

PAVLOVIAN CONDITIONING: LEVELS OF REPRESENTATION AND DATA FROM HUMAN SUBJECTS

Topic

Pavlovian conditioning procedures have been used in a wide variety of contexts, in which roughly similar phenomena have been observed. There are however clear differences between the range of the observed findings for such cases as the conditioning of the simple reflexes in slugs or cockroaches (Carew *et al.*, 1983; Stares *et al.*, 1999; Sutton and Carew, 2002), the effects of Pavlovian procedures on the general behaviour of freely moving dogs and rats (Jenkins *et al.*, 1978; Rescorla, 2000; Timberlake and Grant, 1975) and the interaction of instructions and stimulus-pairings in human subjects (Davey, 1987; Bracha *et al.*, 1997; Ohman and Soares, 1998; Edwards, 2002; Lovibond & Shanks, 2002; Walther *et al.*, 2005; Delgado *et al.*, 2006; Lascelles & Davey, 2006).

There has recently been renewed interest in methods such as eyeblink conditioning with human subjects (Clark *et al.*, 2002; Carter *et al.*, 2003; Herbert *et al.*, 2004; Hermans *et al.*, 2006; Neumann & Waters, 2006), often in the context of investigation into the localization of the brain mechanism responsible for different forms of human learning. "H.M", the patient whose memory deficits have been investigated over several decades, performs within the normal range in eyeblink conditioning, as do other amnesics. (Woodruff-Pak, 1993; Gabrieli *et al.*, 1995; Schugens & Daum, 1999) although some aspects of performance are impaired in amnesics (Carrillo *et al.*, 2001) and it has been suggested that this kind of conditioning is selectively impaired in Alzheimer's disease (Woodruff-Pak, 2001). This suggests that the conditioning process is anatomically separate from other kinds of memory, and there is evidence to support this from the use of methods in which brain activity is mapped or scanned during the performance of various cognitive tasks (e.g. Timmann *et al.*, 2000, Gabrieli, 1998; Buchel *et al.*, 1999; Buchel & Dolan, 2000; Carrillo *et al.*, 2001; Cheng *et al.*, 2003; Knight *et al.*, 2004; Carter *et al.*, 2006; O'Doherty *et al.*, 2006).

There has also for some time been interest in the possible effects of Pavlovian conditioning on physiological responses such as blood glucose level, or nausea, in human as well as animal subjects (Pavlov, 1927; Siegel, 1976; Russell *et al.*, 1984; Klosterhalfen *et al.*, 1999; Ader and Cohen, 1993; Exton *et al.*, 2001; Carey and Burish, 1988; Montgomery & Bovbjerg, 1997; Morrow *et al.*, 1991; Siegel *et al.*, 2000; Siegel, 2001; Siegel & Ramos, 2002; Cardinal & Everitt, 2004; Everitt & Robbins, 2005; Stockhurst *et al.*, 2006).

The most significant form of physiological conditioning would be that related to anxiety, which will be explored further in week 7. (Buchel and Dolan, 2000; Bouton *et al.*, 2001; Cardinal *et al.*, 2002; Ohman and Soares, 1998; Cheng *et al.*, 2003; Knight *et al.*, 2004; Delgado *et al.*, 2006; Wilensky *et al.*, 2006; Brignell & Curran, 2006).

Finally, associative process akin to Pavlov conditioning have been appealed to as explanations for several odd perceptual effects in human subjects, such as the McCollough after-effect (McCollough, 1965; Eisenberg *et al.*, 1995; Siegel *et al.*, 1992; Allan and Siegel 1997; Simpson, 1992; Haijiang *et al.*, 2006)

These different contexts for Pavlovian conditioning can be categorized in terms of the levels of representation of the stimuli used, and assessed according to the nature of the stimuli which the system observed can respond to, and the degree of involvement of attentional and motivational processes. An alternative contrast is that classical conditioning procedures can be applied both to the "molecular question" of memory storage and to the much wider "systems question" of how the whole brain reacts in learning and memory tasks (Kandel and Pittenger, 1999). An additional quotation is that "**Pavlovian conditioning is not a unitary process**" (Cardinal *et al.*, 2002)

Sample Essay

To what extent do the procedures of classical conditioning reveal the operation of a universally applicable associative process?

Main Sources

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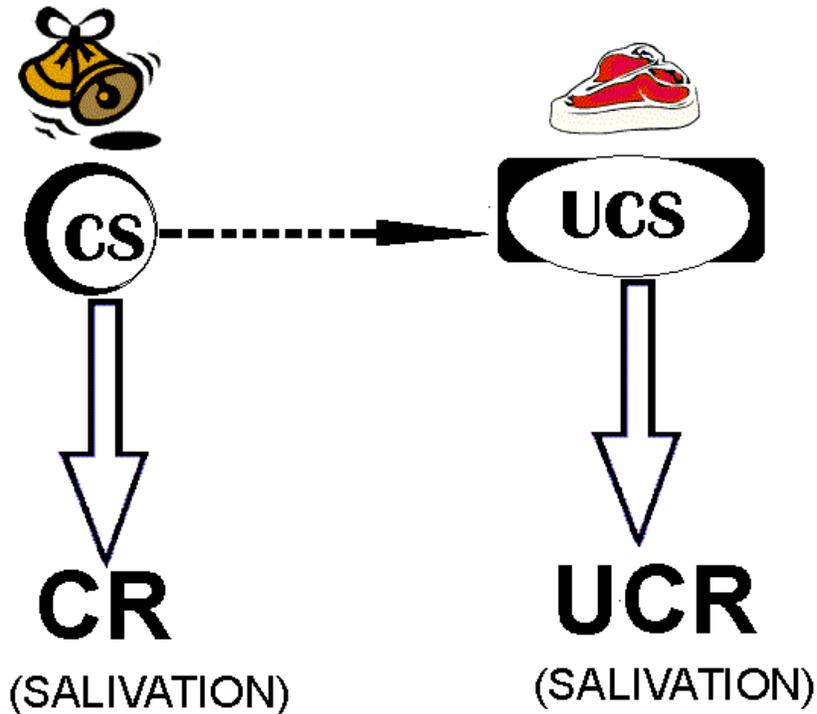
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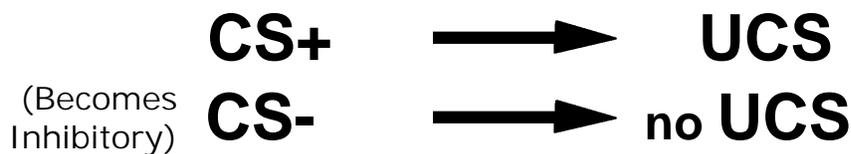
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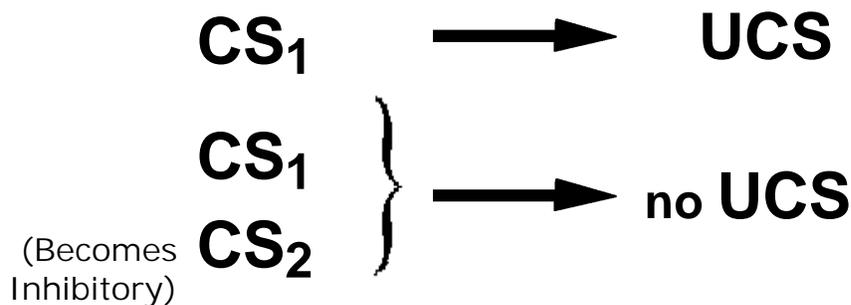


