

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Figure S1: Increase in NMDAr activation by exogenous bicuculline but not D-serine is lower in 3-hit mice, Figure S2: Maximal synaptic NMDAr activation is higher in female 3-hit mice.

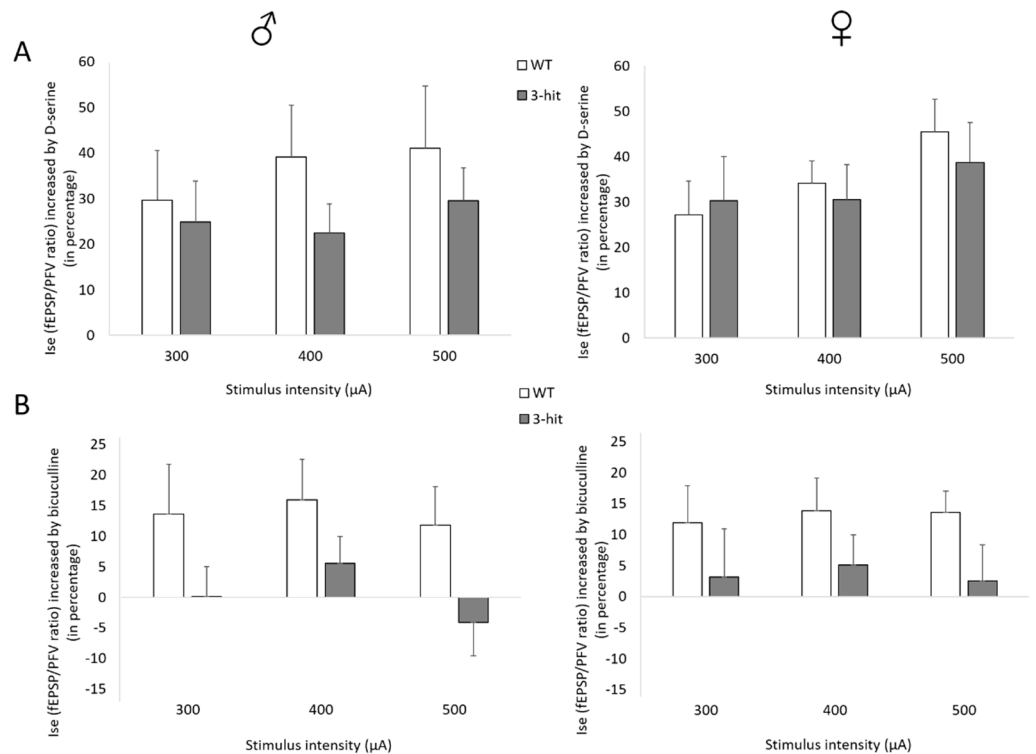


Figure S1. Increase in NMDAr activation by exogenous bicuculline but not D-serine is lower in 3-hit mice. **(A)** Percentage increase in the index of NMDA-r-mediated synaptic efficacy Ise (fEPSP/PFV ratio) in WT and 3-hit slices from male (left) and female (right) mice with increasing stimulus intensity in control vs. D-serine supplemented aCSF (males: WT: $n = 18$ slices vs. 3-hit: $n = 20$ slices; females: WT: $n = 12$ slices vs. 3-hit: $n = 10$ slices). **(B)** Percentage increase in the index of NMDAr-mediated synaptic efficacy Ise (fEPSP/PFV ratio) in WT and 3-hit slices from male (left) and female (right) mice with increasing stimulus intensity in control vs. bicuculline supplemented aCSF (males: WT: $n = 11$ slices vs. 3-hit: $n = 9$ slices; females: WT: $n = 13$ slices vs. 3-hit: $n = 12$ slices). Represented data are Mean $\pm$ SEM; ANOVA or ANOVA with permutation tests.

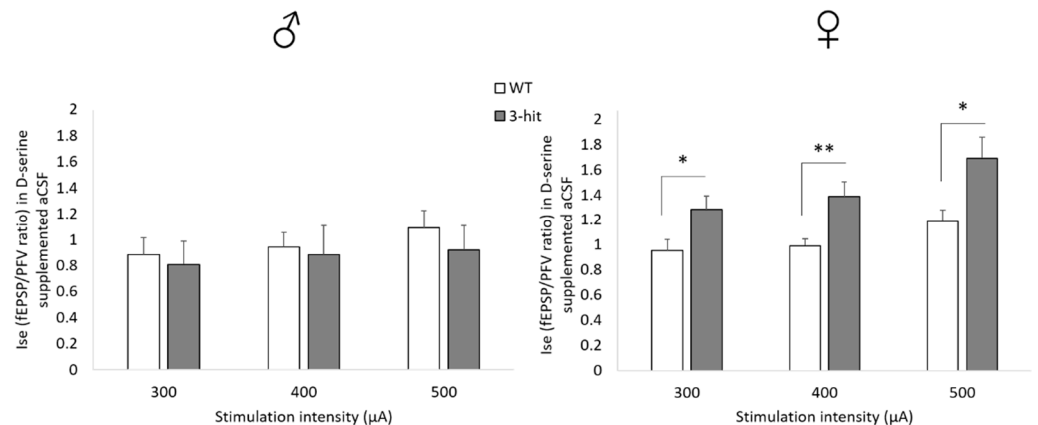


Figure S2. Maximal synaptic NMDAr activation is higher in female 3-hit mice. Index of NMDAr-mediated synaptic efficacy Ise (fEPSP/VA ratio) in hippocampal slices from WT and 3-hit from male (**left**) and female (**right**) mice with increasing stimulus intensity in D-serine supplemented aCSF (males: WT: $n = 18$ slices vs. 3-hit: $n = 20$ slices; females WT: $n = 12$ slices vs. 3-hit: $n = 10$ slices). Represented data are Mean $\pm$ SEM; ANOVA or ANOVA with permutation tests, *: $p < 0.05$; **: $p < 0.01$.