

CHAPTER 5

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On my annual drive home for Thanksgiving last fall, I was in the midst of writing this chapter, and I was thinking about how classical conditioning fits into our everyday lives. We usually think of classical conditioning as a contrived model of learning that happens in the laboratories of scientists who, following in the footsteps of Ivan Pavlov, do things like ring bells and watch dogs salivate. Does classical conditioning also happen in the real world? While pondering this question, I saw the traffic light ahead turn to yellow and moved my foot from the gas pedal to the brake. "Yes!" I thought, "An otherwise neutral stimulus, a yellow light, has come to control my foot!" How did this happen? Of course yellow traffic signal lights are extremely good predictors of red lights that direct us to stop. I had experienced the predictable sequence of yellow light–red light–stop many times. The yellow light had achieved the same power red lights have in evoking my reflexive foot movement to the brakes.

I drove onward to the highway. A sharp curve was ahead; before I reached it, I began to lean in the opposite direction—another conditioned response! The sight of an impending curve predicted that centrifugal forces would press on my body, and I automatically leaned to compensate.

Now I was getting close to the home in which I grew up. I'd exited the highway and was cruising through my hometown. The sight of my old high school made my heart race—an emotional reflex! I'd had many powerful emotional experiences, like exciting sports events and exhilarating (and demoralizing) romances, within that school. And seeing it elicited the feelings I associated with that place and the same emotional responses the actual events once evoked.

Finally I arrived home. My mother came out of the kitchen with the turkey on a platter. I saw that large bird, and my mouth began to water—another example of classical conditioning! I'd eaten that turkey dinner many times, and each time the sight of turkey on a platter predicted turkey in my mouth within minutes. The

sight of turkey had achieved the power of the taste of turkey, reflexively evoking salivation. This kind of classical conditioning is an example of what early psychologists called *psychic secretion*: the release of body fluids in response to seemingly neutral stimuli that predict situations in which reflexive secretions will occur. A doctor named Ivan Pavlov, whom you may remember from Chapter 1, studied gastric reflexes and psychic secretions. His work began the formal study of classical conditioning.

MY THANKSGIVING DRIVE home included many examples of classical conditioning, which happens to us often. The familiar events I described expressed acquired associations between previously neutral stimuli (seeing a curve in the road) and consistent subsequent events (driving along the curve) that evoked reflexive responses (leaning). This form of learning, called **classical conditioning**, gives us much of our motor coordination; such conditioning depends on predictable timing of stimuli and responses. Classical conditioning is pervasive in many human and animal learning and memory systems, and it is the predominant type of learning in motor systems. Researchers use classical conditioning to examine the process of learning and, at the same time, measure the memory for acquired associations between different stimuli and responses. This chapter will highlight some examples of classical conditioning that reveal its particular rules, including how association, predictability, and timing of stimuli influence the process.

Fundamental Questions

1. In what ways does classical conditioning occur in daily life?
 2. What is the nature of memory representation in classical conditioning?
 3. Does classical conditioning apply only to simple motor responses?
 4. How does the brain represent conditioned responses?
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Pavlov Began the Study of Classical Conditioning

Ivan Pavlov was a theology student, but he became interested in chemistry and physiology. His early research focused on connections between the nervous system and other internal organs, including the digestive system. The prevailing view at that time was that digestive fluids were released into the stomach when food particles stimulated the stomach lining. However, Pavlov suspected that the ner-

vous system acted as a critical intermediary between the food stimulus and the stomach's release of fluids. To investigate this possibility, he developed a novel surgical procedure that allowed him to introduce food either directly into the stomach without letting it travel through the mouth or gullet, or instead into the mouth, allowing the food to travel through the upper gullet and then out the opening without going to the stomach.

Pavlov found that food in the mouth caused the release of gastric fluids even when the food never reached the stomach. He concluded that the two organs communicate via the nervous system: Food excites the taste sensors in the mouth and gullet, transmitting signals to the brain stem. Nerves that innervate the stomach then initiate the release of gastric fluids. This kind of pathway is similar to the muscular reflex pathways that begin with sensory stimulation and end in skeletal muscle contractions (see Chapters 2 and 3). For discovering this reflex arc for digestion, Pavlov received the Nobel Prize in 1904.

By then Pavlov had turned his attention to intriguing reports of "psychic secretion." French physiologist Claude Bernard had described how gastric juices of a horse could begin to flow even when the animal only caught sight of hay—before the food entered its mouth. (Another common example of psychic secretion occurs in new mothers as the letdown, or ejection, of breast milk, which is evoked by the sight, smell, or even mention of their infants.) Pavlov replicated this phenomenon in the dogs he studied, noting that the mere sight or smell of food was sufficient to elicit salivary and gastric secretions. But he also found the phenomenon unreliable. Although the dogs would salivate at the sight of beef, they tended to salivate less after repeated visual presentations of beef. But sometimes salivation was triggered by events that preceded the sight of beef—such as when the person who regularly provided the food entered the testing room. How did this occur? And why was this kind of reflex unreliable, contrasting with the standard observation that reflexes are automatic?

In the experimental protocol he developed, Pavlov focused on the automatic salivation that happened when food was placed in a dog's mouth. He implanted a fine tube into the dog's mouth to collect saliva, allowing him to measure the intensity of this digestive reflex by the amount of saliva produced. Pavlov distinguished the automatic, innate, and reliable reflex from the *conditioned* (learned) reflex. The stimulus that triggered an innate reflex (food in this case) was called the **unconditioned stimulus (US)**, and the automatic reaction it triggered (salivation) was called the **unconditioned response (UR)**. In this framework, the **conditioned reflex** (the one learned through experience) is composed of an arbitrary, initially neutral stimulus called the **conditioned stimulus (CS)**, such as a bell or a light, presented with a US to elicit a **conditioned response (CR)**, which typically resembles the automatically generated UR. The general procedure involves presenting the CS for some duration, at the end of which the US overlaps

(Figure 5.1). Early in training, the neutral CS evokes no response; but each presentation of the US automatically evokes the UR. During learning, the CR (which resembles the UR) initially appears shortly before the US; then the CR appears earlier following the beginning of the CS. There are many examples of these stimuli and responses used in classical conditioning (Table 5.1). You can see that the USs in the table would naturally elicit the responses, whereas the CSs, which can be made to evoke the same responses, are neutral stimuli easily manipulated in a laboratory.

Through many systematic studies, Pavlov (1927) identified the importance of two parameters in establishing and maintaining the conditioned reflex: The CS must precede the US by a short interval, and the CS must consistently predict the US. In addition, Pavlov examined the acquisition of the conditioned response as well as its extinction—the gradual disappearance of the learned response when

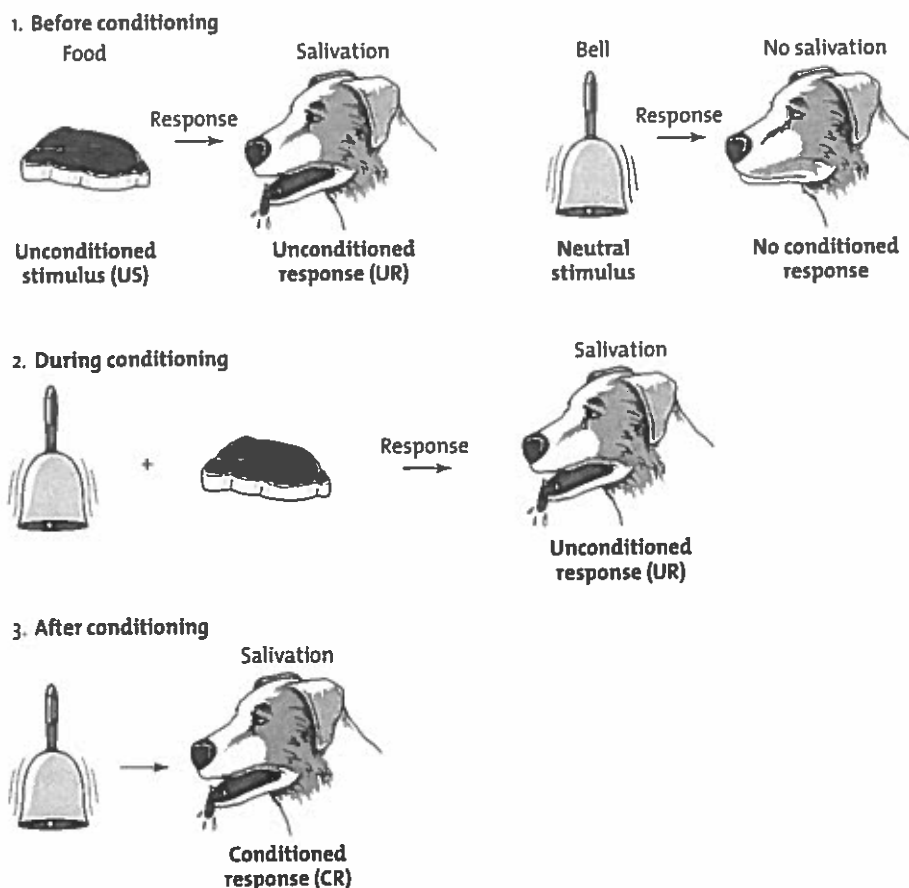


FIGURE 5.1 Stages in conditioning in Pavlov's experiments.

TABLE 5.1 Stimuli and responses in classical conditioning.

Stimulus or Response	Examples
Unconditioned stimulus (US)	Food, loud noises, air puff to the eye
Unconditioned response (UR)	Salivation, startle, eyeblink
Conditioned stimulus (CS)	Tone, light
Conditioned response (CR)	Salivation, startle, eyeblink

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the US ceases to follow the CS. Pavlov noted that the CR sometimes reappeared after extinction: When animals were returned to the training situation after extinction the day before, the CR showed a spontaneous recovery (that is, it reappeared without additional training). These and other observations laid the foundations of research in classical conditioning.

Classical Conditioning Provides Protocols for Studying Simple Motor Responses

Classical conditioning has been used extensively to study the association between an initially neutral stimulus, such as a bell in Pavlov's studies, with stimuli that evoke reflexive responses, such as the taste-evoked salivation reflex. The classical conditioning procedure has received widespread attention because it provides straightforward, measurable behavioral responses to stimuli. Researchers can systematically manipulate the features of these stimuli and their timing. Through many studies, we have learned a lot about what kinds of stimuli effectively result in conditioning and about the critical role of timing the stimulus presentations. But although the laboratory procedures used to explore this kind of learning are artificial, conditioning occurs naturally in many situations.

