Neuroscience & Biobehavioral Reviews, Vol. 13, pp. 181–186. © Pergamon Press plc, 1989. Printed in the U.S.A. 0149-7634/89 $3.00 + .00

Reward or Reinforcement: What's the Difference?

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WHITE, N. M. *Reward or reinforcement: What's the difference?* NEUROSCI BIOBEHAV REV 13(2/3) 181–186, 1989.—The histories of the terms "reward" and "reinforcement" are reviewed to show the difference in their origins. *Reward* refers to the fact that certain environmental stimuli have the property of eliciting approach responses. Evidence suggests that the ventral striatum (nucleus accumbens area) is central to the mediation of this behavior. *Reinforcement* refers to the tendency of certain stimuli to strengthen learned stimulus-response tendencies. The dorsolateral striatum appears to be central to the mediation of this behavior. Neuroanatomical and neurochemical data are adduced suggesting that reward may be mediated by a neural circuit including the neostriatal patch system, together with the hippocampus, limbic system (amygdala, prefrontal cortex) and ventral pallidum. The evidence also suggests that reinforcement, in the form of dopamine release in the striatal matrix, acts to promote the consolidation of sensori-motor associations. Thus, the matrix may mediate stimulus-response memory as part of a circuit including the cerebral cortex, substantia nigra pars reticulata and its projections to thalamic and brainstem motor areas.

Reward Reinforcement

> "When *I* use a word," Humpty Dumpty said, in a rather scornful tone, "it means just what I choose it to mean—neither more nor less."
>
> "The question is," said Alice, "whether you *can* make words mean so many different things." [(5) p. 269]

IF you want to feel like Alice, in a world where anything goes because everyone is stuck on his own point of view, try asking a behavioral neuroscientist the meaning of the term "reward." Worse, try getting one to distinguish between "reward" and "reinforcement." Many of these scientists specialize in research intended to elucidate the physiological basis of behavioral phenomena they describe using terms that mean exactly what they choose them to mean. The importance of clearly defining (and redefining) terms that describe behavioral processes as our knowledge of the underlying physiological mechanisms advances has repeatedly been emphasized [the most recent occasion: (46)]. Nevertheless, we still have trouble with this issue when dealing with the brain-behavior relationship, particularly when discussing reward and reinforcement.

As we have seen in virtually all the talks presented in this symposium, the physiological mechanism we are studying involves the neurotransmitter dopamine, including primarily the so-called mesolimbic and nigrostriatal systems, together with the striatal and nigral mechanisms associated with these systems. To the extent that we fail to consider, define and agree on the meanings of the terms used to describe the behaviors elicited when this substrate is manipulated, we fumble our opportunity to understand its function.

SOME HISTORICAL CONSIDERATIONS

Historically, the terms reward and reinforcement have rather different origins, leading to different operational definitions for them. As discussed in a recent chapter (88), the notion of reward has its origin in the writings of the Epicurean philosophers, who described how behavior is determined as individuals seek to maximize pleasure and minimize pain. This idea has not changed in any substantial way since it was first expressed. In modern psychology the operationalization of affective states, including reward and aversion, by P. T. Young (92,93) provided the model we now use (whether we know it or not) for studying these behavioral processes. According to Young's view, the operational definition of reward is approach; the operational definition of aversion is withdrawal. The most common contemporary measures of reward are electrical self-stimulation or self-administration of drugs, and various place preference techniques. Aversion is generally measured by withdrawal from some environmental stimulus object.

The notion of reinforcement has a more complex history. It has been recognized for over 100 years that certain types of events are capable of influencing memory: in 1857, George Ramsay wrote in his *Principles of Psychology:* "If we could but stimulate the emotions generally, we should certainly improve the memory" [(63) p. 226]. The idea that *general* emotional stimulation may improve memory has an important implication. It means that there is no necessary relationship between the stimulated emotions and the memory that is improved. For example, an animal may acquire a tendency to approach a light. This stimulus(light)-response (approach) association may be strengthened by reinforcement with food or brain stimulation, but this strengthening effect does not depend on any relationship that may exist between either the stimulus or the response and the reinforcer.

In his earliest work with cats (73) Thorndike made this idea more explicit. He recognized that the formation of a simple

stimulus-response (S-R) association does not necessarily involve any ideational processes. Such behavior can be understood as the product of a simple neural connection between stimulus input and response output. Animals do not acquire any information about the stimulus or the response in this type of learning; rather, the neural connection causes the stimulus to elicit the response in an automatic, robot-like manner. In the context of this simple connectionist view of learning it is not unreasonable to suggest that the general activation of a process unrelated to the stimulus or the response can improve memory by strengthening the connection between them. This phenomenon came to be known as the Law of Effect (74).

