Expanded View Figures

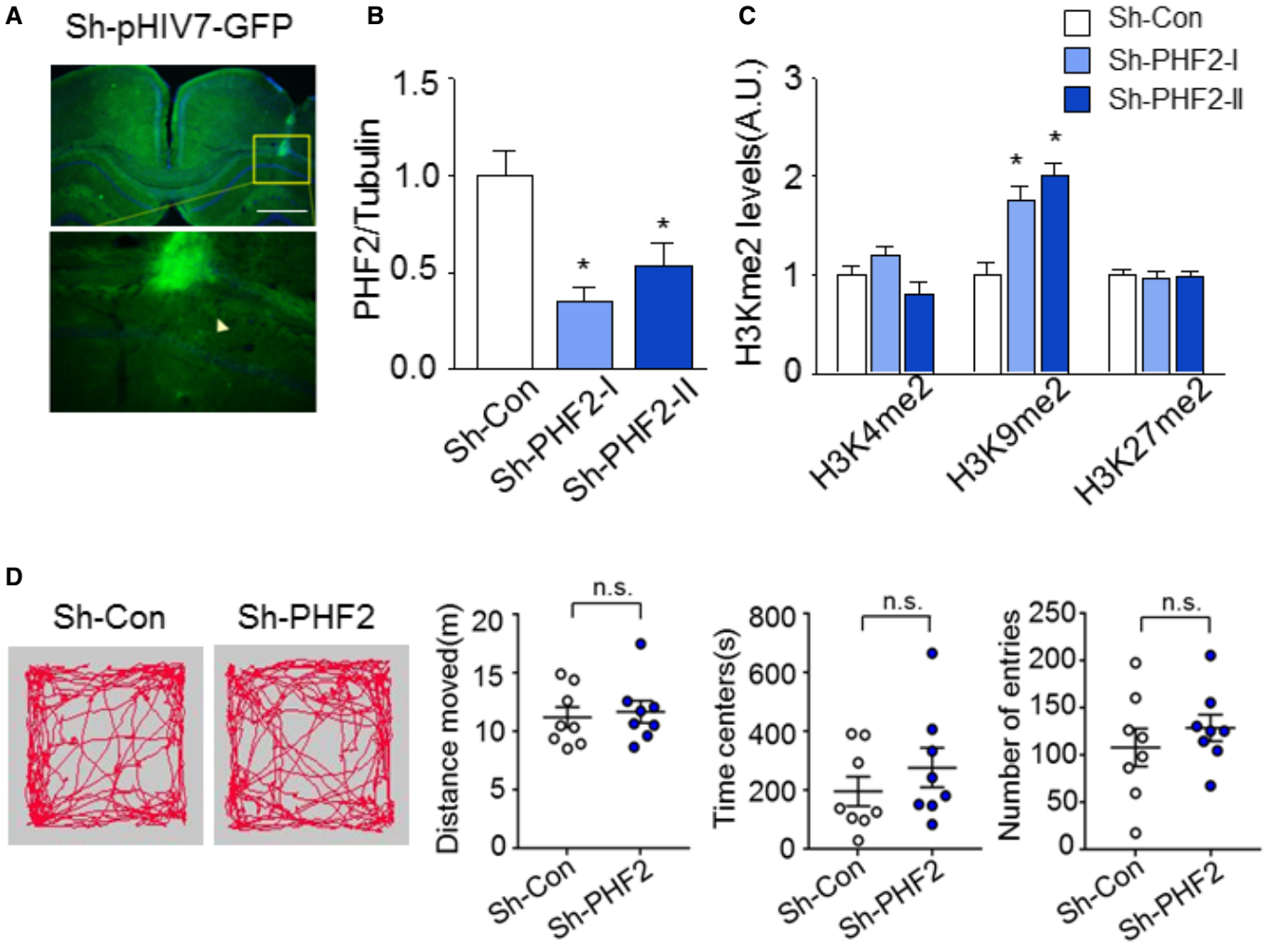

Figure EV1.

Figure EV1. Mice lacking PHF2 show no difference in basal behavior tests.

