SUPPLEMENTAL MATERIAL

Chiang et al., https://doi.org/10.1084/jem.20171484

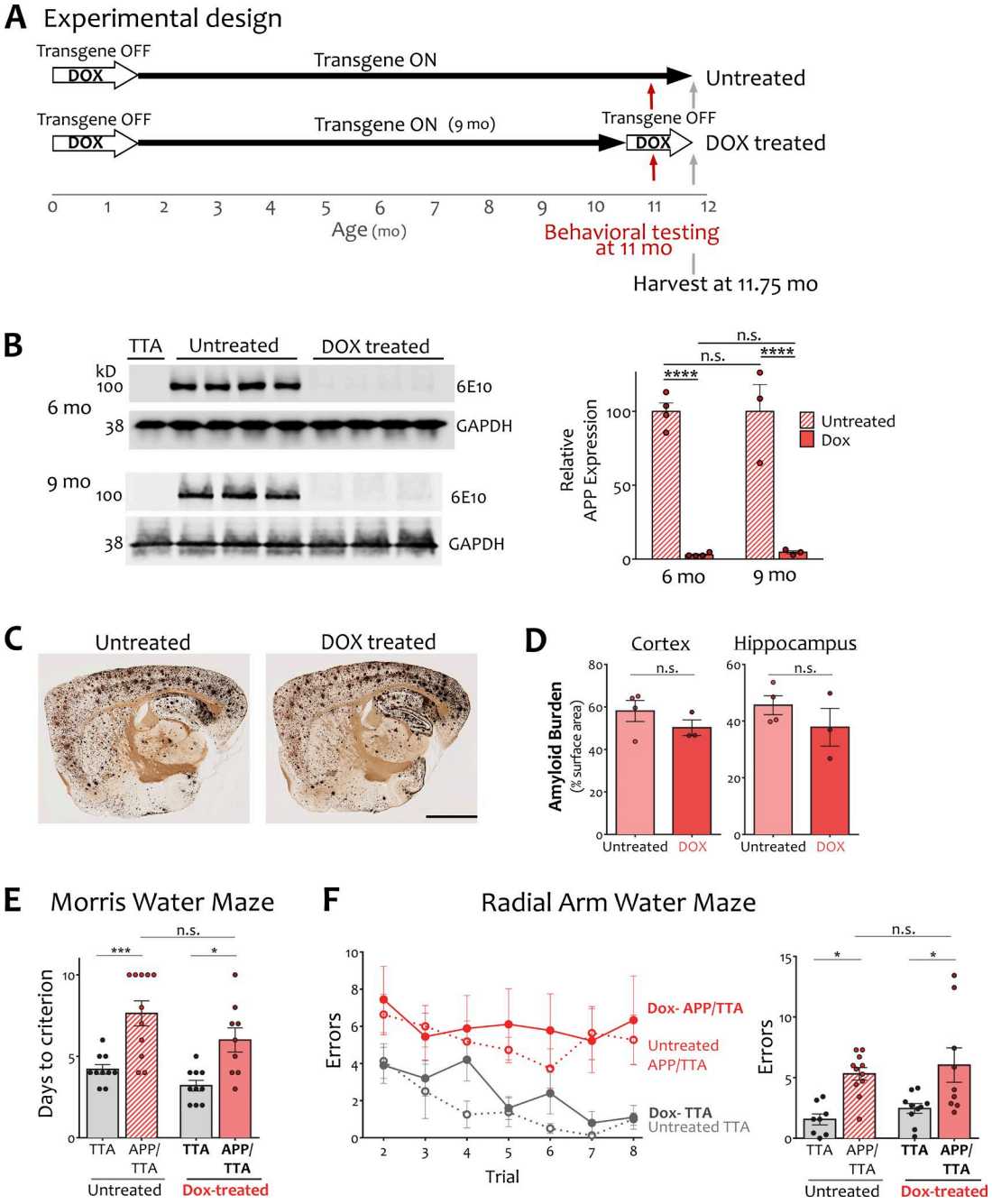

Figure S1. **Acute transgene suppression fails to reverse cognitive impairment in aged APP/TTA mice. (A)** A pilot group of APP/TTA mice overexpressed transgenic APP for 9 mo (from 1.5 until 10.5 mo of age) and was then divided into two treatment groups. Half of the mice were treated with dox to arrest further Aβ overproduction, and the remaining animals served as untreated controls. Behavioral testing began 2 wk later, and mice were harvested for pathological assessment after 5 wk of differential treatment. **(B)** Western blotting with 6E10 confirmed that APP suppression was >95% in the 9-mo cohort (n = 3–4), similar to the efficacy of transgene suppression attained in animals tested after 6 mo of APP overexpression (Fowler et al., 2014). **(C)** Silver staining in the 9-mo animals harvested after behavioral testing. Bar, 2,000 µm. **(D)** Percent of cortical surface area occupied by amyloid in silver-stained sections shows little change between treatment groups (n = 3 untreated and n = 3 