It is possible that, for Thorndike, all learned behavior could be explained on the basis of S-R associations; more recent theorists have presented models for rather complex behavioral processes in which fixed S-R or S-S associations determine behavior [e.g., (1, 41, 65)]. However, recent evidence [e.g., (47,55)] suggests that such associations probably represent only one form of memory among several that mammals are capable of acquiring. In the present paper the focus is on fixed S-R (and/or S-S) learning and on the role of the reinforcement process (Thorndike's Law of Effect) in this type of memory.

It is of some interest to look into the origins of this "Law," because in them lies a possible explanation for the confusion of terminology. In its original version, the Law of Effect stated that when a response was followed by a satisfying state of affairs the probability that the response would be repeated was increased and that when a response was followed by a dissatisfying state of affairs, the probability that it would be repeated was decreased. In other words rewards strengthen stimulus-response associations and punishments weaken them.

Because of Thorndike's academic position at a leading institution for the training of teachers and the promulgation of modern educational theory (Teachers' College, Columbia University), this idea influenced educational practices of the day, with practical consequences in the classroom that can be imagined (32). Possibly because of these consequences, Thorndike reexamined the idea that negative events weakened associations, and eventually concluded that he had been wrong (75). Only the strengthening of associations by positive, or rewarding, events stood up to experimental scrutiny; aversive events (punishment) had no weakening effect. In this way the notions of reward and strengthening of associations became linked; although Thorndike himself maintained the distinction between the two processes, the idea that reward and reinforcement might be independent actions may have been lost for many other workers at that time.

A major experimental paradigm used by Thorndike to test these ideas was the Spread of Effect experiment (76). The experimenter read a list of words to human subjects and required them to respond with whatever word came to mind. Following some randomly selected response, the experimenter replied with the work "good" (a reward). The original list was then reread and the subjects were asked to remember the responses they had given on the first reading. The best remembered response was the one which had been rewarded, a demonstration of the Law of Effect. However, the responses made just before and just after the rewarded response were also remembered significantly better than the others, even though the subject had not been rewarded for making them. This is what Thorndike called Spread of Effect, and it demonstrated that rewarding events can improve memory even when they are *not contingently related* to the behaviors they affect. In fact, the *mere temporal contiguity* of these verbal associations with the reward was sufficient to strengthen them.

The Spread of Effect experiment shows that certain types of events can improve retention when they occur contiguously, but not necessarily contingently, with the creation of new stimulus-response associations. This finding suggests the conclusion that the neural process mediating the strengthening action of these events is independent of the affective properties of the events. Below, I will review evidence concerning the nature of the events that noncontingently improve memory. First, the relationship of the Spread of Effect experiment to research on memory consolidation will be considered.

In 1900 Muller and Pilzecker (50) proposed the idea that, during the period shortly after they are formed, memories are in a labile state susceptible to influence by external events; they become permanent over time by a process called "consolidation." Numerous clinical reports supported this notion over the next 50 years (67). In 1950 Duncan (11) reported the first laboratory demonstration of this phenomenon: electroconvulsive shock disrupted retention of an avoidance response in rats when applied during the immediate posttraining period, but not when applied at a later time. More recently it has been shown that presentation of other events during the posttraining period can improve retention [e.g., (10,42)]. The operational equivalence of these experiments to the Spread of Effect experiment has frequently been pointed out (20, 28, 39, 40, 66). For example, in his typical, pithy manner Peter Milner has written: "Reinforcement, in this sense, means the same as consolidation [Muller and Pilzecker, (50)], a process that occurs during the seconds or minutes after a noteworthy event to fix the long-term memory of the event." [(45) p. 182]. The idea that reinforcers influence memory when they are presented in a contiguous but noncontingent manner is not a new or unusual one. It is simply an idea that not many researchers take into account when thinking about the behavioral processes they denote by the terms reward and reinforcement.

THE NATURE OF THE EVENTS THAT IMPROVE MEMORY

The idea that memory improvement is associated exclusively with reward is not supported by the evidence. When animals are trained on a conditioned emotional response (CER) in which they acquire an association between a tone and the withdrawal response produced by mild footshock, the posttraining, noncontingent consumption of sucrose (44) or a brief application of intense footshock (86) have identical memory-improving effects. Moreover, retention is not improved by posttraining consumption of saccharine solutions in concentrations that are equally preferred to those of retention-improving sucrose (44,84). So, both rewarding and aversive events have memory-improving properties, and the property of being rewarding is neither necessary nor sufficient for an event to improve memory.

