Taste Aversion Learning as a Tool for the Study of Hippocampal and Non-Hippocampal Brain Memory Circuits Regulating Diet Selection

M. Gallo; M.A. Ballesteros; A. Molero & I. Morón

Abstract

Diet selection is the result of different learning experiences that accumulate throughout the life of the organism. The acquisition of aversions to the taste of food followed by mild or severe visceral negative effects plays an important role in food selection. Current knowledge on the role of the critical brain areas (parabrachial area, insular cortex and amygdala) involved in the basic associative neural circuit of taste aversion learning is reviewed. In turn, as shown by a variety of learning phenomena, the development of new aversions to the taste of different types of food is profoundly modulated by the memory of previous learning experiences with the same or different tastes. Some of these phenomena may depend on memory brain systems independent of the basic circuit for taste aversion learning. This seems to be the case for contextual effects and conditioned blocking that depend on the hippocampal integrity. Experimental evidence on the neural basis of complex learning phenomena in taste aversion learning is reviewed. Thus, understanding the way in which taste aversion learning regulates diet selection in daily life requires the study of interactions between hippocampal and non-hippocampal dependent memory systems. Taste aversion learning is proposed as a useful behavioral tool in the investigation of different brain circuits that are critical for food selection.

1. Introduction

The amygdala is part of the limbic system, which is critical for survival. In rats, it is located bilaterally in the medial temporal lobes, and its nuclei are similar to those of primates [1, 2]. In mammals, the amygdala is involved in the expression of many behaviours, such as fear responses, reproduction, aggressiveness and social behaviour and also in physiological processes such as modulation of the neuroendocrine and autonomic systems and homeostasis [3]. The amygdala consists of several nuclei that form a complex network of information processing. The three main nuclei of this structure are the medial, the central and the basolateral nucleus. These nuclei have complex connections with other structures; therefore it is thought that the activity of the amygdala is relevant in the modulation of some types of learning and memory [4]. In particular, the amygdala appears to participate in several complex processes underlying taste learning [5-11].

2. Amygdala and conditioned taste aversion learning

This section will review the studies that implicate the amygdala in taste learning processes [12]. First, a brief description of the phenomenon of CTA will be provided. Then we will analyse the research that points to the amygdala and its nuclei as part of the brain mechanisms of CTA.

2.1. Description of the conditioned taste aversion paradigm

Conditioned taste aversion learning is a particular conditioning paradigm which exists for the subject to associate the consumption of a new taste with a visceral disease that occurs after. Since a delay usually separates the presentation of the taste from the visceral disease, it is suggested that the learning results from the association between the memory trace of that taste and the disease [13]. The CTA learning is vital for numerous species because the learned aversion could reduce the probability of re-experiencing the toxic effects of a harmful substance. Even though this is a conditioning process, it has some special features when compared to most other forms of associative learning. Taste aversion learning is a paradigm widely used in animal research exploring the brain mechanisms of learning and memory [14]. Therefore, we will describe the taste aversion learning paradigm, which was mainly shown in animals. In humans, CTA has also been studied to a much lesser extent than in animals. For example, taste aversion learning has been examined in humans in order to understand the neurobiology of eating behaviour. Studies using positron emission tomography (PET) have shown that the amygdala and orbitofrontal cortex are activated when processing an aversive taste stimuli [15, 16]. Recent research with functional magnetic resonance imaging (fMRI) in humans has confirmed the involvement of the orbitofrontal cortex, anterior cingulated cortex, insular cortex and amygdala in processing highly aversive flavours [17]. Since the amygdala also seems to be involved in conditioned taste aversion in humans, it is possible that the acquisition of this learning requires biological mechanisms that are common in different species of vertebrates [18]. Moreover, because the food aversion associated with chemotherapy treatment is similar to the

experimentally induced taste aversion [19], the CTA paradigm has helped to develop different strategies for dealing with the taste aversion that occurs in patients being treated with chemotherapy [20].

A crucial role in food selection processes is the ability to learn taste aversions [21]. This is particularly relevant for omnivorous species. The discrimination process between edible and harmful, or even potentially deadly, substances starts from the gustatory sensory information. This information stimulates a biological mechanism of precaution against new flavours, which facilitates the evaluation of the consequences of the ingestion of novel substances [22] and subsequently promotes the acquisition of conditioned taste aversions or preferences [8]. The initial response of caution is accompanied by a lower consumption of the novel substances. This phenomenon is called neophobia. If the sensory characteristics of the novel substance are associated with negative visceral consequences (such as poisoning), the animal will then acquire an aversion to that particular taste [23]. If the intake is associated with a positive visceral consequence (as in the case of an energetic food), or non-aversive, the new flavour will be recognized as being safe. Evolution has resulted in the development of neural mechanisms of attention, motivation, learning and memory that allow such identification of edible substances to be made.

Conditioned taste aversion paradigm exhibits three important features of associative learning; each feature exists separately in other classical conditioning paradigms. First, CTA can be acquired with a single pairing between the taste and the visceral discomfort [6, 13, 22-25]. Second, conditioned taste aversion is an example of a biological predisposition to associate certain stimuli more easily. For example, the taste-illness association occurs more easily than sound-disease or odour-disease associations [26]. The third characteristic of CTA learning refers to the delay that separates the presentation of the taste and visceral stimuli, or absence of temporal contiguity. The association between a new taste (the conditioned stimulus -CS-) and visceral consequences following its ingestion (the unconditioned stimulus -US-) results in a subsequent aversion to that taste, even though a delay of minutes or even hours (far superior to that seen in any other type of associative learning) is used. This unusual property of CTA to resist to a long inter-stimulus delay is related to the physiological processes of digestion. Indeed, in physiological conditioning, a delay always separates the ingestion from a potential poisoning. This delay is necessary for the completion of gastric digestion which results in the transport of nutrients through the gastrointestinal system and the gradual absorption of the products of digestion. Consequently, the association between gustatory and visceral stimuli must comply with this temporal requirement [27].

The experimental procedure used to induce conditioned taste aversion is a tool that has been used for decades in research into learning and the biological substrates of learning and memory [6, 11, 13, 14, 24, and 28]. In the laboratory, the procedure involves water deprivation with limited access to a daily amount of water, or water limited to a restricted time period within the day (usually 15 minutes). Once the daily amount of water consumed is stabilized, the animals receive the presentation of a new taste (representing the conditioned stimulus, generally a saccharin solution dissolved in water at 1%) during the conditioning session. The consumption of this taste is followed twenty or thirty minutes later by a gastrointestinal distress (representing the unconditioned stimulus, generally induced by an intraperitoneal injection of lithium chloride (LiCl), although some other aversive agents [29-36] have been used to induce aversion). Forty eight hours after conditioning, CTA tests can be used to detect the strength of the aversion to the CS previously paired with the malaise [37]. The reduction in the consumption of the CS after learning indicates more than a conditioned avoidance response. In fact, the learned aversion to taste really involves a change in the incentive properties of that stimulus, with its hedonic value becoming repulsive [38]. This learning is easily reproduced in the laboratory, and has proven to be a relevant paradigm for discovering important aspects of the neurobiological substrate involved in associative learning and memory. The following section will describe the findings that appear implicate the amygdala in the acquisition of this kind of learning.

