

Expanded View Figures

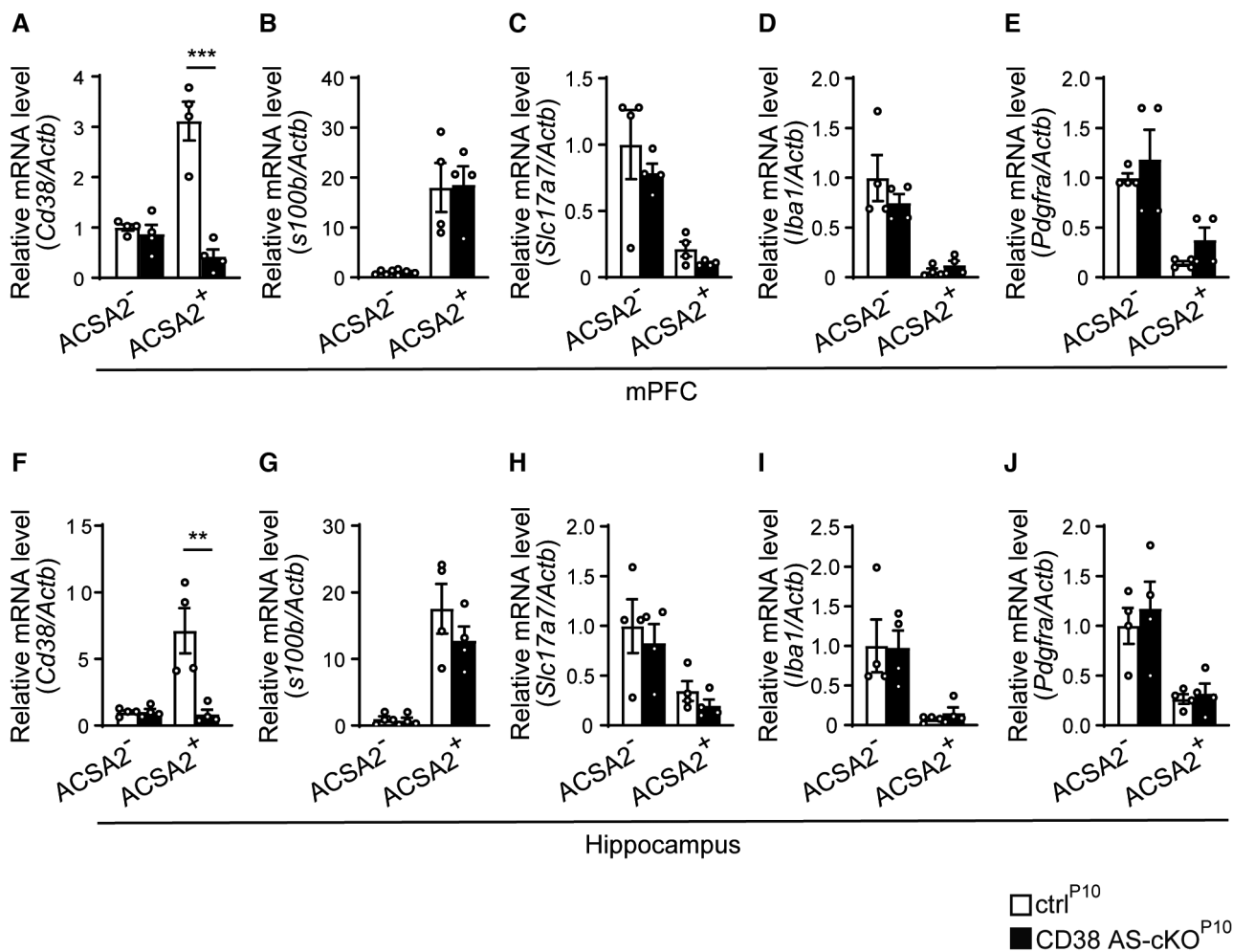


Figure EV1. CD38 is specifically deleted in astrocytes of CD38 AS-cKO^{P10} mice.

A–J RT-qPCR analysis of *Cd38*, *S100b*, *Slc17a7* (VGLUT1), *Iba1*, *Pdgfra* mRNA in ACSA2 negative or positive fraction from the mPFC (A–E) and hippocampus (F–J) of ctrl^{P10} and CD38 AS-cKO^{P10} mice. Astrocytes were enriched by magnetic bead assisted cell sorting (MACS) for astrocytes-specific ACSA2 antigen ($n = 4$ animals per genotype, two-way ANOVA followed by Bonferroni's multiple comparisons test).

