Role of gustatory thalamus in anticipation and comparison of rewards over time in rats

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Schroy, Pearl Lee, Robert A. Wheeler, Collin Davidson, Giuseppe Scalera, Robert C. Twining, and Patricia S. Grigson. Role of gustatory thalamus in anticipation and comparison of rewards over time in rats. Am J Physiol Regul Integr Comp Physiol 288: R966–R980, 2005. First published December 9, 2004; doi:10.1152/ajpregu.00292.2004.—Rats reduce intake of a palatable saccharin solution when it is followed by access to a preferred sucrose solution. This phenomenon, referred to as an anticipatory contrast effect (ACE), is thought to occur because the value of the saccharin conditioned stimulus pales in comparison to the highly rewarding sucrose unconditional stimulus expected in the near future. Although relatively little is known about the underlying neural substrates, lesions of the gustatory thalamus fully disrupt the phenomenon (Reilly S, Bornovalova M, and Trifunovic R. Behav Neurosci 118: 365–376, 2004; Reilly S and Pritchard TC. Behav Neurosci 110: 746–759, 1996). The present set of experiments revisited this issue to determine the nature of this deficit. Rats with bilateral ibotenic acid lesions of the gustatory thalamus were given 3-min access to 0.15% saccharin and, after a 0-s or 5-min interval, were given 3-min access to either the same saccharin solution or a highly preferred 1.0 M sucrose solution. In experiment 1, ACE testing began with the 5-min interstimulus interval (ISI) and then switched to the 0-s ISI. For experiment 2, the order of ISI testing was reversed. The results show that axon-sparing, neurotoxic lesions of the gustatory thalamus prevent ACEs with a 0-s ISI and lead to a reversal (i.e., a reinforcement effect) with a 5-min ISI. Together, the results suggest that the lesion leads to a specific reward comparison deficit, whereby the rats fail to compare the value of an available reward with the memory of a preferred reward that is anticipated in the near future.

anticipatory contrast; memory; sucrose; drugs of abuse; reinforcement effect; taste

PRIMARY TASTE NEURONS in the nucleus of the solitary tract (NTS) terminate in the medulla, making up the first leg of the polysynaptic taste pathway (34, 35). From the NTS, axons project to the pontine parabrachial nuclei (PBN) and then rostrally via two different pathways. The first pathway, the dorsal taste pathway, projects from the PBN to the parvicellular component of the ventral posteromedial nucleus (VPMpc) of the thalamus (also referred to as the gustatory thalamus) and then continues to the agranular insular cortex (27). The second pathway, the ventral taste pathway, includes several diverse projections from the PBN to the substantia innominata, the lateral hypothalamus, the central nucleus of the amygdala, and the bed nucleus of the stria terminalis (21, 32, 33, 44). The present experiments were concerned with the role of the VPMpc, the third relay in the dorsal taste pathway, in the comparison of natural rewards over time.

One type of reward comparison, anticipatory contrast, occurs when rats reduce intake of an otherwise palatable saccharin solution, for example, when it comes to predict access to a more preferred sucrose solution over repeated daily pairings. The reduction in intake of the saccharin cue is measured relative to control conditions in which access to the saccharin cue is followed by access to more saccharin (7, 9, 28). This anticipatory contrast effect (ACE) has been interpreted within the context of classic conditioning where the conditioned stimulus (CS) is the saccharin cue and the unconditioned stimulus (US) is the preferred sucrose solution (16). The phenomenon is thought to occur because the value of the saccharin cue is reduced as it comes to predict the availability of the highly rewarding sucrose US that is anticipated in the near future (Refs. 7, 9, 18; but see Ref. 8).

Although this phenomenon is fundamental to understanding how animals compare and choose rewards over time, relatively little is known about its underlying neurocircuitry. It has been shown, however, that bilateral lesions of the gustatory thalamus (VPMpc) disrupt ACE without affecting innate taste preferences or basic associative learning processes (38–41, 45). Specifically, Reilly and Pritchard (39) used long-term intake tests and Scalera et al. (45) short-term intake tests to show that rats with lesions of the gustatory thalamus (THX) display minimal deficits in response to the four basic taste stimuli. Furthermore, thalamic lesions did not affect the development of a conditioned taste preference, a conditioned odor aversion, or a LiCl-induced conditioned taste aversion (19, 40, 45). The same lesion, however, fully prevented the development of an ACE after daily saccharin-sucrose pairings when the standard 0-s interstimulus interval (ISI) was used (38, 40) and reversed the ACE (i.e., induced a reinforcement effect) when rats with electrolytic lesions of the taste thalamus had to wait 5 min for access to the preferred sucrose reward (i.e., with a 5-min ISI).

The overall disruptive effect of the thalamic lesion on the development of an ACE, then, is fairly well established. Even so, the cause of the lesion-induced deficit and the role of the gustatory thalamus in the comparison of rewards over time remain unclear because anticipatory contrast is not a simple, but rather a multistage, phenomenon. The establishment of an
ACE requires that the rat 1) appropriately detect and respond to the succharin and sucrose solutions, 2) associate the succharin cue with the sucrose US, 3) remember the “value” of the sucrose US on CS presentation, 4) compare the value of the succharin cue with the memory of the sucrose US that is anticipated in the near future, and 5) reduce intake of the succharin cue as a result of this reward comparison process.

As mentioned, published data have shown that the lesion-induced deficit is not likely due to a failure to respond to the taste properties of the gustatory stimuli (39, 45). Nor is an intact gustatory thalamus required to make general CS-US associations, as taste-taste, odor-illness, and taste-illness associations are preserved after the lesion (19, 40, 45). As such, the reinforcement effect obtained in the Reilly and Pritchard (40) ACE study is a key finding because it suggests that the lesion-induced deficit also is not due to a failure to make the specific succharin-sucrose association or a failure of the presentation of the CS to elicit the memory of the sucrose US. That is, with a 5-min ISI, the thalamus-lesioned rats clearly increased licking for the succharin cue in anticipation of the availability of the impending, preferred sucrose reward (i.e., the rats behaved as though they had a clear US representation after presentation of the saccharin CS).

Although these final conclusions are essential to our understanding of the role of the gustatory thalamus in the anticipation and comparison of rewards over time, they must be tempered because in the published experiment described, the lesions were induced with electrical current (40), making it impossible to determine whether the behavior change was attributable to damaged cell bodies within the VPMpc and/or to damaged fibers of passage. In a more recent report, the thalamic lesion was induced with ibotenic acid, but only the 0-s ISI was used and the magnitude of the reinforcement effect (the critical feature for the interpretation of the data) was only marginal (38). The present set of studies, then, used the neurotoxin ibotenic acid to test the role of taste cells in the VPMpc in the expression of an ACE or a reinforcement effect with both a 0-s and a 5-min ISI. In experiment 1, ACE testing began with a 5-min ISI in phase I and then was switched to the 0-s ISI condition in phase II. In experiment 2, ACE testing in a naive set of THLX rats began with a 0-s ISI in phase I and was then switched to the 5-min ISI condition in phase II.