Schematic diagram of the typical classical conditioning procedure. Pairing a conditioned stimulus (CS e.g. a bell) with an unconditioned stimulus (UCS or US, e.g. food) will typically, after a number of pairings, mean that a conditioned response (CR, in this case salivation) is evoked by the CS (redrawn after figure 2.1 in Davey, 1989).

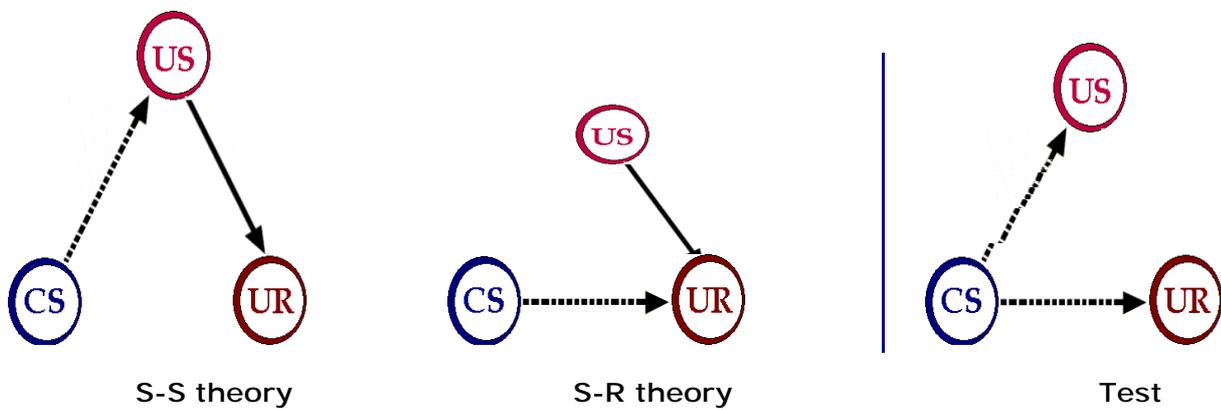
(1) The most basic discrimination procedure: CS- is simply paired with the omission of the UCS.



(2) An alternative procedure in which CS₂ becomes inhibitory because the UCS is omitted on occasions when CS₂ is present at the same time as CS₁, which by itself precedes the UCS.



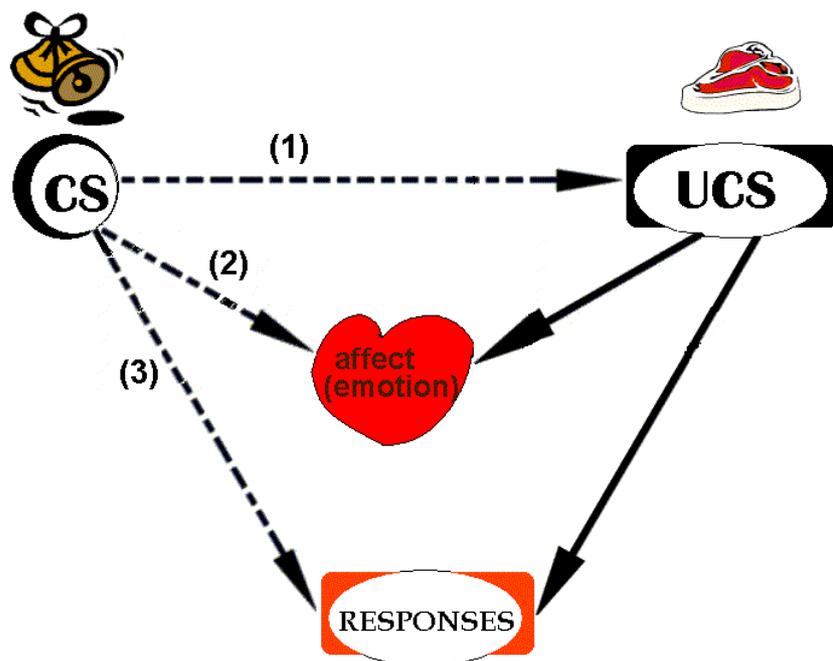
Two procedures for producing inhibitory conditioning (after Davey, 1989, figure 2.2 page 32).



redrawn after Lieberman (2000), page 162 or Lieberman (1993) page 167.

A very simple test of whether the “S-S” or the “S-R” theory is most accurate is to weaken the link between the US and the UR.

According to the S-S theory the conditioned response itself depends on the US-UR link, because the learned association is just between the CS and the US, but for the S-R theory the conditioned response is independent of this US-UR link because of the direct association between the CS and the CR (in this case the same as the UR). Generally, weakening the US-UR link, by prefeeding or taste-aversion training for a food US, weakens the CR (conditioned response), and this supports the original Pavlovian “S-S” interpretation.



This figure is similar in its essentials to figure 1 in the paper by Cardinal et al. (2002). Pavlovian conditioning has the potential to create at least three different kinds of associations. (1) associations between a conditioned stimulus (CS) and representations of the unconditioned stimulus (US). (2) associations between the same CS and central affective or emotional states such as fear. (3) Direct associations between the CS some aspect of the responses initially given to the UCS. Distinctions between different kinds of response in (3) include that between "preparatory" responses (e.g. arousal) and "consummatory" responses (e.g. salivation or blinking.) **Dotted lines** represent the 3 possible kinds of conditioned **associations**.