Data information: Data represent means \pm SEM, ** $P < 0.01$, *** $P < 0.001$.

Figure EV2. Astrocyte-specific deletion of CD38 decreases expression of GFAP, s100 β and Cx43 in the developing mPFC.

- A Representative western blots of CD38, GFAP, Cx43, NDRG2, VGlut1, PSD95, MAG, and β -actin in the mPFC of ctrl^{P10} and CD38 AS-cKO^{P10} mice at P21 (two animals per genotype are shown).
- B–H Relative optical densities of CD38, GFAP, Cx43, NDRG2, VGlut1, PSD95, MAG, and β -actin normalized to the loading control β -actin ($n = 4$ animals per genotype, two-tailed unpaired Student's t -test).
- I Representative western blots of CD38 and β -actin in the mPFC of ctrl^{P42} and CD38 AS-cKO^{P42} mice at P84 (two animals per genotype are shown).
- J Bar graphs depict the relative optical density of CD38 and β -actin normalized to the loading control β -actin ($n = 3$ animals per genotype, two-tailed unpaired Student's t -test).
- K–T (K, M, O, Q, S) Immunohistochemistry for GFAP, s100 β , NDRG2 and SOX9 in the mPFC and MBP in the motor cortex of ctrl^{P10} and CD38 AS-cKO^{P10} mice at P21. Nuclei were counterstained with DAPI. Scale bars, 50 μ m (K, M, O, and Q), and 100 μ m (S). (L, N, P, R, T) Quantification of astrocyte-specific protein-positive cells and MBP intensity ($n = 4$ animals per genotype, two-tailed unpaired Student's t -test).

Data information: Data represent means \pm SEM. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Source data are available online for this figure.

