Supporting Information

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SI Text

Subjects. Eleven common marmosets (*Callithrix jacchus*; 6 females, 5 males) were housed in pairs and maintained on a diet of ≈20 g of MP.E1 primate diet (Special Diet Services/SDS) and either two pieces of carrot or a slice of orange each day for 5 days a week. This diet was supplemented at the weekend with fruit, marmoset jelly (SDS), hard-boiled eggs, whole-meal bread, Farley's Rusk, and nuts.

Test Apparatus. Behavioral testing took place within a sound-attenuated box in a dark room. Each subject was transported to the apparatus in a clear cuboidal Perspex box, which had one side that was removable, thus acting as the door. Both the door (at the front of the box) and the wall on the opposite side (at the back of the box) contained a 30-mm-diameter, centrally located, circular opening. The entire box was then fitted into the internal frame of the apparatus, which comprised two electrically controlled food box units at opposite ends. Both food box units incorporated a circular opening (in line with the circular openings on the Perspex box), which allowed animals in the Perspex box access to a recessed cylindrical food box (internal diameter 52 mm and length 51 mm). Light in the apparatus was provided by a 3W light bulb suspended from the roof and the food box could be illuminated from the inside by a 28V, 0.04W encased light. Two Perspex doors (one black and opaque, the other transparent) formed a barrier between the marmoset and the contents of the food box, both of which had to be opened to enable access to the food. Cameras mounted on the inside walls of the chamber recorded the behavior of the subject and a telemetric receiver below the floor of the apparatus received the cardiovascular information.

Cardiovascular Measurements. To measure BP and HR changes remotely in animals, a PhysioTel Telemetry System (Data Sciences) was used. This consisted of five basic components: an implantable transmitter (TA11PA-C40), which continuously transmitted the BP of subjects; a receiver (RPC-1) located underneath the behavioral testing box; a calibrated pressure output adapter (R11CPA) with an ambient pressure reference monitor (APR-1) to convert the absolute pressure measured by telemetry to a gauge pressure in millimeters of mercury (mmHg); an analogue–digital converter [micro 1401; Cambridge Electronic Design (CED)], and a computer based data acquisition system for collection, analysis, and storage of the accumulated data (PC with the software package Spike2 Version 2.5; CED).

Surgical Procedures. ***Implantation of telemetric devices.*** For implantation of telemetry probes, marmosets were premedicated with ketamine hydrochloride (0.05 ml of a 100 mg/ml solution, i.m.; Amersham Pharmacia and Upjohn), anesthetized with saffan (alphaxalone, 0.9% wt/vol + alphadalone 0.1% solution, 0.4 ml, i.m.; Schering-Plough), given preoperative analgesia with the nonsteroidal antiinflammatory drug, Rimadyl (carprofen; 0.03 ml, s.c.) and administered atropine sulfate (0.1 ml of a 0.6 mg/ml solution, s.c.; Animalcare) for blood vessel dilation. BP transmitters were inserted into the abdominal cavity and the probe catheter implanted into the descending aorta following procedures described previously (1). Nonsteroidal analgesics were given on the day of and the day after surgery, and antibiotics were given both for 2 days before, and up to 10 days after surgery. Marmosets had a 2-week recovery period before testing recommenced.

Excitotoxic lesions of the OFC. Before neurosurgery, all marmosets were assigned to either the control or the OFC-lesion group in balanced pairs according to their preoperative conditioned systolic BP and behavioral responses. On the day of surgery, all marmosets were anesthetized with a combination of ketamine hydrochloride (0.05 ml of a 100 mg/ml solution, i.m.; Amersham Pharmacia and Upjohn), and saffan (alphaxalone 0.9% wt/vol + alphadalone 0.3% wt/vol: 0.4 ml of a 12 mg/ml solution, i.m.; Schering-Plough) and maintained with supplementary doses of 0.3 ml of Saffan for the duration of surgery. For all neurosurgical procedures, animals were placed in a stereotaxic frame (David Kopf) with their head securely fixed in position with specially modified incisor and zygoma bars.

