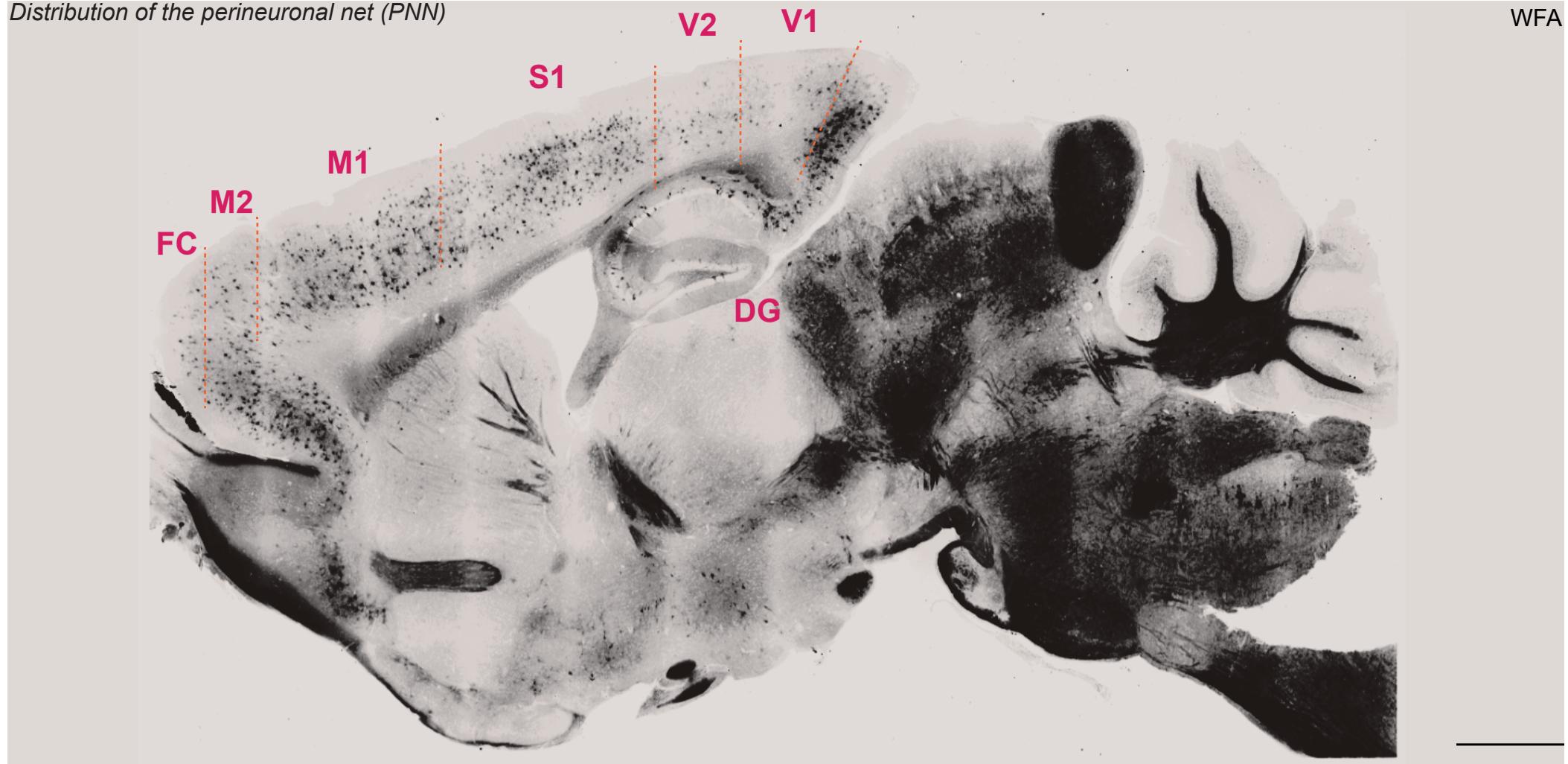


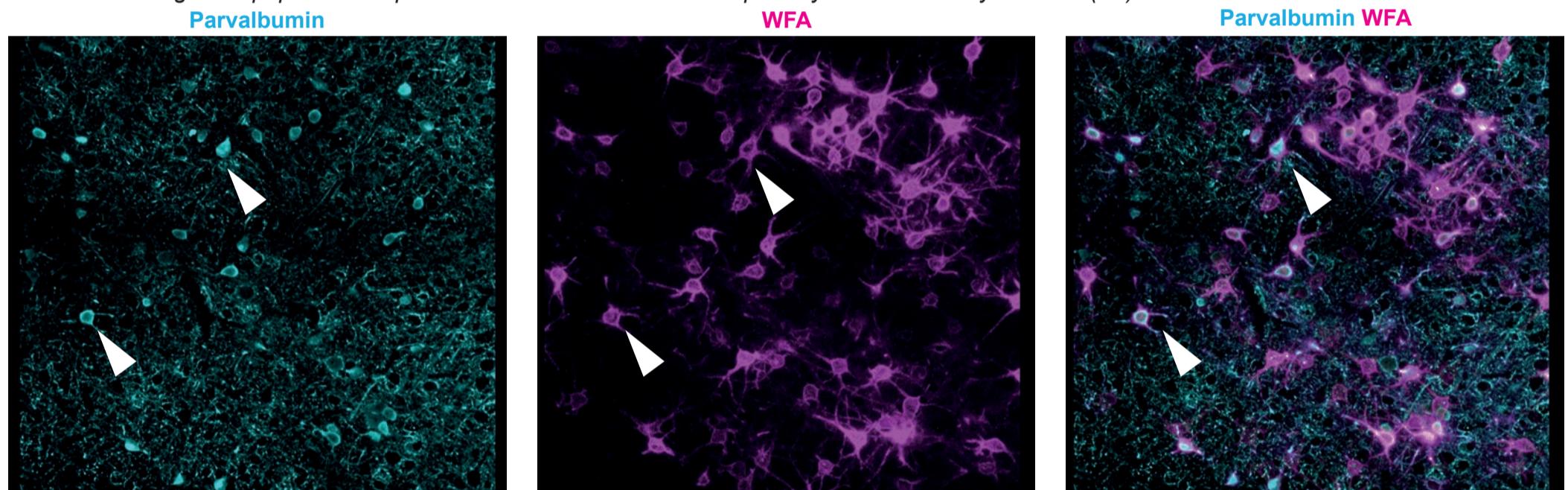
**Figure S1. PNN distribution in the cortex, Related to Figure 1**

**A** Distribution of the perineuronal net (PNN)



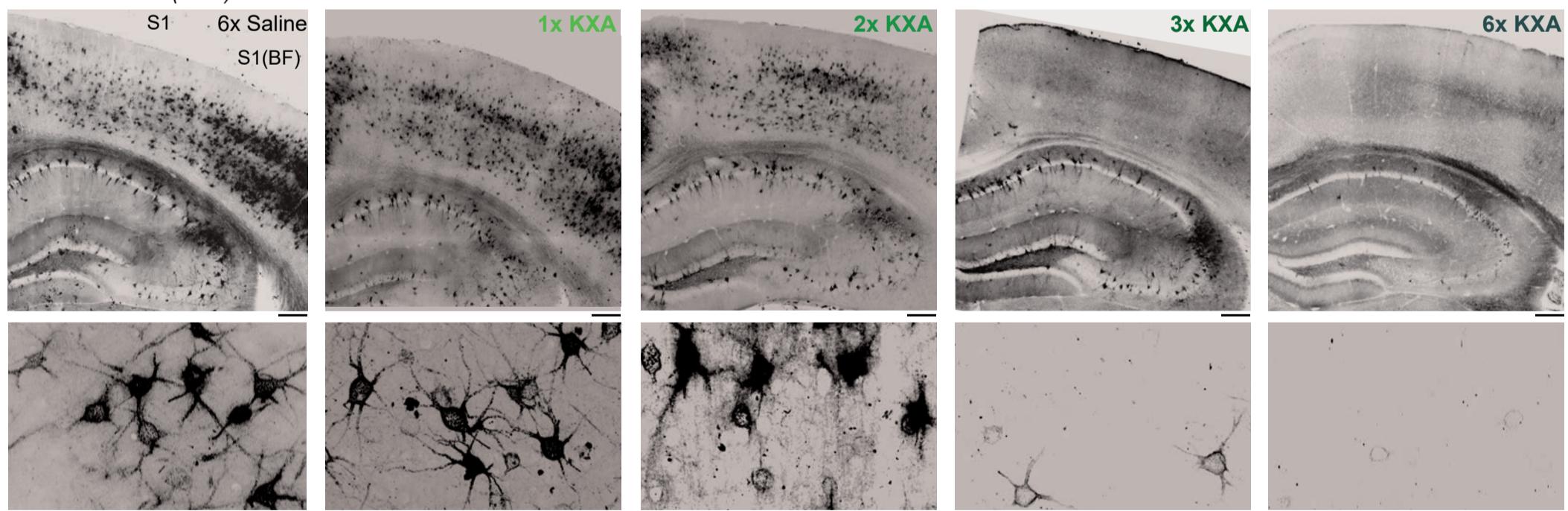
**B**

PNN surrounding a subpopulation of parvalbumin<sup>+</sup> interneurons in the primary somatosensory cortex 1 (S1)