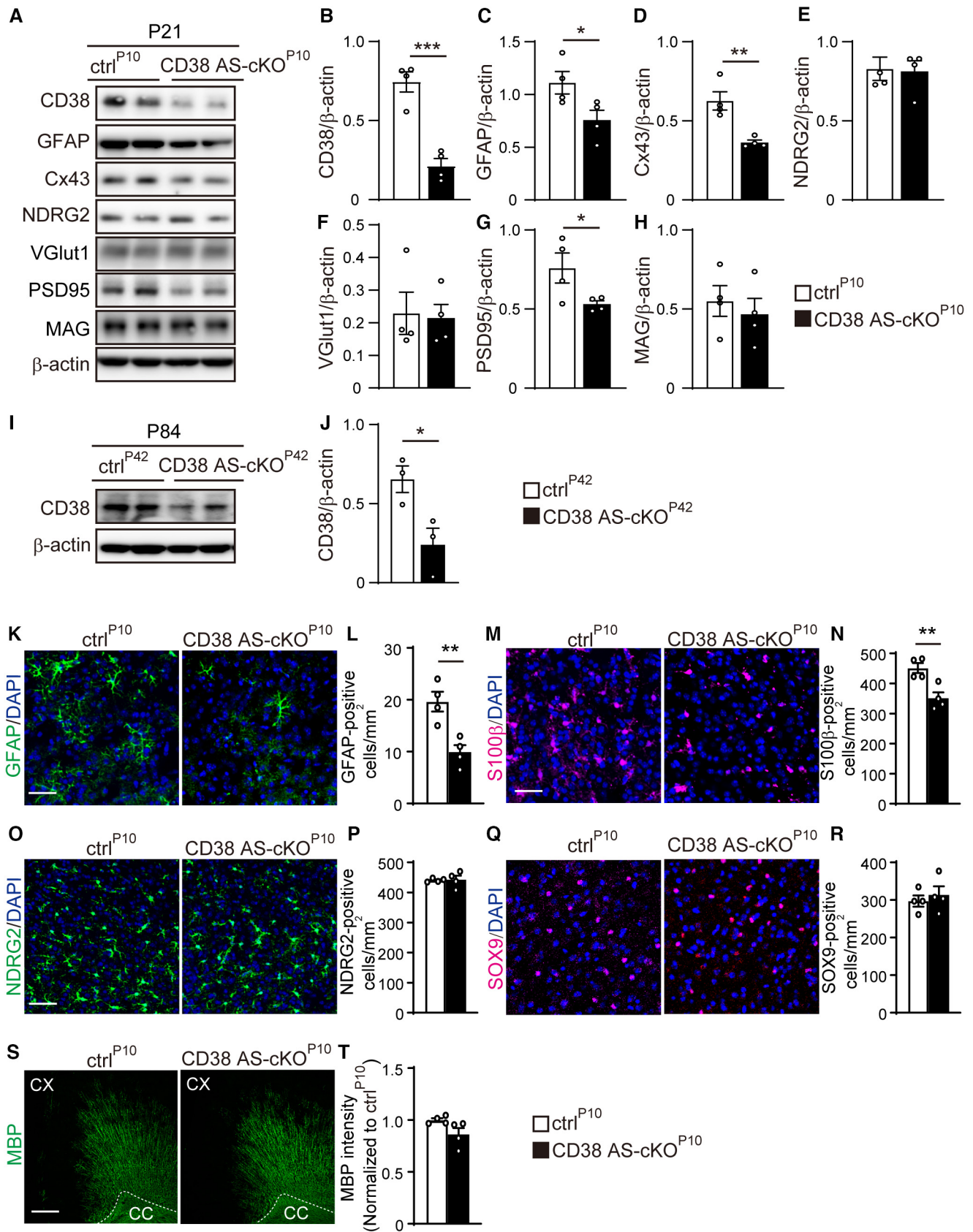


Figure EV2.

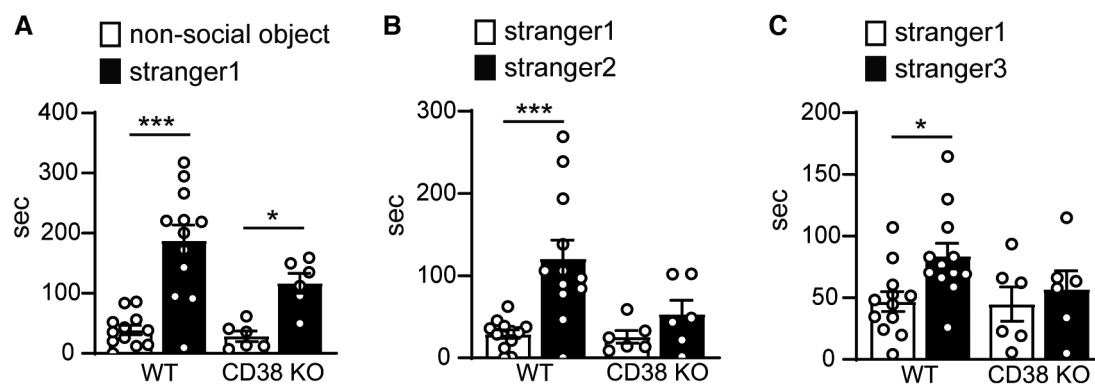


Figure EV3. Social novelty is impaired in constitutive CD38 KO mice.

- A Sociability of WT and CD38 KO mice ($n = 6$ and 12 animals in WT and CD38 KO mice, respectively, two-way ANOVA followed by Bonferroni's multiple comparisons test).
- B Social novelty of WT and CD38 KO mice ($n = 6$ and 12 animals in WT and CD38 KO mice, respectively, two-way ANOVA followed by Bonferroni's multiple comparisons test).
- C Social memory of WT and CD38 KO mice ($n = 6$ and 12 animals in WT and CD38 KO mice, respectively, two-way ANOVA followed by Bonferroni's multiple comparisons test).

Data information: Data represent means \pm SEM. * $P < 0.05$, *** $P < 0.001$.

