Brain mechanisms of conditioned taste aversion learning: A review of the literature

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Animals appear to be innately predisposed to associate such food-related stimuli as taste with internal consequences, such as illness. The neural mechanisms of this taste aversion learning are poorly understood, but have recently been the object of increased experimental scrutiny. This article reviews several dozen published reports concerning the effects of central nervous system manipulations on acquisition and retention of taste aversions. Overall, the evidence indicates that taste aversion learning, as contrasted with traditional passive avoidance, is unusually resistant to disruption. The lateral and ventromedial hypothalamus and the amygdala are consistently implicated as participants in taste aversion learning, although their precise role is unclear. Results of studies dealing with other structures are contradictory and inconclusive. Methodological problems contributing to this confusion are discussed, and potentially profitable directions for further research are indicated.

Animals learn to avoid a novel food or liquid if they become ill within several hours after sampling it (Garcia, Ervin, & Koelling, 1966; Kimeldorf & Hunt, 1965). This "baitshyness" phenomenon has been observed under natural conditions and demonstrated in the laboratory in many species. A wide variety of taste or other food-related stimuli have been used, and methods of inducing illness have included ionizing radiation and ingested and injected toxins. Formation of a conditioned aversion is typically evaluated by comparing experimental and control animals on the basis of absolute amount of the test substance consumed and/or degree of preference for the test substance in a two-choice situation. The two-choice preference tests are reported to be the more sensitive and reliable indicators of specific aversion learning (Dragoin, McCleary, & McCleary, 1971; Grote & Brown, 1971).

Special characteristics distinguish long-delay conditioned aversion learning from traditional learning paradigms. For example, whether in the laboratory or under natural conditions, a strong and persistent aversion is often demonstrated after a single pairing of the food cues (conditioned stimulus, CS) and illness (unconditioned stimulus, US), even with a CS-US interval of up to several hours. The maximum effective CS-US interval for a particular food aversion paradigm can be even further extended by introducing a period of anesthesia between CS and US (Rozin & Ree, 1972). In

addition, a rat can acquire a conditioned food aversion when the US (irradiation or toxic chemical) is administered while the animal is anesthetized (Roll & Smith, 1972). Whether the CS-US association is formed during anesthesia, or whether the stimuli are stored separately and are associated after the animal is awake, remains unclear. The effectiveness of this food-illness conditioning with long CS-US intervals, essentially unheard of before the last decade, cannot be accounted for by the persistence of a peripheral taste trace or aftertaste (Revusky & Garcia, 1970; Rozin, 1969; Rozin & Kalat, 1971).

Long-delay avoidance learning appears to require a particular kind of relationship between food cues and illness. Illness-induced aversions are most readily acquired when the ingested substance is novel rather than familiar (see Best, 1975, and Nachman & Jones, 1974, for discussions of "learned safety") and when the distinctive stimuli associated with this novel substance are of a type normally used by the species in its identification of food (Garcia, Hankins, & Rusiniak, 1974; Revusky & Garcia, 1970; Rozin & Kalat, 1971; Seligman, 1970). Rats, which rely mainly on gustatory stimuli for feeding, associate a novel taste with delayed illness but do not easily acquire a food aversion mediated by visual, auditory, or tactual cues (Garcia & Koelling, 1966; Garcia, McGowan, Ervin, & Koelling, 1968). On the other hand, animals that depend on visual cues for food selection rapidly learn an illness-induced aversion to an unfamiliar food or liquid on the basis of its appearance. Such visual food aversions have been demonstrated with blue jays¹ (Brower, 1969), quail (Wilcoxin, Dragoin, & Kral, 1971), guinea pigs (Braveman, 1974), primates (Johnson, Beaton, & Hall, 1975), and domestic chicks (Gaston, 1977). Further-

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more, predatory animals such as coyotes, wolves, and buteo hawks have been conditioned to avoid attacking and killing, as well as consuming, a particular prey. In these cases, the predatory (instrumental or appetitive) component of the illness-induced aversion is often mediated by visual, auditory, or olfactory cues, while the consummatory aversion (avoidance of ingestion) is based on taste characteristics (Brett, Hankins, & Garcia, 1976; Gustavson, Garcia, Hankins, & Rusiniak, 1974; Gustavson, Kelly, Sweeney, & Garcia, 1976).

Since experimental treatments may readily be introduced during the interval between sampling of the novel food (CS) and onset of illness (US), long-delay conditioned food aversion learning provides a unique and useful paradigm for study of the central processes underlying associative learning and memory formation. Research efforts to elucidate the neural bases for this particular type of learning and memory have been directed to discovering which brain structures and mechanisms are involved and to comparison with the central processes generally thought to participate in more traditional passive avoidance learning.

A framework for such investigations has been offered by Garcia and his associates, who propose a dual neural control system, with one part subserving behavioral adaptation in the *milieu externe* and the other subserving behavioral regulation of the *milieu interne* (Garcia et al., 1974). They cite Herrick's (1948) description of the organization of the somatic and visceral neuropils in the medulla oblongata of the tiger salamander: the auditory system and the cutaneous receptors project to the somatic neuropil, which has outputs to the striated motor system (adaptation in the *milieu externe*), whereas the gustatory system and the visceral receptors project to the visceral neuropil, which has outputs to the smooth muscles of the viscera (regulation of the *milieu interne*). In mammals, the internal control system is quite similar to that of amphibians: both gustatory and visceral receptors, as well as the area postrema, send fibers to the nucleus of the fasciculus solitarius in the medulla (Morest, 1967). Some support for the dual process model of internal and external control systems comes from brain lesion studies, where the general finding has been that lesions produce greater deficits in external than in internal control. Further, extracellular recordings from the brainstem indicate that cells which respond to gustatory stimulation are more likely to respond to visceral stimulation than to cutaneous stimulation, while cells which respond to auditory stimulation are more likely to respond to cutaneous stimulation than to visceral stimulation (Guzman-Flores, Guzman-Flores, & Pacheco; cited in Garcia, Hankins, & Rusiniak, 1974). Garcia et al. (1974) also point out that anatomical separation of gustatory discrimination and palatability functions can be inferred from Norgren and Leonard's (1971, 1973) description of a pontine bifurcation of ascending gustatory projections:

one limb projects to the taste cortex, which may well be involved in discrimination learning; the other limb projects to the feeding areas of the hypothalamus and may therefore mediate palatability adjustments.