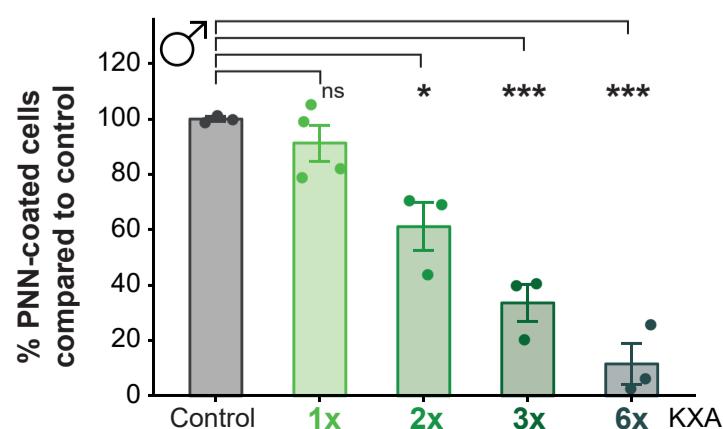


**C**

Perineuronal net (PNN) distribution in S1 of males



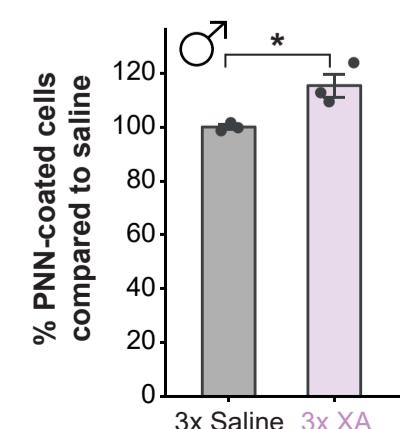
**D** Density of PNN-coated cells



**E** PNN distribution under  $\alpha$ -azne-acepromazine (XA) alone



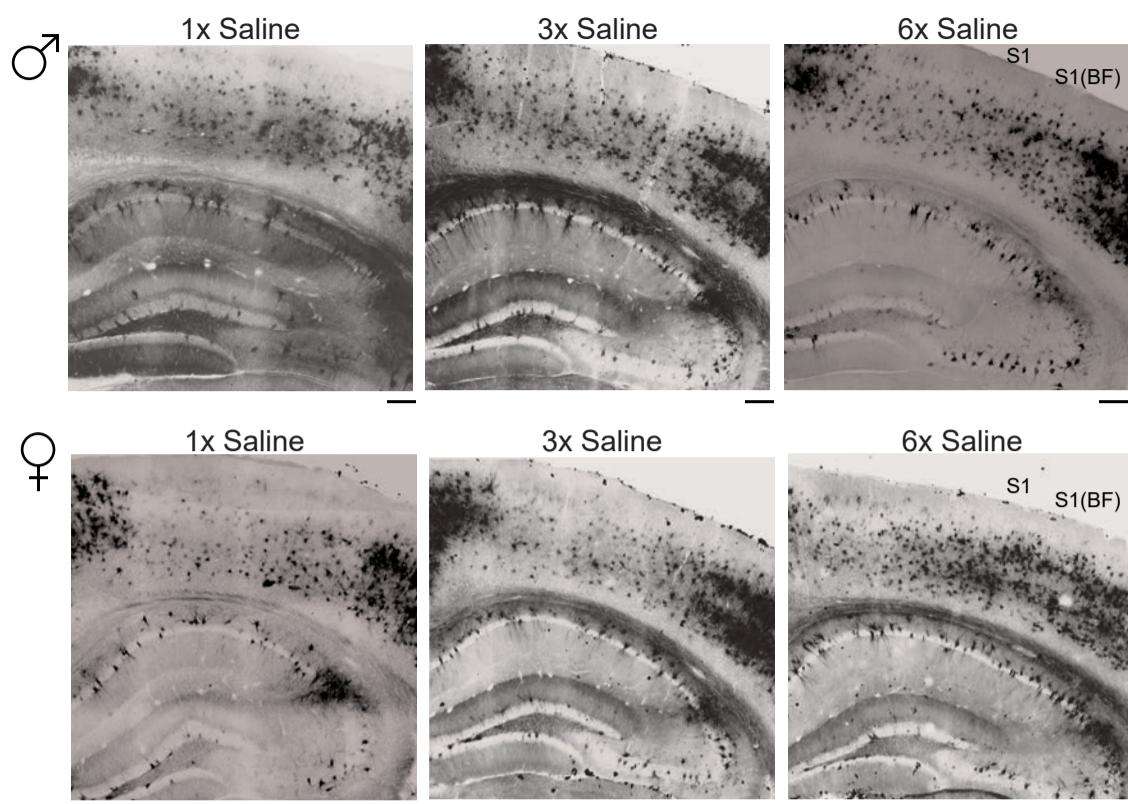
**F** Density of PNN-coated cells



**Figure S2. No PNN loss upon repeated saline injection, and no ketamine-induced apoptosis, Related to Figure 1**

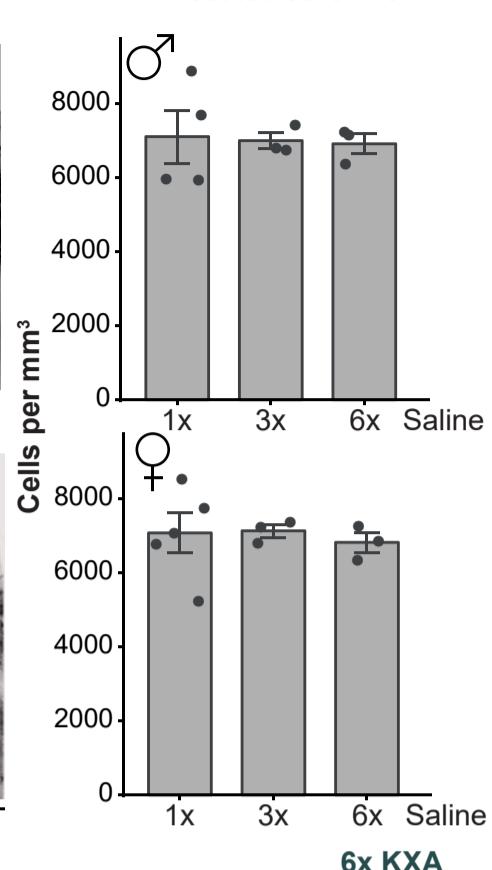
**A**

Perineuronal net distribution in the primary somatosensory cortex (S1)



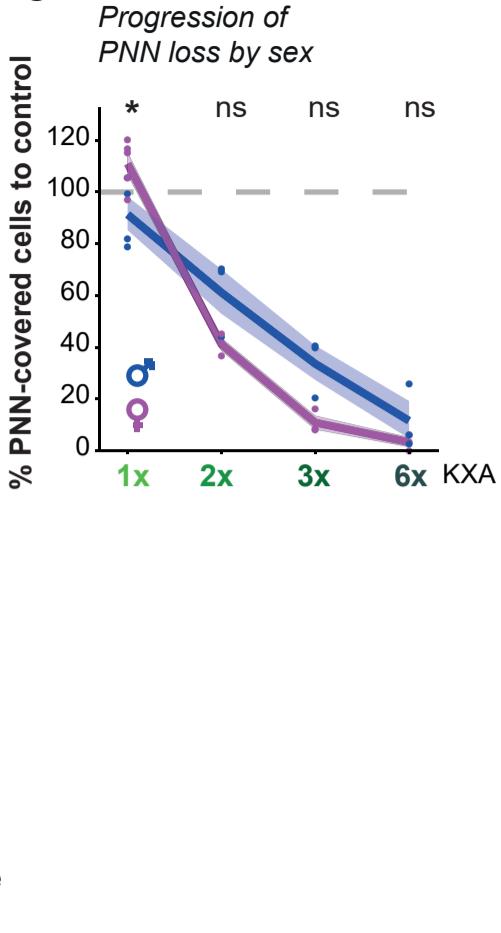
**B**

Number of PNN-coated cells in S1



**C**

Progression of PNN loss by sex

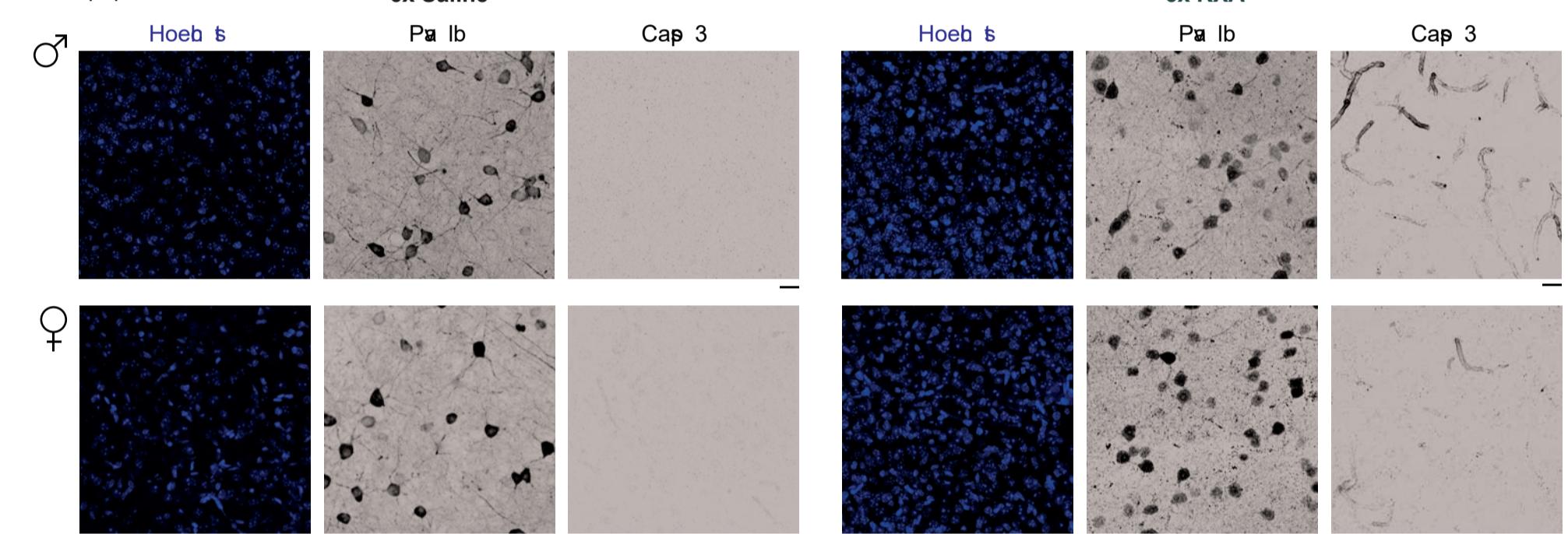


**D**

Apoptotic cells in S1

6x Saline

Cap 3



**E**

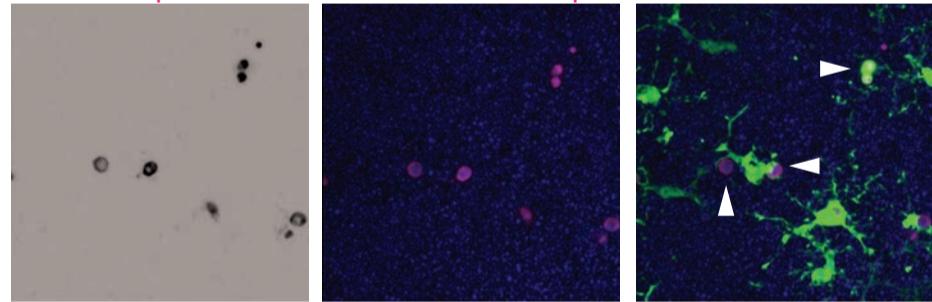
Positive control for caspase-3 staining in the developing retina