A Stereotaxic injection of GFP-expressing lentiviral particles into bilateral hippocampus CA1 in WT mice. Scale bar, 200 μm.
B Quantification of the immunoblot analysis. PHF2 protein levels of hippocampal tissues in sh-PHF2 (I, II) mice were normalized against tubulin and quantified as fold change relative to that seen in sh-Con mice.
C The H3Kme2 protein levels in sh-PHF2 (I, II) mice were normalized against H3 and quantified as fold change relative to that seen in sh-Con mice.
D Open field test shows that basal anxiety and locomotor activity in sh-PHF2 mice were not altered in comparison with sh-Con mice. Path traces of single-trial open field tests were recorded for all sh-Con and sh-PHF2 mice (left). Distance moved, time in center, and number of entries were scored (right).
E Rotarod test showed no differences in motor activity for sh-Con and sh-PHF2 mice.

Data information: In (B, C), data are presented as the mean ± SD ($n = 6$). *$P < 0.05$ (unpaired, two-sided Student's t-test). In (D, E), data are presented as the mean values ± SEM ($n = 8$). Data were analyzed using unpaired, two-sided Student's t-test.

Figure EV2. PHF2 t/g mice show no difference in basal behavior tests.

A Quantification of the immunoblot analysis. PHF2 protein levels of PHF2 t/g mice were normalized against tubulin and quantified as fold change relative to that seen in WT littermate mice.
B Immunofluorescence of hippocampal coronal sections of WT littermate and Flag-PHF2 t/g mice stained with Flag (green), MAP2 (red), and DAPI (blue). Ectopic expression of Flag-PHF2 in the CA1 region of the hippocampus of PHF2 t/g compared to WT littermate mice. Scale bar, 200 μm.
C H3Kme2 protein levels in PHF2 t/g mice were normalized against H3 and quantified as fold change relative to levels in WT mice.
D Path traces of single-trial open field tests for WT littermate and PHF2 t/g mice (left). No differences in distance moved, time spent in the center, or number of entries to the center area were observed between the two groups (right).
E No difference in rotarod motor activity was observed between WT littermate and PHF2 t/g mice.
F No difference in swimming ability was observed between WT littermate and PHF2 t/g mice.

Data information: In (A, C), data are presented as the mean ± SD ($n = 6$). * $P < 0.05$ (unpaired, two-sided Student's t-test). In (D–F), data are presented as the mean values ± SEM ($n = 9$). Data were analyzed using unpaired, two-sided Student's t-test.

