Expanded View Figures

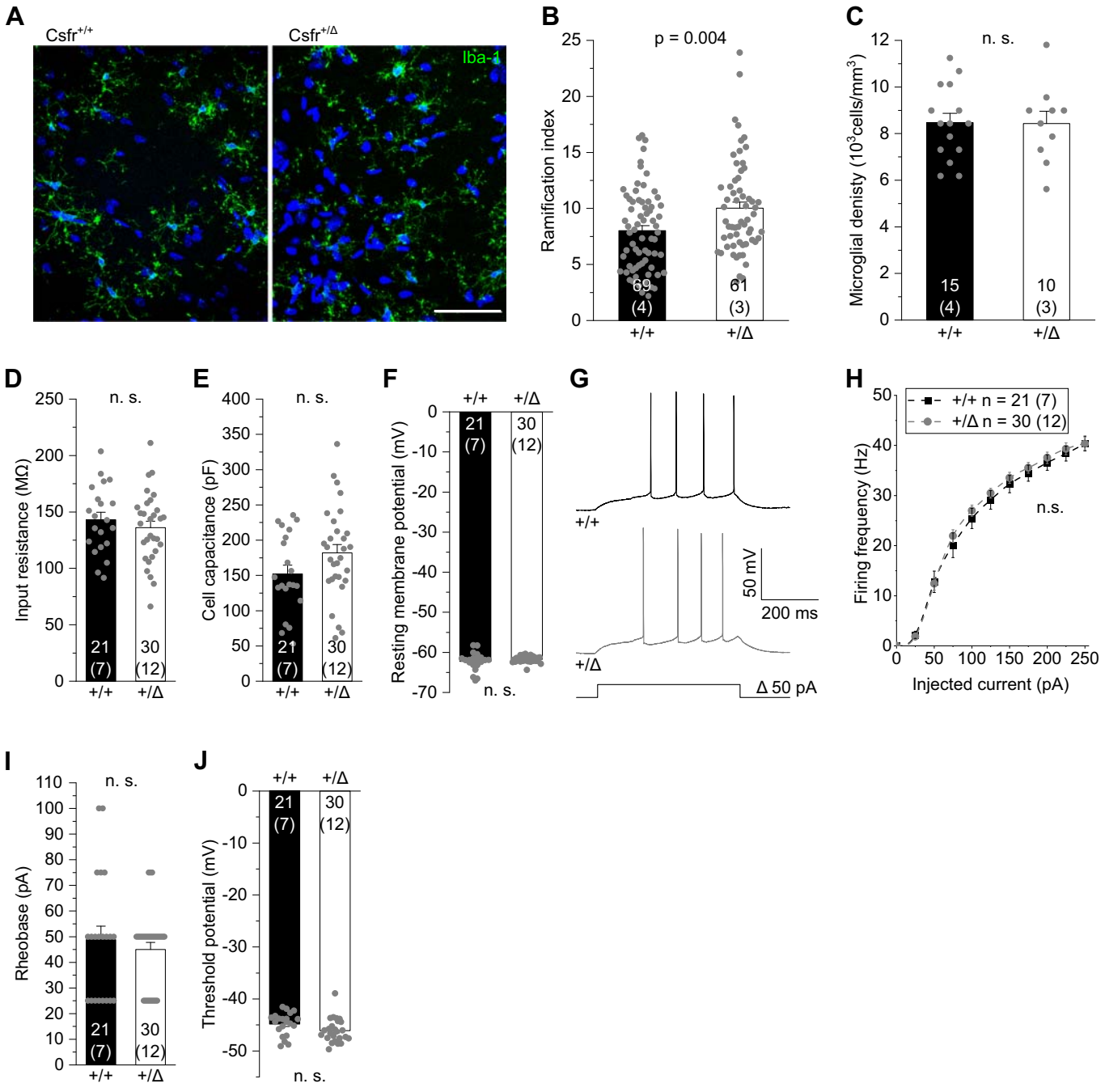

Figure EV1. Normal excitability of CA1 pyramidal cells in heterozygous *Csf1r*$^{+/\Delta FIRE}$ mice.