Cap 3

Hoechst

Cap 3

Caspase 3 GFP het

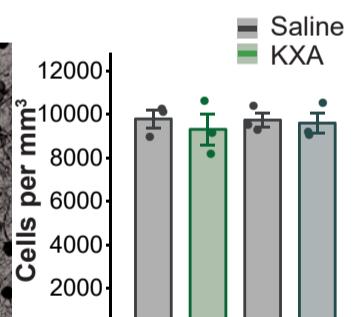
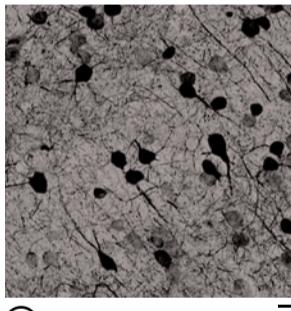


**F**

Density of parvalbumin<sup>+</sup> neurons in S1

♂ 3x Saline

3x KXA



**G**

HABP expression in S1

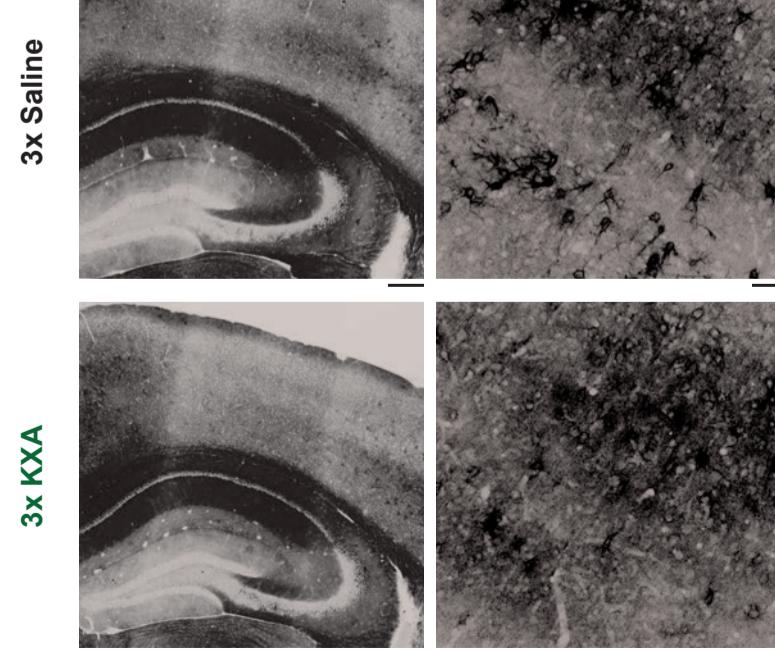
HABP

HABP

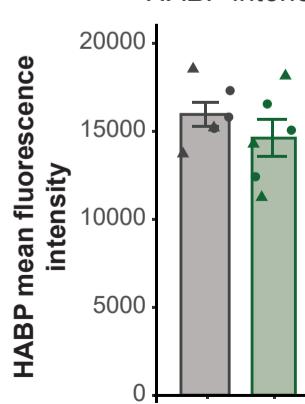
♂

● ♂  
▲ ♀  
■ 3x Saline  
■ 3x KXA

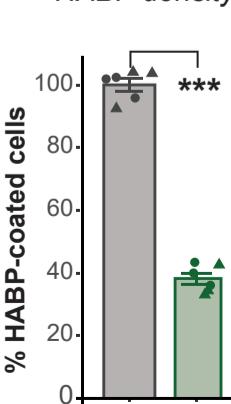
HABP density



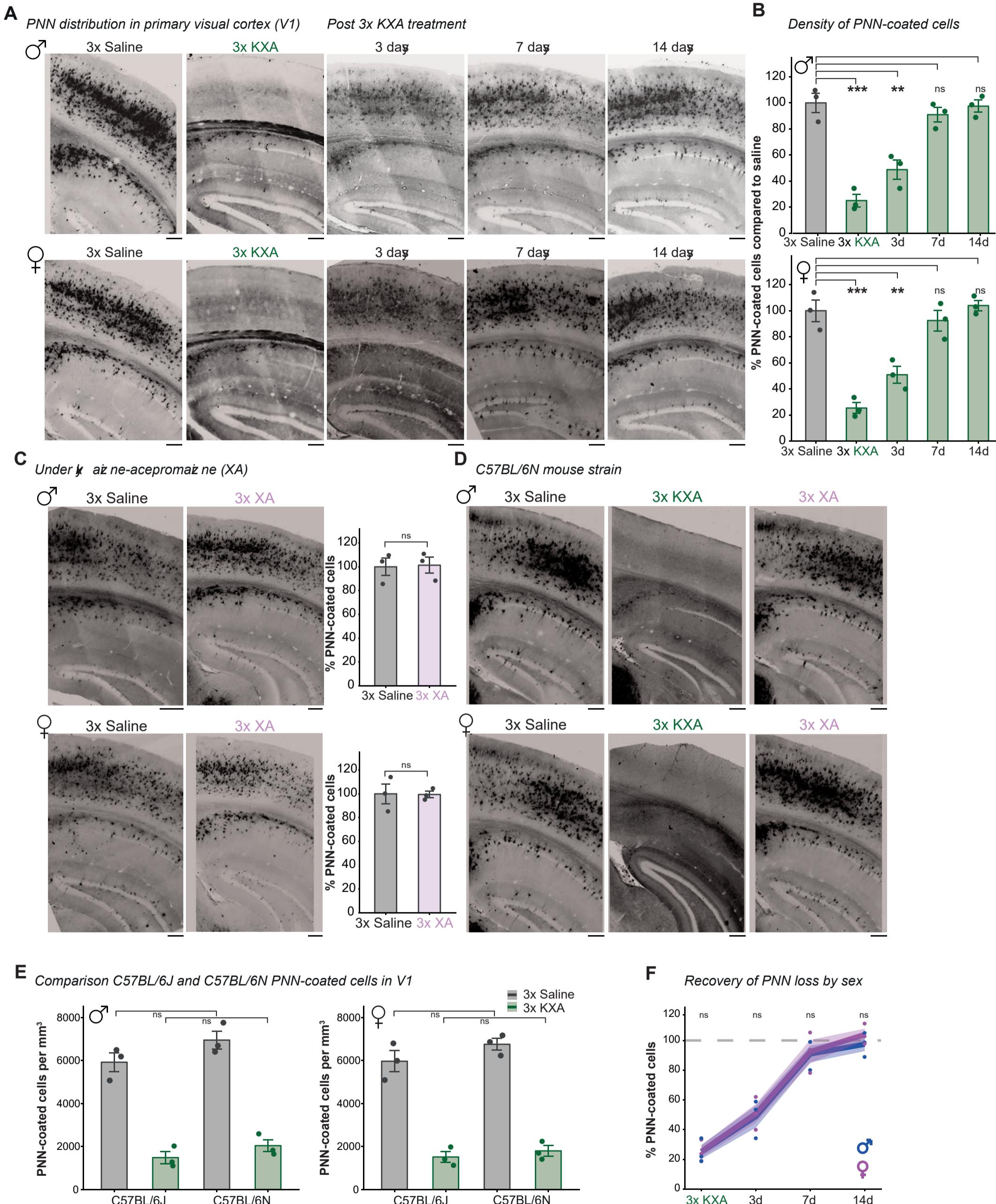
HABP intensity



HABP density

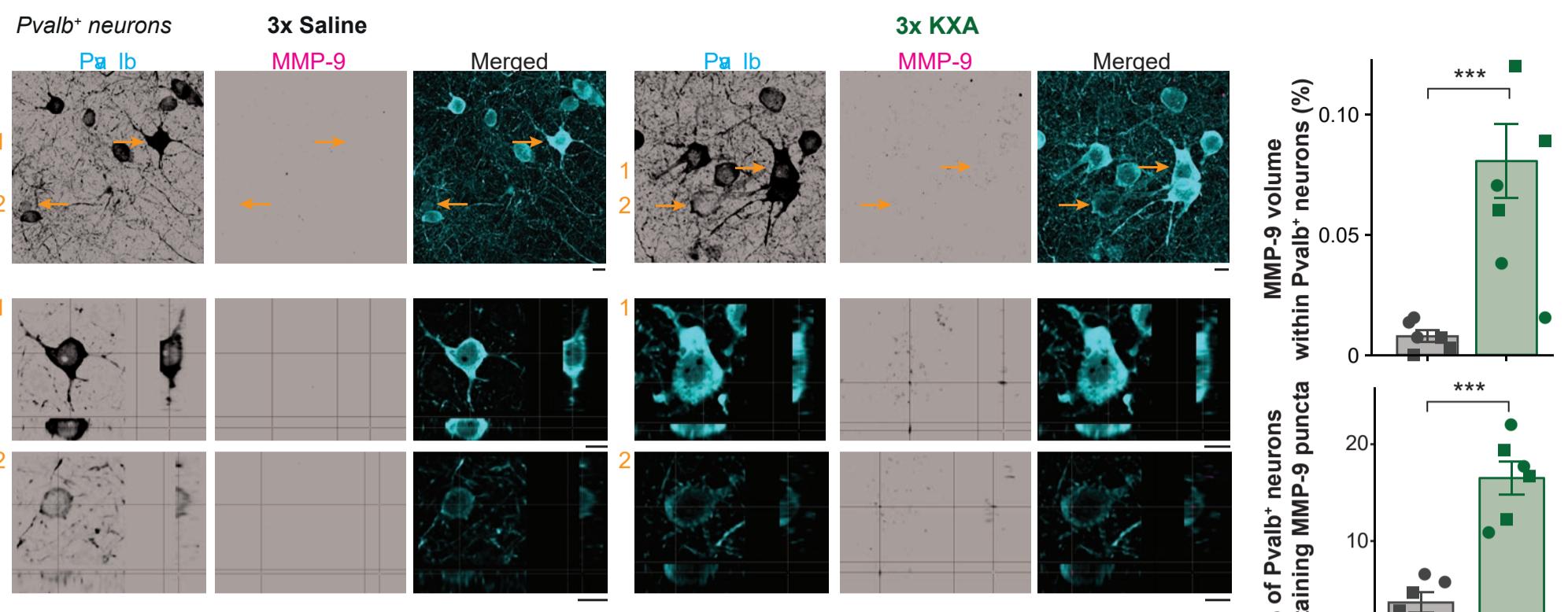


**Figure S3. Ketamine causes transient PNN loss in V1, and is independent from repeated XA treatment alone and mouse strain background. Related to Figure. 1**

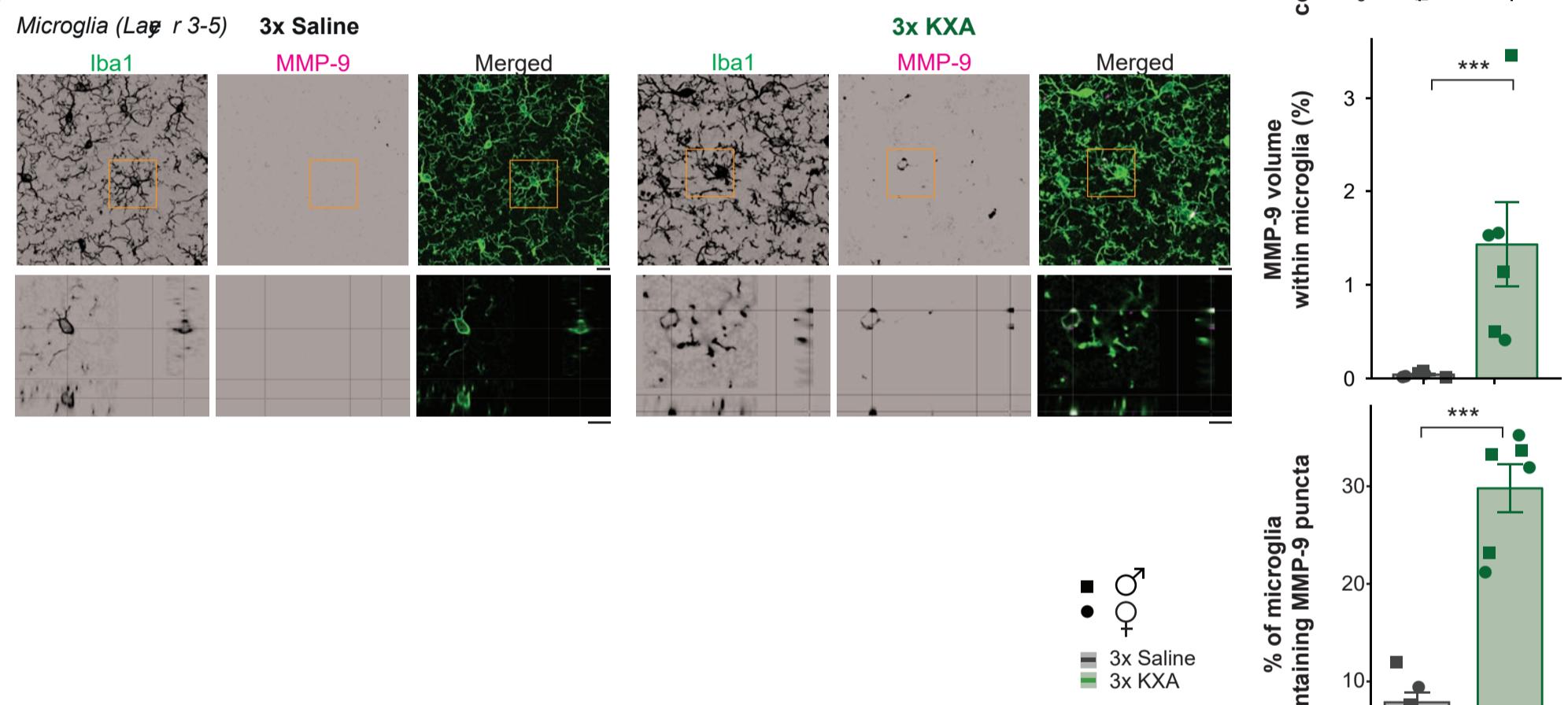


**Figure S4. Repeated KXA treatment increased MMP-9 level in Pvalb<sup>+</sup> neurons and microglia located in cortical layers 3-5, Related to Figure 2.**

