Supporting Information

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SI Methods

Confocal Microscopy Sampling of Dendritic Spines. Transgenic mice expressing GFP in layer V cortical pyramidal neurons (1) were used. Mice were killed by rapid decapitation for dendritic spine analysis using methods similar to those previously described by our group (2): Brains were submerged in 4% paraformaldehyde for 48 h, then transferred to 30% (wt/vol) sucrose, followed by slicing into 40-μm-thick sections on a microtome held at −15 °C. Slices were mounted, and proximal apical dendritic segments (within 120 μm of the cell soma) running parallel to the coronal surface of the section and not overlapping with other segments were imaged on a laser scanning confocal microscope (Olympus Fluoview FV1000) using a 100× 1.4 NA objective with a digital zoom of 3 and laser excitation wavelength at 488 nm. The *z*-steps of 0.5 μm were used to generate stacks that included ∼1 μm above and below the targeted dendritic segment. A Kalman filtration reduced background interference. After imaging, the area was photobleached to allow for post hoc confirmation that the image was collected from the prelimbic cortex. Five segments from each of three mice per group were collected; 148–268 μm per mouse were scored by a single blinded rater.

Collapsed *z*-stacks were analyzed using ImageJ by tracing each dendritic protrusion. Lengths were compared by Kolmogorov-Smirnov test. If a protrusion bifurcated, only the length of the longest arm was measured. Densities (on average one spine per micrometer) were slightly higher than those observed by Golgi impregnation of apical prelimbic prefrontal cortical (PL) layer V branches (3, 4, 5; but see also ref. 6), potentially reflecting greater sensitivity of fluorescence techniques—relative to Golgi impregnation—in detecting smaller spines (7).

Instrumental Conditioning Procedures in Mice. ***Instrumental training.*** Adult male mice were trained to nose poke for grain-based food reinforcers (20 mg; Bioserv) using Med-Associates operant conditioning chambers. Mice were food-restricted to 87–93% of their original body weight, then nose-poke training was initiated with a continuous reinforcement schedule such that 30 pellets were available for responding on each of two distinct apertures, resulting in 60 pellets per session. Four or five such continuous reinforcement sessions were conducted depending on the experiment; all animals acquired the response.

Outcome devaluation. After training, the food pellet was devalued in half of the mice by pairing it with an injection of LiCl. Our techniques were adapted from those reported previously in ref. 8: Mice were placed in clean cages with access to ∼3 g of the same food pellets that were used as reinforcers during instrumental conditioning. After 1 h, mice were injected with either 0.15 M LiCl or PBS (4 mL/100 g, i.p.). Groups were determined by matching mice based on response rates during acquisition (Fig. S3*A*). This procedure was conducted daily for 3 d, at which point mice in the LiCl groups consumed significantly less than mice in the PBS groups (Fig. 2*B*). During this period, mice were fed regular chow in the home cage no sooner than 3 h after injection.

The following day, mice were placed in the operant conditioning chambers; responding during a 15-min test conducted in extinction was analyzed by two-factor ANOVA. Subsequently, mice received a final 15-min posttest consumption test to confirm that the instrumental test session did not alter sensitivity to outcome value (Fig. S3*D*). This experiment in its entirety is represented in Fig. S3.

Contingency degradation. After instrumental training, one nose-poke aperture was occluded, and mice earned unlimited reinforcements on a variable ratio 2 schedule for 25 min, meaning mice were reinforced for every one, two, or three responses on the "active" aperture, as randomly determined by the operating computer. Mice were required to retrieve each pellet before earning more. The following day, the opposite aperture was occluded, and reinforcers were delivered into the magazine at the same rate at which the mouse acquired them during the previous session, but regardless of animals' responding, thus "degrading" the response-outcome contingency. The location of the nondegraded and degraded apertures and the order of the degradation/contingency training sessions were counterbalanced. Next, both apertures were available, and responses made during a 10-min test session conducted in extinction were analyzed by two-factor ANOVA.

