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Reduced palatability in pain-induced conditioned taste aversions

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HIGHLIGHTS

- Gallamine and hypertonic NaCl cause internal pain but not nausea/malaise.
- Gallamine and hypertonic NaCl reduced palatability of the associated tastant.
- Internal pain causes CTAs comparable to those based on emesis-related agents.

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ABSTRACT

The current study investigated whether internal pain-inducing agents can modulate palatability of a tastant in the same way as illness-inducing agents (e.g., lithium chloride). Similar to traditional conditioned taste aversion (CTA) experiments, during conditioning the rats were exposed to a saccharin solution followed by intraperitoneal injections of either gallamine (Experiment 1) or hypertonic sodium chloride (NaCl; Experiments 1 and 2). In addition to the total amount consumed, the time of each lick was recorded for lick pattern analysis. The results showed that both gallamine and hypertonic NaCl caused suppression in saccharin intake. Importantly, both lick cluster size and initial lick rate (the measures of taste palatability) were reduced as well. This pattern of results suggests that these pain-inducing agents reduce the hedonic value of the associated tastant and thus CTA is acquired. The current finding serves as evidence supporting the view that CTA is a broadly tuned mechanism that can be triggered by changes in internal body states following consummatory experience.

1. Introduction

Animals, humans included, avoid eating foods that have previously caused them to experience gastrointestinal malaise. That is, the taste of the food (conditioned stimulus, CS) becomes associated with the aversive post-ingestive effects of food consumption (unconditioned stimulus, US) and a conditioned taste aversion (CTA) is acquired (for reviews see edited volumes by [5,8,43,52]). Not only is intake of the CS suppressed but also, as shown with both taste reactivity (e.g., [10,16,33,48,49,58]) and lick pattern analysis (e.g., [3,4,27]), the CS itself is devalued. That is, the palatability of the CS is reduced consequent to pairings with the US. This latter effect ensures that we do not accidentally or mistakenly consume the toxic food because it is now disgusting and quickly ejected from the mouth. Thus, one can argue that a reduction in taste palatability drives the suppression in consumption of the illness-inducing food.

The present research investigated whether a change in palatability occurs when a taste CS is paired with a US that causes internal pain. A number of studies have found that external pain, induced with footshock, can suppress intake of the associated taste CS (e.g., [30,51]). However, the results of a study by Brett ([11]; discussed in [29]) clearly show that peripheral pain does not cause CTAs. In Brett's experiment, rats, receiving a foot shock at the mid-point of 60-s taste trials, learned to suppress CS intake prior to the shock but drank avidly thereafter. Thus, it appears that taste can serve as a signal for the external pain of footshock but that the taste is not devalued.

The role of internal pain remains largely unresolved, however. Indeed, we are aware of only one study that investigated the palatability of a taste CS followed by an internal pain US (specifically lower gastrointestinal pain caused by lactose malabsorption; [51]). In that study, palatability was assessed using taste reactivity measures, a technique involving analysis of stereotypical orofacial and somatic responses evoked by taste stimuli [32–34]. Although most taste reactivity studies use a procedure in which a small, controlled volume of a tastant is infused directly into the mouth via a cannula implanted in the rat's cheek, the task employed by Pelchat et al. required voluntary ingestion of 40% lactose, which served as both the CS and US. The results show that lactose suppressed intake but had no influence on taste palatability (assessed by the number of rats showing aversive orofacial and somatic responses on the test trial). Because no aversive responses were detected the pattern of results was interpreted as evidence that the internal pain caused by lactose malabsorption produces conditioned taste avoidance not CTA.

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There are, however, a number of reasons why this interpretation of the Pelchat et al. [51] result cannot be accepted with confidence. First, intake of lactose on the first conditioning trial ranged from 0.3 ml to 15.0 ml, indicating wide individual variability in experience with the CS and, perhaps more importantly, the US properties of lactose. Second, because lactose is not very soluble, the 40% solution was presented to the subjects at 35 °C. In turn, to prevent the temperature of the CS from becoming a salient cue during conditioning, all water presented to the thirsty rats during the experiment was also presented at 35 °C. That is, an unconventional experimental procedure was employed with all the attendant concerns about the comparability and generality of the obtained results. Third, intake on the test trial achieved a group mean of less than 0.5 ml and it is not clear, in the absence of intraoral delivery, how much lactose made contact with the mouth or was spilled from the spout. That is, low intake volumes may have influenced detection of aversive taste reactivity responses. For these reasons, the procedure and test stimulus may not have been optimal to evaluate whether internal pain influences taste palatability. Accordingly, the current study sought to reexamine this issue using a procedure more closely resembling that of the traditional LiCl-induced CTA.

In the present study we used 0.1% saccharin as the CS in each experiment where it was paired with gallamine or hypertonic sodium chloride (NaCl) in our standard voluntary intake procedure. Like curare, gallamine blocks cholinergic transmission at the neuromuscular junction [15] thereby inducing paralysis and pain in muscle tissue. Hypertonic NaCl is well established as a laboratory model of visceral pain in rats (e.g., [31]). These two agents were administered intraperitoneally thus providing a better comparison to studies with LiCl as the US. Experiment 1 examined whether gallamine or hypertonic NaCl can significantly reduce CS palatability along with volume consumed. As a positive control, LiCl was included as a US along with a no-US (isotonic saline) control group. Experiment 2 focused on hypertonic NaCl as the US and involved parametric changes intended to increase CS–US contiguity and thus sensitivity to the detection of changes in palatability of the associated saccharin CS.