2.2. Amygdaloid nuclei and acquisition of CTA

Conditioned taste aversion learning depends on a complex neural circuit that includes brainstem areas, as well as subcortical and cortical mechanisms [8, 11, 39, and 40]. Lesion studies have provided important information about the different structures and regions of the brain involved in the acquisition of taste aversion [10, 18, 41, 42-44]. The processing of sensory information necessary for the acquisition of a taste aversion involves multiple systems. The taste system detects information from the lingual papillae and palate via the cranial facial nerve (VII), glossopharyngeal (IX) and vagus (X) [8]. The visceral sensory system receives information via the vagus nerve and area postrema of the brainstem [45]. The information from both sensory systems are transported separately to the primary relay brainstem nuclei (nucleus of the solitary tract) and secondary relay (parabrachial nucleus), as well as to brain structures involved in processing visceral and taste, such as the thalamus, the insular cortex and the amygdala [46]. The processing of taste qualities [47] and subsequent association with the visceral effects of toxicity [48-50] requires complex neuroanatomical relationships in which the amygdala seems to be involved [51].

The amygdala and other cortical and subcortical areas are related to the brainstem associative processes necessary for taste aversion conditioning [41, 52-57]. In reference [52], the blockade of protein synthesis or beta-adrenergic receptors in the central

amygdala blocks acquisition but not extinction of CTA. The same procedure in the basolateral amygdala blocks extinction but not acquisition of this learning. The authors of this research argue that the neural circuit that makes the acquisition of taste aversion memory possible and the extinction of the aversion requires the activity of the amygdala. However, the involvement of the amygdala and other structures in the associative processes of CTA has been studied by examining protein synthesis associated with learning. In one research it has been observed that the long-term aversive taste memory requires protein degradation in the insular cortex and the amygdala [56]. The selective involvement of the amygdala in CTA has also been analysed in other ways in animal models. There are studies of receptor expression during taste aversion learning [58, 59], studies of the c-Fos expression [60] and other genes [61] in the amygdala, studies of receptors blockade of the amygdala [62] and numerous studies using brain lesions [63], all in the CTA paradigm. For example, possible changes of the leptin receptor expression in the basolateral amygdala in relation to CTA acquisition have been analyzed [59]. Leptin receptor mRNA in the brain was analyzed by in situ hybridization and the expression of this receptor was assessed by immunohistochemistry method. Both measures were significantly higher after the formation of CTA. The authors concluded that the amygdaloid leptin receptor is involved in neuronal communication for CTA formation. Other studies [62] have also implicated other amygdaloid receptors in CTA, particularly the noradrenergic receptors. The researchers administered selective bilateral microinfusions of the beta-adrenergic antagonist propranolol into the basolateral amygdala immediately before intraperitoneal LiCl injections. This procedure disrupted CTA memory and the authors proposed that the basolateral amygdala is a critical structure in modulating the consolidation of taste memory. Genetic studies have confirmed the relation between amygdala and CTA. In this regard, studies have recently identified some specific genes in the amygdala (associated with neuropeptides, G protein-coupled receptors, ion channels, kinases and phosphatases) that contribute to CTA acquisition [61].

Regarding the lesion procedure; the studies that describe a lesion in the amygdala have not been decisive so far as they have shown a weak effect on taste learning or even no effect at all. However, electrolytic lesions of amygdala were shown to attenuate or disrupting CTA [64, 65] and also been shown to affect the neophobia phenomenon [65, 66]. Taken together with other studies that reported a selective involvement of the basolateral nucleus in CTA [67], it has been suggested that the effect of the basolateral injury on CTA is due to an alteration of the proper appreciation of the gustatory signal novelty, which could have affected the subsequent expression of taste aversion [63,68]. Subsequent studies have confirmed this hypothesis by reporting a selective effect on CTA [69] or a dual effect on neophobia and taste aversion [70] after basolateral nucleus lesion.

Moreover, electrolytic lesioning of the basolateral nucleus of the amygdala did not induce any effect on the formation of taste aversion in different studies [71-73]. Some authors have argued that the involvement of the basolateral amygdala in CTA is indirectly mediated by its interactions with the nucleus of the solitary tract [74] or the insular cortex [71, 72] therefore showing that the electrolytic lesions indirectly affects the acquisition of taste aversion. Nevertheless, other brain manipulation tools and neurophysiological techniques have also implicated the basolateral nucleus of the amygdala in the acquisition of CTA learning [51, 75-80]. In other studies [51] it has been found that specific neurons in basolateral amygdala respond to convergent taste stimulus and unconditioned stimulus information during CTA. The authors used a procedure of analysis of temporal gene transcription by fluorescence in situ hybridization in order to locate these populations of neurons. In [77], it was shown that CTA memory needs protein synthesis in the basolateral amygdala, and in [79] it has been proposed that the basolateral amygdala interacts with the insular cortex to modulate the memory consolidation because the infusions of the beta-adrenergic antagonist propranolol administered into this nucleus blocked the enhancing effects on CTA of a muscarinic agonist infused into the insular cortex.

The local injection of excitotoxic agents (such as NMDA or ibotenic acid) induces a more selective lesion in the cell bodies of the target structure. Although the excitotoxic lesioning of the amygdala has not always resulted in deterioration of CTA [71, 81, 82], the excitotoxic lesions of the basolateral amygdala often reproduce the effects obtained with electrolytic lesion on CTA [10, 44, 50, 83-86]. In contrast, the excitotoxic lesion of the central amygdala does not affect the formation of taste aversion [44, 83, 84, and 87]. The possible role of the central nucleus of the amygdala in CTA seems to be related to the processing of visceral information. For example, immunohistochemistry has found increased levels of a specific protein kinase associated with the memory of CTA in the cells of the central nucleus of the amygdala after injection of a high dose of LiCl-induced visceral malaise (US) [88]. A local microinjection of an inhibitor of this kinase into this nucleus decreased the strength of the CTA as well as the levels of this protein in the central amygdala. The authors of this study proposed that the intracellular levels of this protein kinase in the central amygdala are critical to process the visceral information in CTA. Therefore, it seems that the amygdaloid nucleus, which is involved in the acquisition of CTA, is the basolateral nucleus. In this regard, an unpublished study conducted in our laboratory has shown that excitotoxic lesions of the basolateral amygdala decreases taste aversion but does not disrupt the learning. In this study we performed bilateral excitotoxic lesions in the basolateral nucleus of the amygdala by local injection of NMDA and compared these animals' learning with two control groups. One was sham-lesioned in the amygdala and one with a lesion in the hippocampus, a structure not involved in CTA. The results showed a learning impairment in the case of animals with a basolateral lesion, compared with both control sham- and hippocampus-lesioned groups (see Figure 1).

Figure 1.Percentage of taste aversion to saccharin in animals with lesion in the hippocampus (HC) or the basolateral amygdala (BL), as well as in the sham group. The percentage was calculated as a ratio between the saccharin consumed the day of acquisition of learning / saccharin consumed the day of acquisition of learning + saccharin consumed the testing day [X100].

Figure 1.

Percentage of taste aversion to saccharin in animals with lesion in the hippocampus (HC) or the basolateral amygdala (BL), as well as in the sham group. The percentage was calculated as a ratio between the saccharin consumed the day of acquisition of learning / saccharin consumed the day of acquisition of learning + saccharin consumed the testing day [X100].

Figures 2 and 3 show stained brain sections of a sham-lesioned animal and an animal with excitotoxic lesion in the basolateral amygdala induced by local injection of NMDA.