Some species, such as the quail, develop stronger avoidance for the visual than for the gustatory properties of a food consumed before illness (Wilcoxin et al., 1971). Compared to the rat, the bird has few taste receptors and a more complex visual system (Pearson, 1972), and birds, unlike rats, swallow their food whole and therefore experience few taste cues. Such species may have developed specialized mechanisms for discriminating toxic foods by forming visual-visceral associations.

Since there is as yet, however, almost no anatomical or experimental evidence regarding the central mechanisms underlying long-delay conditioned food aversions based on other than gustatory cues, this review will be concerned exclusively with research relevant to a description and understanding of the central structures and processes involved in illness-induced *taste* aversion learning. Nearly all of this work has used the laboratory rat as its subject. Studies employing lesion and stimulation methods to elucidate the role of specific brain areas will be discussed first, beginning with the lower brainstem and moving upward through the hypothalamus, thalamus, and limbic system to the neocortex. Subsequently, studies involving electroconvulsive shock and amnesic drugs will be described.

LESION AND STIMULATION STUDIES

Lower Brainstem

Berger (1969, 1972) demonstrated that moderate doses of certain psychoactive drugs (amphetamines, scopolamines, and benzodiazapines) are effective in producing strong food aversions. The effects did not appear to depend on gross poisoning, suggesting that the drugs may directly activate food aversion mechanisms. Berger, Wise, and Stein (1973) have investigated the role of the *area postrema* in taste aversions produced by two of these psychoactive drugs, amphetamine and methyl scopolamine. The area postrema, an emetic chemoreceptor zone in the medulla oblongata of the brainstem, detects toxic agents in the blood (Borison & Wang, 1953) and might reasonably be expected to have a role in taste-illness learning. Destruction of this area by thermal cauterization did not disrupt aversions to flavored milk produced by amphetamine injections and did not affect the anorexic effect of amphetamine. On the other hand, area postrema damage prevented normal acquisition of a flavored-milk aversion after injection of methyl scopolamine. Thus, different agents which are capable of conditioning food aversions may act by different mechanisms. The bait shyness and anorexic effects of amphetamine are not mediated at the level of the area postrema, whereas methyl scopolamine appears

to act as a blood-borne toxin which requires an intact area postrema for effective induction of a taste aversion. The findings suggest that investigators should not expect a single neural mechanism to mediate all taste aversion learning.

Midbrain Reticular Formation

Rats receiving 6 h of electrical stimulation in the mesencephalic reticular formation after LiCl ingestion demonstrated significantly less generalized aversion to equimolar NaCl 4 days later than did nonstimulated controls (Balagura, Ralph, & Gold, 1972). The primary aversion to LiCl was not evaluated. Unfortunately, the investigators do not report the location of their electrodes within the reticular formation, nor do they report any behavioral evidence as to the possible rewarding or punishing effects of the stimulation. The observed decrement in generalized aversion may have resulted from attenuation of the aversiveness of LiCl poisoning (e.g., if the reticular formation stimulation was rewarding) or from a more direct disruption of the taste-illness association.

Hypothalamus and Thalamus

Both the ventromedial and lateral hypothalamic areas are known to be importantly involved in normal feeding behavior. Lesion and stimulation studies have tended, in general, to indicate reciprocal functions for the two areas. Bilateral destruction of the lateral hypothalamus (LHA) produces aphagia (lack of eating) and adipsia (lack of drinking) so profound that the animal will die if not force-fed and hydrated. If the LHA-lesioned animal is kept alive in this way, it will gradually recover relatively normal feeding behavior (Teitelbaum & Epstein, 1962). Bilateral ventromedial hypothalamic (VMH) lesions often result in extreme hyperphagia (overeating) and obesity, as though there were a defective "satiety" mechanism (Teitelbaum, 1961). Stimulation studies of the LHA and VMH report complementary effects: LHA stimulation is likely to initiate feeding behavior, even in a sated animal, whereas stimulation of the VMH tends to cause cessation of feeding, even in a food-deprived animal (Hoebel & Teitelbaum, 1962). In general, stimulation of the lateral hypothalamic area is rewarding (i.e., an animal will work to turn the stimulation on), and stimulation of the ventromedial hypothalamus is apparently aversive (i.e., an animal will not work to turn the stimulation on, and may work to turn it off) (Rolls, 1975).

Lateral hypothalamus. A number of experiments indicate that the lateral hypothalamus is necessary for learning about new consequences associated with ingestion, but not for dietary selection based on previous experiences. Lateral hypothalamic lesioned rats which had recovered the ability to feed voluntarily learned little or no aversion for a preferred flavor of food paired with poison, although this ability seemed to recover

somewhat with time since the lesion. These lateral hypothalamic rats also failed to learn to avoid a preferred flavor that signaled impending electric shock to the tongue (Roth, Schwartz, & Teitelbaum, 1973). In further investigations, Schwartz and Teitelbaum (1974) found that recovered lateral hypothalamic rats retained a taste aversion acquired prior to lesioning, but 7 of 10 failed to learn a new aversion. Recovered lateral hypothalamic rats are also apparently unable to acquire preferences for diets paired with recuperation from poison-induced illness, unlike normal animals (Moscovich & Sullivan, cited in Schwartz & Teitelbaum, 1974).

