Behavioural Brain Research 331 (2017) 205–213

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Reward loss and the basolateral amygdala: A function in reward comparisons

Katsuyoshi Kawasaki[a], Iván Annicchiarico[b], Amanda C. Glueck[b], Ignacio Morón[c], Mauricio R. Papini[b,*]

[a] Department of Psychology, Hoshi University, 2-4-41 Ebara, Shinagawa, Tokyo 142-8501, Japan
[b] Department of Psychology, Texas Christian University, Fort Worth, TX 76129, USA
[c] Department of Psychobiology, and Research Center for Mind, Brain, and Behavior (CIMCYC), University of Granada, Faculty of Psychology, Campus Cartuja, 18071 Granada, Spain

ARTICLE INFO

Keywords:
Basolateral amygdala
Reward loss
Reward devaluation
Successive negative contrast
Autoshaping
Extinction
Open field activity

ABSTRACT

The neural circuitry underlying behavior in reward loss situations is poorly understood. We considered two such situations: reward devaluation (from large to small rewards) and reward omission (from large rewards to no rewards). There is evidence that the central nucleus of the amygdala (CeA) plays a role in the negative emotion accompanying reward loss. However, little is known about the function of the basolateral nucleus (BLA) in reward loss. Two hypotheses of BLA function in reward loss, negative emotion and reward comparisons, were tested in an experiment involving pretraining excitotoxic BLA lesions followed by training in four tasks: consummatory successive negative contrast (cSNC), autoshaping (AS) acquisition and extinction, anticipatory negative contrast (ANC), and open field testing (OF). Cell counts in the BLA (but not in the CeA) were significantly lower in animals with lesions vs. shams. BLA lesions eliminated cSNC and ANC, and accelerated extinction of lever pressing in AS. BLA lesions had no effect on OF testing: higher activity in the periphery than in the central area. This pattern of results provides support for the hypothesis that BLA neurons are important for reward comparison. The three affected tasks (cSNC, ANC, and AS extinction) involve reward comparisons. However, ANC does not seem to involve negative emotions and it was affected, whereas OF activity is known to involve negative emotion, but it was not affected. It is hypothesized that a circuit involving the thalamus, insular cortex, and BLA is critically involved in the mechanism comparing current and expected rewards.

1. Introduction

The role of the amygdala in reward processes was first suggested in the early 1960s by a series of intracranial stimulation experiments. Wurtz and Olds [54] reported that stimulation electrodes placed in the basolateral amygdala (BLA) region yielded mainly escape responses (i.e., rats learned to press a lever that ended weak electrical currents delivered to the region), whereas electrodes located in the central amygdala (CeA) region supported lever approach (i.e., rats learned to press a lever paired with a weak electrical current delivered to the region). Wurtz and Olds [54] (1963, p. 948) concluded that "the amygdaloid complex contains a 'projection area' for environmental rewards and punishments," with the BLA region involved in negative reinforcement and the CeA region in positive reinforcement. Whereas some subsequent results are consistent with this view (e.g., [24,40], the emerging picture of BLA's function includes a role in behavior maintained by rewards. For example, infusion of the $GABA_A$ receptor antagonist muscimol into the BLA region suppressed lever pressing for food, without affecting the consumption of freely available food [51]. Thus, BLA inactivation seemed to affect appetitive (anticipatory) behavior, but not consummatory behavior. Moreover, Hatfield et al. [21] reported that whereas lesions of the BLA region did not affect simple appetitive conditioning (see also [40] or even the development of an aversion to the reward (after food-toxin pairings), the lesion eliminated the reward-devaluation effect. After an aversion to the reward was established, testing with the reward signal in sham animals yielded less responding after reward-toxin pairings than after unpaired reward and toxin presentations (the reward-devaluation effect); however, animals with BLA lesions failed to display such response suppression.

Whereas this research points to a role of the BLA region in reward processes, there is less information on the amygdala's function in

* Corresponding author.
E-mail addresses: kkawasak@hoshi.ac.jp (K. Kawasaki), ivan.annicchiarico@gmail.com (I. Annicchiarico), glueckphd@gmail.com (A.C. Glueck), imoron@ugr.es (I. Morón), m.papini@tcu.edu (M.R. Papini).

http://dx.doi.org/10.1016/j.bbr.2017.05.036
Received 10 April 2017; Received in revised form 8 May 2017; Accepted 10 May 2017
Available online 13 May 2017
0166-4328/

Table 1
Tasks administered in this experiment.

Task	Description
cSNC	Consummatory behavior. In 10 preshift sessions, animals consumed either 32% or 4% sucrose. In 5 postshift sessions, all animals consumed 4% sucrose. There was one 5-min session per day. Thus, some animals were exposed to a 32-to-4% reward downshift whereas other were unshifted controls always exposed to 4% sucrose.
AS	Anticipatory behavior. In 10 acquisition sessions under continuous reinforcement, pairings between the presentation of a lever (CS) and food (US) induced lever pressing (sign tracking) and magazine entries (goal tracking). Food was withheld in 10 extinction sessions. There were 10 CS presentations per session, one session per day.
ANC	Consummatory behavior. In each of 7 sessions, animals received access to sucrose in two 3-min trials separated by 30 s. In one group, animals had access to 4% sucrose followed by 32% sucrose; in the other group, animals had access to 4% sucrose in both trials.
OF	Locomotor behavior. A single 20-min session was administered. Animals were free to move about a well-lit squared area. Distance (cm) traveled was recorded.

Note. All dependent measures were automatically recorded by computers located in adjacent rooms. See details in the text. ANC: anticipatory negative contrast. AS: autoshaping. CS: conditioned stimulus. cSNC: consummatory successive negative contrast. OF: open field. US: unconditioned stimulus.

situations involving reward loss, that is, situations in which a behavior previously yielding a large reward is later paired with either a smaller reward (reward devaluation) or no reward at all (reward omission; [39]. An example of reward devaluation is the consummatory successive negative contrast effect (cSNC), in which animals are first trained with a large reward (e.g., 32% sucrose), and then downshifted to a small reward (4% sucrose), and their performance is compared to that of unshifted controls always exposed to the small reward (4% sucrose). Downshifted animals exhibit a transient reduction in response strength relative to unshifted controls. Reward omission procedures (such as appetitive extinction) involve a downshift from a period of reinforcement to one of nonreinforcement, leading to an initial increase in response strength followed invariably by a reduction in response strength.

Reward loss has been proposed to imply two different, but complementary processes: reward comparison and negative emotion resulting from this comparison, traditionally referred to as frustration, disappointment, or anxiety [2,12,18]. Reward comparison refers to a contrast between the current reward and an anticipated reward retrieved from memory [35]. The comparison between a current reward of low value with an expected reward of higher value creates the conditions for a negative prediction error. The detection of a negative prediction error is necessary, but not sufficient for the ensuing negative emotion. Thus, the reward comparison hypothesis of BLA function does not necessarily require emotionality. A rat may distinguish between two sucrose solutions of different concentration (reward comparison), but not show any evidence of cSNC (negative emotion) if the discrepancy is not significant enough. For example, rats may distinguish 8% and 4% sucrose concentrations, but an 8-to-4% sucrose downshift may not induce a cSNC effect. In principle, therefore, these two processes are dissociable.

Experiments involving BLA manipulations and reward loss do not yield conclusive evidence for a role of the BLA in reward comparison, negative emotion, or both. With respect to *reward comparison*, Becker et al. [5] reported that electrolytic lesions of the lateral amygdala attenuated the cSNC effect without eliminating it. They argued that animals with such lesions seemed to respond to the 32-to-4% sucrose downshift by adjusting to the absolute reward value of 4% sucrose, rather than by comparing the current 4% sucrose value to the remembered value of 32% sucrose from preshift sessions. According to this interpretation, therefore, lateral amygdala lesions had reduced or eliminated the reward comparison mechanism, leaving animals sensitive only to current reward value. Consistent with a reward comparison function, c-Fos expression (a marker of cellular activation) was heightened in the BLA during the first, but not during the second, downshift session [42]. Afferent-efferent connections of the amygdala [44] link it to structures known to affect reward loss. For example, on the afferent side, lesions of the parabrachial nucleus [19], which sends taste information to the CeA region, and of the gustatory thalamus [46], which receives taste information from the parabrachial nucleus and projects to the BLA region, both disrupt cSNC. On the efferent side, microdialysis studies show reduced dopamine release in the nucleus accumbens during reward devaluation in the cSNC situation [15]. Lesions of the insular cortex eliminate the cSNC effect [27], an interesting effect given the feedback loop connecting the parabrachial nucleus, gustatory thalamus, insular cortex, and BLA [44]. This circuit suggests that information about the current reward (via parabrachial-thalamic input) and the expected reward (via thalamic-insular input), both required for reward comparisons, may converge into the BLA.