These results suggest that the basolateral amygdala is part of the brain circuitry of CTA, but is not a necessary structure for this learning. In other studies, the inactivation of the basolateral amygdala has not disrupted the CTA [89], or has impaired the learning but did not prevent its acquisition [7]. Therefore, our study, which used excitotoxic lesions, is consistent with the hypothesis that the formation of taste aversion does not require the integrity of the amygdala, although it does seem to be an important structure in the modulation of CTA [41] since the selective lesion of the basolateral amygdala reduces, but does not prevent, the learning. The reversible lesion studies also suggest that the amygdala, or any of its nuclei, is involved in the neural mechanism responsible for CTA learning. For example, the inactivation of the amygdala using local microinfusions of tetrodotoxin (TTX) has confirmed the involvement of this structure in the acquisition and recovery of CTA [7, 90].

In summary, the evidence indicates that the amygdala is part of the neurobiology of taste aversion learning [51, 63, and 91]. Although the exact mechanism is unknown, the data suggest that anatomical and functional relationships between amygdala and insular cortex are necessary for the correct acquisition of conditioned aversion [79, 92]. Research also indicates that the projections from the amygdala to the hypothalamus [93,94] and, in particular, to the brainstem nuclei involved in taste aversion learning [46,74,95-99] also play a significant role in this kind of conditioning.

References

Abraham, W.C. and Tate, W.P. (1997) Metaplasticity: a new vista across the field of synaptic plasticity. Progress in Neurobiology 52, 303–323.

Ackil, J.L., Mellgren, R.L., Halgren, C. and Frommer, G.P. (1969) Effects of CS preexposures on avoidance learning in rats with hippocampal lesions. Journal of Comparative and Physiological Psychology 69, 739–747.

Aggleton, J.P., Petrides, M. and Iversen, S.D. (1981) Differential effects of amygdaloid lesions on conditioned taste aversion learning by rats. Physiology and Behavior 27, 397–400.

Aguado, L., Del Valle, R. and Pérez, L. (1997) The NMDA-receptor antagonist ketamine as an unconditioned stimulus in taste aversion learning. Neurobiology of Learning and Memory 68, 189–196.

Aguado, L., Hall, G., Harrington, N. and Symonds, M. (1998) Illness-induced context aversion learning in rats with lesions of the dorsal hippocampus. Behavioral Neuroscience 112, 1142–1151

Aguado, L., Sam Antonio, A., Pérez, L., Del Valle, R. and Gómez, J., (1994) Effects of the NMDA-receptor antagonist ketamine on flavour memory: conditioned taste aversion, latent inhibition and habituation. Behavioral and Neural Biology 61, 271–281.

Agüero, A, Arnedo, M., Gallo, M. and Puerto, A. (1993a) The functional relevance of the lateral parabrachial nucleus in lithium chloride-induced aversion learning.. Pharmacology, Biochemistry and Behavior 45, 973–978.

Agüero, A., Arnedo, M., Gallo, M. and Puerto, A. (1993b) Lesions of the lateral parabrachial nuclei disrupt aversion learning induced by electrical stimulation of the area postrema. Brain Research Bulletin 30, 585–592.

Agüero, A., Gallo, M., Arnedo, M. and Puerto, A. (1996) Effects of lesions of the medial parabrachial nucleus (PBNm): taste discrimination and lithium-chloride-induced aversion learning after delayed and contiguous interstimulus intervals. Psychobiology 24, 265–280.

Allen, G.V., Saper, C.B., Hurley, K.M. and Cechetto, D.F. (1991) Organization of visceral and limbic connections in the insular cortex of the rat. Journal of Comparative Neurology 311, 1–16.

Baker, A.G. and Mackintosh, N.J. (1977) Excitatory and inhibitory conditioning following uncorrelated presentations of the CS and UCS. Animal Learning and Behavior 5, 315–319.

Baxter, M.G., Holland, PC. and Gallagher, M. (1997) Disruption of decrements in conditioned stimulus processing by selective removal of hippocampal cholinergic input. Journal of Neuroscience 17, 5230–5236.

Bechara, A., Martin, G.M., Pridgar, A. and Van Der Kooy, D. (1993) The parabrachial nucleus: a brain stem substrate critical for mediating the aversive motivational effects of morphine. Behavioral Neuroscience 107, 146–160.

Berman, D.E., Hazvi, S., Rosemblum, K., Seger, R. and Dudai, Y. (1998) Specific and differential activation of mitogen-activated protein kinase cascades by unfamiliar taste in the insular cortex of the behaving rat. Journal of Neuroscience 18, 10037–10044.

Bermudez-Rattoni, F. and McGaugh, J.L. (1991) Insular cortex and amygdala lesions differentially affect acquisition on inhibitory avoidance and conditioned taste aversion. Brain Research 549, 165–170.

Bermudez-Rattoni, F, Rusiniak, K.W. and García, J. (1983) Flavor-illness aversions: potentiation of odor by taste is disrupted by application of novocaine into amygdala. Behavioral and Neural Biology 37, 61–75.

Bernardis, L.L. and Bellinger, L.L. (1996) The lateral hypothalamic area revisited: ingestive behavior. Neuroscience and Biobehavioral Res 20, 189–287.

Bernstein, I.L. (1999) Taste aversion learning: a contemporary perspective. Nutrition 15, 229–234.

Best, P.J. and Orr, J. (1973) Effects of hippocampal lesion on passive avoidance and taste aversion learning. Physiology and Behavior 10, 193–196.

Bielavska, E. and Bures, J. (1994) Universality of parabrachial mediation of conditioned taste aversion. Behavioral Brain Research 60, 35–42.

Bielavska, E. and Krivanek, J. (1994) Intracerebral injection of polymyxin B blocks the acquisition of conditioned taste aversion in rats. Neuroscience Letters 182, 239–242.

Bielavska, E. and Roldán, G. (1996) Ipsilateral connections between the gustatory cortex, amygdala and parabrachial nucleus are necessary for acquisition and retrieval of conditioned taste aversion in rats. Behavioral Brain Research 81, 25–31.

Boakes, R.A., Westbrook, R.F., Elliot, M. and Swinbourne, A.L. (1997) Context dependency of conditioned taste aversions to water and sweet tastes. Journal of Experimental Psychology 23, 56–67.

Bond, N. and Di Giusto, E. (1975) Amount of solution drunk is a factor in the establishment of taste aversion. Animal Learning and Behavior 3, 81–84.

Bond, N. and Harland, W. (1975) Effect of amount of solution drunk on taste aversion learning. Bulletin of the Psychonomic Society 5, 219–220.

Borsini, F. and Rolls, E.T. (1984) Role of noradrenaline and serotonin in the basolateral region of the amygdala in food preferences and learned taste aversions in the rat. Physiology and Behavior 33, 37–43.

Bouton, M.E. (1993) Context, time and memory retrieval in the interference paradigms of pavlovian learning. Psychological Bulletin 114, 80–99.

Braun, J.J., Slick, T.B. and Lorden, J.F. (1972) Involvement of gustatory neocortex in the learning of taste aversions. Physiology and Behavior 9, 637–641.

Buhusi, C.V., Gray, J.A. and Schmajuk, N.A. (1998) Perplexing effects of hippocampal lesion on latent inhibition: a neural network solution. Behavioral Neuroscience 112, 316–351.

Bures, J. and Buresova, O. (1990) Reversible lesions allow reinterpretation of system level studies of brain mechanisms of behavior. Concepts in Neurosciences 1, 69–89.