METHODS

Subjects

All experimental procedures used were reviewed and approved by the Institutional Animal Care and Use Committee at Pennsylvania State University College of Medicine. The subjects were 35 and 29 naive male Sprague-Dawley rats from Charles River, and body weights initially ranged from 305 to 508 g. They were housed individually in standard wire mesh cages in a colony room, with temperature, humidity, and ventilation automatically controlled. The rats were maintained on a 12:12-h light-dark cycle with all experimental manipulations conducted 4 h into the light phase of the cycle. Food and water were available ad libitum, except where otherwise noted. In experiment 1, 19 rats received bilateral electrophysiologically guided ibotenic acid lesions of the gustatory thalamus (THLX group), and 16 rats served as control subjects (Sham group); 8 of these Sham rats received vehicle infusions of PBS into the taste thalamus and 8 served as nonsurgical controls (NSC). In experiment 2, 17 rats were in the THLX group and 12 rats were in the Sham group (6 PBS and 6 NSC).

Apparatus

The rats were trained and tested in four identical modular operant chambers (MED Associates, St. Albans, VT) measuring 30.5 × 24.0 × 29.0 cm (length × width × height). All chambers had a clear Plexiglas top, front, and back wall. Side walls were made of aluminum. The grid floors consisted of 19 4.8-mm stainless steel rods spaced 1.6 cm apart (center to center). Each chamber was equipped with two retractable sipper tubes that could enter the chamber through 1.3-cm-diameter holes spaced 16.4 cm apart (center to center). In the advanced position, the tip of the sipper tube was aligned in the center of the hole, flush with the right-end wall. A lickometer circuit (0.3 μA) was used to monitor licking. A shaded bulb, which reflected light off the ceiling, was located on the right of the cage, and a white noise speaker was on the left-end wall, opposite to the sipper tubes. Each chamber was housed in a light- and sound-attenuated cubicle that was fitted with a ventilation fan and a white noise source that provided a background noise level of 75 dB. Control of events in the chamber and collection of the data was carried out online with a 33-MHz computer. Programs were written in the Medstate notation language (MED Associates).

Surgery

Twenty minutes before anesthesia, the rats were injected intraperitoneally (ip) with atropine sulfate (0.25 mg/rat) and gentamicin (6 mg/rat). They were then anesthetized with pentobarbital sodium (50 mg/kg ip) and supplemented as necessary throughout surgery. Body temperature was maintained at 37 ± 1°C. The rat’s head was then mounted in a stereotaxic instrument with nontraumatic ear bars, with the skull level between bregma and lambda. The skin over the skull was cleaned with Betadine and opened with a midline incision. With a 4-mm-diameter trephine, a hole was drilled in the skull on either side of the midline, 3.0 mm posterior to bregma. The dura matter was left intact and kept moist throughout surgery with physiological saline.

Gustatory neurons in the VPMpc were located by recording multiunit activity through a glass-insulated tungsten microelectrode (impedance Z = 1.0–1.5 MΩ at 1 kHz) while stimulating the anterior part of the tongue with 0.3 M NaCl. The tongue was rinsed with distilled water (dH2O) both before and after each NaCl stimulation. Neural activity was amplified and continuously monitored with an oscilloscope and an audio monitor. The coordinates for electrode penetrations ranged from −3.5 to −4.1 mm posterior to bregma, ±1.1 to ±1.4 mm lateral to the midsagittal suture, and −5.5 to −6.8 mm below the skull surface. Testing began when the electrode penetrated to −2 mm dorsal to the level of the target and the spontaneous neural activity dropped to a low level that is characteristic as the electrode tip passes from the hippocampus into the dorsal thalamus.

Once the gustatory area had been located on both sides, which required an average of about two penetrations, the search microelectrode was replaced with a double-barreled micropipette-electrode (M/E; OD 50–60 mm; Z = 0.5–1 MΩ at 1 kHz), one lumen of which was glued directly onto the needle of a 1.0-μl Hamilton microsyringe. The microsyringe and its attached micropipette were filled with mineral oil. The other lumen was filled with an etched tungsten wire constructed in a manner identical to the search electrode. The ibotenic acid was drawn in through the tip of the M/E immediately before the injections were made. It was then lowered directly into the hole in the dura that was left by the penetration producing the best response to NaCl. The taste area was relocated electrophysiologically, and 0.2 μl (20 μg/μl) of ibotenic acid was infused over 10 min. After the injection, the M/E remained in place for an additional 10 min, before the procedure was repeated on the opposite side. The PBS rats were treated identically except that 0.2 μl of PBS (pH = 7.40), rather than ibotenic acid, was infused into the VPMpc. After removal of the M/E,
the holes in the skull were filled with Gelfoam and the wound was closed with wound clips. The animals recovered within 2–3 days, and body weight returned to presurgical levels within a week.

Procedure

Food deprivation and habituation. For both experiments, the rats were food deprived to 82% of their free-feeding body weight, maintained by once-a-day feeding with water freely available. Once all rats reached the target weight, they were habituated to the operant conditioning chambers for 5 min/day for 3 days. Both the house light and the white noise were on, but the tubes were empty and out of the reach of the animals. Testing. All animals were placed into the dark operant chamber with the white noise on. Immediately thereafter, the house light was turned on and the first bottle was advanced containing a 0.15% saccharin solution (the CS). After 3-min access, the first bottle was retracted. An ISI of 0 s or 5 min was implemented, followed by the advancement of a second bottle. The second bottle (the US) contained either the same 0.15% saccharin solution or a 1.0 M sucrose solution. After 3-min access to the second bottle, the house light turned off, and the rats were removed from their chambers and returned to their home cages. In experiment 1, there was 1 taste-taste pairing a day for 14 days with a 5-min ISI (phase I) and, after an 18-day interval, 10 additional daily taste-taste pairings with a 0-s ISI (phase II). The 18-day interval was used in an effort to reduce possible carryover effects from the 5-min ISI to the 0-s ISI condition. In experiment 2, there was one taste-taste pairing a day for 16 days with a 0-s ISI (phase I) and, immediately thereafter, 8 additional daily taste-taste pairings with a 5-min ISI (phase II). Dependent measures included the latency (s) to first lick and the number of licks made for the first and second bottles. The number of licks did not differ between the PBS and the NSC rats, so the data from these two groups were collapsed. These subjects are referred to hereafter as the Sham group.