The BLA may also be involved in the *negative emotions* induced by reward loss. Because the BLA is clearly implicated in fear conditioning (e.g., [3,14], and given the parallels between fear and frustration [18,34], it is tempting to argue for a BLA function in emotional learning and expression in reward loss situations. According to this view, the negative prediction errors incurred by reward devaluation and omission tasks induce a variety of behavioral and physiological effects that are modulated by drug treatments and brain regions that, all together, suggest the experience is accompanied by negative emotion [2,34,37,39]. The effect of lateral amygdala lesions on cSNC mentioned above [5] is also consistent with this view. Furthermore, pCREB expression (a marker of synaptic plasticity) was elevated in both CeA and BLA regions in the second downshift session relative to the first downshift session [16].

The present experiment was designed to test these views of BLA's function in reward loss situations by administering four tasks involving reward comparison, negative emotion, or both (see Table 1 for a description). We have used a similar strategy to determine the role of several brain sites on reward loss [23,31,53]. Two tasks concerned reward devaluation effects: cSNC and anticipatory negative contrast (ANC). The cSNC situation involves both reward comparison and negative emotion [12,39]. By contrast, in the ANC task animals received daily sessions in which a 4% sucrose solution was followed by a 32% sucrose solution. The ANC effect does not appear to be accompanied by negative emotion, as suggested by pharmacological [13], lesion [23], and psychogenetic studies [17]. Animals also received autoshaping (AS) acquisition training followed by extinction as a reward omission task. Autoshaping experiments have yielded evidence consistent with negative emotional activation following surprising reward omissions [7,11,32,36,52]. Finally, animals were also tested in the open field (OF). The OF task served a dual purpose, namely, as an activity control and a test for negative emotion that does not involve any obvious reward comparison. Rats exposed to a well-lit arena exhibit reduced activity in the central area, relative to the periphery [8], a behavior accompanied by increased c-Fos expression in the BLA region [20]. Kawasaki et al. [23] also reported that reversible lidocaine lesions in the centromedial amygdala enhanced activity in the OF test, a result interpreted in terms of reduced negative emotion.

Based on the results reviewed above, we predicted that BLA lesions would affect one or more of the tasks included in this experiment. A key aspect was to determine which tasks were actually affected, as the pattern of results could provide support for one of the two hypotheses of BLA function outlined above. If the BLA plays a role in reward comparison and negative emotion, then all these tasks should be affected. However, if BLA lesions disrupt a reward comparison mechan-

ism, then cSNC, AS extinction, and ANC, but not the OF task, should be affected. Finally, if BLA lesions affect negative emotions, then cSNC, AS extinction, and OF, but not ANC, should be affected.

2. Method

2.1. Subjects

The subjects were 33 male, experimentally naïve Wistar rats bred from animals purchased at Harlan Labs (Indianapolis, IN). Rats were weaned at 21–25 days of age and were housed in same-sex groups in polycarbonate cages. At around 40 days of age, rats were moved to individual wire-bottom cages, and about 90 days of age they were assigned to the present experiment. Temperature (18–23 °C) and humidity (50%) were maintained relatively constant in the colony. Lights were on a 12:12 h cycle (lights on at 07:00 h) and behavioral testing took place during the light portion of the cycle. Rats always had free access to water in their cages, but after 90 days of age, food was restricted according to the following schedule. Animals were food deprived to 90% of their free-food weight before surgery and to 81–84% of their free-food weight after a brief period of recovery from surgery. This stepwise deprivation procedure was implemented to reduce the number of postsurgical days before the start of behavioral testing. Supplemental food was given every day at least 15 min after behavioral sessions and up to 2 h after testing, depending on the order of squads, which varied across days. The amount of food provided was determined by an empirically derived formula helping to maintain animals within preestablished values of food deprivation. While on deprivation, animals were weighed daily.

2.2. Surgical procedure

Surgeries were distributed over a 4-week period and, therefore, animals started training at different times. Animals were anesthetized (5%) and maintained (1–2%) with inhalation isoflurane. Then, the head was shaved and cleaned with betadine and alcohol 70%, and mineral oil was applied to the eyes to minimize dryness. Animals were then placed in the stereotaxic frame (Vernier Stereotaxic with Manual Fine Drive, Leica Biosystems, Buffalo Grove, IL, USA), and a midline incision was made, the skull was cleaned from connective tissue, and bregma was located. Cannula guides were placed bilaterally at the following coordinates [41]: −3.3 AP, ± 5.1 ML, and −8.1 and 7.6 D/V. N-methyl D-aspartate (NMDA) was then infused into this location at two dorso-ventral levels with an infusion pump (KDScientific, Model KDS 232 CE, Holliston, MA). NMDA was dissolved in 100 mM of phosphate buffered saline (PBS) at pH 7.4, at a concentration of 20 mg/ml; 2 µl of NMDA were infused at −8.1 D/V and 1 µl was infused at −7.6 D/V, at a rate of 0.1 µl/min. After each infusion, 5 min were allowed for diffusion of the NMDA into the adjacent tissue before removing the cannula. Sham animals received the same treatment, but only the vehicle (PBS) was infused.

Immediately after surgery, all animals were kept under a heat lamp and injected with buprenorphine (0.4 mg/kg, sc, 1.4 µl/dose) to alleviate surgery pain. After recovery from anesthesia (30–45 min after surgery), animals were housed individually in polycarbonate cages until signs of full recovery from surgery were evident (e.g., normal motility about the cage). Then, animals were moved to their home cage and allowed 5–8 days for further recovery and while their weight was gradually brought to the target 81–84% deprivation level and maintained at that level for the duration of the experiment.

2.3. Apparatus and training procedures

Behavioral testing was divided into four phases delivered in a fixed order, but matching groups as far as possible as a function of previous training assignment. Table 2 summarizes the final sample size of each group and phase of training. The phases involved cSNC, AS, ANC, and OF testing. The initial three phases involve different procedures for reward devaluation (cSNC, ANC) and reward omission (extinction in AS); OF testing was added to assess possible effects of these lesions on general levels of locomotor activity. Animals were randomly assigned to the surgical conditions, BLA or sham lesions.

Table 2
Assignment of animals to the four phases of behavioral testing.

		Phase 1		Phase 2		Phase 3		Phase 4	
Lesion	*n*	cSNC	*n*	AS	*n*	ANC	*n*	OF	*n*
Sham	14	32-4	8	CR/Ext	14	4-32	4	Sham	13
						4-4	3		
		4-4	6			4-32	4		
						4-4	3		
BLA	15	32-4	8	CR/Ext	15	4-32	4	BLA	15
						4-4	4		
		4-4	7			4-32	4		
						4-4	3		

Note. In Phases 2 and 4 all animals received the same behavioral treatment. In Phase 3, animals with the same ANC treatment were pooled. For example, four animals in ANC Group BLA/4-32 (n = 8) had experienced reward downshift and four had been in the unshifted condition. This procedure tended to match groups for previous assignments. 32 and 4 refer to the concentration of sucrose solutions. ANC, anticipatory negative contrast. AS, autoshaping. BLA, basolateral nucleus of the amygdala. CR/Ext: continuous reinforcement/extinction. cSNC, consummatory successive negative contrast. OF, open field. See text for further details.

