process itself.

A different way a tangential action could be sine qua non without being an actual part of a rewarding effect comes to light from an analysis of incompatible emotional states. It is reasonable to suppose some reciprocal antagonism of positive and negative emotional conditions. A happy day can be spoiled by a major hurt, and extremes of pleasure and pain seem subjectively to be largely incompatible. If there were central sources of negative and positive emotions, anything which inhibited one might promote the other, while any substantial disinhibition of one might counteract the other. Thus, if a neurochemical substance held in check an important central source of negative emotion, it might seem a sine qua non of reward even if it had nothing directly to do with it.

In the present paper, a search is made for a set of reward neurons among what is fortunately still a rather small number of candidates. These include subsets of noradrenaline neurons, of dopamine neurons, and also of inter-neurons of the gustatory-olfactory sensory system. Both noradrenaline and dopamine neurons seem from some experiments to be strong candidates, but both come under the question of whether they might instead be tangentially related in one of the two ways mentioned above. Either of them might be involved in connecting and learning, or else in the suppressive control of negative emotional states or depressions.

My guess at the end is that both may in fact be involved directly in different reward processes. Noradrenaline neurons might inhibit aversive drive states or negative emotions; and reward the animal in this way. Dopamine neurons might act similarly on drive states that did not have any negative tone; and hedonic states might be the correlate of this action. If it worked this way, then noradrenaline would directly reward the animal when the main problem came from aversive drives; but it could also be secondarily involved at other times, keeping negative emotions in check to make hedonic behavior possible.

Data from a number of brain experiments seemed at first to have relatively direct bearing on central questions of motivation, particularly those related to the steering of behavior toward some things and away from others, and the role of rewards and drives in the problem of learning. The brain experiments promised interesting advances just over the horizon, but so far they have only
added to the puzzles. Considerable thought is still needed to get a sensible thread of meaning from them and to decipher some of the most tractable directions they point toward further understanding. I want to set the outlines of this data on the table and try again to follow some of the best leads*.

BRAIN STIMULATION

The first body of data came from electric stimulation of the brain in behaving animals. Experiments employing this method have resulted in a map of brain locations where electric stimulation caused animals to behave as if the stimulus itself were the goal object of an active drive, or caused a condition so hedonically gratifying that no drive was necessary to get behavior going (Olds, 1962). These abnormal brain rewards motivated not only pedal behavior but also maze running and the crossing of aversive obstructions (Fig. 1).

Rats, cats and monkeys had much the same map (Fig. 2). Even humans would perform nonsense tasks apparently in order to stimulate analogous brain centers, although they often seemed confused as to why they were doing so. In

![Fig. 1. Behaviors motivated by application of electric stimulation in the medial forebrain bundle after each pedal response (0.25 sec trains, 60 Hz alternating current, 50 mA r.m.s.). In the maze and the obstruction box, three pedal responses were rewarded at one pedal and then the animal was required to shuttle to the other for three more, and so forth. In the obstruction box, current of about 60 mA applied through the grid floor stopped hungry rats running for food and these also stopped rats running for 50 mA brain stimuli. However, when the brain “reward” was increased to 200 mA these animals crossed obstructions applying more than 400 mA to the feet.]

* To do this I shall review work in which I personally participated on: (1) behavioral features of “brain reward”, and (2) “unit responses” of hypothalamic neurons, along with work of others on: (3) stimulation and lesions affecting basic drive behavior, and (4) the amine neurotransmitters and their maps.
the rat, the olfactory bulb and much of the floor of the brain connected to it were implicated as areas where stimulation was rewarding.

On the floor of the rat brain a large central region is occupied by the hypothalamus. The borders are its outposts, some of which are in the olfactory parts of the forebrain. Others are located more caudally in the brain. Through the posterior hypothalamic area come sensory messages originating in the

![RAT, Olds & Olds 1963](image)

![CAT, Wilkinson & Peele 1963](image)

![HUMAN, Bishop, Elder & Heath 1963](image)

![MONKEY, Burstyn & Delgado 1958](image)

Fig. 2. Schematic pictures of the parts of the brain yielding brain reward behavior in different species. The map for the rat has been done carefully. Those of other species are estimated from a smaller number of tests, with extrapolation based on anatomical analogies. The marked areas in the brains yielded brain-reward effects. Listed in order from largest to smallest effects they are: (1) large cross hatching = medial forebrain bundle; (2) blackened areas = olfactory bulbs and anterior olfactory areas; (3) small cross hatching = amygdala, septal area, and stria terminalis; and (4) grey areas = “Papez circuit”.

visceral and gustatory receptors. In addition, hormonal messages from the circulation pass directly into the hypothalamus through blood-brain windows.

The reward map covered most of the hypothalamus and neighboring areas (Fig. 3). Within the hypothalamus the map extended from far-anterior to far-posterior, and from far-lateral to the midline. A paradox of the reward map was that this same region was also the locus of aversive effects of electric stimulation (Roberts, 1958). If opposed aversive effects were not immediately obvious, they could usually be demonstrated by careful behavioral analysis. Because the whole hypothalamus was covered by a reward map, while aversive countereffects were also always in evidence, you might suppose that the
Fig. 3. A more detailed map of main areas in the rat brain yielding reward and escape behavior.

The hypothalamus was homogeneous with respect to these maps. It proved not to be.

In the far-lateral parts of the hypothalamus, and in some parts of the far-medial hypothalamus, there were locations where the rewarding effects of stimulation predominated. In these cases the animal was apparently at ease with the self-stimulation. No obvious negative signs were seen during brain pedal behavior, so that careful methods were required to reveal them.

In a large intermediate area there was an obvious mixture of positive and negative effects. The animal would pedal regularly and fast if closeted with an electric stimulus, but if there was a way out it would escape at once. There was no amount of stimulation in these areas that seemed just right. The animal behaved as if it could not stand the stimulation but could not resist it either (Olds and Olds, 1963).

