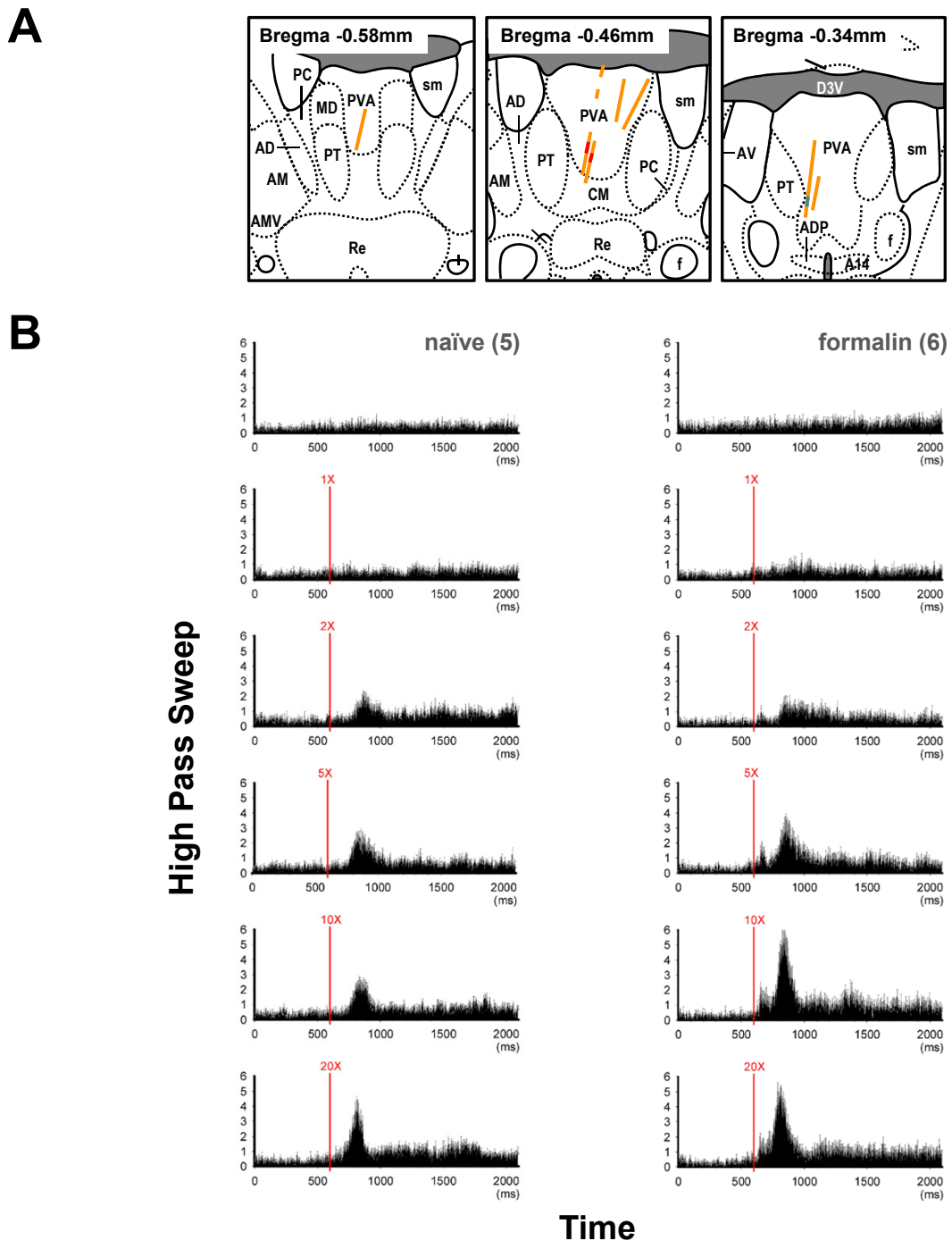
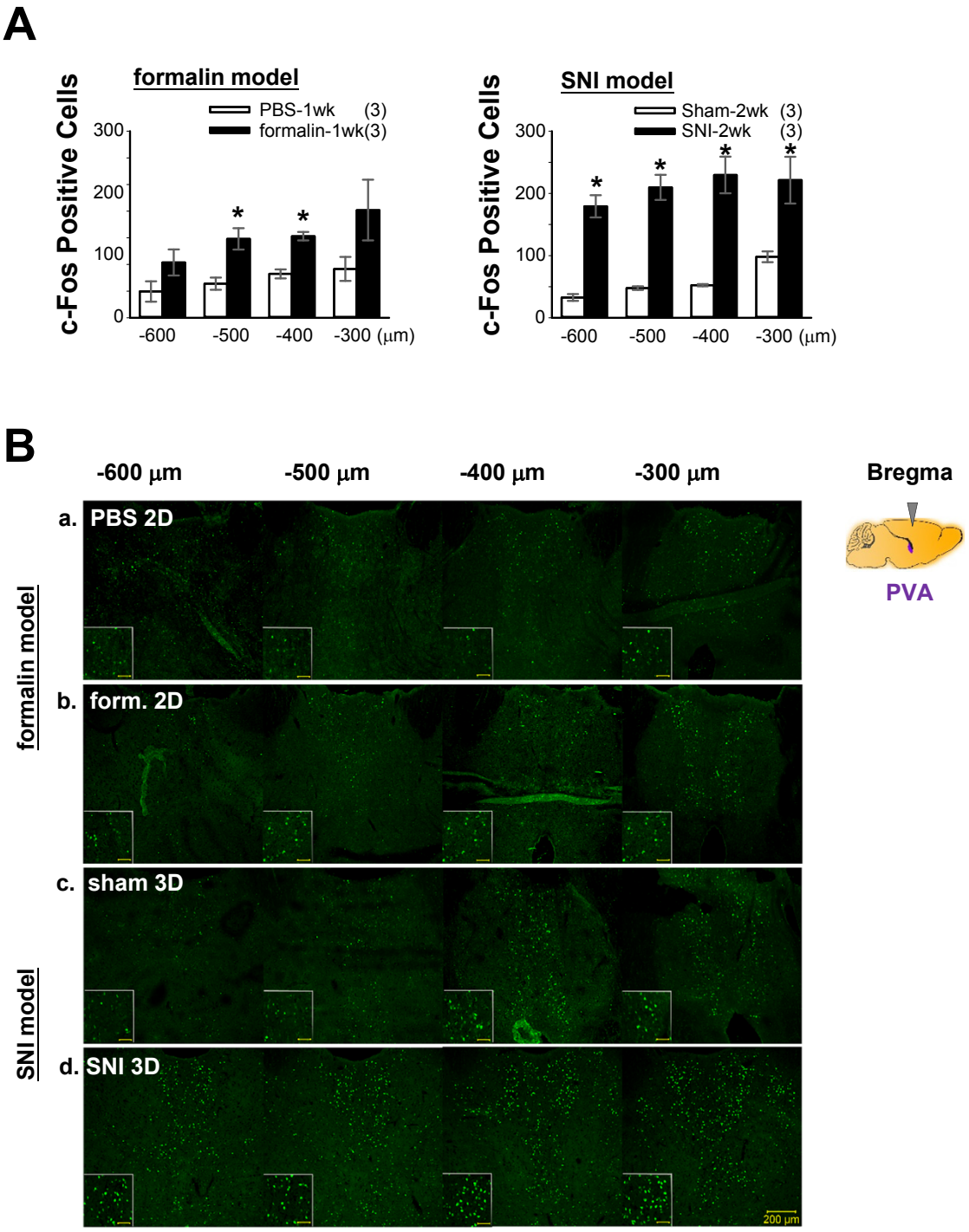
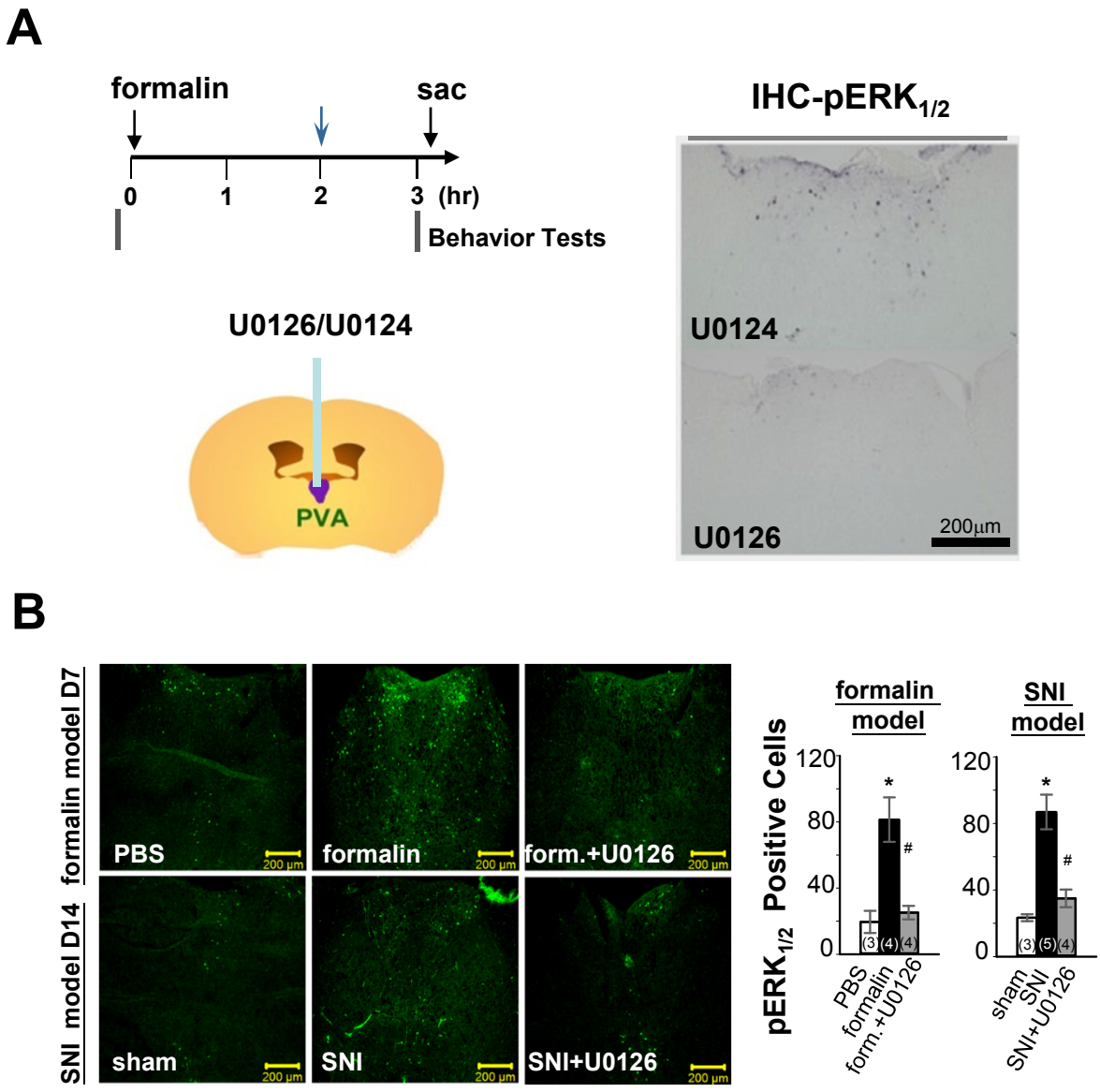


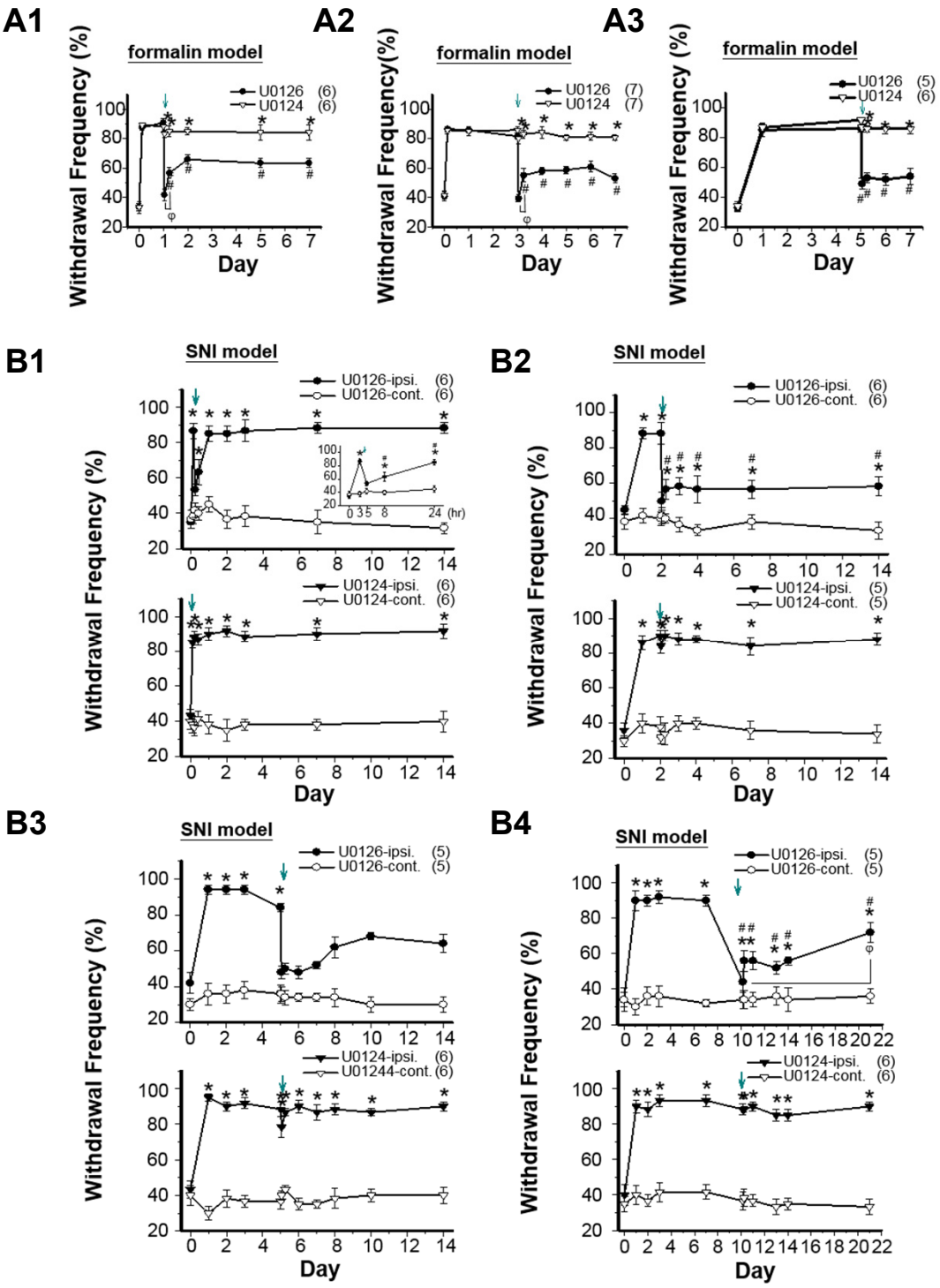
Supplementary Fig. 1 PVA neuronal activities in naïve and formalin treated mice. A. Hot spot analysis of sciatic stimuli responding PVA neurons in naïve mice. After anatomical analysis of the lesion, the PVA responding channels of the multichannel probes were marked in orange within PVA and neighboring regions containing coronal panels from brain atlas (*The Mouse Brain in Stereotaxic Coordinates, Second Edition*) . The lesion channel is marked in red and the responding channel situated at the boarder of PVA is in canyon blue. **B.** Average high-pass sweeps of spontaneous and evoked spike firing of PVA neurons recorded in naïve and formalin treated mice. The sciatic nerve stimulation current was 1-, 2-, 5-, 10-, and 20-fold (X) to the threshold and a red line indicates when the current was applied. The error bar is shown in grey. Sample size is shown in parenthesis.



