For the month of February, we are highlighting Chapter 6 of Reilly and Schachtman’s “Conditioned Taste Aversion: Behavioral and Neural Processes”. This chapter by Parker, Limebeer and Rana is entitled “Conditioned disgust, but not conditioned taste avoidance, may reflect conditioned nausea in rats”.

Parker and her colleagues begin their chapter with a fundamental question, i.e., what is the nature of aversion learning. Specifically, they describe the early work of Garcia and his colleagues who interpreted the avoidance of taste associated with various toxic treatments to be a function of conditioned nausea or conditioned disgust. According to this interpretation, the association between the taste and nausea resulted in conditioned disgust reaction to, and avoidance of, the taste on subsequent exposures. The chapter by Parker and her colleagues reviews the evidence that conditioned disgust is produced by emetic agents (i.e., agents capable of inducing vomiting) and that conditioned disgust mediates conditioned taste avoidance. Several lines of research are described.

One major issue in evaluating disgust (and its possible role in conditioned taste avoidance) is in its measurement. In this context, the authors describe the taste reactivity test introduced by Grill and Norgren in 1978. This test uses intraoral infusions of a taste that has been previously paired with a drug that presumably induces nausea. When intraorally infused with the taste, rats display a number of conditioned reactions, indicative of its unpalatability. According to the Parker et al., conditioned disgust (based on nausea and as measured by the taste reactivity test) is a direct measure of the aversiveness of the taste, i.e., a true taste aversion. This test has revealed that rats display conditioned disgust reactions to tastes that have been paired with a variety of drugs, e.g., LiCl, apomorphine and cyclophosphamide, as well as a number of experimental manipulations, e.g., naloxone-precipitated withdrawal and full body rotation.

The measures of conditioned disgust vary among laboratories, and the authors review several experiments from their own lab to validate the measures of disgust reactions. Based on these assessments, Parker et al. define disgust reactions as the combination of gaping, chin rubbing and paw treading. Interestingly, the authors note that the muscular movements involved in the gaping response in rats (species incapable of vomiting) mimic pre-vomiting oral responses in species capable of vomiting (e.g., shrew).

Having established that drugs that support taste avoidance also produce conditioned disgust (supporting its possible role in this avoidance), the authors describe data inconsistent with this position, specifically that a variety of drugs of
abuse that do not produce conditioned disgust do, in fact, induce taste avoidance. Because the initial demonstrations of conditioned taste aversion learning involved emetic agents as the US, the taste avoidance induced by rewarding drugs was likewise interpreted in terms of conditioned nausea (and conditioned disgust). However, when these drugs were assessed in the taste reactivity design, there was no evidence of conditioned disgust. This failure was not a function of the strength of the taste-drug association in that when drugs of abuse and classical emetics were equated for the strength of taste avoidance only the latter elicit conditioned disgust reactions. Parker et al. conclude from such findings that while nausea appears crucial for conditioned disgust, it clearly is not necessary for taste avoidance. They further conclude that the use of the term “conditioned taste aversion” that is commonly used to describe the suppression of consumption of a drug-paired taste may be inaccurate for some drugs and may better describe an ability of a drug to produce nausea rather than its ability to produce taste avoidance.

If conditioned disgust, but not taste avoidance, is mediated by nausea, anti-nausea treatments should affect these two phenomena differently. Specifically, pretreatment with anti-nausea agents should block conditioned disgust but have no effect on taste avoidance, and in fact this is exactly what Parker and her colleagues report. Two prominent anti-nausea treatments, 5-HT antagonists and CB1 agonists interfere with the development and/or expression of conditioned disgust produced by LiCl, but do not affect the establishment or expression of LiCl-induced taste avoidance. Clearly, nausea is not a necessary condition for taste avoidance, while appears to mediate conditioned disgust.

The issue then becomes what does mediate taste avoidance. Following up on a suggestion made originally by Gamzu (1977), the authors argue that given that the rat is incapable of vomiting, any disruption in its affective homeostasis following the ingestion of food must be perceived as potentially dangerous. This change in homeostatic state is associated with the taste and conditionally signals possible danger, resulting in subsequent avoidance of the taste. Accordingly, taste avoidance is based on conditioned fear and not conditioned disgust. In support of this, the authors describe work using the acute startle response (ASR), a reaction that is potentiated by fear and blunted by illness. They report that tastes paired with LiCl do, in fact, blunt the ASR, while amphetamine paired tastes potentiate it. Such data would suggest that amphetamine results in conditioned fear, while LiCl results in a conditioned disgust. Interestingly, when animals in the LiCl condition were pretreated with the anti-nausea agent, ondansetron, the LiCl-associated taste potentiates the ARR, suggesting that LiCl produces both illness and fear. Presumably the conditioned disgust responses produced by LiCl are mediated by LiCl-induced nausea. Its ability to induce fear may mediate its ability to induce taste avoidance, especially following pretreatment with an anti-nausea agent (see above). It remains to be determined if nausea is sufficient for the establishment of taste avoidance with LiCl.
Indirect evidence for the role of conditioned fear in taste avoidance is provided by comparative studies with the shrew, a species capable of vomiting. According to Parker et al., the shrew may not need to be as careful as the nonemetic rat (given its capacity to vomit). This might explain why shrews develop a preference, rather than avoidance, for tastes paired with rewarding drugs and selectively avoid tastes paired with emetic drugs. When pretreated with an anti-emetic, shrews fail to develop taste avoidance to LiCl-paired taste, suggesting that nausea is necessary for the development of conditioned taste avoidance in the emetic shrew.

Having addressed the nature of taste avoidance learning (possibly based on conditioned fear), the authors briefly discuss an alternative hypothesis introduced earlier by Grigson and her colleagues. This position, the reward comparison hypothesis, offers an alternative explanation to the long-standing paradox wherein rewarding drugs induce taste avoidance. According to the reward comparison hypothesis, rats avoid a taste that has been paired with a rewarding drug, because the taste comes to predict the availability of the more rewarding drug (for a more detailed discussion, see the highlight from the previous chapter of the book). According to Grigson, taste avoidance is based neither on conditioned disgust or conditioned fear. Instead, it is based on reward itself and the relative comparison of the rewarding effects of the taste and subsequent drug. As pointed out by the authors, such an account cannot explain the abovementioned species differences in the ability of rewarding drugs to induce conditioned taste avoidance.

The authors close their chapter with an overview of the different memory systems that appear to serve conditioned disgust and conditioned taste avoidance. This distinction between the neuroanatomy of disgust and avoidance rests on a number of observations. For example, rats lacking gustatory cortex learn LiCl-induced taste avoidance but fail to display disgust reactions. Moreover, lesions of dorsal and median raphe nuclei that reduce serotonin availability prevent development of conditioned disgust reactions but not taste avoidance. Such an analysis serves to illustrate that different processes likely mediate the two behaviors given their very different neuroanatomical mediation.

This chapter provides the reader with a cogent overview of the nature of taste avoidance and the systematic way one can go about sorting out the various mechanisms that may be mediating its display. From its overview, it is clear that the rat avoids tastes that predict a novel change in its homeostatic state. Although nausea mediates the development of conditioned disgust (classical CTA), it is not necessary for the development of taste avoidance (although it may still be sufficient). The behavioral dissociation of conditioned disgust and conditioned taste avoidance is an important consideration in assessing the ability of any compound to induce taste avoidance.

Andrey Verendeev and Anthony Riley