Using classical conditioning, researchers have gotten neutral stimuli to evoke a broad range of simple reflexes involving muscular movements, like the knee jerk reflex, and responses of internal organs, such as cardiac acceleration. The classical conditioning protocol can be used to study many different forms of learning, so it is important to distinguish classical conditioning as an experimental protocol from the specific kinds of memory that are formed during the conditioning procedure. For example, pairing tones with particular tastes can condition reflexive salivation. In addition, this conditioning experience also creates conscious cognitive memories of the stimuli, the responses, and the entire learning experience.

Eyeblink Conditioning: Classical Conditioning of an Elementary Motor Response

If you have visited an eye doctor, you may have been tested for glaucoma with a procedure in which the doctor directs a small, quick burst of air at your eyeball, causing you to blink. The same reflexive eye blinking in response to a mild air puff has been examined extensively in both humans and animals (Gormezano et al., 1987). In a typical experiment, the subject is fitted with a headband containing a nozzle pointed at an eye and a device that records the blink. The US is a brief, gentle puff of air directed at the eye or, in some cases, a mild electrical shock to the area surrounding the eyelids. The CS is typically a light or tone. The UR is typically a rapid, vigorous eye closure, and the learned CR is usually a gradual, less intense blink. Some studies measure the strength and timing (or *latency*) of the onset of the CR, but the most common measure of learning is the percentage of trials in which a CR occurs.

The findings for classical conditioning of the eyeblink reflex are remarkably similar across species. The capacity for classical conditioning of this reflex develops over the first few months of life in human infants and over the first several days after birth in rats (Ivkovich et al., 1999). Although most studies of eyeblink conditioning have used animals, interest is growing in the study of human eyeblink conditioning because of its simplicity and the ability to control aspects of the learning situation (Woodruff-Pak, 1999; Steinmetz, 1999).

Common Conditioning Procedures

As Pavlov recognized, a key feature of classical conditioning is the timing between the CS and US. Several variations of the basic classical conditioning protocol have let researchers examine the underlying basis for this relationship (Figure 5.2). Four such variations are particularly important:

1. **Delay conditioning:** The prototypical procedure involves presentation of the CS for a short period, usually less than one second, with the US presented during the last part of the CS period. Thus, for example, the CS might be a tone presented for 500 milliseconds and the US a 100-millisecond air puff presented during the last part of the CS period. The time between the onset of the CS and the onset of the US is called the **interstimulus interval (ISI)**. Another important temporal measure in classical conditioning protocols is the time between successive presentations of the CS and US, called the **intertrial interval (ITI)**.
2. **Trace conditioning:** This protocol is similar to delay conditioning in that the CS is presented first, followed reliably by the US at a particular ISI. However, in trace conditioning the CS terminates before the US is presented, leaving a gap (or *trace interval*) between the CS and US when no stimulus is present.

1. Delay conditioning



2. Trace conditioning



3. Simultaneous conditioning



4. Backward conditioning



FIGURE 5.2 Pavlovian protocols.

3. **Simultaneous conditioning:** In this procedure, the CS and US are presented at the same time. This might seem to be the most effective way to induce a strong association between the CS and US; but as we will see, it is not the most effective protocol for classical conditioning.
4. **Backward conditioning:** In this protocol, the order of the CS and US is reversed, so the US is presented at a specific interval before the onset of the CS. This technique is used to examine whether the order of conditioned and unconditioned stimuli is critical for learning the association between them.

Control Protocols: Critical Conditions for Learning

Control conditions are also commonly used to test whether the responses learned during conditioning can be attributed to the pairing of the CS and US,

as opposed to the effects of repetition of either stimulus alone. Considering this issue helps us understand exactly what subjects learn when they develop an association between stimuli that is strong enough to change their behavior. The assumption in classical conditioning is that the CS and US have become associated or connected in the subject's mind because they happen close together in time—that is, the subject has learned about their *contiguity*. However, as discussed in Chapter 3, behavioral responses can change without stimulus contiguity—even after a single experience with some types of stimuli. Particularly for intense experiences, a single stimulus can cause sensitization, which increases responsiveness to a variety of stimuli. On the other hand, we also saw in Chapter 3 that repetitive presentation of a stimulus results in habituation (a decrease in behavioral responses). The classical conditioning paradigm presents both the CS and US repeatedly and so could diminish reflexive responses to either stimulus. Also, in typical eyeblink conditioning, the US is moderately aversive and could evoke sensitization of responses to any other stimulus. How can researchers be sure whether the effects they observe are caused by habituation, sensitization, or actual classical conditioning?

To control for the possibility that the CS or US alone could change behavioral responses, and to examine any effects caused specifically by the contiguity of the CS and US, experimenters use different types of control procedures. *CS alone* or *US alone* presentations determine whether either stimulus without the other can affect behavior. The *explicitly unpaired CS and US* condition presents the CS and US separated in time and in alternating or random order. This protocol is often used as a control condition for the standard relationship between the CS and US. However, a possible problem with this kind of control condition is that the subject may learn that the CS reliably predicts the *absence* of the US; in cases where the US is aversive, the subject may learn that the CS is a safety signal indicating that no aversive stimulus will occur. Indeed this protocol sometimes produces a change in response to the CS that is *opposite* that of the UR (such as less than the normal spontaneous rate of blinking). To address this issue, another possibility is to time the CS and US presentations independently, which is called *random control*. In this protocol, the CS and US usually occur separately but sometimes can coincide or occur in close temporal proximity. This might seem to be the most valid control for a reliably predictive temporal relationship between the CS and US. However, several studies have observed that even random control procedures result in learning, possibly because a few rare coincidences of the CS followed by the US may be sufficient to support learning.

With these basic conditioning procedures and control conditions in mind, we can examine the properties of classical conditioning, as well as its neurobiological basis.

Interim Summary



Classical conditioning is defined as a consistent predictive relationship between a CS and a US that reflexively evokes a UR. Conditioning is observed when, after repeated pairings of the CS and US, the CS reliably evokes the CR. This procedure has been applied in a wide variety of situations for different types of stimuli and responses, such as eyeblink conditioning in both animals and humans. The standard version of this kind of learning is delay conditioning, in which the CS begins before and continues through the US; the interval between CS onset and US onset is the ISI. Also used are trace conditioning, in which the CS is transient and most of the ISI is an empty trace interval; simultaneous conditioning, in which the ISI is zero; and backward conditioning, in which the US precedes the CS. Conditioning depends on pairing of the CS and US and is usually most effective with delay conditioning.

Variations in Conditioning Reveal Its Basic Properties

There are many variations of the four classical conditioning protocols (delay, trace, simultaneous, and backward conditioning) described in the previous section. Here we consider examples of these types of classical conditioning that have informed us about a number of issues crucial to understanding how the process works: critical timing of the CS and US, how conditioned responses disappear, how different relationships between the CS and US can affect conditioned responses, and how conditioned responses can generalize or discriminate between stimuli.

Gradual Acquisition of a Conditioned Response Depends on Timing

Classical conditioning of motor responses is typically gradual: The conditioning subject must experience many CS and US pairings before the conditioned response grows to its full magnitude and form (Figure 5.3). On the first few trials, there may be no CRs. Indeed, in a study of four- and five-month-old infants, no conditioning was observed during an initial 30-trial session; but this training was required for learning to occur during a second conditioning session (Ivkovich et al., 1999). With additional training, the likelihood and expected magnitude of a CR increase. Note how the gradual, quantitative classical conditioning of motor reflexes contrasts with the rapid, qualitative learning of conscious memories.

The effectiveness of classical conditioning is also influenced by several factors that provide insights into its properties and mechanisms. One of the most significant aspects of this kind of learning is the intensity of the CS and the US. As you

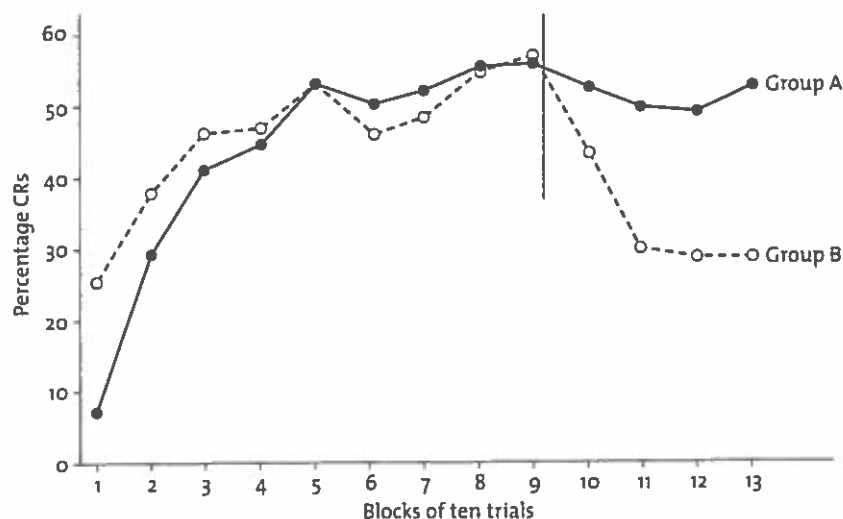


FIGURE 5.3 The acquisition of Pavlovian conditioning.

Group A received a consistently strong US. Group B received the strong US for 90 trials, after which the US intensity was reduced.

might expect, conditioning happens more quickly and attains higher response levels when the CS and US are more intense. Thus in the example shown in Figure 5.3, when the intensity of the US was reduced in Group B, the percentage of trials in which a CR was observed decreased.

In classical conditioning, timing is also critical. As Pavlov discovered, the time between the US onset and the CS onset (the interstimulus interval, or ISI) is crucial to conditioning effectiveness. In general, little learning is observed in simultaneous conditioning, even though a perfectly overlapping CS and US might seem to provide the ideal temporal contiguity of stimuli. Even brief ISIs are not optimal for conditioning. Rather, learning is most rapid at an ideal ISI. In both humans and animals the optimal ISI for classical eyeblink conditioning is about 250–500 milliseconds (Figure 5.4A). Little conditioning is observed at ISIs of less than 100 milliseconds or greater than 2 seconds. The similarity between animals and humans in sensitivity to CS–US timing is remarkable.