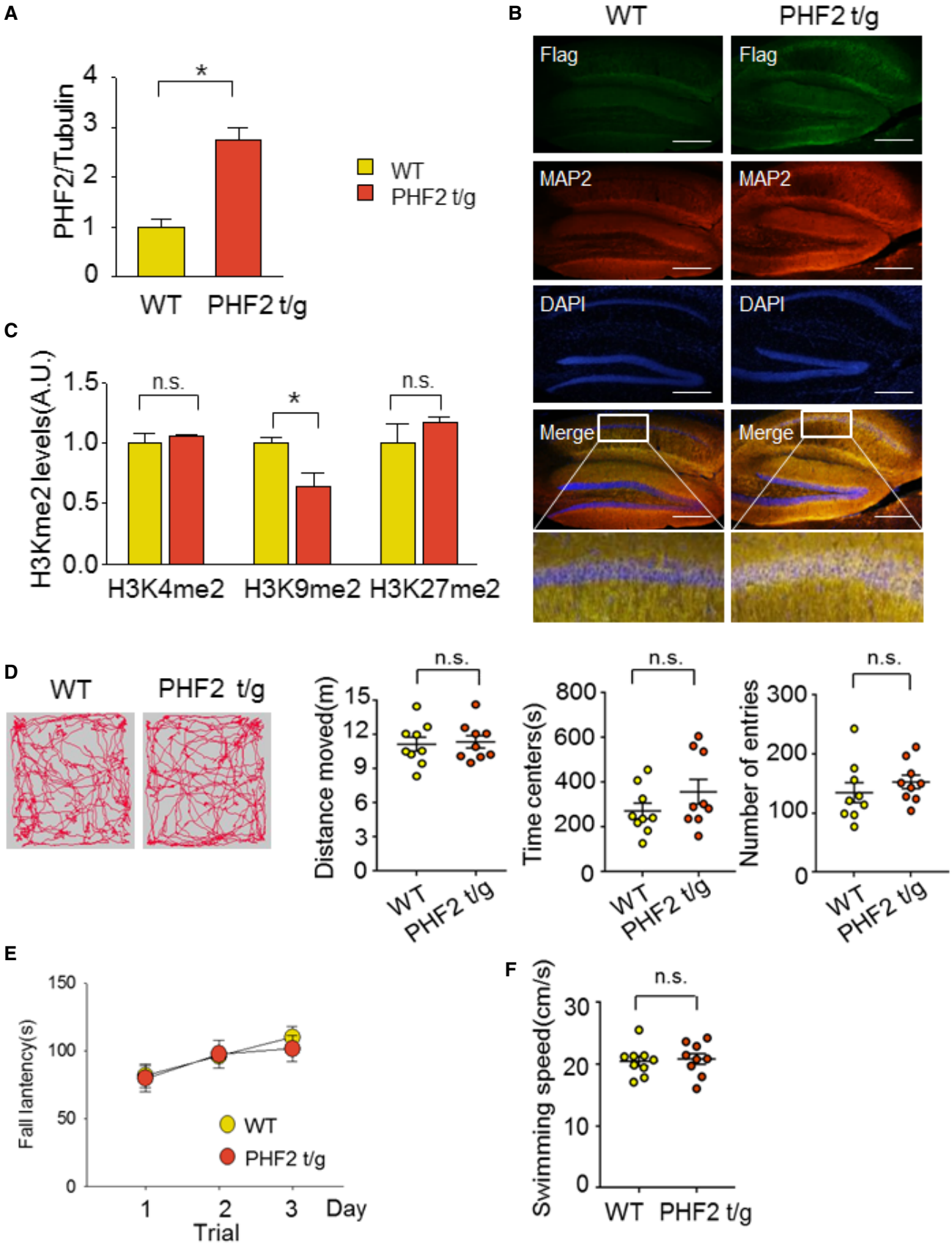

Figure EV2.

Figure EV3. BDNF-HFS mimics the protein synthesis-dependent enhancement of LTP observed in PHF2 t/g mice.

A Input–output of the SC-CA1 synapse of sh-Con or sh-PHF2 expressing mice is represented by fiber volley and fEPSP slope, respectively. Each point represents a mean for a narrow range of fiber volley amplitudes. Representative raw traces are shown for each fiber volley amplitude. Scale bar, 1 mV/5 ms.

B Relationship of PPR of the SC-CA1 synapses in the hippocampus of sh-Con (white) and sh-PHF2 (blue) mice. Example raw traces for PPR are shown for 60-ms intervals. Scale bar: 1 mV/20 ms.

C SC-CA1 synapses of WT and PHF2 t/g mice show no differences in input–output relationship. Representative raw traces are shown for each fiber volley amplitude. Scale bar, 1 mV/5 ms.

D PPR is shown for PHF2 t/g mice in comparison with WT mice. Example raw traces for PPR are shown for 60-ms intervals. Scale bar: 1 mV/20 ms.

E WT hippocampal slices were pre-incubated with BDNF (20 ng/ml) for > 1 h before HFS induction. BDNF-HFS-induced LTP enhancement was blocked by simultaneous application of CHX (60 μM). Example traces of baseline (1: black) and 40 min after LTP induction (2: red) are shown for BDNF-treated and BDNF + CHX-treated WT hippocampal slices (Middle). Scale bar, 1 mV/5 ms. Comparison of LTP at 40 min post-HFS induction (right).

Data information: In (A–E), data are presented as the mean values ± SEM (sh-Con, $n = 8$; sh-PHF2, $n = 6$; WT, $n = 11$; PHF2 t/g, $n = 12$, BDNF on WT slices, $n = 8$; BDNF+CHX on WT slices, $n = 6$). $^{**}P < 0.01$ (unpaired, two-sided Student's t-test).