Studies using stimulation of the lateral hypothalamus have produced confusing but interesting results. Lett and Harley (1974) found that rewarding lateral hypothalamic stimulation during the first 15-20 min of illness resulted in attenuation of a learned taste aversion; stimulation during the interval between CS (taste) and US (illness) had no effect. They suggest the LHA stimulation acted by modifying the sickness experience. In a related study, rats were given lateral hypothalamic stimulation for 6 h after ingestion of a toxic amount of LiCl; when tested 4 days later for a generalized aversion to equimolar NaCl, these rats showed less aversion than unstimulated controls (Balagura et al., 1972). Follow-up revealed that the LHA-stimulated rats displayed a normal primary aversion to the LiCl, despite the lack of generalized aversion to NaCl, and that the same results were obtained whether the electrodes did or did not support self-stimulation (i.e., whether or not the stimulation was rewarding) (Ralph & Balagura, 1974). Since the primary aversion to LiCl was undisturbed, the stimulation must not have disrupted the taste-illness association; since rewarding stimulation was not required for disruption of the generalized aversion to occur, it is unlikely that the LHA-stimulation acted by attenuating the aversiveness of LiCl poisoning. The investigators suggest that the effect observed may have been due either to selective interference with a "generalization mechanism" or to enhancement of the rats' chemosensory discriminative ability.

Wise and Albin (1973) have demonstrated that a conditioned taste aversion to cat food selectively prevented LHA-stimulation-induced eating of the cat food, while not affecting stimulation-induced eating of lab pellets. Thus, a conditioned taste aversion interacted in much the same way with feeding behavior produced by lateral hypothalamic stimulation as it does with feeding produced by "normal" hunger.

Ventromedial hypothalamus. Reports on the effects of ventromedial hypothalamic (VMH) lesions on taste aversion learning are conflicting; meaningful interpretation requires careful consideration of the experimental procedures.

Gold and Proulx (1972) found that hyperphagic VMH-lesioned female rats were slower to acquire an apomorphine illness-induced aversion to saccharin

solution than were controls, and their aversion extinguished more rapidly. The effect was most pronounced when the saccharin was a familiar, rather than a novel, substance. Rats lesioned after learning maintained the aversion postoperatively and extinguished at the same rate as controls. The rats in these studies were maintained on a severe cyclical water-deprivation schedule (23½ h) for at least 2 weeks, and a one-bottle test was used to evaluate the aversion. Under these conditions, normal animals demonstrate weaker conditioned aversion than when less severe deprivation and/or two-bottle preference testing are employed (Dragoin et al., 1971; Grote & Brown, 1971; Peck & Ader, 1974). Hyperphagic VMH-lesioned rats, which are known to be hyperresponsive to many types of stimuli (Grossman, 1966), might thus be expected to perform even more poorly than normals under the above conditions. With a much milder deprivation schedule (24 h at 7-day intervals), nonhyperphagic male VMH rats displayed a stronger methylatropine illness-induced aversion to sweet milk and were more resistant to extinction than sham-operated controls (Weisman, Hamilton, & Carlton, 1972). The results of these two experiments, taken together, suggest that the VMH normally modulates responsivity to internal (interoceptive) cues as it does to exteroceptive cues. In the Gold and Proulx study the experimental conditions favor hyperreactivity to thirst, whereas in the Weisman et al. study the conditions favor a greater-than-normal reaction to illness. The results of a related experiment strongly suggest that accurate interpretation of taste aversion studies with VMH-lesioned animals must take into account the relative drive levels of the lesioned and unoperated groups. Hyperphagic female VMH rats were maintained at 95% body weight, unoperated controls at either 95% or 80% body weight. There were no significant differences between the 95% VMH rats and the 80% control rats, and both showed significantly less aversion to sucrose after a sucrose-LiCl pairing than did the 95% controls. These findings indicate that the VMH rats were "hungrier" than controls maintained at the same percent body weight (Peters & Reich, 1973). Further confusion is introduced, however, by the results of a study by Thomas and Smith (1975), in which both static-phase obese VMH female rats and nonobese hyperphagic female VMH rats, maintained at their preoperative weights, exhibited stronger and more persistent aversions to a sucrose solution after one pairing with LiCl illness than did either male or female unoperated controls. In this experiment, as in the Gold and Proulx (1972) study, a severe cyclical water-deprivation schedule and a single-bottle test were used. Clarification of the role of the VMH in taste aversion learning requires further research. One useful approach would be to combine a relatively mild deprivation schedule with two-bottle preference testing; under these conditions, VMH-lesioned rats would be expected to display taste aversion

learning at least as strong and persistent as normal rats (Roth & Fairbanks, Note 1). In addition, stimulation studies of the VMH and taste aversion learning are needed.

In an attempt to distinguish between brain areas responsible for the changed significance of taste signals and areas executing the results of gustatory processing, Aleksanyan, Burešova, and Bureš (1976) investigated unit activity changes evoked by the taste stimulus in the *gustatory thalamus* (medial part of the ventrobasal thalamus) and the lateral and ventromedial hypothalamus of naive and conditioned taste aversion-trained rats. Unit reactions to mouth perfusion with saccharin and with water were recorded in curarized animals. Saccharin-induced reactions in the gustatory thalamus were equally frequent in trained and naive rats, whereas the percentage of saccharin-induced reactions was lower in the lateral hypothalamus and higher in the ventromedial hypothalamus in trained than in naive rats. These findings suggest that the signal significance of the taste of saccharin activates the "feeding center" and inhibits the "satiety center" of the hypothalamus in naive animals, and that conditioned taste aversion training reverses the effects of saccharin on hypothalamic reactivity. The learning process has apparently changed the sweet saccharin taste from a "reward" stimulus, signaled by activity of neurons in the lateral hypothalamic area, to a "punishment" stimulus, signaled by activity of ventromedial hypothalamic neurons.

Limbic System

The *amygdala*, an important nuclear complex in the limbic system, has extensive anatomical and functional connections with the hypothalamus, including those areas involved in control of feeding behavior, as well as with the hippocampus, midbrain tegmentum, and cingulate gyrus (see Gloor, 1960; Kaada, 1972; Lammers, 1972). Neurons in the amygdala are excited by hypothalamic stimulation which produces eating, drinking, or reward. Amygdaloid lesions (especially basolateral) temporarily attenuate these elicited responses, indicating that it modulates, but is not essential for, these behaviors (Rolls, 1975). Further, amygdaloid lesions disrupt active and passive avoidance learning and impair acquisition of conditioned emotional responses. A rather large body of experimental evidence supports the general view that the amygdala is involved in adjusting the significance of stimuli in accordance with experience (see Gloor, 1972; Hall, Bloom & Olds, 1977; Kaada, 1972). Consequently, it is of interest to speculate on the role of the amygdala in taste aversion learning, wherein the significance of a taste stimulus changes as the result of its association with an aversive experience, illness.