A standardization technique (2) was used to determine the appropriate injection sites for each animal independently, based on the thickness of the marmoset's frontal pole. Excitotoxic lesions of the OFC were then made by infusing 0.5- to 0.6-μl/site of a 0.09 M solution of quinolinic acid bilaterally into six sites. For all placements, infusions were made at a rate of 0.1 μl/20 s by using a 2-μl precision Hamilton sampling syringe (Precision Sampling) through a stainless-steel cannula (30 gauge). The cannula remained in place for 4 min, after which it was withdrawn by 1 mm, where it remained for an additional 2 min before being slowly removed from the brain. The stereotaxic coordinates used to lesion the OFC (in addition to the infusion rate and volume at each site) are described in Table S8. Sham-operated control animals underwent the same surgical procedure as OFC-lesioned animals with the exception that they received infusions of sterile phosphate buffer vehicle bilaterally into the OFC rather than excitotoxin.

After surgery, all animals were administered 5 ml of glucose and saline solution (0.9% saline, 1% sucrose) i.p., followed by a 0.2-ml injection of the antiinflammatory drug, dexamethasone sodium phosphate (4 mg/ml, i.m.; Faulding Pharmaceuticals), to reduce possible brain swelling after surgery. Diazapam (Roche.) in the range of 0.05–0.25 ml was also administered i.m. intermittently over the first 24 h to suppress any epileptic seizure activity and an oral analgesic (0.1 ml Metacam) was given 1 day after surgery for pain relief. Animals then had a 7- to 10-day postoperative recovery period before resuming the testing regime.

Study Design. All marmosets were habituated to the behavioral equipment before telemetry surgery. They were initially placed in the apparatus and preexposed to the sight and sound of the opening doors to the food box. During these sessions, high-incentive foods (such as marshmallows or maltloaf; Soreen) were presented in the food boxes. Preliminary training continued for ≈1 week. After habituation, marmosets were exposed to an appetitive, Pavlovian procedure in which one of two novel sounds (a 4-kHz tone or a computer-generated white noise) was associated with reward (CS^+) and the other, no reward (CS^-). All training sessions began with a variable interval (VI) of between 70 and 110 s with the house light on and all food-box doors closed. There then followed between one and three trials. A trial consisted of a 20-s CS period during which one of the sounds was played. At the end of this period, one or other of the food boxes would open according to a predetermined randomized schedule, accompanied by the house light offset, the onset of the food-box light, and presentation of either an empty food

box or high-incentive food reward (US period). The auditory CS remained "on" for the entire 120-s duration of the US period. In multiple-trial sessions, the offset of the US periods was indicated by termination of the CS, closing of the opaque food box door, and onset of the house light. In the last trial of a session, all lights were extinguished at the end of the US period. Animals never received more than one CS^+ trial in a session (always the final CS) and in no more than 5 of 10 sessions over a 2-week period. The type of food rewards were varied across the sessions. Associations between the different sounds and outcomes were counterbalanced across subjects, with approximately half ($n = 6$) the animals receiving tone as the rewarded sound (CS^+) and white noise as the unrewarded sound and the other half ($n = 5$) trained on the opposite contingencies.

After 2–3 weeks of training, animals were implanted with telemetric probes. The animals then continued their training on the Pavlovian conditioning task until each showed differential BP and behavioral responses to the rewarded and unrewarded sounds. Once animals showed evidence of stable systolic BP conditioning (indicated by a significant difference of at least 3 mmHg between the CS^+ and the CS^-) preoperatively for 10 consecutive days, they each received a selective excitotoxic lesion of the OFC or underwent sham control surgery. Groups were counterbalanced based on the overall number of trials before animals reached stable responding and for their overall conditioned systolic BP scores (CS^+–CS^-). After 10 days of postoperative recovery, animals were then retested on the same behavioral task until their responses to the CS^+ and CS^- were comparable with those they had produced preoperatively. As soon as monkeys showed stable responses across five sessions, they were given two, one-trial extinction sessions (probe tests 1 and 2), spaced at least 1 week apart with reconditioning trials in between:

Probe test session 1: CS termination along with reward omission. A single CS^+ trial was presented. The CS^+ was not followed by reward at the end of the 20 s (i.e., no doors opened). Instead, the CS sound was discontinued, and behavior and cardiovascular responses measured for an additional 70 s.