One of the most common hypotheses about the nature of the events that improve memory during the posttraining period involves the notion that increases in "arousal" during the posttraining period is the critical reinforcing event (20,28). The three events discussed above (sucrose, saccharin and foot-shock) pose certain problems for this idea. Judging by behavioral observations consumption of sucrose and footshock, both of which improve memory, do not appear to produce anything like the same kinds of arousal effects. It is, of course, possible to postulate that behavioral arousal is not the relevant variable here; and to suggest that the important process is some form of affective arousal, regardless of its sign. However, memory was not improved by posttraining consumption of saccharin solutions which, judging by a behavioral measure, produced levels of affective arousal similar to those produced by memory-improving sucrose solutions.

Experiments on the effects on memory of electrical self-stimulation of the brain during the posttraining period (42) pose

similar problems for arousal theory. Rats that self-stimulated during the posttraining period with electrodes in the dorsolateral part of lateral hypothalamus or in substantia nigra showed improved memory; rats that self-stimulated with electrodes in the medial part of lateral hypothalamus or the preoptic area failed to show improved memory. Rates of self-stimulation in all four of these areas were about equal, leading to the conclusion that both the behavioral and affective arousal produced by stimulation in all four sites was also about equal. These findings suggest that arousal, regardless of how it is defined, is not a sufficient explanation for the memory-improving properties of certain events.

In summary, memory-improving events can be rewarding or aversive. Although they all appear to have affectively arousing properties, this is not a sufficient condition for their action. Therefore, although they tend to refute certain hypotheses about the nature of memory-improving events, the data discussed do not suggest an alternative explanation for this behavioral attribute. An exmination of the physiological basis of the memory-improving actions of certain events provides an alternative approach to this question: the precise specification of the neural events that produce the effect of reinforcement on memory.

PHYSIOLOGICAL BASIS OF THE REINFORCEMENT EFFECT

The self-stimulation data already mentioned provide one suggestion about the identity of the neural substrate mediating the memory-improvement effect. The electrode sites at which self-stimulation improved memory were located in brain areas (the dorsolateral lateral hypothalamus and substantia nigra, pars compacta) through which the dopaminergic nigro-striatal bundle (NSB) passes (35,77). In contrast, the brain areas (medial part of lateral hypothalamus and medial preoptic area) at which self-stimulation failed to improve memory have no known dopaminergic innervation. These findings implicated the NSB in the memory improving action of posttraining, noncontingent self-stimulation. A related finding was that pimozide, a postsynaptic dopamine receptor blocker, eliminated the effect of posttraining dorsolateral hypothalamic self-stimulation on memory (87). This finding implicates the release of dopamine in this effect; and it is therefore reasonable to suggest that the memory-improving effect of self-stimulation is caused by the release of dopamine from stimulated NSB neurons in these experiments.

Another posttraining event known to improve memory in a variety of different situations is the systemic injection of amphetamine (10, 13, 37, 43), a drug that promotes the release of dopamine from the terminals of neurons that contain this neurotransmitter. We replicated this finding using a conditioned emotional response, and showed that posttraining amphetamine had no effect on retention in animals with bilateral destruction of dopaminergic nigro-striatal neurons produced by injections of 6-OHDA into substantia nigra (83). This finding is consistent with the hypothesis that posttraining injections of amphetamine improve memory in normal animals by promoting the release of dopamine from the neurons of the NSB.

We were also able to demonstrate a memory-improving effect by training animals on a CER followed by microinjections of amphetamine directly into a site in the dorsolateral striatum (7). This finding is also consistent with the suggestion that the release of dopamine from the terminals of dopaminergic neurons in the striatum is an event that improves retention of learned S-R associations.

An interesting aspect of the effect of intra-striatally injected amphetamine on retention is its anatomical specificity: injections outside of a small area in the dorsolateral striatum were ineffective. Consideration of seveal factors led to an hypothesis about this anatomical specificity. First, among the afferents to the striatum is a topographically organized projection from all areas of the overlying cerebral cortex (52, 79, 82, 91). Second, the effective dorsolateral site coincided closely with the area which receives input from the overlying auditory cortex (29,82). Third, the learned association involved a tone: an auditory stimulus. Accordingly, the hypothesis that the striatum may contain different substrates for learned associations involving different stimulus modalities, and that these substrates may be organized according to the corticostriatal input from corresponding areas of sensory cortex was tested (81).