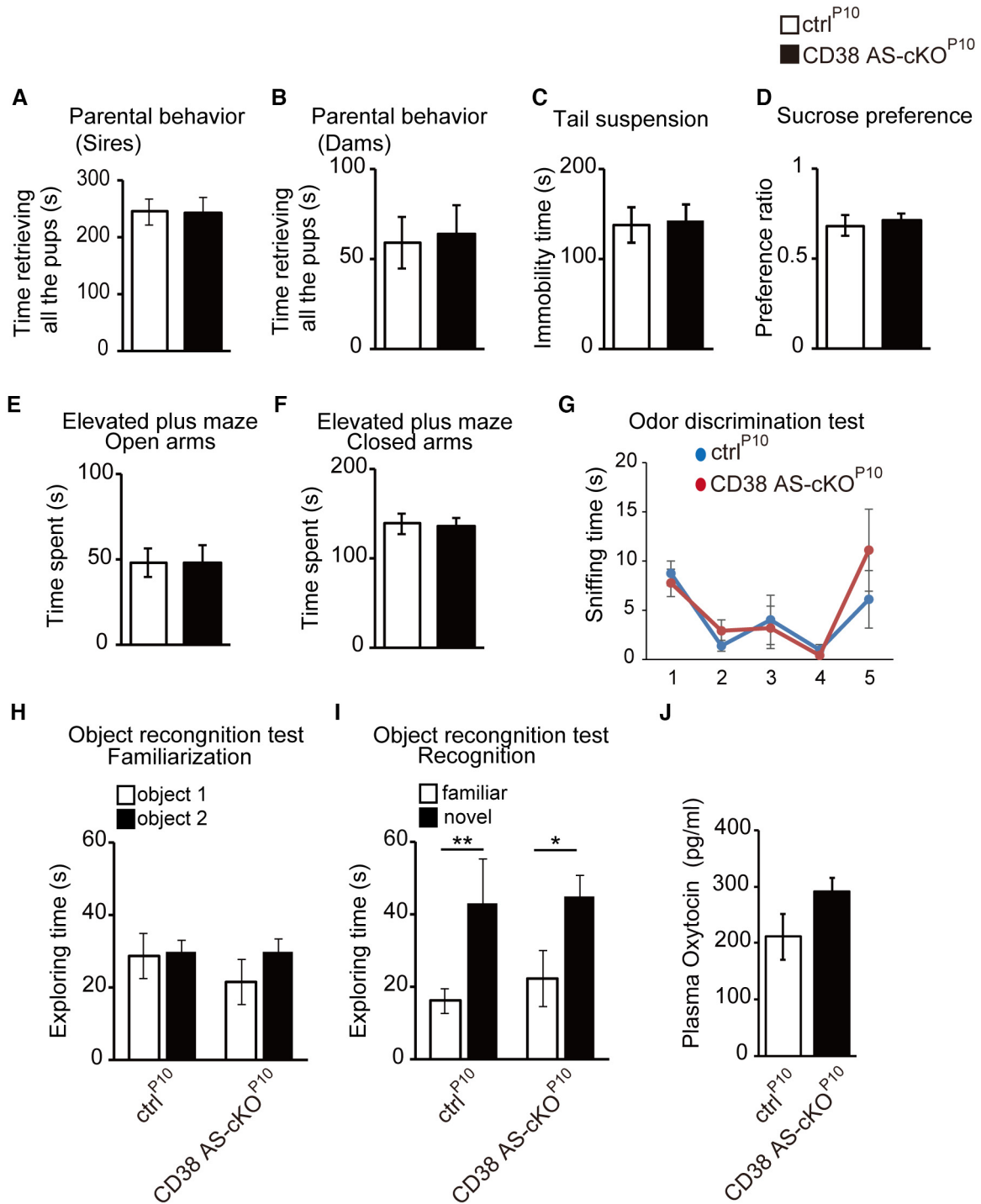


Figure EV4.

Figure EV4. Behavioral phenotypes except social memory are not impaired in CD38 AS-cKO^{P10} mice.

- A, B Pup retrieval behavior. Time to complete retrieving all the pups of ctrl^{P10} and CD38 AS-cKO^{P10} sires (A) and dams (B) (*n* = 5 animals per genotype, two-tailed unpaired Student's *t*-test).
- C Tail suspension test of ctrl^{P10} and CD38 AS-cKO^{P10} mice (*n* = 10 animals per genotype, two-tailed unpaired Student's *t*-test).
- D Sucrose preference test of ctrl^{P10} and CD38 AS-cKO^{P10} mice (*n* = 10 animals per genotype, two-tailed unpaired Student's *t*-test).
- E, F Elevated plus maze test. Time in open arms (E) and closed arms (F) for ctrl^{P10} and CD38 AS-cKO^{P10} mice (*n* = 10 animals per genotype, two-tailed unpaired Student's *t*-test).
- G Odor discrimination test of ctrl^{P10} and CD38 AS-cKO^{P10} mice (*n* = 5 animals per genotype, two-way ANOVA followed by Bonferroni's multiple comparisons test).
- H, I Object recognition test of ctrl^{P10} and CD38 AS-cKO^{P10} mice. Exploring time during the acquisition phase (H) and the recognition trial (I) (*n* = 6 animals per genotype, two-way ANOVA followed by Bonferroni's multiple comparisons test).
- J Plasma oxytocin concentrations in ctrl^{P10} and CD38 AS-cKO^{P10} mice (*n* = 7 and 10 animals in ctrl^{P10} and CD38 AS-cKO^{P10} mice, respectively; two-tailed unpaired Student's *t*-test).

Data information: Data represent means ± SEM. **P* < 0.05, ***P* < 0.01.

