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The effects of amygdala and cortical inactivation on taste neophobia

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ABSTRACT

The current study examined the effects of transient inactivation of the basolateral amygdala (BLA; Experiment 1) and gustatory cortex (GC; Experiment 2) on the expression of taste neophobia and its recovery. We found that inactivation (induced by infusions of baclofen/muscimol) of each structure before exposure to a novel saccharin (0.5%) solution elevated intake on Trial 1 (i.e., taste neophobia was attenuated) and, surprisingly, decreased intake on Trial 2. It seems unlikely that this intake reduction on Trial 2 can be attributed to taste aversion learning caused by drug infusions because in the subsequent experiments with the same set of the implanted animals, the rats did not decrease intake when baclofen/muscimol was infused after taste presentation on Trial 1. The latter result suggests that BLA or GC inactivation that attenuates taste neophobia may also impair memory consolidation of a safe taste experience.

1. Introduction

The decision to ingest a familiar food depends on prior experience with that food. However, such knowledge is not available when a novel food is encountered. In the latter circumstance, the hungry animal is faced with a dilemma: to eat or not to eat. To cope with this situation, animals often show a reluctance to consume a novel food. This phenomenon is termed taste neophobia and is viewed as an innate defensive behavior motivated by the threat posed by the possibility that the unknown food may be poisonous, a behavior traditionally viewed as a fear-evoked response (e.g., Barnett, 1963; Corey, 1978; Domjan, 1977; Hill, 1978; Rozin, 1976; for reviews see Reilly, 2018a). If no aversive systemic effects follow this initial exposure, then intake will increase in subsequent encounters with the food (i.e., taste neophobia habituates). On the other hand, if the food is toxic, and the animal survives the poisoning, the food becomes devalued and avoided in future encounters. This learned defensive behavior is termed conditioned taste aversion (CTA), in which the taste of the food (conditioned stimulus or CS) is associated with the aversive post-ingestive consequence (unconditioned stimulus or US; for reviews see Barker, Best & Domjan, 1977; Braveman & Bronstein, 1985; Bureš, Bermudez-Rattoni & Yamamoto, 1998; Milgram, Krames & Alloway, 1977; Reilly & Schachtman, 2009). Given the relevance to the current topic, it is worth noting that taste neophobia has an important role in CTA acquisition; that is, CTA develops at a much slower rate to a familiar and safe food than to a novel one (a phenomenon termed latent inhibition; Lubow, 1989, 2009). Such a critical involvement in both innate and acquired feeding defensive behaviors encourages investigation of the neural mechanisms underlying taste neophobia (for a review see Reilly, 2018b).

Research from our laboratory demonstrates that the basolateral amygdala (BLA) and the gustatory cortex (GC) are each critically involved in taste neophobia. For instance, Lin, Roman, St. Andre and Reilly (2009) found that, relative to neurologically intact control animals, rats with bilateral lesions of either the BLA or GC over-consumed a novel tastant (also see Lin, Arthurs & Reilly, 2011). Thus, we hypothesized that the BLA and GC have a role in detection/responsivity to the novelty of a taste. This hypothesis receives further support from research that examined the effects of bilateral lesions on CTA acquisition. These studies found that permanent lesions of either structure did not prevent learning. Rather, rats with either BLA or GC lesions required more CS-US pairings to acquire the same magnitude of CTA as control subjects. Indeed, as revealed in these studies, the lesioned subjects acquired CTAs at the same slow rates as that found in non-lesioned rats that were conditioned with a familiar taste (Roman, Lin, & Reilly, 2009; St. Andre & Reilly, 2007). In other words, BLA- (BLAx) or GC-lesioned (GCx) rats appear to treat a novel taste as if it were familiar and safe, and thereby produce a latent inhibition-like effect on CTA acquisition (for reviews see Reilly, 2009; Reilly & Bornovalova, 2005).

Lin, Arthurs and Reilly (2015) conducted a retention experiment to determine the nature of the taste deficits shown in GCx rats. In that experiment, the rats were given a single taste trial, followed by toxicosis

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or no toxicosis, and, three days later, received either GC lesions or no lesions. Subsequently, the rats were tested on taste-only trials. Lin et al. hypothesized that in the CTA acquisition studies a lesion-induced attenuation of taste neophobia might result from either an impairment in taste novelty detection or a failure to properly react to the potential danger conveyed by the taste. If the former is correct, normal CTA expression would be expected because CTA retention does not require taste novelty detection. On the other hand, a retention deficit should emerge if GC is involved in the reaction to the danger conveyed by the taste. As shown in Lin et al. (2015), post-acquisition GC lesions attenuated CTA retention. It should be noted that such a deficit could not be attributed to a lesion-induced failure to recall the taste. This is because a control group in that experiment, which had comparable GC lesions but received a taste-no toxicosis trial prior to surgery, showed normal recovery from taste neophobia, indicating that taste memory was intact in the GCx rats. This pattern of results suggests that the GC, and possibly other components in the same circuit (e.g., BLA), has a role in processing taste-evoked threat responses.

