Supplemental information

Seizure-induced LIN28A disrupts pattern separation via aberrant hippocampal neurogenesis

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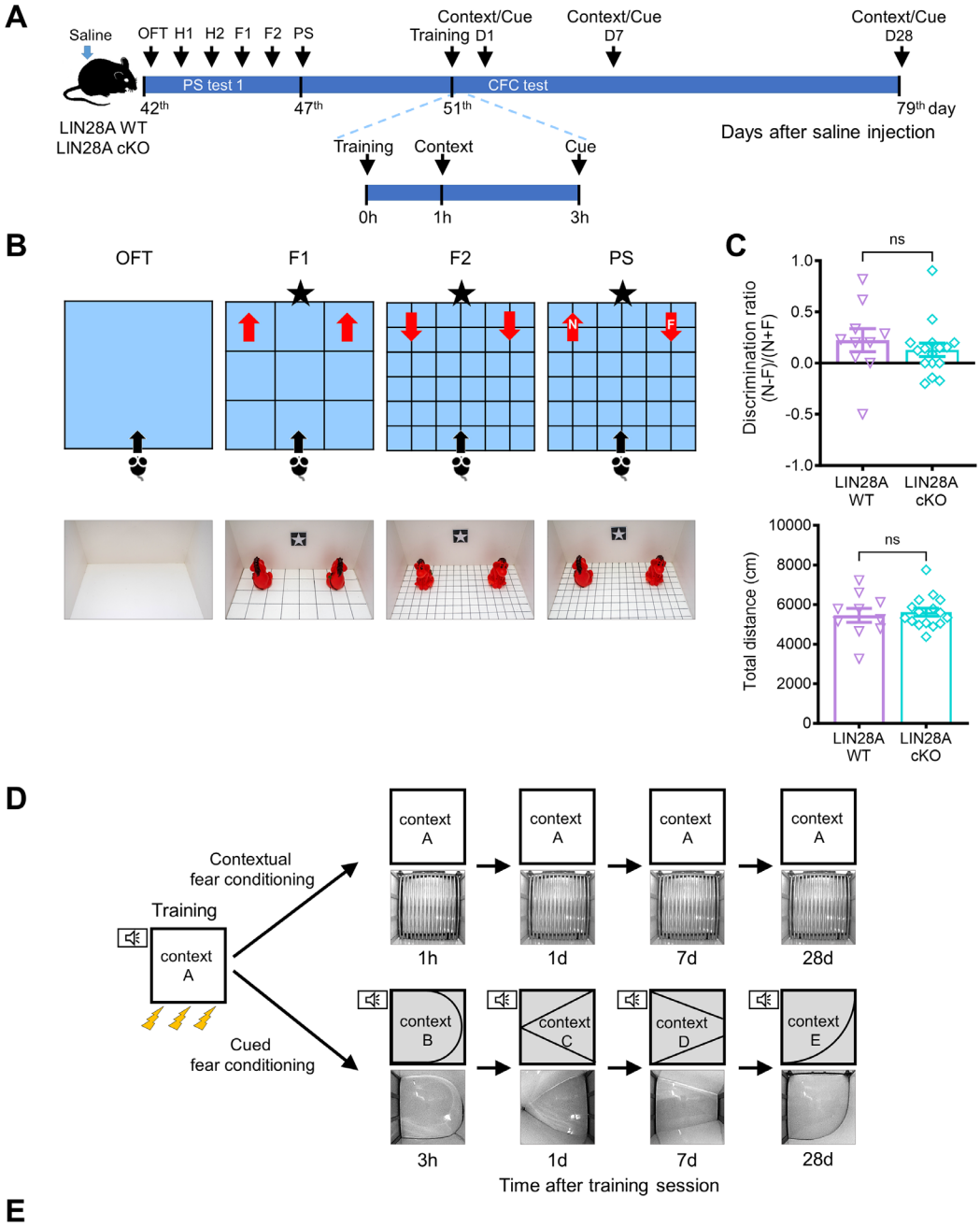
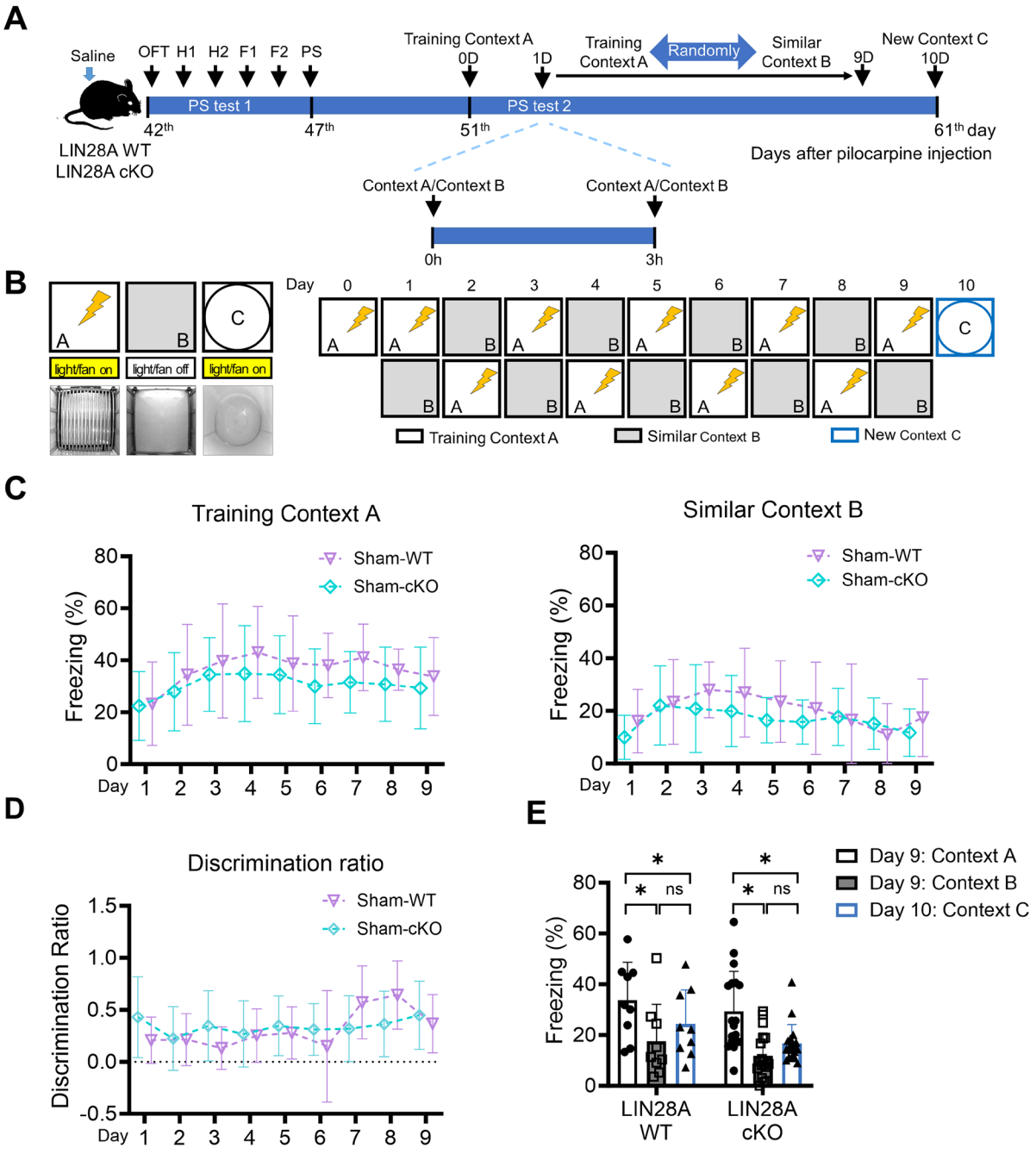
Supplemental figure 1



