

Characterization of Inhibitory Interneurons in Memory Circuits of Alzheimer's Disease Mice

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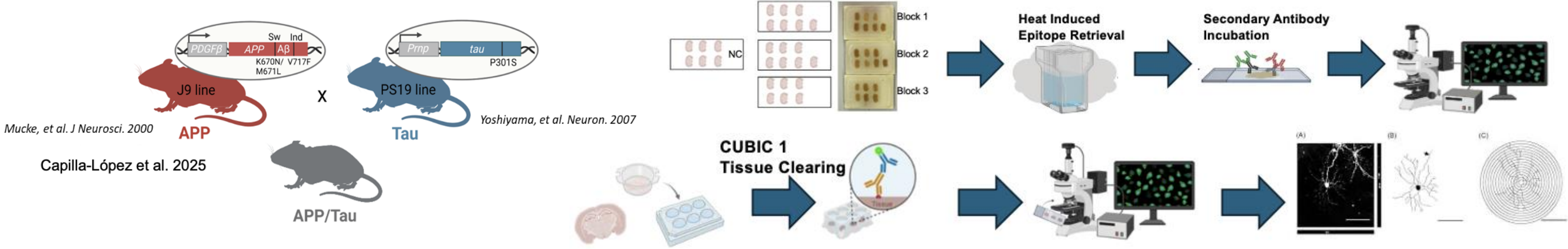
Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by accumulation of amyloid- β (A β) and phosphorylated tau in memory- and emotional-related brain circuits. Parvalbumin (PV)-expressing interneurons, the most abundant cortical inhibitory neurons, regulate neural excitability, synaptic plasticity, and network dynamics, and their dysfunction may cause excitatory/inhibitory imbalance and memory impairment in AD. However, the molecular and pathological mechanisms underlying PV interneuron dysfunction leading to emotional memory impairments in AD are largely unknown. Here, we investigated the role of A β and tau pathologies on the number and morphology of interneurons, particularly PV interneurons, in the hippocampus and basolateral amygdala (BLA) of AD transgenic mice.

Objectives

- To quantify the abundance of inhibitory interneurons in the hippocampus and BLA of AD mice
- To analyze the number and morphology of parvalbumin interneurons in the hippocampus and BLA of AD mice