Phase 1: cSNC. Within each surgery condition, animals were randomly assigned to the two cSNC conditions such that weights were approximately equal across groups: downshifted (32-to-4% sucrose) and unshifted (4% sucrose) reward devaluations. Assignment was done such that animals assigned to the contrast conditions were trained concurrently as far as possible. cSNC testing took place in eight conditioning boxes (MED Associates, St. Albans, VT) made of aluminum and Plexiglas (29.4 × 28.9 × 24.7 cm, L × H × W). In each conditioning box, the floor was made of steel rods (0.5 cm in diameter, 1.2 cm apart); there was a tray filled with corncob bedding and placed underneath the steel rods (bedding was replaced as needed); diffuse light was provided by a light (GE 1820); and the sipper tube (1 cm diameter) was presented through an elliptical opening (1 × 2 cm, W × H, 3.5 cm from the floor). Fully inserted, the sipper tube was flush against the wall. A computer located in an adjacent room controlled the presentation and retraction of the sipper tube, and recorded contacts with the sipper tube through a circuit involving the steel rods. Each conditioning box was placed in a sound-attenuating chamber. A speaker delivered masking white noise and a fan provided ventilation; together, they provided 80.1 dB, SPL scale C (Digital Sound Lever Meter, Extech, Waltham MA) of background noise.

Training started after animals were fully recovered from surgery and reached the 81–84% target deprivation weight (approximately 6–10 days after surgery). A Contrast (downshifted, unshifted) by Lesion (BLA, Sham) by Session (preshift 1–10, postshift 11–15) design was used in this phase. Groups were labeled BLA/32, Sham/32, BLA/4, and Sham/4 ("32" refers to the 32-to-4% sucrose downshifted condition, whereas "4" refers to the 4% sucrose unshifted condition). About half the animals received downshift training, with access to 32% sucrose on sessions 1–10 followed by access to 4% sucrose on sessions 11–15 and the rest were given access to 4% sucrose throughout training. Each day, animals were transported to a waiting room in squads of four; a given animal was assigned to the same squad and trained in the same box, but squad order was scrambled across days to minimize possible sequential effects. The house light, white noise, and fan were on during the session. At the start and end of each session there was a mean interval of 30 s (range: 15–35 s) with the sipper tube retracted. A session started with the presentation of the sipper tube and lasted 5 min from the first

recorded contact with the sipper tube. After each session, animals were returned to their home cage and the conditioning boxes were wiped with a damp paper towel, feces removed, and bedding material replaced as needed. The target weight was maintained by providing food at least 15 min after the session. Sucrose solutions were prepared weight by weight by mixing 32 (or 4) g of commercial sugar for every 68 (or 96) g of distilled water. The dependent variable was lick frequency, that is, the total number of licks in the 5-min session.

Phase 2: AS. Four standard operant chambers (MED Associates, St. Albans VT) each enclosed in a sound-attenuating chamber were used for AS training. Each box (20.1 × 28 × 20.5 cm, W × L × H) had a grid floor with steel bars (0.4 cm in diameter, 1.6 cm apart from center to center); a tray filled with corncob bedding; two retractable levers located 1 cm to the right and left of the feeder, and 6 cm above the floor; a food cup was located inside a hole in the front wall of the chamber (2 cm above the floor); and a pellet dispenser. Each food pellet (45-mg food pellets; Bio-Serv, Frenchtown NJ) contained protein (18.8%), fat (5.0%), carbohydrate (61.5%), fiber (4.6%), ash (4.4%), and moisture (5.0%), and provided 3.68 kcal/g. Only the lever located at the left of the magazine was used in this experiment. This lever was 4.8 cm wide, when fully inserted protruded 1.9 cm into the chamber, it took 0.2 s to be fully inserted or retracted, and it was adjusted so that a minimum forced applied on it would be detected. The hole with the feeding cup contained a photocell placed (1.1 cm inside this hole) designed to detect head entries. The sound-attenuating chambers provided diffuse illumination (GE 1820), white noise, and ventilation; background masking noise (speaker and fan) registered 80.1 dB, SPL, scale C (Digital Sound Lever Meter, Extech, Waltham MA). A computer located in an adjacent room recorded lever presses and goal entries, and also inserted and retracted the lever, and delivered pellets.

AS training started a day after the last cSNC session. Behavioral training was the same for all animals; thus, there were only two factors in this phase: Lesion (BLA, Sham) and Session (acquisition 1–10, extinction 11–20). Animals were matched for prior experience in the cSNC task (Table 2). Animals were moved in a transport rack in squads of four whenever possible to the room housing the AS conditioning boxes. Between sessions, animals were left in a lighted room across the hall from the testing room. Acquisition involved ten 10-trial sessions. Each trial involved the presentation of the lever for 10 s followed by the response-independent delivery of five 45-mg food pellets at a rate of one every 0.2 s. The intertrial interval was 90 s on average (range: 60–120 s). Acquisition was followed by ten 10-trial extinction sessions with the same training parameters, except that no pellets were delivered at the end of each trial. Each box was cleaned with a damp paper towel and feces were removed after each session. The dependent variables were the number of lever presses per trial and the number of goal entries per trial. In addition, a response bias measure was calculated by subtracting goal entries per trial from lever presses per trial. A positive number indexes the strength of sign-tracking (i.e., responding to the lever CS), whereas a negative number indexes the strength of goal-tracking (i.e., responding to the location of food presentations).

Phase 3: ANC. Training occurred in the same conditioning boxes used for cSNC training in Phase 1, except for the following. A second sipper tube located in the front wall and to the right of the sipper tube used during cSNC training was introduced. The original sipper tube, located in the middle of the front wall, delivered 4% sucrose, whereas the new sipper tube delivered either 32% or 4% sucrose depending on the group. Events and behavioral recordings were controlled by a computer located in an adjacent room.

Training in the ANC situation started a day after the last session of AS extinction. Animals were assigned to match as far as possible for prior experience (Table 2). This phase involved ANC (upshifted, unshifted) by Lesion (BLA, Sham) by Session (1–7) design. Each lesion condition was segregated into two behavioral conditions. Two groups of animals, one with each lesion condition, were assigned to the upshifted, 4-32 condition and the other two groups with each lesion condition were assigned to the unshifted, 4-4 condition. Animals were transported in squads of up to eight rats to the room housing the contrast conditioning boxes. Between sessions, animals were left in a lighted room across the hall from the testing room. All animals received access to two solutions per day, each lasting 3 min from the first recorded lick and separated by a 30-s intersolution interval. The first bottle in each session provided access to 4% sucrose for all animals. For groups labeled 4-32, the second bottle provided access to 32% sucrose, whereas for groups labeled 4-4 the second bottle allowed access to 4% sucrose. A total of 7 sessions were run for all animals. Each box was cleaned with a damp paper towel after each session. Lick frequency for each bottle was the dependent measure.

Phase 4: OF. Open field testing was carried out in three units (MED Associates, St. Albans, VT) measuring 43 × 30 × 43 cm (L × H × W). A single 20-min session was administered, between 9:00 and 15:00 h. Rats were tested in squads of three whenever possible. A light bulb (100 W) was suspended on top of each field, above the central area. The room lights were off.

The day after the last ANC session, animals were transported to the room housing the OFs (this was the same room housing consummatory conditioning boxes; however, only one type of behavioral testing was scheduled at any single time in this room). Between sessions, animals were left in a lighted room across the hall from the testing room. Because there was only a single behavioral treatment, groups differed only in terms of the Lesion (BLA, Sham). At the start of the trial, the rat was placed in the center of the open field and allowed free movement. Each field was cleaned with a damp paper towel after each session. A computer located in an adjacent room recorded the distance traveled (cm) during the session as the dependent variable.

Histology and cell count. Animals were humanely sacrificed with a CO_2 overdose the day after the last training session. Brains were immediately extracted and embedded in 4% paraformaldehyde for at least 3 days and then transferred to 30% sucrose for at least 2 days. Tissue was sectioned with a cryostat in 40-μm slices. Slices were stained with cresyl violet and mounted in glass slides. All slices were photographed with an Olympus CX41 light microscope with Q-Color 3 digital camera; an adaptor and Image-Pro Express were used for image capture and analysis. The A/P position of each section was identified based on the Paxinos and Watson [41] atlas of the rat brain. Using a 4x enlargement, all images were subjected to a cell count procedure using ImageJ software. The same protocol for the cell count was used in all images. Images were open at 2592 × 1944 pixels, at 8-BIT. An area of 4.91 cm^2 on the monitor screen was selected for cell counts, always located in the center of the structure (BLA or CeA). A/P coordinates from Paxinos and Watson [41] were used to classify the location of each image. The cell diameter chosen was 5.2 μm, a diameter consistent with granular cells.