To strengthen the conclusion that taste neophobia is a BLA-GC dependent behavior, the current study employed transient bilateral neural inactivation to refine understanding of the nature of the involvement of BLA and GC in taste neophobia. That is, prior to exposure to a novel taste the BLA (Experiment 1A) or GC (Experiment 2A) were inactivated with intracranial infusions of GABA receptor agonists (baclofen and muscimol; BM), a well-established approach that has been used to examine a range of behaviors (Baker & Ragozzino, 2014; Fuchs, Branham, & See, 2006; McFarland & Kalivas, 2001). A benefit of using transient inactivation is that, unlike permanent lesions, intracranial infusions of BM have been shown to decrease neural activity within minutes (< 5-min; Baker & Ragozzino, 2014; Hikosaka & Wurtz, 1985; Krupa, Ghazanfar & Nicolelis,1999) and last over 40-min (Baker & Ragozzino, 2014; Kawabe, Chitravanshi, Kawabe & Sapru, 2008; McMullan & Pilowsky, 2012). Thus, transient inactivation of neural activity can be used to determine the involvement of a target structure at a specific time in a behavioral process. Additionally, the transient nature of the neural inactivation minimizes the likelihood of the development of any compensatory mechanisms that might be seen following permanent neural manipulations. Furthermore, with transient inactivation we could potentially uncover the influence of the disruption of taste neophobia on taste processing by examining performance during non-inactivated encounters with the taste stimulus. To maintain comparability with prior work from our laboratory (e.g., Lin et al., 2009, 2011; Lin, Amodeo, Arthurs & Reilly, 2012). and the literature (e.g., Gutiérrez, Rodriguez-Ortiz, De La Cruz, Núñez-Jaramillo & Bermudez-Rattoni, 2003; Monk, Rubin, Keene & Katz, 2013; Wilkins & Bernstein, 2006), we used 0.5% saccharin as the stimulus for taste neophobia testing because it evokes a significant neophobic reaction that habituates after 1 or 2 benign exposures. To provide comparability across experiments, in the current experiment our standard taste neophobia procedure was used in which rats were given daily 15-min access to saccharin until asymptotic intake of the taste was reached.

Based on the results from our prior lesion studies, we have proposed that the BLA- or GC-lesioned rats fail to respond to the threat conveyed by a novel taste. If this analysis is correct, then the inactivation of the BLA or GC before the novel taste exposure was expected to increase Trial 1 intake (i.e., when taste neophobia is maximal) but have little influence on subsequent trials as the taste becomes safe/familiar. This prediction was confirmed. Unexpectedly, a reduction in intake was also found on Trial 2 in the rats that received BM infusions before Trial 1, an outcome that does not occur following permanent lesions. One potential interpretation of this Trial 2 intake reduction is that the intracranial BM somehow functioned as a US to support the acquisition of a CTA. Therefore, using the same set of rats to assure the location of intracranial infusions, follow-up experiments (Experiment 1B and 2B) were conducted in the same way as the main experiments, except that quinine (0.0001 M) was used as the taste stimulus and BM was infused after the Trial 1 taste exposure. CTAs can be acquired after a single CS-US pairing and to a wide variety of taste stimuli, including sweet, sour, salty and bitter tastants (for bibliographies see, Riley & Clarke, 1977; Riley & Tuck, 1985). Therefore, if the intake reduction on Trial 2 of the main experiments was due to the acquisition of a CTA we might expect to observe a more pronounced reduction in taste intake on Trial 2 in Experiments 1B and 2B.

2. Experimental procedures

2.1. Animals

The subjects were 72 naïve male Sprague-Dawley rats (275–300 g) obtained from Charles River Laboratory (Wilmington, MA). The rats were individually housed in polycarbonate cages (26.5 × 48 × 20 cm) in a vivarium maintained at 21 °C with a 12-h light cycle (light on at 7:30 am). Food and water were available at all times except during behavioral testing (see below). Animal care and experimental procedures were approved by Animal Care Committee of University of Illinois at Chicago and in accordance with the guidelines set by the American Psychological Association (2012) and National Institutes of Health (2011).

2.2. Surgery

Thirty-six rats were used in each experiment: 26 were given cannulation surgery and 10 served as non-surgical control subjects that were anesthetized (ketamine/xylazine; 100/10 mg/kg) but received no surgical procedures. For cannulations, each rat was anesthetized, shaved and fixed in a stereotaxic instrument (David Kopf Instruments, Tujunga, CA) with blunt ear bars and a bite bar. Thereafter, a midline incision was made to expose the skull sutures and a trephine hole (~3 mm diameter) was drilled above the target structure in each hemisphere. A 22-gauge stainless steel cannula (Plastics One, Roanoke, VA) was then lowered to a position 2 mm above the center of the target structure (coordinates shown in Table 1). The cannulas were fixed in place at those locations with 4 screws secured in the skull and dental cement. During surgery, body temperature was monitored with a rectal thermometer and maintained at ~37 °C with a heating pad (Harvard Apparatus, Holliston, MA). When the dental cement hardened, a stainless steel dummy cannula was inserted into each guide cannula to protect the brain and maintain patency. After recovery from anesthesia, the rat was returned to the vivarium.

2.3. Apparatus

All behavioral testing occurred in the home cages. Water and taste stimuli were presented in 100-ml graduated cylinders with silicone stoppers and open tip stainless drinking tubes that could be attached to the front panel of the cage. Intake was measured with a resolution of 0.5 ml.

Table 1
Stereotaxic coordinates (relative to bregma in mm) used for cannulation placements in the BLA and GC. For the GC placements, the cannulas were lowered at an angle of 10° in the ML plane.

Site	AP	ML	DV
BLA	−2.5	± 5.0	−5.5
GC	+1.2	± 3.0	−5.0

AP: Antero-posterior; ML; Medio-lateral; DV; Dorso-ventral; BLA; Basolateral amygdala; GC; Gustatory insular cortex.