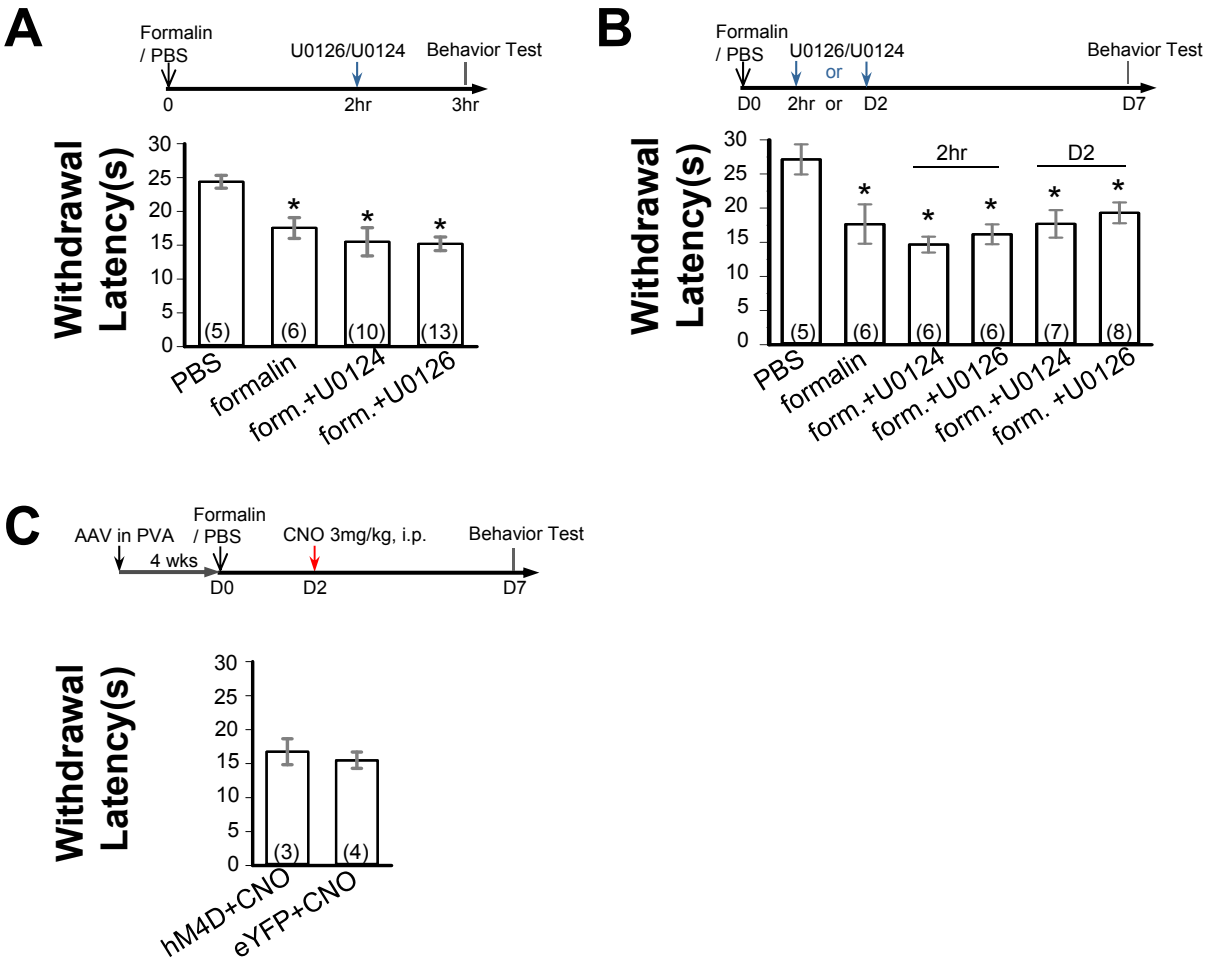
Supplementary Fig. 2 Increased c-Fos expressing in PVA in formalin and SNI models. A. Quantification of c-Fos positive cells in the PVA. c-Fos signals was detected from 600 to 300 μm posterior to bregma 1 wk after formalin or PBS injection and 2 wks after SNI or sham operation. **B.** Representative immunofluorescent staining of c-Fos signals in PVA. Brain slices containing PVA at the same rostrocaudal level, from 600 to 300 μm posterior to bregma, are shown. c-Fos staining on PVA (**a**) 2 days after PBS, (**b**) 2 days after formalin (form.) (F) injection, and (**c**) 3 days after sham operation, (**d**) 3 days after SNI surgery. Scale bar = 200 μm. Insert, enlarged images of the up-right corner of PVA, scale bar = 50 μm. Immunofluorescent staining of c-Fos was repeated in at least 2 mice in each treatment group. (Quantification of cell count was analyzed by one-way ANOVA. Data are mean±SEM. * $p<0.05$ compared to control; sample size is shown in parenthesis.)