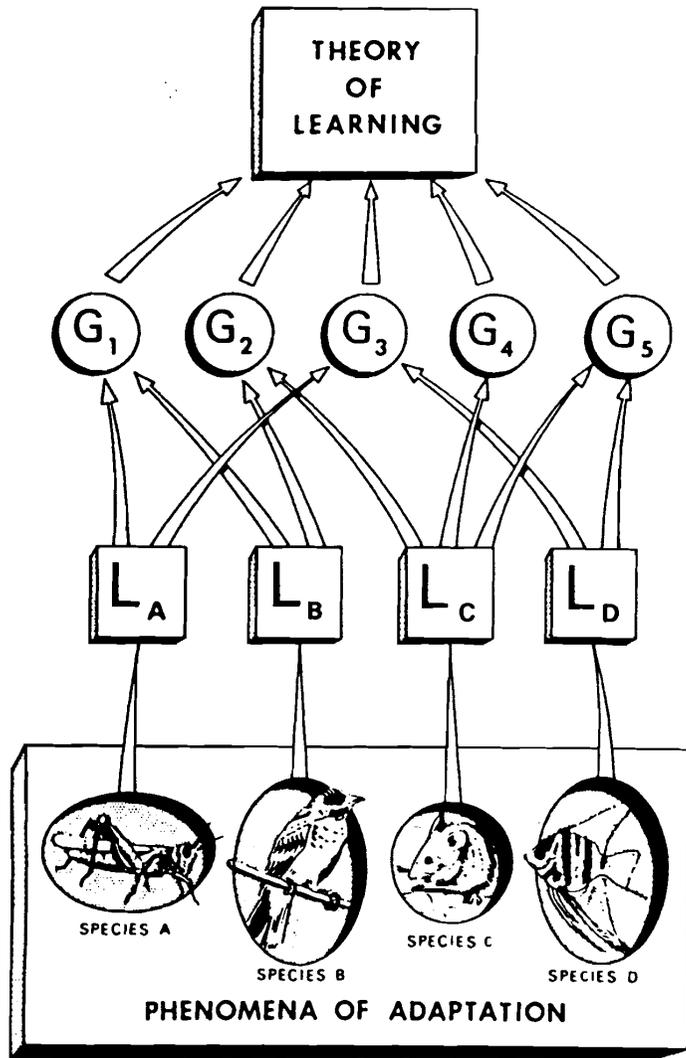


Figure 1.2 The ecological approach to learning. The four phenomena of adaptation represent the study of animals in their natural environments, and description and analysis of adaptation within each of these ecosystems provides the basis for local principles of adaptation ($L_A - L_D$). Each local principle may then contribute to one or more global (or general) principle of adaptation. Note that not all global principles may apply to all species studied. (Adapted from Johnston, 1981a)

from DAVEY (1989)

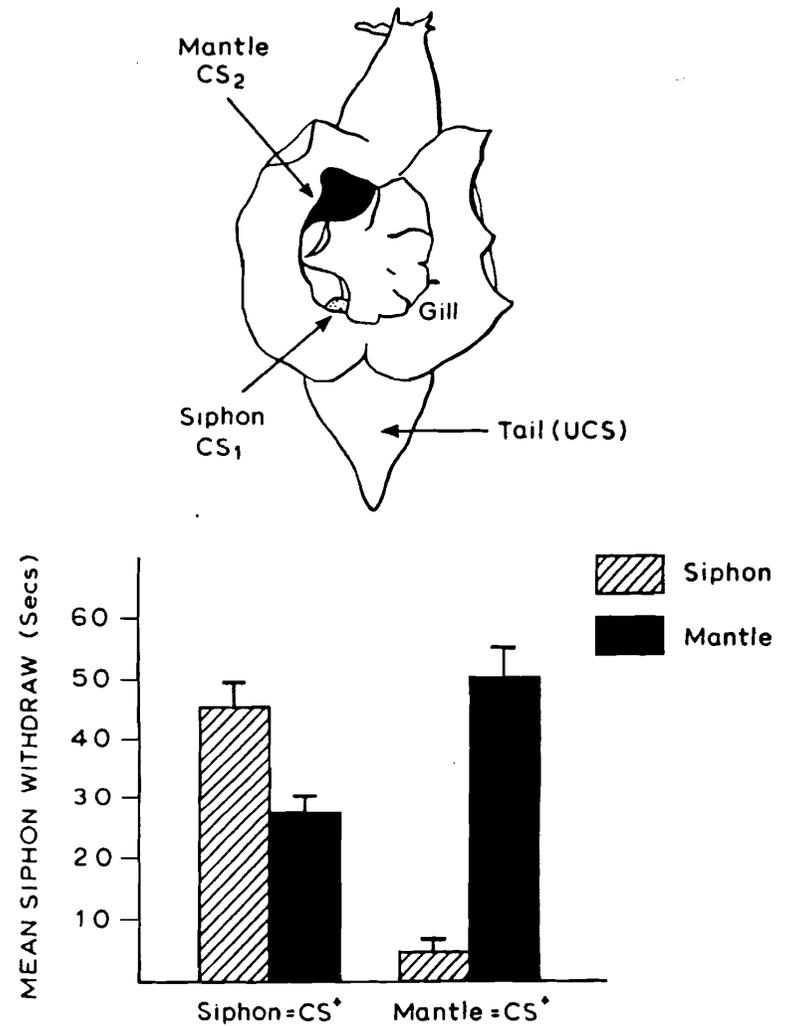


Figure 2.3 A dorsal view of aplysia illustrating the siphon and mantle shelves which were used as sites for CS presentation. The UCS was an electric shock to the tail. The bottom half of the figure shows the results of a differential conditioning procedure. On the left, the group that had CS^* presented to the siphon (siphon = CS^*) showed significantly more CRs to the siphon CS than the mantle CS (the latter of which was not paired with the UCS). On the right, the group which had CS^* presented to the mantle (mantle = CS^*) showed more CRs to the mantle CS than to the siphon CS. (From Carew, Hawkins, and Kandel, 1983)