Histology

At the end of all behavioral tests, the rats were given an overdose of pentobarbital sodium (100 mg/kg ip) and, once deeply anesthetized, were perfused transcardially for 5 min with physiological saline, immediately followed by 10% buffered formalin for 25 min. The brains were removed and stored in a solution of 30% sucrose for at least a week. They were then frozen and cut coronally in 50-μm sections. One series of alternate sections was stained for cell bodies with cresyl Lecht violet and the other for fibers with the Weil procedure. The adequacy of the lesions was judged by comparing the acellular areas in the brains that had been injected with ibotenic acid with comparable areas in the brains of the PBS-injected controls. The boundaries of the VPMpc were defined from neuroanatomic and electrophysiological data from this and other laboratories (27, 34, 35, 36).

RESULTS

Histology

In experiment 1, the data from four THLX rats were eliminated because of inadequate lesion placement, and the data from four other THLX rats were eliminated because they failed to lick in the apparatus. Thus, in experiment 1, 11 rats served as the THLX group and 16 rats served as the Sham group (8 PBS and 8 NSC). In experiment 2, the data from eight rats were eliminated from the analyses, seven because of misplaced lesions and one because of failure to lick in the apparatus. Thus 9 THLX rats and 12 Sham rats contributed data to experiment 2.

Lesions were assessed at four levels that correspond roughly to Figs. 31–34 in Paxinos and Watson (37). Level I is considered pretaste and occurs at the final point at which the medial lemniscus splits. Level II demarcates the point at which taste cells first spill into the thalamus. The fasciculus retroflexus (FR) is just evident. Level III is thought to fall right in the middle of the thalamic taste area. At this level the FR and the parafascicular nucleus (PF) are frankly evident. Level IV is best demarcated by the PF, which runs in long parallel lines dorsal to ventral and is thought to be the location of the most posterior taste cells in this nucleus. An example of the brain of a PBS-treated control at level III of the gustatory thalamus is shown in Fig. 1A. As demonstrated here, the PBS-injected brains sustained no evidence of damage, aside from an occasional electrode track.

All 20 rats in the THLX group that contributed data in experiments 1 and 2 had complete bilateral damage to levels II, III, and IV of the VPMpc. Most lesions extended beyond the boundaries of the VPMpc to include parts of the reuniens, centromedial (CM), ventromedial, paracentral, centrolateral, VPM, posterior (Po), PF, subparafascicular, and mediiodorsal thalamic nuclei. Damage to these structures was at most partial, with the exception of the CM, which was damaged completely and bilaterally in all but a few lesioned rats. The VPMpc, then, is the only structure that sustained complete bilateral damage in all lesioned subjects. The data from one THLX rat in experiments 1 and 2 are shown in Fig. 1, B and C, respectively. The subject shown in Fig. 1B had bilateral damage to the VPMpc that was both symmetrical and complete. Damage extended into the VPM and, to a lesser extent, into the Po. The PF also sustained partial damage, but only on the left. Otherwise, neighboring nuclei were largely spared. Damage to the VPMpc also was bilateral and complete for the subject shown from experiment 2 in Fig. 1C. The Po and PF were spared on the left but partially damaged, along with the VPM, on the right. The CM was fully damaged on the right and partially damaged on the left.

Behavior (Experiment 1)

The intake data (total licks/3 min) and the latency (s) to make the first lick were averaged into 2-day blocks for bottle 1 and for bottle 2 and were analyzed with $2 \times 2 \times 7$ repeated-measures ANOVAs varying lesion (Sham vs. THLX), US (saccharin vs. sucrose), and blocks (1–5 or 1–7). Post hoc tests were conducted, where appropriate, using Newman-Keuls tests with $\alpha$ set at 0.05.

CS intake (bottle 1). The Sham rats suppressed intake of the saccharin CS when paired with the preferred sucrose reward, whether 5 min or 0 s elapsed between CS and US presentation. The suppressive effect of the sucrose US, however, was reversed in rats with bilateral ibotenic acid lesions of the gustatory thalamus when testing began in phase I with a 5-min ISI. When animals were switched after an 18-day interval to the 0-s ISI in phase II, the ACE persisted in the Sham rats but was eliminated in the THLX rats. These conclusions were supported by the following statistical analyses.

PHASE I: 5-MIN ISI. When tested in the 5-min ISI condition, the Sham animals demonstrated an ACE (see Fig. 2, left). The Sham rats that were given a sucrose US (Sac-Suc group) consumed less first-bottle saccharin than the Sham rats in the Sac-Sac condition. The THLX rats, on the other hand (see Fig. 2, right), demonstrated a reinforcement effect such that the rats...
in the Sac-Suc condition actually licked more of the first-bottle 0.15% saccharin solution than the Sac-Sac THLX controls. These effects were confirmed by post hoc Newman-Keuls tests of a significant lesion × US × block interaction \( F(6,138) = 3.28, P < 0.005 \). Thus Sham rats in the Sac-Suc condition made fewer licks for first-bottle saccharin than their Sac-Sac controls, and this effect attained statistical significance on blocks 2, 4, and 5 (all \( P < 0.05 \)). Rats in the THLX group, in comparison, made significantly more licks for first-bottle saccharin when it predicted access to the preferred sucrose reward across blocks 2–7 (all \( P < 0.05 \)). Finally, it should be noted that the THLX rats in the Sac-Sac condition made significantly fewer licks of first-bottle saccharin than the Sham rats in the same condition, and this effect was significant on blocks 2–7 (\( P < 0.05 \)).

**Phase II: 0-s ISI.** The contrast effect that was obtained with a 5-min ISI in the Sham rats in phase I persisted when the ISI was switched to a 0-s ISI in phase II of the experiment (see Fig. 3, left). The reinforcement effect obtained in the THLX rats, on the other hand, was eliminated (see Fig. 3, right). Post hoc tests of a significant lesion × US interaction \( F(1,23) = 5.51, P < 0.03 \) confirmed that the contrast effect remained significant in the Sham rats (i.e., Sham rats in the Sac-Suc condition made fewer licks for the saccharin cue overall than did Sham rats in the Sac-Sac condition). The reinforcement effect in the THLX rats, however, was abolished (\( P > 0.05 \)). Together, these data show that cells intrinsic to the VPMpc, rather than fibers of passage, are required for the comparison of disparate natural rewards over time. Bilateral ibotenic acid lesions of the gustatory thalamus reversed the ACE when a 5-min ISI was used and eliminated the ACE when a standard 0-s ISI was used. The occurrence of the reinforcement effect in phase I with these THLX rats is important because it stands as evidence that the lesion-induced deficit in ACE is not due to a simple inability to associate the CS with the US.

**Latency to lick (bottle 1).** **Phase I: 5-min ISI.** Analysis of the latency (s) to lick bottle 1 saccharin showed that neither the Sham nor the THLX rats demonstrated a significant contrast effect or reinforcement effect in latency (see Table 1). This conclusion was supported by a nonsignificant lesion × US × block interaction (\( F < 1 \)).