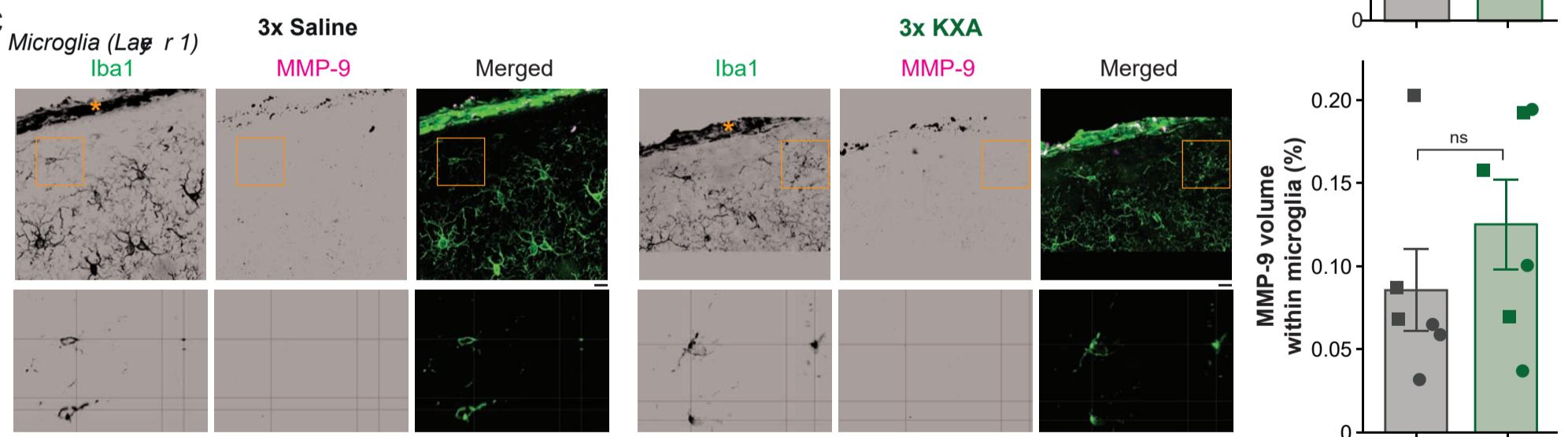
**A**



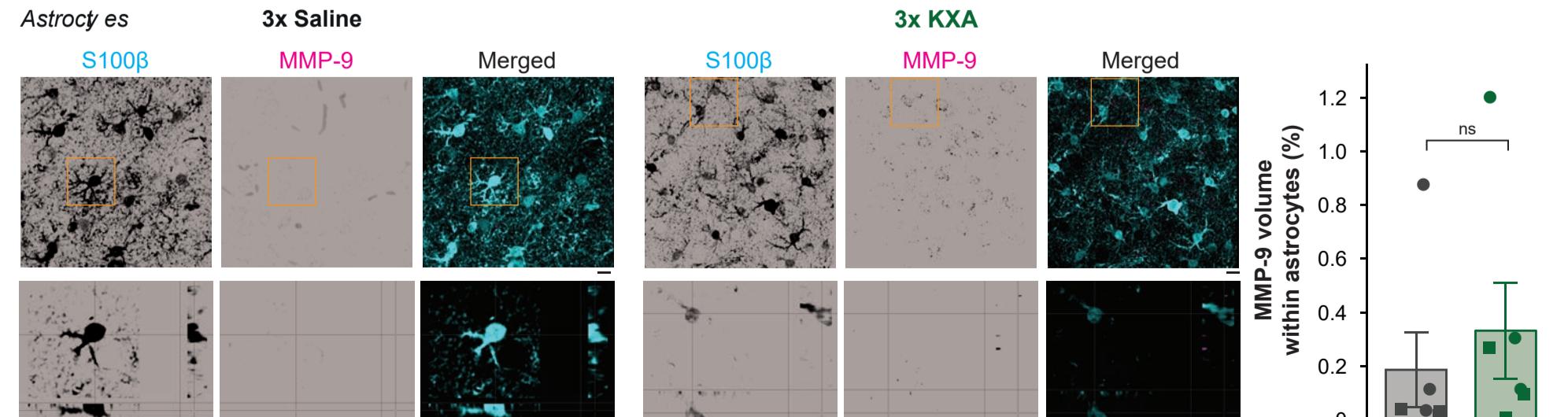
**B**



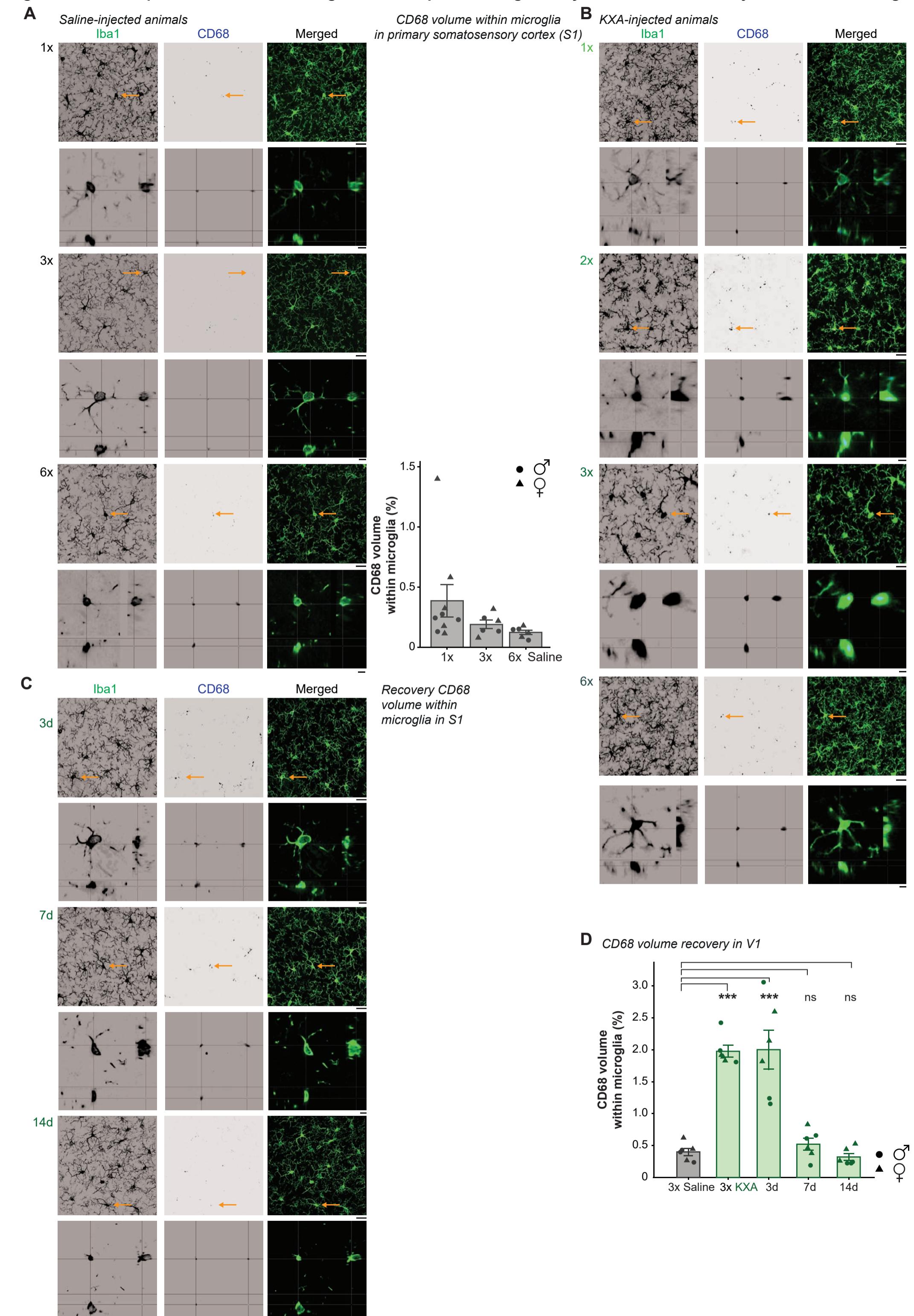
**C**



**D**



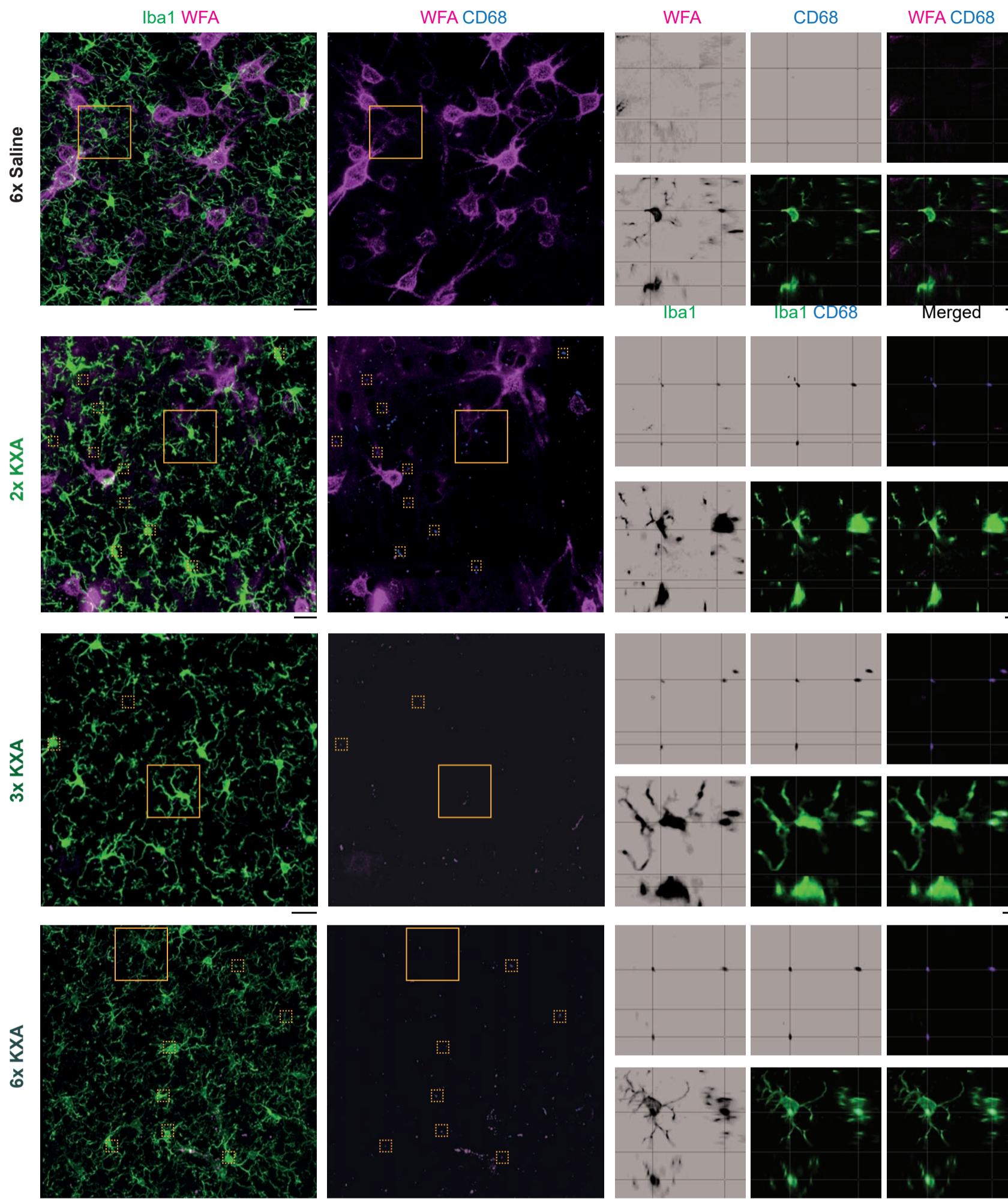
**Figure S5. CD68 expression increased during ketamine exposure and gradually recovered after last injection, Related to Figure 2.**



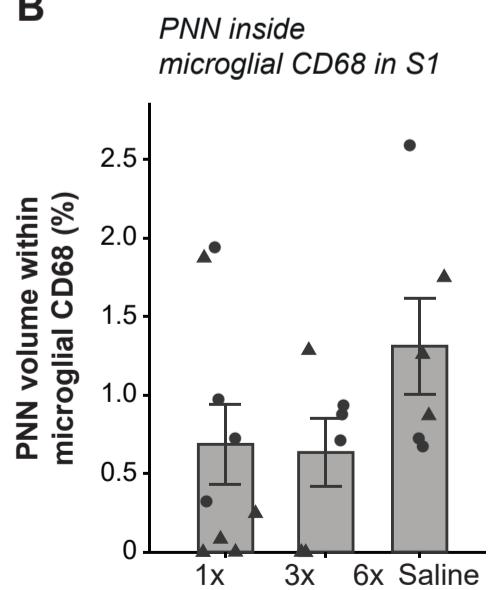
**Figure S6. Multiple microglia contain PNN/CD68 fragments after ketamine exposure, Related to Figure 2.**

**A**

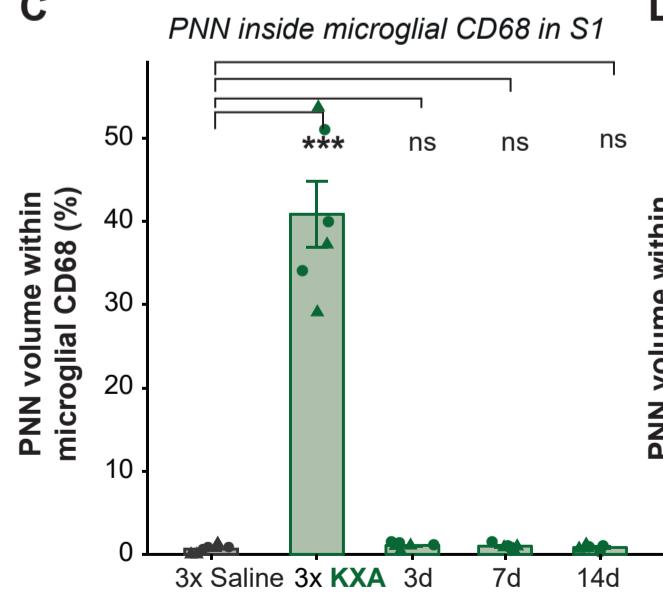
Perineuronal net fragments inside microglia in primary somatosensory cortex (S1)