Bures, J., Bermudez-Rattoni, F. and Yamamoto, T. (1998) Conditioned Taste Aversion: Memory of a Special Kind (Oxford: Oxford University Press).

Bures, J., Buresova, O. and Krivanek, J. (1988) Brain and Behavior: Paradigms for Research in Neural Mechanisms (Prague: John Wiley and Sons), pp. 185–237.

Buresova, O. and Bures, J. (1973) Cortical and subcortical components of the conditioned saccharin aversion. Physiology and Behavior 11, 435–439.

Caulliez, R., Meile, M.-J. and Nicolaidis, S. (1996) A lateral hypothalamic D1 dopaminergic mechanism in conditioned taste aversion. Brain Research 729, 234–245.

Davidson, T.L., McKernan, M.G. and Jarrard, L.E. (1993) Hippocampal lesions do not impair negative patterning: a challenge to configural association theory. Behavioral Neuroscience 107, 227–234.

Davis, M. (1997) Neurobiology of fear responses. The role of the amygdala. Journal of Neuropsychiatry and Clinical Neurosciences 9, 382–402.

De Oliveira Mora, P., Fouquet, N., Oberling, R, Gobaille, S., Graeff, F.G. and Sandner, G. (1999) A neurotoxic lesion of serotonergic neurones using 5,7-dihydroxytryptamine does not disrupt latent inhibition in paradigms sensitive to low doses of amphetamine. Behavioral Brain Research 100, 167–175.

Di Lorenzo, P.M. (1988) Long-delay learning in rats with parabrachial pontine lesions. Chemical Senses 13, 219–229.

Di Lorenzo, P.M. (1990) Corticofugal influence on taste responses in the parabrachial pons of the rat. Brain Research 530, 73–84.

Di Lorenzo, P.M. and Monroe, S. (1992) Corticofugal input to taste-responsive units in the parabrachial pons. Brain Research Bulletin, 29, 924–930.

Dunn, L.T. and Everitt, B.J. (1988) Double dissociations of the effects of the amygdala and insular cortex lesions on conditioned taste aversion, passive avoidance and neophobia in the rat using the excitotoxin ibotenic acid. Behavioral Neuroscience 102, 3–23.

Eichenbaum, H., Otto, T. and Cohen, N.J. (1992) The hippocampus. What does it do? Behavioral and Neural Biology 57, 2–36.

Ellenbrock, B.A., Knobbout, D.A. and Cools, A.R. (1997) The role of mesolimbic and nigrostriatal dopamine in latent inhibition as measured with the conditioned taste aversion paradigm. Psychopharmacology 129, 112–120.

Escobar, M.L., Alcocer, I. and Chao, V. (1998a) The NMDA receptor antagonist CPP impairs conditioned taste aversion and insular cortex long-term potentiation in vivo. Brain Research 812, 246–251.

Escobar, M.L., Chao, V. and Bermudez-Rattoni, F. (1998b) In vivo long-term potentiation in the insular cortex: NMDA receptor dependence. Brain Research 779, 314–319.

Escobar, M.L., Russell, R.W., Booth, R.A. and Bermudez-Rattoni, F. (1994) Accelerating behavioral recovery after cortical lesions. I Homotopic implants plus NGF. Behavioral and Neural Biology 61, 73–80.

Fanselow, M.S. (1998) Pavlovian conditioning, negative feedback and blocking: mechanisms that regulate association formation. Neuron 20, 625–627.

Fernández-Ruiz, J., Escobar, M.L., Piña, A.L., Díaz-Cintra, S., Cintra-McGlone, F.L. and Bermudez-Rattoni, F. (1991) Time-dependent recovery of taste aversion learning by fetal brain transplants in gustatory neocortex-lesioned rats. Behavioral and Neural Biology 55, 179–193.

Fitzgerald, R.E. and Burton, M.J. (1981) Effects of small basolateral amygdala lesions on ingestion in the rat. Physiology and Behavior 27, 431–437.

Galarraga, E., Hernández-López, S., Reyes, A., Miranda, M.I., Bermudez-Rattoni, F., Vilchis, C. and Bargas, J. (1999) Cholinergic modulation of neostriatal output: a functional antagonism between different types of muscarinic receptors. Journal of Neuroscience 19, 3629–3638.

Gallagher, M. and Holland, C. (1992) Preserved configural learning and spatial learning impairment in rats with hippocampal damage. Hippocampus 2, 81–88.

Gallo, M. and Bures, J. (1991) Acquisition of conditioned taste aversion in rats is mediated by ipsilateral interaction of cortical and mesencephalic mechanisms. Neuroscience Letters 133, 187–190.

Gallo, M. and Cándido, A. (1995a) Dorsal hippocampal lesions impair blocking but not latent inhibition of taste aversion learning in rats. Behavioral Neuroscience 109, 413–425.

Gallo, M. and Cándido, A. (1995b) Reversible inactivation of dorsal hippocampus by tetrodotoxin impairs blocking of taste aversion selectively during the acquisition but not the retrieval in rats. Neuroscience Letters 186, 1–4.

Gallo, M., Bielavska, E., Roldán, G. and Bures, J. (1998) Tetrodotoxin inactivation of the gustatory cortex disrupts the effect of the NMDA antagonist ketamine on latent inhibition of conditioned taste aversion in rats. Neuroscience Letters 240, 61–64.

Gallo, M., Márquez, S.L., Ballesteros, M.A. and Maldonado, A. (1999) Functional blockade of the parabrachial area by tetrodotoxin disrupts the acquisition of conditioned taste aversion induced by motion-sickness in rats. Neuroscience Letters 265, 57–60.

Gallo, M., Roldán, G. and Bures, J. (1992) Differential involvement of gustatory cortex and amygdala in the acquisition and retrieval of conditioned taste aversion in rats. Behavioral Brain Research 52, 91–97.

Gallo, M., Valouskova, V. and Cándido, A. (1997) Fetal hippocampal transplants restore conditioned blocking in rats with dorsal hippocampal lesions: effect of age. Behavioral Brain Research 88, 67–74.

Garrud, P, Rawlins, J.N.P., MacKintosh, N.J., Goodal, N.J., Cotton, M.M. and Feldon, J. (1984) Successful overshadowing and blocking in hippocampectomized rats. Behavioral Brain Research 12, 39–53

Good, M. and Honey, R.C. (1991) Conditioning and contextual retrieval in hippocampal rats. Behavioral Neuroscience 105, 499–509.

Gray, J. A., Moran, P.M., Grigoryan, G., Peters, S.L., Young, A.M.J. and Joseph, M.H. (1997) Latent inhibition: the nucleus acumbens revisited. Behavioral Brain Research 88, 27–34.

Gray, N.S., Pickering, A.D., Hemsley, D.R., Dawling, S. and Gray, J.A. (1992) Abolition of latent inhibition by a single 5 mg dose of d-amphetamine in man. Psychopharmacology 107, 425–430.

Grecksch, G., Bernstein, H.G., Becker, A., Hollt, V. and Bogerts, B. (1999) Disruption of latent inhibition in rats with postnatal hippocampal lesions. Neuropsychopharmacology 20, 525–532.

Grigson, P.S., Reilly, S., Shimura, T. and Norgren, R. (1998a) Ibotenic acid lesions of the parabrachial nucleus and conditioned taste aversion: further evidence for an associative deficit in rats. Behavioral Neuroscience 112, 160–171.

