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Research report

Role of the gustatory thalamus in taste learning

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HIGHLIGHTS

- Gustatory thalamus lesions do not disrupt drug-induced CTA learning.
- Gustatory thalamus plays a critical role in taste neophobia.
- Gustatory thalamus lesion-induced neophobia deficit does not delay learning.

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ABSTRACT

The present study re-examined the involvement of the gustatory thalamus (GT) in the acquisition of drug- and toxin-induced conditioned taste aversions (CTAs) using a standardized procedure involving 15-min taste trials in rats injected with morphine (Experiment 1), lithium chloride (Experiment 2) or amphetamine (Experiment 3). Contrary to previous results, GT lesions did not eliminate drug-induced CTAs. Rather, GT-lesioned rats acquired aversions of comparable magnitude to non-lesioned subjects but from an elevated intake on the first conditioning trial. A similar pattern of lesion effects was found in the acquisition of an illness-induced CTA. Thus, we conclude that GT lesions do not differentially influence CTAs conditioned with drugs or toxins. The lesion-induced elevated intake of a novel tastant confirms an unappreciated role for the GT in taste neophobia.

1. Introduction

Taste neophobia and conditioned taste aversion (CTA) are phenomena that defend against the ingestion of toxic foods. The former refers to the reluctance, in the absence of knowledge about post-ingestive consequences, to consume a new food (e.g., [7,8,10,15]) whereas the latter refers to the reduced intake of a food that is known to have aversive post-ingestive consequences (e.g., [6,9,39,52]). In the laboratory the oral (taste) and post-ingestive (visceral malaise) features of the toxic food are usually separated and termed, respectively, the conditioned stimulus (CS) and the unconditioned stimulus (US).

Because it is a taste-guided behavior, neurobehavioral investigations of CTA learning have tended to focus on the roles of the components of the central gustatory system (e.g., [46–48]). In the rat, taste information is relayed from the parabrachial nucleus to the gustatory insular cortex (GC) via the gustatory thalamus (GT; for reviews see [36,65]). The present article is concerned with the role of the GT in CTA acquisition. The overwhelming majority of studies that have examined the effects of GT lesions on CTA have employed a toxin (e.g., lithium chloride; LiCl) as the US (e.g., [19,40,49,51,59]). Moreover, these studies uniformly found that GT lesions have no influence CTA acquisition. In marked contrast, however, there are two experiments that reported that GT lesions eliminated CTA acquisition [21,53]. These latter two experiments are notably different from the former studies in that they used a rewarding dose of morphine (i.e., a dose that supports place preference learning) as the US. Together, this pattern of results encouraged the view that malaise-inducing toxins/poisons and rewarding drugs of abuse support qualitatively different types of taste learning dependent on different neural substrates (e.g., [21,22]).

The view that there are different forms of taste suppression that can be fractured apart by a neural manipulation (in this case, GT lesions) is critically dependent on all aspects of the behavioral procedures being the same, except, of course, the USs. However, the two morphine experiments involved taste trials that were 5 min in duration whereas the aforementioned LiCl studies typically employed 15 min taste trials. It is, we believe, unsafe to form strong conclusions about the existence of different processes of taste suppression on the basis of experiments that used such short access periods. In particular, 5-min trials are prone to ceiling effects on intake (which is constrained to a maximum of about 10–12 ml) that

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might obscure differences that otherwise would be revealed when a longer trial duration is employed. The goal of the present study was to reexamine the role of the GT in taste suppression induced with a drug of abuse (Experiments 1 and 3) and LiCl (Experiment 2). To ensure comparability, 15-min trials were used in each experiment. If the GT has a significant role in drug-induced taste suppression then lesions of this nucleus should, like those reported by Grigson et al. [21] and Reilly and Trifunovic [53], eliminate this form of learning irrespective of trial duration. On the other hand, if a different outcome is obtained with 15-min taste trials then the role of the GT in taste learning requires reevaluation.

2. Experiment 1

As noted above, only two experiments, those reported by Grigson et al. [21] and Reilly and Trifunovic [53], have investigated the influence of GT lesions on the acquisition of drug-induced taste learning. Both of these experiments employed the same design that involved 5-min CS access per trial and a 15-mg/kg morphine US. In each experiment it was found that GT-lesioned (GTX) rats injected with the morphine US drank the same amount of the taste CS as the control GTX subjects injected with the saline vehicle. Thus, GTX rats conditioned with morphine failed to show any evidence of CS intake suppression. Experiment 1 re-examined the influence of GT lesions on drug-induced taste learning with a procedure that permitted 15-min saccharin access each trial and a 15-mg/kg morphine US.