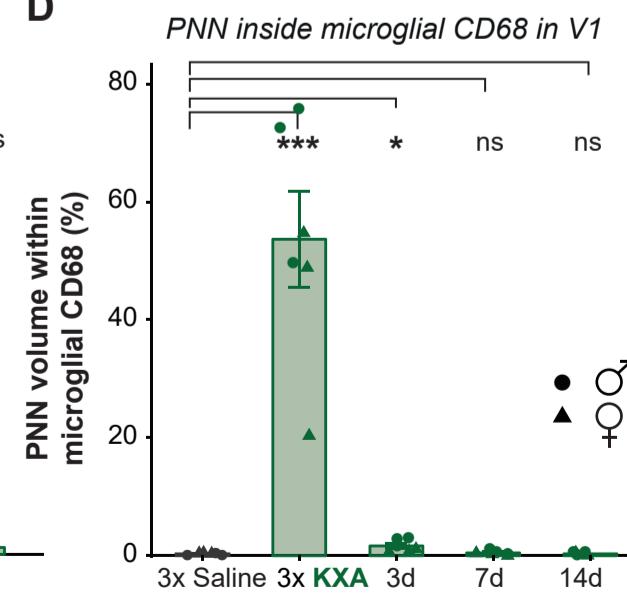
**B**



**C**



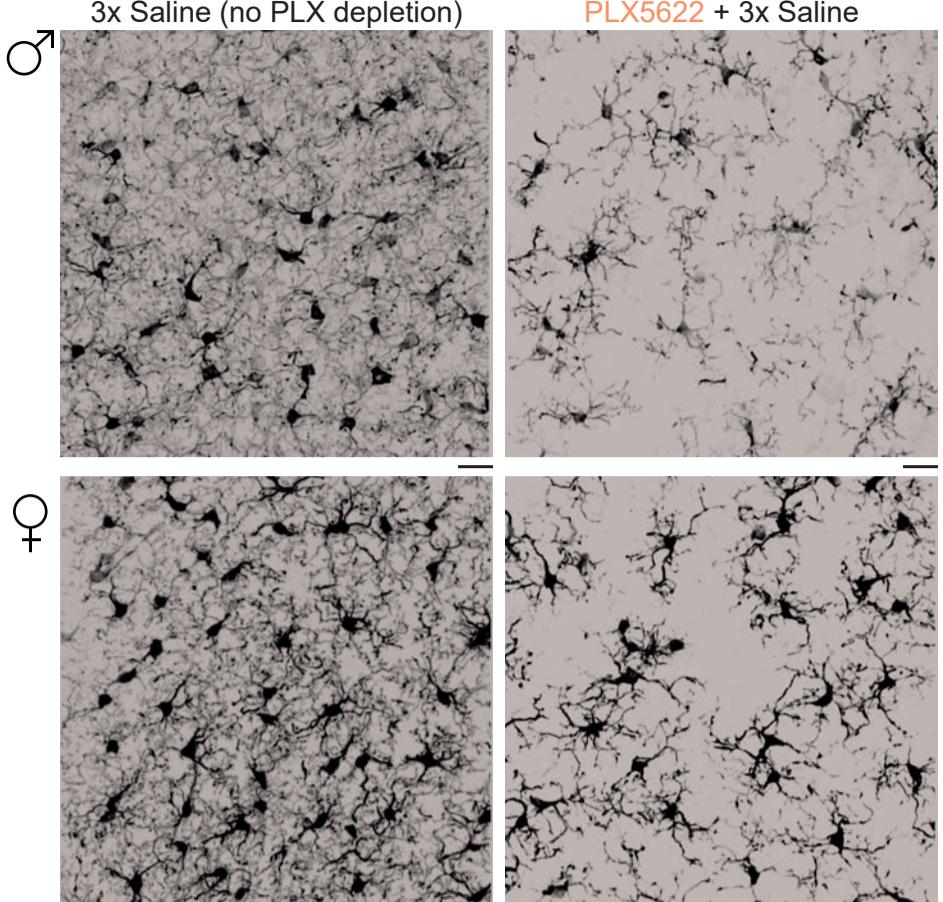
**D**



**Figure S7. Consequences of microglial manipulation, Related to Figures 3 and 4.**

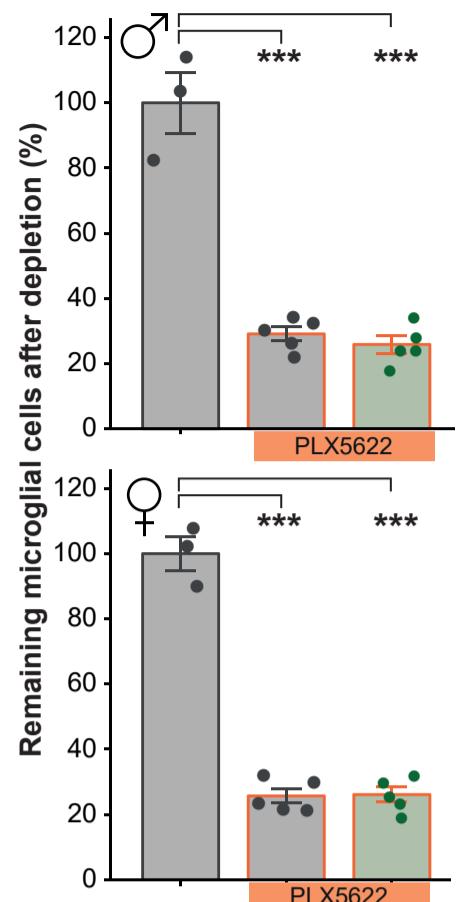
**A**

*Efficiency of microglia depletion with PLX5622 in primary somatosensory cortex (S1)*



