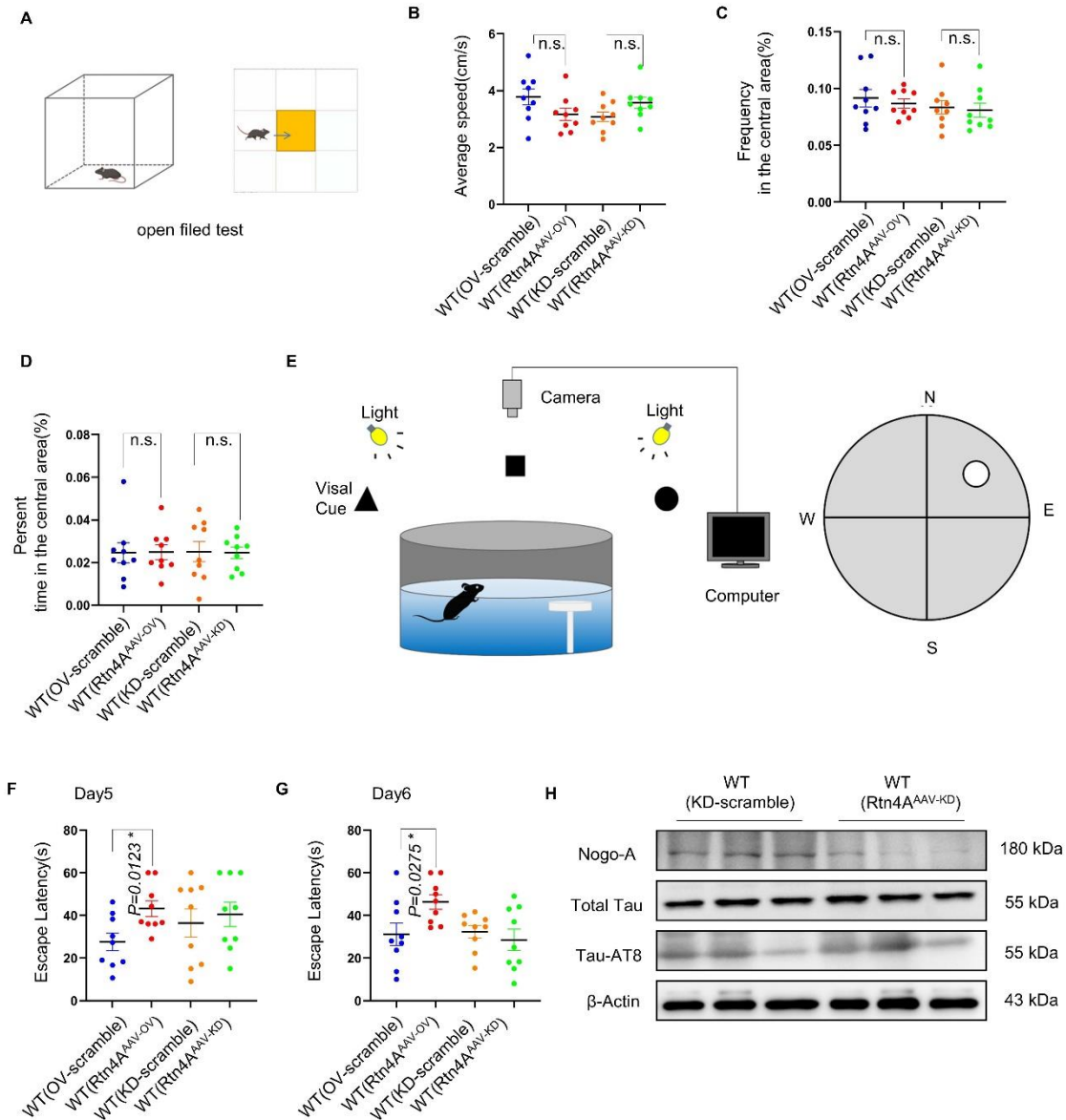SUPPLEMENTARY DATA

# Nogo-A Drives Alzheimer's Disease Progression by Inducing Tauopathy Vulnerability

Zijian Wang, Jun-ping Pan, Jiayuan Geng, Shijie Lv, Guisi Chen, Nian Fang, Zheng Zhang, Junliang Li, Xinke Xu, Rui Wang, Qing Zheng, Li Yan, Guobing Chen, Fei Xiao
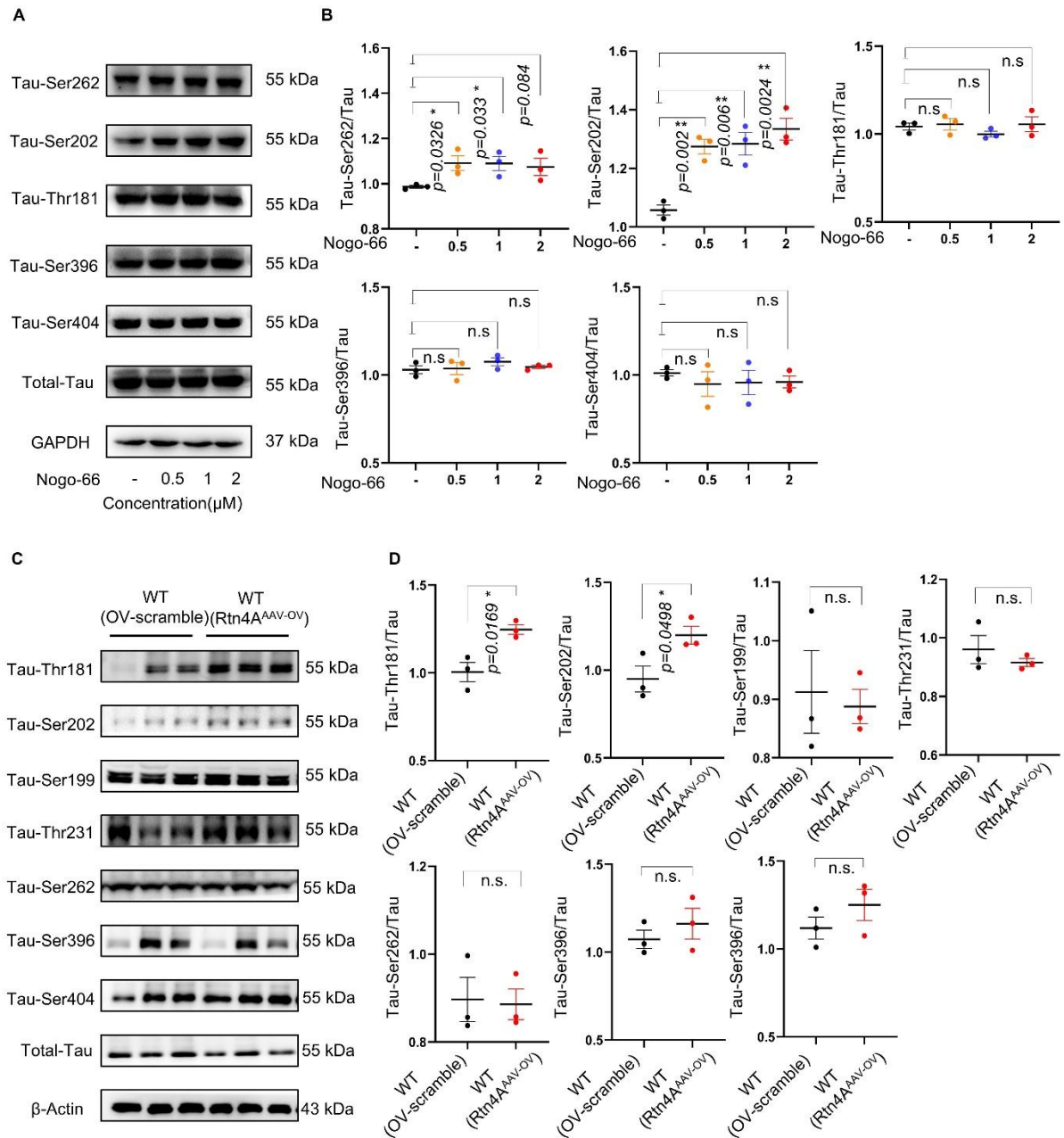
SUPPLEMENTARY DATA

Supplementary Figure 1. Behavior and tau phosphorylation effects of Nogo-A overexpression or knockdown in C57BL/6 N mice. (A) Schematic diagram of the open field test. **(B)** The average speed of the mice, n=9 for each group. **(C-D)** The frequency **(C)** and time spent **(D)** in the central area of each group were statistically analyzed. n=3 for each group. **(E)** Schematic diagram of the Morris water maze. **(F-G)** The escape latency of each group was statistically analyzed on days 5 and 6. n=9 for each group. **(H)** Representative western blots showing the levels of Nogo-A and tau phosphorylation at AT8 sites in the WT (KD-scramble) group and WT (Rtn4AAAV-KD) group. Data sets were tested for normal Gaussian distribution via Shapiro-Wilk test. Significance was determined by Kruskal-Wallis test, followed by Dunn's multiple comparisons with a significant difference set at 0.05. n.s.=not significant, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Each point represents an individual animal.