The available evidence suggests that the amygdala is, indeed, involved in long-delay conditioned taste aversion learning, but its specific role remains unclear. Lesions

of the amygdala generally produce deficits in acquisition or retention of a taste aversion. Nachman and Ashe (1974) observed that basolateral amygdaloid lesions caused a permanent partial deficit in rats' ability to acquire a new taste aversion to sucrose paired with LiCl-induced illness, as well as complete loss of an aversion learned prior to lesioning. These rats also displayed a decreased neophobic response to the novel taste of sucrose (i.e., they did not inhibit consumption, as normal rats do, during their first exposure to the novel substance) and had an abnormal generalized aversion to water after the sucrose-illness experience. When the unoperated control rats were familiarized with the sucrose solution prior to training, differences between normals and amygdaloid rats disappeared: that is, the lesioned rats learned an aversion as well to a novel solution as controls did to a familiar one, suggesting that the amygdaloid lesions did not affect learning ability directly, but rather disrupted the animals' ability to recognize a novel stimulus as significant.

More widespread lesions in the amygdala also resulted in rats' failure to learn an illness-induced aversion (saccharin-LiCl) after one conditioning session (Kemble & Nagel, 1973) or after repeated trials (McGowan, Hankins, & Garcia, 1972). These lesions also disrupted conditioned suppression of drinking in a noise-shock paradigm (McGowan et al., 1972). Kemble and Nagel (1973) found that their amygdaloid rats consumed about the same amount of the novel saccharin solution prior to LiCl injection as did normal controls, in contrast to the reduced neophobia to sucrose solution reported by Nachman and Ashe (1974).

Subseizure amygdaloid stimulation disrupted rats' acquisition of a taste aversion if administered up to 3 h after illness; the degree of disruption was inversely related to the interval between onset of illness and stimulation (Kesner, Berman, Burton, & Hankins, 1975). No particular area of the amygdala appeared to be critical for the effect. The amygdaloid stimulation had no effect on recovery from neophobia or on the development of behavior presumed to reflect apomorphine-induced illness, nor did it affect acquisition of the taste aversion if it was administered after the CS (taste) rather than after the US. Kesner et al. (1975) argue that these findings indicate that the amygdaloid stimulation is acting directly to disrupt formation of the taste-illness association. However, a memory-disruption effect cannot be eliminated on the basis of the data. Post-training subseizure amygdala stimulation has been shown to produce retrograde amnesia for other passive avoidance learning (Gold, Macri, & McGaugh, 1973). Moreover, since the amygdaloid stimulation itself may have been either rewarding or punishing, depending on electrode placement, the extent of the taste aversion may have been influenced through some motivational route rather than by a direct effect on associative learning or consolidation processes.

Arthur (1975) disrupted acquisition of a taste aversion by administering suprathreshold stimulation of the amygdala during the interval between CS (saccharin) and US (LiCl injection). The effect was not dependent on the occurrence of seizure activity. If stimulation was delayed until 15 min after the LiCl injection, taste aversion learning was normal. Arthur concludes that the amygdala is involved in learning over long delays and that the taste-illness association is consolidated quickly and is therefore only briefly susceptible to disruption by electrical stimulation. The conflicting results reported by Arthur (1975) and by Kesner et al. (1975) are probably due primarily to differences in electrode placements within the amygdala and differences in the parameters of electrical stimulation used.

Electrical stimulation of the *pyriform cortex* overlying the amygdala failed to affect taste aversion learning (Arthur, 1975).

The role of the *olfactory bulbs* in taste aversion learning has been examined in rats and hamsters. The olfactory bulbs have important connections with the corticomedial amygdala and with other areas of the limbic system (Lammers, 1972). The rostral portions of the olfactory bulbs have been found to be involved in the acquisition of conditioned taste aversions in both species (Hobbs, Clingerman, & Elkins, 1976; Elkins, Fraser, & Hobbs, Note 2). In rats, at least, the disruptive effect of bulbectomy on baitshyness is probably not related to the sensory function of the olfactory bulbs. Hankins, Garcia, and Rusiniak (1973) have shown that bulbectomy, but not peripheral anosmia, disrupts acquisition of baitshyness.

The *septal area* appears not to be as importantly involved in taste aversion learning as the amygdala. Both medial and lateral septal nuclei receive efferents from the medial olfactory tract and are reciprocally related to the hypothalamus and hippocampus. In general, lesions of the septal area, especially of the lateral nucleus, have been found to improve performance during the acquisition of active avoidance behavior, impair passive avoidance, and interfere with appetitive response inhibition (see Isaacson, 1974). However, lateral septal lesions which disrupted conditioned suppression of drinking by a noise which had been paired with painful shock had no effect on acquisition of a conditioned taste aversion (Hobbs, Elkins, & Peacock, 1974; McGowan et al., 1972). Large medial septal lesions which did not affect noise/shock conditioning have been reported to facilitate taste aversion learning (saccharin-irradiation or saccharin-LiCl) (McGowan, Garcia, Ervin, & Schwartz, 1969; McGowan et al., 1972) and to increase resistance to extinction (McGowan et al., 1972). Somewhat smaller medial septal lesions did not enhance the aversion produced by pairing sweet milk with LiCl-induced illness, and the aversion extinguished more rapidly for the lesioned rats than for normals (Siegel, 1976). Siegel

suggests that the difference in lesion size may account for the conflicting results of his and McGowan et al.'s experiments, or that saccharin may have been a more salient taste cue than sweet milk, or, finally, that irradiation and LiCl may interact differently with brain lesions.

