Materials and Methods

Subjects

Male B6129 F1 hybrids (8-12 weeks) from Taconic were used in these experiments. Mice were housed two per cage, given free access to food and water and maintained on a 12-h light/dark cycle. Behavioral tests were performed during the light phase of the cycle. All experiments were approved by the University of Virginia Animal Research Committee.

Morris watermaze

The pool (122 cm diameter x 61 cm height) was located in an isolated testing room with distinct cues on the walls (Med Associates Inc., St. Albans, VT). It was filled with opaque water that was kept at 20°C by a submerged pond heater. A platform (11 cm diameter) was located .5 cm beneath the surface of the water in the NE quadrant of the pool. A video tracking system (Actimetrics, Wilmette, IL) was used to control the trial sequence and collect/analyze the behavioral data. The mice received 4 training trials per day. Each trial began from a randomly chosen starting position and ended when the mouse found the platform or 60 s had elapsed. The latency to reach the platform was calculated on each trial and averaged for a single day. The mice received 1 day of pre-training where the platform was marked with a visual cue. Hidden training (with the visual cue removed) began the next day. Mice received 5 consecutive days of hidden platform training. On day 6 the mice received a 60 s probe test. On this trial, the platform was removed and the mouse released from a novel starting position. Spatial memory was assessed by comparing the percentage of time spent in the target quadrant relative to the other 3 quadrants.
**Fear conditioning**

The fear conditioning equipment and automated scoring system have been described previously (Anagnostaras et al., 2010; Tayler et al., 2011). In context A, visible light was turned on, a grid floor was inserted, and the chambers were cleaned with 95% ethanol prior to conditioning. Context B was the same as context A except that a black plastic triangular tent was inserted into each chamber. During training, the mice were placed in the context and allowed to explore for 3 minutes prior to shock onset. Three shocks (0.5 mA, 2s) were delivered, each separated by a 30s intertrial interval. One minute after the final shock, the mice were removed from the conditioning chambers and returned to their home-cages. In the immediate shock experiment, mice received 3 shocks 5 seconds after they were placed in context B. In all experiments, memory for context A was tested 1 day after training by returning mice to the chamber for 5 minutes and measuring the freezing response.

**Intraperitoneal injections**

The NMDAR-antagonist CPP (10mg/kg; Sigma-Aldrich, St. Louis, MO) was dissolved in 0.9% saline (pH 7.4) and injected 30 minutes prior to training.