**Phase II: 0-s ISI.** As in phase I, rats failed to demonstrate either a contrast or a reinforcement effect in the latency to initiate licking the saccharin cue, as evidenced by a nonsignificant lesion × US interaction \( F(1,23) = 2.18, P < 0.15 \) and lesion × US × block interaction \( F(4,92) = 1.0, P < 0.4 \) (see Table 1).

**US intake (bottle 2 licks).** **Phase I: 5-min ISI.** The main effect of US was significant \( F(1,23) = 160.5, P < 0.0001 \), indicating that both Sham and THLX rats made more licks for second-bottle 1.0 M sucrose than 0.15% saccharin overall (see Fig. 4). The main effect of lesion also was significant \( F(1,23) = 6.08, P < 0.03 \), showing that the THLX rats made fewer licks than the Sham rats overall. Neither the lesion × US \( F(1,23) = 2.96, P = 0.09 \) nor the lesion × US × block \( F(6,138) = 1.48, P = 0.19 \) interaction attained statistical significance. Even so, the significant main effect of lesion on intake appears to be influenced by differences in the ingestion of second-bottle saccharin. As a consequence, the number of licks made for second-bottle saccharin was reanalyzed across the Sham and the THLX rats, and the results of this analysis showed a highly significant lesion × block interaction \( F(6,72) = 4.70, P < 0.0004 \). Post hoc tests revealed that the THLX rats made fewer licks for second-bottle saccharin than the Sham rats on blocks 2–7 (all \( P < 0.05 \)). A similar analysis of the number of licks made for second-bottle 1.0 M sucrose,
in comparison, found no differences in intake between the Sham and THLX rats (all $F < 1$).

**PHASE II: 0-s ISI.** Again, these patterns of behavior persisted when the rats were switched to the 0-s ISI (see Fig. 5). The main effect of the lesion was significant [$F(1,23) = 9.60, P < 0.006$], with the THLX rats consuming less than the Sham rats overall. The main effect of US also was statistically significant [$F(1,23) = 278.1, P < 0.0001$], such that all rats made more licks for second-bottle sucrose than for second-bottle saccharin. Neither the lesion $\times$ US ($F < 1$) nor the lesion $\times$ US $\times$ block [$F(4, 92) = 2.43, P < 0.053$] interaction was significant. Once again, given that the significant main effect of the lesion appeared to be influenced by differences in saccharin intake, an additional $2 \times 5$ ANOVA was conducted on second-bottle saccharin intake, varying lesion and blocks. The results of this analysis revealed a significant interaction [$F(4,48) = 4.63, P < 0.003$], and post hoc tests showed that the THLX rats in the Sac-Sac condition made fewer licks for second-bottle saccharin than the Sham rats in the Sac-Sac control group on blocks 2, 4, and 5 (all $P < 0.05$). A similar analysis of second-bottle sucrose intake also found a significant $2 \times 5$ interaction [$F(4,44) = 6.09, P < 0.0005$], and post hoc tests indicated that THLX rats made fewer licks for second-bottle sucrose on blocks 4 and 5 (both $P < 0.05$) than the similarly treated Sham rats.
rats. This decline in licks made for the 1.0 M sucrose solution during the terminal blocks was carried by one sick animal. These data were not eliminated from the analysis, however, because they did not affect the interpretation of the results.

**Latency to lick (bottle 2). PHASE I: 5-MIN ISI.** Analysis of the bottle 2 latency data revealed a significant main effect of US \[F(1, 23) = 5.02, P < 0.05\], whereby both control and THLX rats initiated licking more quickly for second-bottle sucrose than for second-bottle saccharin (see Table 1). Neither the main effect of lesion \[F(1, 23) = 1.37, P = 0.25\] nor any interaction thereof was statistically significant (all \(F < 1\)).

**PHASE II: 0-S ISI.** As in phase I, a significant main effect of US \[F(1,23) = 6.39, P < 0.02\] showed that both Sham and THLX rats were faster to make the first lick of second-bottle sucrose than second-bottle saccharin (see Table 1). Other factors and interactions, however, were not significant, including the main effect of lesion \[F(1,23) = 3.15, P = 0.09\], the lesion \(\times\) US interaction \[F(1,23) = 1.82, P = 0.19\], and the lesion \(\times\) US \(\times\) US interaction.

### Table 1. Latency to lick for first-bottle 0.15% saccharin or second-bottle 0.15% saccharin or 1.0 M sucrose for Sham and THLX rats in saccharin-saccharin or saccharin-sucrose condition

<table>
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<tr>
<th>Experiment 1a: 5-min ISI</th>
<th>BL 1</th>
<th>BL 2</th>
<th>BL 3</th>
<th>BL 4</th>
<th>BL 5</th>
<th>BL 6</th>
<th>BL 7</th>
<th>BL 8</th>
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<tbody>
<tr>
<td>Sham</td>
<td>31.07</td>
<td>6.44</td>
<td>5.98</td>
<td>5.94</td>
<td>5.29</td>
<td>3.86</td>
<td>6.17</td>
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<td>Sac-Sac</td>
<td>9.92</td>
<td>1.95</td>
<td>1.51</td>
<td>1.17</td>
<td>1.32</td>
<td>0.74</td>
<td>2.05</td>
<td>0.58</td>
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<tr>
<td>Sac-Suc</td>
<td>46.31</td>
<td>8.71</td>
<td>8.47</td>
<td>9.38</td>
<td>3.61</td>
<td>7.14</td>
<td>9.14</td>
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</tr>
<tr>
<td>THLX</td>
<td>14.96</td>
<td>1.71</td>
<td>2.12</td>
<td>3.46</td>
<td>0.53</td>
<td>1.63</td>
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<table>
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<th>Experiment 1b: 0-s ISI</th>
<th>BL 1</th>
<th>BL 2</th>
<th>BL 3</th>
<th>BL 4</th>
<th>BL 5</th>
<th>BL 6</th>
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<tr>
<td>Sham</td>
<td>40.98</td>
<td>34.12</td>
<td>13.88</td>
<td>11.45</td>
<td>8.16</td>
<td>4.27</td>
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<td>3.30</td>
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<td>0.99</td>
<td>0.59</td>
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<tr>
<td>THLX</td>
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<td>3.67</td>
<td>1.59</td>
<td>1.46</td>
<td>0.77</td>
<td>0.62</td>
<td>0.23</td>
<td>1.19</td>
</tr>
</tbody>
</table>

Data (in s) are mean \(\pm\) SE values for experiment 1a and experiment 1b, using a 5-min and a 0-s interstimulus interval (ISI), respectively, and for experiment 2a and experiment 2b, using a 0-s and then a 5-min ISI. Sham, control nonlesioned; THLX, gustatory thalamus lesioned; BL1–BL8, blocks 1–8; Sac-Suc, saccharin followed by sucrose; Sac-Sac, saccharin followed by saccharin.
block interaction ($F < 1$). The latency data parallel the intake data by showing that the THLX rats, like the Sham rats, can appropriately detect and respond to the absolute rewarding properties of the saccharin and sucrose US. Thus, although the THLX rats drank less second-bottle 0.15% saccharin than the Sham rats, both groups exhibited a clear magnitude of reinforcement effect by making more licks for 1.0 M sucrose than 0.15% saccharin and by initiating licking more quickly for the stronger solution.