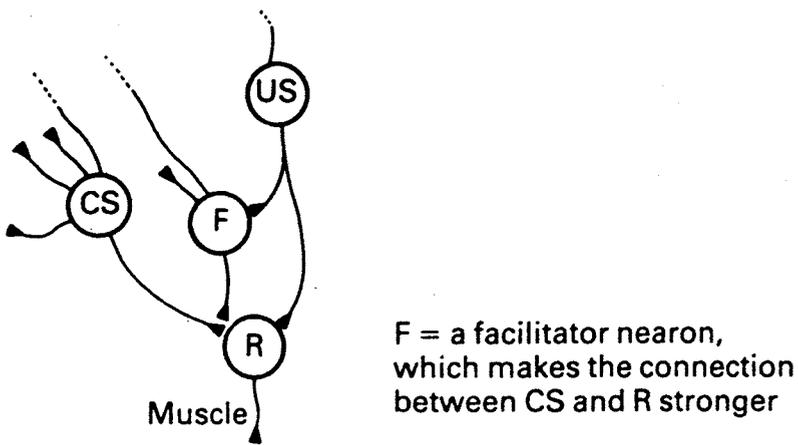


Figure 3.3 *The conditioned reflex modelled as a simple neural circuit.*

US is a neuron which is activated by the unconditioned stimulus, and is directly connected to the neuron R, which outputs the unconditioned response. CS is a neuron which has a connection to R, but which does not normally fire R. However, the CS becomes able to fire R if the CS output to R is accompanied by the output from the facilitator neuron, F. Thus the connection between CS and R is made stronger when CS and US are active at the same time. After Hawkins *et al.* (1983).

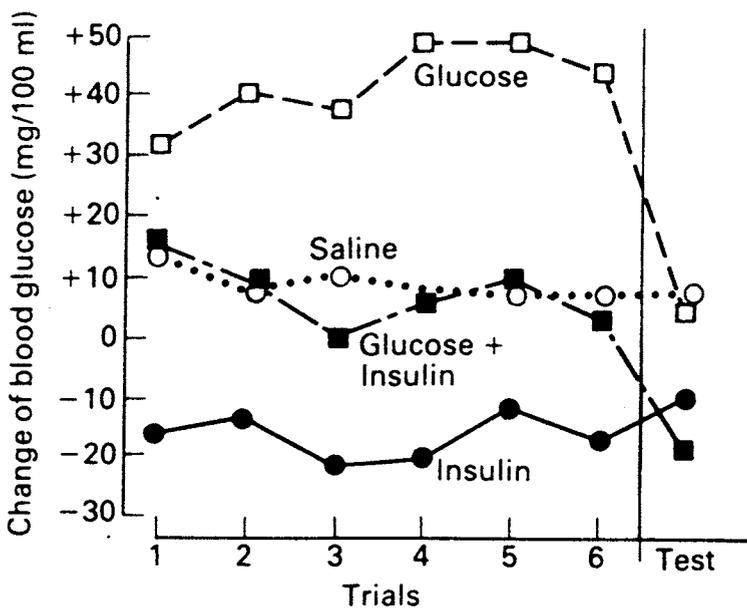


Figure 3.4 *Conditioned lowering of blood sugar level.*

Four groups of rats were given the test, at the right of the figure, of an injection of a weak salt solution (saline), and their blood sugar level was measured immediately afterwards. Groups with previous experience of receiving injections of insulin, or insulin with glucose, showed a lowering of blood glucose in response to the saline injection. Control groups with previous injections of saline or glucose did not. After Woods (1976).

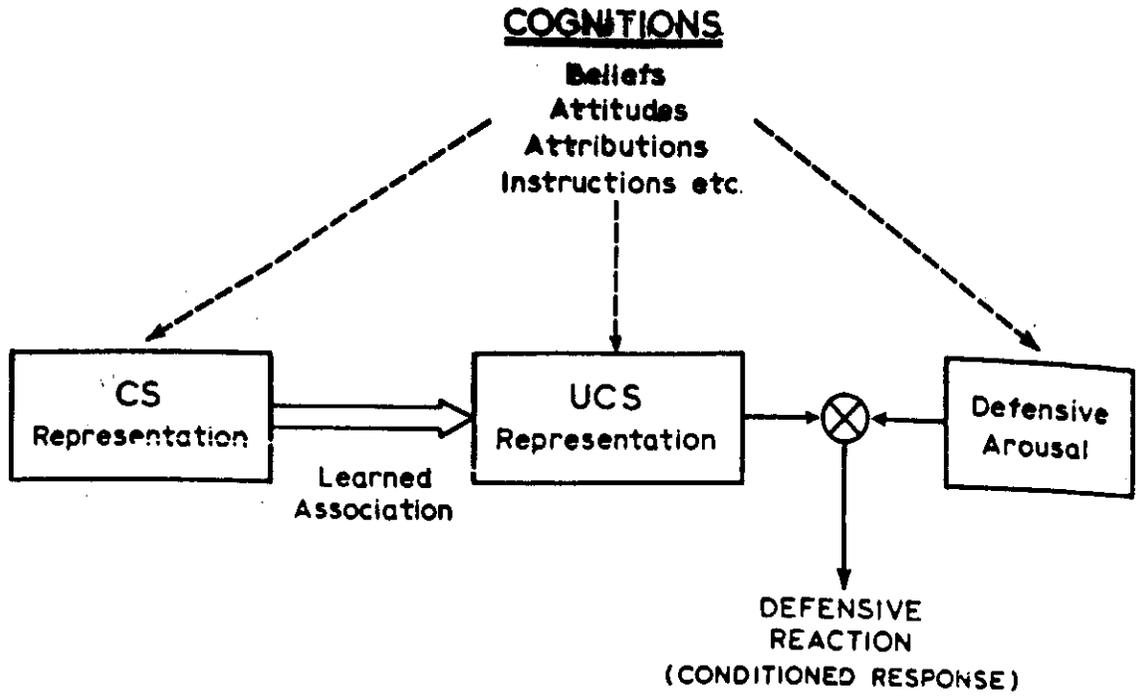
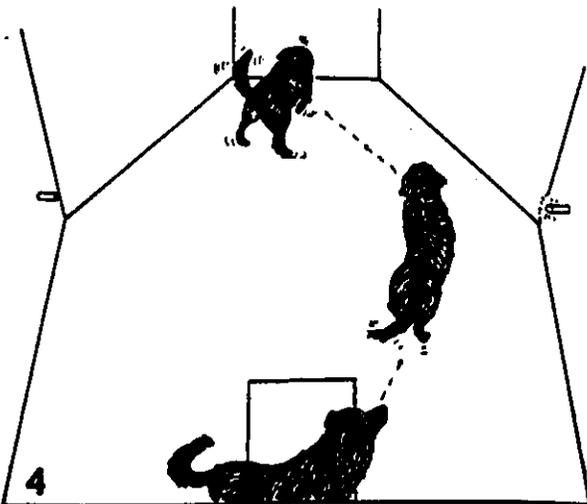
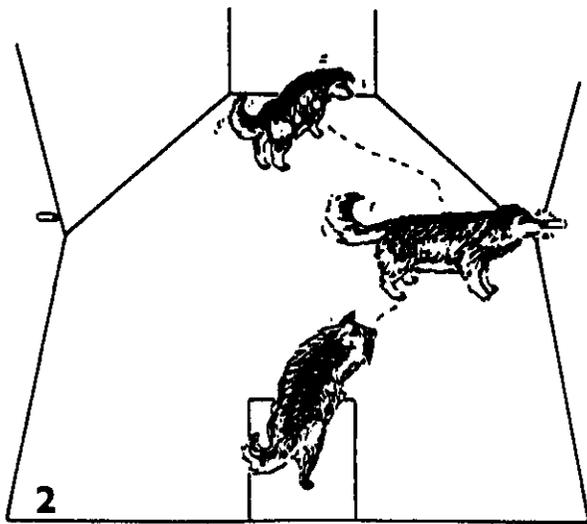


