Supplementary Methods

Social Preference Test

Subjects

Seventy-four Long-Evans, male rats served as subjects (*S*-rats) in the food-preference test, with 40 assigned to the CXT-Same (CXT-S) Condition and 34 to the CXT-Different (CXT-D) Condition. Thirty-five rats received hippocampal (HPC) lesions and 39 were controls. All rats were about 5 months old at the beginning of this test. In addition, 10 normal rats served as demonstrators (*D*-rats).

Training Procedures

Training on the social preference task began at least two weeks after surgery. For this task, *D*- and *S*-rats were placed on a food restriction schedule (17g/day) for 1 week prior to being transferred to the test cages. The cages were constructed of wire-mesh (42 \(\times\) 24 \(\times\) 27 cm.) and divided into two equal compartments by a wire mesh-partition.

Training consisted of four distinct stages: (1) A pair of *D*- and *S*-rats were placed individually in the separate compartments of a test cage and left undisturbed for 2 days with unlimited access to standard lab chow and water. This allowed each pair to become familiar with each other and the new environments. (2) The next day, food was removed from each cage. (3) After 23-hr of food deprivation, the *D*-rat was removed to another room and, for 60 min., fed a sample food of powdered rat chow mixed with commercially prepared cocoa (2% by weight) or commercially prepared cinnamon (1% by weight). (4) Immediately thereafter, the *D*-rat was returned to its compartment and allowed to interact with its *S*-rat for 30 min through the wire-mesh partition.
Following Stage 4, *S-rats* were returned to their home cages for 1 day (short delay) or 8 days (long delay), during which time they were fed 17g of standard rat chow in pellet form once each day.

**Testing Procedures**

One or 8 days following training, *S-rats* in the CXT-S Condition were returned individually to the original test compartment. *S-rats* in the CXT-D Condition were transferred, 1 or 8 days following training, to a different box that was located in a different room. Care was taken to ensure that the latter room and the general context (size and shape of room, lighting, furniture, etc.) contrasted significantly from those associated with acquisition of the food preference. The only elements common to both the CXT-S and CXT-D test chambers were that both boxes contained 2 food-cups, with one cup containing 30 g. of the cocoa-flavored diet and the other, 30g. of the cinnamon-flavored diet. In both conditions, *S-rats* were allowed 2 hr. to eat freely from the food-cups, with water available at all times. The amount of food in the cups was weighed at 1- and 2-hr intervals. The measure of preference for the sample food was the amount of that food consumed, expressed as a percentage of the total amount of food consumed.

The number of rats in each cell of the food preference study is indicated in Supplementary Table 1:

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<tr>
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<th>CXT-Same</th>
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<td></td>
<td>1 day</td>
<td>8 days</td>
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<tr>
<td>HPC</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Control</td>
<td>12</td>
<td>11</td>
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Context Fear-Conditioning

Subjects

Fifty-five rats served as subjects in the fear conditioning test study. Of these, 27 were assigned to the CXT-S Condition and 28 to the CXT-D condition. Twenty-six rats had HPC lesions and 29 were controls. All had participated previously in the social-preference test, and were 7 – 8 months old at the time that fear conditioning was initiated.

Training and Testing Environments

All rats received fear conditioning in a wood-framed box (50x40x18-cm) that consisted of four walls made of clear Plexiglas, a hinged clear Plexiglas roof with holes to allow ventilation, and a floor that consisted of metal rods, spaced 1.3 cm apart.

The box was placed on a table, 1.3 m above the floor, and situated in the centre of a standard laboratory room. The room contained standard furniture (eg., desk, table, bookshelf along one wall, etc.), as well as pictures, light fixtures, etc. on the walls. Illumination was provided by overhead fluorescent lights under rheostatic control.

Rats assigned to the CXT-S Condition were tested in the same box and environment as in training. Rats in the CXT-D Condition were tested in a smaller box (40x30x18-cm), also made of Plexiglas but with walls that were lined with opaque gray material. The roof was clear Plexiglas with ventilation holes and the floor consisted of metal rods, spaced 1.3 cm apart. This test box was placed in a different room on a table that was situated against a wall. Care was taken to ensure that the configuration of furniture, pictures, etc, was different from that of the room in which fear conditioning took place.