**Behavior (Experiment 2)**

**CS intake (bottle 1).** As with the results of experiment 1, lesions of the thalamus eliminated, but did not reverse, the ACE when testing began with a 0-s ISI in phase I. With the switch to the 5-min ISI in phase II, however, a reinforcement effect in CS intake became immediately apparent in these same experimental subjects (i.e., the reinforcement effect became evident after a single CS-US pairing). Statistical support for these conclusions is provided below.

**PHASE I: 0-s ISI.** An ACE was demonstrated by the Sham animals when testing began with the 0-s ISI (see Fig. 6, left), and this ACE was eliminated by lesions of the gustatory thalamus. These conclusions were confirmed by post hoc tests of significant lesion × US interaction [$F(1,17) = 14.55, P < 0.002$] and lesion × US × block interaction [$F(7,119) = 4.59, P < 0.0002$]. Post hoc tests of the three-way interaction showed that Sham rats in the Sac-Suc condition made fewer licks for first-bottle saccharin than their Sac-Sac controls on blocks 3–8 (all $P < 0.05$). Rats in the THLX group, on the other hand, showed no significant differences in licks generated for first-bottle saccharin as a function of US condition (all $P > 0.05$). Finally, it should be noted that the THLX rats in the
Sac-Sac condition, once again, made significantly fewer licks for first-bottle saccharin than the Sham rats in the same condition, and this effect was statistically significant on blocks 3–8 (all $P < 0.05$).

**Phase II: 5-Min ISI.** As alluded to above, the contrast effect obtained in the Sham rats in phase I (0-s ISI) persisted when the ISI was switched to 5 min in phase II of the experiment. The ACE in similarly treated THLX rats, on the other hand, tended to be reversed (see Fig. 7).

Post hoc tests of a significant lesion × US interaction [$F(1,17) = 10.74, P < 0.005$] confirmed that the contrast effect remained significant in the Sham rats (i.e., Sham rats in the Sac-Suc condition made fewer licks for the saccharin cue overall than did Sham rats in the Sac-Sac condition). Post hoc tests on this same interaction, however, confirmed that the reinforcement effect did not attain statistical significance for the THLX rats ($P > 0.05$). Neither the main effect of US [$F(1,17) = 1.24, P < 0.28$] nor the lesion × US × block interaction [$F(3,51) = 1.7, P < 0.17$] was statistically significant. Finally, as has been the case previously, additional post hoc tests of the significant lesion × US interaction showed that THLX rats in the Sac-Sac condition made fewer licks for first-bottle saccharin than their Sham lesioned counterparts ($P < 0.05$).

To more closely investigate intake of first-bottle saccharin in the Sham and THLX rats, these same data were unblocked and graphed across each of the eight individual trials (see Fig. 8, right).

The data were analyzed with a $2 \times 2 \times 8$ ANOVA varying lesion, US, and trials (1–8). The results of this analysis revealed a significant lesion × US interaction [$F(1,17) = 10.74, P < 0.005$].
10.74, \( P < 0.005 \), and post hoc tests confirmed that, although the Sham rats exhibited a significant contrast effect, the THLX rats demonstrated a significant reinforcement effect overall (all \( P < 0.05 \)). The lesion \( \times \) US \( \times \) trials interaction did not attain statistical significance (\( P > 0.05 \)). Even so, in an effort to track the rapidity with which the reinforcement effect emerged, a separate 2 \( \times \) 2 ANOVA was conducted for the THLX rats, varying US and trials (1 and 2 only). Post hoc Neuman–Keuls tests of a highly significant US \( \times \) trials interaction [\( F(1,7) = 14.77, P < 0.007 \)] confirmed that the THLX animals in the Sac-Suc condition increased licks for the first-bottle saccharin solution from trial 1 to trial 2 (\( P < 0.05 \)). Intake of the same solution for the THLX rats in the Sac-Sac condition, on the other hand, did not change from trial 1 to trial 2 (all \( P > 0.05 \)). Indeed, on trial 2, the THLX animals made more licks for first-bottle saccharin when it predicted access to sucrose than when it predicted access to more saccharin (\( P < 0.05 \)). Thus, once having experienced the 5-min ISI for the first time on trial 1, the THLX rats demonstrated a reinforcement effect as of trial 2.

**Latency to lick (bottle 1).** **Phase I: 0-S ISI.** Analysis of the latency (s) to lick first-bottle saccharin showed that neither the Sham nor the THLX rats demonstrated a contrast effect or a reinforcement effect (see Table 1). This conclusion was supported by a nonsignificant lesion \( \times \) US \( \times \) block interaction (\( F < 1 \)). A significant main effect of lesion [\( F(1,17) = 5.22, P < 0.04 \)], however, indicated that THLX rats were slower to initiate licking than control rats overall.

**Phase II: 5-MIN ISI.** As in phase I, there was no contrast effect in latency for either group. To the contrary, post hoc tests of a significant lesion \( \times \) US \( \times \) block interaction [\( F(3,51) = 4.20, P < 0.01 \)] indicated that, on block 2, THLX animals were, in fact, faster to make the first lick for first-bottle saccharin when it predicted access to sucrose than when it predicted access to more saccharin (see Table 1). Neither the main effect of lesion \( [F(1,17) = 1.12, P = 0.3] \) nor the lesion \( \times \) US interaction \( [F(1,17) = 1.88, P = 0.19] \) was statistically significant. This reinforcement effect in the latency to lick first-bottle saccharin when it predicts subsequent access to sucrose provides further evidence that rats with lesions of the gustatory thalamus can associate the saccharin CS with the sucrose US and can anticipate the availability of the US on CS presentation.

**US intake (bottle 2).** **Phase I: 0-S ISI.** The main effect of US was significant [\( F(1,17) = 134.1, P < 0.0001 \)], indicating that all rats made more licks for second-bottle 1.0 M sucrose than for 0.15% saccharin overall (see Fig. 9).

The main effect of lesion was not significant (\( F < 1 \)), confirming that there was no difference in overall consumption between the THLX and the Sham rats. Furthermore, neither the lesion \( \times \) US (\( F < 1 \)) nor the lesion \( \times \) US \( \times \) block (\( F < 1 \)) interaction attained statistical significance. As in experiment 1, the number of licks made for second-bottle saccharin was analyzed alone for the Sham and the THLX animals. In this case, neither the main effect of lesion [\( F(1,8) = 1.46, P < 0.26 \)] nor the lesion \( \times \) block interaction (\( F < 1 \)) was statistically significant. A similar analysis of the number of licks made for second-bottle 1.0 M sucrose also found no differences in intake between the Sham and the THLX rats (all \( F < 1 \)). Thus the THLX animals detected and responded appropriately to both saccharin and sucrose.