(**A**) Specimen confocal images illustrating microglia by Iba1 immunoreactivity (green) in acute hippocampal slices of *Csf1r*$^{+/\Delta FIRE}$ (+/Δ) and WT littermates (+/+). DAPI labeling of cellular nuclei in blue. Scale bar, 50 µm. (**B**, **C**) Quantification of microglial ramification (**B**) and cell density (**C**) in the CA1 *stratum radiatum*. (**D–F**) Analysis of input resistance (**D**), cell capacitance (**E**) and resting membrane potential (**F**) of CA1 pyramidal cells. (**G**) Specimen traces showing action potential firing patterns of CA1 pyramidal cells in response to 500 ms depolarizing current injections. (**H**). Corresponding course of action potential firing frequencies of CA1 pyramidal cells on increasing depolarizations. (**I**, **J**) Values for rheobase (**I**) and action potential threshold voltage (**J**). Data information: Data indicate mean ± SEM. Numbers on bars show tested cells or number of slices (**C**) and (number of animals). *P* values are from unpaired Student's *t* (**B–F**, **J**) or Mann–Whitney tests (**I**) and two-way ANOVA (**H**).

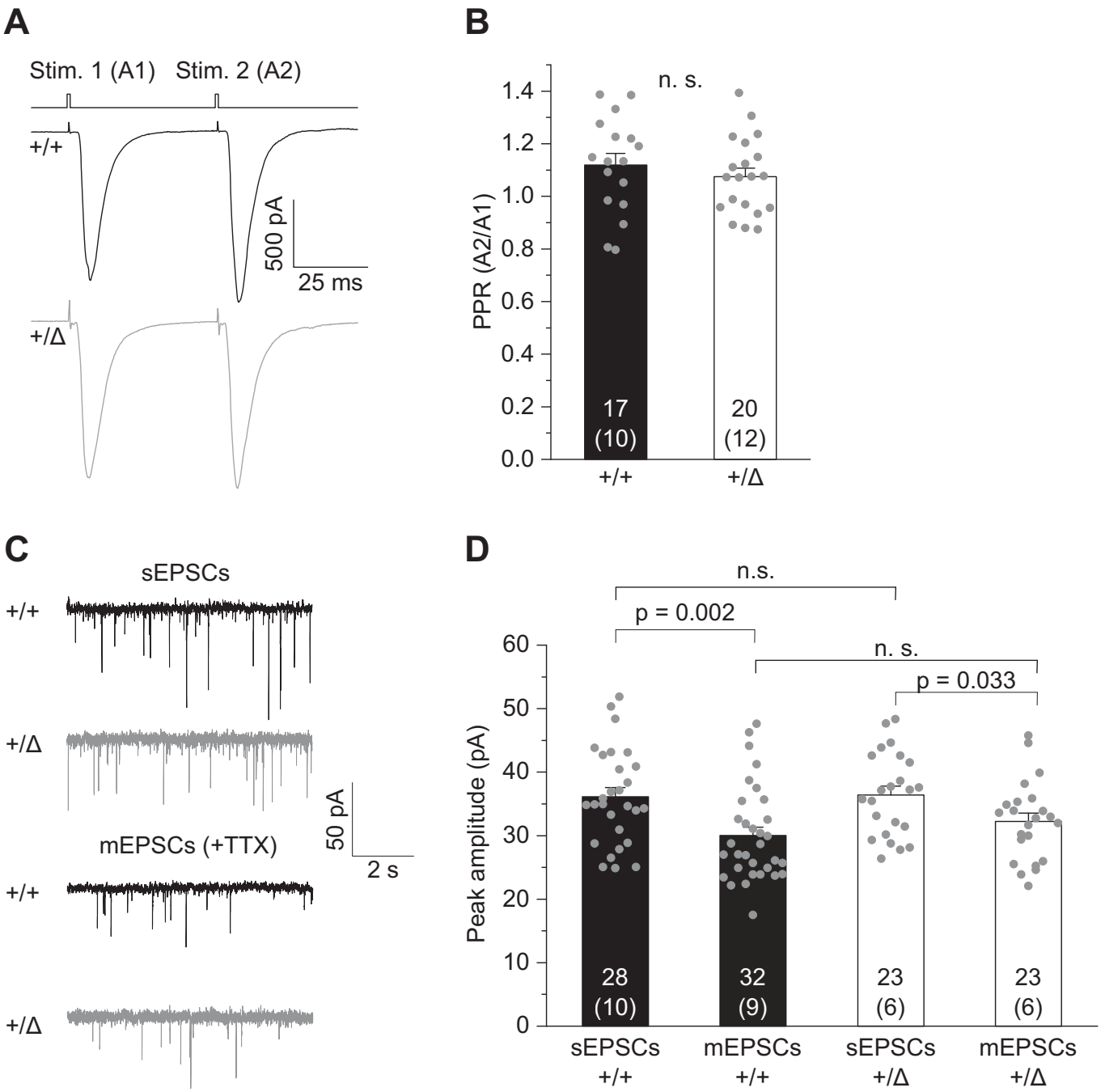

Figure EV2. Normal glutamatergic transmission in heterozygous *Csf1r*$^{+/\Delta FIRE}$ mice.

(**A**) Example traces (EPSCs) of CA1 pyramidal cells after paired-pulse stimulation at 50 ms inter-stimulus intervals. (**B**) Comparison of paired-pulse ratios (PPR) as the quotient of the second vs first EPSC amplitude (A2/A1) of CA1 pyramidal cells. (**C**) Specimen traces showing AMPAR-mediated spontaneous EPSCs (sEPSCs) and miniature EPSCs (mEPSCs) in the presence of 300 nM TTX of CA1 pyramidal cells. (**D**) Comparison of peak amplitudes of sEPSCs and mEPSCs. Data information: Data are represented as mean ± SEM. Numbers on bars indicate tested cells and (number of animals). *P* values are from unpaired Student's *t* (**B**, **D**, for +/Δ and sEPSC comparison) or Mann–Whitney tests (**D**, for +/+ and mEPSC comparison).