Given the use of a voluntary drinking procedure, lick pattern analysis was used to assess the conditioned changes in the palatability of the taste CS. The raw data from such an analysis supply lick counts and inter-lick interval times which reveal that rats, during trials that typically last 30 min, produce sustained runs of rapidly occurring licks (termed clusters) that are separated by pauses of varying durations [1,12,23]. Thus, a number of measures can be extracted including: total licks, initial and overall lick rates, number of clusters, inter-cluster interval and lick cluster size. However, not all of these variables reflect taste palatability [17]. Total licks and number of clusters are each highly correlated with amount consumed but not the concentration of the tastant [9,25,56,59]. Similarly, inter-cluster intervals, which show a skewed distributed, do not seem to code palatability [19,23]. Indeed, long inter-cluster intervals (ranging from 5 s to over 100 s) indicate that the rat has stopped licking and is engaged in other behaviors such as grooming or exploring. Cluster size, however, is highly controlled by sensory input from the taste solution [20,21]. For example, for a palatable taste like sucrose, there is a monotonic relationship between concentration and cluster size — as the former increases or decreases so too does the latter. It should also be noted that larger cluster size does not necessarily imply a larger volume consumed. There is, in fact, an inverted U-shaped function between volume consumed and the concentration of palatable solutions [18,23,59,60]. On the other hand, for an unpalatable tastant like quinine, cluster size decreases monotonically as concentration increases [36,61].

Another line of evidence that supports the use of cluster size as an index of taste palatability comes from studies in which manipulations that influence taste palatability produce comparable effects on both cluster size and taste reactivity responses. For instance, benzodiazepines are considered to stimulate feeding by enhancing taste palatability as revealed by an increased frequency in the occurrence of ingestive taste reactivity responses (e.g., [50,53,57]) and an increase in the size of lick clusters (e.g., [35]). As noted already, illness-induced with LiCl decreases the palatability of the associated taste CS as determined with taste reactivity methodology and cluster size analysis. Overall, these findings, which in many instances have been used as cross-validation for the two approaches, along with those in the preceding paragraph support the view that cluster size is a reliable measure of taste palatability during voluntary intake tasks (e.g., [18,22,23,35,39,59]; for a review see [26]).

Finally, it has been suggested that initial lick rate also represents the affective reactions to a tastant (e.g., [20,47]). However, this measure may have less utility than cluster size. For example, initial lick rate is defined by an arbitrary break (e.g., 1 min or 3 min) determined by the experimenter and not by a pause in licking. Furthermore, given that this measure is taken from a relatively small portion of the whole drinking period, the influence of experimental manipulations on initial lick rate may, in some circumstances, be obscured by ceiling effects in lick rate [59]. Nonetheless, initial lick rate is considered a relatively pure measure of the sensory properties of the taste solution because the short sample period minimizes post-ingestive feedback [22], which, of course, is one of the merits of using taste reactivity methodology to assess palatability. Therefore, in addition to cluster size, initial lick rate was included as an additional measure of taste palatability in the current study.

2. Experiment 1

This experiment examined whether the internal pain-inducing USs gallamine and hypertonic NaCl, like the illness-inducing US LiCl, reduce palatability as well as CS intake. To prevent the rapid development of floor effects in CS consumption, the LiCl US (0.075 M) was half our standard concentration and hypertonic NaCl (1.0 M) was half the concentration employed by Sakai and Yamamoto [55]. To our knowledge, two studies [37,40] have investigated whether gallamine can suppress intake of a taste CS. In the first of these studies, Ionescu and Buresova [37] reported that all rats given a 40-mg/kg dose of gallamine (which failed to induce taste suppression in a one-trial procedure) had to be placed on artificial respiration for the duration (1–2 h) of muscular paralysis. A preliminary study in our laboratory of gallamine-induced taste suppression using 10 and 20 mg/kg found that the lower dose was sufficiently high to suppress CS intake without generating lethal consequences in the absence of support from artificial respiration. Accordingly, the 10-mg/kg dose of gallamine US was used in the present, multiple-conditioning trial experiment.

2.1. Materials and methods

2.1.1. Subjects

A total of 40 experimentally naïve male Sprague–Dawley rats (Charles River Laboratory, Wilmington, MA) were used as subjects. The rats were individually housed in hanging steel cages (Acme Metal Product, Chicago, IL) with free access to food and water in a colony room that was illuminated for 12 h each day beginning at 7:00 am. Prior to the behavioral treatments, the subjects were acclimated to a water deprivation schedule that permitted 15 min access each morning in the drinking chambers and 15 min access each afternoon in the home cages; food was always available in the home cages. The University of Illinois at Chicago Animal Care and Users Committee approved all procedures employed in the present study. At all times, rats were treated according to guidelines recommended by the American Psychological Association [2] and the National and the Institutes of Health [45].

2.1.2. Apparatus

Eight identical drinking chambers (Med Associates, St. Albans, VT; 30.5 cm × 24.0 cm × 29.0 cm) were employed, each housed in a sound-attenuating cubicle fitted with a ventilation fan. The sidewalls