Probe test session 2: Reward omission only. A single CS^+ trial was again presented. This time the CS^+ was not followed by reward after 20 s (i.e., no doors opened). However, unlike Probe session 1, the CS^+ remained on for the duration of the 120-s "no-reward" US period.

Reversal of reward contingencies. After both one-trial extinction test sessions and approximately a week of additional Pavlovian training to allow BP and behavioral responses to restabilize, animals were subjected to reversal of the contingencies. During this phase of testing, the reward contingencies were switched, such that the previously rewarded stimulus was no longer rewarded, and the previously unrewarded stimulus became rewarded. All animals received an identical set of sessions across the reversal, i.e., session 1: one CS^-, one CS^+, session 2: two CS^-, session 3: one CS^-, one CS^+, etc., until they reached criterion on the reversal (described below).

Histological Analysis. All marmosets were euthanized with Euthatal (1 ml of a 200 mg/ml solution, pentobarbital sodium, i.p.; Merial Animal Health). Animals were then perfused transcardially with 500 ml of 0.1 M PBS (pH 7.4), followed by 500 ml of 0.4% formaldehyde-buffered solution, washed through over 10 min. The entire brain was removed and placed in fixative solution overnight before being transferred to a 30% sucrose solution in 0.01 M PBS for a minimum of 48 h. For verification of lesions, coronal sections (60 μm) of the brain were cut by using a freezing microtome and cell bodies stained by using Cresyl Fast Violet. The sections were viewed under a Leitz DMRD microscope, and lesioned areas were defined by the presence of major neuronal loss, often with marked gliosis. For each animal, areas with cell loss were schematized onto drawings of standard marmoset coronal sections and composite diagrams were then made to illustrate the extent of overlap between lesions.

Behavioral and Cardiovascular Analyses. ***Cardiovascular responses before and after training.*** For the telemetric data, recording failures and outliers were removed (typically BP values >400 mmHg or <0 mmHg or other abnormal spikes), and then the systolic and diastolic BP events were extracted as local minima or maxima for each heartbeat cycle. Outliers or missing values were filled with cubic spline interpolation, although any disruptions in the trace >0.4 s were treated as missing values in the resulting dataset. A mean value was calculated over the 20-s CS period for the systolic BP. The 20-s period immediately preceding the onset of the CS served as its baseline (BL) for comparison purposes. Systolic BP was used as the primary measurement for affective physiological responses because it proved to be less variable across sessions in all animals and is known to be unaffected by initial BL levels or movement (1). Other measurements also analyzed were diastolic BP and HR, but the strength of these responses were found to depend more on initial BL values than systolic BP as determined by a correlation analysis on preoperative data (systolic BP: $r = 0.04$, $P = 0.8$; diastolic BP: $r = -0.28$, $P = 0.02$; HR: $r = -0.25$, $P = 0.04$).

The values for the US periods were calculated over the 60 s after the animal had reached into the food box in the case that this happened in the first 20 s after access becomes available or, alternatively, the 60 s directly after access when no approach was made within the first 20 s.

Behavior. All behavior was recorded on DVD and then subsequently scored by a researcher blind to the experimental groups.

CS period before and after training. Head jerks (HJs) were seen throughout the 20-s CS period. They were very seldom seen at any other time, i.e., the intertrial intervals (BL: controls, 0.85 ± 0.3, OFC, 0.54 ± 0.27) or during presentation of the stimulus that was not paired with reward (CS^-: controls, 2.8 ± 0.5, OFC, 2.0 ± 0.5). HJs were observed and scored from DVD recordings of the behavioral sessions. The number of HJs during the CS^- and CS^+ presentations (minus the number of HJs observed in their respective 20-s BLs) were used as quantitative difference measures of CS-directed conditioned behavior.