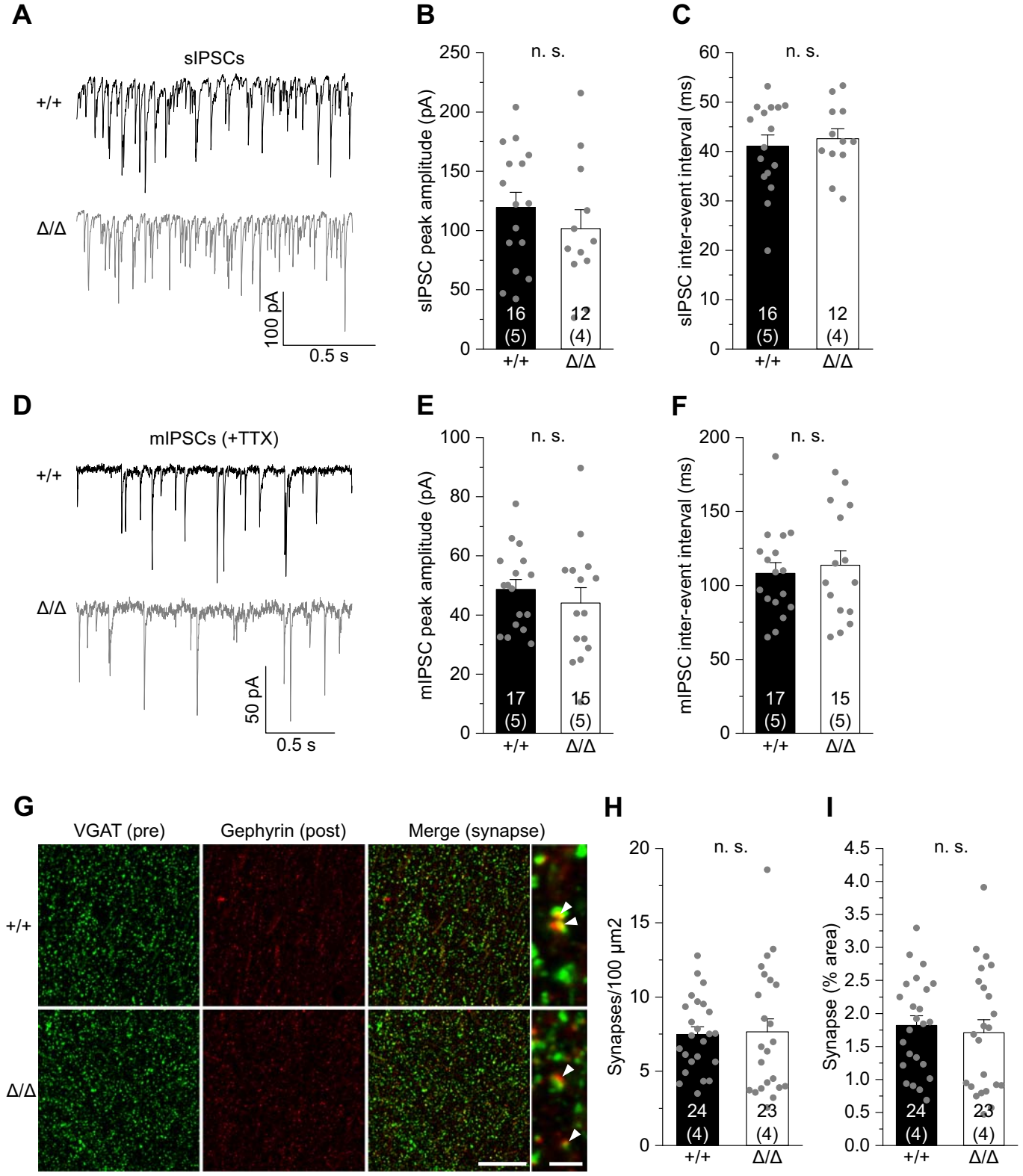
A
sIPSCs
+/+
Δ/Δ
100 pA
0.5 s
B
n. s.
sIPSC peak amplitude (pA)
250
200
150
100
50
0
16
(5)
12
(4)
+/+
Δ/Δ
C
n. s.
sIPSC inter-event interval (ms)
60
50
40
30
20
10
0
16
(5)
12
(4)
+/+
Δ/Δ
D
mIPSCs (+TTX)
+/+
Δ/Δ
50 pA
0.5 s
E
n. s.
mIPSC peak amplitude (pA)
100
80
60
40
20
0
17
(5)
15
(5)
+/+
Δ/Δ
F
n. s.
mIPSC inter-event interval (ms)
200
150
100
50
0
17
(5)
15
(5)
+/+
Δ/Δ
G
VGAT (pre)
Gephyrin (post)
Merge (synapse)
+/+
Δ/Δ
H
n. s.
Synapses/100 µm2
20
15
10
5
0
24
(4)
23
(4)
+/+
Δ/Δ
I
n. s.
Synapse (% area)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
24
(4)
23
(4)
+/+
Δ/Δ

Figure EV3. Unaltered inhibitory synaptic transmission of CA1 pyramidal cells in *Csf1r*$^{\Delta FIRE/\Delta FIRE}$ mice.

(**A**) Specimen traces showing $GABA_A$ receptor-evoked spontaneous inhibitory postsynaptic currents (sIPSCs) of CA1 pyramidal cells in +/+ and Δ/Δ mice. (**B**, **C**) Comparison of sIPSC peak amplitudes (**B**) and inter-event intervals (**C**). (**D**) Specimen traces showing miniature IPSCs (mIPSCs) of CA1 pyramidal cells. (**E**, **F**) Comparison of peak amplitudes (**E**) and inter-event intervals (**F**). (**G**) Confocal images showing VGAT-labeled presynaptic puncta (green) and Gephyrin-labeled postsynaptic puncta (red) in the CA1 *stratum radiatum* (left and middle) and colocalization of puncta (right, arrowheads). Scale bars, 20 μm and 2 μm (for expanded view). (**H**, **I**) Quantification of colocalized puncta (inhibitory synapses) per 100 μm^2 (**H**) and their area covered (**I**). Data information: Data indicate mean ± SEM. Numbers on bars show tested cells and (number of animals). *P* values are from unpaired Student's *t* (**B**, **C**, **E**, **F**, **I**) and Mann–Whitney (**H**) tests.