dox). **(E)** The number of days required for 9 mo APP/TTA mice to reach criteria performance in MWM is unchanged by acute transgene suppression. Both untreated (n = 11) and dox-treated APP/TTA (n = 9) mice are significantly impaired compared with age-matched TTA single transgenic controls (n = 10). **(F)** The mean number of errors per trial (left) and mean total errors across trials (right) on RAWM. Both dox-treated and untreated APP/TTA (n = 10) mice made significantly more errors than respective TTA controls (n = 10 dox, n = 8 untreated). *, P < 0.05; ***, P < 0.001; ****, P < 0.0001. Error bars show means ± SEM.

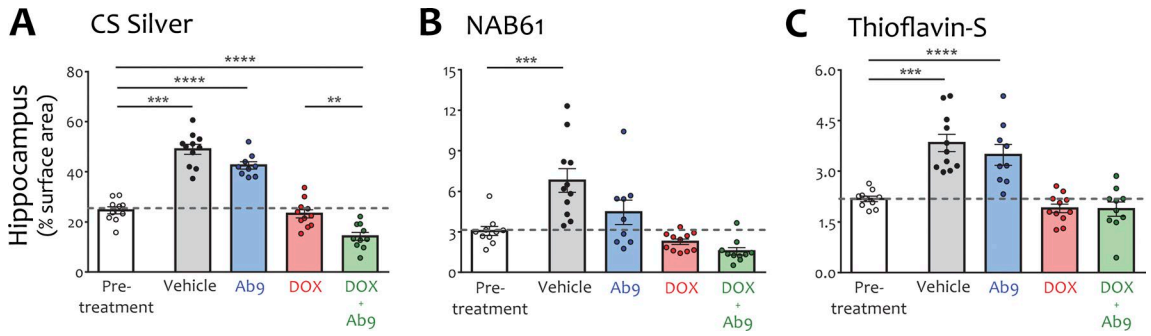

Figure S2. **Histological analysis of plaque burden in hippocampus. (A–C)** Quantification of hippocampal plaque area: CS silver (A), NAB61 (B), and thioflavin-S (C). Dashed line in scatter plots indicates the pretreatment plaque load for each stain. Significant comparisons against pretreatment or between dox and dox + Ab9 are shown; other comparisons are listed in Table S1. *n* = 9–11/group. **, P < 0.01; ***, P < 0.001; ****, P < 0.0001. Error bars show means ± SEM.