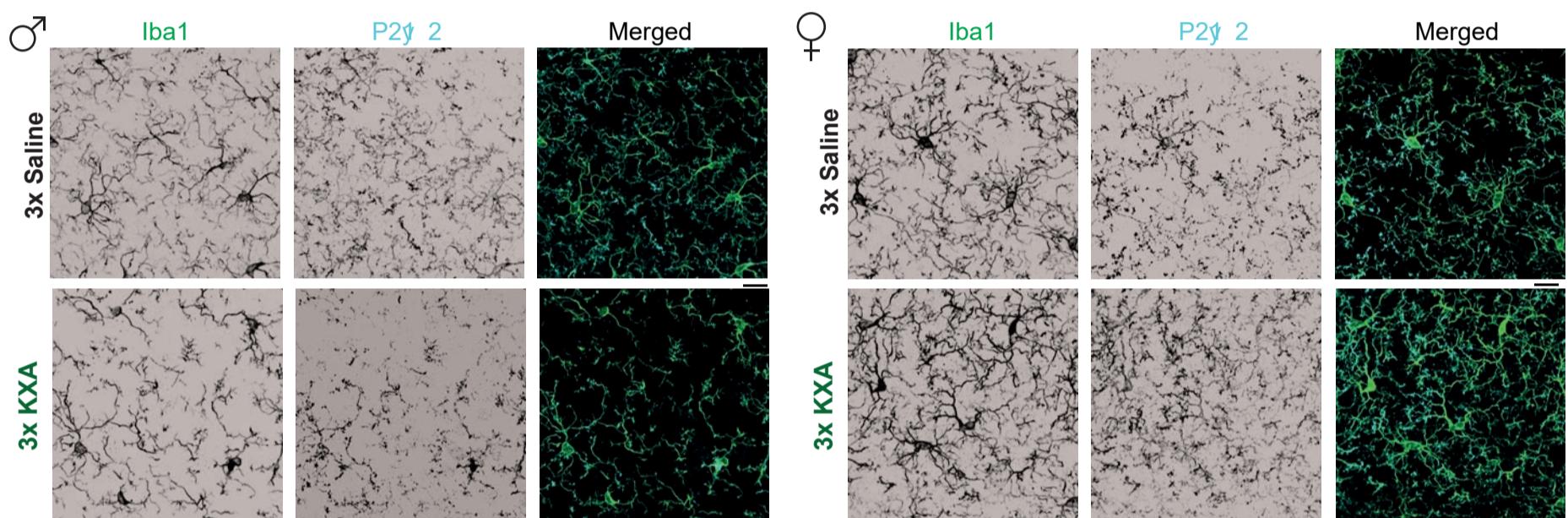
**B**

3x Saline  
3x KXA



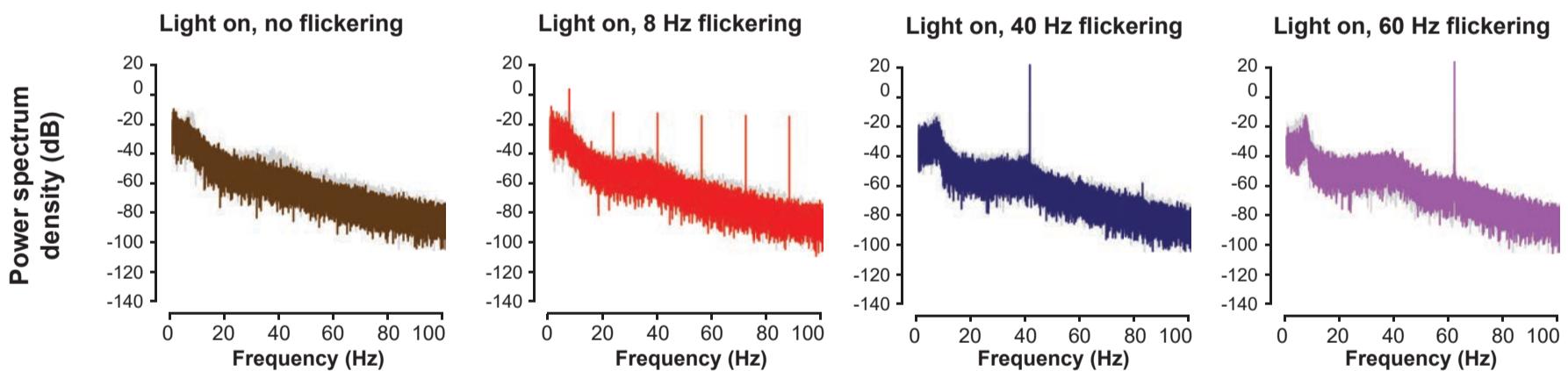
**C**

*P2y<sub>2</sub> receptor expression in S1*



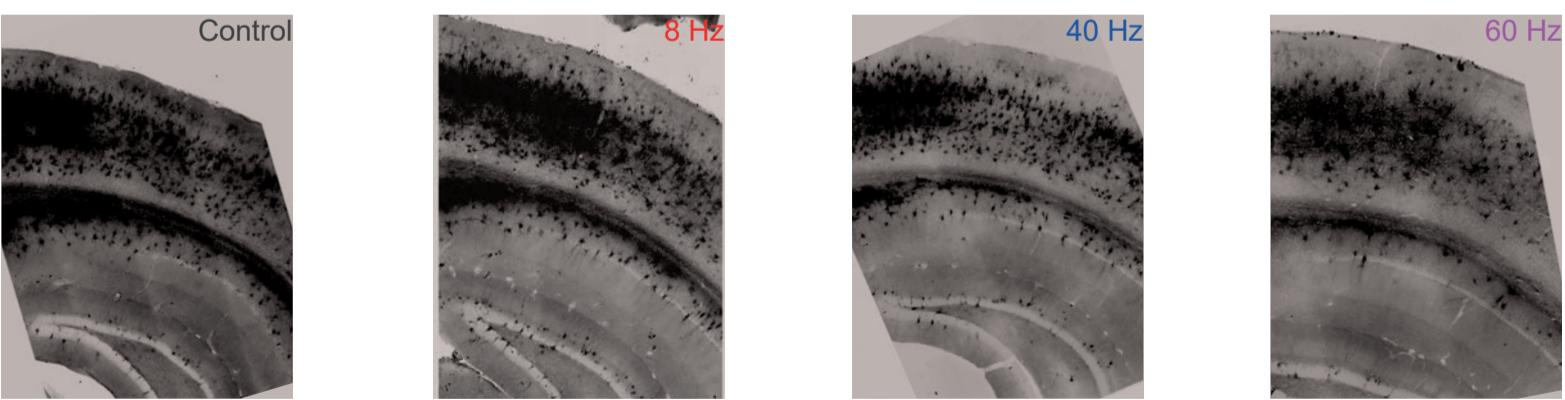
**D**

*In-vivo power spectrum density in primary visual cortex (V1)*



