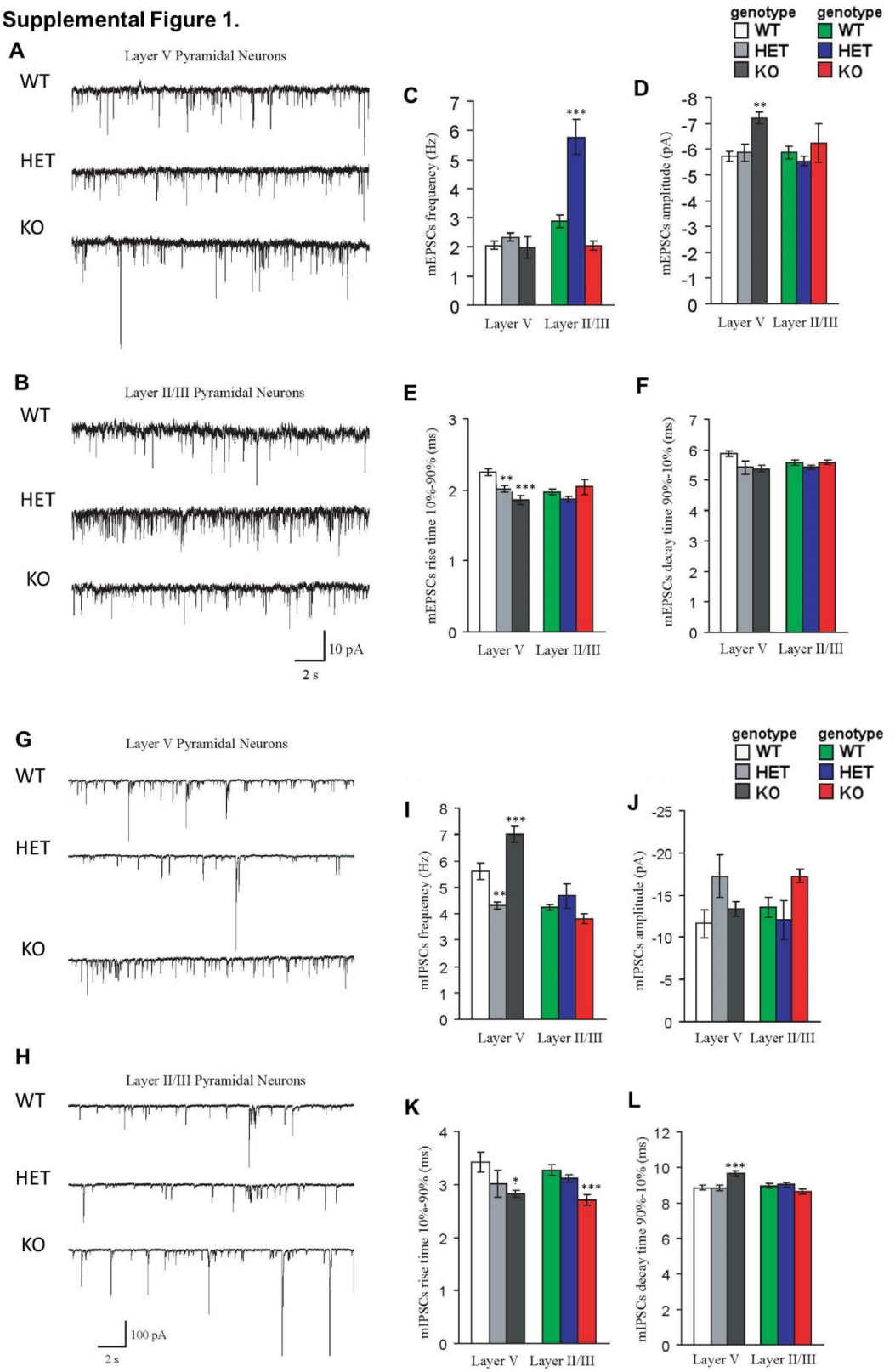
Supplemental Figure 1.