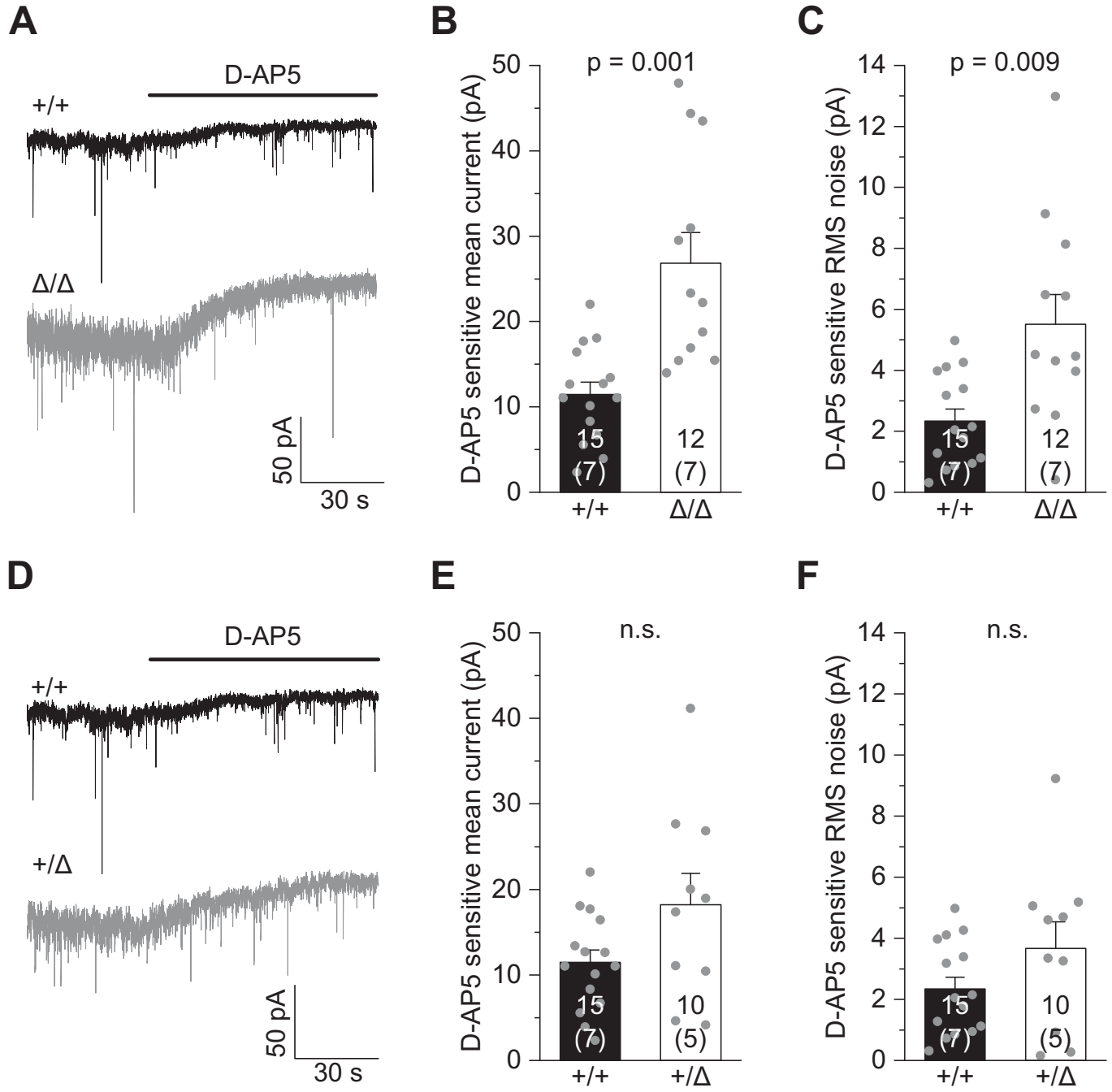

Figure EV4. Increased tonic NMDA current in *Csf1r*$^{\Delta FIRE/\Delta FIRE}$ mice.