Importantly, ISI duration affects CR timing. In his studies of salivary reflexes, Pavlov varied the ISI from a few seconds to a few minutes and observed that the CR onset varied to occur shortly before the US, as if the CR “anticipated” the timing of the US (Figure 5.4B). Studies of human and animal eyeblink conditioning have similarly shown that with relatively long ISIs (like one second), the blink (CR) initially appears just before the puff of air (US), and the timing of the CR progressively shortens so that the conditioned blink (CR) is at its maximum when the

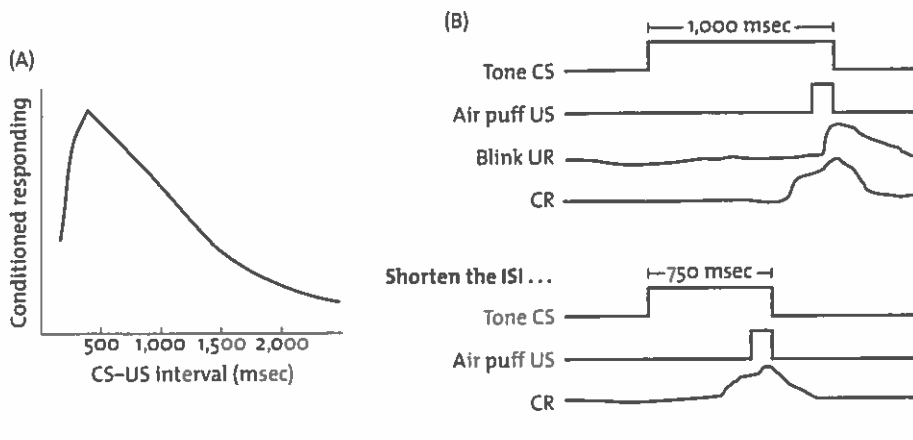


FIGURE 5.4 Classical conditioning at different ISIs.

A. The strength of conditioning is maximal at an intermediate CS-US interval.
B. Conditioned responses in conditioning with different CS-US intervals. The CR is timed to anticipate the onset of the US.

US occurs. These findings also suggest that the CR is timed to anticipate the US. Given these learning patterns, what do you think happened in backward conditioning when Pavlov presented the US before the CS—that is, when Pavlov gave the dogs their food and *then* rang the bell? Because the CS was not in position to predict the US in this procedure, no learning resulted. These observations show that learning is not limited to an acquired *association* between the CS and US. Rather, during conditioning, subjects also learn the *temporal relationship* between them. Specifically, they learn that the CS predicts that the US will occur at a particular time. Recall that when I was driving home for Thanksgiving, the timing of the yellow signal light in predicting the impending red signal light was vital. The normal interval between these events told me when and how forcefully I should step on the brakes.

Conditioned Response Extinction Is Not Forgetting

There is typically little “forgetting” (actual loss of memory) for a classically conditioned reflex. Even after considerable time, conditioned responses are strong as soon as conditioning trials are again presented. However, this does not mean conditioned responses are permanent and immutable. Rather, if a CS is presented repeatedly in the absence of a US, this reduces the CR, which eventually disappears. In other words, a CS, such as Pavlov’s bell, occurring in the absence of a US, such as food, on multiple occasions causes extinction of the conditioned response. For example, as shown in Figure 5.5, following successful conditioning

of the human eyeblink response, repeated presentations of the CS tone or light in the absence of the US air puff gradually decrease the probability of the CR blink in response to the light or tone.

Following extinction, the subject behaves just as observed prior to conditioning, showing no response to the initially neutral CS. Therefore, we might conclude that the conditioned response has been unlearned—that is, that the CS–US association formed during conditioning has somehow been eliminated. However, multiple lines of evidence indicate that conditioning's effects are not simply erased from the mind. One such clue is the phenomenon of spontaneous recovery. Following conditioning and extinction in an initial session, typically the subject is removed from the training situation and then brought back the next day for additional testing. Upon presentation of the CS trials on the second day, strong CRs are typically observed even though the response was fully extinguished at the end of the previous day's training. This reappearance of the CR without retraining is known as **spontaneous recovery**. Indeed, after spontaneous recovery, only repeated presentations of the CS alone will reduce and ultimately again extinguish the CR. Typically the CR will spontaneously recover again the next day, though with reduced initial strength. If extinction trials are again presented, the response will diminish further, then spontaneously recover again the next day at a lower level, and so on until the response may completely disappear.

What is the mechanism for spontaneous recovery? Pavlov proposed that just as the initial conditioning can be viewed as the acquisition of an *excitatory association* between the CS and US, CS presentations without the US may lead to a separate *inhibitory association* in which the CS is associated with the absence of the US. According to this view, when extinction is complete, the strength of the inhibitory association has become as strong as the original excitatory association, and the two contradictory associations cancel each other. If this is true, though, why isn't a single extinction session sufficient to cancel the initial training session? A key assumption here is that inhibitory associations are more fragile and tran-

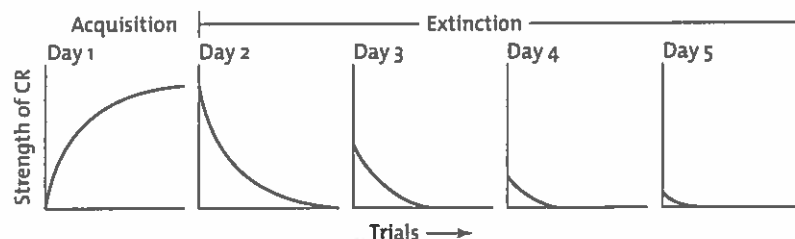


FIGURE 5.5 Human eyeblink conditioning and the reduction of responses during extinction.

sient than excitatory associations; so unlike excitatory associations, they fade with time. After the extinction session, the inhibitory association diminishes between testing sessions; when it becomes weaker relative to the excitatory association, the excitatory association "wins" and the CR reappears. Additional extinction trials strengthen the inhibitory association so that it eventually becomes strong and persistent enough to produce lasting cancellation of the excitatory association.

Here's an alternative perspective: During extinction the repeated presentation of the CS without the consequence of the US causes loss of attention to the CS, regardless of its previously formed association with the US. Conditioned responses cease when the attention level for the CS is so low that it is no longer processed and therefore cannot evoke the CR. According to this view, following an interval between testing sessions, attention is again focused on the CS, which can again elicit the CR, resulting in its spontaneous recovery. These two accounts of spontaneous recovery are not mutually exclusive; perhaps both are correct.

Another line of evidence indicating that conditioned responses are not lost during extinction is the phenomenon of **disinhibition**, in which an extinguished CR reappears not spontaneously but in response to another, typically arousing stimulus. Imagine a situation in which conditioning with a tone CS is completed and followed by extinction so that eyeblink CRs are no longer observed. Now imagine a loud bell sounding shortly before the CS is presented. Typically the CR reappears: It is disinhibited following the noise (similar to the phenomenon of sensitization). According to Pavlov's theory, the fragile inhibitory associations are not only more susceptible than the excitatory associations to the passage of time (as observed in extinction); they are also affected more by the bell. So the loud noise of the bell disrupts the balance between excitatory and inhibitory associations, and the stronger excitatory association trumps the weaker inhibitory one, again generating conditioned responses. According to the alternative attentional account of extinction, the noise, like the passage of time, increases attention to all stimuli, including the CS (an example of sensitization). This results in a recovery of CS processing and renewed generation of the CR.

Finally, a conditioned response can be retrained more readily following extinction than during its initial conditioning. Such **rapid reacquisition** of the CR following its extinction indicates that even when no CRs are observed, at least some subtle association between the CS and US must have been retained. Some rapid reacquisition might be due to spontaneous recovery of the CR. However, even when extinction sessions are repeated until spontaneous recovery ceases, reacquisition of the learned association between stimuli happens more rapidly than original conditioning. Whether spontaneous recovery, disinhibition, and rapid reacquisition involve the same mechanism remains unclear. However, the combined observations for all three phenomena strongly show that once a response is conditioned, it does not disappear following extinction. Some mental represen-

tation of the association remains and can be recovered under the right circumstances. These findings clearly distinguish forgetting (true memory loss) from extinction of previously elicited behaviors, which involves new learning to inhibit an unnecessary or inappropriate response.

Conditioning Can Also Involve Learning Not to Respond

As we've just discussed, extinction may involve the development of conditioned inhibitory associations between a CS and the absence of a US. In addition, other protocols have focused explicitly on demonstrating **conditioned inhibition**: the conditioning of a decrease in CRs to a CS. Conditioned inhibition can be observed only when the conditioned response is apparent, so that there is a baseline of CRs that can be reduced by the inhibitory association. Pavlov designed a procedure for demonstrating conditioned inhibition in a single situation that combines excitatory and inhibitory conditioning. One conditioned stimulus (such as a tone) signals the US (food) and is called the CS+. Another stimulus (a light) signals the absence of a US and is called the CS-. On some trials the tone CS+ is followed by the food US in the usual excitatory conditioning protocol; this provides a baseline level of the salivation CR from which we can test inhibition effects. On other trials, randomly intermixed, the tone CS+ and light CS- are presented together without the food US. Salivation responses to the compound tone/light CS+ / CS- occur initially but gradually diminish, suggesting that the light CS- inhibits conditioned responses to the tone CS+.

Generalization and Discrimination: Conditioned Responses Transfer to Other Stimuli

Two other common phenomena in classical conditioning are **generalization** (the tendency of CRs to result from a stimulus similar to the CS) and its opposite, **discrimination** (the ability to acquire a conditioned response to one stimulus but no response to a similar but distinguishable stimulus). Typically when animals are conditioned to respond to a specific stimulus, such as a tone of a particular frequency, they are likely to show a CR in response to neighboring frequencies. That is, the CR production transfers, or generalizes, to similar stimuli. For example, when rabbits are extensively conditioned to blink when they hear a tone CS of 1,200 Hz, they will also blink in response to similar tones, producing considerable CRs to tones at 800 Hz and 1,600 Hz and fewer CRs to tones at lower or higher frequencies (Figure 5.6). This pattern of graded transfer, called a *generalization gradient*, occurs for a broad range of stimuli used in classical conditioning.

Generalization typically occurs when animals are trained initially with a particular CS and then tested with a variety of similar stimuli. Discrimination occurs

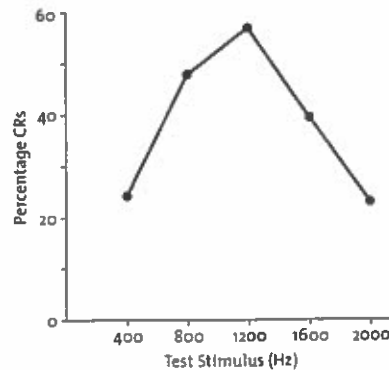


FIGURE 5.6 A typical generalization gradient observed in classical eyeblink conditioning in rabbits.

Note that the response is optimal at the conditioning frequency of 1,200 Hz, and the response is stronger for neighboring frequencies and weaker for more distant frequencies.

when animals are trained from the outset with a combination of the same CS paired with the US and other stimuli presented in the absence of the US. Thus, for example, if an animal is conditioned with a 1,200 Hz tone, it usually shows considerable generalization of the conditioned response to an 800 Hz tone. However, this doesn't mean the animal can't tell the difference between the two tones. If instead it experiences a mixture of trials composed of the 1,200 Hz tone (the CS+) paired with the US and the 800 Hz tone (the CS-) not followed by the US, the difference between the two becomes more meaningful, and conditioning will occur only for the CS+ and not for the CS-. This discrimination can be explained by a combination of excitatory conditioning to the CS+ and conditioned inhibition to the CS-.