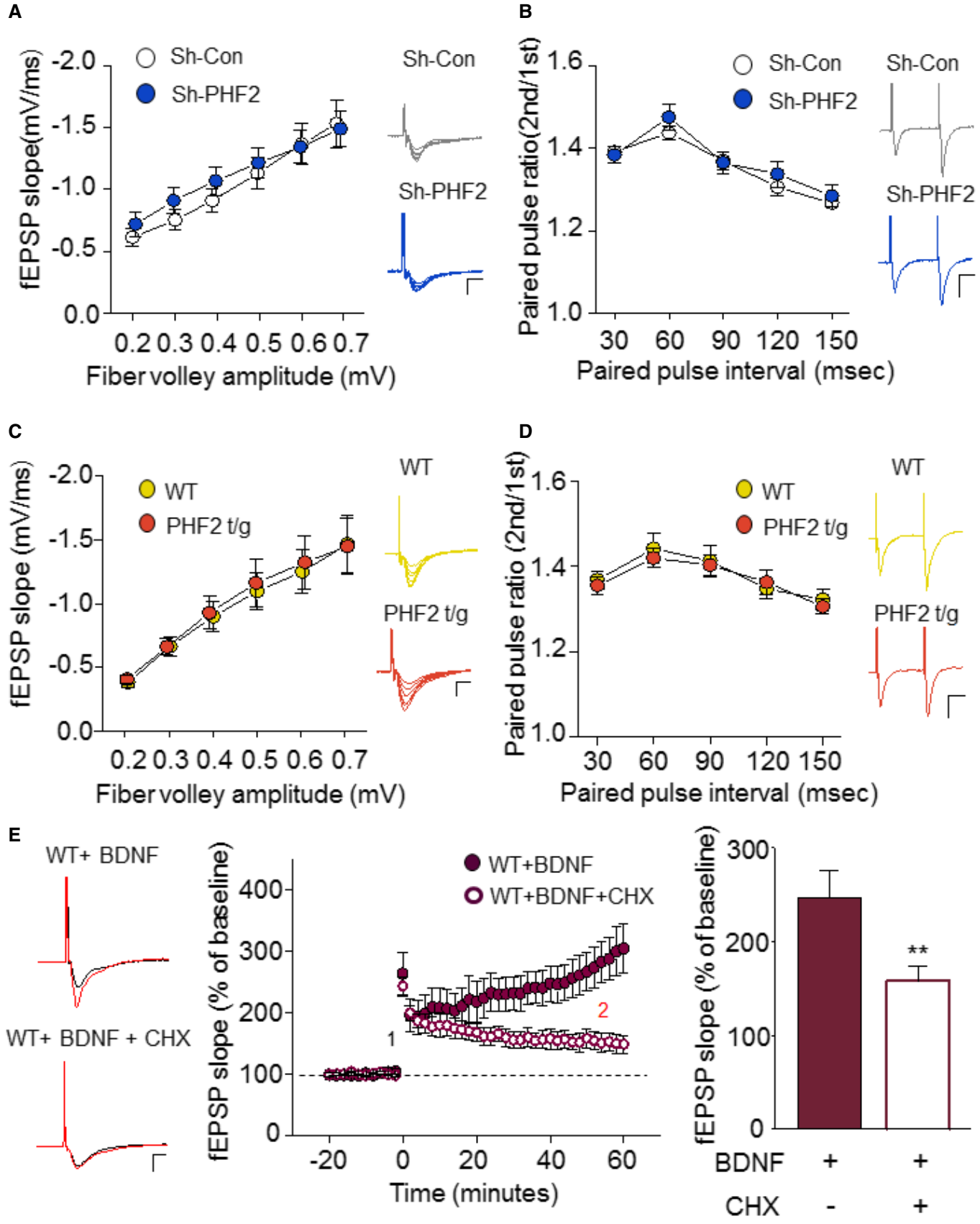

Figure EV3.