Other conditioned behaviors scored during the session were US-directed "looking" and "nose poking" at the food boxes. These were discrete events, and thus the number rather than the time spent engaged in the behaviors was scored. These US-directed behaviors were found to vary both between and within subjects, most likely as a result of the food location being randomized across sessions. Mean values in retention for controls were 0.6 ± 0.2 (CS^+) and 1.2 ± 0.7 (CS^-) and for lesions, 0.2 ± 0.3 (CS^+) and 1.3 ± 1.4 (CS^-), respectively. Thus, these were not a robust measure of conditioned behavior. Also, due to the relatively confined nature of the testing environment, general activity was limited and did not differentiate between BL, CS, and US periods. No other significant behaviors were observed.

US period: before and after training. Behaviors during the US periods were also measured pre- and postoperatively. Latencies to look at the food box after US^+ onset, latencies to reach in for the food reward, latencies to start eating, and total food consumed (in grams) were measured for all animals.

Cardiovascular and Behavioral Responses. ***One-trial extinction tests.*** During probe test sessions 1 and 2, the BL, "probe-CS" and "no-US" periods were analyzed in 10-s time bins to capture time-dependent autonomic and behavioral changes more accurately. Changes in responses were then monitored from the second 10 s of the probe-CS and across each 10 s of the following no-US period for 70 s. The CS-evoked responses were calculated

as a difference value, where the BP/HJs during the last 10 s of the preceding BL were subtracted from the probe-CS (last 10 s) and no-US period (70 s).

Reversal. Mean responses to the new CS^+ and CS^- over the reversal for each animal were calculated as a running mean of six consecutive CS^+ trials and intervening CS^- trials (6–14), i.e., means of CS^+ trials 1–6, 2–7, 3–8, etc. The number of sessions animals took to reach "chance" performance (based on systolic BP or behavior) was determined as the point where responses to the reversed CS^+ and CS^- were not significantly different from one another ($P > 0.02$), i.e., when animals were responding equally to both stimuli. Animals were considered to have reversed successfully (reversal criterion) when their mean systolic BP response across six consecutive CS^+ trials was significantly greater than that for the intervening CS^- trials ($P < 0.02$).

1. Braesicke K, *et al.* (2005) Autonomic arousal in an appetitive context in primates: A behavioural and neural analysis. *Eur J Neurosci* 21:1733–1740.
2. Roberts AC, *et al.* (2007) Forebrain connectivity of the prefrontal cortex in the marmoset monkey (*Callithrix jacchus*): An anterograde and retrograde tract-tracing study. *J Comp Neurol* 502:86–112.

Table S1. Mean autonomic data for control and OFC-lesioned animals, pre- and postoperatively during baseline, CS, and US periods

Group	Surgery	Measure	BL	CS^+ (CS^+-BL)	CS^- (CS^--BL)	US^+ (US^+-BL)	US^- (US^--BL)
Control	Pre	Systolic	131.2 ± 2.3	9.2 ± 1.2	−0.5 ± 0.4	19.9 ± 2.2	−1.0 ± 0.7
		Diastolic	92.1 ± 2.6	6.8 ± 1.2	−1.0 ± 0.4	16.0 ± 1.6	0.4 ± 0.7
		HR	304.1 ± 22.6	21.0 ± 8.3	−15.7 ± 4.7	48.1 ± 12.1	−0.7 ± 5.4
	Post	Systolic	126.5 ± 1.7	7.7 ± 1.5	−0.4 ± 0.9	22.2 ± 2.8	−0.7 ± 1.2
		Diastolic	88.9 ± 1.8	6.4 ± 2.3	−0.8 ± 1.1	18.5 ± 2.2	0.6 ± 1.4
		HR	298.9 ± 24.9	21.5 ± 11.3	−13.9 ± 7.2	52.5 ± 16.9	−5.7 ± 10.5
OFC	Pre	Systolic	120.8 ± 3.7	7.7 ± 0.4	−1 ± 0.4	23.1 ± 2.1	−1.9 ± 0.7
		Diastolic	85.7 ± 4.2	6.7 ± 0.4	−0.2 ± 0.3	18.1 ± 1.5	−0.7 ± 0.6
		HR	235.2 ± 18.3	33.6 ± 8.4	6.9 ± 3.3	64.5 ± 11.1	4.8 ± 5.0
	Post	Systolic	123.2 ± 3.7	5.4 ± 0.5	−0.9 ± 0.4	16.9 ± 2.6	−2.1 ± 1.1
		Diastolic	90.4 ± 4.4	4.0 ± 0.5	−0.3 ± 0.4	12.2 ± 2.0	−1.1 ± 1.3
		HR	267.9 ± 22.1	28.4 ± 12.6	6.5 ± 6.1	32.1 ± 15.5	−7.1 ± 9.6