A number of investigations comparing the involvement of the *hippocampus* in taste aversion learning with its important role in traditional passive avoidance (see Isaacson, 1974) have produced conflicting results and one clear generalization: it is easier to disrupt other types of passive avoidance than it is to disrupt taste aversion learning. Kesner et al. (1975) report that neither post-CS nor post-US stimulation of the hippocampus had any disruptive effect on learning of a taste aversion. Large hippocampal lesions did not affect the speed of acquisition, strength, or resistance to extinction of an aversion to sucrose paired with LiCl illness (Murphy & Brown, 1974). Extensive hippocampal lesions which significantly impaired locomotor passive avoidance did not affect the acquisition or strength of a cyclophosphamide illness-induced aversion to saccharin, although the lesioned rats did extinguish the aversion more quickly than controls (Miller, Elkins, Fraser, Peacock, & Hobbs, 1975). When the toxic agent was irradiation rather than a drug poison, however, rats with extensive hippocampal lesions failed to acquire a saccharin aversion (Miller, Elkins, & Peacock, 1971). Best and Orr (1973) restricted lesions to the ventral or posteroventral hippocampus and found that the lesioned rats displayed normal or facilitated taste aversion learning (saccharin-apomorphine) but failed to show simple passive avoidance of footshock or conditioned suppression of drinking (noise-shock). These investigators suggest that their lesions may have extended into the fimbria, thereby destroying outputs from a larger area of the hippocampus. Similarly, McGowan et al. (1972) found that ventral, but not dorsal, hippocampal lesions disrupted conditioned suppression of drinking (noise-shock) and facilitated acquisition of a conditioned taste aversion (saccharin-irradiation). Fornicotomy was found to have no effect on rats' acquisition of an aversion to mouse-killing induced by LiCl poisoning, nor did it affect extinction of the aversion (DeCastro & Balagura, 1975).

Cortex

The results of experiments investigating the role of neocortical areas in long-delay taste aversion learning are equivocal, but generally tend to indicate that cortical participation is not essential.

Lesions of the anterolateral (gustatory) neocortex which produced degeneration in the ventromedial two-thirds of the ventral thalamic nucleus and occasionally in the ventromedial portion of the dorsal lateral geniculate disrupted rats' ability to associate the taste of saccharin with drug-induced illness. These rats maintained a normal preference for saccharin over water,

and had no deficit in associating the unpleasant taste of quinine with illness, suggesting that the gustatory neocortex lesions affected associative ability but not the palatability of a taste (Braun, Slick, & Lorden, 1972). Hankins, Garcia, and Rusiniak (1974) found that all anterior cortical lesions produced deficits in both flavor-illness and noise-shock conditioning and that involvement of the gustatory neocortex was not required. The effects depended more on the size than the location of the lesions. In the same study, posterior cortical lesions disrupted noise-shock conditioning but did not affect taste aversion learning. Lesions of the anteromedial cortex (which receives projections from the lateral part of the mediodorsal thalamic nucleus), the dorsal bank of the rhinal sulcus (which receives fibers from the medial portion of the same nucleus), or the anteromedial part of the neostriatum did not produce any deficit in taste aversion learning in rats (Divac, Gade, & Wikmark, 1975). Micrencephalic rats, with up to 60% reduction in the size of the forebrain as a result of prenatal exposure to methylazoxymethanol acetate (MAMA), acquired taste aversions as easily as normal controls, and both learned to reverse a relative preference between two flavors easily and repeatedly (Woods, Lawson, Haddad, Rabe, & Lawson, 1974).

In addition to lesion techniques, functional decortication produced by KCl-induced cortical spreading depression (CSD) has been used in an effort to elucidate the role of the cortex in taste aversion learning. Best and Zuckerman (1971) trained rats under unilateral CSD (25% KCl) to avoid drinking saccharin by pairing the taste with apomorphine injections. When tested under contralateral CSD, the untrained hemisphere was able to demonstrate the aversion. In a second experiment, rats were successfully trained on the same task while under bilateral CSD. However, repeated training trials, requiring multiple applications of KCl, were used in these experiments. Cortical depression is less likely to be complete when multiple sessions are used (Lehr & Nachman, 1973), which weakens any argument that these results are evidence for subcortical mediation of taste aversion learning. Lehr and Nachman (1973) conditioned a one-trial aversion to drinking LiCl in rats under unilateral CSD (25% KCl), and found no transfer of the aversion to the opposite hemisphere (contralateral CSD), as measured in one-bottle tests at intervals of 3 days. They interpret these results as evidence that one-trial conditioned taste aversions are normally cortically mediated. Contradictory results were obtained by Davis (1975). Rats were given one pairing of saccharin and LiCl injection under unilateral CSD (25% KCl). When tested the next day in a two-bottle preference test, the aversion transferred to the untrained hemisphere. Nonillness CSD controls had a preference for saccharin, indicating that in this case the spreading depression did not itself induce an aversion to saccharin. There is accumulating evidence, however, that spreading

depression may have aversive properties which, under certain circumstances, are sufficient to condition a food aversion. Rats which drank a novel saccharin solution and then were given a 1-h treatment of 25% KCl-induced bilateral CSD showed a long-lasting conditioned aversion to the saccharin, as compared with controls treated with isotonic Ringer's solution or controls treated with CSD but not exposed to saccharin (Freedman & Ward, 1976). These findings suggested the possibility that CSD may mimic some of the central consequences of gastrointestinal distress, acting directly on a part of the central mechanism which mediates long-delay aversion learning. They certainly indicate that results of taste aversion experiments employing CSD to investigate neocortical involvement must be interpreted with extreme caution. In a related set of experiments, Winn, Kent, and Libkuman (1975) found that rats receiving unilateral or bilateral application to the cortex of 12%, but not 25%, KCl immediately after access to a novel sucrose solution acquired an aversion to the sucrose. These results were interpreted as evidence that cortical spreading depression has both aversive and amnesic properties, as well as that the cortex is not necessary for learning a taste aversion. When the novel taste stimulus was saccharin rather than sucrose, unilateral application of either 12% or 25% KCl effectively produced a taste aversion (Winn, Todd, & Elias, 1977). The authors suggest the possibility that CSD induced by topical application of KCl may produce a taste aversion through direct stimulation of hypothalamic structures which are known to be affected by CSD (Weiss & Fifkova, 1961).