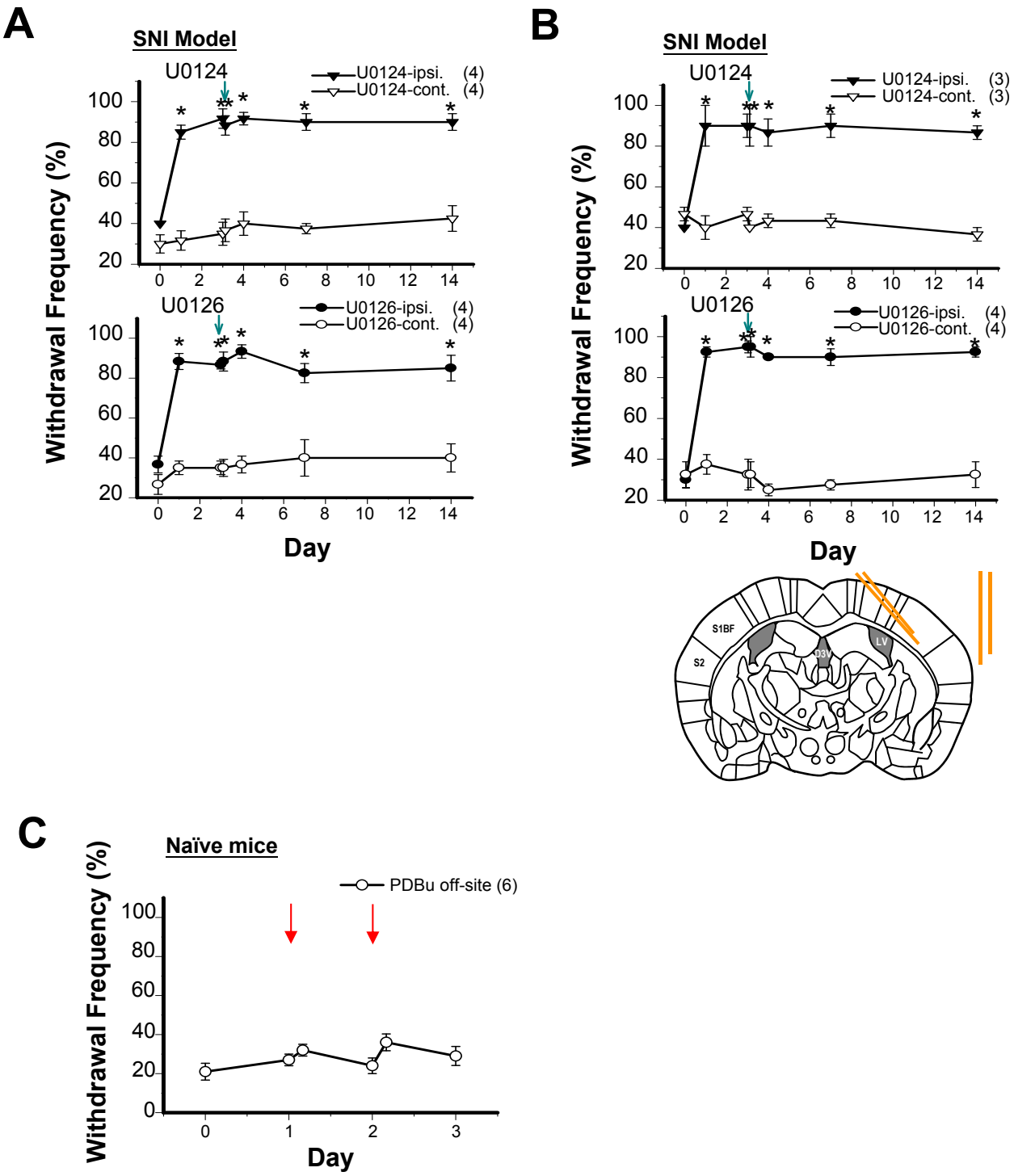
Supplementary Fig. 3 Intra-PVA infusion of U0126 reduces formalin- and SNI-induced increase of IHC-pERK$_{1/2}$ signals in PVA. A Mice receiving a microinfusion of 5mM U0124 or U0126 in PVA 2 hours after formalin injection underwent a behavioral test. The brain was then harvested after behavioral tests 3-hr after formalin injection. Immunochemistry staning of pERK$_{1/2}$ signals were then detected on 5-μm paraffin sections containing PVA. **B** Mice receiving a microinfusion of 5mM U0126 in PVA at 2 days after formalin injection or 3days after SNI surgery. Immunofluorescent staining of pERK$_{1/2}$ signals were detected on 20-μm cryo-sections containing PVA regions. Right panel: the quantification of PVA pERK1/2 positive cells in each treatment group analyzed by one-way ANOVA. (Data are mean±SEM. * p<0.05 compared to control, # p<0.05 compared to formalin or SNI;. Sample size is shown in parenthesis.)