Control (n = 5) and OFC-lesioned (n = 6) animals. All BP values are in mmHg and HR values are in beats per minute (bpm). Three-way ANOVA revealed that all subjects showed a significant main effect of incentive during the CS period for systolic: [$F(1,9) = 6.3$, $P = 0.03$], diastolic BP (log transformed): [$F(1,9) = 108$, $P < 0.001$], and HR: [$F(1, 9) = 18.9$, $P < 0.01$]. Analysis of the systolic BP also revealed a significant main effect of surgery [$F(1,9) = 176.6$, $P < 0.001$] as well as a significant surgery × incentive interaction [$F(1,9) = 13.2$, $P = 0.005$]. The diastolic BP also showed a significant surgery × incentive interaction [$F(1,9) = 5.7$, $P = 0.04$]. Post hoc analysis revealed that these interactions were due to a significantly reduced BP during the CS^+ period postoperatively for all animals, lesions, and controls, [systolic BP: $F(1,9) = 12.5$, $P = 0.006$; diastolic BP: $F(1,9) = 7$, $P = 0.03$], most likely the result of habituation to the task. There were no interactions with groups (Fs < 1). Three-way ANOVA of autonomic responses during the US periods (change from BL) demonstrated a main effect of incentive [systolic BP (log transformed): $F(1,9) = 160.2$, $P < 0.001$; diastolic BP (log transformed): $F(1,9) = 129.5$, $P < 0.001$; HR: $F(1,9) = 20.8$, $P = 0.001$]. There was a trend for HR to show a main effect of surgery [$F(1,9) = 5.0$, $P = 0.052$] and a surgery × group interaction ($F(1,9) = 4.7$, $P = 0.059$] but this was primarily due to the lesioned group, presurgery, showing higher levels of HR during the US than controls and then showing a small decline, postsurgery. There were no statistically significant group effects on BL systolic BP [group: $F < 1$; group × surgery: $F(1,9) = 1.1$, $P = 0.3$], diastolic BP (group: $F < 1$; group × surgery: $F(1,9) = 2$, $P = 0.2$] or HR [group: $F(1,9) = 1.4$, $P = 0.3$; group × surgery: $F(1,9) = 2.7$, $P = 0.1$].

Table S2. Median latency and consumption data pre- and postoperative

Group	Surgery	Latency Measures				Consumption
		Look (US^+)*	Look (US^-)*	Reach**	Eat***	total, g
Control	Pre	0.4 ± 0.1	0.7 ± 0.2	15.8 ± 3	22 ± 6.1	4.7 ± 0.4
	Post	0.6 ± 0.2	0.5 ± 0.2	13.6 ± 3.1	16.4 ± 3.2	4.4 ± 0.4
OFC	Pre	0.4 ± 0.1	0.7 ± 0.2	14.4 ± 4.2	16.6 ± 4.1	4.5 ± 0.3
	Post	1.1 ± 0.3	0.6 ± 0.1	12.4 ± 1.2	14.4 ± 1.3	4.5 ± 0.6

There were no significant main effects or interactions in the looking latencies [incentive: $F(1,9) = 4.1$, $P = 0.07$, all other Fs < 1], reaching latencies [surgery: $F < 1$; group: $F(1,9) = 1.3$, $P = 0.3$; surgery × group: $F(1,9) = 2.2$, $P = 0.2$], or eating latencies [surgery: $F(1,9) = 1.7$, $P = 0.2$; group: $F < 1$; surgery × group: $F < 1$]. There were also no significant effects in the amount of food consumed pre- or postoperatively in any of the groups (all Fs < 1).