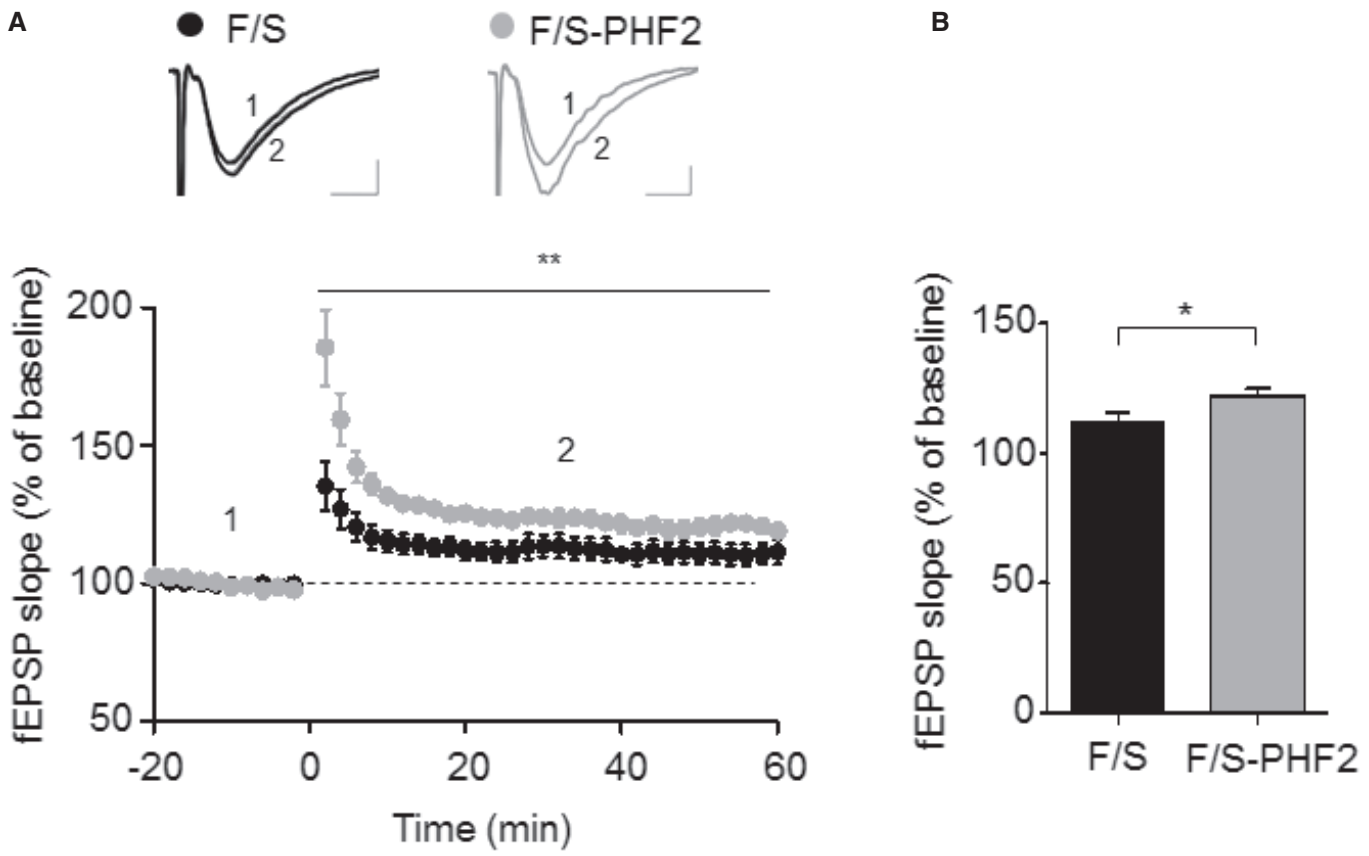

Figure EV4. Transient ectopic expression of PHF2 facilitates long-term potentiation (LTP) in the hippocampal Schaffer collateral-CA1 synapses.

A Field excitatory postsynaptic potentials (fEPSPs) induced by a single 1-s training at 100 Hz HFS. LTP was significantly greater in slices derived from transiently Flag-PHF2 expressing mice compared to those from control mice ($P < 0.05$). Measurements correspond to the time points indicated on the time course graph in this figure. Error bars show the standard error of the mean (**$P = 0.0055$, 2-way ANOVA). Scale bar, 0.25 mV/5 ms.

B LTP of control mice was 111 ± 4.11% of baseline during the 10 min before and after time point 2 ($n = 5$ slices from 3 mice). In Flag-PHF2 overexpressing mice, fEPSPs were 120.5 ± 2.75% of baseline during the 10 min before and after time point 2 ($n = 9$ slices from 4 mice). Error bars show the standard error of the mean (*$P = 0.0465$, 2-way ANOVA).

Figure EV5. Basal synaptic transmission of NMDA- and AMPA-mediated EPSCs do not differ by PHF2 expression levels.

A, B Recording of NMDAR- (A) and AMPAR-mediated (B) PPR at 50, 100, 150, and 200 ms intervals. Insets indicate raw trace of PPR (Top). Scale bars, 100 pA/150 ms.