**Phase II: 5-MIN ISI.** Again, these patterns of behavior persisted when the rats were switched to the 5-min ISI (see Fig. 10). As in phase I, the main effect of lesion was not statistically significant (\( F < 1 \)), showing that there was no difference in consumption between the THLX and the Sham rats overall. In addition, neither the lesion \( \times \) US nor the lesion \( \times \) US \( \times \) block interaction reached statistical significance (all \( F < 1 \)). Once again, the number of licks made for second-bottle saccharin and second-bottle sucrose was analyzed separately across lesion condition. The results of these analyses found that neither the main effect of lesion nor the lesion \( \times \) block interaction was significant (all \( F < 1 \)). Thus, at least in this instance, the THLX rats made as many licks for second-bottle saccharin and second-bottle sucrose as the Sham rats.

**Latency to lick (bottle 2).** **Phase I: 0-S ISI.** Analysis of the bottle 2 latency data revealed a significant main effect of US...
[\( F(1,17) = 9.14, P < 0.008 \)], whereby all rats were found to initiate licking more quickly for second-bottle sucrose than for second-bottle saccharin (see Table 1). Consistent with the findings from experiment 1, these data show that the THLX rats, like the Sham rats, could appropriately detect and respond to the absolute rewarding properties of the saccharin and the sucrose US. The main effect of the lesion, the lesion × US interaction, and the lesion × US × block interaction all failed to attain statistical significance (all \( F < 1 \)).

PHASE II: 5-MIN ISI. As in phase I, a significant main effect of US \( F(1,17) = 12.73, P < 0.003 \) showed that both the Sham and the THLX rats were faster to make the first lick of second-bottle sucrose than second-bottle saccharin (see Table 1). Once again, the main effect of lesion \( (F < 1) \), the lesion × US interaction \( (F < 1) \), and the lesion × US × block interaction \( [F(3, 51) = 1.58, P = 0.21] \) were not statistically significant.

DISCUSSION

In two experiments, Sham rats reduced intake of a saccharin cue when it predicted access to a preferred 1.0 M sucrose solution. This ACE was evident in the Sham rats whether testing began or ended with a 0-s or a 5-min ISI. As such, these data are consistent with published data showing that intact rats will suppress intake of a saccharin cue whether it predicts immediate (0 or 15 s) or delayed (e.g., 5, 10, or 30 min) access to a preferred sucrose reward (2, 7, 10). It should be noted, however, that although the Sham rats in our experiment appropriately reduced intake of a saccharin cue when having to wait
blocks 3–8. That is, although for Sham rats the ACE was significant on 5 min for access to the preferred sucrose reward, the magnitude and the persistence of the ACE was somewhat reduced for these subjects in the 5-min, relative to the 0-s, ISI condition. That is, although for Sham rats the ACE was significant on blocks 3–8 when testing began with the 0-s ISI in experiment 2, the ACE was significant only on blocks 2, 4, and 5 when testing began with the 5-min ISI in experiment 1. Similarly, when animals were switched from the 0-s to the 5-min ISI in experiment 2, the ACE failed to attain statistical significance on the fourth 2-day block in these subjects. A similar, slight diminution in the magnitude of the ACE has been reported for intact rats (3, 7, 29) when access to a saccharin CS was followed by access to a sucrose US across increasing ISI conditions. Thus, even in intact rats where the ACE is robust, the magnitude of the effect can be slightly reduced by a reinforcement effect when hungry rats have to wait for access to a preferred sucrose reward.

Bilateral ibotenic acid lesions of the gustatory thalamus fully prevented the development of the ACE when access to the saccharin CS was immediately followed by access to the preferred sucrose reward (i.e., when tested with the 0-s ISI). Moreover, the ACE not only was eliminated, but actually was reversed, when hungry THLX rats had to wait 5 min for access to a preferred sucrose solution. This pattern was obtained when testing began with the 5-min ISI in experiment 1 and, although somewhat smaller in magnitude, when animals were switched to the 5-min ISI in experiment 2. Thus, in two experiments, bilateral ibotenic acid lesions of the gustatory thalamus eliminated the ACE when testing began or ended with the 0-s ISI and reversed the ACE when testing began or ended with the 5-min ISI. Damage to cell bodies in the taste thalamus, then, can lead to either an elimination or a reversal of the ACE, and the reversal of the effect (the reinforcement effect) is most reliable and most robust when hungry THLX rats are required to wait 5 min for access to the preferred sucrose reward.

Before considering why rats with bilateral lesions of the gustatory thalamus might exhibit a reinforcement effect when tested with a 5-min ISI, it is reasonable to address the default condition whereby this lesion fully prevents the establishment of an ACE when access to the saccharin cue is immediately followed by access to the preferred sucrose reward. As described here, the establishment of an ACE requires that the rat 1) appropriately detect and respond to the saccharin and sucrose solutions, 2) associate the saccharin cue with the sucrose US, 3) remember the value of the sucrose US on CS presentation, 4) compare the value of the saccharin cue with the memory of the sucrose US, and 5) reduce intake of the saccharin cue as a result of this reward comparison process. First, although saccharin intake has not been assessed across a range of concentrations in THLX rats, the disruption in contrast is not likely due to either a detection or a perception deficit. A detection deficit would seem an unlikely possibility because, as discussed above, rats with similar lesions have been found to respond appropriately to representatives of the four basic tastes in both short- and longer-term intake tests (20, 39, 45). Although there is some support for the alternative hypothesis that the THLX rats might suffer from a perceptual deficit (e.g., they may make fewer licks for saccharin than the Sham rats because they perceive the solution as more aversive than intact rats), it should be noted that the failure to reduce intake was not due to a floor effect because there remained ample room for suppression by the THLX rats in the Sac-Suc condition. In addition, Reilly et al. (38) reported a similar lesion-induced deficit in ACE in THLX rats that did not evidence a reduction in baseline licking for saccharin. Finally, ACEs readily develop even when the saccharin CS is adulterated with an aversive quinine solution (10). Thus it would appear unlikely that the failure to reduce CS intake by the lesioned rats relates to simple differences in the detection or perception of either the saccharin CS or the sucrose US.