Fig. 4. Map of areas in rat brain yielding instrumental and consummatory behaviors aimed at different drive-object targets.
In this same intermediate area a second paradox of the reward maps was found: the same electric stimulus often provoked drives as well as rewards. The drives depended partly on the location of the stimulus (Fig. 4). With probes implanted in anterior hypothalamus there were both sex responses and responses that adjusted the body temperature (Roberts et al., 1967). In the anterior part of the middle hypothalamus there were both eating and drinking responses, but the drinking responses predominated. In the posterior part of the middle hypothalamus there were still more eating and drinking responses, but here it was the eating response which predominated (Valenstein et al., 1970). In the posterior part of the hypothalamus sex responses were again evoked (Herberg, 1963). Because there were many overlapping effects, and sex responses were evoked in areas on both sides of the feeding and drinking areas, the idea of sharp localizations was rejected. But because this area could be mapped into four contiguous regions where stimulation caused, respectively, temperature, drinking, eating and sexual behavior as the most likely responses, the idea of totally unlocalized drive systems was equally rejected. The truth obviously lay somewhere in between.

One feature of the "in between" answer was discovered. The goal objects of the "drives" caused by these stimulations were often changed by training. If the animal was stimulated regularly in the presence of a drive object, after a while the stimulus began to evoke an appropriate drive, that is one with the

Fig. 5. Valenstein effect: modification of drive-object by training (Valenstein et al., 1968). Prior to "training" the electric brain stimulus caused at first little drive behavior and then, after some repetition of the stimulus in the presence of food and water, the stimulus evoked feeding. Then after a long period of stimulation in the presence of water only, the electric stimulus evoked drinking.
available drive object as its target (Fig. 5). In one test, for example, probes were placed in what originally seemed to be a feeding point (i.e., the stimulation evoked feeding as opposed to drinking in original choice tests). Then with only water present, 30-sec trains of stimulation were applied every 5 min for many days. Under the impetus of this the feeding point changed, so that in the end it had become a drinking point! This can be called the Valenstein effect after its discoverer (Valenstein et al., 1968).

Because drives were mapped into different areas of the brain to begin with it seemed strange that they could be modified by training. One possible answer to this puzzle was that a family of drive neurons might be initially related to a specific drive by their sensitivity to particular visceral inputs or to particular hormones, but their outputs might become functionally connected during development or learning to appropriate drive objects. The Valenstein effect might be evidence that electric stimulation could interfere with this normal learning mechanism. It is possible to assume that the stimulus was applied in a “hunger center” but that gradually the training artificially caused the animal to respond as if the water were a hunger drive object.

To recapitulate the picture developed by hypothalamic stimulation: there were far-lateral and far-medial areas where reward predominated, plus in-between areas where aversive effects and drive effects were overlapped with reward.

LESIONS

A second body of data came from restricted destruction of small and deep “brain centers”. These studies have divided the hypothalamus and neighboring structures into a focus where lesions had one kind of effect, and a set of three surrounding areas where different kinds of opposed effects were observed (Fig. 6). Anatomically, the focus was the same lateral hypothalamus where electric stimulation had produced predominantly positive effects. It included also the boundary regions of the hypothalamus: among these the substantia nigra is one we will be most interested in later on. Lesions in lateral hypothalamus or along its boundary regions caused a loss of positive drive-reward behaviors and other operant behaviors (even ones aimed at avoiding noxious stimulation; Teitelbaum and Epstein, 1962; Balinska, 1968).

If, however, animals were kept alive for a few days after these lesions there was often good recovery of some of the reward behaviors. Animals died if not force-fed at first but they recovered in 1–3 weeks if kept alive by force-feeding or other methods. After recovery the animals were dependent in a surprising way on the cortex for drive behavior (Teitelbaum and Cytwara, 1965). This was shown by application of KCl to the cortex, which causes in normals a 4–8 hr period during which all instrumental behavior is abolished (and abnormal electric activity is recorded from the head). This treatment may be thought of as causing a temporary shut-down of cortical function and, in normals, there appeared to be essentially full recovery after several hours. In animals with functional recovery from lateral hypothalamic lesions, on the other hand, the same KCl application to the cortex had a much more devastating effect, causing
the full 3 week recovery period to need redoing. This dependence of drive behavior upon cortical integrity after lateral hypothalamic damage suggests that recovery was in fact not really complete.

There were other signs pointing in the same direction. The experimental animals, after recovery from lesioning, did not respond to cellular water deficits by drinking, but drank only to wet their mouths (Teitelbaum and Epstein, 1972). Similarly, they did not respond to glucose deficits by eating, and also failed to respond appropriately to sodium deficits. With their repertoire of redundant hunger controllers or learned feeding behaviors, however, the animals managed to survive, and even succeeded in looking robust and well-fed. It is conceivable that a learned cortical repertoire of drive behaviors recovered, while a hypothalamic initiator of these drives was gone.

![Diagram of lesions](image)

Fig. 6. Map of lesions in and near the hypothalamus affecting targeted instrumental-approach and consummatory behaviors. In the lateral-hypothalamic substantia nigra focus, lesions halted such behavior temporarily and modified it permanently. In three neighboring areas there were opposed effects. Lesions in medial hypothalamus caused episodes of approach and consummatory behavior aimed at food to occur too frequently. Lesions in the caudate nucleus caused compulsive instrumental behavior aimed at moving "nonsense" objects. Lesions in the amygdaloid region caused attempts to perform consummatory behavior with non-goal objects.

Fitting this view, a most important food learning mechanism was also absent, the animals failing to learn to exclude foods on the basis of poisoning or illness. A normal rat responds to foods that preceded illness as if they were aversive, called the Garcia effect after its discoverer (Garcia and Ervin, 1968). This may be thought of as the learning of aversive reactions to poison, and it disappeared following lateral lesions. In normal rats, there is also learning of special positive reactions to foods that are correlated with recovery from illness, and these learned positive reactions too were gone after lateral lesions (Roth et al., 1973). Because these food-learning phenomena matched the drive-target learning of the Valenstein experiments, it seemed doubly likely that the hypothalamus might be involved in the learning of drive targets: that is, in the learned attachments of animals to objects.

