iScience, Volume *25*

Supplemental information

Familial natural short sleep mutations reduce Alzheimer pathology in mice

Qing Dong, Nicholas W. Gentry, Thomas McMahon, Maya Yamazaki, Lorena Benitez-Rivera, Tammy Wang, Li Gan, Louis Ptáček, and Ying-Hui Fu

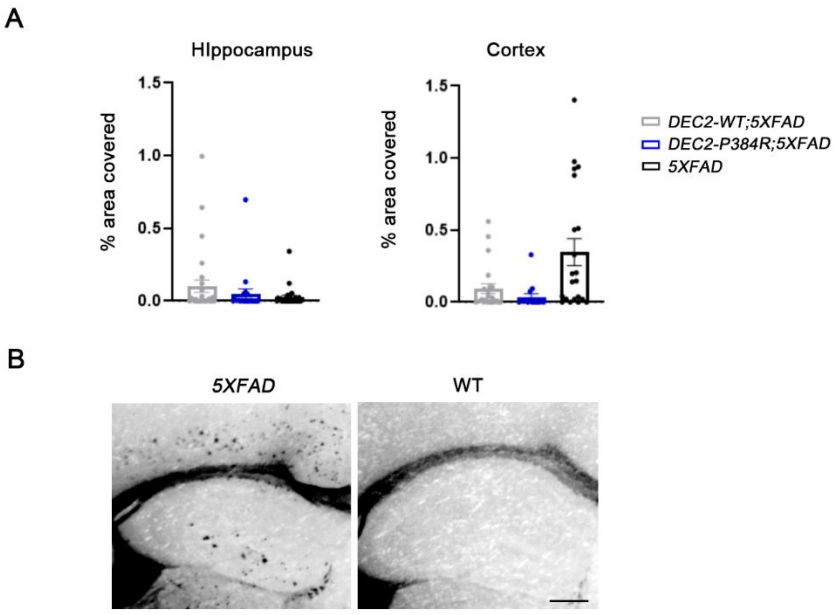

Figure S1 Plaques in 3- and 6-month-old mouse, related to Figure 1.

(A) % area of silver-stained brain slice from hippocampus and cortex covered by plaques in 3 months old mice. Hippocampus: *DEC2-WT;5XFAD*, $n = 4$ ($N = 28$ slices); *DEC2-P384R;5XFAD*, $n = 3$ ($N = 21$ slices); *5XFAD*, $n = 4$ ($N = 28$ slices); cortex: *DEC2-WT;5XFAD*, $n = 4$ ($N = 22$ slices); *DEC2-P384R;5XFAD*, $n = 3$ ($N = 15$ slices); *5XFAD*, $n = 4$ ($N = 21$ slices). (B) Representative silver staining of plaques for 6-month-old hippocampus in *5XFAD* and WT mice at high magnification. Scale bars, 500 μm. Data expressed as mean ± SEM with individual measures displayed.