Figure 4.11 A schematic representation of the possible interaction between cognitions, evaluations, and CR strength during conditioning

BEHAVIOR ON POSITIVE (CS+) TRIALS



SIGNAL-CENTERED ACTION PATTERNS

BEHAVIOR ON NEGATIVE (CS-) TRIALS

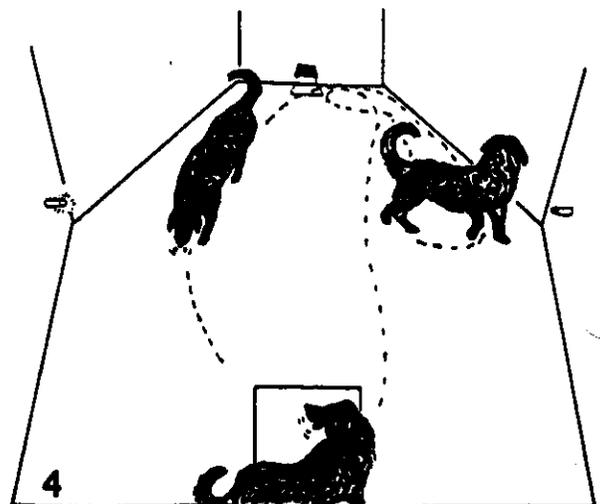
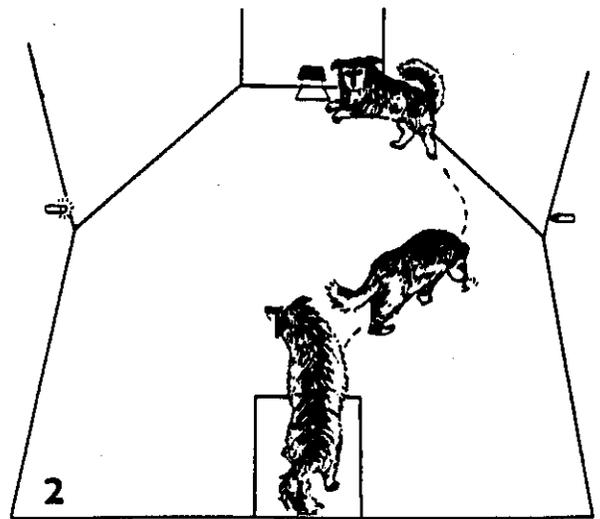


FIG. 2. Typical sequence of postures in Dogs 2 (top panel) and 4 (lower panel) on positive trials.

FIG. 3. Typical sequences in Dogs 2 (top panel) and 4 (lower panel) on negative trials.

Classical conditioning of Metabolic responses (animals)

1 Woods (1976)

UCS was presence of insulin in an injection.

CS was getting an injection + being placed in a holding cage smelling of mentholatum (for 20 mins, after which blood sample was taken from the tail)

2. Russell et al (1984)

Guinea pigs tested for **plasma histamine release** - 10 minutes after a trial animal anaesthetised and blood withdrawn for testing

US was bovine serum albumen

CS+ and CS- were sulphur and fish smells - only one paired with US /

Trials given one week apart

3. Siegel (1975,1976, Siegel et al., 2000, Siegel & Ramos, 2002)

Rats were made tolerant to morphine in one of two environments (different rooms with different enclosures) and then assessed for morphine tolerance in both. They only showed tolerance in the **same** room they had previous experience of. Theory is that the body antagonises the drug (so it's less effective) and **that it is antagonism to the drug that is conditioned to environmental stimuli**

Extinction is produced if cues given without the drug i.e. saline injections in room bring back the original effects of the same dose of morphine. (Siegel, 1975)

cf stimulus-substitution theory

What is associated may vary - different components of the UCR may be moved to the CR, and what is produced as the CR may also depend upon the precise characteristics of the signal and “affective responses”.

Simpson, B. (1992) **The escalator effect**. *The Psychologist*, 5, No 10 (October) 462-3.

The phenomenon

"Upon setting foot on the first tread of a stationary escalator, the traveller experiences a strange sensation of movement."

The explanation

“From a physiological point of view, it seems that we become so well prepared to receive certain messages from our vestibular (inner-ear balance) mechanism and from muscular proprioceptors that such messages, when they arrive, are effectively discounted. Only if the escalator is stationary are we suddenly made aware of it – as a strip of floor that is moving backwards relative to our expectations.

Such mental preparation is apparently unconscious, and it would appear to take the form of a reflex that becomes strongly **conditioned** to the whole range of visual stimuli associated with escalators (i.e. to the *appearance* of escalators and not just to the *movement* of their treads and handrails).

The escalator effect is not at all easy to disrupt, diminish or destroy, however much one concentrates on the fact that the stationary escalator is just like any normal staircase. Perhaps it is only for some Northern Line passengers, with their unparalleled experience of stationary escalators, that the effect is ever **extinguished**.” (My bold print.)