Davis and Bureš (1972) found that rats' acquisition of a LiCl-induced aversion to saccharin was disrupted by CSD induced by 25% KCl 3 h after saccharin ingestion and 2 h before LiCl injection. Less effect was produced by CSD evoked 5 min after saccharin or 15 min before LiCl injection. The investigators suggest that a cortical gustatory trace prolongs the temporal storage of taste cues at the level of the medulla oblongata (cf. Garcia & Ervin, 1968) and therefore bridges the long CS-US delays typically found in gustatory-visceral learning.

Burešova and associates have reported an interesting series of CSD studies. First, bilateral CSD (25% KCl) applied immediately after a saccharin-LiCl pairing did not interfere with rats' acquisition of a saccharin aversion. The saccharin intake of nonillness controls was not depressed by CSD, in direct contrast to the results obtained by Freedman and Ward (1976) and by Winn et al. (1975, 1977). When bilateral CSD was induced 15 min after saccharin consumption, then LiCl injections administered 30 min to 2 h after the saccharin were effective in conditioning taste aversions; when the CS-US interval was more than 2 h, the procedure was ineffective. Non-CSD controls were able to acquire taste aversions when the CS-US interval was as long as 4 h. These results suggest a subcortical short-term memory

for the taste of saccharin. If bilateral CSD was applied before force-feeding saccharin, then LiCl poisoning did not result in a conditioned aversion, indicating that the cortex is necessary for the formation of the gustatory engram. The strength of this engram appeared to be related to the amount of cortex functional during initial gustatory memory formation: when CSD was applied to one hemisphere before saccharin ingestion, the subcortical trace decayed faster than in the case where CSD was induced in both hemispheres 15 min after drinking saccharin. The question of whether cortical function is required for retrieval of the stored taste aversion learning was investigated by measuring hippocampal theta activity. A strong conditioned aversion was established in rats by three pairings of saccharin with LiCl injections. Then hippocampal EEG was recorded during oral perfusion with either saccharin solution or water. Saccharin infusion of trained intact rats produced marked activation of theta activity; saccharin infusion of naive rats or of trained rats under bilateral CSD did not result in increased theta activity, indicating failure of retrieval. While the functionally decorticate (CSD) rats did not exhibit either aversive behavioral reactions or activated theta activity in response to saccharin, forced feeding of saccharin prior to retention testing resulted in extinction of the taste aversion comparable to that produced in intact rats. This suggests that functionally decorticate rats are able to retrieve some types of gustatory information (Brozek, Burešova, & Bureš, 1974; Burešova & Bureš, 1973, 1974).

ECS AND DRUG STUDIES

The effects of electroconvulsive shock (ECS) on memory for long-delay conditioned taste aversions generally appear to be less reliable than the effects of ECS on more traditional kinds of memories. In addition, the nature of the toxic agent employed in the taste aversion paradigm seems to influence the effectiveness of ECS as a memory disrupting treatment.

Using a saccharin-irradiation paradigm, Riege (1969) found that ECS disrupted taste aversion learning whether it was administered after drinking and before irradiation, after irradiation and before drinking, or after drinking and during irradiation. When LiCl is used instead of irradiation, both length of exposure to the taste CS and position of the ECS treatment becomes more important. With a CS-US interval of just 5 min, Nachman (1970) found that ECS given immediately after 30 sec of drinking saccharin had no amnesic effect (i.e., a strong aversion was formed), whereas ECS given immediately after 5 or 10 sec of saccharin drinking had some amnesic effect in some rats. In addition, ECS was found to be ineffective as a US for inducing a taste aversion. Kral (1970) reported that ECS given at any time during a long CS-US interval (saccharin-LiCl

injection) disrupted formation of a taste-illness association. Giving ECS immediately after rats drank the novel-tasting liquid did not impede habituation to the taste, as evidenced by increased intake during a later test. Thus, the ECS did not act by producing retrograde amnesia for the novel taste, since habituation implies memory. Further, when the CS-US interval was 4 h, ECS interpolated during the interval did not appear to be acting via proactive inhibition (decreased memory of the illness experience), since the degree of attenuation of the taste aversion was not related to ECS-US recency. Proactive inhibition would predict that the attenuation would be greatest when ECS was given closest to the onset of illness (Kral, 1971a). This evidence is interpreted as favoring a disassociation theory; that is, ECS acts directly on the central associative mechanism, and the taste and illness events are preserved independently in memory. That ECS actually prevents associative learning rather than inducing amnesia for an already-formed association is suggested by the fact that ECS effectively disrupted taste aversion learning only if it was given immediately after the US (LiCl injection), and therefore functionally within the CS-US interval. ECS given 5 min after the injection (i.e., during illness) did not affect conditioning (Kral & Beggerly, 1973). ECS of a particular intensity and duration was more disruptive when the current was delivered across the posterior rather than the anterior portion of the brain (Kral, 1972); this evidence is consistent with the view that the posterior brain is critical to the formation of taste-illness associations, compared to the greater importance of the anterior brain for other passive avoidance learning (Gold, Farrell, & King, 1971).

In contrast to the results with electroconvulsive shock, amnesic effects of a convulsant drug, pentylenetetrazol (Metrazol), were most pronounced if it was administered after the US (LiCl injection), although some amnesia was evidenced when the drug was given within a 15-min CS-US interval (Ahlers & Best, 1972).

There is one reported study of the amnesic effects of the antibiotic cycloheximide (CXM), a potent protein synthesis inhibitor, on taste aversion learning. Tucker and Gibbs (1976) found that total amnesia resulted when intraventricular CXM was administered at 5, 7, or 9 h before taste aversion training, whereas CXM given 1, 3, or 17 h before training or 7 h before preference testing had no amnesic effect. Unfortunately, there are a number of ambiguities in the report of these results. Data were apparently eliminated for all rats whose overall licking was depressed, but the authors fail to report the numbers eliminated for each group, leaving unanswered the question of whether there were significant differences between groups. No nonillness CXM rats were included in the study to control for the possible effects of CXM on saccharin preference. Finally, the *ns* are very small: 77 rats began the experiment and 14 groups were formed, so initially there were fewer than 6 rats per group; how many remained in each group after the depressed lickers were eliminated is unknown.