Grigson, P.S., Reilly, S., Scalera, G. and Norgren, R. (1998b) The parabrachial nucleus is essential for acquisition of a conditioned odor aversion in rats. Behavioral Neuroscience 112, 1104–1113.

Grigson, P.S., Shimura, T. and Norgren, R. (1997a) Brainstem lesions and gustatory function: II. The role of the nucleus of the solitary tract in Na+ appetite, conditioned taste aversion and conditioned odor aversion in rats. Behavioral Neuroscience 111, 169–179.

Grigson, P.S., Shimura, T. and Norgren, R. (1997b) Brainstem lesions and gustatory function: III. The role of the nucleus of the solitary tract and the parabrachial nucleus in retention of a conditioned taste aversion in rats. Behavioral Neuroscience 111, 180–187.

Grigson, P.S., Spector, A.C. and Norgren, R. (1994) Lesions of the pontine parabrachial nuclei eliminate successive negative contrast effects in rats. Behavioral Neuroscience 108, 714–723.

Gutierrez, H., Hernández-Echeagaray, E., Ramirez-Amaya, V. and Bermudez-Rattoni, F. (1998) Blockade of NMDA receptors in the insular cortex disrupts taste aversion and spatial memory formation. Neuroscience 89, 751–758.

Gutierrez, H., Miranda, M.I. and Bermudez-Rattoni, F. (1997) Learning impairment and cholinergic deafferentation after cortical nerve growth factor deprivation. Journal of Neuroscience 17, 3796–3803.

Hawkins, R.D., Greene, W. and Kandel, E.R. (1998) Classical conditioning, differential conditioning and second-order conditioning of the Aplysia gill-withdrawal reflex in a simplified mantle organ preparation. Behavioral Neuroscience 112, 636–645.

Hirsh, R. (1980) The hippocampus, conditional operations and cognition. Physiological Psychology 8, 175–182.

Holland, P.C. (1992) Occasion setting in pavlovian conditioning. In: Medin, D.L. (Ed.) The Psychology of Learning and Motivation (San Diego: Academic Press). Vol. 28, pp. 69–125.

Holland, P.C. (1997) Brain mechanisms for changes in processing of conditioned stimuli in pavlovian conditioning: implications for behavior theory. Animal Learning and Behavior 25, 373–399.

Holland, P.C. and Bouton, M.E. (1999) Hippocampus and context in classical conditioning. Current Opinion in Neurobiology 9, 195–202.

Honey, R.C. and Good, M. (1993) Selective hippocampal lesions abolish the contextual specifity of latent inhibition and conditioning. Behavioral Neuroscience 107, 23–33.

Houpt, T.A., Berlin, R.A. and Smith, G.P. (1997) Subdiaphragmatic vagotomy does not attenuate c-fos induction in the nucleus of the solitary tract after conditoned taste aversion expression. Brain Research 747, 85–91.

Houpt, T.A., Philopena, J.M., Joh, T.H. and Smith, G.P. (1996) c-fos induction in the rat nucleus of the solitary tract by intraoral quinine infusion depends on prior contingent pairing of quinine and lithium chloride. Physiology and Behavior 60, 1535–1541.

Illich, P.A., Salinas, J.A. and Grau, J.W. (1994) Latent inhibition, overshadowing and blocking of a conditioned antinociceptive response in spinalized rats. Behavioral and Neural Biology 62, 140–150.

Ivanova, S.F. and Bures, J. (1990a) Acquisition of conditioned taste aversion in rats is prevented by tetrodotoxin blockade of a small midbrain region centered around the parabrachial nuclei. Physiology and Behavior 48, 543–549.

Ivanova, S.F. and Bures, J. (1990b) Conditioned taste aversion is disrupted by prolonged retrograde effects of intracerebral injection of tetrodotoxin in rats. Behavioral Neuroscience 104, 948–954.

Jaeger, T.V. and Van der Kooy, D. (1993) Morphine acts in the parabrachial nucleus, a pontine viscerosensory relay, to produce discriminative stimulus effects. Psychopharmacology 110, 76–84.

Jaeger, T.V. and Van der Kooy, D. (1996) Separate neural substrates mediate the motivating and discriminative properties of morphine. Behavioral Neuroscience 110, 181–201.

Jarrard, L.E. (1993) On the role of the hippocampus in learning and memory in the rat. Behavioral and Neural Biology 60, 9–26.

Jia, H.-G., Rao, Z-R. and Shi, J-W. (1994) An indirect projection from the nucleus of the solitary tract to the central nucleus of the amygdala via the parabrachial nucleus in the rat: a light and electron microscopic study. Brain Research 663, 181–190.

Karimnamazi, H. and Travers, J.B. (1998) Differential projections from gustatory responsive regions of the parabrachial nucleus to the medulla and forebrain. Brain Research 813, 283–302.

Kessner, R.P., Berman, R.F. and Tardif, R. (1992) Place and taste aversion learning: role of basal forebrain, parietal cortex and amygdala. Brain Research Bulletin 29, 345–353.

Kiefer, S.W. and Orr, M.R. (1992) Taste avoidance, but not aversion, learning in rats lacking gustatory cortex. Behavioral Neuroscience 106, 140–146.

Kiefer, S.W., Leach, L.R. and Braun, J.J. (1984) Taste agnosia following gustatory neocortex ablation: dissociation from odor and generality across taste qualities. Behavioral Neuroscience 98, 590–608.

Kiefer, S.W., Metzler, C.W. and Lawrwence, G.J. (1985) Neocortical involvement in the acquisition and retention of learned alcohol aversions in rats. Alcohol 2, 597–601.

Kiefer, S.W., Rusiniak, K.W. and García, J. (1982) Flavor-illness aversions: gustatory neocortex ablations disrupt taste but not taste-potentiated odor cues. Journal of Comparative and Physiological Psychology 96, 540–548.

Kim, J.J., Krupa, D.J. and Thompson, R.F. (1998) Inhibitory cerebello-olivary projections and blocking effect in classical conditioning. Science 279, 570–573.

Krivanek, J. (1993) Protein kinase C in nucleus parabrachialis: effect of drugs inducing conditioned taste aversion. Brain Research 629, 327–330.

Krivanek, J. (1996) Conditioned taste aversion and protein kinase C in the parabrachial nucleus of rats. Neurobiology of Learning and Memory 65, 154–162.

Krivanek, J. (1997) Protein kinase C in the parabrachial nucleus of rats during conditioned taste aversion induced by amphetamine. Neuroscience Letters 236, 17–20.

Lamprecht, R., Hazvi, S., Dudai, Y. (1997) cAMP response element-binding protein in the amygdala is required for long-but not short-term conditioned taste aversion memory. Journal of Neuroscience 17, 8443–8450.

Lasiter, P.S. (1982) Cortical substrates of taste aversion learning: direct amygdalocortical projections to the gustatory cortex do not mediate conditioned taste aversion learning. Physiological Psychology 10, 377–383.

Lasiter, P.S. and Glanzman, D.L. (1985) Cortical substrates of taste aversion learning: involvement of dorsolateral amygdaloid nuclei and temporal neocortex in taste aversion learning. Behavioral Neuroscience 99, 257–276.

Ledoux, J. (1998) Fear and the brain. Where have we been and where are we going. Biological Psychiatry 44, 1229–1238.