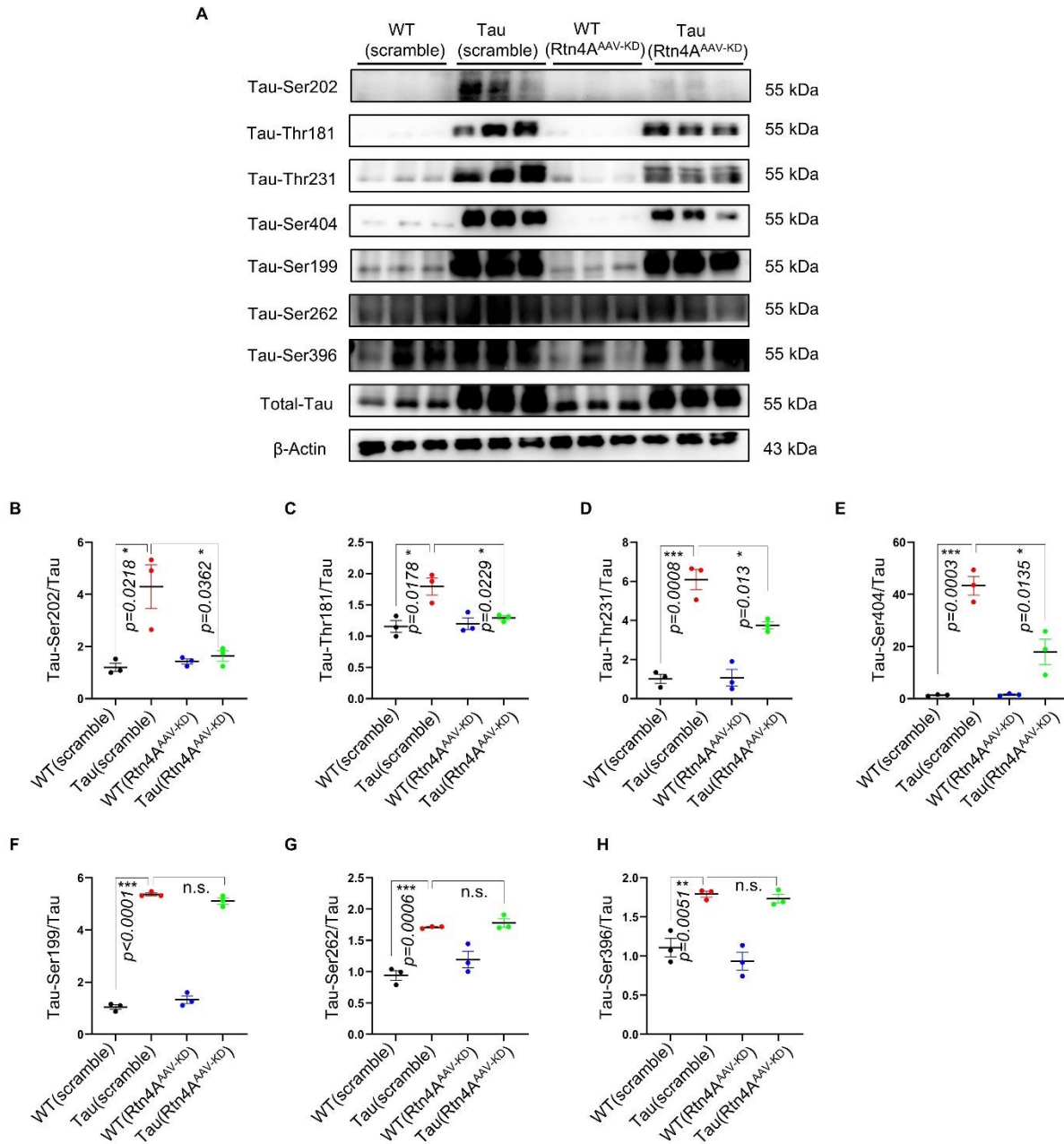
SUPPLEMENTARY DATA
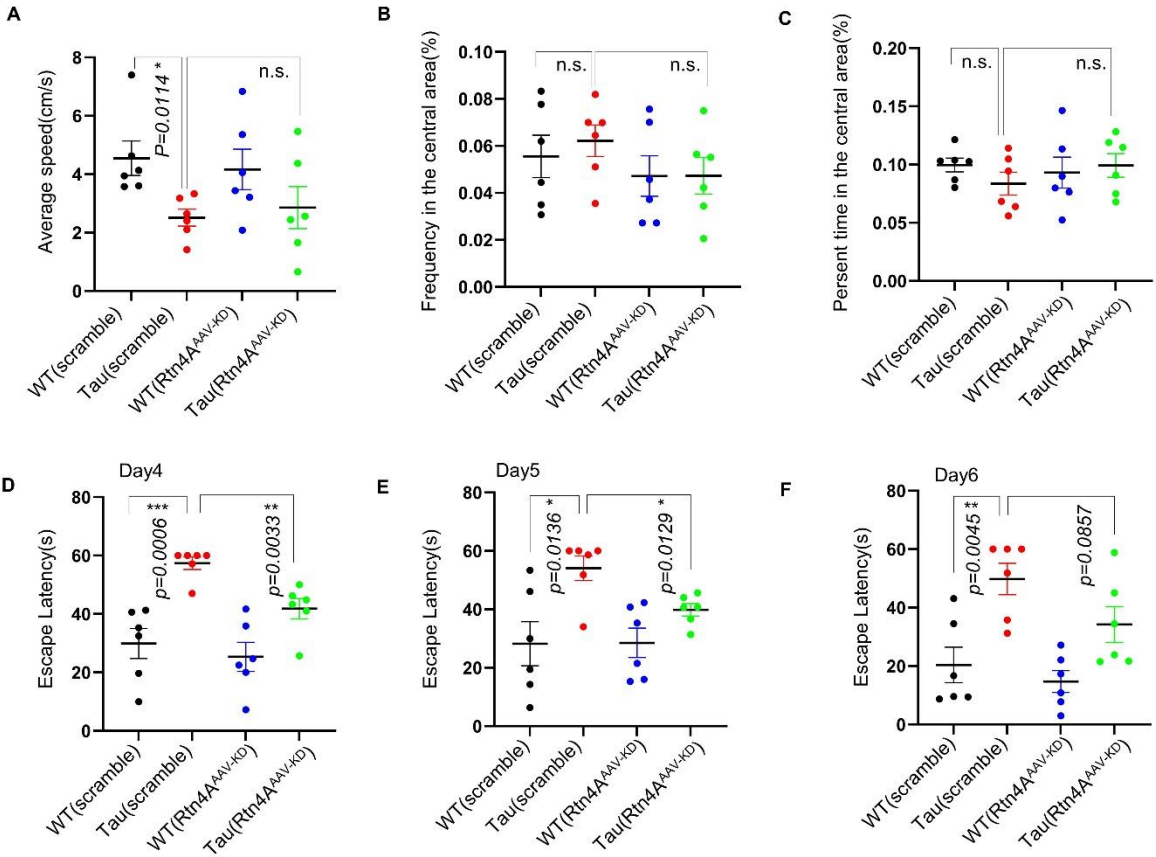
Supplementary Figure 2. Behavioral effects of Nogo-A knockdown in hTau. P301S mice. (A) The average speed of each group. n=6 mice per group. (**B-C**) The frequency (**B**) and the time spent (**C**) in the central area of each group were statistically analyzed. n=6 for each group. (**D**) The escape latency of each group was statistically analyzed on days 4, 5 and 6. *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$, groups analyzed by one-way ANOVA. Dunnett's multiple comparisons test followed by Tukey's multiple comparisons test were used for statistical analysis, with a significant difference set at 0.05. n.s.=not significant, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Supplementary Figure 3. Nogo-A overexpression promoted tau phosphorylation at multiple sites in rat cortical neurons and C57BL/6 N mice. (**A-B**) Western blots showing the levels of tau phosphorylation at Ser262, Ser202, Thr181, Ser396 and Ser404 at different concentrations of Nogo-66 in rat cortical neurons. n=3 in each group. (**C-D**) Western blots showing the levels of tau phosphorylation at Thr181, Ser202, Ser199, Thr231, Ser262, Ser396 and Ser404 in the hippocampus of the WT (scramble) and WT (Rtn4A-AAV-OV) groups. n=3 in each group. *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$, Data sets were tested for normal Gaussian distribution via Shapiro-Wilk test. Significance was determined by Kruskal-Wallis test, followed by Dunn's multiple comparisons with a significant difference set at 0.05. n.s.=not significant, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Each point represents an individual animal.

SUPPLEMENTARY DATA

Supplementary Figure 4. Nogo-A knockdown ameliorated tau phosphorylation at multiple sites in hTau. P301S mouse. (A) Western blots showing the levels of tau phosphorylation at Thr181, Ser202, Ser199, Thr231, Ser262, Ser396 and Ser404 in the hippocampi of the WT (scramble), Tau (scramble), WT (Rtn4A-AAV-KD) and Tau (Rtn4A-AAV-KD) groups. n=3 in each group. (**B-H**) Data sets were tested for normal Gaussian distribution via Shapiro-Wilk test. Significance was determined by Kruskal-Wallis test, followed by Dunn's multiple comparisons with a significant difference set at 0.05. n.s.=not significant, * $p < 0.05$, ** $p < 0.01$, *** $p <$ 0.001. Each point represents an individual animal.