Preexposure to the Unconditioned Stimulus in Nausea-Based Aversion Learning

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For the month of December, we are highlighting Chapter 4 of Reilly and Schachtman's "Conditioned Taste Aversion: Behavioral and Neural Processes". This chapter by Hall is entitled "Preexposure to the unconditioned stimulus in nausea-based aversion learning".

This chapter summarizes the attenuating effects of exposure to the unconditioned stimulus (US) on taste aversion conditioning. It does so by discussing various demonstrations of the attenuating effects of such preexposure, the conditions under which the attenuation occurs and the possible mechanisms underlying the effect.

As an example of the US preexposure effect, Hall describes how consumption of saccharin paired with lithium chloride (LiCl) differs in subjects with a history of LiCl exposure (weaker than nonpreexposed subjects). Although Hall points out that US preexposure can be seen with other compounds, he focuses on LiCl in order to discuss the mechanisms underlying the US preexposure effect. The complexity of the US preexposure effect lies in trying to determine these mechanisms.

As Hall describes, there are two major classes of interpretations, specifically, associative and non associative. Within two classes, the two major interpretations receiving the most attention are associative blocking and habituation (or tolerance), respectively. Associative blocking argues that during drug preexposure the animal acquires an association between various external cues (like the environment) and the preexposed drug. During subsequent taste aversion conditioning with that same drug, the taste-drug association is blocked by the environmental cues that had already been associated with the drug. Habituation, instead, argues that the effectiveness of the US diminishes following repeated exposure. That is, the initial preexposures to the drug result in the development of habituation (or tolerance) such that upon subsequent exposure the compound produces a weaker subjective effect. When conditioning is then attempted, the drug supports a weaker taste aversion. Habituation as an explanation is immediately dismissed (due to evidence that the attenuating effects of preexposure with LiCl are evident with no obvious habituating effects on other behavioral indices), and the chapter focuses on evidence for associative blocking (specifically via environmental cues associated with the effects of preexposure).

For associative blocking to be a viable interpretation of the US preexposure effect in aversion learning, evidence must be presented that environmental cues can be associated with the drug (in this case LiCl). After initially describing early work by Garcia arguing that exteroceptive cues generally are not effective stimuli in aversion conditioning, Hall provides evidence that context can, in fact, function as a CS. First, he

cites work from Symonds and Hall (1997) in which taste aversion conditioning with LiCl was blocked if this conditioning was attempted in the presence of environmental cues previously paired with LiCl. Secondly, he notes that while context control of consumption may be relatively weak unless animals are drinking immediately prior to drug injection, such control (suppression of consumption) is more evident if LiCl is given immediately prior to context exposure, even in animals which do not have fluid access during conditioning. Clearly, context can be an effective CS.

Based on the abovementioned findings, Hall then argues that the US preexposure effect with LiCl is a function of associative (context) blocking. That is, injections of LiCl in some context results in an association of that context with LiCl-induced nausea. That context then blocks subsequent taste aversion conditioning. If this is true, such blocking should be context dependent , specifically, aversions should be attenuated only when the preexposure and conditioning contexts are the same. As Hall notes, this prediction has been supported by a number of studies. He further notes that manipulations, e.g., overshadowing, extinction, latent inhibition, that affect the strength of the context US association should impact the US-preexposure effect. Again, such is the case.

Although the above arguments do support the blocking hypothesis, Hall notes that many studies have reported US preexposure effects in the home cage (albeit often weaker). The issue here is that one would expect that latent inhibition might be evident with the environmental context of the home cage that would limit (prevent?) its association with LiCl during preexposure. Consequently, there would be limited blocking of the association of the novel taste with LiCl during taste aversion conditioning. The issue becomes why there would be any attenuation if the context conditioning was weak as a function of latent inhibition. Hall describes work by De Brugada et al. (2003) that indicates that when the preexposure environment is familiar (as when it is given in the home cage), injection cues are the reliable predictor of LiCl. During taste aversion conditioning, these cues block the ability of the taste to become associated with LiCl. Such control by injection cues is not evident when preexposure occurs in a novel environment. Under this condition, the context itself is associated with LiCl and blocks taste aversion learning, but only when animals are conditioned in that same environment. The preexposure effect is diminished if animals are given aversion conditioning in an environment different from preexposure (see above).

In order to provide evidence that injection cues may be important for the US preexposure effect with LiCl (in the familiar home cage environment), Hall cites early work by Willner (1978) who demonstrated that preexposure effects with LiCl were weakened when saline was administered randomly throughout the preexposure phase (reducing the ability of the injection itself to predict sickness). Similarly, when saline injections are given between LiCl preexposure and conditioning, the US preexposure effect is weakened (De Brugada & Aguado, 2000; De Brugada et al., 2003).

The most convincing evidence that injection cues may mediate the US preexposure effect with LiCl (at least when preexposure and conditioning are given in the home cage) was reported by De Brugada et al. (2004). In this work, De Brugada and her

colleagues injected rats with LiCl prior to taste aversion conditioning in which LiCl was given orally. Under these conditions, injected LiCl had no impact on aversions induced by the orally administered LiCl. Interestingly the initial LiCl injections did attenuate a subsequent aversion in these same animals when given another flavor paired with injected LiCl, an attenuation that is presumably due to blocking by the injection cues.

Based on the evidence described, contexts, including the cage and injection cues, serve as CSs in the CTA preparation and mediate the US preexposure effect with LiCl. Habituation does not appear to be involved in this attenuation given that it can occur when there is no preexposure effect and the preexposure effect has been demonstrated without habituation. Hall provides an important caveat to his overall conclusion by noting that the "US" event itself is likely more complex than credited and that certain aspects of that event may be susceptible to blocking while others may be susceptible to habituation. Further, the effects seen with LiCl and classical emetics may not be the same as those that occur when other substances (e.g., drugs of abuse) and should be further investigated. The chapter provides a critical review of the procedures necessary to isolate the specific mediation of the attenuating effects of drug preexposure in taste aversion conditioning. Such procedures need to be applied to other compounds to assess the generality of the associative account of the effects of such exposure.