Some attempt has been made to determine whether cholinergic synapses are importantly involved in taste aversion learning and memory. Injections of an anticholinergic drug such as atropine or scopolamine either before or during an original taste-poison pairing had no effect on learning a conditioned taste aversion (Kral, 1971b; Smith & Morris, 1964). However, interpretation of these results is complicated by reports that scopolamine or methylscopolamine can act as an aversive US and effectively induce a taste aversion (Berger, 1972; Kral, 1971b). Injection of various doses of scopolamine hydrobromide before testing had no apparent effect on rats' retention of a moderately strong learned aversion to sucrose (Gadusek & Kalat, 1975), in contrast to the large effects reported for retention of other tasks (Deutsch, 1971). These findings suggest that taste aversion learning may not depend on the cholinergic transmitter system thought to be involved in many types of learning.

DISCUSSION

Despite extensive experimental effort, we do not yet know what changes occur in the brain, or even where in the brain they occur, when a rat learns to press a lever to obtain food or when a dog is conditioned to salivate at the sound of a bell. The unusual characteristics and obvious adaptive value of illness-induced taste aversion learning suggest that this may be a relatively "primitive" learning ability based on specialized central mechanisms which might be particularly easy to identify.

Contrary to the view of traditional learning theory that all stimuli are equally associable, the organism seems to be uniquely "prepared," as a result of evolutionary selection in response to environmental pressures, to associate certain kinds of stimuli. It is tempting to postulate the existence of specialized, prewired brain mechanisms which favor the formation of associations between food-related cues and illness and which mediate this associative learning over unusually long delays. The nature of such prewiring might be easier to discover than the neural processes underlying other, less prepared, types of learning and might therefore serve as a valuable model for associative processes in general.

Thus far, simple explanations for the ability of animals to form taste-illness associations over long delays have not been forthcoming. No investigator has found, or claimed to have found, a brain "center" for taste aversion learning. Garcia et al. (1974) have argued that the convergence of gustatory and visceral afferents from cranial nerves VII, IX, and X in the brainstem's nucleus solitarius, and the projections from there to the posterior thalamus, may provide the basic neuroanatomical substrate for the formation of taste-illness associations. While preliminary evidence from brainstem recordings is at least consistent with this view, there are no reported studies which directly support it.

The available research does not yet permit firm conclusions about the central physiological mechanisms underlying taste aversion learning. The methods and

Table 1
Summary of Studies Involving Brainstem, Hypothalamic, and Limbic Structures

Reference	CNS Manipulation	Time of Manipulation										Results									
		Structure	Lesion	Stimulation	Before				Illness-Inducing Agent		Method of Testing		Effect on Learning/Memory		Effect on Resistance to Extinction						
					Training	After-Training	CS-US Interval	Illness	Irradiation	LICI	Apomorphine	One Bottle	Two Bottle	Im-paired	Facilitated	N	De-creased	In-creased	N	O	
Berger et al. (1973)	AP	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Berger et al. (1973)																					
Balagura et al. (1972)	MRF	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Balagura et al. (1972) and Ralph & Balagura (1974)	LHA	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Roth et al. (1973)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Schwartz & Teitelbaum (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Schwartz & Teitelbaum (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Lett & Harley (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Lett & Harley (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Gold & Proulx (1972)	VMH	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Gold & Proulx (1972)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Weisman et al. (1972)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Peters & Reich (1973)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Thomas & Smith (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
McGowan et al. (1972)	AMG	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Kemble & Nagel (1973)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Nachman & Ashe (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Nachman & Ashe (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Arthur (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Arthur (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Kesner et al. (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Kesner et al. (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Hankins et al. (1973)	OB	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Elkins et al. (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Hobbs et al. (1976)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
McGowan et al. (1972)	SA	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
McGowan et al. (1972)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Hobbs et al. (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Siegel (1976)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Miller et al. (1971)	HP	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Best & Orr (1973)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Murphy & Brown (1974)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Kesner et al. (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Kesner et al. (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Miller et al. (1975)		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Note—O = other; N = none; AP = area postrema; MRF = midbrain reticular formation; LHA = lateral hypothalamic area; VMH = ventromedial hypothalamus; AMG = amygdala; OB = olfactory bulbs; SA = septal area; HP = hippocampus.

Table 2: Summary of Studies Involving Cortex

Table 2. Summary of Studies Involving CSD																								
Reference	Time of Manipulation										Results													
	CNS Manipulation		Through-Dur-					Illness-Inducing Agent			Method of Testing			Effect on Learning/Memory		CSD-Induced Aversion								
	Le- sions	Unilat- eral CSD	Bilat- eral CSD	Before Train- ing	Inter- val	Ill- ness	Dur- out Train- ing	LiCl	O	N	One Bottle	Two Bottle	Contra- lateral CSD	O	paired	N	Transfer		Yes	No	Yes	No	O	
																	Yes	No						
Best & Zuckerman (1971)	*	*		*			*		*		*		*			*			*					
Braun et al. (1972)	*				*				*		*					*								
Davis & Bureš (1972)		*				*		*				*				*								
Davis & Bureš (1972)		*							*			*					*							
Lehr & Nachman (1973)		*				*		*			*		*			*			*					
Burešova & Bureš (1973, 1974) and								*			*						*							
Brozek et al. (1974)		*			*				*		*						*					*		
Brozek et al. (1974)		*			*			*			*						*					*		
Brozek et al. (1974)		*			*			*			*					*						*		
Brozek et al. (1974)		*			*		*	*			*			*		*						*		
Hankins et al. (1974)	*			*				*			*					*						*		
Hankins et al. (1974)	*			*				*			*					*						*		
Davis (1975)		*				*						*		*			*			*				
Davis (1975)		*				*				*		*		*			*							*
Winn et al. (1975)		*			*				*		*		*				*				*	*	*	*
Winn et al. (1975)		*			*				*		*		*				*				*	*	*	*
Freedman & Ward (1976)		*			*				*		*		*				*				*	*	*	*
Winn et al. (1977)		*			*				*		*		*				*				*	*	*	*