Lipinski, W.J., Rusiniak, K.W., Hilliard, M. and Davis, R.E. (1995) Nerve growth factor facilitates conditioned taste aversion learning in normal rats. Brain Research 692, 143–153.

López-García, J.C., Fernández-Ruiz, J., Bermudez-Rattoni, F. and Tapia, R. (1990) Correlation between acetylcholine release and recovery of conditioned taste aversion induced by fetal neocortex grafts. Brain Research 523, 105–110.

Lorden, J.F. (1976) Effects of lesions of the gustatory neocortex on taste aversion learning in the rat. Journal of Comparative and Physiological Psychology 90, 665–679.

Lubow, R.E. (1989) Latent Inhibition and Conditioned Attention Theory (Cambridge, Cambridge University Press).

Mackey, W.B., Keller, J. and Van der Kooy, D. (1986) Visceral cortex lesion block conditioned taste aversions induced by morphine. Pharmacology, Biochemistry and Behavior 24, 71–78.

Mackintosh, N.J. (1975) A theory of attention: variations in the associability of stimuli with reinforcement. Psychological Re 82, 276–298.

Mackintosh, N.J., Kaye, H. and Bennett, C.H. (1991) Perceptual learning in flavour aversion conditioning. Quarterly Journal of Experimental Psychology 43B, 297–322.

Masugi, M., Yokoi, M., Shigemoto, R., Muguruma, K., Watanabe, Y., Sansig, G., Van der Putten, H. and Nakanishi, S. (1999) Metabotropic glutamate receptor subtype 7 ablation causes deficit in fear response and conditioned taste aversion. Journal of Neuroscience 19, 955–963.

McCaughey, S.A., Giza, B.K., Nolan, L.J. and Scott, T.R. (1997) Extinction of a conditioned taste aversion in rats: II Neural effects in the nucleus of the solitary tract. Physiology and Behavior 61, 373–379.

McFarland, D.J., Kostas, J. and Drew, W.G. (1978) Dorsal hippocampal lesions: effects of preconditioning CS exposure on flavor aversion. Behavioral Biology 22, 398–404.

Mediavilla, C., Molina, F. and Puerto, A. (1998) Bilateral lesions in the cerebellar interpositus-dentate region impair taste aversion learning in rats. Physiology and Behavior 65, 25–33.

Mediavilla, C., Molina, F. and Puerto, A. (1999) Inferior olive lesions impair concurrent taste aversion learning in rats. Neurobiology of Learning and Memory 72, 13–27.

Meiri, N., Masos, T., Rosenblum, K., Miskin, R. and Dudai, Y. (1994) Overexpression of urokinase-type plasminogen activator in transgenic mice is correlated with impaired learning. Proceedings of the National Academy of Sciences USA 91, 3196–3200.

Miller, R.R. and Matzel, L.D. (1988) The comparator hypothesis: a response rule for the expression of associations. In: Bower, G.H. (Ed.) The Psychology of Learning and Motivation (San Diego: Academic Press). Vol. 22, pp. 51–92.

Miranda, M.I. and Bermudez-Rattoni, F. (1998) Acetylcholine determination of microdialysates of fetal neocortex grafts that induce recovery of learning. Brain Research Protocols 2, 215–222.

Miranda, M.I. and Bermudez-Rattoni, F. (1999) Reversible inactivation of the nucleus basalis magnocellularis induces disruption of cortical acetylcholine release and acquisition, but not retrieval, of aversive memories. Proceedings of the National Academy of Sciences USA 96, 6478–6482.

Miranda, M.I., López-Colomé, A.M. and Bermudez-Rattoni, F. (1997) Recovery of taste aversion learning induced by fetal neocortex grafts: correlation with in vivo extracellular acetylcholine. Brain Research 759 (141–148).

Mogenson, G.J. and Wu, M. (1982) Electrophysiological and behavioral evidence of interaction of dopaminergic and gustatory afferents in the amygdala. Brain Research Bulletin 8, 685–691.

Montag-Sallaz, M., Welzl, H., Kuhl, D., Montag, D. and Schachner, M. (1999) Novelty-induced increased expression of immediate-early genes c-fos and arg 3.1 in the mouse brain. Journal of Neurobiology 38, 234–246.

Morris, R., Frey, S., Kasambira, T. and Petrides, M. (1999) Ibotenic acid lesions of the basolateral, but not the central, amygdala interfere with conditioned taste aversion: evidence from a combined behavioral and anatomical tracttracing investigation. Behavioral Neuroscience 113, 291–302.

Nachman, M. and Ashe, J.H. (1974) Effects of basolateral amygdala lesions on neophobia, learned taste aversions and sodium appetite. Journal of Comparative and Physiological Psychology 87, 622–643.

Nader, K., Bechara, A. and Van der Kooy, D. (1996) Lesions of the lateral parabrachial nucleus block the aversive motivational effects of both morphine and morphine withdrawal but spare morphine's discriminative properties. Behavioral Neuroscience 110, 1496–1502.

Naor, C. and Dudai, Y. (1996) Transient impairment of cholinergic function in the rat insular cortex disrupts the encoding of taste in conditioned taste aversion. Behavioral Brain Research 79, 61–67.

Nerad, L., Ramírez-Amaya, V., Ormsby, C.E. and Bermudez-Rattoni, F. (1996) Differential effects of anterior and posterior insular cortex lesions on the acquisition of conditioned taste aversion and spatial learning. Neurobiology of Learning and Memory 66, 44–50.

Nicolle, M.M., Barry, C.C., Veronesi, B. and Stanton, M.E. (1989) Fornix transections disrupt the ontogeny of latent inhibition in the rat. Psychobiology 17, 349–357.

Nishijo, H., Uwano, T., Tamura, R. and Ono, T. (1998) Gustatory and multimodal neuronal responses in the amygdala during licking and discrimination of sensory stimuli in awake rats. Journal of Neurophysiology 79, 21–36.

Nolan, L.J., McCaughey, S.A., Giza, B.K., Rhinehart-Doty, J.A., Smith, J.C. and Scott, T.R. (1997) Extinction of a conditioned taste aversion in rats: I. Behavioral effects. Physiology and Behavior 61, 319–323.

Norgren, R. (1976) Taste pathways to hypothalamus and amygdala. Journal of Comparative Neurology 166, 17–30.

Norgren, R. (1995) Gustatory System. In: Paxinos, G. (Ed) The Rat Nervous System (San Diego: Academic Press, 2nd edn).

Ormsby, C.E., Ramírez-Amaya, V. and Bermudez-Rattoni, F. (1998) Long-term memory retrieval deficits of learned taste aversions are ameliorated by cortical fetal brain implants. Behavioral Neuroscience 112, 172–182.

Pavlov, I.P. (1927) Conditioned Reflexes (London: Oxford University Press).

Papas, S. and Ferguson, A.V. (1990) Electrophysiological characterization of reciprocal connections between the parabrachial nucleus and the area postrema in the rat. Brain Research Bulletin 24, 577–582.

Pearce, J.M. and Hall, G. (1980) A model for pavlovian learning: variations in the effectiveness of conditioned but not of unconditioned stimuli. Psychological Re 87, 532–552.

Petrovich, G.D. and Swanson, L.W. (1997) Projections from the lateral part of the central amygdala nucleus to the postulated fear conditioning circuit. Brain Research 763, 247–254.