There were three areas surrounding the lateral hypothalamus (LH) where lesions had the opposite effect to LH lesions. The first set of opposed lesions was in the medial hypothalamus, and caused the reverse of starvation. The animals thus ate too often, because the beginning of meals occurred too early (as if no visceral or chemical trigger were needed; Le Magnen et al., 1973).
The second set of opposed lesions was situated in the caudate nucleus. This is a motor center which reciprocally inhibits the substantia nigra. Lesions here caused meaningless instrumental behavior directed at anything that moved (Villalba, 1974). This effect looked as if it might represent the inversion of the loss of pursuit behavior that occurred with lateral hypothalamus lesions.

The third set of opposed lesions was found in the amygdala, an outpost in the olfactory forebrain. These lesions caused consummatory behavior toward dangerous objects or untested foods, or even toward “wrong” objects. For example, there were attempts to eat or mate with, respectively, non-food or non-sex objects (Klüver and Bucy, 1937).

The fact that lesions in a central area stopped reward behaviors, whereas lesions in three surrounding areas caused different kinds of excessive approach behavior, suggests a multiple opponent process system: a central positive region in lateral hypothalamus and substantia nigra inhibiting and being inhibited by three neighboring regions. In such a system a shifting balance of excitation and inhibition would determine the presence or absence of approach behavior, and electric stimulation along the communication links might well have double or mixed effects.

Besides these, another set of lesion studies which is more specifically related to self-stimulation deserves special mention. Many lesions failed to halt this type of behavior; for instance, even the very extensive damage from ablating all of the neocortex, paleocortex and basal ganglia (Huston and Borbély, 1974). Animals with these lesions behaved as if they had lost all nuances of behavior. Gross behaviors such as rearing on the hindlegs could still be reinforced, however. When such behaviors were clearly characterized, they could be greatly increased in frequency by electrical brain rewards. Furthermore, after the reward was withdrawn the behavior showed no signs of extinguishing, leaving the impression that, although the telencephalon was not required for operant learning of gross behavior patterns, it was needed for normal extinction. The only way the response could be suppressed in these animals was to reinforce its opposite. This study has many important implications for questions about why brain reward often extinguishes very rapidly. However, one of the main imports is that at least some of the “reward” neurons do not reside in the front end of the medial forebrain bundle system.

THE BRAIN AMINES

A third body of data came from neurochemical maps showing where certain brain chemicals reside and what neurons and fiber pathways carry them. These maps have identified a set of apparent brain reward neurons, and thus may give the beginnings of an interpretation of brain reward behavior — and possibly the beginnings of an explanation of other reward behaviors as well. Small clumps of neurons in focal centers of the hindbrain, midbrain, and the boundaries of the forebrain send axons which radiate from the focal centers to the farthest reaches (Ungerstedt, 1971a, b). There are several similar clumps and several overlapping sets of diverging fibers. The localized origins and the widely diffusing fibers make these look like command centers that could send YES-NO
messages to the whole brain (Fig. 7). The synaptic transmitters used by these neurons to transmit signals are noradrenaline, dopamine, and serotonin.

The noradrenaline fibers started farthest back and went farthest forward. They ran from a crossroads of the brain in the medulla to all of its outposts: the cerebellum, thalamus, paleocortex and neocortex. The serotonin fibers started in the middle of the midbrain and ran a less well-defined course to many parts of the forebrain. The dopamine fibers started in the rostral part

![Diagram showing three catecholamine fiber systems](image)

**Fig. 7.** Schematic diagram of three catecholamine fiber systems. From the locus coeruleus of the medulla to the cerebellum, hippocampus, and cortex runs the dorsal noradrenaline bundle (dashes). From the ventral midbrain to the olfactory tubercle runs the mesolimbic dopamine system (scrambled markings and cross hatch). From the substantia nigra to the caudate nucleus runs the nigrostriatal dopamine system (black lines). It is questionable whether these last two should be separated; and it is likely that at least one of them runs beyond the diagrammed targets because dopamine is found in the cortex. The raphe-paleocortex serotonin system is not shown: it starts between the noradrenaline and the dopamine systems and runs to the paleocortex (and likely also to parts of the neocortex).

of the midbrain and caudal part of forebrain. They run a shorter course ending mainly in structures below the cortex, i.e., in parts of the extrapyramidal motor system (which might be the main control system for purposive instrumental behavior) and in some poorly understood centers of the olfactory forebrain. Most likely not all of the fibers end at their main subcortical stations, for dopamine itself was found along with noradrenaline in the cortex.
For all of these amine fiber systems one property stood out; namely, there was a restricted source of origin, together with a very wide radius of influence. The noradrenaline, serotonin, and dopamine systems thus suggest a central triad of command stations deep within the brain.

These fibers pervaded the drive-reward systems in such a way as to match the drive-reward maps (German and Bowden, 1974). New maps based on the theory that these were reward neurons showed new rewarding locations that tracked the noradrenaline pathway toward the medulla, and the dopamine pathway towards the substantia nigra (Fig. 3; Crow, 1971; Ritter and Stein, 1973). While stimulation at the sources of the two different catecholamines both appeared to be rewarding, some interesting differences appeared. When stimulation was applied at the source of the noradrenaline system in locus coeruleus, the behavior caused was quiet and paced. When the stimulation was applied instead at one source of the dopamine pathways, in the substantia nigra, the behavior was much more frenzied: it appeared more highly “motivated” (Crow, 1972a, b).

Furthering the view that these could be reward neurons were pharmacological studies too numerous to mention here. Chemicals such as amphetamine, which liberate catecholamines from their inactive “capsules”, were found to
promote hedonic states in humans and added to self-stimulation behavior in animal experiments. Chemicals which blocked the degradation of catecholamines such as MAO inhibitors, and others which blocked inactivation by reuptake (e.g., imipramine) added to these positive effects. On the other hand, chemicals such as haloperidol and chlorpromazine (which block catecholamine receptors), caused depressed conditions in both humans and animals, and in addition blocked brain reward behavior. In sum, the drug studies were consistent with the view that catecholamine neurons could well be reward neurons.