*Latency to look at the food box after US onset.

**Latency to reach into the food box after US onset.

***Latency to start eating after US onset.

Table S3. Mean changes in autonomic activity during the one-trial extinction, probe test 1

Parameter	CS-BL	"No-US" bins							"No-US" mean
		10	20	30	40	50	60	70	
Systolic BP									
Control	9.2 ± 1.7	6.3 ± 0.8	1.5 ± 1.5	2.1 ± 1.0	−0.4 ± 1.9	−0.8 ± 2.4	1.0 ± 1.8	−1.5 ± 1.9	1.2 ± 1.0
OFC	10.4 ± 1.8	11.0 ± 1.8	5.9 ± 1.1	5.8 ± 1.5	4.5 ± 0.5	4.3 ± 1.1	3.1 ± 1.4	3.7 ± 1.9	5.5 ± 1.0
Diastolic BP									
Control	5.9 ± 1.2	3.1 ± 0.9	0.2 ± 1.2	0.5 ± 1.1	−1.0 ± 1.5	−1.7 ± 2.1	−0.2 ± 1.8	−2.1 ± 1.8	−0.2 ± 0.7
OFC	7.0 ± 1.6	6.9 ± 1.4	4.0 ± 0.9	4.3 ± 1.1	3.2 ± 0.6	3.1 ± 0.8	2.2 ± 1.0	2.6 ± 1.5	3.8 ± 0.6
HR									
Control	−4.9 ± 11.9	−16.5 ± 9.4	3.8 ± 10.3	−5.7 ± 11.0	−3.6 ± 13.5	−5.6 ± 16.0	−8.3 ± 17.1	−16.8 ± 12.3	−7.5 ± 2.8
OFC	39.7 ± 10.2	28.0 ± 8.1	24.1 ± 7.3	27.4 ± 10.2	19.1 ± 9.0	20.2 ± 10.4	21.7 ± 12.9	7.2 ± 15.5	21.1 ± 2.6

One-trial extinction, probe test 1 (CS termination and reward-omission), showing the systolic/diastolic BP and HR values during the last 10 s of the CS (left columns) and during each successive 10 s bin of the no-US period (70 s; right columns; including mean US values during "no-US" period on far right). Two-way ANOVA of the autonomic responses during the no-US period revealed a main effect of "bin" in all animals in the BP [systolic: $F(6,54) = 11$, $P < 0.001$; diastolic: $F(6,54) = 7.8$, $P < 0.001$], where appetitive BP responses tended to decline over the 70 s following CS offset. There was also an overall effect of group in the BP [systolic: $F(1,9) = 6.8$, $P = 0.03$; diastolic: $F(1,9) = 6.9$, $P = 0.03$]. There were no statistically significant effects found in the HR responses during the no-US period [bin: $F(6,54) = 1.8$, $P = 0.1$; group: $F(1,9) = 3.8$, $P = 0.09$; bin × group: $F < 1$], although any changes were in the same direction as for BP.

Table S4. Mean changes in autonomic activity and behavior during the one-trial extinction, probe test 2