C, D Recording of NMDAR- (C) and AMPAR-mediated (D) PPR at 50, 100, 150, and 200 ms intervals. Insets indicate raw trace of PPR (Top). Scale bars, 100 pA/150 ms.

Data information: In (A-D), data are presented as mean values ± SEM (sh-Con, $n = 14$; sh-PHF2, $n = 13$; wild type, $n = 16$; PHF2 t/g, $n = 26$).

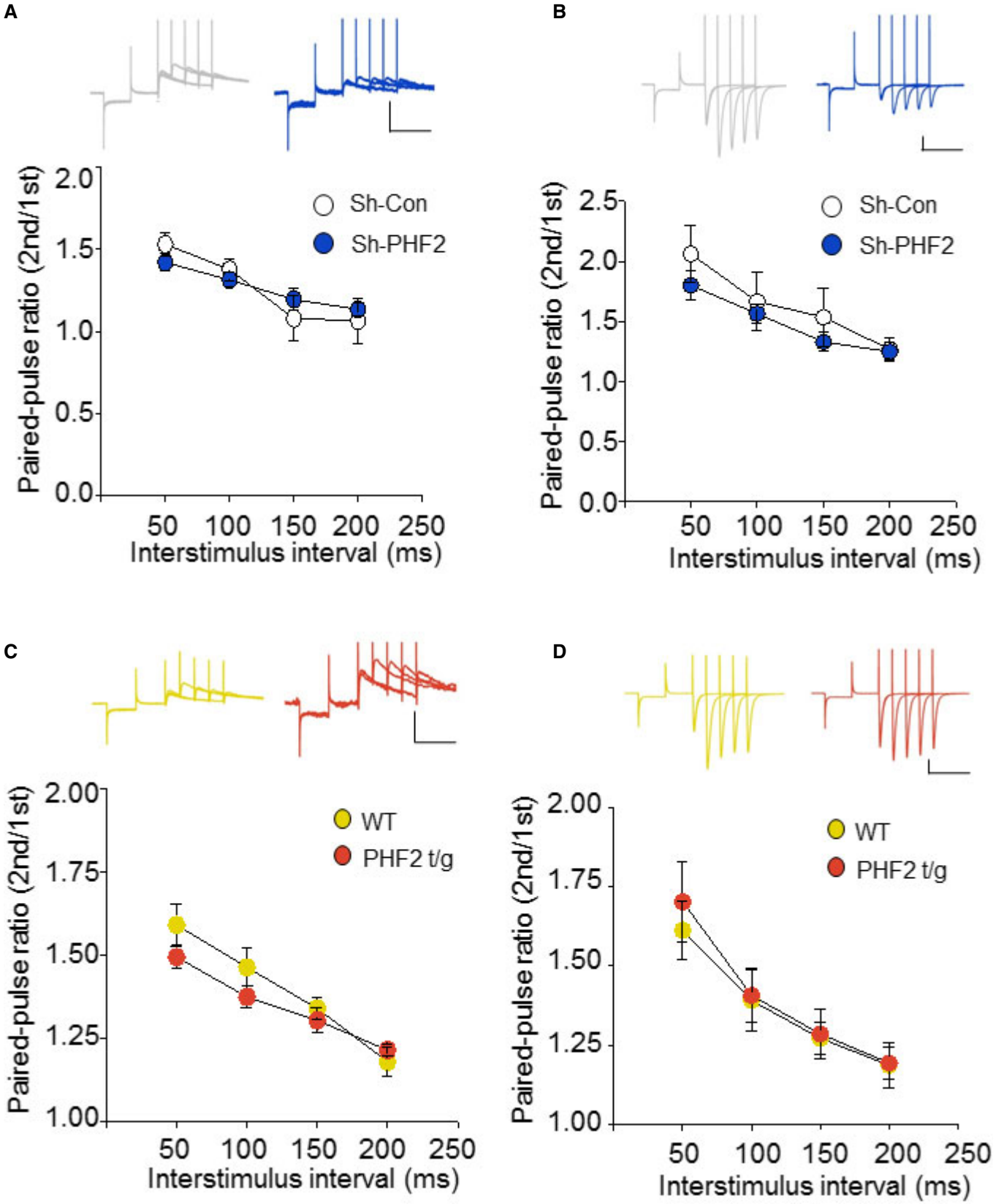

Figure EV5.