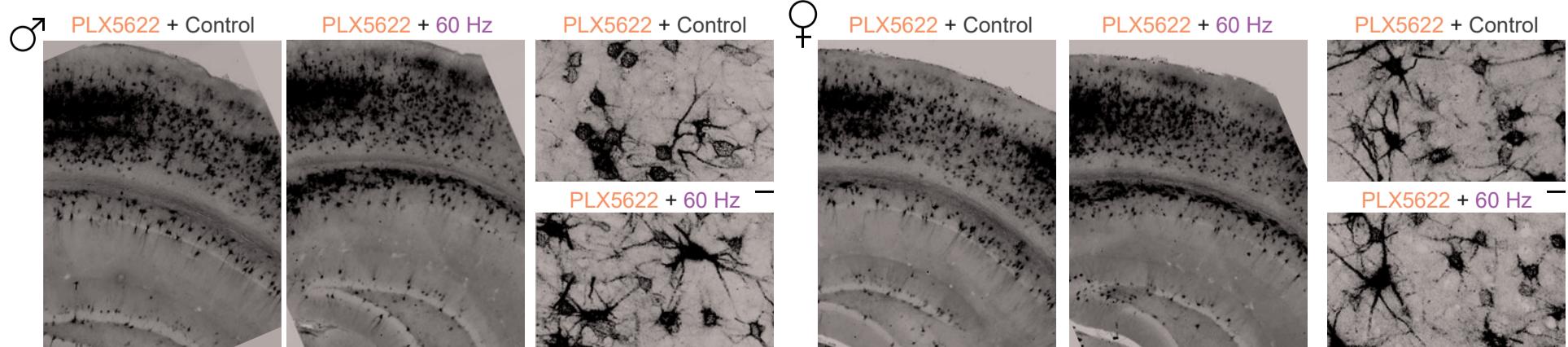
**E**

*PNN distribution in V1*



**F**

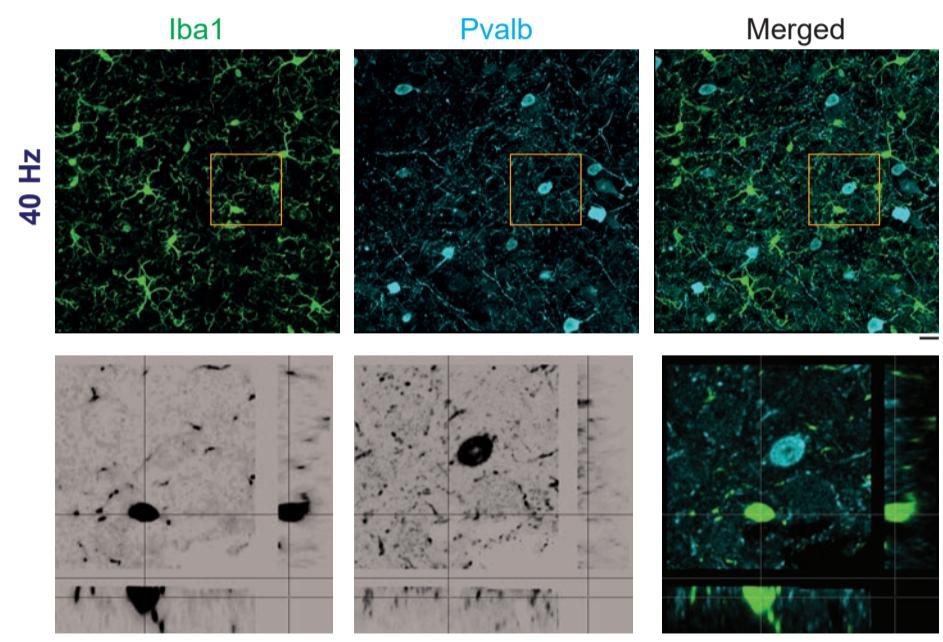
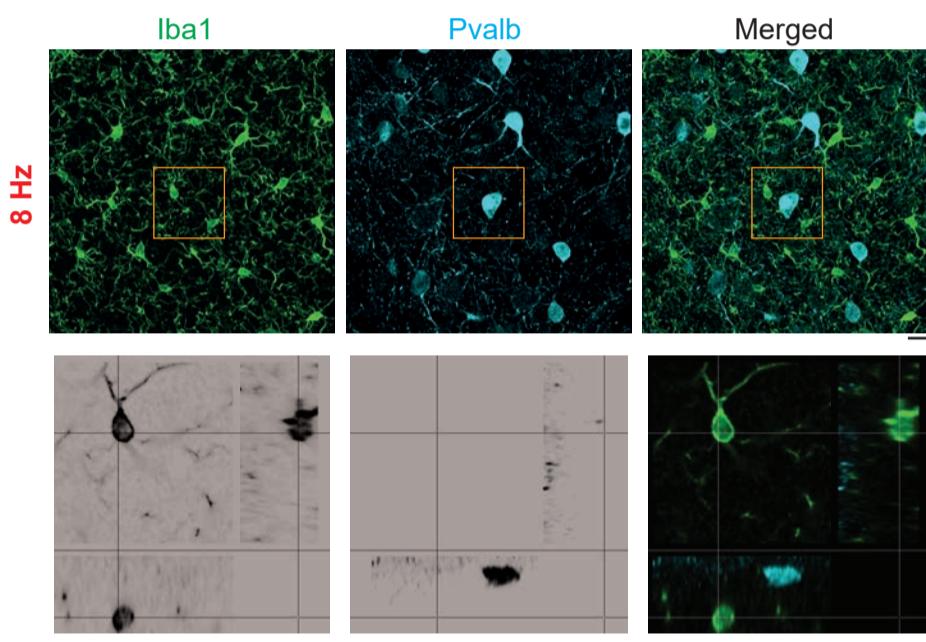
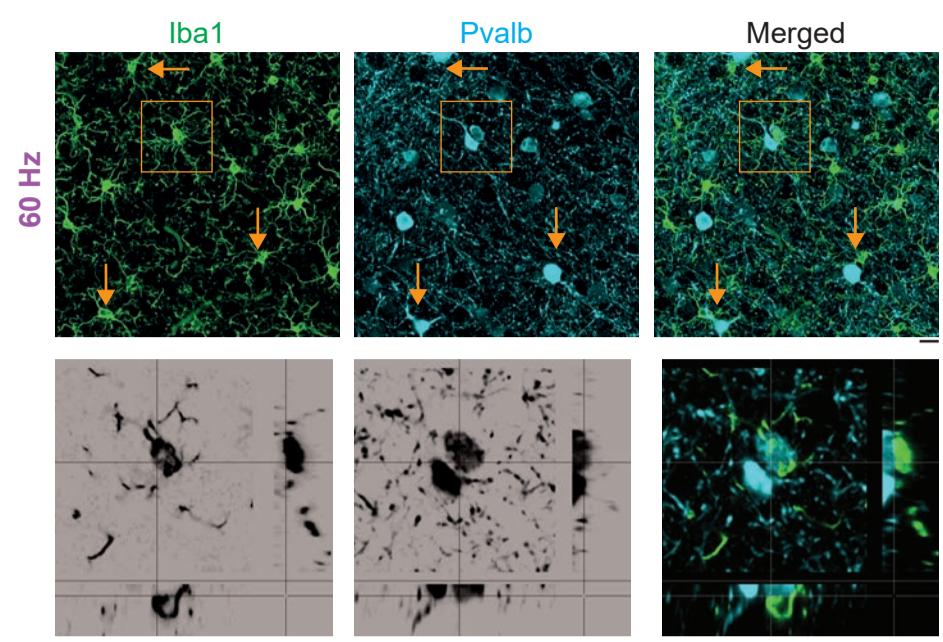
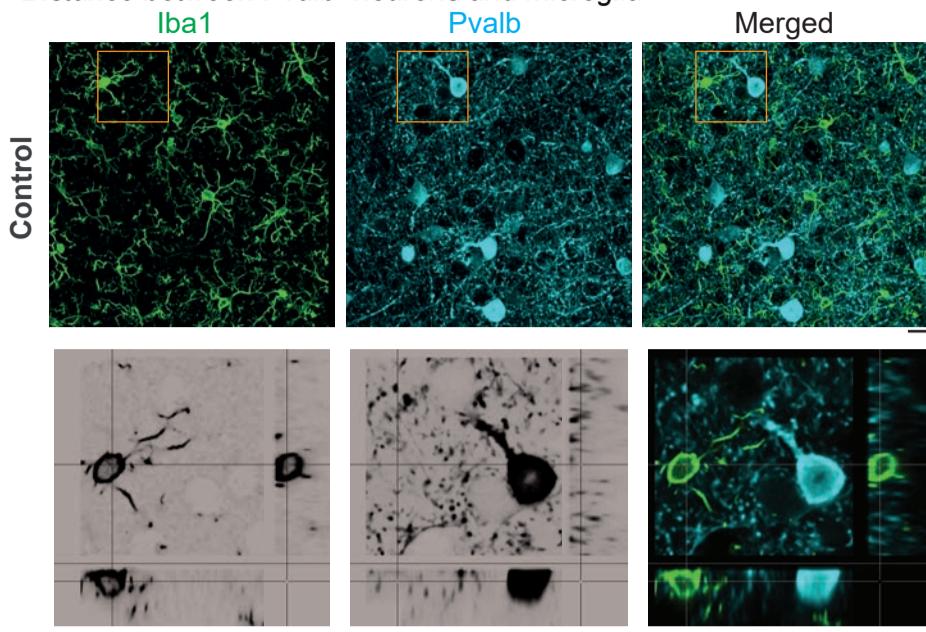
*PLX5622 depletion in V1*



