Neural Mechanisms of Reinforcement

The primary goal of ***Learning and Complex Behavior*** (***LCB***) is to identify fundamental principles based upon the experimental analysis of behavior and then to use those principles to interpret complex human behavior under circumstances that preclude experimental analysis. If behavioral research is the basis for the principles, then why should we be concerned with the neural mechanisms that underlie behavior?

The text indicates one type of reason—the imperfect correspondence between the ability of a stimulus to elicit behavior and its ability to function as a reinforcer. Some reinforcers do not elicit any clearly identified behavior, such as most conditioned reinforcers (e.g., the approval of others). And, some eliciting stimuli do not function as reinforcers even though they clearly evoke behavior, such as papillary dilation by lowering the illumination. If a unified reinforcement principle is to interpret such cases, it must be assumed that, whatever neural mechanisms underlie selection by reinforcement, those mechanisms are engaged in the first case but not in the second. However, without independent knowledge of the status of the neural mechanisms, our accounts are not compelling and invite circular reasoning. For example, suppose that we answer the question, "Why do some stimuli (e.g., expressions of approval) function as conditioned reinforcers?" with the reply, "Because they engage the neural mechanisms of reinforcement." However, if we are then asked, "How do you know that these stimuli engage the neural mechanisms of reinforcement," we cannot reply, "We know this because approval functioned as a reinforcer." Such a sequence exemplifies circular reasoning: We have based our "explanation" on the very observation that led to the explanation.

Problems of the preceding sort are not unique to analyses at the behavioral level. Such puzzling phenomena always exist at the boundary between one science and its neighbors. These phenomena require information from both sciences to be fully understood. Skinner (1974) unambiguously allied the science of behavior with biology as shown in the following quotation: "The experimental analysis of behavior is a rigorous, extensive, and rapidly advancing branch of biology" (p. 255). He noted further, "The … gap between behavior and the variables of which it is a function can be filled only by neuroscience, and the sooner … the better" (Skinner, 1988, p. 460). Thus it is quite consistent with the experimental analysis of behavior to integrate observations at the behavioral level with those at the level of neuroscience to interpret some phenomena.

A second type of reason for behavioral science to interface with other biological sciences is more fundamental, and—in the larger picture—perhaps more important: If behavioral principles are to be accepted as adequate for the interpretation of complex behavior, it may be politically necessary—if not scientifically so—for those principles to be coordinated with the neural mechanisms that implement them. Consider the fate of Darwin's principle of natural selection, now generally accepted as the fundamental insight in biology. Darwin revealed his proposal for evolution through natural selection with the publication of *The Origin of Species* in 1859. However, it was not until the 1930s that most biologists fully embraced natural selection. What was responsible for the delay and what caused the principle ultimately to be accepted? Its acceptance was due to several factors, the chief of which was that Darwin did not know the biological mechanisms that implemented natural selection. Mendel's work on genetics was not rediscovered until after Darwin's death and quantitative methods that could trace the changes in gene frequency produced by natural selection were not devised until much later. (See Donahoe, 2003 for a historical review of the factors that led to the acceptance of Darwinism in biology.)

Even though Darwin's principle of natural selection was based on extensive research and naturalistic observations, his functional account of evolution through natural selection was not accepted until the biological mechanisms that implemented it were uncovered through experimental work at other levels of analysis. If the historical parallel holds, the general acceptance of selection by reinforcement as the central insight into complex human behavior may await the discovery of the neural mechanisms that implement it.

Neural System of Reinforcement

Research on the biological mechanisms of reinforcement is one of the most vigorously pursued areas in neuroscience. When ***LCB*** was published in 1994, strong—but indirect—evidence implicated a broadly projecting, dopamine-releasing neural system in reinforcement. Behavioral research showed that a wide range of stimuli could control any of a wide range of responses, which required a neural system that could simultaneously affect synaptic efficacies throughout large portions of the brain. Neuroanatomical research indicated that dopamine-releasing (*dopaminergic*) neurons projected widely in the brain. Biobehavioral research demonstrated that electrical stimulation of these dopaminergic neurons increased the subsequent strength of behavior that preceded the stimulation; i.e., the release of dopamine served as a reinforcer. (*See pp. 54 ff.*) Since the publication of ***LCB***, considerable direct evidence has accumulated that is consistent with the original proposal.