Parameter	CS	No-US bins							No-US mean
		10	20	30	40	50	60	70	
Systolic BP									
Control	5.4 ± 2.7	6.8 ± 2.7	5.3 ± 2.3	5.5 ± 2.8	5.5 ± 2.8	3.2 ± 2.6	5.0 ± 2.2	4.1 ± 2.5	5.0 ± 0.4
OFC	8.9 ± 2.2	8.4 ± 2.2	10.0 ± 2.3	6.9 ± 2.7	8.4 ± 2.8	8.1 ± 2.3	6.1 ± 2.4	6.9 ± 2.8	7.8 ± 0.5
Diastolic BP									
Control	4.0 ± 2.5	4.9 ± 2.5	4.0 ± 2.5	3.6 ± 2.5	4.2 ± 2.5	2.6 ± 2.4	3.7 ± 2.0	2.7 ± 2.0	3.7 ± 0.3
OFC	8.0 ± 2.0	8.1 ± 2.2	8.9 ± 2.1	7.2 ± 2.4	8.0 ± 2.1	8.0 ± 2.0	6.8 ± 2.1	7.7 ± 2.5	7.8 ± 0.3
HR									
Control	−4.1 ± 12.3	−16.5 ± 13.5	−2.2 ± 17.7	6.5 ± 18.1	10.0 ± 13.6	16.2 ± 14.6	14.9 ± 8.9	12.1 ± 16.8	5.8 ± 4.4
OFC	25.8 ± 16.6	38.8 ± 15.6	34.0 ± 16.6	33.0 ± 14.8	39.2 ± 14.7	25.8 ± 11.5	32.3 ± 14.9	31.5 ± 11.7	33.5 ± 1.7
HJs*									
Control	5 ± 1.4	3.2 ± 1.2	2.4 ± 0.5	1.4 ± 0.5	2.4 ± 0.5	2.0 ± 0.3	1.2 ± 0.7	2.0 ± 0.4	14.6 ± 3.2
OFC	2.6 ± 0.6	0.9 ± 0.5	1.9 ± 0.9	1.7 ± 0.5	1.3 ± 0.7	1.5 ± 0.6	0.5 ± 0.4	0.5 ± 0.4	8.0 ± 3.2

Includes responses during the last 10 s of the probe CS (left columns) and during each successive 10-s bin of the no-US period (right columns; far right column shows overall mean responses during the no-US period for the autonomic measures and the total HJs). Two-way ANOVA of the autonomic responses during the no-US period of probe 2 revealed a main effect of bin in all animals for BP [systolic: $F(6,54) = 2.3$, $P = 0.05$; diastolic: $F(6,54) = 2.6$, $P < 0.02$], where (similar to the effect seen during probe 1) the BP tended to decline across the US bins. However, unlike the effect seen in probe 1, there was no overall effect of group on the BP [systolic: $F < 1$; diastolic: $F(1,9) = 1.6$, $P = 0.2$]. ANOVA on the HR responses failed to reveal any main effects [bin: $F(6,54) = 1.5$, $P = 0.2$; group: $F(1,9) = 2$, $P = 0.2$]. However, there was a bin × group interaction [$F(6,54) = 3.8$, $P = 0.003$]. Further analysis showed that this was due to a significant difference in HR responses between OFC-lesioned and control groups during the first US 10-s bin [$F(1,9) = 6.9$, $P = 0.03$] but not in subsequent bins [20 s: $F(1,9) = 2.2$, $P = 0.2$; 30 s: $F(1,9) = 1.3$, $P = 0.3$; 40 s: $F(1,9) = 2$, $P = 0.2$; 50–70 s: all Fs < 1]. However, there was also a trend for a difference between the control and lesioned groups during the last 10 s of the preceding CS period, and when these two periods were directly compared by using ANOVA, no significant differences were seen ($F < 1$). Two-way ANOVA of the behavior during the no-US period of probe 2 revealed a main effect of bin for all animals [$F(6,54) = 2.6$, $P = 0.03$]. There were no other significant effects [group: $F < 1$; bin × group: $F(6,54) = 1.3$, $P = 0.3$].

*Total number of HJs (minus HJs during BL) during the last 10 s of the probe CS (left column) and during each successive 10-s bin of the no-US period (up to 70 s; right columns).