Second, data argue against the conclusion that the THLX rats failed to suppress intake of the saccharin cue because they failed to associate the saccharin CS with the sucrose US or because, once the association was made, the saccharin CS failed to elicit the memory or the “representation” of the sucrose US. As discussed above, published data show that rats with bilateral lesions of the gustatory thalamus readily form taste-taste, taste-illness, and odor-illness associations (20, 39, 45). Furthermore, the THLX rats in the present report exhibited a clear reinforcement effect in both bottle licks and latency when having to wait 5 min for access to the preferred sucrose reward. This stands as evidence that these animals can associate the saccharin cue with the sucrose consequence and that presentation of the saccharin cue must elicit anticipation of (i.e., memory for) the preferred sucrose reward. There is, then, no support for an associative deficit or for the suggestion that the saccharin CS fails to elicit the memory of the preferred sucrose reward that is anticipated in the near future.

A third consideration is that rats with bilateral lesions of the gustatory thalamus fail to exhibit an ACE because, once having associated the CS with the US, they fail to compare the relative value of the two disparate rewards. In support of this, rats with lesions of the gustatory thalamus not only fail to demonstrate an ACE but also a successive negative contrast effect that occurs when intact rats are unexpectedly shifted from a greater to a lesser reward (40, 42, 43). In this case, intake of the lesser 0.15% saccharin reward is reduced in the lesioned rats when downshifted from a 1.0 M sucrose solution, but only to the level of the unshifted saccharin controls (42). Oddly, although fully impaired in these two contrast paradigms, rats with similar lesions of the gustatory thalamus exhibit perfect simultaneous contrast effects when given the opportunity to compare the same saccharin and the sucrose solutions closely in time in the same daily session (41). Indeed, the clear lack of dependence upon the gustatory thalamus in this basic reward comparison paradigm is underscored by the fact that decerebrate rats (rats with an intact brain stem but no neural connection between the brain stem and the forebrain) also exhibit normal simultaneous contrast effects (22). The gustatory thalamus, then, does not appear to be the seat of reward comparison per se.

If the gustatory thalamus is not the “seat” of reward comparison, then why do rats with lesions of this structure fail to exhibit an ACE? An answer to this question might be provided, in part, by considering that which is common between an ACE and a successive negative contrast effect (both disrupted by the lesion) and how, in turn, these phenomena differ from simultaneous contrast effects (which are not disrupted by the lesion). Each of these phenomena involves the comparison of disparate levels of reward in food-deprived rats. Indeed, in each case, the role of the gustatory thalamus has been assessed when comparing 0.15% saccharin to 1.0 M sucrose. In the simultaneous
contrast paradigm, the rewards are compared within a daily session over a relatively short time frame (5, 14). Specifically, the rats are given a total of three alternating 60-s access periods to each of the two levels of reward within a daily session (41). Intake during these alternating trials is then compared with intake on other days when the rats are given six repeated 60-s access periods to only one of the levels of reward (referred to as continuous trials). A simultaneous negative contrast effect occurs when intake of the lesser reward (e.g., 0.15% saccharin) is reduced on trials when alternated with access to the greater reward (e.g., 1.0 M sucrose) compared with continuous trials where only the lesser of the two rewards is presented. This phenomenon does not appear to be due to simple receptor adaptation because simultaneous contrast effects persist when as much as 8 min elapses between successive stimulus presentations (38). In addition, Grigson, Cornelius, and Reich (unpublished data) found that simultaneous contrast effects also persist unchanged when rats are required to rinse their tongues with water between each successive stimulus presentation and when access is alternated between two gustatory stimuli (i.e., sucrose and Polycose) that bind to two distinct receptor populations in the oral cavity (31, 46). Thus, together, the evidence suggests that simultaneous contrast is a brain stem-mediated reward comparison process involving short-term memory, not adaptation of peripheral taste receptors (22).

As discussed briefly above, a successive negative contrast effect is a multistage process that occurs when rats with a history of experience (e.g., 5 min/day for 10 days) with a highly preferred sucrose solution such as 32% sucrose are unexpectedly downshifted to a lesser reward such as 4% sucrose or 0.15% saccharin (for discussion see Refs. 4, 42). The first stage, which typically occurs on the first postshift day, involves detection, rejection, and a search for the missing reward. According to Flaherty (4), the shifted rats appear to “detect” the lesser reward in 10–20 s, after which licking stops and the rats begin to search for the missing reward. At this point, contrast is associated with an increase in the number of bursts initiated (a burst was defined as a run of licks without a 500-ms pause) but fewer licks per burst (24), an increase in arm entries in a radial arm maze, and an immediate approach to a second arm where the preferred reward previously was presented (4). The second stage, which generally occurs on the second postshift day, involves a conflict where a hungry rat (having failed to find the missing reward) must choose whether to accept a reward of lesser value. In accordance, it is during this stage that circulating corticosterone levels are elevated and benzodiazepines attenuate the successive negative contrast effect. There is no evidence that anticipatory contrast involves conflict, and, in accordance, treatment with benzodiazepines is not effective in reducing the magnitude of an ACE (2). Rats recover from successive negative contrast effects over trials, whereas ACEs develop throughout testing. Finally, as further evidence that these two phenomena differ, rats bred for sensitivity to successive negative contrast were not found to differ when tested in the anticipatory contrast paradigm (13). Strain differences, however, might have been revealed with testing using a more sensitive (i.e., less robust) anticipatory contrast paradigm (25).

Despite the clear differences between ACE and successive negative contrast, two similarities can be noted. A first similarity between the two phenomena relates to foraging. When an animal suddenly receives a lesser reward than expected in the successive negative contrast paradigm, the animal begins to search for the missing reward. Flaherty (4) described this when rats, after having been shifted from 32% to 4% sucrose, increased entries into other arms of an eight-arm radial maze and rapidly entered one particular arm where they had, on occasion, received the preferred 32% sucrose reward. A similar behavioral response was described in 1928 by Tinklepaugh (49) when a monkey searched about after having unexpectedly received a piece of lettuce in place of a piece of banana. Although different from the searching behavior described in successive negative contrast, the anticipatory contrast paradigm has been described as an animal model of foraging (28, 48). Specifically, “when prey frequency in the current patch falls below the expected average or frequency of prey, the animals may give up on the current patch and move on to other locations” (for a discussion, see Ref. 11). This is not to suggest that the ACE is due solely to competing responses, because, although the effect is larger when the CS and US are presented at separate locations, ACEs still occur in the experimental chambers when the CS and the US are presented at the same spatial location or “patch” (7, 11). When the CS and the US are
presented in opposite arms of a T maze, however, the reduction in saccharin intake in the left arm is accompanied by (actually preceded by) an increase in time spent in the right arm where the preferred sucrose reward will be presented (11). Thus both phenomena involve a giving up of the available, lesser reward to search for the missing (successive negative contrast) or the anticipated (anticipatory contrast) preferred reward. In light of these data, one might hypothesize that rats with lesions of the gustatory thalamus may be able to compare the available reward with the memory of the preferred reward but simply fail to “give up” the lesser reward in search of the greater reward (i.e., they may be impulsive). This hypothesis (which is readily testable) would have to assume, however, either that simultaneous contrast effects (which are not disrupted by the lesion) do not depend upon foraging/searching or that an intact gustatory thalamus is not necessary for giving up an available lesser reward when alternated over very similar time periods with access to the preferred reward in the same daily session. Although not impossible, this seems an unlikely conclusion.