Methodology



Results

Unchanged interneurons subtypes in APP, Tau and APP/Tau mice

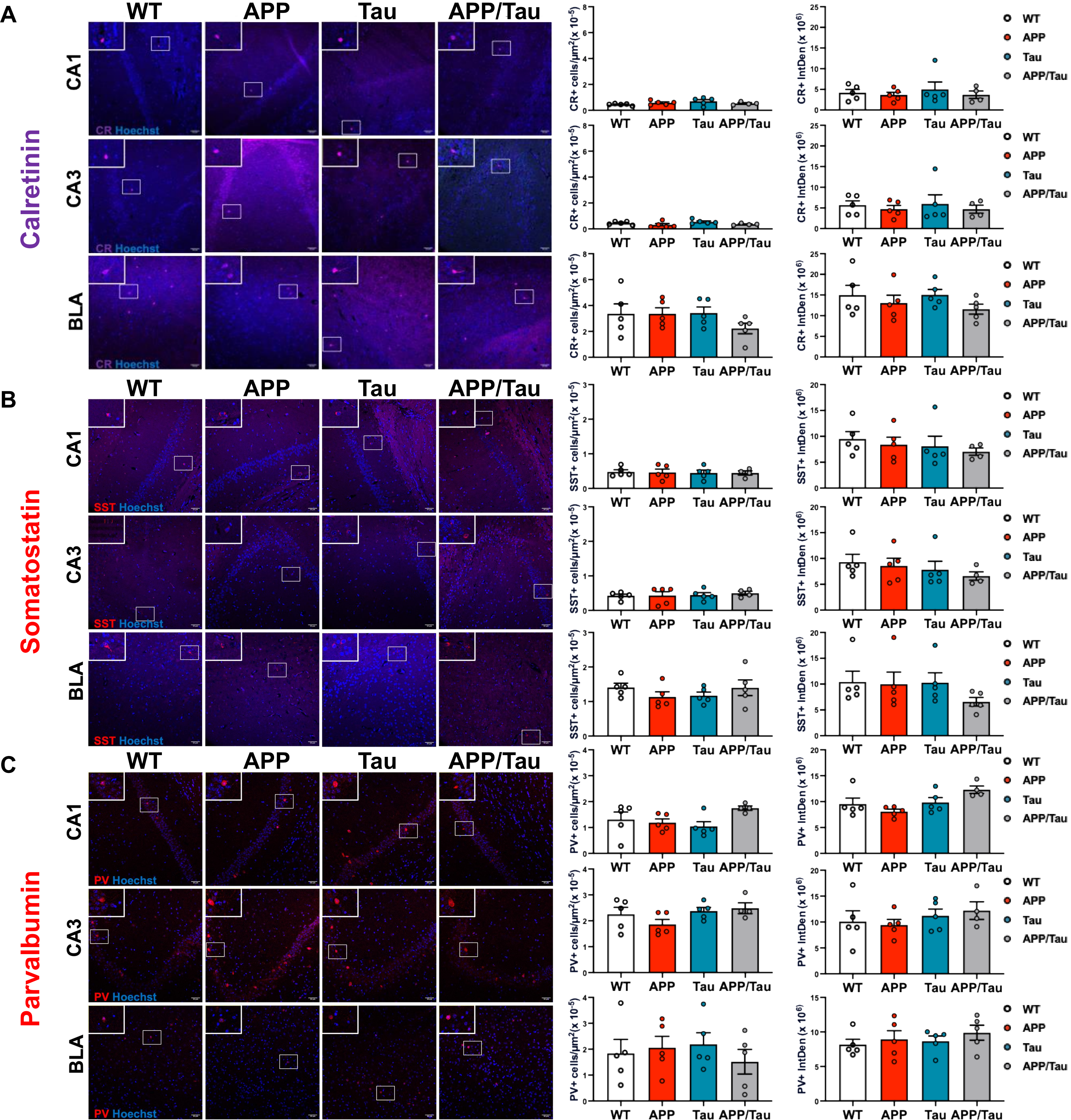


Figure 1. (A–C) Representative confocal microscopy images and quantification of calretinin (CR; A), somatostatin (SST; B), and parvalbumin (PV; C) neurons in coronal brain sections (100 μ m) of 9-month-old control (WT), APP, Tau and APP/Tau mice. Interneurons number and integrated density (IntDen) were quantified in CA1 and CA3 hippocampus and basolateral amygdala (BLA) of AD mice (n=3 sections/mouse). Each point represents an individual mouse. Scale bar: 50 μ m. Data are presented as mean $\pm$ SEM. Statistical analysis was determined by one-way ANOVA.

Results

Reduction of Parvalbumin interneurons in the hippocampus of APP/Tau mice

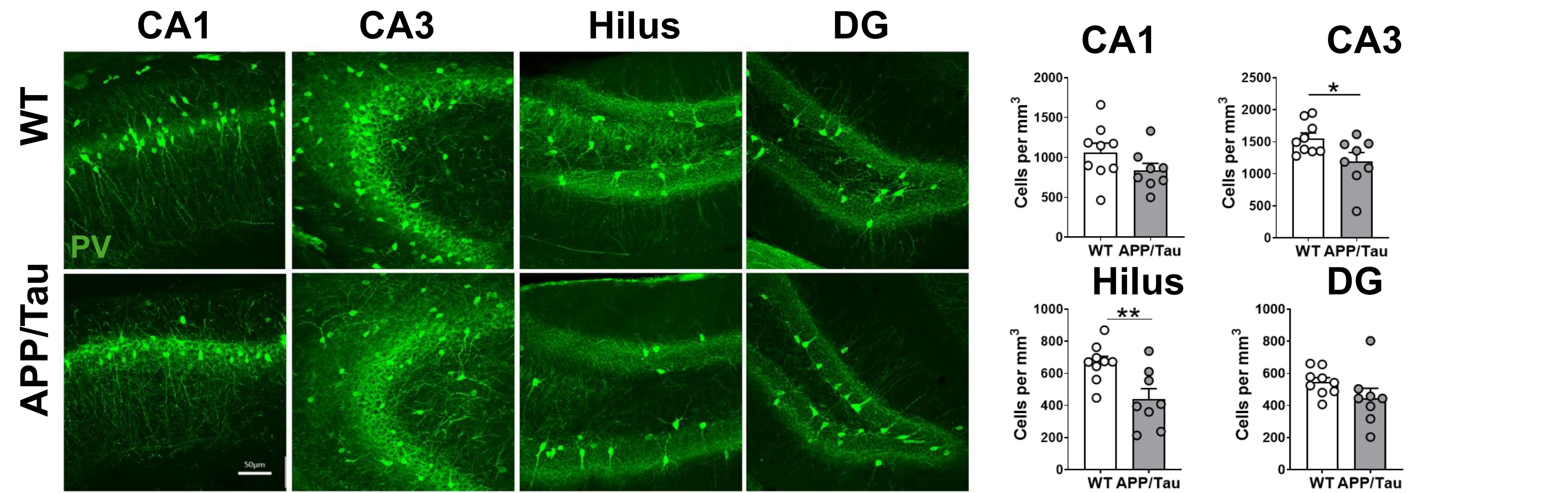


Figure 2. Coronal brain sections (100 μ m) and quantification of Parvalbumin (PV)-positive cells (green) in CA3, CA1, Hilus and DG of WT and APP/Tau at 6 months of age (n=8-9). Scale bar: 100 μ m. Data represent mean $\pm$ SEM. Statistical analysis was determined by unpaired t-test. * $P < 0.05$, ** $P < 0.01$. Scale bar: 50 μ m