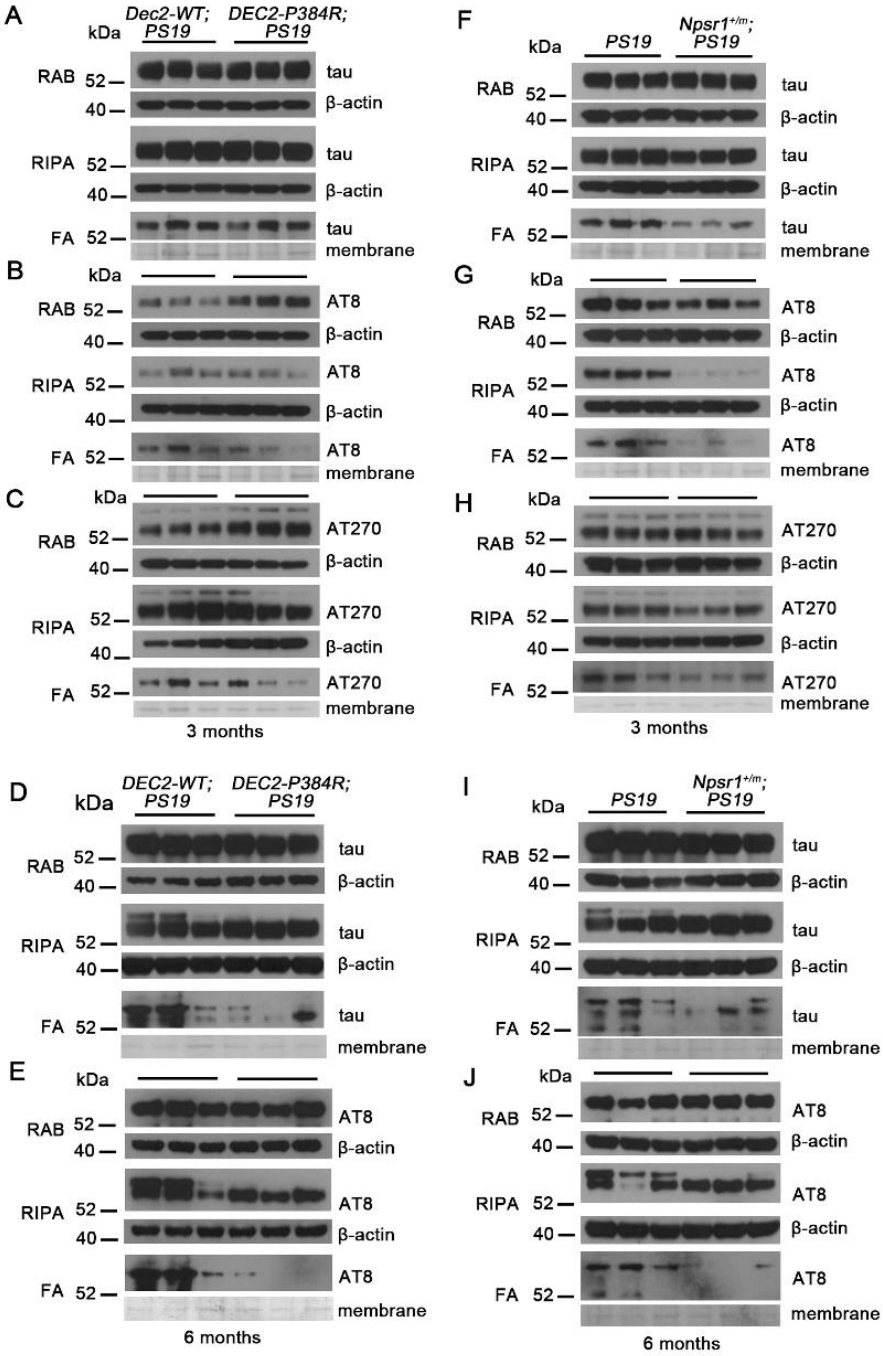

Figure S2 Representative Western blot for tau protein in *FNSS;PS19* mice, related to Figure 2.

(A-J) Representative Western blot analysis of the hippocampus of three-month-old and six-month-old mice for total tau or phosphorylated tau in soluble (RAB), less soluble (RIPA) and insoluble (FA) fractions, respectively. β-actin served as loading control for RAB and RIPA fractions. Membranes stained with Coomassie brilliant blue (CBB) served as loading control for FA fractions.

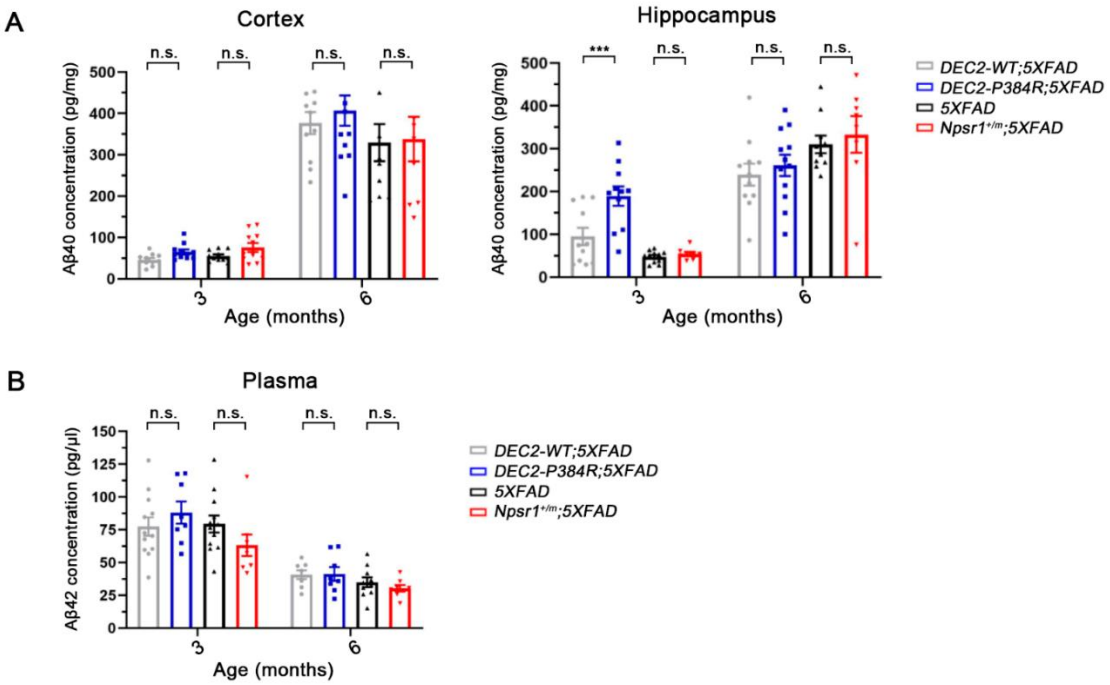

Figure S3 Aβ40 and Aβ42 from *FNSS:5XFAD* measured by ELISA, related to Figure 3.