Cannulas were implanted into the posteroventral striatum, which is innervated by the visual cortex, or into ventrolateral striatum which is innervated by olfactory cortex, in different groups of rats. Groups of animals with cannulas aimed at each site were trained on CERs consisting of learned associations between a visual stimulus (a bright light) and shock-induced withdrawal, or between an olfactory stimulus (the smell of amyl acetate) and withdrawal. Posttraining injection of amphetamine into the posteroventral site improved retention of the visual, but not the olfactory CER. Posttraining injection of amphetamine into the ventrolateral site improved retention of the olfactory, but not the visual CER. This double dissociation of the effect of posttraining amphetamine with respect to site of injection and sensory modality of the learned association is consistent with the hypothesis that corticostriatal innervation of the dorsolateral striatum organizes memory-related functions in this brain area.

In summary, the release of dopamine from the terminals of NSB neurons in the dorsolateral striatum during the posttraining period is an event that improves memory. It appears that the released dopamine interacts in some manner with the topographically organized corticostriatal innervation of this part of the striatum to produce this effect.

PHYSIOLOGICAL BASIS OF THE REWARD EFFECT

The reward effect is similar to reinforcement in that the available evidence suggests that it too is mediated by the release of dopamine in the striatum. It appears to be distinct from reinforcement anatomically, however, since behavioral functions associated with reward are generally affected by manipulations of ventral rather than dorsal striatum. [As suggested by Heimer (30), the term "ventral striatum" refers to nucleus accumbens and surrounding areas.] One type of reward for which this is the case is that thought to be produced by intravenously self-administered drugs such as morphine (90) and amphetamine (58). Microinjections of amphetamine (33), morphine (53) and m-enkephalin (9) are self-administered directly into nucleus accumbens, while morphine is self-administered into the ventral tegmental area (VTA) (3) from which dopaminergic neurons project to nucleus accumbens. These data suggest that the ventral striatum may contain both dopaminergic and opiate substrates of reward.

Systemically administered morphine (49) and amphetamine (64,69) also give evidence of their rewarding properties in the conditioned place preference (CPP) paradigm. The rewarding effect of amphetamine in this paradigm can be blocked by 6-OHDA lesions of ventral striatum (69). Central microinjections of both morphine (78) and amphetamine (6) also produce CPPs when injected into ventral, but not dorsal striatum, implicating ventral striatal dopaminergic and opiate mechanisms in reward.

Recently it has been demonstrated that systemic injections of a specific dopamine D2 receptor agonist, quinpirole (LY171555), produces a conditioned place preference (34). We replicated this

finding and showed that microinjection of the same D2 agonist directly into nucleus accumbens also produces a conditioned place preference (85). Systemic injections of a D1 agonist, SKF38393, tend to produce a conditioned place aversion (34,85), but we found that intrastriatal injection of the D1 agonist into the same brain area produced a place preference (85). It therefore appears that reward may be mediated by both D1 and D2 dopamine receptors in the ventral striatum. The aversive effect of the D1 agonist that is observed when it is injected systemically may be mediated elsewhere in the brain, in a manner similar to the aversive effect of amphetamine (8), or in the periphery in a manner similar to the aversive effects of morphine (2).

Dopaminergic and opiate function in ventral striatum are also implicated in the rewarding properties of self-stimulation. It is likely that the reduction in rate of self-stimulation produced by systemic dopaminergic blockade is at least partly due to an attenuation of its rewarding effect (12, 16, 89). Blockade of dopamine function with specific D1 blockers also reduces rates of self-stimulation (51), and microinjection of a specific D2 blocker directly into ventral striatum has a similar effect (48). Ipsilateral dopamine-specific lesions of the mesotelencephalic pathway block self-stimulation with electrodes in the ventral tegmental area (14). Opiate mechanisms may also be involved in the rewarding effects of self-stimulation (68); however, beyond characterizing the effect of opiate manipulations on this behavior as "modulatory," little is known about its precise nature. Nevertheless, the data suggest that both dopaminergic and opiate mechanisms play a role in mediating the rewarding effects of self-stimulation. The dopaminegic mechanism seems to be localized to ventral striatum.

The role of the striatum in the mediation of conditioned reward has also been investigated. Intracerebral microinjections of amphetamine into ventral, but not dorsal striatum enhance responding in the presence of a conditioned rewarding stimulus (71), and 6-OHDA lesions of the ventral, but not of the dorsal striatum, blocked the amphetamine-induced increase in responding to the conditioned stimulus (72). These findings implicate the ventral striatum in responding to conditioned rewards.

The amygdala has also been implicated in the enhancement of responding to conditioned rewards produced by ventral striatal injections of amphetamine. Lesions of the amygdala do not affect responding to primary reward, but they attenuate performance in situations which require responding to a conditioned reward (4).