Second, although the comparison processes are different (one retrograde and one anterograde), both anticipatory contrast and successive negative contrast involve comparison of an available reward with some “engram” or memory. In successive negative contrast, the rat adjusts its response to a lesser reward (4% sucrose or 0.15% saccharin) because it expects (on the basis of prior experience) to have received access to a highly preferred 1.0 M sucrose solution. In anticipatory contrast, the rat adjusts its response to the lesser reward because it is anticipating (on the basis of prior experience) access to the preferred 1.0 M sucrose solution in the near future. In each case, then, the response to an available reward changes as it is compared with the memory of an alternative reward. As such, the lesion may disrupt anticipatory contrast and successive negative contrast because an intact gustatory thalamus is necessary to compare the value of an available reward with the long-term memory of an alternative reward. This interpretation would have to suggest that THLX rats failed to exhibit a successive negative contrast effect, even when downshifted 7.5 min after a final access period to the preferred 1.0 M sucrose reward (43), because contrast, in this case, depended upon comparison with the long-term memory of the preferred reward, not with the characteristics of the stimulus that was received 7.5 min earlier. Were the important comparison that between the available reward and the characteristics of the stimulus received 7.5 min earlier, then this would have been a simultaneous, rather than a successive, contrast paradigm and the contrast behavior of the THLX rats should not have been impaired (41). According to this account, although the taste cells in the VPMpc are not critical for memory (THLX rats demonstrate a reinforcement effect) or for reward comparison (the lesion does not disrupt simultaneous contrast) per se, intact taste cells in the VPMpc are essential for comparing the value of an available gustatory stimulus with the long-term memory of a preferred reward. As such, the lesion-induced deficit is very specific.

Finally, consideration must be given to the overresponding that was obtained in the lesioned rats when the 5-min ISI was used. Why do the lesioned rats overrespond under these circumstances, and what does it mean? As discussed above, overresponding to the CS has been obtained in intact rats in the ACE paradigm, but only under very specific circumstances. In the first example (18), a reinforcement effect occurred when the CS had no intrinsic reward value (e.g., when a hungry rat licked an empty spout or water before gaining access to the preferred sucrose reward). In the second case (10), intact Sprague-Dawley rats overresponded for a 2% sucrose CS when, after a 15-s ISI, an 8% sucrose reward was presented. This finding showed that overresponding can occur when a short ISI is used, but only when value of the CS approaches that of the US. A similar trend was obtained when access to 0.125% saccharin predicted access to 0.15% saccharin (17). A final instance of overresponding for the CS in the anticipatory contrast paradigm occurred when the rat was hungry, the CS had caloric value (i.e., 2% sucrose), and the animal had to wait 5 min for access to a preferred 32% sucrose reward (10).

The first of these three options (use of a neutral CS) does not provide a ready explanation because, although the THLX rats consumed less of the 0.15% saccharin solution than the Sham rats, the THLX rats made many more licks for this solution than were reportedly made for water or on an empty bottle (18). The saccharin solution does not appear to be a neutral stimulus. The second possibility that overresponding occurred in the THLX rats because the value of the saccharin cue approached that of the sucrose reward also is not plausible because the second-bottle lick data show that the THLX rats, like the Sham rats, clearly distinguished between the two stimuli by making many more licks for second-bottle sucrose than for second-bottle saccharin. Finally, although not perfectly concordant, there is overlap with the third instance as outlined by Flaherty et al. (10). The rats in the present report were food-deprived, and they had to wait 5 min for access to the preferred sucrose reward. The saccharin CS, however, did not have caloric value. The thalamus-lesioned rats, then, were more sensitive to induction (i.e., more likely to exhibit a reinforcement effect) when food-deprived and when having to wait 5 min for access to the preferred sucrose reward, even when the CS was devoid of calories. Again, why might this be so? By way of explanation, Flaherty and Grigson (9) obtained evidence for competition between the expression of a reinforcement effect and the expression of an ACE. Indeed, evidence of such competition was provided here, as the ACE in the Sham rats was slowly degraded by an apparent reinforcement effect in the 5-min ISI condition. Thus the lesion-induced disruption in contrast may contribute to overresponding in the 5-min ISI condition because, in the absence of contrast, the reinforcement effect stands unsupported.

In summary, bilateral ibotenic acid lesions of the gustatory thalamus eliminate the development of an anticipatory contrast effect when tested with a 0-s ISI and reverse it when tested with a 5-min ISI. These data verify that cell bodies in the gustatory thalamus, not fibers of passage, are essential for the establishment of an ACE. In addition, the data suggest that the failure to suppress intake of the saccharin cue after saccharin-sucrose pairings in THLX rats is not due to a failure to detect or respond appropriately to either the saccharin CS or the sucrose US. The disruption also is not due to an associative deficit. The reinforcement effect in bottle licks and latency confirms that the THLX rats are able to use the saccharin cue to predict access to the preferred sucrose reward. The gustatory thalamus is not thought to be essential for reward comparison per se, because these same lesioned rats can readily compare rewards when presented in close temporal proximity in the
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simultaneous contrast paradigm. Finally, the engram is assumed to be intact because the THLX rats overconsume the saccharin cue in anticipation of the future availability of sucrose—suggesting that they remember the stimulus characteristics of the coming reward. Although the lick and latency data suggest that the memory for the US is likely intact, the complexity of data suggests that rats with lesions of the gustatory thalamus fail to demonstrate an ACE (and a successive negative contrast effect) because the rats fail to compare the available lesser reward with the memory of the preferred reward. It is, therefore, both a reward comparison and a memory deficit.

An intact gustatory thalamus, then, is essential for comparing the value of different rewards over time, particularly when comparing the value of an available reward with the memory of a preferred reward. Indeed, the involvement of this structure is not limited to the comparison of sapid stimuli (i.e., natural rewards). Rats with these same lesions also fail to avoid intake of a saccharin CS when it predicts the future administration of morphine (23). These data are consistent with other reports in which head direction cells in the anterodorsal thalamus anticipate the future direction of the head (1), cells in the posterior thalamus anticipate the value of a sucrose or an intracranial self-stimulation reward on the basis of the presentation of auditory and visual cues (26), and abnormal methylphenidate-induced activation of the thalamus (possibly the mediodorsal nucleus) as measured by PET is associated with greater cocaine craving (anticipation of cocaine) in cocaine-dependent subjects (50). Together, the data suggest that the thalamus is involved in the anticipation and the comparison of rewards over time and that this reward comparison process, which can be retrograde (expectancy) or anterograde (anticipation), serves to amplify differences in perceived reward value in an effort to affect the appropriate selection of behavior over time.

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