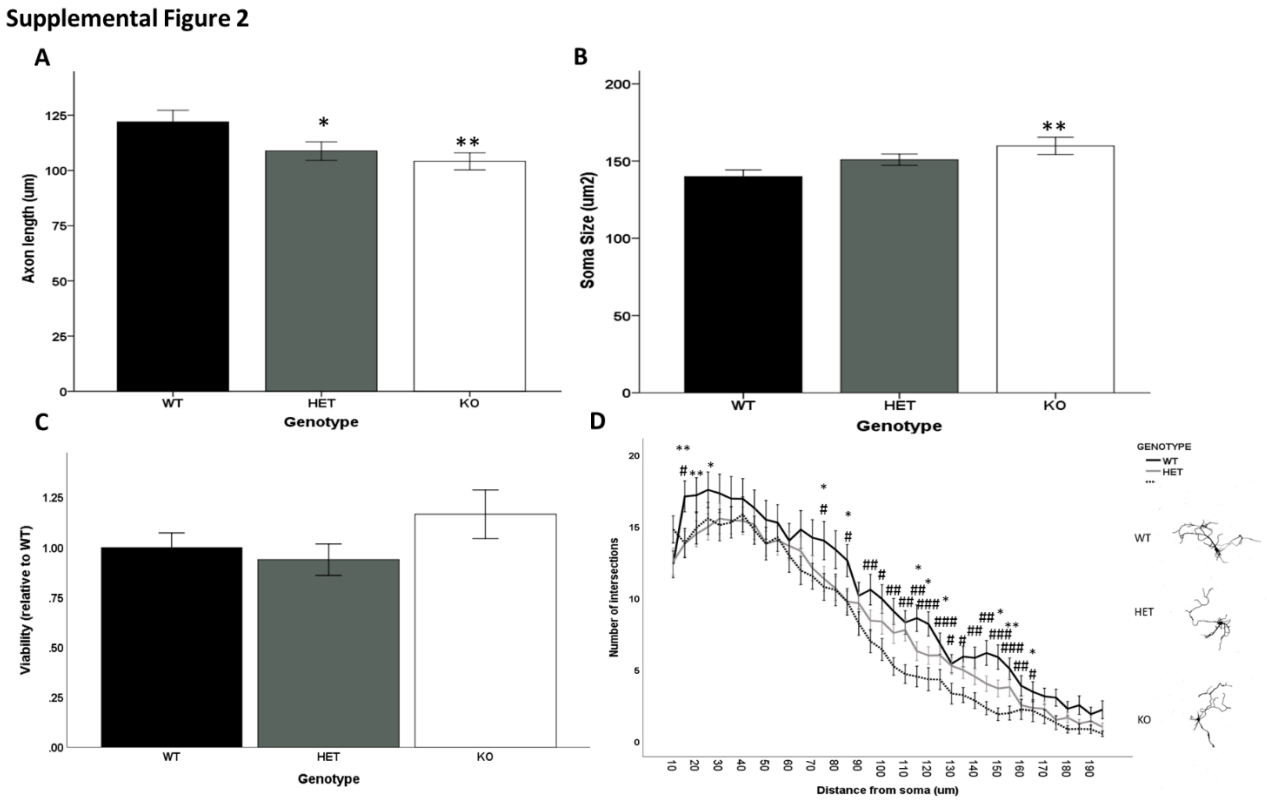


Supplemental Figure 1. Abnormal excitatory and inhibitory inputs onto pyramidal neurons in the lamina V and lamina II/III of mPFC in *Akt2* HET and KO mice.