Supplemental Figure 1. No difference in newborn neuron- and hippocampus-associated memory function between sham-manipulated LIN28A WT and cKO mice. (A) Experimental timeline. Animals with chronic epilepsy were subjected to an open-field test (OFT), pattern separation (PS) test 1, and fear conditioning test. **(B)** A schematic presentation of OFT and PS test 1. **(C)** Graphs showing the discrimination ratio and the distance moved. The LIN28A WT and cKO mice showed no difference in their ability to recognize a novel object from analogous experiences. Discrimination ratio: Mann-Whitney U test was performed. $P = 0.151$, U = 52.500. WT (n = 10), cKO (n = 16); distance moved: Student's *t*-test was performed. $P = 0.680$, t(24) = 0.417. WT (n = 10), cKO (n = 16). **(D)** A schematic illustration of the fear conditioning paradigm. **(E)** Graphs showing the percentage of freezing behavior in contextual and cued fear conditioning tests. The LIN28A WT and cKO mice showed a similar freezing percentage in response to contextual and cued fear conditioning, indicating intact hippocampal memory function. Repeated measures ANOVA was performed. Contextual fear conditioning: $P = 0.199$, F(1,19) = 0.011. WT (n = 9), cKO (n = 12); cued fear conditioning: $P = 0.829$, F(1,19) = 0.048. WT (n = 9), cKO (n = 12). Data are presented as mean ± SEM. ns, not significant.

Supplemental figure 2



Supplemental Figure 2. No difference in fear-based pattern separation between sham-manipulated LIN28A WT and cKO mice. (A) Experimental timeline. Saline-injected sham animals were subjected to an open-field test (OFT), pattern separation (PS) test 1, and PS test 2. **(B)** A schematic presentation of PS test 2. **(C)** Graphs showing the percentage of freezing behavior in training context A and similar context B. Note that LIN28A WT and cKO mice showed comparable freezing behavior in both context A and B. Repeated measures ANOVA was performed. Context A: $P = 0.247$, $F(1,25) =$

1.407. Context B: P = 0.338, F(1,25) = 0.954. WT (n = 9), cKO (n = 18). **(D)** A graph showing discrimination ratio with no change between LIN28A WT and cKO mice. Repeated measures ANOVA was performed. P = 0.661, F(1,25) = 0.197. WT (n = 9), cKO (n = 18). **(E)** A graph showing the freezing percentage when sham-manipulated LIN28A WT and cKO mice were exposed to training context A, similar context B, and completely new context C. Note that both LIN28A WT and cKO mice could recognize context B and C as different contexts compared to original context A. Student's paired t-test was performed. LIN28A WT: context A vs. B, P = 0.011, t(8) = 3.288; context B vs. C, P = 0.092, t(8) = 1.910; context A vs. C, P = 0.034, t(8) = 32.543. LIN28A cKO: context A vs. B, $P < 0.001$, t(17) = 4.619; context B vs. C, P = 0.090, t(17) = 1.795; context A vs. C, P = 0.002, t(17) = 3.686. WT (n = 9), cKO (n = 18). Data are presented as mean ± SEM. *$P < 0.05$. ns, not significant.