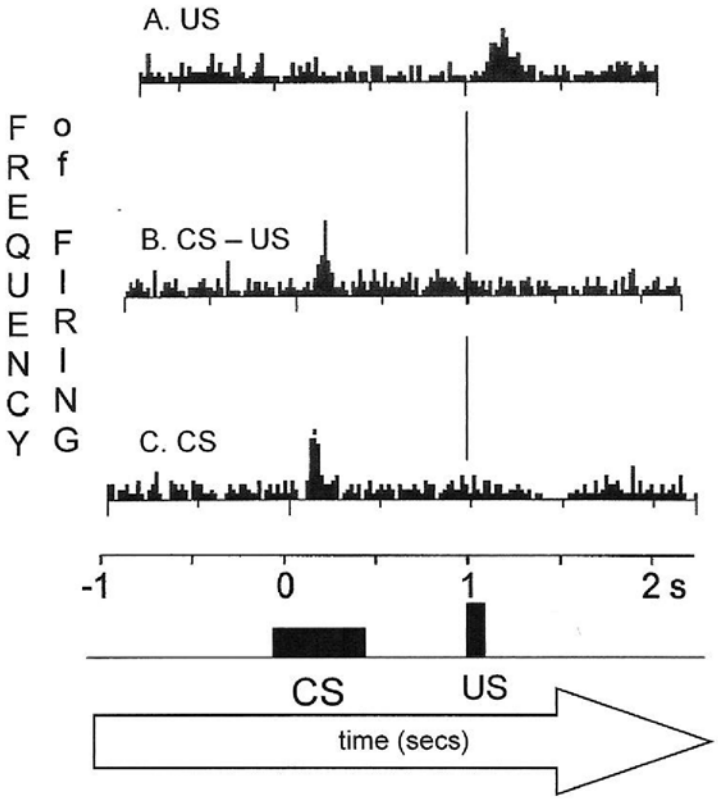

Figure 2.A *The frequency of firing of a single dopaminergic neuron during three phases of a classical procedure*
Panel A shows responding during the US before conditioning. *Panel B* shows the responding during the CS and US after conditioning. Panel C shows responding during the CS alone after conditioning.

The neural system of reinforcement has been most systematically studied by Wolfram Schultz and his colleagues. Both classical and operant procedures were used. In a typical operant task, reaching and touching a target was reinforced in monkeys by a squirt of orange juice into the mouth. While the monkey was behaving in the task, the neural responses (firing) of individual dopamine-secreting neurons in midbrain nuclei (the *ventral tegmental area* and *substantia nigra*) were recorded with electrodes. As noted in ***LCB***, neurons whose cell bodies are found in these nuclei project widely to the frontal lobes and subcortical structures that mediate between environmental input to the brain and output from the brain to muscles. (*See* ***Figure 2.12*** *in* ***LCB***.) **Figure 2.A** depicts the rate of firing of a dopaminergic neuron detected by an electrode during three phases of a classical procedure (Schulz, 1997; 2001). Panel A shows that when the US was presented alone (or during the first trial of an experiment), the frequency of firing of the neuron increased dramatically. Note one other characteristic of these neurons—they fire at substantial baseline rates even when no discrete stimulus is presented. Other work, not shown here, indicated that a wide variety of stimuli—visual, auditory, and touch—initially cause small increases in firing, but that these increases habituate unless the stimulus can function as an effective reinforcer. Panel B shows that, after a number of pairings of the CS with the US, the increase in firing now occurred when the CS was presented but no longer occurred during the US (reinforcer). The increase in dopaminergic activity during the CS demonstrates that stimuli that function as conditioned, or secondary, reinforcers acquire the ability to activate the same neural system of reinforcement as unconditioned reinforcers. As the result of conditioning, a formerly "neutral" stimulus, such as a tone that originally instigated only small transitory increases in firing, now evoked pronounced increases in the firing of dopaminergic neurons. (*See pp. 96 ff. in* ***LCB***) Whereas the CS was now able to activate dopaminergic neurons, the US was no longer effective. The inability of the US to increase the firing of dopaminergic neurons means that it could not longer function as a reinforcer when presented in the context of the CS. This is the neural basis of the *blocking effect.* (*See pp. 47 ff. in* ***LCB***) Panel C depicts the firing of a dopaminergic neuron on a test trial when the CS was presented alone. At the normal time of occurrence of a US-elicited increase in firing, the firing of dopaminergic neurons *decreased.* That is, the presentation of the CS inhibited the firing of dopaminergic neurons at that time.

To summarize, recent work on the neural systems of reinforcement provides direct support for the view that a diffusely projecting, dopaminergic system plays a central role in the behavioral process of reinforcement.

Cellular Mechanisms of Reinforcement

Recent work also provides insight into the cellular mechanisms that implement reinforcement. (*See footnote 70, pp. 66 ff. of* ***LCB***) **Figure 2.B** depicts some of the cellular events that occur when the synaptic efficacy changes between a presynaptic and postsynaptic neuron. Neurons affect one another though the liberation of compounds called *neurotransmitters*. The primary excitatory neurotransmitter in the brain is *glutamate*. An excitatory transmitter is a molecule that facilitates the production of an action potential in the postsynaptic neuron. Glutamate is liberated by the presynaptic neuron and acts upon two main types of glutamate receptors located on protuberances (*spines*) in the membrane of postsynaptic neurons. One glutamate receptor—the AMPA receptor—rapidly facilitates the initiation of a nerve impulse in the postsynaptic neuron. A second glutamate receptor—the NMDA receptor—plays a different role, but one that is crucial if glutamate-induced firing is to produce long-lasting changes in synaptic efficacies. (See http://www.bris.ac.uk/Depts/Synaptic/info/glutamate.html for a more detailed discussion of