Another source of support came from studies of lesions which damaged the CNS, and were supposed to have specially damaging effects on catecholamine neurons, either destroying the cell bodies or their active endings. When lesions of this kind were placed in the dopamine bundles (or when catecholamine poisons were applied in the ventricles where they presumably had relatively widespread effects) the results were to abolish reward and drive behaviors, almost exactly mimicking the lateral hypothalamic syndrome referred to earlier (Ungerstedt, 1971b; Stricker and Zigmond, 1974). Brain reward behavior was abolished by this kind of ventricular poisoning. In other experiments it was also greatly set back, or altogether absent, after electrolytic lesions applied to the origin of the main ascending noradrenaline pathway (M.E. Olds, private communication; Eilman, private communication). When chemical lesions were placed so as to directly affect only the secondary noradrenaline pathway (directed at the medial hypothalamus) there were quite opposite effects, which apparently mimicked the medial lesions that caused animals to overeat (Ahlsgkog and Hoebel, 1972). It was surprising that this catecholamine lesion had such a different effect from the one in the dopamine bundle, but this was assumed to be due to subtle differences in function.

In other experiments (Pickel et al., 1974), electrolytic lesions in the main noradrenaline fiber system caused a great regrowth and proliferation of the damaged fibers. This brought them in quite a different way into accord with the self-stimulation data, because the time course of this remarkable regrowth matched well the time course of a well known (but rarely reported) behavioral change. This was that self-stimulation behavior improved (thresholds declining and rates increasing) for a period of about 2–3 weeks after probe implantation. The improvement progressed steadily from the time or surgery whether or not the animals were provided with any stimulation during the 3 week period. The surprising proliferation of catecholamine fibers during the 3 weeks after surgery, matching as it did the improvement of self-stimulation (whose probes must have damaged some catecholamine fibers), may thus explain what has heretofore been a mystery to me (Olds, 1958). Another important link may herewith be forged connecting catecholamine systems to reward behaviors.

Even stronger support for the catecholamine theory of reward is the finding that direct application of catecholamines into the ventricle has positive effects on brain reward behavior, either restoring it if it had been blocked by drugs or lesions, or promoting it if stimulation be applied at or near threshold levels (Wise et al., 1973).

Many of the experiments that pointed strongly toward dopamine or noradrenaline being involved in brain reward or drive behavior pointed
ambiguously at the third important amine, serotonin (Porschel and Ninteman, 1971). Drugs that manipulated this neurohormon could be positive or negative with respect to brain reward behavior, depending on other ill-defined aspects of a given experiment. Quite different researches were more clear in pointing to an involvement of serotonin in quieting the animal for sleep or in suppressing pain (Jouvet, 1974; Yunger and Harvey, 1973). It seemed possible, therefore, that some self-stimulation aimed at pain reduction might be promoted by serotonergic drugs, while other behavior aimed at producing a euphoric state might well be damped by the same drugs.

In any event, the two catecholamines were strongly related to the basic drives and to rewards. Before leaving the topic, it is fair to set forth the substance of a current debate about the noradrenaline neurons and the dopamine neurons with evidence enumerated for and against each of them being "reward neurons".

**Noradrenaline neurons**

The fibers radiate from the locus coeruleus. Because they spread to cerebellum, diencephalon, paleocortex and neocortex, they have the possible neuroanatomical character of a major integrative net. Self-stimulation was observed at most locations where these fibers were concentrated. This made it possible to suggest them to be reward neurons. Pharmacological evidence was not incompatible with the idea that noradrenaline neurons had reward functions, although most of the evidence could equally well be applied to a dopamine theory.

Blocking the conversion of dopamine to noradrenaline with the drug disulfiram caused brain reward behavior to cease, whereas application of noradrenaline in the ventricles at this time rapidly restored the behavior (Stein, 1974). However, the blocking drug also caused many signs of general dishabilitation, and this "disease" was to some degree cured by the ventricular application of noradrenaline, so that there may not have been any specific effect on brain reward mechanisms. Moreover, blocking with a different drug seemed to leave self-stimulation intact. Cutting ascending fibers in a region where locus coeruleus axons passed through the midbrain caused self-stimulation behavior to cease in some cases, even if the behavior was provoked by stimulation in non-noradrenaline areas (Stein, 1974).

All these facts pointed to noradrenaline neurons as candidates for reward neuron status, but there were substantial arguments on the other side. One was that a very large deletion of locus coeruleus neurons by ablations in and around this nucleus sometimes did, but at other times did not cause a lasting change in self-stimulation behavior (Clavier, 1976). The large loss of noradrenaline neurons was incompatible with the relative lack of permanent loss of self-stimulation if these were in fact a large family of reward neurons. This made it seem that noradrenaline, while it might be involved in or related to brain reward in the normal animal, was nevertheless only tangentially related in some cases. Pointing in the same direction, pharmacological manipulations that caused near depletion of all noradrenaline in the forebrain, or at least in the
telencephalon, did not cause a major and lasting change in self-stimulation behavior (Breese and Cooper, 1976).

Those were the two major difficulties, but there was another unclear problem, namely, that drugs which caused catecholamines to be freed from synaptic vesicles and from neurons, and thus to become active in the interstitial fluid, seemed to promote rather than retard self-stimulation behavior. This left the question: why were the animals stimulating the fibers if they no longer contained catecholamines? I conclude from all this conflicting data that noradrenaline is in some way involved in the reward process in the normal animal, but is not the key factor in most brain-stimulation reward processes. For example, noradrenaline might be involved in the inhibitory control of negative emotional mechanisms which would themselves be incompatible with reward behavior. If so, noradrenaline might mediate reward when this consisted in the suppression of aversive mechanisms; and noradrenaline depletion might release central wellsprings of aversion or depression, thereby temporarily suppressing other reward processes until the system had adapted to the new low noradrenaline levels.