(**A**) Example traces showing changes in holding current after application of 50 µM D-AP5 for Δ/Δ compared with +/+ mice, reflecting blockade of all tonic NMDAR-mediated currents in CA1 pyramidal cells. Measurements were done in nominally Mg^{2+}-free extracellular solution in the presence of 300 nM TTX and 10 µM glycine. (**B**, **C**) Comparison of the D-AP5-sensitive mean holding current (**B**) and root mean square (RMS) noise (**C**) for the different genotypes. Note the contribution of both synaptic and extrasynaptic NMDA receptors to these parameters. (**D–F**) Same as for (**A–C**), but comparison of wild-type (+/+) and heterozygous phenotype (+/Δ). Data information: Data are represented as mean ± SEM. Numbers on bars indicate tested cells and (number of animals). *P* values are from unpaired Student's *t* tests.

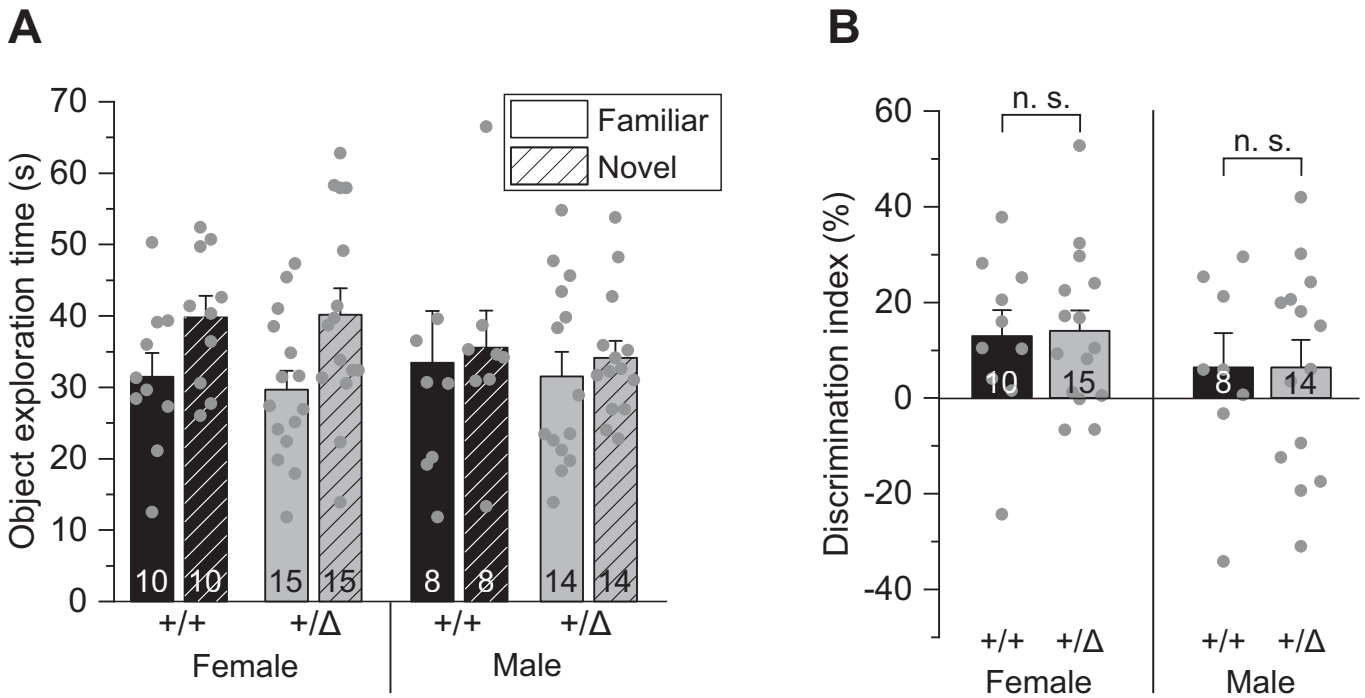

Figure EV5. Unaltered object recognition memory in heterozygous *Csf1r*$^{+/\Delta FIRE}$ mice.

(**A**) Comparison of exploration times of the familiar and novel object after habituation for male and female +/Δ and +/+ mice. (**B**) Comparison of the respective discrimination indices (see "Methods"). Data information: Data are represented as mean ± SEM. Numbers on bars indicate number of tested animals. *P* values are from two-way ANOVA (**B**).