Comment: The effect is independent of rational cognitive analysis (i.e. it is involuntary).

Four patients (44–58 years old, mean age 51 years) with varying degrees of unilateral cerebellar pathology participated in this study. These subjects with cerebellar pathologies were recruited among former patients treated at Barrow Neurological Institute.

Case 1

Male, 58 years old. This subject had a tumour (40 × 30 mm) in the left cerebellar cortex. The tumour at the undersurface of the tentorium was surgically excised in 1988. His MRI scans as well as neurological examinations indicate no, or only a mild, pathology of the nuclei on the left side of the cerebellum. At the time of testing (1996), he displayed mild ataxia and target oscillations with his left upper extremity. In addition, he has a slight gait ataxia.

Case 2

Male, 44 years old. This patient had a 30 × 70 mm dysplastic gangliocytoma surgically removed from his right cerebellar hemisphere in 1991. Before the surgery, he had an upper extremity ataxia and a slightly ataxic gait. Following the surgery, he completely recovered and, at present, does not display any signs of cerebellar deficits. He currently works as a machinist.

Case 3

Male, 49 years old. This individual had an arterio-venous malformation in the right cerebellar hemisphere. The malformation was resected in 1992. His CT scans indicate a large lesion in the right cerebellum involving the cerebellar hemispheric cortex, parts of the vermis and the cerebellar nuclei. Presently, he displays dysarthria, a strong cerebellar ataxia of the right arm and leg, and a significant intention tremor which interferes with any writing or fine movements. He has impaired balance and uses a cane to ambulate. After surgery, he had a slight diplopia related to the residual palsy of the right superior oblique muscle. This deficit, however, completely recovered. In addition, he has a slight ptosis (1 mm) on the right side.

Case 4

Male, 53 years old. In 1995, he had a lesion resected from his right cerebellar cortex. Recent MRI scans indicate a 11-mm lesion in the dorso-lateral aspect of the right cerebellar hemisphere with no involvement of the lateral cerebellar nucleus. Presently, he has a slight cerebellar ataxia and intention tremor in his right arm. He has developed a set of compensatory strategies which allow him to continue his hobby of artistic drawing. This patient is right-handed and he draws using his dominant and slightly ataxic arm. He experiences difficulties when drawing straight lines and

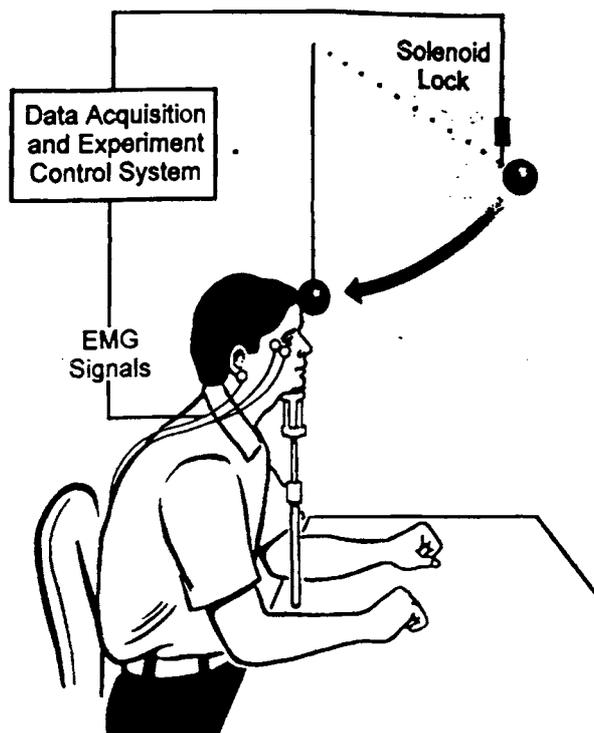


Fig. 1 Schematic diagram of the experimental set-up used in the VTER paradigm. For description see text.

1404 V. Bracha et al.

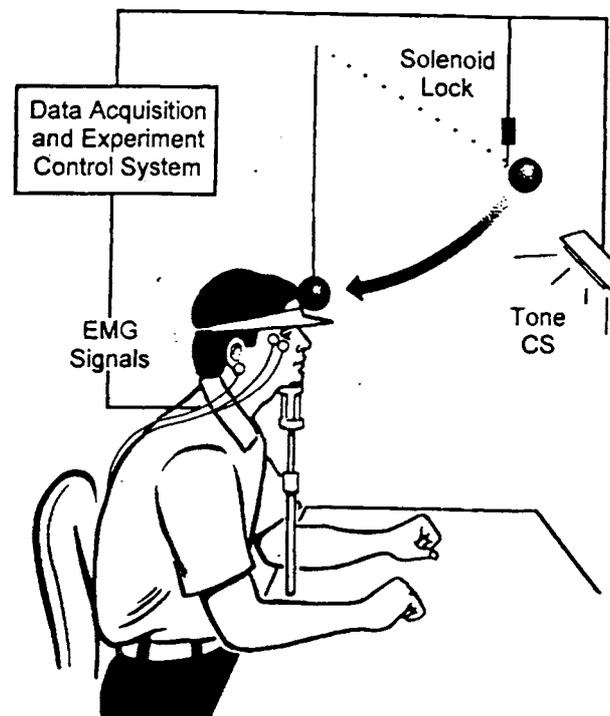


Fig. 2 Schematic diagram of the experimental set-up used in the classical conditioning paradigm. For description see text. Note that the subject wears a visor which prevents him from seeing the ball.

of Helsinki.

12.

Bracha, V., Zhao, L., Wunderlich, D.A., Morrissy, S.J. and Bloedel, J.R. (1997) Patients with cerebellar lesions cannot acquire but are able to retain conditioned eyeblink reflexes. *Brain*, 120, 1401-1413.