glutamate receptors.) Normally, the channel in the NMDA receptor is blocked by a magnesium ion. However, if the postsynaptic neuron is sufficiently stimulated through the action of AMPA receptors, the electrical potential across the membrane of the postsynaptic neuron changes and the magnesium ion migrates out of the channel. The opening of the ion channel of the NMDA receptor permits calcium ions (Ca^{2+}) to enter the cell. When calcium enters the postsynaptic neuron, a sequence of intracellular events occurs: A key event is thought to be the placement of a molecular "tag" on nearby AMPA receptors that have just been acted upon by glutamate. This tag, which lasts several hours, labels those receptors as having been recently stimulated by glutamate (Frey & Morris, 1998).

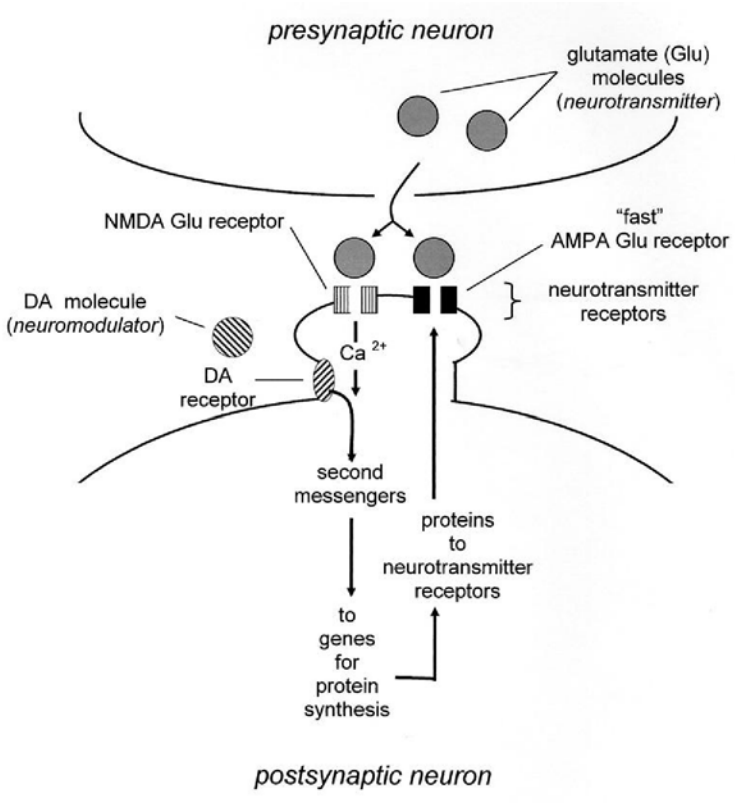

Figure 2.B *Neurotransmitters and intracellular events that play a role in increasing synaptic efficacies between neurons during conditioning.*
See the text for discussion of the sequence of events that occur during conditioning.

If the neural pathways that have recently been active are followed by behavior that produces a reinforcer, then dopaminergic neurons in midbrain nuclei are stimulated. The neuromodulator dopamine is liberated from enlargements (*varicosities*) distributed along the axon of these neurons and diffuses into extracellular space where it can act upon many neurons. When dopamine receptors are engaged together with AMPA and NMDA receptors, their concerted action initiates a series of intracellular events (*second messengers*) that cause genes in the nucleus of the cell to synthesize new proteins. These proteins then migrate down the axon and, when they contact tagged receptors, change the structure of those receptors and/or cause new receptors to emerge in the membrane of the postsynaptic cell. At the conclusion of this sequence of events, there is a higher probability of initiating an action potential in the postsynaptic neuron

when the presynaptic neuron liberates glutamate because AMPA receptors have become more sensitive (or more numerous). The net result is that synaptic efficacies are increased along the neural pathways in which environmental stimuli initiated activity that led to the reinforced behavior. Note that the synaptic tags that mark recently active receptors allow the delayed synthesis of proteins to be distributed generally but to have their effects on only specific AMPA glutamate receptors.

The details of the cellular mechanisms of reinforcement will likely be modified and elaborated by further research, but the general picture is already emerging. The conceptual similarity between how proteins act on specific synapses of the entire neuron and how reinforcers act on specific environment-behavior relations of the whole organism is striking. In the reinforcement of behavior, a general reinforcement "signal"—the release of dopamine—contacts synapses within a large population of neural pathways but has the cumulative effect of changing only those synapses that are recently active before the reinforcer. Likewise, in the strengthening of synaptic efficacies, a general diffusion of proteins contacts a large population of receptors (some neurons have over 10,000 synapses) but has the cumulative effect of changing only those receptors that have been recently active. In both cases, natural selection has evolved a general mechanism that cumulatively has specific effects.

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