2.4. Statistical analyses

The dependent variables were subjected to analysis of variance with an alpha value set at the 0.05 level. Pairwise comparisons using the LSD test were derived from the main analysis whenever justified by appropriate significant interactions. The IBM SPSS 24 package was used to compute all the statistics. For brevity, significant F and p values are reported in most cases.

3. Results

3.1. Histology

Four animals were lost at various stages of the experiment, leaving the $N = 29$. In 2 sham animals, the histological material was inadequate to compute a cell count and therefore their data were excluded. The resulting sample sizes as well as the trajectory through the four

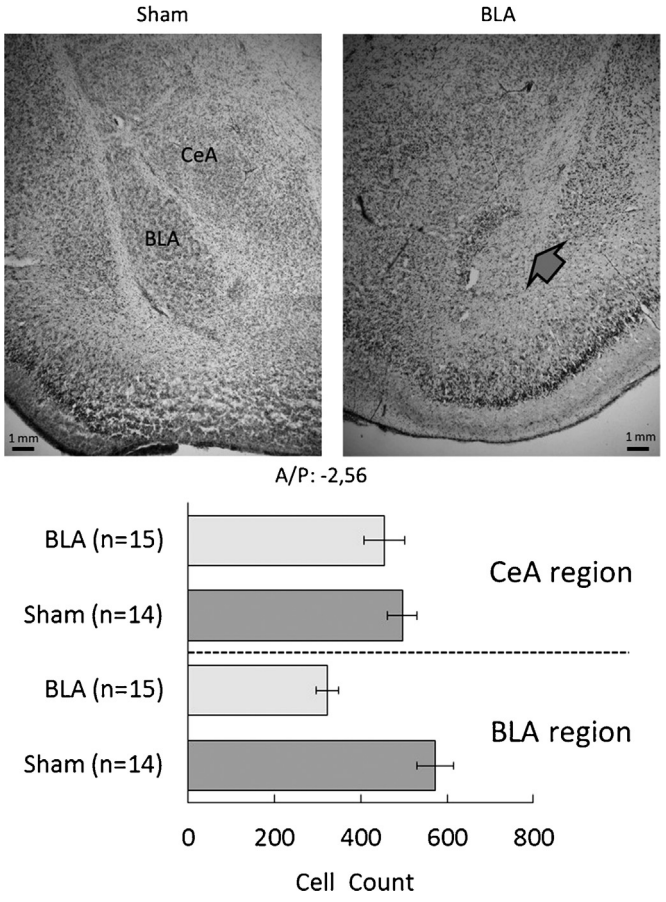

Fig. 1. Top: Photomicrographs of coronal sections stained with Cresyl Violet showing the BLA. The left picture shows an animal with a sham lesion and the right picture a BLA lesion. The arrow points to an area damaged by the NMDA infusion. Cell bodies are visible in the case of the sham slice, but the BLA is substantially depleted of cell somas after the NMDA lesion. **Bottom:** Mean (± SEM) of cell count in the BLA and CeA for groups of rats given neurotoxic lesions or sham lesions in the BLA. All cell counts were calculated in slices from A/P -2.8 to -3.3.

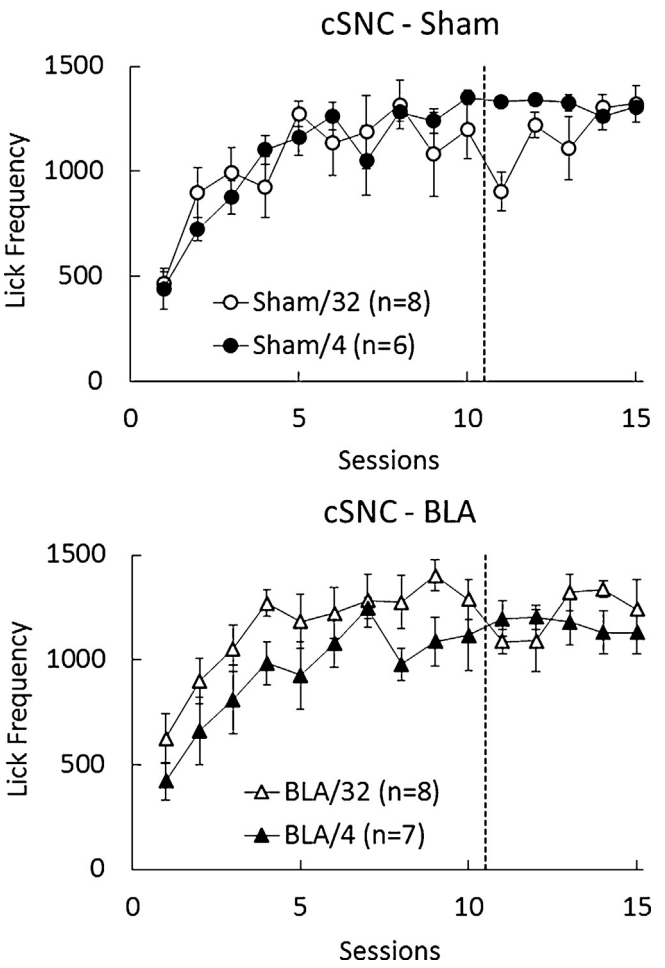

Fig. 2. Mean (± SEM) lick frequency in groups given access to 32% or 4% sucrose during preshift. All animals received access to 4% sucrose during postshift sessions 11–15. Thus, "32" denotes the 32-to-4% sucrose downshift condition and "4" the 4% sucrose unshifted condition. The top panel shows the results for sham-operated animals and the bottom panel for animals with BLA lesions. Data from Phase 1.

phases of this experiment are presented in Table 2. The sample size for each group is also included in each figure. Fig. 1 shows histological slices of two selected brains (top) and cell counts in the BLA and sham groups (bottom). These stained slices were selected because they clearly show the deletion of cell somas in the BLA region after NMDA infusions, relative to the sham control. Some lesions were not as visible as this one, but the cell count procedure provided an objective indication that the number of cells was reduced in the BLA region.

Fig. 1, bottom, shows the results of the cell count. Each animal contributed to the final computation with 1–4 slices from slides corresponding to the A/P coordinates matching cannula insertion in the BLA and the area immediately rostral to it (A/P −2.8 to −3.3). When cell count was assessed in more than one slice, a mean was calculated for the animal, such that each animal contributed one value to the analysis. There was a significantly smaller cell count for the lesioned area than in sham controls, $F(1, 27) = 25.67$, $p < 0.001$. As a control, cell counts were computed for the CeA region in animals with sham and BLA lesions using the same procedure (A/P −2.8 to −3.3). The results are also shown in Fig. 1, bottom. In this case, the difference was not significant, $F < 1$, thus suggesting that the lesion did not spread to the adjacent CeA region. All the behavioral analyses that follow were computed on these animals.

Phase 1: cSNC. Preshift data were analyzed by a Lesion (BLA, Sham) × Contrast (32%, 4%) × Session (1–10) analysis, with Session as a repeated-measure factor. Lick frequency increased across the 10 preshift sessions, $F(9, 225) = 18.53$, $p < 0.001$. The contrast and contrast by lesion effects came close to significance, $Fs < 3.83$, $ps < 0.07$. This was due to a similar lick frequency in sham animals, but a higher average lick frequency in BLA/32 than in BLA/4 animals. None of the effects involving lesion as a factor was significant, $Fs < 1$. By the end of the preshift (see session 10 in Fig. 2), groups were responding at about the same level and nondifferentially.