Progressive-ratio test. Mice tested on a progressive-ratio schedule of reinforcement constituted separate groups that were first trained to nose poke on a single aperture: one, two, or three responses were reinforced, as randomly determined by the operating computer (i.e., variable ratio schedule of reinforcement) during 1-h training sessions until responding was stable. Corticosterone (CORT) exposure, *Bdnf* knockdown, or chronic RU38486 administration were then achieved as described in the main text, before shifting the animals to a progressive-ratio schedule in which the response requirement increased by 4 with each reinforcement. (Groups were designated by matching mice based on response rates during acquisition.) Sessions ended when mice executed no active responses for 5 min. The highest response: reinforcement ratio—termed "break-point ratio"—was analyzed by ANOVA with repeated-measures or two-factor ANOVA as appropriate.

Extinction test. Mice were trained to nose poke for food as above (under progressive-ratio test) then exposed to CORT, as described in the main text. After CORT exposure, nonreinforced responding—rather than progressive-ratio responding—was quantified in three daily 15-min sessions and analyzed by repeated-measures ANOVA.

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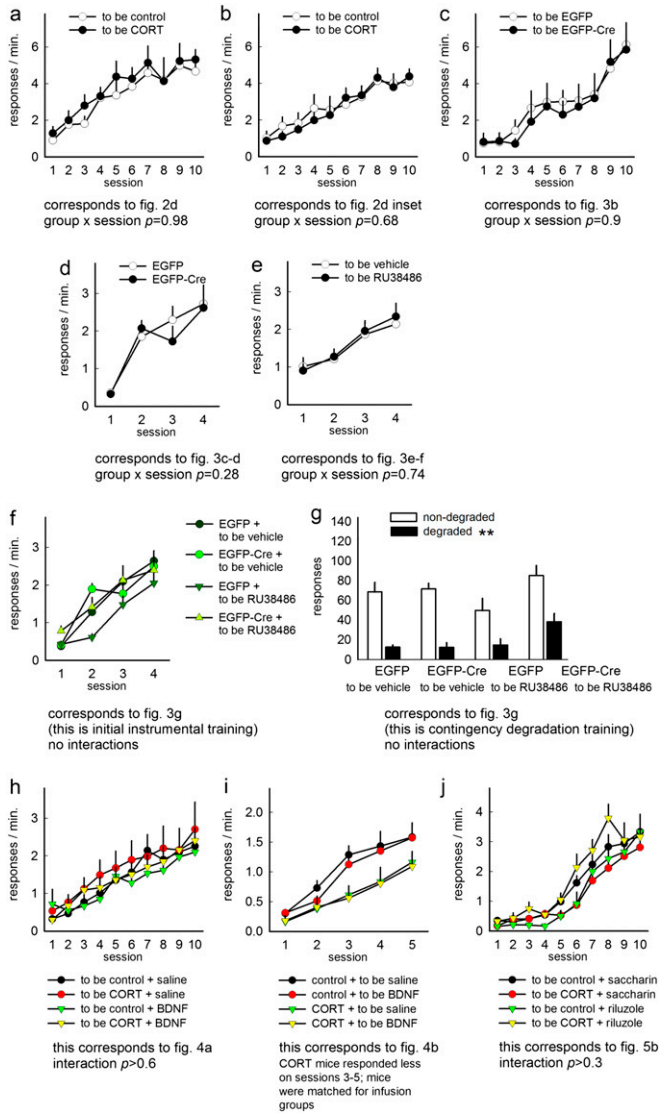

Fig. S1. Response acquisition curves. (*A–J*) Response acquisition curves not shown in the main text are shown here. The graph in the main text with which they correspond is indicated below each curve. Bars and symbols represent group means + SEM, $^{**}P < 0.001$.