The purpose of these experiments was to examine the role of the human cerebellum in the acquisition and retention of conditioned reflexes. Normal human subjects and patients with cerebellar lesions were tested for their capacity to acquire, retain and express conditioned eyeblink responses. In acquisition tests, subjects were trained in a delay classical conditioning paradigm using a tone conditioned stimulus and a midline forehead tap as an unconditioned stimulus. While normal subjects developed anticipatory eyeblinks to the tone in one session, patients with cerebellar lesions failed to acquire conditioned responses in four consecutive training sessions. The conditioning deficit was bilateral even in patients with a unilateral cerebellar pathology. The same groups of subjects were tested for the presence of eyeblinks to a visual threat. In these experiments, both normal subjects and patients with cerebellar lesions exhibited a high level of responding when they saw an object approaching their face. These eyeblinks to the visual threat are probably naturally acquired conditioned responses because they extinguish in normal subjects if they are not reinforced by the unconditioned cutaneous stimulus. In addition, the stimulus of seeing an approaching object blocks the acquisition of classically conditioned eyeblinks to a new conditioned stimulus in normal subjects. These data imply that patients with cerebellar lesions who cannot acquire new classically conditioned responses are able to retain and express conditioned eyeblinks which were acquired before the onset of the pathology. Consequently cerebellum-dependent neural substrates which are involved in learning new conditioned reflexes do not seem to be required for the storage of naturally learned conditioned responses.

Ohman, A. and Soares, J.J.F. (1998) Emotional conditioning to masked stimuli: Expectancies for aversive outcomes following nonrecognized fear-relevant stimuli. *Journal of Experimental Psychology-General*, 127, 69-82.

The role of conscious awareness in human Pavlovian conditioning was examined in 2 experiments using masked fear-relevant (snakes and spiders; Experiments 1 and 2) and fear-irrelevant (flowers and mushrooms; Experiment 1) pictures as conditioned stimuli, a mild electric shock as the unconditioned stimulus, and skin conductance responses as the primary dependent variable. The conditioned stimuli were presented briefly (30 ms) and were effectively masked by an immediately following masking stimulus. Experiment 1 demonstrated nonconscious conditioning to fear-relevant but not to fear-irrelevant stimuli. Even though the participants could not recognize the stimuli in Experiment 2, they differentiated between masked stimuli predicting and not predicting shocks in expectancy ratings. However, expectancy ratings were not related to the conditioned autonomic response.

Schugens, M.M. and Daum, I. (1999) Long-term retention of classical eyeblink conditioning in amnesia. *Neuroreport*, 10, 149-152.

THE retention of classical eyeblink conditioning was investigated in amnesic patients 10 days and 2 months after original learning. During reacquisition, the first CR occurred earlier and the CR frequencies during the first 10 trials were higher than in the baseline session. The overall CR rates increased significantly across sessions during both acquisition and extinction. The amnesics did not differ from matched controls on any of these effects, although they did not recall previous conditioning sessions and did not become fully aware of CS-US contingencies. The smaller number of electrodermal responses to the CS tone during extinction in the amnesics may relate to their lack of insight into the change in the reinforcement schedule. (C) 1999 Lippincott Williams & Wilkins.

Twitmyer, E. B. (1974). A study of the knee jerk. *Journal of Experimental Psychology*, 103(6), 1047-1066.

Knee-jerks to the sound of a bell were obtained from 6 college students after 150-238 trials, during which the 2 patellar tendons were struck 0.5 sec after the sound of the bell. These knee-jerks to the bell alone were not the result of S's voluntary effort, and attempts to inhibit the kicks were wholly unsuccessful. With increased numbers of paired stimulations, the regularity of responding to the bell alone was greatly increased, and the pattern of the knee-jerks was exactly the same as that of knee-jerks resulting from blows to the patellar tendon. The knee-jerks to the bell can be explained only in terms of reflex action, wherein repeated association of the functioning of the motor cells of the lumbar segment of the spinal cord with excitation of centers of the medulla resulting from the sound of the bell resulted in the development of an unusual reflex arc.

Notes

6 Ss. 150-238 trials until knee-jerks to sound of a bell. the two patellor tendons were struck 0.5 sec after bell. Twin lead hammers on both legs.

Lots of individual variation. After more trials regularity of responding to bell greatly increased. Responding was not the result of voluntary efforts, and attempts to inhibit responses were wholly unsuccessful. '...on the unanimous testimony of the subjects it was not produced voluntarily ie. there was noidea of the movement in consciousness, antecedent to the movement itself.' — he used special apparatus and chair at 45 degrees with legs dangling.

Haijang, Q., Saunders, J. A., Stone, R. W., & Backus, B. T. (2006). Demonstration of cue recruitment: Change in visual appearance by means of Pavlovian conditioning. *Proceedings of the National Academy of Sciences of the United States of America*, 103(2), 483-488.

Until half a century ago, associative learning played a fundamental role in theories of perceptual appearance [Berkeley, G. (1709) *An Essay Towards a New Theory of Vision* (Dublin), 1st Ed.]. But starting in 1955 [Gibson, J. J. & Gibson, E. J. (1955) *Psychol. Rev.* 62, 32-41], most studies of perceptual learning have not been concerned with association or appearance but rather with improvements in discrimination ability. Here we describe a "cue recruitment" experiment, which is a straightforward adaptation of Pavlov's classical conditioning experiment, that we used to measure changes in visual appearance caused by exposure to novel pairings of signals in visual stimuli. Trainees viewed movies of a rotating wire-frame (Necker) cube. This stimulus is perceptually bistable. On training trials, depth cues (stereo and occlusion) were added to force the perceived direction of rotation. Critically, an additional signal was also added, contingent on rotation direction. Stimuli on test trials contained the new signal but not the depth cues. Over 45 min, two of the three new signals that we tested acquired the ability to bias perceived rotation direction on their own. Results were consistent across the eight trainees in each experiment, and the new cue's effectiveness was long lasting. Whereas most adaptation aftereffects on appearance are opposite in direction to the training stimuli, these effects were positive. An individual new signal can be recruited by the visual system as a cue for the construction of visual appearance. Cue recruitment experiments may prove useful for reexamining of the role of experience in perception.

Pavlovian Conditioning in Human Subjects?

In some cases conscious cognitive processes in human subject appears to over-ride any simpler conditioning effects (see Davey, 1987). In other cases however there is evidence that associative process in human learning occur without or in spite of conscious awareness.