Training Procedures
Training procedures and testing for conditioned fear were similar to those of Anagnostaras, Maren, & Fanselow, (1). Each rat received one fear conditioning trial that began with the rat being placed in the chamber and allowed to explore freely for 5 min. Near the end of the exploration period and over a 64-sec. period, 8 observations of freezing behavior were recorded every 8 sec in order to obtain a pre-shock measure of freezing. Following Anagnostaras et al. (2), freezing was defined by an immobilized crouching response in which the only detectable movement was the rat’s breathing. The time spent freezing during that period was manually recorded using a stopwatch. The rat then received 10 tone-shock pairings at 2 min. intervals (tone: 2000 Hz; 80 – 90 db, 30 sec.; shock: 1.5 mA; 1 sec.). The tone was presented through a centrally mounted speaker attached to the box and the shock was delivered by TechServe; Model 452A shock generator. Immediately following the last shock and over a 64-sec. period, freezing behavior was recorded every 8 sec. (8 observations). The rat was then removed from the box and returned to its home cage.

**Testing Procedures**

For testing, rats were assigned to a CXT-S or CXT-D Condition and tested 1 day (short delay) or 28 days (long delay) following fear conditioning. Rats were assigned randomly to CXT and delay conditions, with no attempt made to relate their assignments to their previous experience in the food preference test.

Testing procedures were identical in both context conditions. Testing consisted of a single trial in which the rat was placed in the appropriate box for 8 min. and, in the absence of the tone, the amount of time spent freezing was recorded. The rat was then removed from the box and returned to its home cage.
The number of rats in each cell of the fear conditioning study is indicated in Supplementary Table 2:

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<tr>
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<td>1 day</td>
<td>28 days</td>
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<tr>
<td>HPC</td>
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<td>7</td>
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<tr>
<td>Control</td>
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**Surgery and Histology**

Rats were anesthetized with isoflurane respiratory anesthetic. All lesions were stereotaxically placed with coordinates, based on the Paxinos and Watson (3) atlas, measured in relation to bregma and the horizontal skull surface. The procedure for making hippocampal lesions was slightly modified from the technique developed by Jarrard and Meldrum (4). Using a small dental burr, 8 holes were drilled through the skull directly above the hippocampus in each hemisphere. Hippocampal lesions were produced by 10 intra-cranial micro-injections of a solution containing the cellular neurotoxin, NMDA (5 mg/1 phosphate buffer per site) into each hemisphere. The injection coordinates were calculated from a level head with respect to bregma: 3.1 mm posterior (p), 1 mm lateral (l), and 3.6 mm ventral (v); 3.1 (p), 2 (l), 3.6 (v); 4.1 (p), 2 (l), 4 (v); 4.1 (p), 3.5 (l), 4 (v); 5 (p), 3, (l), 4.1 (v); 5 (p), 5.2 (l), 5 (v); 5 (p), 5.2 (l), 7.3 (v); 5.8 (p), 4.4 (l), 4.4 (v); 5.8 (p), 5.1 (l); 6.2 (v); 5.8 (p), 5.1 (l), 7.5 (v). The solution was infused through 30-gauge stainless steel needles for 38 seconds, using a 10-1 syringe attached to a motorized infusion pump. The last two ventral hippocampal sites were injected for 2 minutes each. The needles were removed 2 minutes after each injection. In the control
procedure, incisions and burr holes were identical to the lesioned animals with the exception that there was no penetration of brain tissue. To facilitate recovery from surgery, all rats were given injections of diazepam (10 mg/kg ip).

Following behavioral testing, rats with hippocampal lesions were deeply anesthetized with sodium pentobarbital (65 mg/kg) and perfused with 0.9% saline followed by 10% formalin. The fixed brains were removed from the skull and stored in 10% formalin. Brains were transferred to a 20% buffered sucrose solution 36 hours prior to sectioning. The brains were then frozen and sliced at 40 m. Every fifth section was mounted on gelled glass slides and stained with cresyl violet.

**References**