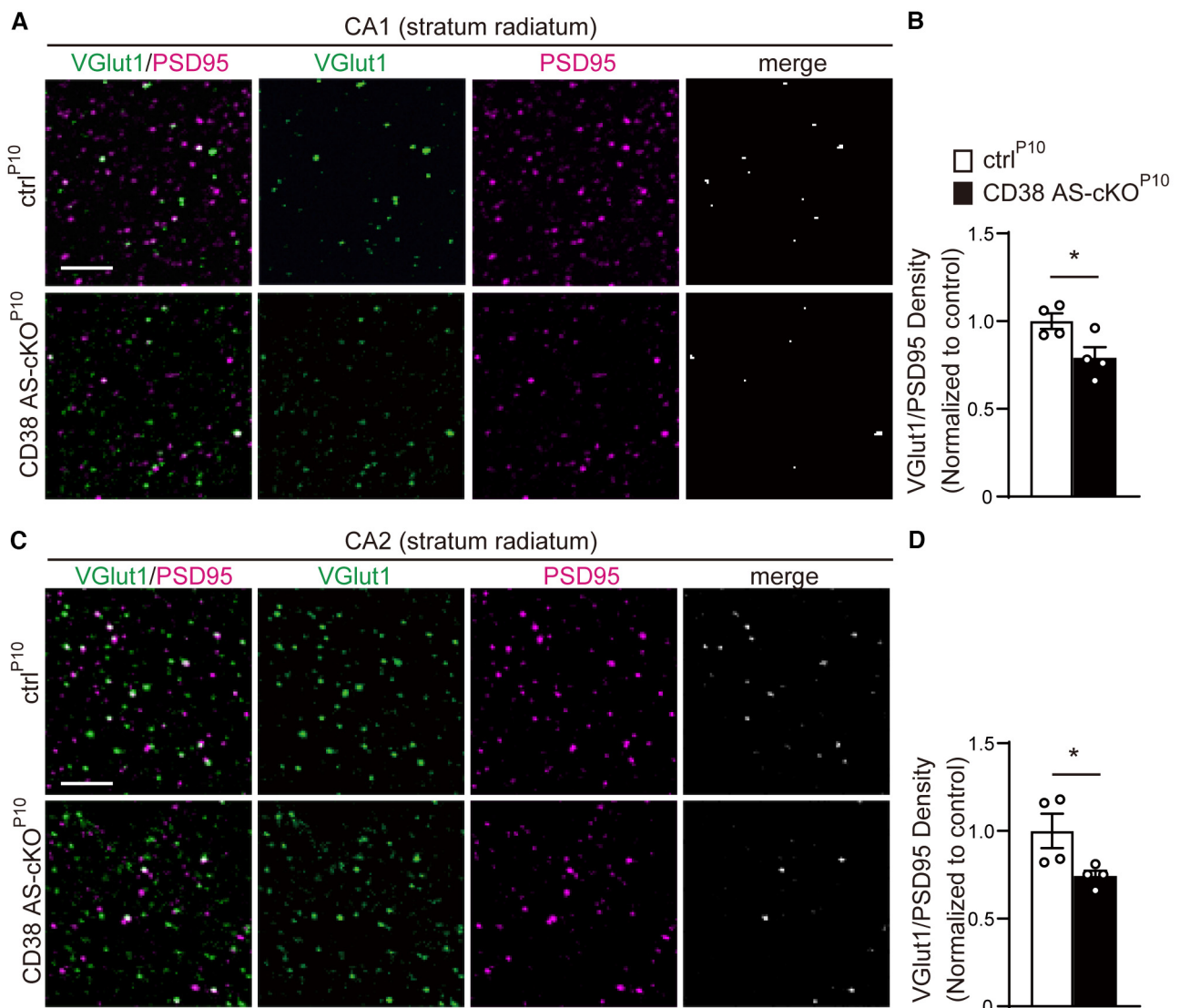


Figure EV5.

**Figure EV5. Excitatory synapses are reduced in the hippocampal neurons in CD38 AS-cKO^{P10} mice.**

A–D (A, C) Immunohistochemistry for VGLut1 (green) and PSD95 (magenta) in the stratum radiatum of the CA1 (A) and CA2 (C) of ctrl^{P10} and CD38 AS-cKO^{P10} mice at P70. The VGLut1 and PSD95 channels are separated in the middle panels. Right panels are colocalized VGLut1 and PSD95 puncta. Scale bar, 10 μ m. (B, D) Quantification synapses (colocalization of VGLut1 and PSD95) in each area of the hippocampus ($n = 4$ animals per genotype, two-tailed unpaired Student's t -test).

Data information: Data represent means \pm SEM. * $P < 0.05$.