Fig. 2 also shows the effects of reward downshift separately for sham groups (top) and BLA groups (bottom). The BLA lesion eliminated the cSNC effect. A Lesion × Contrast × Session (11–15) analysis confirmed these conclusions with a significant contrast by session effect, $F(4, 100) = 2.99$, $p < 0.03$. The interaction between lesion and contrast approached significance, $F(1, 25) = 4.10$, $p = 0.054$. Pairwise follow-up comparisons derived from the main analysis indicated that whereas the cSNC effect was significant in sham groups, $F(1, 25) = 4.36$, $p < 0.05$, there was no evidence of such an effect among BLA groups, $F < 1$. Because most of the change occurred in session 11 (see Fig. 2), we computed a Lesion × Contrast analysis on just this session and found that the interaction was significant, $F(1, 25) = 4.51$, $p < 0.05$. The main effect of contrast was also significant, $F(1, 25) = 12.73$, $p < 0.002$. Follow-up LSD pairwise comparisons indicated that whereas the cSNC effect was significant in Sham animals, $F(1, 25) = 15.54$, $p < 0.002$, the difference between downshifted and unshifted groups was not significant among BLA animals, $F(1, 25) = 1.09$, $p > 0.30$. As far as the authors know, these are the first results suggesting that the BLA is involved in reward devaluation in the cSNC situation.

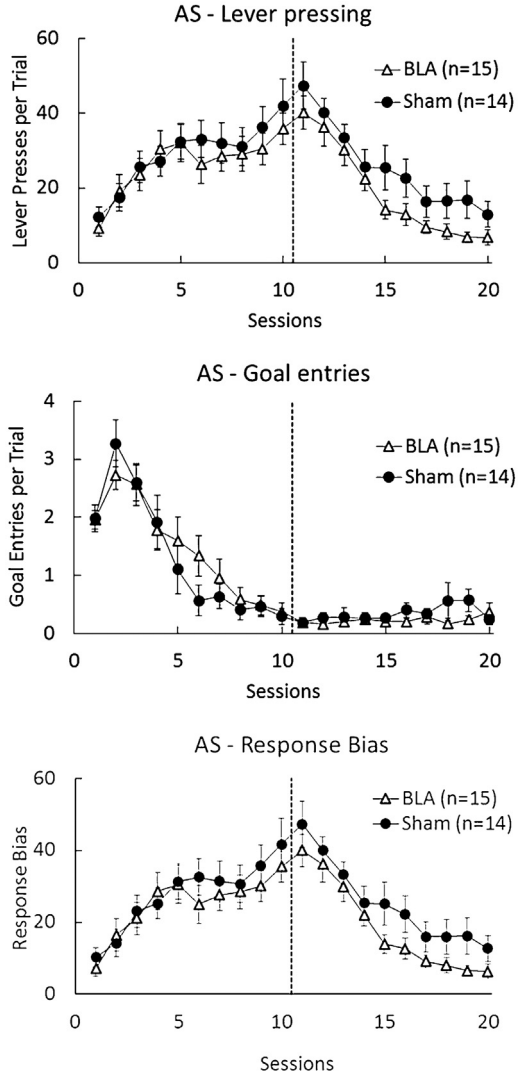

Fig. 3. Mean (± SEM) lever presses per trial (top), goal entries per trial (middle), and response bias (bottom) for sham-operated and BLA-lesioned groups. Response bias corresponds to the difference between lever presses minus goal entries per trial. The dashed vertical line signals the transition from acquisition (reinforced lever presentations) to extinction (nonreinforced lever presentations). During acquisition, every presentation of the lever was followed by the response-independent delivery of 5 food pellets (continuous reinforcement). Data from Phase 2.

Phase 2: AS. Fig. 3 shows the effects of BLA lesions on AS acquisition and extinction, and for three different measures: lever pressing (top), goal entries (middle), and a response bias measure that combines the previous two (bottom).

Consider *lever pressing*. There was an increase in lever pressing during acquisition sessions, $F(9, 243) = 16.59$, $p < 0.001$, but the lesion had no effect either on its own or in terms of a session interaction, $Fs < 1$. There was also a modest increase in lever pressing in the transition from acquisition to extinction, but it was similar in both sham and BLA groups. An analysis of sessions 10–11 showed no evidence of an extinction spike, $Fs < 2.99$, $ps > 0.09$. Fig. 3, top panel, shows that extinction performance was lower in BLA animals than in sham animals, but an analysis including all extinction sessions failed to detect anything either in terms of a main effect or an interaction with sessions, $Fs < 2.73$, $ps > 0.10$. There was a significant decrease in lever pressing across extinction sessions, $F(9, 243) = 37.51$, $p < 0.001$. To further explore this apparent effect of the BLA lesion on extinction of lever pressing, we computed the mean responding for each animal in the first and second halves of extinction. For sessions 11–15, the groups were not different, $F(1, 27) = 1.25$, $p > 0.27$. However, for session 16–20 BLA animals responded significantly below shams, $F(1, 27) = 4.34$, $p < 0.05$.

Fig. 3, middle panel, shows the results of *goal entries*. As expected based on previous results [53], goal entries increased sharply in early acquisition and then decreased to a low level for the rest of training. There was no obvious change either during the transition from acquisition to extinction or during extinction sessions. Whereas the change across acquisition sessions was significant, $F(9, 243) = 36.24$, $p < 0.001$, none of the other factors, whether in acquisition or extinction, were significant.

The bottom panel in Fig. 3 shows the results for *response bias*, that is, lever pressing minus goal entries per session. Notice that all values were positive, a fact implying that these animals were predominantly sign trackers (i.e., responding to the lever CS), rather than goal trackers (i.e., responding to the US site). Analyses of acquisition and extinction indicated that only changes across sessions were significant, $Fs(9, 243) > 18.53$, $ps < 0.001$. All other effects were nonsignificant. The usual increase in responding in early extinction relative to late acquisition (i.e., extinction spike) was not evident in terms of response bias and the BLA lesion had no effect, $Fs < 3.15$, $p > 0.08$. Again, there was a trend toward a lower response bias in extinction in BLA animals. However, a comparison of groups during the first and second halves of extinction revealed no effect on sessions 11–15 and only a borderline, but still nonsignificant effect on sessions 16–20, $F(1, 27) = 4.13$, $p = 0.052$.

AS data has shown very little in terms of BLA involvement. There was a statistically weak tendency for BLA animals to exhibit enhanced extinction during the second half of these sessions. But there were no lesion effects on acquisition, overall extinction, or on the extinction spike, whether in terms of lever pressing, goal entries, or response bias.

Phase 3: ANC. Fig. 4 shows the results of this phase for the first bottle (top) and second bottle (bottom), averaged over the last two sessions of training. Lesion (BLA, Sham) × ANC (4-32, 4-4) analyses on data from the first and second bottles yielded no evidence of significant effects, although the ANC effect on the first bottle came close, $F(1, 36) = 3.48$, $p = 0.074$. Because Fig. 4 (top) suggested that the ANC effect was present in sham animals, but not in BLA animals, separate analyses comparing 4-32 vs. 4-4 groups were calculated for each lesion group. Indeed, sham animals showed significant suppression of licking in the first bottle—that is, an ANC effect, $F(1, 12) = 6.41$, $p < 0.03$, whereas BLA groups did not exhibit differences in the 4-32 vs. 4-4 conditions. None of the three comparisons were significant for the second bottle. Thus, BLA lesions appear to have also eliminated the ANC effect.

Phase 4: OF. Fig. 5 shows the results of the OF test in terms of distance traveled as a function of lesion and field area. There was lower activity in the central area of the field than in the periphery, $F(1, 26) = 75.90$, $p < 0.001$, but no statistical evidence of a lesion or a lesion by area interaction. Thus, BLA lesions appeared to cause their effects by means other than by affecting activity levels or the tendency of rats to move more in the periphery than in the central area of the field.