**Dopamine neurons**

The dopamine-containing fibers from the zona compacta of the substantia nigra and from the adjacent ventral tegmental area have a radiation similar to, but not as extensive as, that of the locus coeruleus system. They could nevertheless be a major integrative net for the forebrain, although from anatomical appearances they would seem to be of secondary importance in comparison with the locus coeruleus system. Their output is more addressed to the extrapyramidal system than to the cortex, and thus they were thought to be possibly involved in response execution rather than basic integration. However, there were also pathways to many parts of the paleocortex, and even to neocortex. They would be more likely than locus coeruleus neurons to receive convergent inputs from the olfactory and telencephalic centers. This might provide them with afferents from discriminated rewards and punishments, or from distance receptors as Crow (1973) suggested, and make them less likely to receive visceral afferent messages directly.

Brain reward behavior was better correlated with the dopamine system than with the noradrenaline one. Thus, with probes implanted in its pathways, self-stimulation was more nearly “pure”; i.e., less contaminated by apparently aversive side-effects. This was true in my experience for lateral hypothalamus, and for some parts of the far-medial hypothalamus, and for the cingulate cortex.

Pharmacologically, most of the evidence supporting the existence of noradrenergic reward neurons applied equally well to the dopamine hypothesis, in addition to which there is other evidence favoring dopamine more directly. Blocking the conversion of tyrosine to dopamine (which also blocked the further step to noradrenaline) always stopped self-stimulation behavior (Stinus and Thierry, 1973). Adding DOPA, which bypassed the block, restored self-stimulation. Cutting the dopamine fiber bundle from the substantia nigra
to the caudate nucleus stopped self-stimulation in the caudate nucleus (Phillips et al., 1976). This could be accomplished unilaterally; and the retained self-stimulation of probes placed on the other side gave at least some evidence that the reward mechanism rather than the behavior was impaired. The effect was irreversible. “Neurotoxic” manipulations which caused nearly total depletion of dopamine in the forebrain also caused near-complete abolition of self-stimulation behavior (Breese and Cooper, 1976).

Proponents of the noradrenaline neurons had some rebuttals but these served more to suggest that an abrupt drop in telencephalic noradrenaline levels could block dopaminergic and other self-stimulation than to displace the dopamine hypothesis. Transection in the midbrain behind the dopamine system sometimes stopped self-stimulation even though the behavior was caused by stimulation in more anteriorly placed dopamine pathways. This was given as evidence that the noradrenaline path transected was a prerequisite to the self-stimulation. In other studies, blocking the conversion of dopamine to noradrenaline by disulfiram stopped self-stimulation and this could be restored by placing noradrenaline in the ventricles (Stein, 1974). However, both lesions in noradrenaline neuron systems and neurotoxic damage to them could apparently be repaired by time. Thus, either the telencephalon has mechanisms of supersensitivity which allow it to get along on very little noradrenaline, or a loss of noradrenaline neurons can be compensated for by other mechanisms. These rebuttals therefore left the view that while dopamine was essential for at least some self-stimulation, and possibly for all, noradrenaline was possibly not essential.

Another objection to the dopamine neuron view, which carried more weight, was speculative in nature. It turned on the idea that the dopamine system, being part of the extrapyramidal system, was more involved in correlating the response with the reward, or in organizing the response, than in the rewarding condition itself. One experiment indicated that extremely gross self-stimulation behaviors were still possible after cutting a dopamine pathway even though pedal-press behaviors were no longer possible (Huston and Ornstein, 1976). In another experiment, food-reward learning of pedal behavior disappeared but there was still gross movement toward goals, and consummatory behavior still occurred (Grossman, 1976). The possibility remained, however, that in these cases the cuts left dopamine fibers with access to extremely gross behavior controllers, but removed the dopamine afferents of pedal behavior controllers. Thus the dopamine-reward hypothesis survived.

I would guess from this set of data that the dopamine neurons could well be a final common pathway in the reward system, acting in one direction to inhibit certain types of drive neurons, or in another direction to cement connections between drives and other neuronal systems — or both. Why such neurons would point most selectively to the extrapyramidal system, to similar components of the paleocortex system, and to cingulate cortex is not clear. To judge from neuroanatomical arrangement alone, the noradrenaline neurons are better suited than the dopamine ones to inhibit lateral hypothalamic drive neurons and, at the same time, to modify their functional connections in the cortex.
UNITS

A fourth set of experiments was aimed at explaining some of the other results, by means of recording directly from neurons in and near the lateral hypothalamic centers.

In one set of studies (Hamburg, 1971) neurons were recorded from the middle part of the lateral hypothalamus (an area which is sometimes called the “feeding center”) and from more posterior parts of the lateral hypothalamus and from adjacent areas in the substantia nigra. The recordings were made in chronically prepared animals which were hungry and were provided with food to eat. In all parts of this rather extensive region there were neurons that were decelerated during eating. Analysis showed that it was not the eating that stopped them so much as the cessation of instrumental behaviors. The units were firing briskly during the high drive state which was used in these tests. When a dish of feed was presented, the neuronal activity subsided abruptly as the animal began to eat; this happened even though eating, of course, could not have caused the metabolic deficiency to subside in this brief time. If the experimenter tried to remove the dish, the animal would counter the effort by various strategies to retain it. During this period of renewed instrumental behavior the unit activity would recur even though the animal was still consuming food. Thus, it was the cessation of instrumental behavior rather than the occurrence of consummatory behavior that matched the cessation of this particular unit activity.

The question arose, therefore, whether these neurons were the cause or the consequence of the instrumental behavior. Some light was shed on this by experiments showing that neurons recorded from the same area were activated by promising, conditioned stimulus (CS) signals which turned the animals toward the food tray (Olds, 1973; Linseman and Olds, 1973). In these tests (Fig. 9) the hypothalamic unit response occurred first, and the observed behavior some milliseconds later; thus, the unit activity did not appear to result from the behavior. Because conditioned stimuli activated these units, but only after the animals had been deprived of food, it looked as if both the CS and the deficiency condition were required to activate the units. Because the units became active first, and the food approach behavior came second, the former presumably mediated the latter. Because the conditioned stimulus which activated these units also caused a temporarily heightened state of behavioral arousal or drive, it appeared that these neurons might in fact mediate one component of drive, namely, the one that directly instigates, i.e., instrumental behavior. This would account for their being turned on jointly by deprivation plus environmental signals, and also for their being terminated as soon as instrumental behavior stopped. Were they also directly inhibited by rewards?