Poremba, A., Jones, D. and Gonzalez-Lima, F. (1997) Metabolic effects of blocking tone conditioning on the rat auditory system. Neurobiology of Learning and Memory 68, 154–171.

Purves, D., Bonardi, Ch. and Hall, G. (1995) Enhancement of latent inhibition in rats with electrolytic lesions of the hippocampus. Behavioral Neuroscience 109, 366–370.

Ramírez-Amaya, V., and Bermudez-Rattoni, F. (1999) Conditioned enhancement of antibody production is disrupted by insular cortex and amygdala but not hippocampal lesions. Brailz, Behavior and Immunity 13, 46–60.

Ramírez-Amaya, V., Alvarez-Borda, B. and BermudezRattoni, F. (1998) Differentiai effects of NMDA-induced lesions into the insular cortex and amygdala on the acquisition and evocation of conditioned immunosuppression. Brain, Behavior and Immunity 12, 149–160

Ramírez-Amaya, V., Alvarez-Borda, B., Ormsby, Ch.E., Martínez, R.D., Pérez-Monfort, R. and BermudezRattoni, F. (1996) Insular cortex lesions impair the acquisition of conditioned immunosuppression. Brain, Behavior and Immzmity 10, 103–114.

Reilly, S. (1999) The parabrachial nucleus and conditioned taste aversion. Brain Research Bulletin 48, 239–254.

Reilly, S., Grigson, P.S. and Norgren, R. (1993a) Parabrachial nucleus lesions and conditioned taste aversion: evidence supporting an associative deficit. Behavioral Neuroscience 107, 1005–1017.

Reilly, S., Harley, C. and Revusky, S. (1993b) Ibotenate lesions of the hippocampus enhance latent inhibition in conditioned taste aversion and increase resistance to extinction in conditioned taste preference. Behavioral Neuroscience 107, 996–1004.

Reilly, S. and Pritchard, T.C. (1996) Gustatory thalamus lesions in the rat: II. Aversive and appetitive conditioning. Behavioral Neuroscience 110, 746–759.

Reilly, S. and Pritchard, T.C. (1997) Gustatory thalamus lesions in the rat: III. Simultaneous contrast and autoshaping. Physiology and Behavior 62, 1355–1363.

Rescorla, R.A. and Wagner, A.R. (1972) A theory of pavlovian conditioning: variations on the effectiveness of reinforcement and nonreinforcement. In: Black, A.H. and Prokasy, W.F. (Eds.) Classical Conditioning II: Current Research and Theory (New York, Appleton Century Crofts).

Rickert, E.J., Bennett, T.L., Lane, P. and French, J. (1978) Hippocampectomy and the attenuation of blocking. Behavioral Biology 22, 147–160.

Rickert, E.J., Lorden, F.J., Dawson, R. and Smyly, E. (1981) Limbic lesions and the blocking effect. Physiology and Behavior 26, 601–606.

Roldán, G. and Bures, J. (1994) Tetrodotoxin blockade of amygdala overlapping with poisoning impairs acquisition of conditioned taste aversion in rats. Behavioral Brain Research 65, 213–219.

Rosenblum, K., Berman, D.E., Hazvi, S. and Dudai, Y. (1996) Carbachol mimics effects of sensory input on tyrosine phosphorylation in cortex. Neuroreport 7, 1401–1404.

Rosenblum, K., Berman, D.E., Hazvi, S., Lamprecht, R. and Dudai, Y. (1997) NMDA receptor and the tyrosine phosphorylation of its 2B subunit in taste learning in the rat insular cortex. Journal of Neuroscience 17, 5129–5135.

Rosenblum, K., Meiri, N. and Dudai, Y. (1993) Taste memory: the role of protein synthesis in gustatory cortex. Behavioral and Neural Biology 59, 49–56.

Rosenblum, K., Schul, R., Meiri, N., Hadari, Y.R., Zick, Y. and Dudai, Y. (1995) Modulation of protein tyrosine phosphorylation in rat insular cortex after conditioned taste aversion training. Proceedings of the National Academy of Sciences USA 92, 1157–1161.

Sacchetti, B. and Bielavska, E. (1998) Chelerytrine, a specific PKC inhibitor, blocks acquisition but not consolidation and retrieval of conditioned taste aversion in rat. Brain Research 799, 84–90.

Sakai, N. and Yamamoto, T. (1997) Conditioned taste aversion and c-fos expression in the rat brainstem after administration of various USs. Neuroreport 8, 2215–2220.

Sakai, N. and Yamamoto, T. (1998) Role of the medial and lateral parabrachial nucleus in acquisition and retention of conditioned taste aversion in rats. Behavioral Brain Research 93, 63–70.

Saper, C. (1982) Reciprocal parabrachial-cortical connections in the rat. Brain Research 242, 33–40.

Saper, C.B. (1995) Central autonomic system. In: Paxinos, G. (Ed.) The Rat Nervous System (SanDiego: Academic Press, 2nd edn).

Scalera, G., Spector, C.A. and Norgren, R. (1995) Excitotoxic lesions of the parabrachial nuclei prevent conditioned taste aversion and sodium appetite. Behavioural Neuroscience 109, 997–1008.

Scalera, G., Grigson, P.S. and Norgren, R. (1997) Gustatory functions, sodium appetite and conditioned taste aversion survive excitotoxic lesions of the thalamic taste area. Behavioral Neuroscience 11, 633–645.

Schafe, G.E. and Bernstein, I.L. (1996) Forebrain contribution to the induction of a brainstem correlate of conditioned taste aversion: I. The amygdala. Brain Research 741, 109–116.

Schafe, G.E. and Bernstein, I.L. (1998) Forebrain contribution to the induction of a brainstem correlate of conditioned taste aversion: I. Insular (gustatory) cortex. Brain Research 800, 40–47.

Schafe, G.E., Thiele, T.E. and Bernstein, I.L. (1998) Conditioning method dramatically alters the role of amygdala in taste aversion learning. Learning and Memory 5, 481–492.

Schmajuk, N.A. and Blair, H.T. (1993) Stimulus configuration, spatial learning and hippocampal function. Behavioral Brain Research 59, 103–117.

Schmajuk, N.A. and DiCarlo, J.J. (1992) Stimulus configuration, classical conditioning and hippocampal function. Psychological Re 99, 268–305.

Schmajuk, N.A., Lam, Y.W. and Christiansen, B.A. (1994) Latent inhibition of the rat eyeblink response: effect of hippocampal aspiration lesions. Physiology and Behavior 55, 597–601.

Schmajuk, N.A., Lam, Y.W. and Gray, J.A. (1996) Latent inhibition: a neural network approach. Journal of Experimental Psychology: Animal Behavior Processes 22, 321–349.

Serova, O.N., Solovea, N.A. and Lagutina, L.V. (1996) Formation of taste aversion and preference in protein synthesis inhibition in rats. Neuroscience and Behavioral Physiology 26, 477–481.

Shimura, T., Suzuki, M. and Yamamoto, T. (1995) Aversive taste stimuli facilitate extracellular acetylcholine release in the insular gustatory cortex of the rat: a microdialysis study. Brain Research 679, 221–226.

Shimura, T., Tanaka, H. and Yamamoto, T. (1997) Salient responsiveness of parabrachial neurons to the conditioned stimulus after the acquisition of taste aversion learning in rats. Neuroscience 81, 239–247.