1. Minor motor reflexes

Knee-jerk	Twitmeyer (1902/1974)
Leg flexion	Timmann <i>et al.</i> , (1996, 1998, 2000), Kolb & Timmann (1996), Dimitrova <i>et al.</i> (2002), Maschke <i>et al.</i> (2002)
Eyeblink	Woodruff-Pak (1993, 1996, 2001), Blaxton <i>et al.</i> , (1996), Logan and Grafton (1995), Bracha <i>et al.</i> (1997), Gabrieli <i>et al.</i> (1995) Gabrieli, (1998), Carillo <i>et al.</i> (2001), Kinder and Lachnit (2002), Clark <i>et al.</i> (2002)

2. Autonomic and metabolic effects

Aversive UCS e.g.skin-resistance measures and shock UCS	Ohman <i>et al.</i> (1975a/b), Esteves <i>et al.</i> (1994) Wik <i>et al.</i> (1997), Ohman and Soares (1998), Buchel and Dolan (2000) Bouton <i>et al.</i> , (2001), Ploghaus <i>et al.</i> (2001), Mineka and Ohman (2002), Delgado <i>et al.</i> (2006).
Immune system	Russell <i>et al.</i> (1984), Ader and Cohen, (1993); Exton <i>et al.</i> (2000), Miller and Cohen (2001),
Blood-glucose	Woods (1976), Woods & Ramsay (2000), Stockhurst <i>et al.</i> (2000, 2004).
Drug administration/ tolerance effects	Siegel (1976-2001: animals), Powell (1995), Ramsay and Woods (1997), Montgomery and Kirsh (1997); Kim and Siegel (2001), Siegel & Ramos (2002), McDonald <i>et al.</i> (2004) Everitt and Robbins (2005).
Anticipatory nausea and taste-aversion	Carey and Burish (1988), , Hu <i>et al.</i> (1996), Morrow and Black (1991), Montgomery and Bovbeg (1997); Cameron <i>et al.</i> (2001); Stockhorst <i>et al.</i> (2006)

3. Sensory and perceptual effects

Direction of rotation of an ambiguous figure (Necker cube)	Qi <i>et al.</i> , (2006)
The 'escalator effect': sensations associated with movement	Simpson (1992) - see handout
McCollough Effects: associations between colour and shape (see below)	Holding and Jones (1976), Allan and Siegel (1993), Siegel <i>et al.</i> (1992) below. McCollough (2000); Ans <i>et al.</i> (2001)

The McCollough after effect — e.g. Holding and Jones (1976)

If red vertical and green horizontal stripes are followed by black and white vertical and horizontal stripes then these vertical stripes appear green, and the horizontal stripes appear red.

In Holding and Jones (1976) Ss were asked to null the effect on black/white gratings by using a colour mixer.

Very long persistence of the after-effect was found: 4, 24, 96 hours and 2000 hours (3 months) could elapse before the first black and white test.

But a single test series initiated a decay process lasting several days.

Some use the word 'conditioning' for this association between pattern and colour (e.g. Allan and Siegel, 1993; Siegel *et al.*, 1992)

Allan, L.G. and Siegel, S. (1993) McCollough effects as conditioned responses: Reply to Dodwell and Humphrey. *Psychological Review*, 100, 342-6.

Allan, L. G., & Siegel, S. (1997). Assessing a new analysis of contingent color aftereffects. *Cognition*, 64(2), 207-222.

Siegel, S., Allan, L.G. and Eissenberg. T. (1992) The associative basis of contingent color after-effects. *Journal of Experimental Psychology: General*, 121, 79-94.

Kandel, E. R., & Pittenger, C. (1999). The past, the future and the biology of memory storage. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences*, 354(1392), 2027- 2052.

We here briefly review a century of accomplishments in studying memory storage and delineate the two major questions that have dominated thinking in this area: the systems question of memory, which concerns where in the brain storage occurs; and the molecular question of memory, which concerns the mechanisms whereby memories are stored and maintained. We go on to consider the themes that memory research may be able to address in the 21st century. Finally, we reflect on the clinical and societal import of our increasing understanding of the mechanisms of memory, discussing possible therapeutic approaches to diseases that manifest with disruptions of learning and possible ethical implications of the ability which is on the horizon, to ameliorate or even enhance human memory.

2. THE PROBLEM OF MEMORY HAS A SYSTEMS COMPONENT AND A MOLECULAR COMPONENT

The work of Ramon y Cajal at the beginning of the century (Cajal 1893) and of Donald Hebb in 1949 (Hebb 1949) established a useful conceptual framework for the study of memory, based on the idea that memory is stored as changes in the strength of specific synaptic connections. This framework divides the study of memory into two components: the systems problem and the molecular problem. The systems problem of memory is concerned with where in the brain memory is stored and how neural circuits work together to create, process and recall memories. The molecular problem of memory is concerned with the mechanisms whereby synapses change and information is stored. Most early work on memory focused on the systems problem, focusing on the question ‘Where is memory stored?’ (pp. 2027-8

14. CONCLUSION

We have at this point a clearer understanding of biologically meaningful subdivisions of memory storage and clearer understanding in outline of some molecular mechanisms of storage relevant to each of these subdivisions. Most impressive is the finding that explicit and implicit storage seems to use a common and limited set of mechanisms to convert short- to long-term memory.

Whereas satisfactory insight into even the details of the storage mechanisms are in sight, the systems problems are much more difficult and will continue to occupy us for many decades. This is because the anatomical system that stores explicit memory is complex, as is the nature of the memory that is stored. Moreover, explicit memory is intimately joined with conscious recollection, an area of neuroscience into which we have little insight. Because the complexity of explicit memory will take time to dissect (probably another century) it will be advisable to continue to analyse instances of implicit memory storage, including the simple implicit memory systems of vertebrates and invertebrates, and use them as prototypes for understanding more complex explicit systems. Because explicit memory storage is so deeply embedded in perception, action and consciousness, its future is the future of neuroscience. (pp. 2048).

Clark, R. E., Manns, J. R., & Squire, L. R. (2002). Classical conditioning, awareness, and brain systems. *Trends in Cognitive Sciences*, 6(12), 524-531.

Memory is composed of several different abilities that are supported by different brain systems. The distinction between declarative (conscious) and nondeclarative (non-conscious) memory has proved useful in understanding the nature of eyeblink classical conditioning -the best understood example of classical conditioning in vertebrates. In delay conditioning, the standard procedure, conditioning depends on the cerebellum and brainstem and is intact in amnesia. Trace conditioning, a variant of the standard procedure, depends additionally on the hippocampus and neocortex and is impaired in amnesia. Recent studies have sharpened the contrast between delay and trace conditioning by exploring the importance of awareness. We discuss these new findings in relation to the brain systems supporting eyeblink conditioning and suggest why awareness is important for trace conditioning but not for delay conditioning.