That this might be so was suggested by experiments of Ito (1972). In his studies, the vast majority of neurons recorded from the same lateral hypothalamic areas was directly (though usually temporarily) inhibited by the onset of a rewarding brain stimulus (Fig. 8). A substantially smaller minority of units here was driven by the brain reward. In more anterior regions of the medial forebrain bundle at the preoptic level, the majority of neurons was
accelerated or driven by the brain reward, and a much smaller number was decelerated. Taken together these studies implicate a family of neurons in the lateral hypothalamus that are activated during levels of heightened instrumental performance and quieted by rewards.

Furthering the idea that these might be drive neurons which are inhibited by rewarding stimuli were experiments on morphine-addicted rats (Kerr et al., 1974). “Drive” and “reward” were both easily manipulatable in this situation. The withdrawal state (the drive state) could be heightened by application of naloxone (which counters morphine). The reward state could be induced (and the drive state thus lowered) by application of morphine. Neurons of the lateral hypothalamus were most often accelerated by the drive-inducing manipulation and quieted by the rewarding one. Medial hypothalamic units, on the contrary,

![Diagram](image)

**Fig. 9.** Behavior and hypothalamic unit responses before and after conditioning. The upper trace portrays the average output of a detector attached to the head that measured head movements in arbitrary units. The lower trace represents the spike frequency of a lateral hypothalamic unit, the vertical bar at the left representing a rate of 5 spikes/sec. The traces represent 3 sec. At the end of the first sec a tone (CS+) was started which then continued to the end. During conditioning a pellet dispenser (UCS) was triggered at the end of 2 sec. Prior to conditioning (pseudoconditioning) the tone caused minor changes in the unit and behavior responses. After conditioning it caused behavior changes with a 90–170 msec latency and unit changes with a 20–40 msec latency. (From Linseman and Olds, 1973.)

were accelerated during the reward condition, and decelerated by the rewarding one.

A different set of candidates for drive neuron status, also inhibited by rewards, was added by the studies in monkeys of Hayward and Vincent (1970) and of Vincent et al. (1972) on osmotic detectors (thirst neurons?) and their responses to drinking (water reward). Neurons were recorded from a part of the lateral preoptic area, and from the smaller nucleus supraopticus nearby, which contains vasopressin-secreting cells. “Thirst” and water preservation mechanisms were directly triggered by piping hyperosmotic solutions directly into the carotid body. This caused excessive osmotic concentrations and thus a perceived water deficiency. It activated a group of neurons in the lateral preoptic region, which were thus conceived of as being possible osmodetectors, responding directly to the “water deficiency”. Their response was correlated with a burst of activity in the nearby vasopressin-containing neurons of the
supraoptic nucleus, which presumably released vasopressin (which then acts upon the kidney to retain water).

Both the osmocytodetector neurons and the vasopressin neurons had their responses to the osmotic stimulus reversed by the ensuing drinking; the reversal was immediate, well preceding the compensation of the effective water deficit. If they were drive neurons, this suggested again that drive neurons in this general region might be inhibited by rewarding inputs. At least, there was a temporary suppression of the activity caused by the rewarding input.

There were also reward neuron candidates nearby. Interdigitated with, or slightly offset from, the osmocytodetector neurons was a second family of preoptic area elements, whose activity was suppressed by the osmotic stimulus and accelerated during drinking. At first sight these seemed like obvious reward neuron candidates but Rolls objected — pointing out that such neurons might be responding similarly to low drive levels and to actual rewarding conditions (being activated in both cases). His view was that true reward neurons would respond exclusively to rewards and be insensitive to drive levels, except, of course, insofar as these might themselves accentuate responses to reward stimuli. This did not seem to be a devastating argument against the idea that Vincent’s “drinking neurons” might be reward neurons, but it did make it important to consider other units that might be accelerated by rewards, but have no response to drive levels alone.

Neurons of this kind were evidently observed in the experiments of Rolls and his group (Rolls, 1975, 1976; Burton et al., 1976), done with monkeys. Neurons were recorded from the lateral hypothalamus and adjacent “substantia-inominata” regions. Cells responded to visual food objects, and some to the taste of food. Some of the responses were accelerations, whereas others were decelerations. The background firing rates were reported to be unchanged by drive level manipulations; but responses to the “rewards” were augmented by the drive. These units thus responded not to drives but to conditioned stimuli related to rewards, or to real rewards; in addition, their response to rewards increased when drive levels were heightened.

In summary, a small but growing body of evidence points to a family of neurons whose firing rate is jointly controlled by excess or deficiency conditions, and by external stimulus inputs. The kinds of effect observed most often were: acceleration by drive-increasing manipulations, or by conditioned stimuli associated with rewards, and deceleration during consummatory behavior — or complete suppression by rewarding stimulation. The deceleration occurred immediately, i.e., before the deficiency condition was remedied. There is a smaller family of observations pointing to nearby neurons being accelerated directly by rewards, but the data are still unclear. Some of the neurons which were accelerated during drinking might be “low drive neurons”, unrelated to rewards. The accelerated neurons of Rolls’ experiments might have been activated mainly by conditioned stimuli related to rewards. Still, the taste neurons of Rolls and the drinking neurons of Vincent, as well as the brain-reward neurons of Ito (1972), Keene (1973) and Rolls (1975, 1976), all suggest that reward neurons might overlap drive neurons in this area. If not, they most certainly project there from surrounding areas (to mediate the observed inhibition).
THEORY AND PERSPECTIVES

The concept of “drive” can be divided into two parts. One is an incentive part, and suggests that certain neurons would become active during approach conditions, and would be the motivation involved in operant behavior. The other is an alarm part, and suggests that some neurons might become active when supplies become dangerously low, or when harm is imminent. If so, these “alarm” neurons could be inhibited by reward elements that signal the end of the danger. The incentive kind of drive could be inhibited by rewards that trigger consummatory responses and suppress operant behaviors. It seems possible that the noradrenaline system might inhibit alarm neurons and mediate their appropriate connections to instrumental behaviors, and the dopamine system might have a similar action or incentive neurons. This would put both catecholamine systems in the reward category, and put both kinds of drive neurons outside this category. For reasons I will not go into here, I suspect that the drive neurons involve muscarinic actions of acetylcholine, and are involved in the transport of peptide hormones.

