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Supporting Information

Object Recognition test

The apparatus was formed by a glass box (30 X 60 X 30 cm). The apparatus was illuminated by a 100 W lamp suspended 70 cm above the box in a darkened room. The day before testing, rats were habituated to the test environment by exploring the box for 6 min without objects. On the day of the test, a session of two trials was given. The inter-trial interval was 60 min. In the first trial, two identical objects were placed on the centerline of the long axis of the floor, 5 cm from each end of the apparatus. Rats were placed into the center of the box and allowed to explore the two objects for 6 min. The time spent exploring each object was recorded. During the second trial, one of the objects presented in the first trial was replaced by a novel object and rats were left in the box for 6 min. The time spent for the exploration of the familiar (Tf) and the novel object (Tn) was recorded separately. Exploration was considered sniffing at the object within a distance of 2 cm from the object and/or touching it with the nose. A discrimination index (Tn-Tf/Tn+Tf) was calculated. For each animal, one pair of objects in the first trial was selected at random from a set of three

plastic objects that differed in shape and color (red cubes, green pyramids, and blue cylinders of 6 cm height), and the role (familiar and novel object) and the position of the two objects in the second trial were randomly changed to avoid object and place preference. After each exposure, the apparatus and the objects were cleaned carefully with 70 % alcohol to avoid olfactory stimuli.

T-maze spontaneous alternation

Spontaneous alternation was investigated in an acrylic T shaped runway. It consisted of a start box (20 X 18 cm) and start arm (60 cm long), and two identical goal arms (both 50 cm long). All arms were 10 cm wide and 10 cm high. Rats were placed in the start box of the T-maze and a maximum time of 5 min was allowed for them to explore the maze. Spontaneous alternation was defined as following: the rat entered with all four feet into one goal arm, came back, and then entered with all four feet into the opposite goal arm. The number of rats that alternated was recorded.

T-maze left/right discrimination memory retention

The dimensions of the T-maze apparatus were described above. The exit of the start box and the entrances of the goal arms could be blocked by guillotine doors. Careful consideration was given to avoid providing the

animals with any spatial cues. To minimize olfactory cues, the maze was wiped carefully after each run with 70 % alcohol.

Training sessions for left/right discrimination memory retention

The day before training, after the spontaneous alternation test, rats were habituated for 15 min to the presence of food pellets (Bacon Softies; Bio-Serv, Frenchtown, NJ, USA) placed at the end of each arm in the T-maze. On days 1 to 3, the rats were food-deprived for 8 to 12 hours each day before the T-maze left/right discrimination training. This training consisted of 3 stages. In the performance of the training, half of the rats from each group were randomly selected and reinforcement (food reward) placed on the right arm; for the other half of the rats from each group, the reinforcement was placed on the left arm. The reinforced arm then remained consistent throughout the remainder of the training period. The first stage consisted of 5 trials. In this stage, a guillotine door was placed to close off one arm, and the animal was forced to enter the open arm, which was baited with a food reward that the animal was allowed to eat. For all runs the animals remained on the maze until 2 min had elapsed; they were then placed in the start box for 2 min. The second stage consisted of 5 trials. In this stage, a guillotine door was placed to close off the same arm as that in the first stage, and the animal was forced to enter the open arm, which was not baited with a food

reward. When the animal entered into the open arm, a food reward was given and the animal was allowed to eat the food. The animals remained on the maze for 2 min and were then placed in the start box for 2 min. In the third stage, a guillotine door was removed, and the animal could enter into either arm (correct side and incorrect side). If the animal chose the arm on the correct side the animal received a food reward and was allowed to eat for 2 min after which it was placed in the start box for 2 min. If the animal chose the incorrect side-arm, the animal was picked up immediately and placed in the start box for 2 min. The third stage was continued until the animals made 4 consecutive correct choices or until they had had 20 training sessions (the training ceiling). This procedure was performed daily on three successive days.

Left/right discrimination memory retention test session

The retention of left/right discrimination memory was evaluated at 1, 2, 3, 5, 7, 10 and 14 days after the training session. The animals were given 10 trials on each testing day. An entry was defined as all four paws entering the arm. The total number of correct entries was recorded. This paradigm was repeated at 2, 6 and10 weeks after surgery.

Histopathology

Coronal brain sections were incubated for 1 hr in 0.1 M PBS containing 0.3% Triton X-100 for permeabilisation. Ten percent donkey serum was applied for blocking followed by incubation overnight in primary antibody (SMI 311, Covance Research Products, Inc., Berkeley, CA, USA) in a dilution of 1:500. The sections were subsequently incubated with a biotinylated anti-mouse IgG raised in donkey (Jackson Immuno Research Labs, West Grove, PA, USA, 1:2000) for 1 hr, and then incubated with an avidin-biotin peroxidase complex solution (Vector Laboratories, Burlingame, CA, USA, 1:100) for 1 hr. After each incubation, the sections were rinsed for 30 min with 0.1 M PBS containing 0.3% Triton X-100. The immunoreaction products were visualized with diaminobenzidine (DAB kit, Vector Laboratories, Burlingame, CA, USA). Endogenous peroxidase was inactivated by immersing the sections in a solution of 0.3% hydrogen peroxide in 10% methanol/0.1M PBS for 30 min. To block nonspecific staining, sections were incubated in 5% normal horse serum in 0.1 M PBS containing 0.3% Triton X-100 for 1 hr. After blocking, the sections were incubated overnight with the following antibodies (mouse or goat anti-rat) (dilutions in parentheses): against the major histocompatibility complex (MHC) class II (Ia) antigen (OX 6, Serotec, Raleigh, NC, USA, 1:100), against TNF (YC032, Yanaihara Institute, Fujinomiya, Shizuoka, Japan

1:800) and against E-selectin (R and D systems, Minneapolis, MN, USA, 5 μg/ml). The sections were subsequently incubated with a biotinylated anti-mouse IgG or a biotinylated anti-goat IgG raised in horse (Vector Laboratories, Burlingame, CA, USA, 1:200) for 1 hr, and then incubated with an avidin-biotin peroxidase complex solution (Vector Laboratories, Burlingame, CA, USA, 1:100) for 1 hr. After each incubation other than that for blocking nonspecific staining, the sections were rinsed for 15 min with 0.1 M PBS containing 0.3% Triton X-100. Finally, the immunoreaction products were visualized with diaminobenzidine (DAB kit, Vector Laboratories, Burlingame, CA, USA).