Interim Summary

The success of classical conditioning is gradual and depends on optimal timing of the CS and US; learning occurs as the CS consistently predicts US onset. Extinction of the CR is not forgetting. The CR can reappear spontaneously or be inhibited by conditioning with an opposite prediction of the US; can be disinhibited by arousing stimuli; and can be retrained readily. Just as pairing a CS and a US leads to excitatory conditioning, pairing a CS with the absence of a US leads to inhibitory conditioning or conditioned inhibition. Excitatory conditioning and conditioned inhibition combine to determine the extent of generalization or discrimination of responses to a CS.

Learning & Memory in Action

How Do Clinicians Treat Phobias?

Sometimes when people have been exposed to particular stimuli repeatedly in dangerous situations, they develop irrational fears of those and other similar stimuli. A common example occurs when people take elevators to high floors of a building, where they then fear falling. A treatment for such phobias is to gradually expose the person to the fear-producing stimulus. For elevator phobia, a person would be exposed briefly to a view of an elevator, then successively exposed for longer periods. On the first occasion, anxiety might occur immediately and intensively. But after repeated exposures without riding in the elevator, the conditioned anxiety extinguishes. In addition, therapy for this phobia also involves a cognitive component in which the person is encouraged to think about the valuable and important events that will occur when he or she arrives at the end of the elevator ride. This helps people associate positive feelings with arrival at the end of the ride. The combination of extinguishing the conditioned anxiety (the negative UR) and conditioned inhibition of that response by counterconditioning a positive response to the CS often successfully treats specific phobias.

Complex Associations in Classical Conditioning

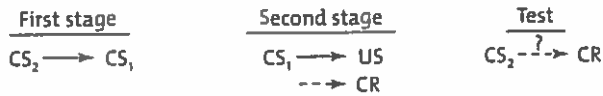
Several variants of classical conditioning show that this type of learning extends to a broad range of situations (Wasserman & Miller, 1997; Rescorla, 1988). These higher-order forms of classical conditioning may involve increased complexity both in the nature of the associations and in the brain circuits that mediate classical conditioning of motor reflexes (Figure 5.7).

1. *Second-order conditioning:* The standard form of classical conditioning discussed thus far is called **first-order conditioning** because it involves a direct association between a CS and a US. **Second-order conditioning** occurs when animals initially develop a first-order conditioned response, and presentation of the first-order CS is preceded by another CS. Thus, for example, an animal might be trained initially in eyeblink conditioning with a tone CS. When the conditioned response to the tone is established, the animal might see a light before each tone,

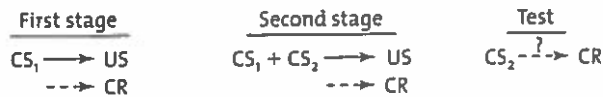
1. Second-order conditioning



2. Sensory preconditioning



3. Blocking



Latent inhibition



4. Contextual conditioning



FIGURE 5.7 Higher-order forms of classical conditioning.

In each type, the solid arrow represents the sequence of stimuli presented during training, and the dashed arrow represents the development of a CR as a result of training. A question mark indicates that the CR may or may not be observed, depending on whether conditioning has occurred in the preceding stage. In the bottom panel on contextual conditioning, the rectangle and oval represent different contexts.

with the US discontinued. After several presentations of the light, CRs would begin to appear even though the light was never paired directly with the US. A good example of second-order conditioning was my conditioned braking response to the yellow traffic signal light during my Thanksgiving trip. The original CS was the red light that initially conditioned the braking response. The yellow light predicted the red light and became a second-order CS that produced the same response as the primary CS (the red light).

2. *Sensory preconditioning*: The phenomenon of **sensory preconditioning** is similar to second-order conditioning except that the two CSs are paired before any excitatory conditioning involving the US. In a sensory preconditioning protocol, the light and tone would be paired for several trials before any presentations of the US. Then the animal would be trained with pairings of the tone and the US until CRs were consistently observed. Sensory preconditioning would have occurred if the light alone could elicit CRs. In advertising, a common approach is to expose potential buyers to a combination of the product name and its purpose many times before the buyer uses the product. If use of the product produces positive feelings, the product name itself should produce positive responses.
3. *Blocking and latent inhibition*: Experience with potential conditioned stimuli before training can impair the efficacy of conditioning. In the phenomenon of **blocking** (Kamin, 1968), conditioning is initially accomplished with pairings involving CS1 and the US. Then CS1 is presented in combination with another stimulus (CS2), and conditioning continues as the CS1–CS2 combination is paired with the US. In a subsequent test with CS2 alone, CRs are not evoked. Thus prior conditioning with a stimulus prevents conditioning of a newly added stimulus even though the new stimulus has been paired with a US repeatedly. Similarly, in the phenomenon of **latent inhibition**, a neutral stimulus such as a tone is presented repeatedly without a US before conditioning. Subsequently the efficacy of that stimulus in supporting conditioning is reduced. Both blocking and latent inhibition show that experience with stimuli before conditioning can affect how well they act as conditioned stimuli. A related problem product makers face is that once buyers have been conditioned to associate one product name with the positive values of a product, it is difficult to establish new associations with that product. Many of us are so conditioned to associate “Kleenex” with the tissue we use to blow our noses that it is difficult to learn the names of competitors’ tissues; this is an example of blocking.
4. *Contextual conditioning*: During conditioning, information about the environmental context is also acquired, and the CS–US association can become closely bound to environmental cues in what we call **contextual conditioning**. In an example, Penick and Solomon (1991) varied the context in which rabbits were trained in eyeblink conditioning. One group of animals were transported to a distinct testing laboratory in individual boxes; each animal was placed in a large restraining box inside a wooden, well-lit, sound-insulating chamber scented with sandalwood oil. Another group of animals was transported together in an open cart to a different laboratory; each animal was placed in a small restraining box inside a metallic, dimly lit, sound-insulating chamber scented with lemon. Both groups were trained with a 1,000 Hz tone as the

CS and an air puff as the US, and they showed equivalent conditioning over six sessions. Subsequently these animals were retested in the same context or switched to the new context. Continued testing in the same context improved performance, presumably due to the previous training under the same circumstances. But the animals showed considerably fewer CRs when tested in the novel context. So animals learn about the context in which they are trained, and whether or not the conditioned response is expressed depends on this contextual learning.

Contextual conditioning occurs every day in situations where we develop emotional responses to stimuli associated with happy or unhappy events that occurred in a particular context. When I was a child, I used to become anxious at the sight of my dentist walking out of his office to greet me for an appointment. But seeing him on the street did not produce this conditioned anxiety. This place-specific emotional reaction is an everyday example of a contextually conditioned response.

In some situations a context itself can evoke conditioned responses even in the absence of the specific CS. An example is fear conditioning in which repeated presentations of a neutral cue, such as a tone, consistently precede a painful stimulus, such as a shock, that evokes a fearful unconditioned response such as freezing in place. Animals and humans learn to produce conditioned freezing responses to the tone. However, subjects also commonly freeze as soon as they enter the environment or context where they experienced the shocks. This is an example of the context itself becoming a CS.

Interim Summary

Several complex forms of classical conditioning involve combinations of stimuli that interact in their roles as CS. Second-order conditioning occurs when neutral stimuli predict an already conditioned CS. Here the neutral stimulus becomes a CS itself, with the former CS acting like a US; in this way chains of associations can be made. In sensory preconditioning neutral stimuli can be associated by pairing before the conditioning procedure; subsequently when one stimulus become a CS, both can elicit the CR. Blocking and latent inhibition have the opposite effect. In blocking, initial conditioning with one CS prevents subsequent conditioning to the combination of the CS and another stimulus. In latent inhibition, initial presentation of a stimulus without a US makes it less able to become an effective CS in later conditioning. Finally, during classical conditioning animals and people sometimes learn not only about the CS but also about the context or environment in which the CS was presented; so conditioning to the CS is less effective in other contexts, or the context itself can evoke the conditioned response.

The Nature of the Association in Classical Conditioning

Two fundamental issues that Pavlov raised remain the subject of examination in studies of classical conditioning. One issue is the nature of the association with the CS formed during learning. Is the critical association between the CS and the learned response it evokes? Or is the critical association an acquired link between the CS and the US, which then indirectly brings about the conditioned response? The other issue has to do with how the association between stimuli is formed. Is mere contiguity of the CS and the US sufficient to support the learned association between them, or is this contiguity only one of several factors required for learning? We will consider these questions in the next sections.

Is Conditioning Based on S-S Associations or S-R Associations?

Exactly what association is learned in classical conditioning? Pavlov proposed that through repeated presentations of a CS and US, the CS comes to substitute for the US in evoking the CR. Pavlov's *stimulus substitution theory* seems to account for learning in the case of eyeblink conditioning because the CS indeed takes on the property of the air puff in eliciting eyelid closures. However, the stimulus substitution theory falls short of providing a complete explanation for conditioning because the CR and UR are not identical. Typically, even in eyeblink conditioning, UR eyelid closures are stronger and faster than the gentler, more gradual eyelid closures that constitute the CR. More problematic is that not all UR components are duplicated in every CR. When food is presented to condition a salivary response, the unconditioned responses to the food stimulus include chewing and swallowing as well as salivation; yet only the salivation component appears in the CR. In addition, some CRs include components that do not appear in their corresponding URs. For example, in salivary classical conditioning, animals orient toward a salient CS (such as the speaker from which a tone CS originates), which does not occur during presentation of the food US. In yet another circumstance that calls Pavlov's theory into question, a CR may take a form opposite that of its UR. If electric shock is used as a US to produce cardiac acceleration, conditioning causes the CR of cardiac deceleration.

These results do not rule out Pavlov's stimulus substitution theory, but they suggest an alternative to the notion that the CS forms a direct association with the response-generating mechanism. Pavlov speculated that the brain contains distinct areas or "centers" (Figure 5.8) for representing the US (the US center) and the CS (the CS center), as well as another area that generates the UR (the response center). He assumed that an innate connection between a US center and the response center created the unconditioned reflex. Pavlov proposed that during classical conditioning, the CS center somehow becomes directly connected with

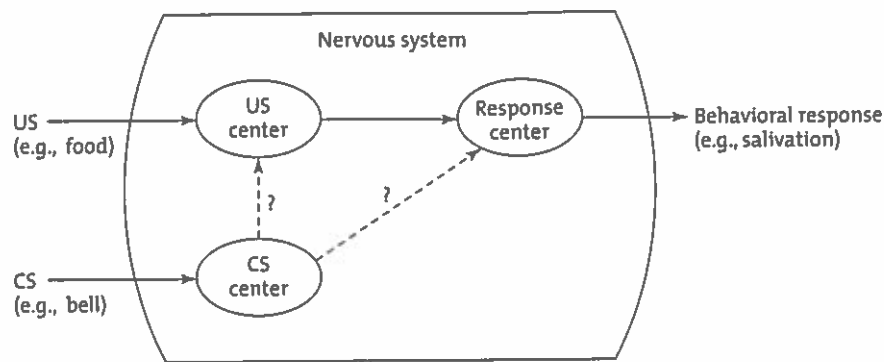


FIGURE 5.8 Possible loci for learning in stimulus substitution theory.