The opponent process interaction between catecholamine systems and drive neurons might be the main target of transactions between medial and lateral hypothalamus. The other two lesions affecting approach behavior (in the caudate nucleus and in the amygdala) had to do with a different problem, viz., the channeling of drives onto specific targets. The experiments of Garcia and Valenstein (op. cit.) pointed to changeable targets of brain stimulated drives and also of naturally occurring ones. The locus of Valenstein’s probes and of lesions countering Garcia’s effects pointed to the lateral hypothalamic region. One interpretation was that the same drive or learned drive neurons that we have been talking about had not only some modifiability on the input side but also some at the other end. That is, they might have changed output connections depending on “good” or “bad” after effects of consummatory behavior.

The “law of learning” for this changing of drive targets might be that the drive axons would become connected to basal ganglia and cortex cell assemblies active at the time of drive inhibition. The long-predicted hypothalamocortical axons to mediate this have recently been amply demonstrated with horseradish peroxidase (Kievet and Kuypers, 1975). Thus, the possibility exists that drive neurons which are excited by visceral inputs, hormones and conditioned signals, are silenced by rewards and become functionally connected during development or learning to basal ganglia and cortex cell assemblies which are active at the time of their “silencing” (Fig. 10).

The widespread ramifications of the catecholamine axons suggested that, if these were reward neurons, they must have other functions besides that of inhibiting lateral hypothalamic neurons. This brings me to my final set of points. There are several different ways that reward neurons should be involved in more specialized behavioral steering mechanisms. At least three different ways would be appropriate to different levels of CNS organization (Table I). At the level of motor skills, reward might directly cause “connections” to form between a warp of axons and a woof of dendrites. This kind of process would
Fig. 10. A new "drive-reduction theory of reward". Noradrenaline neurons from the medulla would be triggered by rewarding gustatory and visceral inputs. They would act to silence drive neurons housed in or near the lateral hypothalamus (some of which could be dopamine neurons). Silencing of the drive neurons would cause them to become coupled to cortex cell assemblies active at the time. $\oplus$ = excitatory and $\ominus$ = inhibitory connections.

fit readily into the cerebellar cortex, where the parallel fibers form such a warp and the Purkinje dendrites the woof.

At a second level there would be sequential memory, as when a rat runs a maze or a human remembers how he got somewhere, and takes the same route a second time. In these cases, recordings would be made of successive events on the first occurrence of a behavior sequence. These would have some characteristics of a movie film, or a magnetic tape recording; but a better metaphor would be the sequential memory locations in a computer. Successive small episodes with their sensory, motor and reward components would be recorded in sequential memory addresses. Later, near-matching sensory inputs would re-arouse a memory, and this would re-arouse its successors. A "dry run" (without behavior) would occur first. If an appropriate reward memory was discovered among the near successors, this would cause a predisposition toward expression of some of the recorded behaviors. From observations in the hippocampus of highly organized axonal systems that run like the digit lines of a computer core-memory through oriented dendrite systems that look like the

### TABLE I

**DIFFERENT LEARNING FUNCTIONS POSTULATED TO INVOLVE DIFFERENT BRAIN SYSTEMS, DIFFERENT MECHANISMS OF LEARNING AND PERFORMANCE, AND DIFFERENT ROLES OF REWARD**

<table>
<thead>
<tr>
<th>Function</th>
<th>Possible anatomical correlate</th>
<th>Mechanism</th>
<th>Role of reward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning motor skills</td>
<td>Cerebellum</td>
<td>Sensorimotor connections</td>
<td>&quot;Stamp-in&quot; connections</td>
</tr>
<tr>
<td>Learning behavior</td>
<td>Hippocampus</td>
<td>Convert temporal sequences to spatial memory arrays</td>
<td>Cause rewarded behaviors to recur</td>
</tr>
<tr>
<td>sequences</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Learning maps and</td>
<td>Cortex</td>
<td>Make behavioral-topographic maps of external objects</td>
<td>Cause object to be pursued</td>
</tr>
<tr>
<td>objects</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
memory lines of such a device, it has seemed possible that this kind of process might occur there.

At a third level, there would be representations of objects and object-arrangements. These would be sensorimotor or cognitive maps, with control elements at any one node pointing toward a behavior with one hand, and toward a second node (the representation of the expected outcome) with the other. These control elements could be the layer 5 pyramidal cells, while the nodes could be the "columns" of the neocortex. Motive cells at a second node would need to "point back" to motivate the control elements pointing toward them. The motive cells could be either other pyramidal cells or cells of different type. Reward in this kind of system would serve to connect drives to motive elements of those columns, or to cell assemblies which were active at the time of the rewarding events. This would be the same function which I indicated earlier by saying that drive neurons might become attached to cell assemblies which are active at the time of their being inhibited.

The suggestions contained here, therefore, are that reward neurons may exist, and have the following four functions: (1) to inhibit drive neurons in the lateral hypothalamus, (2) to facilitate certain sensorimotor connections, (3) to plant "emotional" codes on certain sequential memories, and (4) to connect drives to cell assemblies in neocortex which were active at the time of the reward. It was also suggested that noradrenaline neurons might be the reward neurons addressed to negative drives and dopamine neurons to positive drives.