2.1. Method

2.1.1. Subjects

Forty-one, experimentally naïve, male Sprague–Dawley rats (275–300 g) obtained from Charles River Laboratories (Wilmington, MA) served as subjects. They were individually housed in stainless steel hanging cages (Acme Metal Product, Chicago, IL) in a vivarium maintained at 21 °C on a 12 h light–dark cycle (lights on at 7:00 am). Animals were allowed to habituate to the facility for 3–5 days before surgery. All experimental treatments and procedures were conducted during the light phase of the cycle. Food and water were available at all times in the home cage except during behavioral testing as noted below. Animals were treated in accordance with guidelines from the American Psychological Association [2] and the National Institutes of Health [43]. The University of Illinois at Chicago Institutional Animal Care and Users Committee approval was obtained for all treatments.

2.1.2. Surgery

A total of 20 rats received bilateral GT lesions using the procedures of Sastre and Reilly [58]. These animals (Group GTX) were anesthetized with intraperitoneal (IP) injections of sodium pentobarbital (55 mg/kg) and secured in a Kopf Model 1900 stereotaxic instrument equipped with a digital readout (David Kopf Instruments, La Jolla, CA) using non-traumatic earbars. Cranial sutures were exposed by a midline incision; a single trephine hole (5 mm diameter) was drilled on the skull centered over the transverse sinus at the level of the GT. Excitotoxic lesions were created with 0.15 M N-methyl-D-aspartate (Sigma–Aldrich; St Louis, MO) backfilled into a glass micropipette (tip diameter ~70 μm) and infused iontophoretically into the GT with a Midgard precision current source (Stoelting, Wood Dale, IL). There was a single 6 min −10 μA current infusion per hemisphere at −3.70 mm posterior to bregma, ±0.80 mm medial/lateral to the midline, −6.30 mm ventral to dura. Body temperature was monitored throughout the surgical procedure via a rectal thermometer and maintained at 37 °C with a heating pad (Harvard Apparatus, Holliston, MA). Twenty-one rats served as control subjects (Group SHAM): 10 rats received the same surgical procedures as GTX rats except no N-methyl-D-aspartate was infused and 11 rats received only pentobarbital anesthesia.

2.1.3. Apparatus

All testing was conducted in the home cage with fluids presented in plastic graduated cylinders fitted with silicone stoppers and stainless steel sipper tubes secured to the front of the home cage by stainless steel springs. Volumes were measured to the nearest 0.5 ml.

2.1.4. Procedure

The rats were acclimated to a deprivation schedule permitting 15 min access to water each day. The experiment began when water intake stabilized (12 days) at which time the rats in each group (SHAM and GTX) were divided into subgroups according to the drug (saline or morphine) to be administered as the US on conditioning days. Each conditioning trial consisted of 15 min access to 0.15% saccharin followed, 5 min later, by an IP injection of either physiological saline (1 ml/kg body weight) or morphine sulfate (15 mg/ml/kg). A saccharin trial occurred every third day and the rats were otherwise maintained on the water deprivation schedule as described above. Conditioning trials continued until stable performance emerged in the experimental and control groups. Thus, there were a total of four conditioning trials with US injections and a single CS only test trial; US injections were omitted on the test trial because they were superfluous. Volume consumed served as the dependent measure.

2.1.5. Data analysis

Behavioral data was analyzed with repeated-measures analysis of variance (ANOVA) with Group as the between-subjects variable and Trial as the within-subjects variable. Significant main effects and interactions were followed-up by appropriate post hoc analyses, either planned comparisons (simple main effects) with the adjusted error term from the overall ANOVA or Tukey HSD tests. All analyses were conducted using Statistica 6.0 software (StatSoft, Inc., Tulsa, OK) with alpha level set at $p < .05$.

2.1.6. Histology

Once all experimental procedures were completed, GTX rats were injected with sodium pentobarbital (100 mg/kg; IP) and then transcardially perfused with physiological saline followed by 4% formaldehyde. Brains were extracted and stored in 4% formaldehyde and then 20% sucrose for two days each. Thereafter, the brains were frozen, sliced at 50 μm on a cryostat and stained with cresyl violet. Using a light microscope (Zeiss Axioskop 40), photomicrographs were taken with a Q-Imaging camera running Q-Capture software (Quantitative Imaging Corporation, Burnaby, B.C., Canada). Damage to the GT and surrounding regions was identified and evaluated based on the Paxinos and Watson [44] atlas.

2.2. Results and discussion

2.2.1. Anatomical

Complete bilateral destruction of the GT was required for rats to be included in statistical analyses of Group GTX (see Fig. 1). Of the rats that were included some minor damage extended into the centromedian, paracentral, parafasicular, and subparafasicular thalamic nuclei, as well as the VPM, but damage was unilateral and non-systematic in all animals. Misplaced lesions tended to be placed dorsolateral to the GT resulting in subtotal GT damage while increasing damage to the VPM, centromedian nucleus, and paracentral nucleus. Groups included in the behavioral analysis were: SHAM-Saline ($n = 11$), SHAM-Morphine ($n = 10$), GTX-Saline ($n = 8$), and GTX-Morphine ($n = 8$). GT Lesions in the current study were