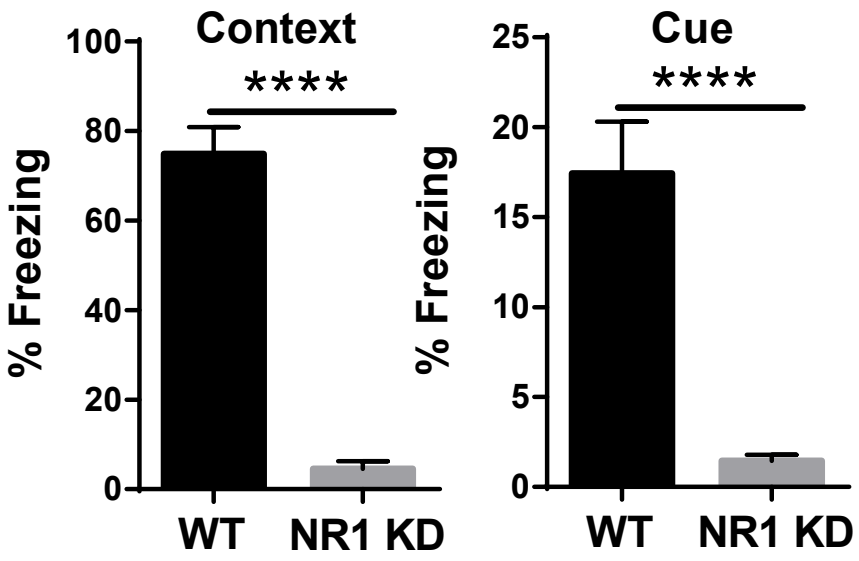
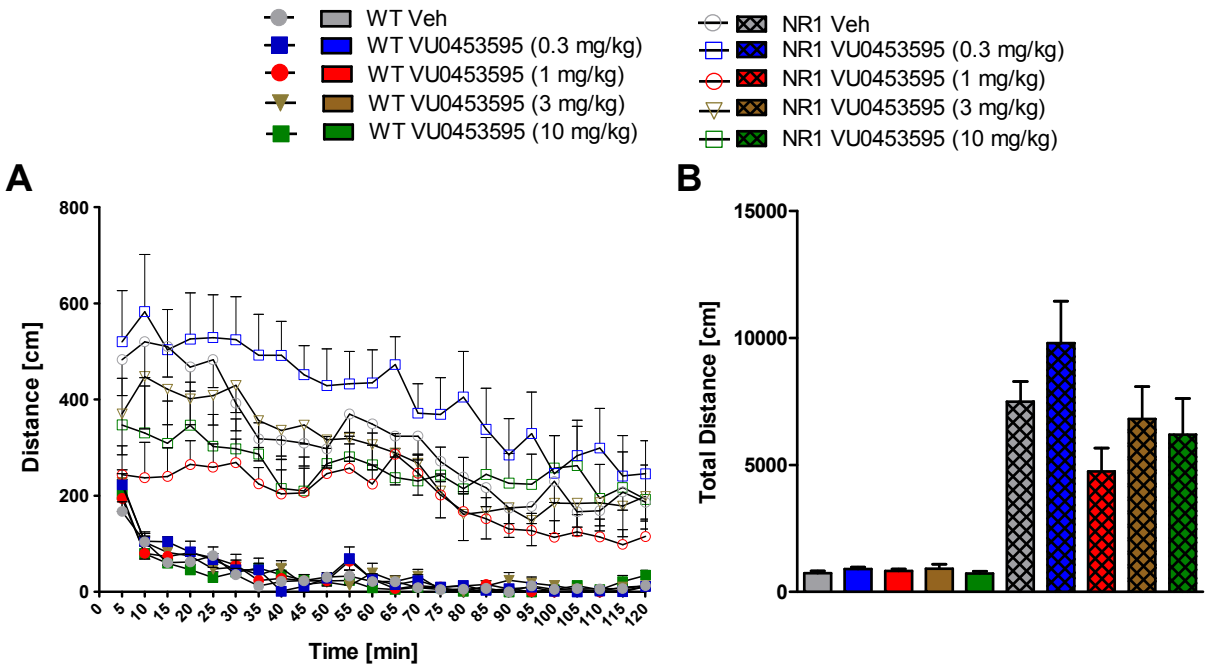
Supplementary Figure 1. Comparison of NR1 KD and WT littermate control mice in context and cue-mediated fear conditioning. Left, NR1 KD mice displayed a significant reduction in time spent freezing compared to WT littermate controls. Right, Similar results were observed in the cue-mediated fear conditioning paradigm. (Unpaired t-test, ****$p < 0.0001$).

Supplementary Figure 2. VU0453595 does not reduce hyperlocomotor activity in NR1 KD mice. Vehicle-treated NR1 KD mice showed excessive locomotor activity when compared to WT littermate controls. Pretreatment with VU0453595 (0.3-10 mg/kg) did not significantly affect locomotor response in NR1 KD or WT mice. (n =9-14/treatment group).



Supplementary Figure 1.



Supplementary Figure 2.

SUPPLEMENTARY METHODS

Contextual- and cued-mediated conditioned freezing. Studies were conducted using conditioning chambers in sound attenuating cubicles equipped with a stainless steel grid floor for shock delivery and a video camera for recording freezing behavior (MedAssociates, Allentown, NJ). To assess ability of NR1 KD mice to learn both contextual and cue-mediated associative learning, we conducted studies across a 72 h period, with initial training occurring on Day 1, testing of contextual conditioned freezing on day 2, and testing cue-mediated conditioned freezing on Day 3. Wildtype and NR1 KD mice were handled for three days prior to study initiation. On the conditioning day, mice were habituated for 1 h in an anteroom. Mice were then placed into the chamber - scented with 1.0 mL 10% vanilla extract and illuminated by a white house light - and exposed to the following events during an 8-min session: 90 s habituation followed by four 30 s tone presentations (85 dB, 2500 Hz) co-terminating with a shock (0.7mA, 1 s) with an inter-tone interval of 60 s, followed by a 90 s interval without any stimuli. Approximately 24 h after conditioning (Day 2), mice were placed in the anteroom for 1 h and then exposed to the same conditioning context (identical environment and conditioning chamber including tactile, light, and odor cues). Freezing behavior, defined as motionless posture, excluding respiratory movements, was measured in the absence of any tone or shock stimuli for 8 min. After this 8 min test mice were returned to their homecage. Approximately 48 h after conditioning (Day 3), mice were returned to the anteroom and habituated under infrared light for 1 h. The test room and chamber were also illuminated by an infrared light only. The context of the chamber was altered with the addition of a white plexiglass floor on top of the shock grid, a black teepee to alter the shape/size of the chamber, and a 0.5 mL 10% *Eucalyptus* oil odor cue. Mice were exposed to the identical testing paradigm as on the conditioning day (e.g. presentation of the 4 tones) but without the shock stimuli. Again, freezing behavior was measured in the absence of any shock stimuli for 8 min. Data are presented as means ± S.E.M. and analyzed by one-way ANOVA followed by Bonferroni's test.