**Figure S8. Effects of light flickering on parvalbumin<sup>+</sup> neuron-microglia distance and MMP-9 expression level, Related to Figure 4.**

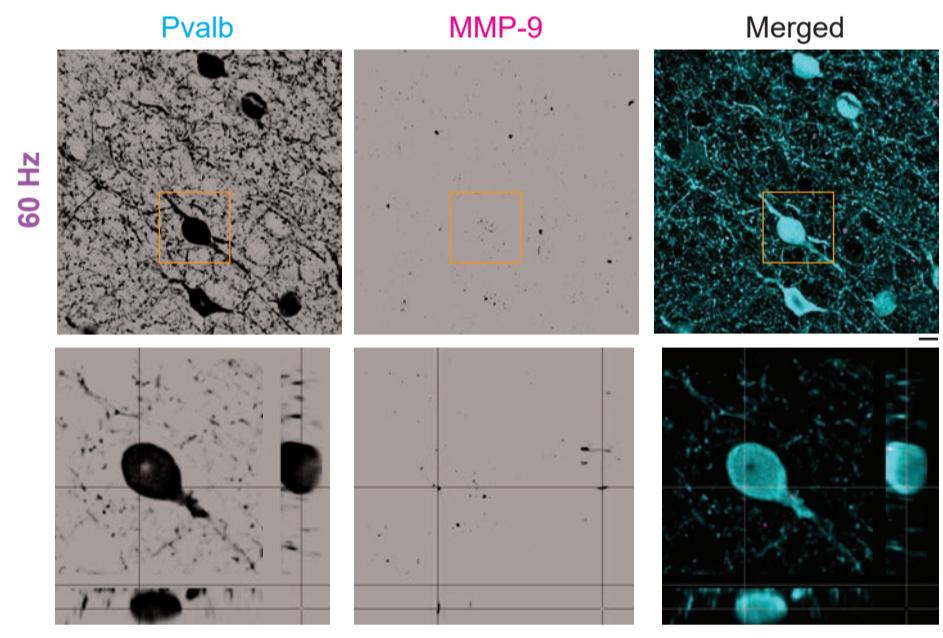
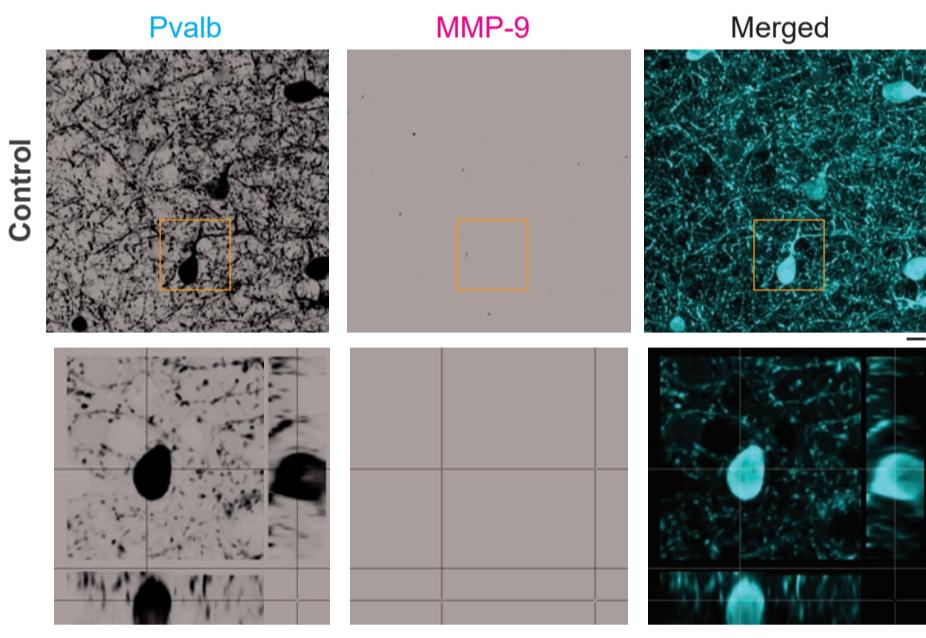
**A**

*Distance between Pvalb<sup>+</sup> neurons and microglia*



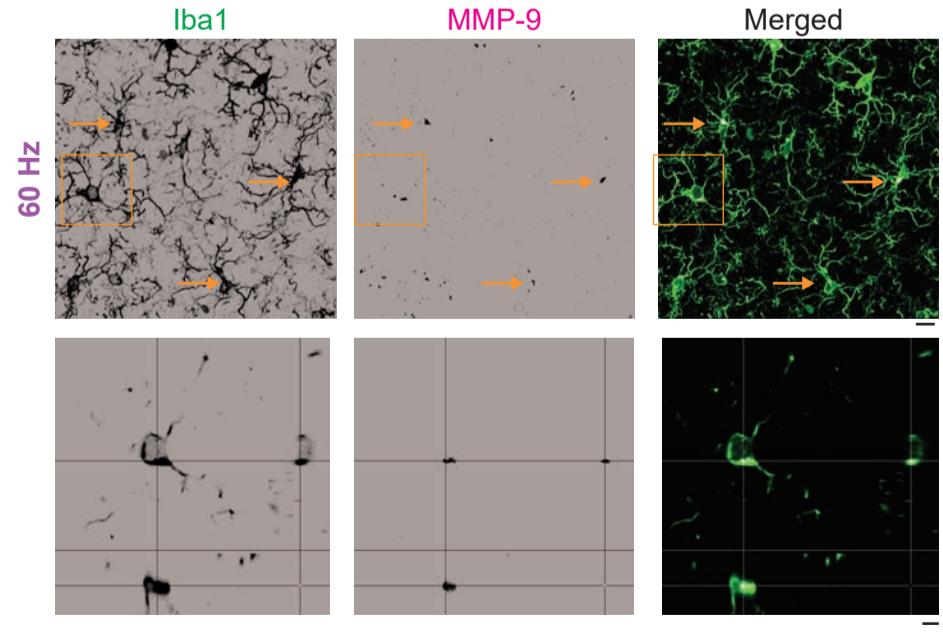
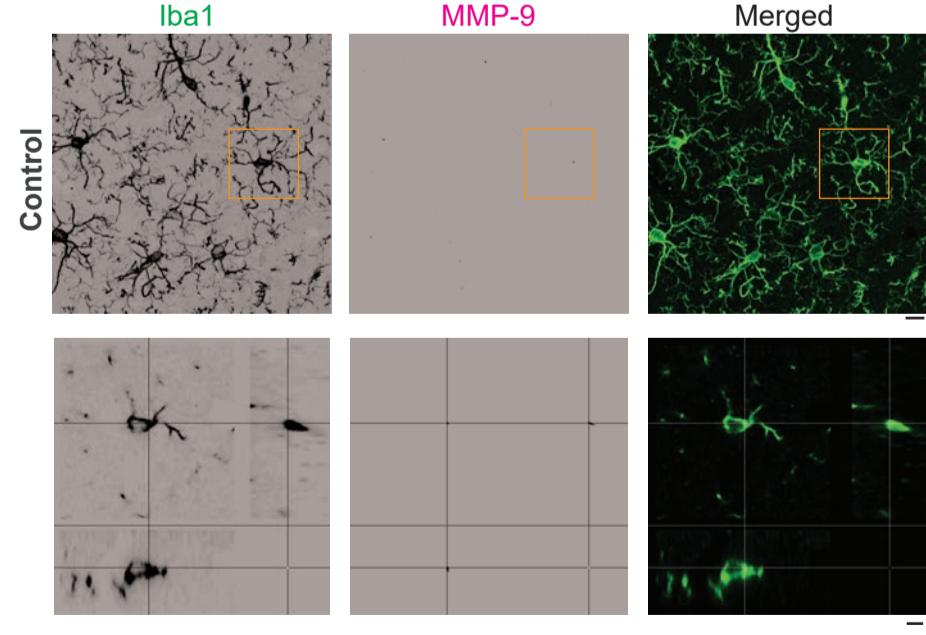
**B**

*Pvalb<sup>+</sup> neurons*



**C**

*Microglia*



**Figure S9. 60 Hz light-flickering induces PNN removal via microglia, Related to Figure 4.**