(A) Soluble Aβ40 from mouse cortex (left) of indicated genotypes measured by ELISA at 3 months of age (n = 11 mice per group) and 6 months of age (*DEC2-WT;5XFAD*, n = 11; *DEC2-P384R;5XFAD*, n = 12; *5XFAD*, n = 10; *Npsr1*$^{+/m}$*;5XFAD*, n = 9); soluble Aβ40 from hippocampus (right) at 3 months of age (*DEC2-WT;5XFAD*, n = 11; *DEC2-P384R;5XFAD*, n = 11; *5XFAD*, n = 12; *Npsr1*$^{+/m}$*;5XFAD*, n = 8) and 6 months of age (*DEC2-WT;5XFAD*, n = 11; *DEC2-P384R;5XFAD*, n = 12; *5XFAD*, n = 10; *Npsr1*$^{+/m}$*;5XFAD*, n = 8). (B) Plasma Aβ42 from indicated genotypes measured by ELISA at 3 months of age (*DEC2-WT;5XFAD*, n = 12; *DEC2-P384R;5XFAD*, n = 8; *5XFAD*, n = 12; *Npsr1*$^{+/m}$*;5XFAD*, n = 8) and 6 months of age (*DEC2-WT;5XFAD*, n = 8; *DEC2-P384R;5XFAD*, n = 8; *5XFAD*, n = 10; *Npsr1*$^{+/m}$*;5XFAD*, n = 8). Data expressed as mean ± SEM with individual measures displayed. Statistical analysis performed through one-way ANOVA with post-hoc Tukey's multiple comparisons test between relevant conditions. ***$p < 0.001$; n.s., not significant.

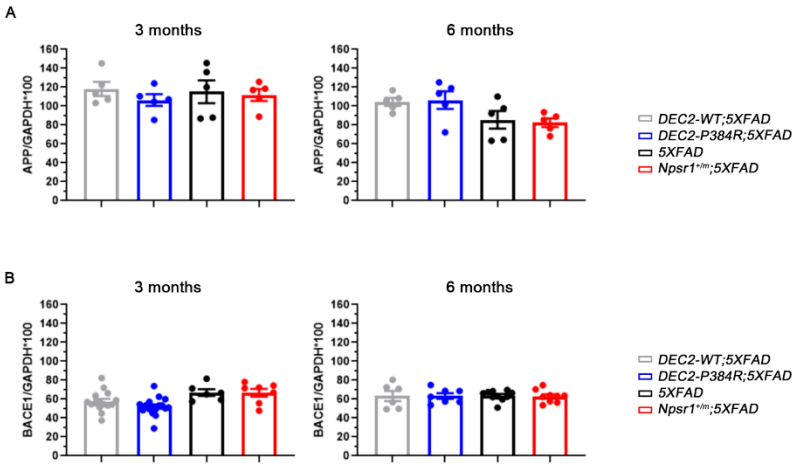

Figure S4 Quantitative results from Western blots for APP and BACE, related to Figure 3.

(A) APP levels at 3 and 6 months of age (n = 5 mice per group). (B) BACE1 levels at 3 months of age (*DEC2-WT;5XFAD*, n = 15; *DEC2-P384R;5XFAD*, n = 17; *5XFAD*, n = 6; *Npsr1*$^{+/m}$*;5XFAD*, n = 7) and 6 months of age (*DEC2-WT;5XFAD*, n = 6; *DEC2-P384R;5XFAD*, n = 7; *5XFAD*, n = 10; *Npsr1*$^{+/m}$*;5XFAD*, n = 10). Data expressed as mean ± SEM with individual measures displayed.

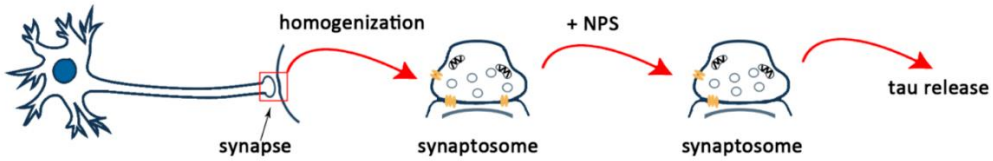

Figure S5 Schematic for synaptosome preparation and treatment with NPS, related to Figure 4.