Shipley, M.T. and Sanders, M.S. (1982) Special senses are really special: evidence for a reciprocal, bilateral pathway between insular cortex and nucleus parabrachialis. Brain Research Bulletin 8, 493–501.

Simbayi, L.C. (1987) Effects of anterior basolateral amygdala lesions on taste aversions produced by high and low oral doses of LiCl and lactose in the rat. Behavioral Brain Research 25, 131–142

Simbayi, L.C., Boakes, R.A. and Burton, M.J. (1986) Effects of basolateral amygdala lesions on taste aversions produced by lactose and lithium chloride in the rat. Behavioral Neuroscience 100, 455–465.

Solomon, P.R. (1977) Role of the hippocampus in blocking and conditioned inhibition of the rabbit's nictitating membrane response. Journal of Comparative and Physiological Psychology 91, 407–417.

Solomon, P.R. and Moore, J.W. (1975) Latent inhibition and stimulus generalization of the classically conditioned nictitating membrane response in rabbits (Oryctolagus cuniculus) following dorsal hippocampal ablation. Journal of Comparative and Physiological Psychology 89, 1192–1203.

Spector, A.C. (1995) Gustatory function in the parabrachial nuclei: implications from lesion studies in rats. Res in Neurosciences 6, 143–175.

Spector, A.C., Norgren, R. and Grill, H.J. (1992) Parabrachial gustatory lesions impair taste aversion learning in rats. Behavioral Neuroscience 106, 147–161.

Sutherland, R.J. and Rudy, J.W. (1989) Configural association theory: the role of the hippocampal formation in learning, memory and amnesia. Psychobiology 17, 129–144.

Swank, M.W. and Bernstein, I.L. (1994) c-fos induction in response to a conditioned stimulus after single trial taste aversion learning. Brain Research 636, 202–208.

Swank, M.W., Ellis, A.E. and Cochran, B.N. (1996) c-Fos antisense blocks acquisition and extinction of conditioned taste aversion in mice. Neuroreport 7, 1866–1870.

Swank, M.W., Schafe, G.E. and Bernstein, I.L. (1995) c-fos induction in response to taste stimuli previously paired with amphetamine or LiCl during taste aversion learning. Brain Research 673, 251–261.

Thiele, T.E., Roitman, M.F. and Bernstein, I.L. (1996) c-fos induction in rat brainstem in response to ethanol- and lithium chloride-induced conditioned taste aversions. Alcoholism: Clinical and Experimental Research 20, 1023–1028.

Touzani, K., Taghzouti, K. and Velley, L. (1997) Increase of the aversive value of taste stimuli following ibotenic acid lesion of the central amygdaloid nucleus in the rat. Behavioral Brain Research 88, 133–142.

Tucci, S., Rada, R and Hernández, L. (1998) Role of glutamate in the amygdala and lateral hypothalamus in conditioned taste aversion. Brain Research 813, 44–49.

Usuda, I., Tanaka, K. and Chiba, T. (1998) Efferent projections of the nucleus accumbens in the rat with special reference to subdivision of the nucleus: biotinylated dextran amine study. Brain Research 797, 73–93.

Wang, Y, Cummings, S.L., Gietzen, D.W. (1996) Temporalspatial pattern of c-fos expression in the rat brain in response to indispensable amino acid deficiency. II. The learned taste aversion. Molecular Brain Research 40, 35–41.

Wasserman, E.A. and Miller, R.R. (1997) What's elementary about associative learning?. Annual Re of Psychology 48, 573–607.

Weiner, I. and Feldon, J. (1997) The switching model of latent inhibition: an update of neural substrates. Behavioral Brain Research 88, 11–25.

Weiner, I., Feldon, J., Tarrasch, R., Hairston, I. and Joel, D. (1998) Fimbria-fornix cut affects spontaneous activity, 2-way avoidance and delayed non-matching-to-sample, but not latent inhibition. Behavioral Brain Research 96, 59–70.

Whishaw, I.Q. and Tomie, J.A. (1991) Acquisition and retention by hippocampal rats of simple, conditional and configural tasks using tactile and olfactory cues: implications for hippocampal function. Behavioral Neuroscience 105, 787–797.

Yamamoto, T. (1993) Neural mechanisms of taste aversion learning. Neuroscience Research 16, 181–185.

Yamamoto, T. (1994) A neural model for taste aversion learning. In: Kurihara, K. and Suzuki, N. (Eds.) Olfaction and Taste XI (Tokyo: Springer-Verlag).

Yamamoto, T, Azuma, S. and Kawamura, Y. (1981) Significance of cortical-amygdalar-hypothalamic connections in retention of conditioned taste aversion in rats. Experimental Neurology 74, 758–768.

Yamamoto, T., Azuma, S. and Kawamura, Y. (1984) Functional relations between the cortical gustatory area and the amygdala: electrophysiological and behavioral studies. Experimental Brain Research 56, 23–31.

Yamamoto, T., Fujimoto, Y., Shimura, T. and Sakai, N. (1995) Conditioned taste aversion in rats with excitotoxic brain lesions. Neuroscience Research 22, 31–49.

Yamamoto, T., Matsuo, R. and Kawamura, Y. (1980) Localization of cortical gustatory area in rats and its role in taste discrimination. Journal of Neurophysiology 44, 440–455.

Yamamoto, T., Nagai, T., Shimura, T. and Yasoshima, Y. (1998) Roles of chemical mediators in the taste system. Japanese Journal of Pharmacology 76, 325–348.

Yamamoto, T., Sako, N., Sakai, N. and Iwafune, A. (1997) Gustatory and visceral inputs to the amygdala of the rat: conditioned taste aversion and induction of c-fos-like immunoreactivity. Neuroscience Letters 226, 127–130.

Yamamoto, T., Shimura, T., Sako, N., Azuma, S., Bai, W.Z. and Wakisaka, S. (1992) c-fos expression in the rat brain after intraperitoneal injection of lithium chloride. Neuroreport 3, 1049–1052.

Yamamoto, T., Shimura, T., Sakai, N. and Ozaki, N. (1994a) Representation of hedonics and quality of taste stimuli in the parabrachial nucleus of the rat. Physiology and Behavior 56, 1197–1202.

Yamamoto, T., Shimura, T., Sako, N., Yasoshima, Y. and Sakai, N. (1994b) Neural substrates for conditioned taste aversion in the rat. Behavioral Brain Research 65, 123–137.

Yasoshima, Y. and Yamamoto, T. (1997) Rat gustatory memory requires protein kinase C activity in the amygdala and cortical gustatory area. Neuroreport 8, 1383–1367.

Yasoshima, Y. and Yamamoto, T. (1998) Short-term and long-term excitability changes of the insular cortical neurons after the acquisition of taste aversion learning in behaving rats. Neuroscience 84, 1–5.

Yasui, Y., Itoh, K., Takada, M., Mitani, A., Kaneko, T. and Mizuno, N. (1985) Direct cortical projections to the parabrachial nucleus in the cat. Journal of Comparative Neurology 234, 77–86.

Yee, B.K., Feldon, J. and Rawlins, J.N.P. (1995) Latent inhibition in rats is abolished by NMDA-induced neuronal loss in the retrohippocampal region, but this lesion effect can be prevented by systemic haloperidol treatment. Behavioral Neuroscience 109, 227–240.

Zald, D.H., Lee, J.T., Fluegel, K.W. and Pardo, J. (1998) Aversive gustatory stimulation activates limbic circuits in humans. Brain 121, 1143–1154.