Table S5. Performance on the reversal test

Group	Sessions to	Sessions
Control	Chance (based on systolic BP)	9.0 ± 2.4
	Chance (based on behavior)	9.6 ± 1.4
	Reversal criterion (systolic BP)	32.6 ± 3.9
OFC	Chance (based on systolic BP)	6.8 ± 1.5
	Chance (based on behavior)	7.3 ± 1.9
	Reversal criterion (systolic BP)	59.3 ± 9.1*

Mean number of sessions to reach (*i*) chance levels of performance based on systolic BP and behavior and (*ii*) reversal criterion based on systolic BP only. One-way ANOVA confirmed that there were no significant group differences in mean number of sessions to systolic chance ($F < 1$) or behavioral chance ($F < 1$). There was a significant group difference (*), however, in mean number of sessions to systolic BP reversal criterion [$F(1,9) = 6.2$, $P = 0.03$].

Table S6. Median latency and consumption data at different stages of the reversal

Group	Stage	Latency measures				Consumption total, g
		Look (US^+)*	Look (US^-)*	Reach**	Eat***	
Control	To chance	0.4 ± 0.1	0.4 ± 0.2	13.5 ± 2.6	16 ± 2.1	5.2 ± 0.5
	To criterion	0.3 ± 0.04	0.3 ± 0.03	10.3 ± 2.1	11.9 ± 1.9	4.6 ± 0.3
	At criterion	0.3 ± 0.04	0.3 ± 0.05	9.6 ± 0.7	11.4 ± 3.9	4.5 ± 0.5
OFC	To chance	0.5 ± 0.3	0.4 ± 0.08	8.3 ± 1.8	11.1 ± 2.3	5.1 ± 1.3
	To criterion	0.3 ± 0.04	0.3 ± 0.02	8.3 ± 1	10.8 ± 0.9	5.3 ± 0.5
	At criterion	0.3 ± 0.04	0.3 ± 0.1	7.7 ± 0.7	9.8 ± 0.7	5.2 ± 0.7

There were no significant main effects or interactions in the looking latencies [stage: $F(1,9) = 2.3$, $P = 0.1$; stage × incentive: $F(1,9) = 1.1$, $P = 0.4$; incentive/incentive × group: $Fs < 1$]. There was, however, a significant main effect of stage in the reaching [$F(1,9) = 11.6$, $P = 0.001$] and eating latencies [$F(1,9) = 3.5$, $P = 0.05$] but no group interactions [reaching: $F(1,9) = 1.4$, $P = 0.3$; eating: $F < 1$]. This effect demonstrated that as animals learned the new contingencies during reversal, they became faster to reach into the food box and start eating. Nevertheless, there were no significant differences in amount of food (in grams) consumed between the animals during the stages ($Fs < 1$). Asterisks are as described in Table S2.

Table S7. Response correlations during reversal

sys BP vs HJs	*r*	*P*	sys BP vs HJs	*r*	*P*
Control 1	0.92	0.001*	OFC1	0.17	0.59
Control 2	0.78	0.036*	OFC2	−0.11	0.75
Control 3	0.86	0.001*	OFC3	0.37	0.16
Control 4	0.68	0.022*	OFC4	0.77	0.015*
Control 5	0.52	0.185	OFC5	0.39	0.101
			OFC6	0.53	0.035*

Correlation coefficients (*r*) and significance values for behavior (head jerks, HJs) and systolic BP responses over the course of the reversal for each animal. * denotes a significant correlation within individuals ($P < 0.05$).

Table S8. Surgical parameters

Lesion	AP	LM (+/−)	Infusion volume, μl	Infusion rate, μl/20 s
OFC	16.75	2.5	0.5	0.1
0.09 M quinolinic acid	16.75	4.8	0.5	0.1
	17.75	2.0	0.5	0.1
	17.75	4.8	0.5	0.1
	18.5	2.0	0.6	0.1
	18.5	4.0	0.5	0.1

Stereotaxic coordinates (in millimeters), excitotoxin infusion volumes, and infusion rates for the OFC lesions (six injections per side at 0.7 mm from the base). Injection locations along the anterior–posterior (AP) plane were adjusted *in situ* according to a cortical depth check, see description in *Excitotoxic Lesions of the OFC* in *SI Text*.