The solid arrow indicates an innate connection between the US and a response center that elicits the behavioral response. The dashed arrows represent possible learned connections.

the response center, thus acquiring the ability to make the UR center generate conditioned responses. Pavlov was basically right about the existence of these centers; we will consider their anatomical locations later when we examine the neural circuitry that supports classical conditioning.

This association between an arbitrary stimulus and a response-generating mechanism is called an *S-R association*. However, if the CR is not identical to the UR, perhaps the CS center becomes connected with the US center rather than the response center. According to this view, through pairing of the CS and US, the CS may develop the capacity to make the subject "think of" the US and then generate an appropriate response that is similar to the UR. Such an association between an arbitrary stimulus (CS) and the mental representation of the unconditioned stimulus constitutes what some call an *S-S association*.

If the S-S association idea is correct, Rescorla (1973) reasoned, then manipulating the connection between the innate US and its related response center should affect the nature of the CR. On the other hand, if the critical connection is between the CS and response centers directly, then modifying the US-response center connection should not affect the CR. To test the nature of these associations, Rescorla invented a *US devaluation* procedure in which he first trained a conditioned response, then separately "devalued" the US, then measured the effect of US devaluation on responses to the CS. Specifically, using a conditioned emotional response paradigm, he trained rats to press a lever to receive rewards. Next he conditioned an association between a light CS and a loud noise US that startled the rats, causing them not to press the lever for several seconds. Then, for the rats in the experimental group, he habituated the emotional response to the loud noise by

presenting the noise repeatedly. Rats in the control group received no other noise exposures. Subsequently, Rescorla measured lever press responses to the light CS. In the control group, which had not been habituated to the noise, he observed far fewer lever press responses after the light was presented. However, the rats that were habituated to the noise continued pressing the lever even when the light was presented. The observation that devaluing the US diminishes the effectiveness of the CS suggests a direct link between the US and the CS, thus supporting the notion of S-S associations.

Is Conditioning Based on Stimulus Contiguity or Information?

Pavlov viewed the contiguity of the CS and the US as the critical basis of conditioning. The fact that the strength of the CR depends on the timing of the CS-US contiguity supports this view. However, early observations of blocking (Kamin, 1968) suggested that appropriate temporal contiguity of stimuli is *not* sufficient to produce conditioning. In the blocking effect, recall that initially the CS is conditioned; then it is presented in combination with another stimulus and paired reliably with US presentations. Subsequent CRs are evoked by the original CS but not by the new stimulus. Note that during presentations of the compound stimulus, the new stimulus is paired with the US enough times for the two to form an excitatory association; yet the new stimulus clearly has been blocked from doing so.

Why does the initial CS block conditioning of the new stimulus? Kamin suggested that a US has to be "surprising" to enter a new association. In his protocol, the US is not a surprising consequence when the compound of the CS and the new stimulus is presented because the CS itself already fully predicts the US. This realization was described in an influential account of classical conditioning known as the **Rescorla-Wagner model**. According to Rescorla and Wagner (1972), the effectiveness of the US depends on the extent to which its occurrence or magnitude differs from what is expected based on experience. Quite different from Pavlov, Rescorla and Wagner proposed that the critical issue determining the efficacy of conditioning is the match between the subject's expectancy of the strength of the US and the actual strength of the US. According to their model, learning occurs only when there is a mismatch between the expectancy of a US following the CS and the actual outcome. In real life, this view is another way of saying that we learn mainly from our mistakes—situations in which actual outcomes do not meet our expectations.

In this analysis, whenever the strength of a US is greater than expected, excitatory conditioning will occur for all CSs present. The larger the mismatch between the expectation about the US and the actual US, the greater the amount of conditioning; when the US simply meets expectations, no conditioning will occur.

Conversely, if the US is less intense than expected, inhibitory conditioning will occur for all CSs present. If two or more CSs are presented together, the US expected by the subject is the sum of the expectancies for each CS. (This resembles Pavlov's account of how excitatory and inhibitory associations of equal strength cancel one another.)

Based on these premises, the Rescorla-Wagner model handily accounts for many phenomena in classical conditioning. It predicts that incremental excitatory conditioning will occur when a CS is first paired with a US, and conditioning will strengthen until the subject can fully predict the US based on presentation of the CS. It also explains blocking: After initial conditioning with a CS, the CS fully predicts the US; so when a compound stimulus is presented that includes a new event, the new event does not add to the subject's expectancy and does not cause new conditioning. In extinction and conditioned inhibition, inhibitory conditioning occurs for the CS— to the extent that the expected US does not occur. The response in any subsequent situation is additive, so further presentations of the CS— reduce the likelihood of the CR.

An additional confirmation of the Rescorla-Wagner model came with the novel prediction of what will occur when the magnitude of a US is "overexpected." In this situation, two distinct CSs (such as a light and a tone) are separately paired with the same US until conditioning is complete for both CSs. Subsequently the light and tone are presented as a compound CS followed by the same conditioned US. Later the light and tone are again presented separately, and the magnitude of the CR is measured. The CRs of animals trained with the compound stimulus are weakened in comparison with those of animals trained only with the independent stimuli. Consistent with the Rescorla-Wagner model, presenting the compound CS created an expectancy that the magnitude of the US would be *double* that following either CS alone—derived from the sum of the magnitudes of the US expected from each light and tone. Yet during conditioning with the compound, the magnitude of the US was exactly the same as that presented following either CS alone—less than expected—leading to inhibitory conditioning for the light and the tone. According to this theory, subsequent responses to the light and tone alone should be, and indeed were, reduced.

Interim Summary

Classical conditioning does not link a CS directly to a UR-generating mechanism, forming an S-R association, because the CR is not always identical to the UR. Rather it appears that a representation of the CS forms a direct association with the US in an S-S association. This idea was validated by Rescorla's experiments showing that devaluation of a US affects its CR. Also, mere contiguity (pairing of a CS and a US) is

not the critical basis of conditioning: The effectiveness of contiguity can be prevented by prior pairing of the US with another CS (the blocking effect). Instead, according to the Rescorla–Wagner model, a CS is effective only when there is a mismatch between the expectancy of a US and the actual outcome. Excitatory conditioning for the CS will occur only when the strength of the US is greater than expected; conversely, inhibitory conditioning will occur when the strength of the US is less than expected.

Neural Circuits Build Reflex Arcs to Support Classical Conditioning

Two systems have been used as models to study the neural circuits that support classical conditioning of simple motor reflexes. One involves the invertebrate *Aplysia*, which you may remember from the neurobiological studies of habituation and sensitization described in Chapter 3. The other is the rabbit eyeblink paradigm discussed earlier in this chapter. Each system provides insights into different types of neural representations that underlie the classical conditioning of basic motor responses.

Classical Conditioning in Aplysia Modifies Reflex Circuitry

One of the simplest animals that displays classical conditioning is the sea slug *Aplysia*. Kandel and his colleagues (Carew et al., 1981) developed a procedure for classically conditioning these animals based on an elaboration of their habituation and sensitization processes and neural circuits, which were discussed in Chapter 3 (Figure 5.9). This protocol combined the same neuroanatomical circuits involved in those simpler learned behaviors, involving two sensory (CS) pathways and a common pathway by which the unconditioned stimulus (US) influences them. One CS pathway directly connects the sensory neurons of the mantle shelf skin to motor neurons that withdraw the gill. The second CS pathway connects siphon sensory neurons to motor neurons. These two potential CS pathways offer the ability to condition one of those paths but not the other. The US pathway indirectly connects the tail via an interneuron to the presynaptic elements of both the mantle skin and siphon sensory neurons.

The classical conditioning protocol that Kandel's team used with *Aplysia* involved the animal learning a discriminative response: conditioning for the mantle CS+ and not the siphon CS-. In some trials the mantle shelf skin was lightly stimulated with a brush; shortly afterward the tail was shocked at a low level insufficient to produce sensitization. In this configuration, the mantle shelf stimulation acted as the CS+ and the tail stimulation was the US. In other trials the siphon was stimulated, and no tail shock was given. Thus siphon stimulation served as

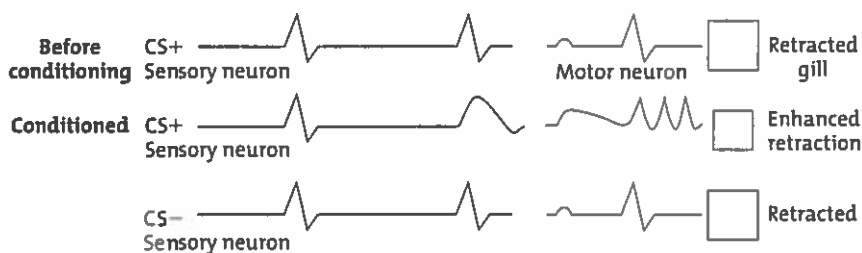
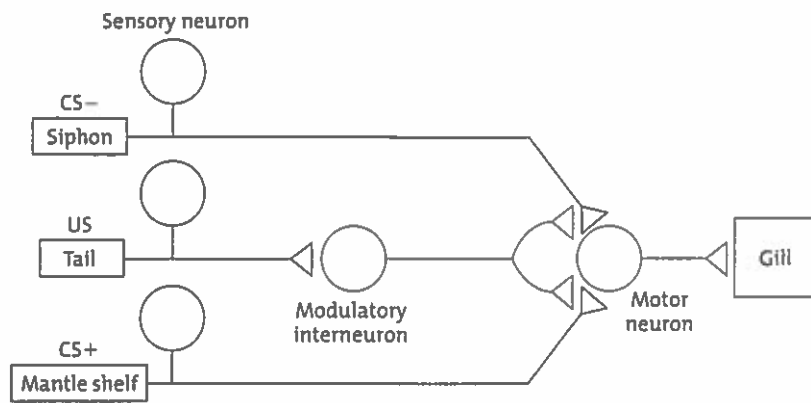


FIGURE 5.9 Classical conditioning in *Aplysia*.