SUMMARY

Electric stimulation in certain parts of the brain causes behavioral signs of reward: mammals, at least, seek out the brain stimulus as if it were a goal. Lesion studies, pharmacological studies, unit studies, and anatomical studies, mainly from other laboratories, are reviewed here with a view to explaining these observations. Lesions in these parts of the brain cause deficient goal-directed behaviors; animals no longer learn tasks for food or water rewards, and temporarily do not eat or drink. Learned avoidance behaviors are also deficient. The regions of the brain where these effects have been best obtained were parts where fibers containing noradrenaline, dopamine, and serotonin were concentrated. Fitting in with this, pharmacological studies showed that electrically stimulated and natural reward behaviors depended on dopamine and noradrenaline in some special way, and relief from pain depended on serotonin. It seemed possible that these were all involved in different kinds of reward by mediating the inhibition of aversive conditions or drives. For reasons I do not spell out completely here, I have proposed that (1) serotonin inhibits a kind of aversive condition that depends on the external environment; (2) noradrenaline inhibits a different kind of aversive condition that depends on the internal environment; and (3) dopamine inhibits a milder kind of drive that has no aversive component but which is involved in most normal behavior. In several different experiments, neurons were directly recorded from "hypothalamic reward centers" during behavior. Such neurons responded to a variety of conditions in a way that suggested they were "drive
neurons" rather than "reward neurons". In experiments where deficiency conditions were imposed, the majority of the affected neurons was accelerated by these manipulations. In experiments where conditioned stimuli related to rewards were used, the same result was obtained. In experiments where goals and consummatory behaviors were used, on the other hand, the majority of affected units was decelerated. In iontophoretic application studies with noradrenaline, the majority of affected units showed a deceleration in firing rate. In all these series of observations, there was a smaller group of neurons showing opposite responses. In histofluorescence studies, noradrenaline or dopamine terminals were found in the hypothalamic "reward" regions, and in horseradish peroxidase studies neurons were observed with projections directly to neocortex. For all these reasons, it is concluded that drive ("command")? neurons in this area might be inhibited by noradrenaline- or dopamine-containing "reward neurons". By this means alone, or plus some added action, the inhibited neurons might, at the time of their inhibition by rewards, become functionally connected to active cortex cell assemblies. This could make environmental objects which are reflected by the activity of these cortical cell groups into targets of pursuit on later occasions.

REFERENCES


**DISCUSSION**

N.J. SPITERI: You talked about drives in general, but most of these experiments have been done in the feeding and drinking motivational systems. Were all of the catecholamine experiments done in just these two systems, or for sexual behavior as well? And also: how many experiments have been performed where people used sexual behavior as a reward, and single unit recording studies from populations of neurons?

J. OLDS: You are right about feeding and drinking being the best studied. However, electric stimulation and lesions have caused instigation and loss of sexual behavior respectively. These effects were shown with probes in both anterior and posterior hypothalamus. Operant behavior with a sexual reward has not been used in stimulation and lesion studies. It is not an easy kind of experiment for a physiological psychology laboratory because the rewards are of necessity few and far between. Therefore the studies of sexual effects of stimulation and lesions were carried out without using instrumental behaviors. Lesions in the lateral hypothalamus or in the nigrostriatal bundle have been reported to abolish several different operant responses at once, however, leaving the impression that all operant responses were temporarily disrupted. Instrumental responses directed toward food, water, temperature adjustment and the avoidance or delay of aversive stimulation were all disrupted by these lesions. It therefore appears that lesions in this part of the lateral hypothalamus, where you can cut both the nigrostriatal bundle and the mesolimbic bundle, can cause a type of motivational defect which is as broad as we have yet been able to test. By the same token, an animal under chlorpromazine has very great difficulty in performing any purposive behavior task. If he gets very close to food, so that he is almost with his feet planted in it, he goes through the response: that is the reflex part of the mechanism. The consummatory mechanisms are thus satisfactory, but the operant mechanisms are in very bad shape.

P.B. BRADLEY: Would it be reasonable to suggest from what you have said that the cholinergic mechanisms are not involved in reward behavior.
J. OLDS: The muscarinic aspect of the cholinergic system is quite definitely acting in some opposition to this brain reward mechanism, and we don't know whether it is acting in opposition to the noradrenaline attention mechanism, or in opposition to the brain reward mechanism per se. The nicotinic aspect of the cholinergic system, however, may well be a positive link in some parts of the brain reward mechanism.

S.P.R. ROSE: In that Valenstein learned-drive experiment that you set up, when the animal learned to replace eating by drinking, is it then given a choice in the drinking situation between food and water?

J. OLDS: The safest thing to say is that it can go either way: it can prefer water entirely, it can retain its original preference, or the two can be equal. The important thing in these experiments is the tremendous difference in the animals before and after training. I came to speak in favor of Valenstein's study — I was an opponent of it at first — when he explained that with all hypothalamic stimulated drives you often get nothing when you first put the probes in. In all studies of hypothalamically stimulated drive behaviors there is commonly a lag period after the probes are planted and stimulation tests begun before positive effects are observed. The lag has been an enigma and caused many young investigators to abandon the problem early. Persistence often yielded success, but the reason for the initial failures was not clear. Valenstein's study clarified the fact that stimulating the animal in the presence of goals is a form of training and that the stimulus gradually brings goal-directed behaviors under control by an almost "developmental" chain of events. Valenstein thus put us onto the idea that there is a great deal of training in any hypothalamic drive behavior. My view of it is that you are stimulating a pot pourri of things in the hypothalamus, and the animal practically has to organize all of that into a drive for the first time.

F.H. LOPES DA SILVA: About your units: you showed one which stops firing when you start with stimulation and then starts up again. Are these phasic changes — changes that last for a very short time and then return to normal while the behavior continues as it was — or are they tonic changes?

J. OLDS: They are phasic changes but tightly coupled, meaning that every time the animal presses the pedal, the neuronal inhibition is strong at the beginning and becomes attenuated to some degree later in the stimulus train. We sometimes can predict when he will release the pedal by looking at the attenuation of the inhibition. As he lets go a burst occurs, and then the inhibition is restored as he presses again. If he walks around in between the operant periods, the neurons are relatively active during this interval.