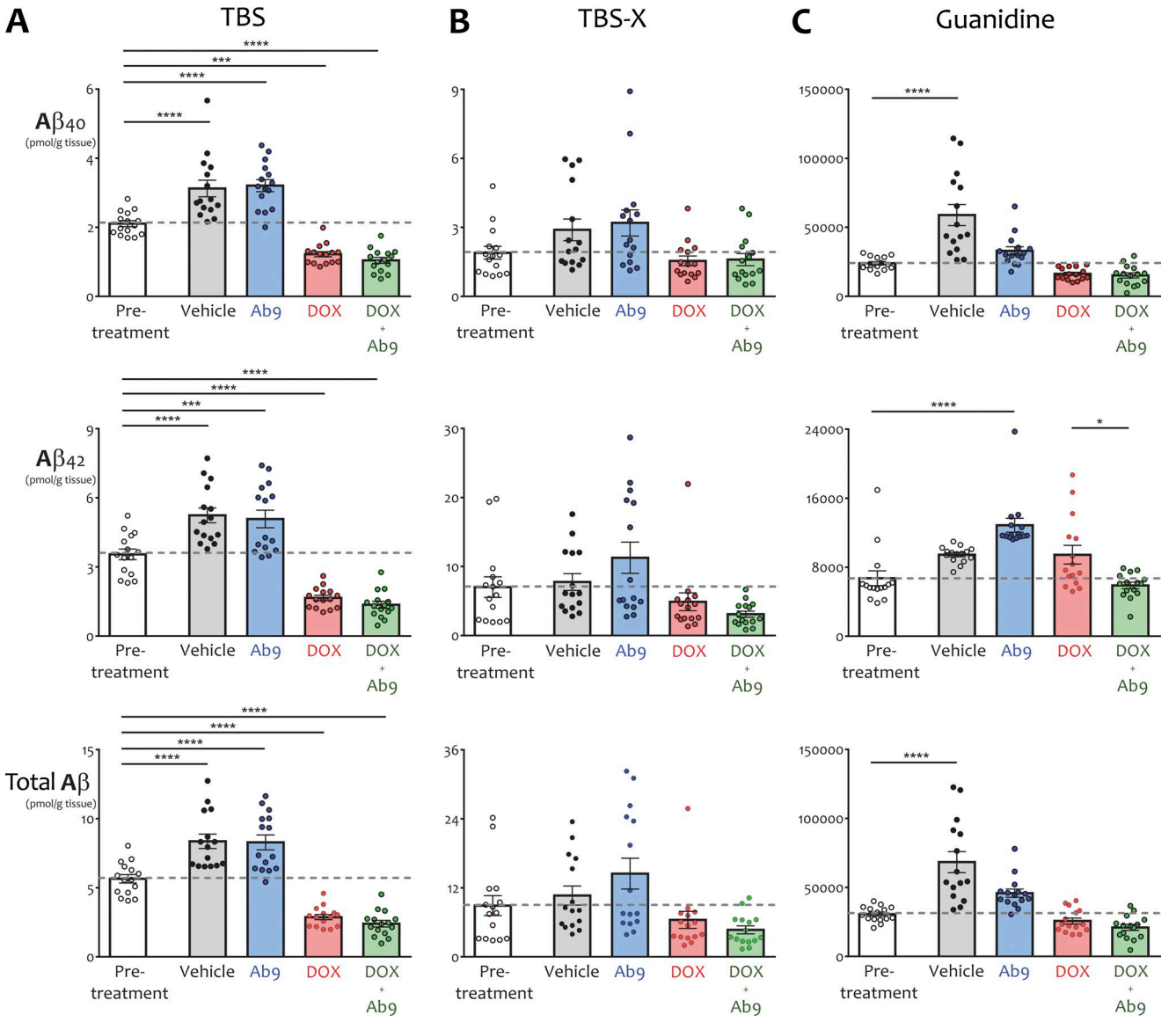

Figure S3. **Biochemical measurements of Aβ40, Aβ42, and total Aβ concentration for each treatment group. (A–C)** Concentration of cortical Aβx-40 (top row), Aβx-42 (middle row), and total Aβ (bottom row) measured by ELISA for each treatment condition after extraction into TBS (A), TBS-X (B), or guanidine (C). Dashed line in scatter plots indicates the pretreatment concentration for each measure. Significant comparisons against pretreatment or between dox and dox + Ab9 are shown; other comparisons are listed in Table S1. *n* = 15/group. *, P < 0.05; ***, P < 0.001; ****, P < 0.0001. Error bars show means ± SEM.