Top: Components of the circuit that supports classical conditioning. Bottom: Neural activity in components of the circuit before (naive) and after conditioning.

the CS-. Over repeated trials, the animals developed vigorously enhanced withdrawal responses (the CR) to mantle stimulation but not to siphon stimulation. In other words, the animals learned to discriminate between the relevant CS+ and an irrelevant CS-. As is true of classical conditioning in mammals, timing was critical: The conditioned response occurred only if the CS+ and US were contiguous.

What cellular mechanisms could be involved in the association between the CS+ and US in this neural circuit? The critical cellular mechanisms occur in both the presynaptic and postsynaptic elements of the reflex circuit and involve electrical activity at the synapses and molecular events in both types of cells (Figure 5.10). The CS+ (mantle shelf stimulation) causes an action potential in the sensory neurons that reaches the presynaptic site, resulting in the influx of calcium (Ca^{++}), which causes neurotransmitters to dock to the presynaptic membrane

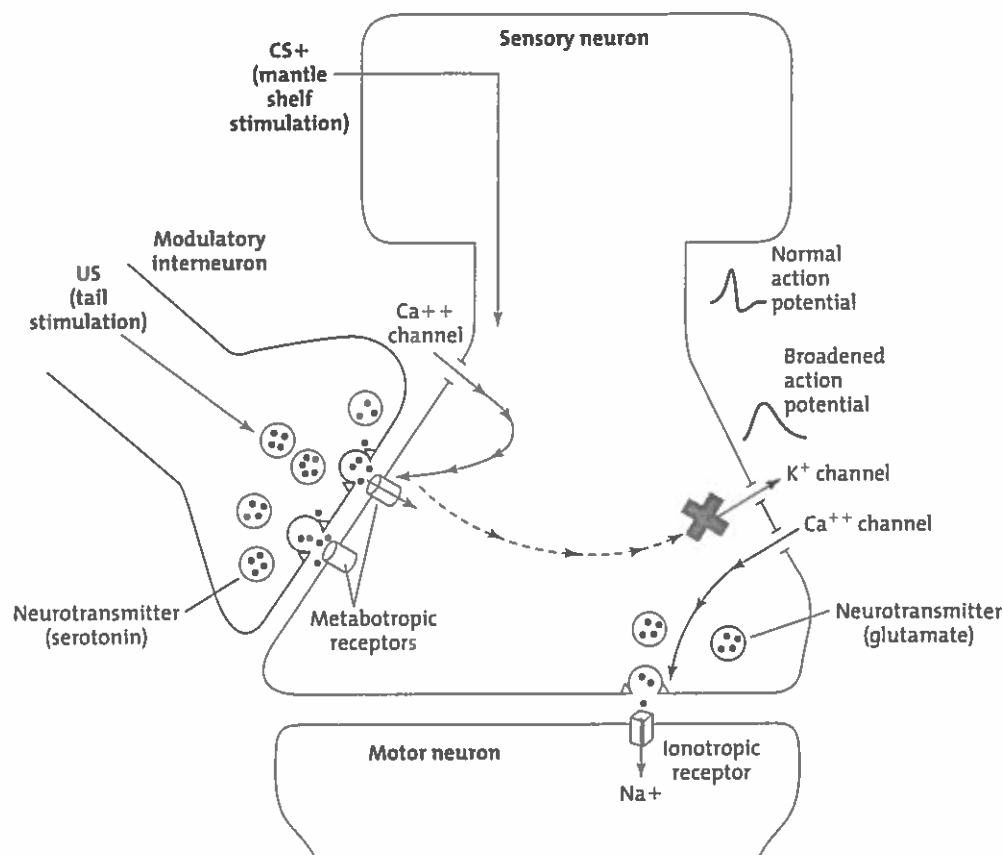


FIGURE 5.10 Cellular events that underlie classical conditioning in *Aplysia*.

and release. Closely following US (tail stimulation) activates a different type of receptors, called metabotropic receptors. When primed by the increased level of Ca^{++} , the US-produced activation of the metabotropic receptors sets off a chain of molecular events that prevent the K^{+} channel from opening. As you read in Chapter 2, the opening of K^{+} channels ends the depolarization phase of the action potential. So, the result of prolonging the action potential is that an especially large amount of Ca^{++} enters the presynaptic element, consequently prolonging neurotransmitter release. This happens only in the mantle sensory neurons (that is, the CS+ pathway). Because the US never occurs with siphon stimulation (the CS-), there is no facilitation of Ca^{++} entry and therefore no prolonged transmitter release in that sensory neuron (the CS- pathway).

In addition to these presynaptic element changes, a postsynaptic element change also supports the conditioned response. This change involves the same mecha-

nisms as those of long-term potentiation (LTP), which you read about in Chapter 2. You may recall that the neurotransmitter for the reflex pathway is glutamate. This neurotransmitter activates two types of receptors in the postsynaptic elements. One is a conventional receptor that regulates Na^+ influx. The other is a special receptor, called the NMDA receptor, that regulates Ca^{++} flow. During normal reflex operation and habituation and sensitization, the NMDA receptors are blocked by another charged molecule, magnesium (Mg^{++}). However, NMDA receptors have an unusual property: When the membrane potential is reduced (depolarized), the magnesium block is eliminated and Ca^{++} can flow into the cells.

During classical conditioning the membrane becomes depolarized (more positive) when the CS+ activates the conventional receptors, allowing Na^+ influx. This depolarization briefly unblocks the NMDA channels. If a US occurs soon afterward, a long train of action potentials occurs, and the open NMDA receptors allow Ca^{++} to flow into the postsynaptic elements. The influx of Ca^{++} results in a cascade of molecular events that creates long-lasting changes to the postsynaptic elements. The fact that classical conditioning in *Aplysia* uses the same LTP phenomenon studied in mammals supports the widely held view that LTP is a cross-species mechanism for memory in many different brain systems.

Classical Eyeblink Conditioning Involves Cerebellum Circuitry

Recent studies have also examined the brain circuit supporting classical conditioning of a simple mammalian motor reflex. Richard Thompson and colleagues pioneered neurobiological examinations of eyeblink conditioning in rabbits (Thompson & Kim, 1996; Christian & Thompson, 2003), and the model they developed has received considerable experimental support (Steinmetz, 1996; Mauk, 1997). Such studies have produced compelling evidence that the cerebellum stores the critical associations for this particular excitatory conditioning.

The cerebellum is a brain structure long associated with motor learning; its circuitry is organized to play a key role in reflex adaptations. The cerebellum has two main components: the cerebellar cortex and the underlying deep cerebellar nuclei. One of the cerebellar nuclei is the interpositus nucleus (Figure 5.11). During classical conditioning, cells in both the cerebellar cortex and the cerebellar nuclei receive two excitatory inputs (one representing the CS and another the US), making these ideal places for forming CS-US associations.

In the circuit shown in Figure 5.11, the unconditioned reflex (UR) pathway carries air puff sensory inputs into a part of the brain stem called the trigeminal nucleus. Outputs of the trigeminal nucleus travel to the cranial motor nuclei either directly or by passing through another brain stem structure called the reticular formation. The cranial motor nuclei send direct motor outputs to the facial mus-

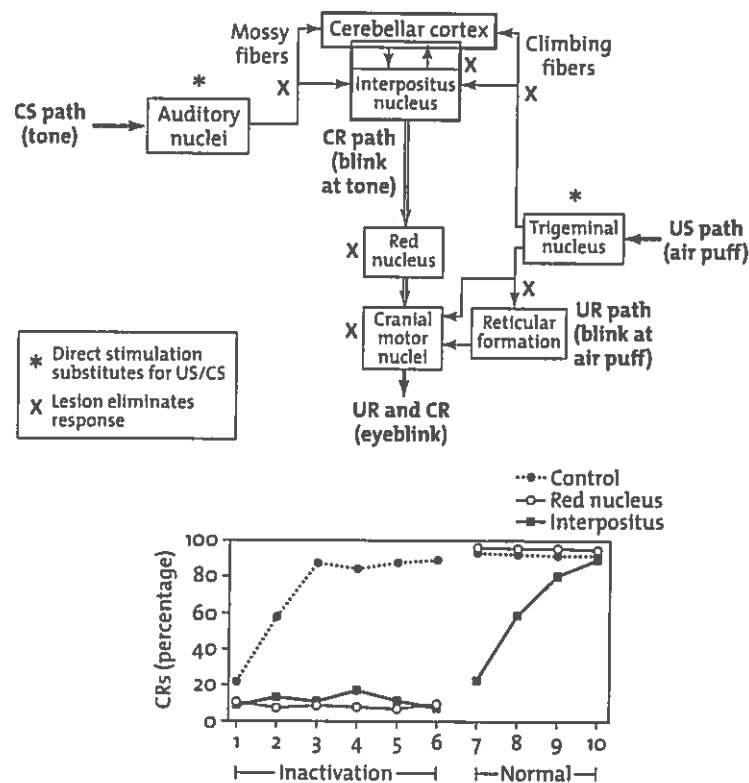


FIGURE 5.11 The cerebellum and the circuit for classical eyelid conditioning. Top: Schematic diagram of the sensory and motor pathways in the circuit. * denotes locations in the circuit where electrical stimulation can substitute for a natural stimulus. X indicates locations in the circuit where a lesion prevents conditioning. Bottom: Course of conditioning in normal control animals and in animals where neurons were inactivated in the red nucleus or interpositus nucleus.

cles that evoke the blink. This pathway was difficult to identify; but its vital role has been demonstrated by an elegant combination of studies showing that (1) cells in these brain areas fire reliably along with the UR and (2) inactivation of these brain areas prevents the UR. This pathway puts the US signal near the CS signals described earlier.

Additional studies have also identified the circuit for the US and CS in the conditioned reflex (CR). The US input travels from the trigeminal nucleus through another brain stem area to the cerebellar cortex as well as to one of the cerebellar nuclei called the interpositus nucleus. The pathway for a tone CS sends auditory nuclei inputs through the brain stem and then to the cere-

bellar cortex, where the CS and US signals meet and critical synaptic changes occur (Mauk, 1997). The output of this interaction is sent from the cerebellar cortex to the interpositus nucleus, where additional synaptic changes support the development of a CR. The CR output travels from the interpositus to a brain stem area called the red nucleus, which projects to the cranial motor nuclei that control the facial muscles.

The evidence for cerebellar circuit involvement in eyeblink conditioning is substantial. Studies by Steinmetz and colleagues (1996) have shown that electrical stimulation of the auditory pathway can substitute for a tone CS in establishing the conditioned response. Similarly, stimulation of the brain stem area where the air puff US signal enters the circuit can substitute for the air puff. Thus these areas are critical in generating the CS and US signals.