(A-B) Representative traces and quantification of mEPSCs of *Akt2* HET, KO and their WT littermates mice. The excitatory synaptic transmission to pyramidal neurons in the lamina V and lamina II/III of mPFC was detected by whole-cell recordings, in the presence of 1.5 μM TTX and 50 μM bicuculline. (C) mEPSCs frequency (Hz) (univariate one-way ANOVA: $F(2,43) = 19.540$; $p \leq 0.001$. Bonferroni post-hoc: ***$p \leq 0.001$ HET vs WT). (D) mEPSCs amplitude (pA) (univariate one-way ANOVA: $F(2,45) = 5.890$; $p = 0.005$. Bonferroni post-hoc: **$p = 0.006$ KO vs WT). (E) mEPSCs rise time (ms) (univariate one-way ANOVA: $F(2,45) = 11.863$; $p \leq 0.001$. Bonferroni post-hoc: **$p = 0.004$ HET vs WT, ***$p \leq 0.001$ KO vs WT). (F) mEPSCs decay time (ms). Lamina V: N = 3 WT (10 slices, 19 cells), 3 HET (10 slices, 20 cells), 3 KO (9 slices, 9 cells). Lamina II-III: N = 3 WT (9 slices, 17 cells), 3 HET (10 slices, 19 cells), 3 KO (9 slices, 10 cells). Data represent mean ± SEM.

(G-H) Representative traces and quantification of mIPSCs of *Akt2* HET, KO and their WT littermates. The inhibitory synaptic transmission to pyramidal neurons in the lamina V and lamina II/III of mPFC was detected by whole-cell voltage clamp, in the presence of 1.5 μM TTX, 50 μM APV and 50 μM CNQX. (I) mIPSCs frequency (Hz) (Lamina V univariate one-way ANOVA: $F(2,41) = 21.637$ $p \leq 0.001$; Bonferroni post hoc: ** $p = 0.005$ HET vs WT, ***$p = 0.001$ KO vs WT). (J) mIPSCs amplitude (pA). (K) mIPSCs rise time (ms) (Lamina V univariate one-way ANOVA: $F(2,41) = 4.147$ $p = 0.023$; Bonferroni post hoc: *$p \leq 0.02$ KO vs WT; Lamina II-III univariate one-way ANOVA: $F(2,35) = 10.229$ $p \leq 0.001$; Bonferroni post hoc: ***$p \leq 0.001$ KO vs WT, ##$p = 0.001$ KO vs HET). (L) mIPSCs decay time (ms) (Lamina V univariate one-way ANOVA: $F(2,41) = 11.407$ $p \leq 0.001$; Bonferroni post-hoc: ***$p \leq 0.001$ KO vs WT). Lamina V:

N = 3 WT (10 slices, 15 cells), 3 HET (9 slices, 11 cells), 3 KO (9 slices, 18 cells). Lamina II-III: N = 3 WT (9 slices, 14 cells), 3 HET (9 slices, 11 cells), 3 KO (9 slices, 11 cells). Data represent mean ± SEM. $^{*}p \leq 0.05$, $^{**}p \leq 0.01$, $^{***}p \leq 0.001$.



Supplemental Figure 2. Altered neuronal morphology, and dendritic complexity without effects on viability in *Akt2* HET and KO *ex vivo* hippocampal cultures.

(A) Axon length of hippocampal neurons at DIV3 derived from WT, HET and KO *Akt2* embryos at E18. Axon length is significantly decreased in HET and KO neurons compared to WT neurons ($p<0.05$ and <0.01, respectively). (B) Soma size of hippocampal neurons at DIV3 derived from WT, HET and KO *Akt2* embryos at E18. Soma is significantly larger in KO neurons compared to WT neurons ($p<0.01$). WT=120 neurons, HET=150 neurons, KO= 120 neurons derived from ≥3 embryos/genotype. (C) Neuronal viability in hippocampal neurons derived from WT, HET and KO *Akt2* embryos at E18 is unaffected at DIV4. WT= 11 embryos, HET=15 embryos, KO-6 embryos. (D) Sholl analysis of dendritic complexity in DIV 10 hippocampal neurons derived from WT, HET and KO *Akt2* embryos at E18. Dendritic complexity is

significantly reduced in HET and KO neurons compared to WT neurons ($p<0.05$ and <0.01, respectively). WT=112 neurons, HET=82 neurons, KO= 47 neurons derived from ≥3 embryos/genotype. Right, representative traces of DIV 10 neurons. Data represent mean ± SEM. $^{*}p \leq 0.05$, $^{**}p \leq 0.01$, $^{***}p \leq 0.001$.