4. Discussion

The BLA lesion eliminated the two reward devaluation effects included in this study (the cSNC and ANC effects) and affected behavior in reward omission (appetitive extinction in AS). Both cSNC and ANC effects were based on consummatory behavior. Thus, these results are at variance with those reported by Simmons and Neill [51], who found that BLA inactivation with muscimol affected anticipatory, but not consummatory behavior. However, these results are consistent with the reduced cSNC effect reported by Becker et al. [5] and with the disruption of the reward devaluation effect reported by Hatfield et al. [21]. BLA lesions also reduced lever pressing performance toward the end of AS extinction; this effect was not observed in terms of goal entries and it was only marginal in terms of response bias. None of these effects were dependent upon an effect of BLA lesions on the acquisition

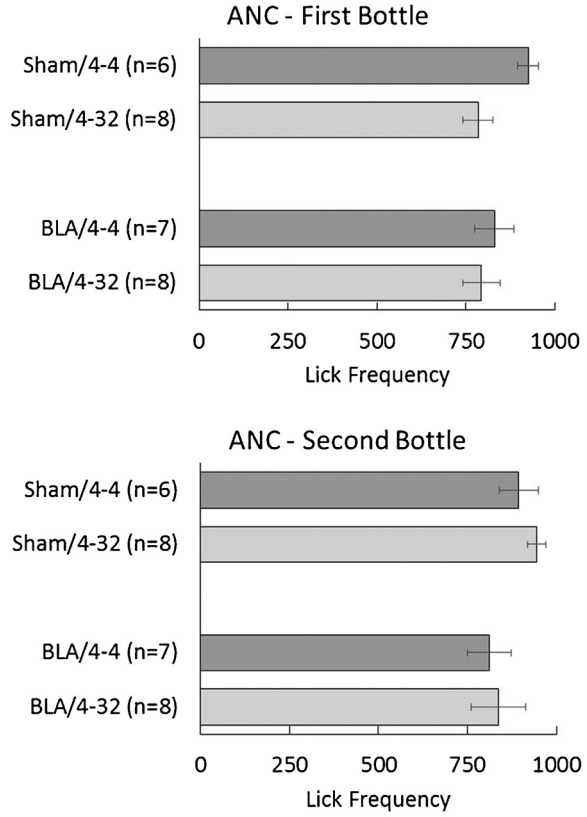

Fig. 4. Mean (± SEM) lick frequency in groups receiving two trials per day. The first trial (top, First bottle) involved access to 4% sucrose for all groups. The second trial (bottom, Second bottle) involved access to 32% or 4% sucrose depending on the groups (4-32, 4-4). Each bar represents the mean over the last two sessions of anticipatory negative contrast (ANC) training, either for sham-operated or BLA-lesioned groups. Data from Phase 3.

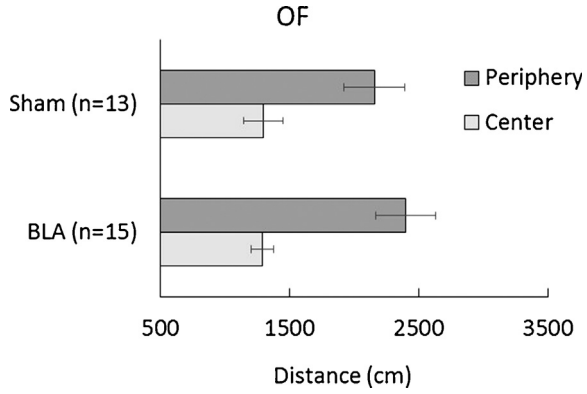

Fig. 5. Mean (± SEM) distance (cm) traveled during 20-min test sessions in the OF segregated according to whether the animal was in the central area or in the peripheral area of the field. Data from Phase 4.

of responding, either in cSNC's preshift sessions or during autoshaping acquisition (see [40]. Moreover, there was no evidence of a BLA lesion effect on the open field test either in terms of general activity or in term of differentially lower activity levels in the central area of the arena. The possibility that the BLA lesion impaired other motor responses (e.g., grooming; see [22] cannot be completely dismissed. The rest of the discussion focuses on the implications of these results for the two accounts of BLA's function in reward loss presented in the introduction: the negative emotion and reward comparison hypotheses.

Previous researchers had reported that lesions in the centromedial region of the amygdala disrupted cSNC [5,23]. Moreover, infusions of diazepam in the CeA region also attenuated cSNC [26]. Amygdala regions were also found to express high levels of both c-Fos and pCREB after the first downshift event [16,42]. Thus, there is good evidence for a role of the CeA in reward loss situations, but the same could not be said for the BLA. Becker et al. [5] also included groups with more lateral lesions that might have encompassed portions of the BLA; however, these ablations were large compared to the current study and also damaged fibers of passage. These animals showed evidence of contrast, but it was reduced relative to sham controls. Becker et al. suggested that amygdala lesions reduced the control of behavior by the negative emotion induced by the reward downshift, leaving the animals to respond in terms of the absolute value of the reward, rather than its relative value. Responding to the relative value of a reward requires a comparison mechanism [35]. In the cSNC and ANC situations studied here, that comparison must be between a current reward (4% sucrose) and the reactivated memory of the expected reward (32% sucrose). The BLA lesion may interfere with such a comparison, thus leaving the animal sensitive mostly or only to the current reward—another way of saying that the animal responds to absolute reward value. This interpretation would work reasonably well with the present results. In the case of cSNC and also ANC, consummatory behavior was adequate to the level supported by 4% sucrose. Thus, the ANC effect was eliminated because animals with BLA lesions responded at a level comparable to unshifted controls with sham lesions. In the case of AS extinction, lower lever pressing in animals with BLA lesions relative to shams would reflect an adjustment to the current reward conditions, that is, the absence of reward in extinction sessions. The lack of effects in goal tracking may be attributed to the generally low level in this behavior during extinction, which has been observed before [53].

Results at least partially consistent with this interpretation were reported in an experiment in which BLA lesions were tested in the instrumental SNC situation (iSNC). Salinas et al. [50] trained rats in a runway to collect either 10 pellets or 1 pellet before they were downshifted to 1 pellet, with 6 trials per session and an intertrial interval of 30 s. While animals with BLA lesions exhibited a normal iSNC effect during the initial downshift session, the effect was gone in BLA animals, but not in sham animals, during the next session. iSNC is analogous to AS in one respect: They both involve anticipatory behavior (i.e., latency to reach the goal in iSNC or lever pressing before food delivery in AS). In both cases, the effect of BLA lesions became evident only after some experience with the new conditions, either after one session in iSNC or after five sessions in AS extinction. Salinas et al. [50] favored an interpretation suggesting that while the amygdala is not a site of storage for stimulus-reward associations, its output modulates the consolidation of such emotionally significant memories in other brain sites. However, the results in the iSNC situation could also reflect incomplete damage of the mechanism necessary to compare postshift (current) and preshift (expected) rewards; such incomplete damage may have produced evidence of contrast during the initial downshift session, but the iSNC effect disappeared in the following sessions.

The hypothesis that damage to the BLA region disrupts the comparison between current and expected reward value is also consistent with the lack of effects of this lesion in preshift performance in the cSNC situation, acquisition in the AS situation, and activity in the OF test. Presumably, none of these situations involved comparisons between current and expected rewards or induced a negative prediction error. However, such apparent consistency must be taken with caution for one simple reason: The present design involved tandem testing animals in four situations, thus opening the possibility that there were reward comparisons across phases. These transfer effects were minimized by redistributing animals so as to balance group compositions by prior experience (see Table 2). Moreover, one would expect that current performance would be affected by the most recent prior training, especially when administered in the same situation. Still, the issue of transfer across situations involving reward loss merits further scrutiny (e.g., [10]; [49].