Thompson and his colleagues have provided compelling evidence that the interpositus nucleus of the cerebellum is the critical site of this CS-US association. They have shown that injury or inactivation of the interpositus nucleus impairs the acquisition and retention of classically conditioned eyeblink reflexes, indicating that this area is a vital part of the conditioning pathway. In addition, blocking the molecular events that underlie interpositus nucleus plasticity prevents establishment of the conditioned reflex, demonstrating that crucial changes in cellular structure occur within the interpositus itself.

Additional compelling data come from rabbit eyeblink conditioning studies using reversible inactivations of particular areas (Krupa et al., 1993). Temporary inactivation of the red nucleus or motor nuclei that are essential to producing the CR and UR also prevented the rabbits from outwardly responding to the stimuli during training. However, as soon as the inactivated areas were allowed to function again, CRs appeared in full form. So the circuit that supports the unconditioned eyeblink is not critical for conditioned learning about *when* to blink, but only for producing the actual blinking. In contrast, inactivation of the interpositus nucleus and overlying cortex does not affect UR production, showing that it does not generate motor responses. Yet inactivation of the interpositus resulted in failure of CR development; when the inactivation later wore off, conditioning occurred at the same rate as if there was no previous training (Figure 5.11). These results indicate that inactivating the interpositus specifically prevented learning but not unconditioned blinking—and point to the interpositus nucleus and overlying cerebellar cortex as the essential locus of some sort of memory trace.

Notably, the same cerebellar circuitry is critical to human eyeblink conditioning. In an elegant study exploiting the fact that the left and right cerebellar circuits are specific for the left and right eyes, respectively, Woodruff-Pak and colleagues (1996) conditioned subjects who had experienced damage to either the right or the left side of the cerebellum. The subjects were impaired in acquiring classically

conditioned eyeblink responses on the same side of the head as their cerebellar damage; but they normally acquired the conditioned response when trained on the intact side.

Other studies have confirmed the importance of the cerebellum in classical eyeblink conditioning, shedding light on the neural coding that mediates learning in the cerebellar cortex and interpositus nucleus. During training, neurons in both areas increased their firing in response to the CS. During subsequent extinction trials, during which the US was withheld while the CS was presented repeatedly, the CR gradually disappeared as interpositus cells ceased firing. But the neural representation for conditioning remained in the activity of the cerebellar cortex long after extinction. Perhaps this lasting representation supports spontaneous recovery, dishabituation, and accelerated relearning of conditioned responses (Steinmetz, 1996; Figure 5.12).

Finally, a pathway from the interpositus to the inferior olive (a structure deep in the brain stem that activates eyeblink muscle contractions) may influence the efficacy of the US, suggesting a mechanism for conditioned inhibition. Kim and colleagues (1998) used drugs to prevent inhibition in the inferior olive and observed decreased neural output from the olive to the cerebellum. The same drug treatment also eliminated blocking of the conditioned eyeblink reflex. (Recall that in blocking, prior training with one CS prevents learning about another CS presented in combination with the first one.) These findings suggest that during normal blocking, the cerebellar signal inhibits the US representation in the olive and, via that mechanism, prevents conditioning.

Interim Summary

The neural circuitry of two different model systems for classical conditioning of motor responses has been identified and outlined in detail. In the *Aplysia* withdrawal reflex, conditioning requires appropriately timed activation of the CS and US pathway to produce both selective enhancement of neurotransmitter release from the CS sensory neuron and LTP in the motor neuron. In the eyeblink reflex in mammals, conditioning involves complex circuitry where CS and US inputs meet in the interpositus nucleus of the cerebellum. There a trace is stored that engages the reflexive blinking response.

Classical Conditioning Can Illuminate Other Memory Systems

So far we have focused on classical conditioning of elemental salivary and muscular reflexes. This focus let us examine the behavioral properties, neural cir-

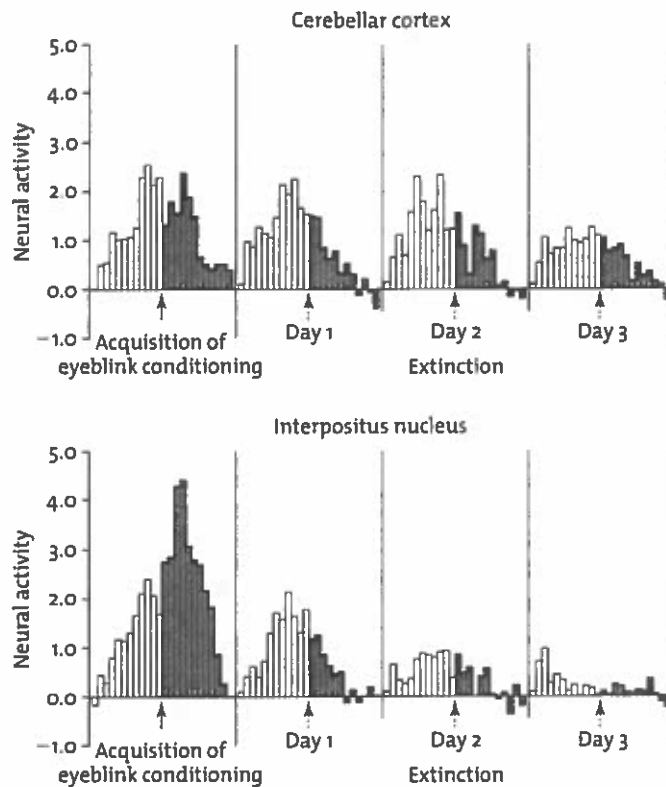


FIGURE 5.12 Firing patterns in the cerebellar cortex and interpositus nucleus during acquisition of the conditioned eyeblink and during three successive days of extinction.

In each panel, neural activity in successive 20-millisecond periods is shown during the CS period and following the US presentation (arrow); in extinction sessions, the dotted arrow indicates when the US would normally have been presented.

cuitry, and mechanisms that support learning in these motor reflex circuits. But classical conditioning as a training protocol is not limited to the study of elemental reflexes. It is also used to study emotional responses and various complex forms of learning.

Among the most widely used types of classical conditioning are methods for conditioning emotional responses. An example is the conditioned suppression paradigm, in which rats initially trained to press a bar at a constant rate are presented with either a light or a tone (CS) paired with a foot shock (US), briefly suppressing the bar pressing. Another example is fear conditioning, in which rats are presented with paired tone CSs and foot shocks. In subsequent mem-

ory tests, the tone CS makes the rats freeze and exhibit fearful cardiac and respiratory responses. These emotional conditioning protocols will be discussed in detail in Chapter 7.

Here, to demonstrate the broad utility of classical conditioning, we will discuss two interesting extensions of classical conditioning to other learning supported by higher brain systems.

Taste Aversion Learning Breaks the Rules of Contiguity

One behavioral paradigm that has received widespread attention in studies of classical conditioning is **taste aversion learning**. When animals or humans ingest a food and later experience gastrointestinal distress, they subsequently avoid that food. Most people can recall instances in which they ate something, became ill shortly later, and subsequently avoided that food. Such avoidance persists even when people are certain the food did not cause the illness (perhaps they came down with the flu coincidentally just after a meal). Therefore, the conditioning occurs even when we know that there was contiguity but no causal relationship between the food and the illness. A common example is that people undergoing chemotherapy for cancer often develop an aversion to a food they ate before the therapy made them ill, even though they know it was the therapy and not the food that caused the illness. In animals this kind of learning is sometimes called *bait shyness*, a term borrowed from the observation that mice that survive eating poisoned bait subsequently avoid the trap.

In the laboratory, taste aversion is typically conditioned by having animals consume a novel and appealing flavor (such as sweetened water), then inducing illness by drug treatment or irradiation. Subsequently we can measure learning in terms of a decrease in the normal preference for sweetened water versus tap water. In the taste aversion paradigm, the food is the CS, the illness is the US, and aversion to the food is the CR. This kind of learning is often obvious after a single conditioning trial, unlike the slow process of eyeblink conditioning; and the memory for taste aversion can last a long time. So taste aversion learning is considered an unusual and especially robust example of classical conditioning.

Taste aversion learning is also unique in that it occurs even when the interval between the CS and the US is extended for hours. In one experiment, rats were allowed to drink a sweetened water solution, then irradiated immediately or at intervals ranging from a half hour to 24 hours after drinking. Irradiation at intervals of up to 6 hours produced strong conditioning, and even at 12 hours some conditioning was observed (Figure 5.13A). In eyeblink conditioning, the critical ISI is about a few seconds; so the long effective interval in taste aversion conditioning seems to be an exception to the contiguity principle. But consider the condi-

tions that typically surround taste aversion learning: The effectiveness of long delay conditioning seems appropriate. Usually a poisonous food does not make us ill immediately; rather substantial time is required for the toxin to affect the gastrointestinal organs or enter the bloodstream. So at the usual brief ISI, taste aversion learning would not be adaptive.

Another feature of taste aversion learning is its specificity to flavor as the critical CS. Thus, whereas rats immediately learn an aversive association between a flavor and illness, associations between, say, flavor and shock are not easily acquired. Rats readily learn to avoid a fluid food marked by distinctive visual cues (like water with blue food coloring) when they are shocked for licking its drinking tube. But they do not easily associate other cues with illness (Garcia & Ervin, 1968; Figure 5.13B). This experiment showed that taste-illness and visual-shock combinations have adaptive significance—that is, they belong together—whereas taste-shock and visual-illness combinations do not. These findings shake the Pavlovian assumption that learning can occur between any arbitrary neutral stimulus and any unconditioned stimulus. Instead a new principle for classical conditioning, called *belongingness*, says that the CS and US must “belong” together for conditioning to occur. According to this idea, some types of CS and US stimuli have a natural or adaptive connection and others do not; it remains to be determined how stimuli acquire these natural connections.

Long-delay conditioning and the belongingness of CS-US associations challenge a general principle of CS and US contiguity as the fundamental basis of classical

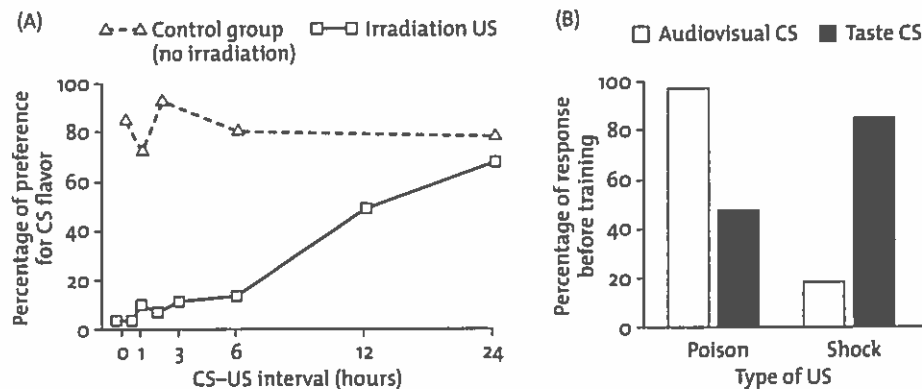


FIGURE 5.13 Taste aversion learning.