In summary, manipulations involving dopaminergic function in the ventral striatum affect behavioral paradigms that measure reward: self-administration, self-stimulation and the conditioned place preference. There is also some evidence for a role for opiate systems and an interaction with the amygdala in the mediation of learning about this reward.

A PROPOSAL CONCERNING THE ANATOMICAL BASES OF REINFORCEMENT AND REWARD

Recent neurochemical investigations of the striatum have revealed the existence of two distinct, partly interposed compartments. One of these, called the "patch" system, has high concentrations of opiate receptors (56), and exhibits dense immunohistochemical reactivity to enkephalin (26,31), and substance P (17). The patches are distributed throughout the striatum, although there are numerous suggestions (18, 22, 24–26, 54, 56, 80) that the dorsolateral striatum may contain fewer patches, and that the patches may be more extensive and diffuse in the ventral striatum. The second compartment, called the "matrix," is distinguished neurochemically by high density acetylcholinesterase (AChE) (24,31) and choline acetyltransferase (ChAT) (23) staining. The patches react weakly to these stains. The matrix is distributed in the dorsolateral striatum, and surrounds the patches in the central area. The compartmentalization of opiate and AChE staining has been confirmed in both the cat (26) and rat (31) by staining alternate sections of the same brain for each of the two markers. Recently, a three dimensional reconstruction of the patch compartment (27) has revealed it to be composed of an interconnected array of columns and "fingers" invading all areas of striatum.

Anatomical studies of the two compartments have revealed important differences in their efferent and afferent connections. In the rat the prelimbic (medial prefrontal) cortex innervates striatal patch areas identified by l-enkephalin and substance P immunoreactivity (17). The ventral striatal area, where the patches are most prominent, is also innervated by limbic cortex, including hippocampus and amygdala, as well as by the medial prefrontal cortex which is itself innervated by hippocampus (36, 57, 70). The patches give rise to a diffuse projection to substantia nigra (15,18). Dopaminergic neurons originating in pars compacta and in a cluster within pars reticulata of substantia nigra innervate the patches in ventral and dorsal striatum respectively (19).

In contrast, the matrix, as defined by dense AChE staining, receives the topographically organized input from neo-cortex (21, 38, 62) and thalamus (31). Efferents from the matrix topographically innervate globus pallidus and pars reticulata of substantia nigra (18), both areas mediating direct motor output (29). Dopaminergic neurons originating in ventral tegmental area and pars compacta of substantia nigra innervate the matrix in the ventral and dorsal striatum, respectively (19).

Various features of the reward and reinforcement functions discussed above appear to coincide with the neurochemical and anatomical properties of the patch and matrix systems, respectively. As described, data from self-stimulation studies and from experiments in which dopamine function was manipulated localize the reward function in ventral striatum, the area where the patch system is most prominent. Another feature of the patch system is the presence of opiate receptors, and evidence that opiates play some role in mediating reward has been reviewed. The ventral striatum (patch system) receives afferents from limbic cortex and amygdala, structures which have also been implicated in the effect of rewards upon behavior. Finally, efferents from the patches affect dopamine neurons in substantia nigra, which have been implicated in reward (89).

The effect of reinforcement on memory is localized in dorsolateral striatum, the area where the matrix is most prominent. The major neurochemical attribute of the matrix is the presence of acetylcholine; the role of striatal acetylcholine in memory is well established (59–61). The matrix receives topographically organized afferents from neo-cortex. As described, this arrangement provides a substrate for the site-specific facilitation of visual and olfactory conditioning. The output of the matrix to motor relay centres mediates the response aspect of the learned stimulus-response associations.

The hypothesis proposed, on the basis of neurochemical and anatomical considerations, is that the patches mediate reward, and that the matrix mediates stimulus-response memory, a function that is influenced by reinforcement. Both patch-related reward and matrix-related reinforcement are mediated by dopamine released from separate divisions of the nigro-striatal system projecting to the two compartments. To the extent that this functional distinction between the patch and matrix compartments can be supported by the available evidence and by additional experiments that test the hypothesis, the behavioral distinction between reward and reinforcement will be confirmed. The association of the reward and memory/reinforcement functions with the patch and matrix systems would be a major step forward in our understanding of the neural control of learned and motivated behavior.

ACKNOWLEDGEMENTS

Preparation of this manuscript was supported by grants from the Medical Research Council of Canada, the National Sciences and Engineering Research Council of Canada, and from Fonds FCAR, Province of Quebec.

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