The amygdala is most clearly associated with emotionally signifi-

cant events, such as the emotional memory for conditioned fear. The BLA region has been specifically suggested to be part of a circuit important for fear extinction (e.g., [3,14]. For example, infusions of the $GABA_A$ agonist muscimol into the BLA before the start of fear extinction trials based on a discrete tone CS accelerate freezing extinction [1]. This result is reminiscent of the reduction in lever pressing observed during AS extinction in the present experiment. However, pretraining excitotoxic lesions of the BLA region also affect acquisition of fear conditioning to a discrete CS, especially after limited training [28,29]. Rats with BLA lesions do eventually acquire the freezing response, but they require extensive training. This seems at odds with the lack of acquisition effects in both the cSNC and AS tasks, in the present experiment (see also [40], although it is consistent with other experiments showing BLA effects on appetitive behavior (e.g., [51]. One possibility is that the cSNC and AS tasks used here are simply not sensitive enough to detect the effects of BLA lesions during acquisition training. This is not necessarily incompatible with a reward comparison mechanism, but the idea would have to be extended to include the unexpected occurrence of a reward early in acquisition before any prior experience in that situation with other rewards. This is often referred to as positive prediction error—current reward is higher than expected reward [25]. A second possibility is that different cell populations in the BLA are engaged by appetitive vs. aversive environmental conditions, such that similar lesions have different effects depending on the task. For example, [30]; see also [6] identified distinct cell populations in the BLA that respond to either aversive cues (audiovisual CS paired with shock) or appetitive cues (audiovisual CS paired with sucrose). The neurons encoding negative valence projected to the CeA, whereas those encoding positive valence projected to the NAc. Although the behavioral procedures used in these BLA experiments did not involve reward loss, similar results, but for the CeA region, were reported in response to signals for shock vs. signals for reward omission [45]. Whether this is also the case for BLA neurons remains to be determined.

Several aspects of the present results suggest caution in the interpretations. First, although significant, the effects reported for sham animals were relatively small, whether for cSNC, ANC, or appetitive extinction in AS. Surely training parameters could be adjusted to increase the size of these effects without losing significance for the reward loss event. For example, reducing food deprivation is known to enhance the cSNC effect [9], but this may also imply a reduction in the emotional strength induced by the reward downshift (e.g., less intense conflict over consumption of the devalued reward). Second, the infusion of PBS in sham animals may have caused itself a small or moderate BLA damage affecting behavior. This can be assessed by including intact controls in future experiments. Our lab has extensive experience with the cSNC situation and variation in the size of the effect is common. An extensive secondary analysis of such variation using latent growth mixture modeling has even detected three different profiles for recovery from reward devaluation [38]. Thus, some of the variation in the size of the cSNC effect across experiments may be caused by a larger-than-usual proportion of animals relatively less sensitive to the effects of reward devaluation (see [43], Experiment 3). Third, although we favored an interpretation of BLA function in reward loss in terms of reward comparison, other studies have led to somewhat different interpretations. For example, Balleine et al. [4] reported that rats with BLA lesions failed to discriminate between two responses (instrumental lever pressing and chain pulling) when only one was differentially reinforced (with food pellets or maltodextrin, counterbalanced) in any given session. Based on this and additional findings, the authors argued that the BLA was necessary to integrate the sensory components of different rewards into the action-outcome association guiding instrumental performance. It is possible that a similar deficit may account for the results presented here if BLA rats cannot discriminate, for example, the sensory components of a current 4% sucrose and a remembered 32% sucrose, their response comparison tasks such as cSNC and ANC would be compromised. However, a failure of reward comparison in BLA animals could also explain Balleine et al. Balleine et al.'s (2003) results. In their Experiment 4, animals were exposed to one reward per session, but different rewards across sessions, responding selectively to the manipuladum paired with the available reward in any given session would have required a comparison between the reward expectancy evoked by each manipulandum with the currently available reward. This is the function we are hypothesizing to be compromised in animals with BLA lesions. Finally, it should be noted also that the hypothesis that the BLA is less concerned with negative emotion related to reward loss requires further empirical attention. We based that idea on only two pieces of evidence: The lack of evidence for an anxiolytic effect in the ANC situation [12], coupled with its disruption in BLA animals reported here, and the lack of a BLA effect on OF performance in the present experiment, coupled with OF sensitivity to centromedial inactivation in a previous experiment [23].

The present results are more consistent with a view of BLA function in reward loss situations emphasizing reward comparisons, rather than negative emotional learning. The key components of the underlying circuitry for reward comparisons in the cSNC situation may be the gustatory thalamus-BLA connection, which may provide information about the current reward, and the gustatory thalamus-insular cortex-BLA, which may retrieve information about the expected reward [33]. The BLA would then be in a position to compare information from these two sources. Lesions of these structures disrupt the cSNC effect [47,27]; present experiment), whereas lesions of two of them, gustatory thalamus and BLA, also disrupt ANC [48]; present experiment). Clearly, lesions of the insular cortex should also disrupt ANC if this hypothesis were correct.

Acknowledgments

The authors thank Brandon Grant for assistance with animal maintenance and histology. Carmen Torres and Joanna Thompson made useful comments on an earlier draft of this article. This research was partially supported by a Sabbatical grant to KK from Hoshi University, Japan, and from a TCU/RCAF grant # 60672 to MRP. IA was supported by a Fulbright/Colciencias (Colombia) scholarship. Send correspondence to M. R. Papini (m.papini@tcu.edu).

References

[1] I. Akirav, H. Raizel, M. Maroun, Enhancement of conditioned fear extinction by infusion of the $GABA_A$ agonist muscimol into the rat prefrontal cortex and amygdala, Eur. J. Neurosci. 23 (2006) 758–764.
[2] A. Amsel, Frustration Theory, Cambridge University Press, Cambridge, UK, 1992.
[3] E. Baldi, C. Bucherelli, Brain sites involved in fear memory reconsolidation and extinction of rodents, Neurosci. Biobehav. Rev. 53 (2015) 160–190.
[4] B.W. Balleine, A.S. Killcross, A. Dickinson, The effect of lesions of the basolateral amygdala on instrumental conditioning, J. Neurosci. 23 (2003) 666–675.
[5] H.C. Becker, M.F. Jarvis, G.C. Wagner, C.F. Flaherty, Medial and lateral amygdalectomy differentially influences consummatory negative contrast, Physiol. Behav. 33 (1984) 707–712.
[6] A. Beyeler, P. Namburi, G.F. Glober, C. Simonnet, G.G. Calhoon, G.F. Conyers, R. Luck, C.P. Wildes, K.M. Tye, Divergent routing of positive and negative information from the amygdala during memory retrieval, Neuron 90 (2016) 348–361.
[7] R.L. Boughner, M.R. Papini, Survival of the partial reinforcement extinction effect after contextual shifts, Learn. Motiv. 37 (2006) 304–323.
[8] J.A. Bouwknecht, F. Spiga, D.R. Staub, M.W. Hale, A. Shekhar, C.A. Lowry, Differential effects of exposure to low-light or high-light open field on anxiety-related behaviors; relationship to c-Fos expression in serotonergic and non-serotonergic neurons in the dorsal raphe nucleus, Brain Res. Bull. 72 (2007) 32–43.
[9] L. Cuenya, I. Annicchiarico, M. Serafini, A.C. Glueck, A.E. Mustaca, M.R. Papini, Effects of shifts in food deprivation on consummatory successive negative contrast, Learn. Motiv. 52 (2015) 11–21.
[10] L. Cuenya, M. Sabarieto, R. Donaire, A. Fernández-Teruel, C. Torres, M.R. Papini, Transfer across reward devaluation tasks in inbred Roman rat strains, Learn. Motiv. 52 (2015) 22–31.
[11] R.T. Dudley, M.R. Papini, Pavlovian performance of rats following unexpected reward omissions, Learn. Motiv. 26 (1995) 63–82.
[12] C.F. Flaherty, Incentive Relativity, Cambridge University Press, Cambridge, UK, 1996.