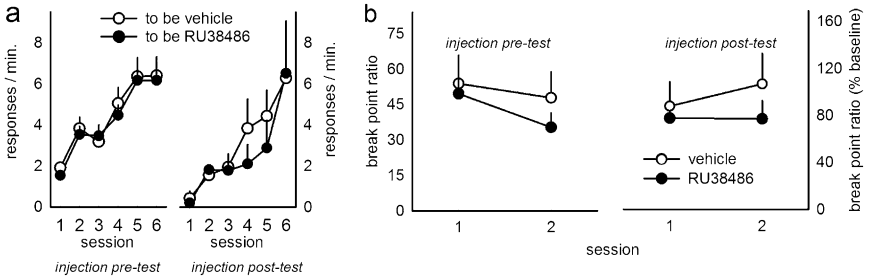

Fig. S2. GR blockade does not impact progressive-ratio responding. (*A*) Naïve mice were trained to perform a nose-poke response for food reinforcement, then matched based on response-acquisition curves. Curves are shown for two distinct experiments. (*B*) Although posttraining RU38486 disrupted response-outcome decision-making (see main text), neither chronic exposure before the progressive-ratio test (*Left*), nor injection immediately after the test (*Right*), affected break-point ratios. Symbols represent group means + SEM.

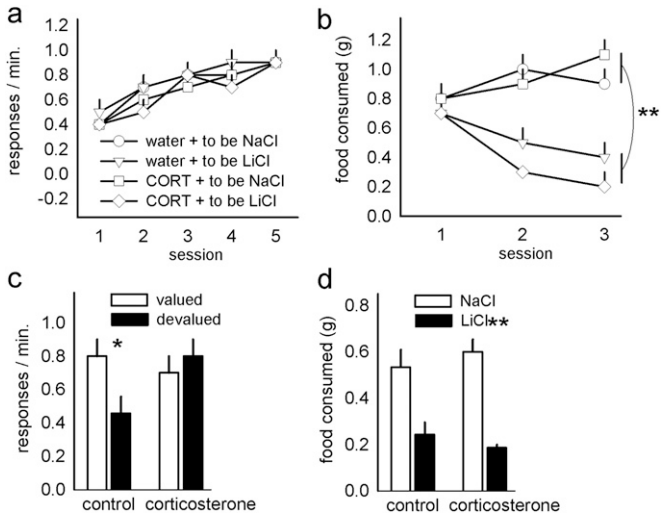

Fig. S3. Corticosteroid exposure eliminates instrumental sensitivity to outcome devaluation without impacting conditioned taste aversion. (*A*) Mice were exposed to CORT as described in the main text, then trained to respond for food reinforcers on a continuous reinforcement schedule. Response rates did not differ based on CORT exposure status or between groups that were next assigned to the NaCl or LiCl groups ($F < 1$). (*B*) Food intake during taste aversion conditioning is shown. Injection followed free access to food, thus mice had not been injected at session 1; divergence between the LiCl- and NaCl-injected group followed, with LiCl-injected mice consuming less in each subsequent session relative to control groups and relative to their own baseline. CORT-exposed animals did not differ from control animals in their degree of conditioned aversion. This graph is reprinted from the main text. (*C*) Despite this pattern, responding for the devalued outcome was unchanged in CORT-exposed mice. Control mice were, in contrast, sensitive to outcome devaluation, in that those that were exposed to LiCl showed reduced response rates relative to NaCl-injected animals. This graph is reprinted from the main text. (*D*) In a posttest consumption test, LiCl-injected animals consumed less than NaCl-injected animals, providing further evidence that a history of CORT exposure does not impair taste aversion conditioning but significantly disrupts animals' ability to use the value of an appetitive outcome to engage goal-directed decision-making [main effect of LiCl $F_{(1,27)} = 36.4$, $P < 0.001$; no effect of CORT or CORT × LiCl interaction ($F \leq 1$)]. Means + SEM; *$P < 0.05$, **$P < 0.001$.