Table 3: Summary of ECS and Drug Studies

Reference	CNS Manipulation		Time of Manipulation				Illness-Inducing Agent		Method of Testing		Results				
	Drug	ECS	Before Training	After Training	CS-US Interval	Illness	Before Testing	Irradiation	LiCl	N	Testing		Effect on Learning/Memory		
											One Bottle	Two Bottle	Impaired	N	O
Riege (1969)		*				*		*			*	*			
Riege (1969)		*				*		*			*	*			
Riege (1969)		*		*		*		*			*	*			
Kral (1970)		*			*			*	*		*	*			
Nachman (1970)		*			*			*	*		*	*		*	
Nachman (1970)		*			*			*	*	*	*	*		*	
Kral (1971a)		*			*			*	*	*	*	*		*	
Kral (1971a)		*			*			*	*	*	*	*		*	
Ahlers & Best (1972)	M				*			*	*		*	*		*	
Ahlers & Best (1972)	M			*	*			*	*		*	*		*	
Kral (1972)		*		*	*			*	*	*	*	*		*	
Kral & Beggerly (1973)		*			*			*	*	*	*	*		*	
Kral (1971b)	SH				*			*	*	*	*	*		*	
Gadusek & Kalat (1975)	SH						*		*	*	*	*		*	
Tucker & Gibbs (1976)	CX		*					*	*	*	*	*		*	
Tucker & Gibbs (1976)	CX		*					*	*	*	*	*		*	
Tucker & Gibbs (1976)	CX						*		*	*	*	*		*	

Note—N = none; O = other; M = metrazol; SH = scopalamine hydrobromide; CX = cycloheximide.

major findings of most of the studies reviewed here are summarized in Tables 1, 2, and 3. As inspection of these tables reveals, there has been wide variation in the methodology, as well as in the results, of experiments investigating the role of a brain area or process in taste aversion learning. Some of the major procedural differences between studies include the use of different tastes (CSs), illness-inducing agents (USs), and CS-US intervals; one-trial learning vs. extended training; one- vs. two-bottle tests; and deprivation schedules which range from very mild to extremely severe. CNS manipulations produced at various times during the course of training interact in unknown ways with the preceding experimental conditions, and interpretation of lesion and stimulation studies is further complicated by the frequent lack of adequate reported information on electrode placement or extent of tissue damage.

Despite the different procedures used and the contradictory results reported, however, a few tentative generalizations do emerge from the confusion. First, the evidence indicates that taste aversion learning is more resistant to disruption than are other types of learning. For example, experimental interventions such as surgical or functional brain lesions or electroconvulsive shock are more likely to impair acquisition or retention of other passive avoidance tasks than they are to affect taste aversion learning. Further, it is apparent that taste aversion learning does not simply depend on entirely different and less vulnerable areas of the brain, for disturbances of many of the areas known to be involved in other types of learning do affect taste aversion learning as well, albeit less readily.

The lateral and ventromedial hypothalamus, the amygdala, and the hippocampus, areas of the brain which have a role in primitive regulation of feeding behavior, detection of the motivational significance of environmental stimuli, and inhibition of responding, respectively, all appear to participate to some extent in the formation, retention, or behavioral demonstration of taste-illness associations.

Lateral hypothalamic lesions severely impair an animal's ability to acquire a new taste aversion without disturbing its ability to remember and demonstrate an aversion acquired preoperatively. Lesions of the ventromedial hypothalamus, on the other hand, are variously reported to impair, facilitate, or have no effect on taste aversion learning. Which effect is observed appears to depend on the nature of the experimental conditions (e.g., deprivation regimen or type of test). That similar lesions are able to produce such directly contrasting effects suggests that the VMH does not have either a simple or an essential role in taste aversion learning, but rather that it may have an indirect motivational or emotional influence.

Whatever the experimental procedures, surgical or functional lesions of the amygdala almost always impair taste aversion learning and memory and decrease

neophobia. This evidence indicates that the amygdala is required for normal acquisition and retention of a taste aversion and, further, that its contribution has to do with enabling the animal to recognize the significance of novel taste stimuli. Unlike the amygdala, the septal area has no apparent role in normal taste aversion learning. Septal lesions never impair learning, and there is one report of facilitation. Lesions of the hippocampus have been found to impair or facilitate taste aversion learning, to decrease resistance to extinction, or to have no effect at all.

Evidence from studies employing lesions or KCl-induced spreading depression tends to indicate that the neocortex may participate to some extent in taste aversion learning, but that it is not essential for the formation and storage of gustatory-visceral associations. Interpretation of the spreading depression studies is complicated by substantial evidence that the procedure itself has aversive consequences which may be sufficient to condition a taste aversion.

Electroconvulsive shock, on the other hand, does not seem to be effective as a US in a taste aversion paradigm. In general, ECS is reported to have less profound amnesic effects on taste aversion learning than it typically does on other types of learning. Some impairment of learning is generally found, however, no matter what the temporal placement of the ECS treatment (i.e., during the CS-US interval, during illness, or after training is completed), suggesting that ECS is disrupting the associative process rather than producing amnesia for an established association. Further, ECS does not result in amnesia for the individual taste or illness experiences.

It is hoped that future research will employ greater systematic control of experimental parameters, thereby permitting more precise determination of the specific contributions each participating brain structure makes to taste aversion learning. Thoughtful biochemical work will also be needed in order to identify the neurotransmitter system or systems involved. In addition, physiological investigations might profitably be extended to include comparison of the neural substrates of taste aversion learning with those of other "prepared" types of learning, such as imprinting; comparison of predatory and consummatory food aversions; and analysis of the central bases of food aversion learning which is mediated by other than gustatory stimuli.

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NOTE

1. The blue jays apparently reject monarch butterflies on sight after their bitter taste has been associated with emesis.

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