[13] C.F. Flaherty, G.A. Rowan, Effect of intersolution interval, chlordiazepoxide, and amphetamine on anticipatory contrast, Anim. Learn. Behav. 16 (1988) 47–62.
[14] C. Furini, J. Myskiw, I. Izquierdo, The learning of fear extinction, Neurosci. Biobehav. Rev. 47 (2014) 670–683.
[15] R.F. Genn, S. Ahn, A.G. Phillips, Attenuated dopamine efflux in the rat nucleus accumbens during successive negative contrast, Behav. Neurosci. 118 (2004) 869–873.
[16] A.C. Glueck, T. Dennis, L. Perrotti, C. Torres, M.R. Papini, Brain expression of pCREB in rats exposed to reward devaluation, Neurosci. Lett. 587 (2015) 93–97.
[17] M.J. Gómez, M.D. Escarabajal, L. de la Torre, A. Tobeña, A. Fernández-Teruel, C. Torres, Consummatory successive negative and anticipatory contrast effects in inbred Roman rats, Physiol. Behav. 97 (2009) 374–380.
[18] J.A. Gray, N. McNaughton, The Neuropsychology of Anxiety, 2nd ed., Oxford University Press, Oxford, UK, 2000.
[19] P.S. Grigson, A.C. Spector, R. Norgren, Lesions of the pontine parabrachial nuclei eliminate successive negative contrast effects in rats, Behav. Neurosci. 108 (1994) 714–723.
[20] M.W. Hale, J.A. Bouwknecht, F. Spiga, A. Shekhar, C.A. Lowry, Exposure to high- and low-light conditions in an open-field test of anxiety increases c-Fos expression in specific subdivisions of the rat basolateral amygdaloid complex, Brain Res. Bull. 71 (2006) 174–182.
[21] T. Hatfield, J.S. Han, M. Conley, M. Gallagher, P. Holland, Neurotoxic lesions of basolateral, but not central, amygdala interfere with Pavlovian second-order conditioning and reinforcer devaluation effects, J. Neurosci. 16 (1996) 5256–5265.
[22] W. Hong, D.-W. Kim, D.J. Anderson, Antagonistic control of social versus repetitive self-grooming behaviors by separable amygdala neuronal subsets, Cell 158 (2014) 1348–1361.
[23] D. Kawasaki, A.C. Glueck, A. Annicchiarico, M.R. Papini, Function of the centro-medial amygdala in reward devaluation and open-field activity, Neuroscience 303 (2015) 73–81.
[24] E. Knapska, G. Walasek, E. Nikolaev, F. Neuhäusser-Wespy, H.-P. Lipp, L. Kaczmarek, T. Werka, Differential involvement of the central amygdala in appetitive versus aversive learning, Learn. Memory 13 (2006) 192–200.
[25] S.S.Y. Li, G.P. McNally, The conditions that promote fear learning: prediction error and Pavlovian fear conditioning, Neurobiol. Learn. Mem. 108 (2014) 14–21.
[26] R.-M. Liao, F.-J. Chuang, Differential effects of diazepam infused into the amygdala and hippocampus on negative contrast, Pharmacol. Biochem. Behav. 74 (2003) 953–960.
[27] J.-Y. Lin, C. Roman, S. Reilly, Insular cortex and consummatory successive negative contrast in the rat, Behav. Neurosci. 123 (2009) 810–814.
[28] S. Maren, Neurotoxic basolateral amygdala lesions impair learning and memory but not the performance of conditional fear in rats, J. Neurosci. 19 (1999) 8696–8703.
[29] S. Maren, Is their savings for Pavlovian fear conditioning after neurotoxic basolateral amygdala lesions in rats? Neurobiol. Learn. Mem. 76 (2001) 268–283.
[30] P. Namburi, A. Beyeler, S. Yorozu, G.G. Calhoon, S.A. Halbert, R. Wichmann, S.S. Holden, K.L. Mertens, M. Anahtar, A.C. Felix-Ortiz, I.R. Wickersham, J.M. Gray, K.M. Tye, A circuit mechanism for differentiating positive and negative associations, Nature 520 (2015) 675–678.
[31] L.A. Ortega, A.C. Glueck, M. Uhelski, P.N. Fuchs, M.R. Papini, Role of the ventrolateral orbital cortex and medial prefrontal cortex in incentive downshift situations, Behav. Brain Res. 244 (2013) 120–129.
[32] L.A. Ortega, J.N. Norris, M.F. Lopez-Seal, T. Ramos, M.R. Papini, Correlates of recovery from incentive downshift: a preliminary selective breeding study, Int. J. Comp. Psychol. 27 (2014) 160–186.
[33] L.A. Ortega, J.L. Solano, C. Torres, M.R. Papini, Reward loss and addiction: opportunities for cross-pollination, Pharmacol. Biochem. Behav. 154 (2017) 39–52.
[34] M.R. Papini, R.T. Dudley, Consequences of surprising reward omissions, Rev. General Psychol. 1 (1997) 175–197.
[35] M.R. Papini, S. Pellegrini, Scaling relative incentive value in consummatory behavior, Learn. Motiv. 37 (2006) 357–378.
[36] M.R. Papini, H.W. Ludvigson, D. Huneycutt, R.L. Boughner, Apparent contrast effects in autoshaping with rats, Learn. Motiv. 32 (2001) 434–456.
[37] M.R. Papini, M. Wood, A.M. Daniel, J.N. Norris, Reward loss as psychological pain, Int. J. Psychol. Psycholog. Therapy 6 (2006) 189–213.
[38] S. Papini, I.R. Galatzer-Levy, M.R. Papini, Identifying profiles of recovery from reward devaluation in rats, Behav. Brain Res. 275 (2014) 212–218.
[39] M.R. Papini, P.N. Fuchs, C. Torres, Behavioral neuroscience of psychological pain, Neurosci. Biobehav. Rev. 48 (2015) 53–69.
[40] J.A. Parkinson, T.W. Robbins, B.J. Everitt, Dissociable roles of the central and basolateral amygdala in appetitive emotional learning, Eur. J. Neurosci. 12 (2000) 405–413.
[41] G. Paxinos, C. Watson, The rat brain in stereotaxic coordinates. 6th ed., Academic Press, New York, 2007.
[42] N. Pecoraro, M.F. Dallman, c-Fos after incentive shifts: expectancy, incredulity, and recovery, Behav. Neurosci. 119 (2005) 366–387.
[43] S. Pellegrini, M. Wood, A.M. Daniel, M.R. Papini, Opioid receptors modulate recovery from consummatory successive negative contrast, Behav. Brain Res. 164 (2005) 239–249.
[44] J.L. Price, Comparative aspects of amygdala connectivity, Ann. N.Y. Acad. Sci. 985 (2003) 50–58.
[45] R.J. Purgert, D.S. Wheeler, M.A. McDannald, P.C. Holland, Role of amygdala central nucleus in aversive learning produced by shock or by unexpected omission of food, J. Neurosci. 32 (2012) 2461–2472.
[46] S. Reilly, R. Trifunovic, Gustatory thalamus lesions eliminate successive negative contrast in rats, Behav. Neurosci. 113 (1999) 1242–1248.
[47] S. Reilly, R. Trifunovic, Gustatory thalamus lesions eliminate successive negative contrast in rats: evidence against a memory deficit, Behav. Neurosci. 117 (2003) 606–615.
[48] S. Reilly, M. Bornovalova, R. Trifunovic, Excitotoxic lesions of the gustatory thalamus spare simultaneous contrast effects but eliminate anticipatory negative contrast: evidence against a memory deficit, Behav. Neurosci. 118 (2004) 365–376.
[49] R.R. Ross, Positive and negative partial-reinforcement extinction effects carried through continuous reinforcement, changed motivation, and changed response, J. Exp. Psychol. 68 (1964) 491–502.
[50] J.A. Salinas, M.B. Parent, J.L. McGaugh, Ibotenic acid lesions of the amygdala basolateral complex or central nucleus differentially affect the response to reductions in reward, Brain Res. 742 (1996) 283–293.
[51] D.A. Simmons, D.B. Neill, Functional interaction between the basolateral amygdala and the nucleus accumbens underlies incentive motivation for food reward on a fixed ratio schedule, Neuroscience 159 (2009) 1264–1273.
[52] B. Thomas, M.R. Papini, Adrenalectomy eliminates the extinction spike in autoshaping with rats, Physiol. Behav. 62 (2001) 543–547.
[53] C. Torres, A.C. Glueck, S.E. Conrad, I. Moron, M.R. Papini, Dorsomedial striatum lesions affect adjustment to reward uncertainty, but not to reward devaluation or omission, Neuroscience 332 (2016) 13–25.
[54] R.H. Wurtz, J. Olds, Amygdaloid stimulation and operant reinforcement in the rat, J. Comp. Physiol. Psychol. 56 (1963) 941–949.