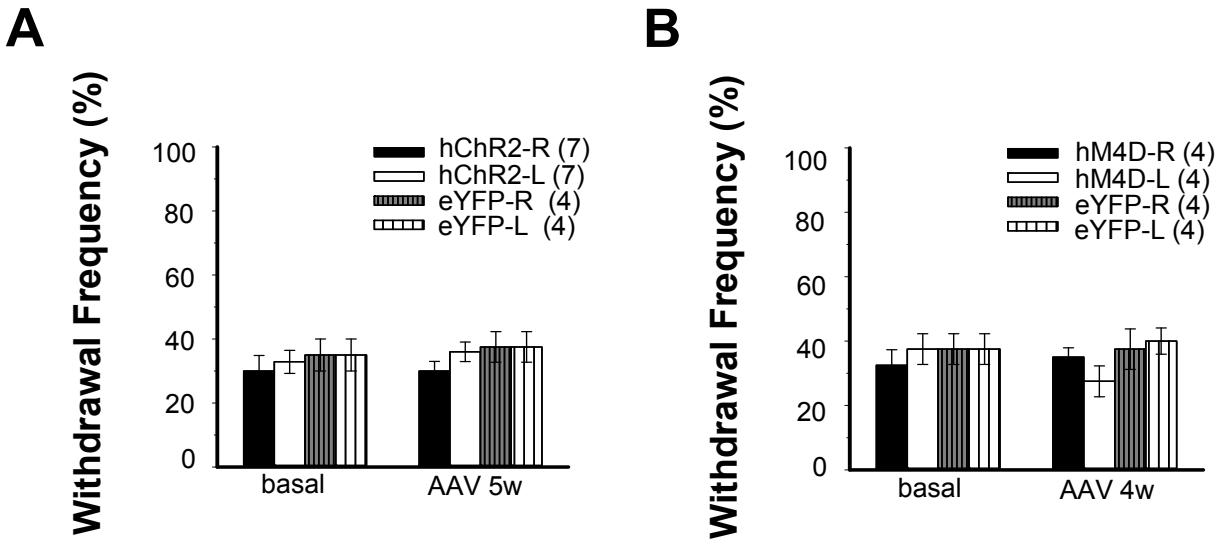
Supplementary Fig. 4 Inhibition of PVA ERK$_{1/2}$ activity attenuates SNI- and formalin-induced chronic mechanical hyperalgesia. U1026 and U0124, the inactive structural analogue of U0126, were infused into PVA at different times in formalin and SNI models. Effect of intra-PVA infusion of U0126 at **A1.** 1 day (1D) after formalin, **A2. 3** days (3D) after formalin, **A3.** 5 days (5D) after formalin, **B1.** 4 hr (4H) after SNI, **B2**. 2 days (2D) after SNI, **B3**. (5D) after SNI, and **B4.** 10days (10D) after SNI. (Data are mean±SEM. * $p<0.05$ compared to control, # $p<0.05$ compared to basal level, φ $p<0.05$ compared to previous time point; sample size is shown in brackets.).