Age-dependent morphology changes of Parvalbumin interneurons in the basolateral amygdala APP/Tau mice

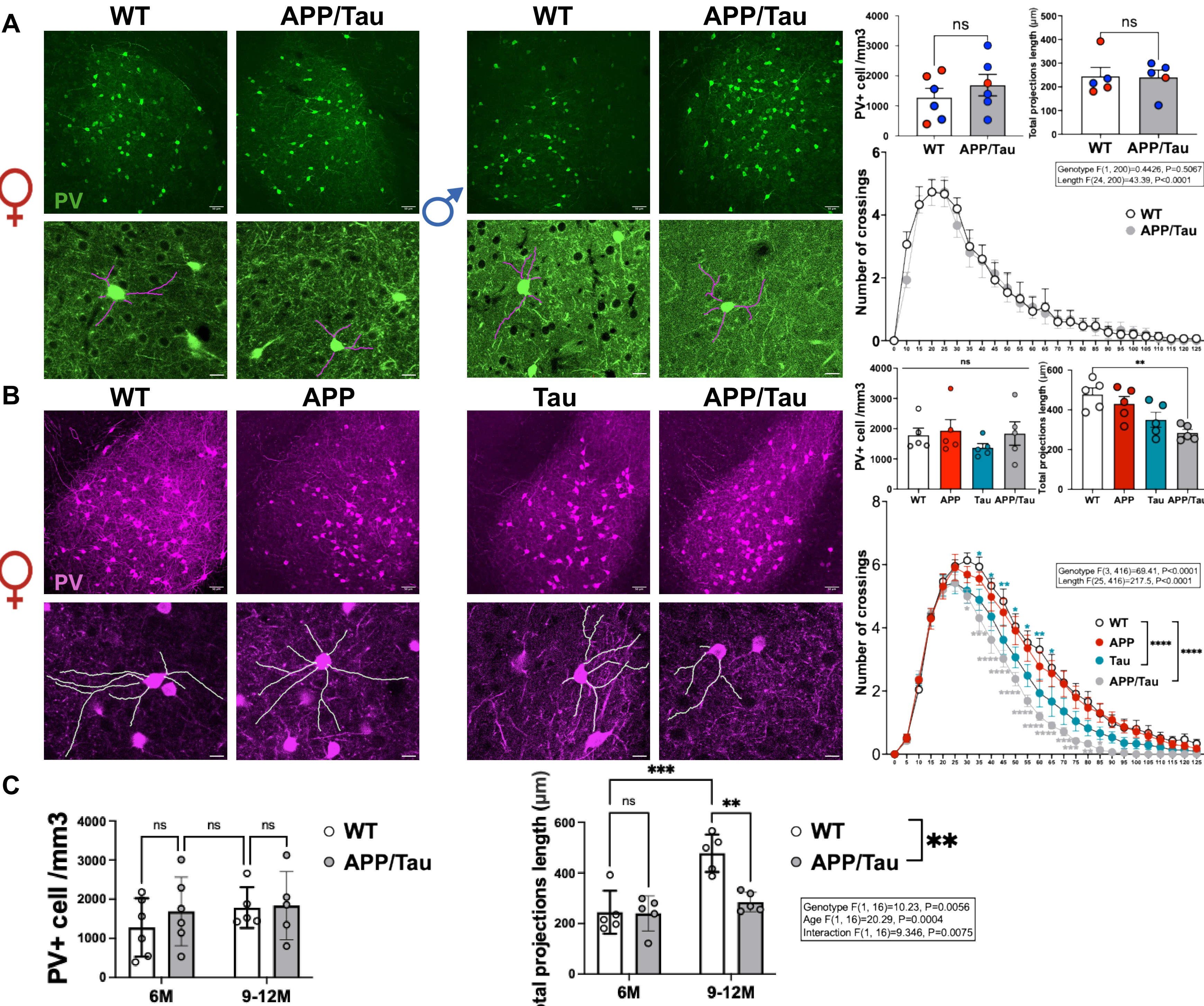


Figure 3. (A, B) Quantification of number and morphology (dendritic length and complexity) of PV interneuron in the basolateral amygdala of 6-month-old male and female WT and APP/Tau mice (A), and 9–12-month-old female WT, APP, Tau, and APP/Tau mice (B). (C) Comparison of PV+ number and projections WT and APP/Tau mice at 6 and 9–12 months of age. Data represent mean $\pm$ SEM. Statistical analysis was determined by one-way ANOVA or Two-way ANOVA or unpaired t-test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Scale bar: 50 μ m

Conclusions

A β and tau pathologies converge to affect hippocampal and amygdalar PV neurons implicating vulnerability of PV interneuron as a cellular substrate of emotional and memory disturbances in AD.