A. Success in learning at different ISIs. Animals in the control group are not given the US.
B. Success in conditioning with different CS-US combinations.

conditioning. How does the brain know which ISI and which stimulus pairing are appropriate for different kinds of classical conditioning? The answer is that different brain systems support classical conditioning, but each system has its own operating principles and rules about contiguity. Taste aversion, for example, is mediated by the gustatory cortex, a part of the frontal lobe that processes flavor perception. Damage to this area prevents taste aversion learning.

Learning & Memory in Action

Can Coyotes Be Trained Not to Prey on Sheep?

In the western United States a big problem for sheep farmers is predation of their livestock by coyotes. The farmers hunt coyotes and lay traps with poisons that sometimes also kill other harmless and even endangered species. To solve the predation problem while preserving the coyote population and protecting other wild animals, the principles derived from studies of taste aversion learning have been applied to manage coyotes' predatory behavior in a nonlethal way—specifically by using conditioned taste aversion to teach coyotes not to prey on lambs. Gustavson and his colleagues (1974) exposed coyotes to lamb meat that was tainted with lithium chloride to induce nausea and vomiting. One to three conditioning trials were sufficient to prevent captive coyotes from attacking live lambs that were introduced into their pens. Follow-up studies in the western U.S. and Canadian rangelands have demonstrated the efficacy of this classical conditioning procedure in reducing coyote predation of sheep. The success of this approach has reduced the use of traps and poisons and has preserved the coyote's role in the ecosystem.

Trace Conditioning Requires the Hippocampus

Simple eyeblink reflex conditioning can be accomplished within the cerebellar circuitry described earlier in this chapter, without necessary support by higher brain areas. However, some higher brain areas, including the hippocampus, influence simple reflex conditioning and are necessary for more complex forms of eyeblink conditioning (Solomon, 1980; Disterhoft et al., 1996). For example, several studies have shown that the hippocampus is not required for acquisition of the conditioned eyeblink response in the standard delay conditioning paradigm (the version of classical conditioning in which the CS and US overlap). However, damage to or removal of the hippocampus sometimes accelerates delay eyeblink conditioning (Port et al., 1985). Also, hippocampal neurons develop increased activity associated with the appearance and timing of the CR.

These findings indicate that the hippocampus plays some role in simple eyeblink conditioning.

Other studies involving more complex forms of classical eyeblink conditioning show how the hippocampus may be involved. For example, damage to the hippocampus disrupts learning when subjects are initially trained to blink to a CS+ and not blink to a CS-. Then the CS and US pairings are *reversed*: The former CS+ becomes the CS-, and the former CS- becomes the CS+. Normal animals typically switch their CRs to match the reversed CS-US contingencies. However, animals with hippocampal damage produce CRs to *both* the CS+ and the CS-. In addition, damage to the hippocampus abolishes blocking and latent inhibition (Solomon, 1980), as well as the dependence of conditioning on environmental context (Penick & Solomon, 1991). These studies demonstrate that the hippocampus plays a decisive role in various situations where subjects normally inhibit a conditioned response, which is prominent in all of these paradigms.

In addition, the hippocampus is required for the classical conditioning variant called trace conditioning discussed earlier in this chapter (see p. 148). Recall that in the typical version of this task, the CS involves a brief (100-millisecond) tone followed by a silent 500-millisecond "trace" interval punctuated by the US. Trace conditioning therefore challenges the nervous system's ability to associate a CS and a US that are not actually contiguous, although the CS still predicts the subsequent occurrence of the US. Rabbits and humans develop CRs in this form of eyeblink conditioning, and hippocampal neurons also are active during presentation of the CS and US. This variant of eyeblink conditioning is prevented by hippocampal damage (Moyer et al., 1990).

Why does adding a brief trace interval between the stimuli cause their connection to be processed mainly by the hippocampus rather than by the cerebellum? Clark and Squire (1998) suggest that the hippocampus is required in trace conditioning because when the CS and US are not contiguous, learning an association between them requires conscious awareness of the CS-US contingency. As you will read in Chapter 9, the hippocampus plays a key role in such conscious memory. In Clark and Squire's studies, normal and amnesic humans were tested in both delay and trace eyeblink conditioning, then interviewed about their awareness of the temporal relationship between the CS and US. Amnesic subjects with hippocampal damage acquired conditioned responses in the delay conditioning task involving contiguous stimuli but failed to develop trace conditioning. Normal subjects were successful in delay conditioning regardless of their awareness of the contingency, but they succeeded in trace conditioning only when they were also aware of the CS-US relationship.

In a subsequent study, the same investigators either promoted or prevented awareness of the CS-US contingency during delay and trace conditioning in normal subjects (Clark & Squire, 1999). For some subjects, they promoted awareness by explaining the temporal contingency before training. These subjects then

watched a movie during training. For other subjects, the investigators prevented awareness. They did not explain the contingency in advance and during conditioning engaged subjects in a demanding task that required them to detect strings of odd digits. The groups prevented from awareness performed well during the delay task but not during the trace conditioning. In contrast, advance awareness of the contingency facilitated trace conditioning. These findings show that human awareness is closely related to success in trace conditioning, and hippocampal damage prevents such awareness and trace conditioning. It appears that hippocampal processing of the CS and memory for the CS-US relationship mediate the temporal gap in trace conditioning—a capacity not supported by the cerebellar system.

Interim Summary

Two examples of classical conditioning show how this formal learning protocol can be applied to other brain systems and other forms of learning and memory. *Taste aversion learning* involves pairing a taste CS with gastrointestinal distress as the US. This form of classical conditioning is unique in that it occurs over long ISIs (hours) and in that only particular stimuli are meaningful in learning to avoid poisonous foods. *Trace eyeblink classical conditioning* involves a variant of standard delay conditioning: A brief blank interval separates the CS and US, challenging brain systems to appreciate the CS-US contingency in the absence of contiguity between those stimuli. Trace conditioning, unlike delay conditioning, requires the hippocampus and involves conscious awareness of the contingency in humans. These examples show that classical conditioning is a training procedure, rather than a form of learning and memory, that can apply to many brain systems with different types of information and different operating rules.

Chapter Summary

1. Classical conditioning is a training procedure that applies to a broad range of situations, learning and memory systems, and species. Classical conditioning is best understood as the predominant form of learning in motor systems. Conditioning in such systems involves several rules of operation and stimuli timing that determine the success of contiguity and make classical conditioning unique among different types of learning and memory.

2. Classical conditioning is a learning protocol in which there is usually a strict temporal relationship between the presentation of an arbitrary stimulus (the CS) and a nonarbitrary stimulus (the US) that reflexively incites an unconditioned response (the UR). The outcome is a conditioned response (CR) that mimics the UR. The CS must predict the occurrence of the US, and the temporal relationship between the CS and US is learned. Learning can be either excitatory (increasing the CR) or inhibitory (decreasing the CR), depending on the extent to which the CS bears new information and the nature of that information. Conditioning occurs when the actual US is not already fully predicted by the CS, and the strength and direction of learning are determined by the mismatch in prediction.

3. Variations of the classical conditioning protocol have shown that extinction is not an unlearning but an inhibition of the conditioned response, which can spontaneously recover in relearning. Excitatory and inhibitory influences from multiple sources can modulate the expression of conditioned responses. Conditioned responses can generalize to stimuli similar to the CS, but we can learn to discriminate between stimuli that predict and do not predict the US. Also, potential CSs can become associated with one another by direct pairing (as in second-order conditioning, sensory preconditioning, and contextual conditioning); a CS can block the effectiveness of another potential CS that confers no new information; and a potential CS can be rendered ineffective by prior presentation without the US (latent inhibition). Each of these effects shows that neutral stimuli can enter a variety of associations with one another and with the US.

4. The neural system for classical conditioning has been characterized in several brain systems. In *Aplysia* conditioning is mediated by modulation of the intensity of sensory motor reflexes. In eyeblink conditioning, a circuit involving the cerebellum and other brain stem areas mediates learning, and a small component of that circuit stores a representation of the CS-US contingency. Conscious awareness of the CS-US contingency is not required for many forms of classical conditioning; but it is required at least sometimes when there is a temporal gap (trace interval) between the CS and the US. In trace conditioning, the hippocampus is crucial in bridging the gap between the CS and the US.

5. Examples of classical conditioning include fear conditioning, which imparts a set of emotional responses to a previously neutral stimulus and is supported by distinct circuitry. Taste aversion learning occurs only for stimuli that are related to feeding and occurs even at very long interstimulus intervals; the critical site of taste memories is in the gustatory cortex. The broad range of circumstances in which these phenomena are observed tells us that classical conditioning is a protocol for generating learning in multiple brain systems.

KEY TERMS

classical conditioning (p. 144)	disinhibition (p. 155)
unconditioned stimulus (US) (p. 145)	rapid reacquisition (p. 155)
unconditioned response (UR) (p. 145)	conditioned inhibition (p. 156)
conditioned reflex (p. 145)	generalization (p. 156)
conditioned stimulus (CS) (p. 145)	discrimination (p. 156)
conditioned response (CR) (p. 145)	first-order conditioning (p. 158)
extinction (p. 146)	second-order conditioning (p. 158)
delay conditioning (p. 148)	sensory preconditioning (p. 160)
interstimulus interval (ISI) (p. 148)	blocking (p. 160)
intertrial interval (ITI) (p. 148)	latent inhibition (p. 160)
trace conditioning (p. 148)	contextual conditioning (p. 160)
simultaneous conditioning (p. 149)	Rescorla-Wagner model (p. 164)
backward conditioning (p. 149)	taste aversion learning (p. 174)
spontaneous recovery (p. 154)	

REVIEWING THE CONCEPTS

- What are the basic protocols for different types of classical conditioning and their controls?
- What role does timing of the CS and the US play in the success of classical conditioning?
- Is extinction of a conditioned reflex accomplished by unlearning of the conditioned response or new learning to inhibit the previously learned response? How do extinction and learned inhibition of behavioral responses differ from forgetting?
- How do conditioned excitation and conditioned inhibition of responses interact in classical conditioning?
- What are second-order conditioning, sensory preconditioning, blocking, and contextual conditioning? What do they tell us about classical conditioning?
- Is the association in classical conditioning based on S-S or S-R learning? On stimuli contiguity or on the information contained in events?

- Describe the circuits for classical conditioning of the gill withdrawal reflex in *Aplysia* and the eyeblink reflex in mammals.
- What are fear conditioning, trace eyeblink conditioning, and taste aversion conditioning? How do they differ from the classical conditioning of elementary motor reflexes?