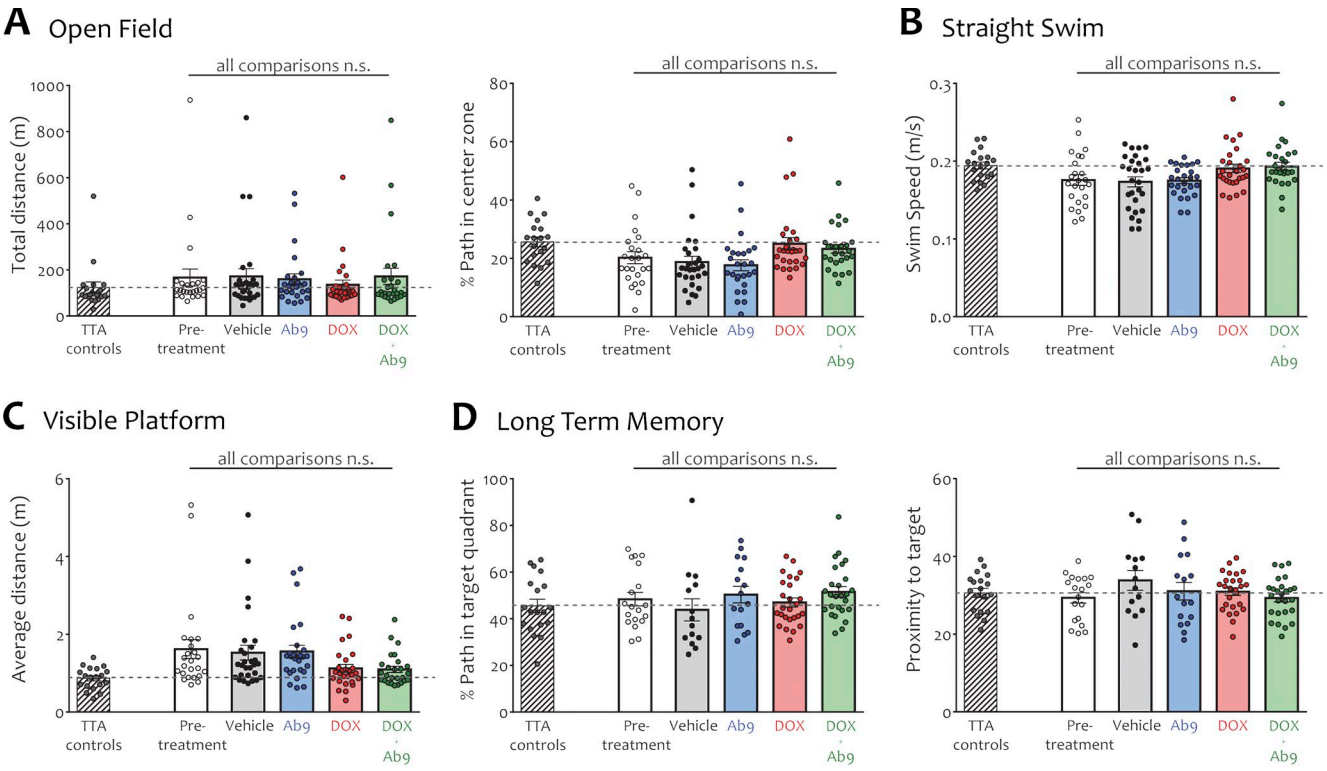

Figure S4. **Additional control data from behavioral testing of aged APP/TTA mice. (A)** No differences were observed across treatment groups in open field distance or percentage path traveled in center of the arena. **(B)** Swim speed in an enclosed channel was similar across treatment groups. **(C)** Visual acuity measured as path length to a marked platform was not significantly different between treatment groups. **(D)** Once animals reached criteria performance in the MWM, long-term memory for the trained escape location was similar between treatment groups whether measured by percentage of swim path in the trained quadrant (right) or proximity to the trained location (left). Dashed line in each plot indicates the mean performance of age-matched TTA controls. TTA values are for illustration only; statistical comparisons included only APP/TTA groups. *n* = 24–28/group (19 for TTA). Error bars show means ± SEM.

Provided online as a PDF is Table S1, showing detailed statistical information for all quantitative comparisons performed in this study

Reference

Fowler, S.W., A.C. Chiang, R.R. Savjani, M.E. Larson, M.A. Sherman, D.R. Schuler, J.R. Cirrito, S.E. Lesné, and J.L. Jankowsky. 2014. Genetic modulation of soluble Aβ rescues cognitive and synaptic impairment in a mouse model of Alzheimer's disease. *J. Neurosci.* 34:7871–7885. https://doi.org/10.1523/JNEUROSCI.0572-14.2014