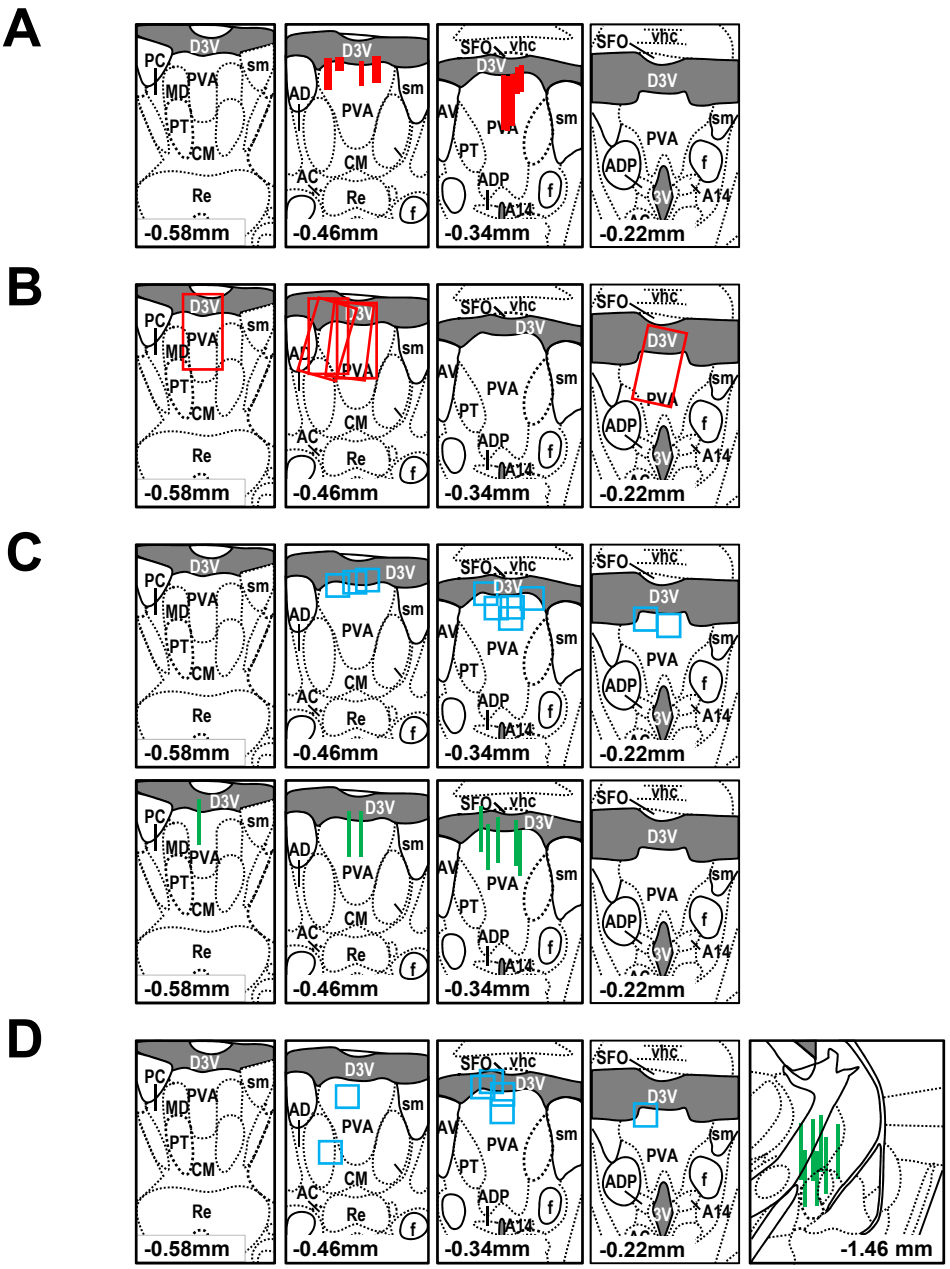
Supplementary Fig. 5 Inhibition of PVA neuronal activity has no effect on formalin-induced thermal hyperalgesia. Formalin-induced shortening of withdrawal latency of limbs was detected on a 50°C hot plate. **A.** Effect of intra-PVA infusion of U0126 at 2 hr after formalin injection on formalin-induced thermal hyperalgesia. Thermal sensitivity was tested 3 hs after formalin injection. **B.** Effect of intra-PVA infusion of U0126 at 2 hr or 2 days after formalin injection on thermal hyperalgesia. Thermal sensitivity was tested 7 days after formalin injection. **C**. Effect of activation of hM4D with CNO on the withdrawal latency compared to the viral (AAV-eYFP) infection control 1 wk after formalin induction. (Data are mean±SEM. *p<0.05 compared to the PBS control; sample size is shown in brackets.)



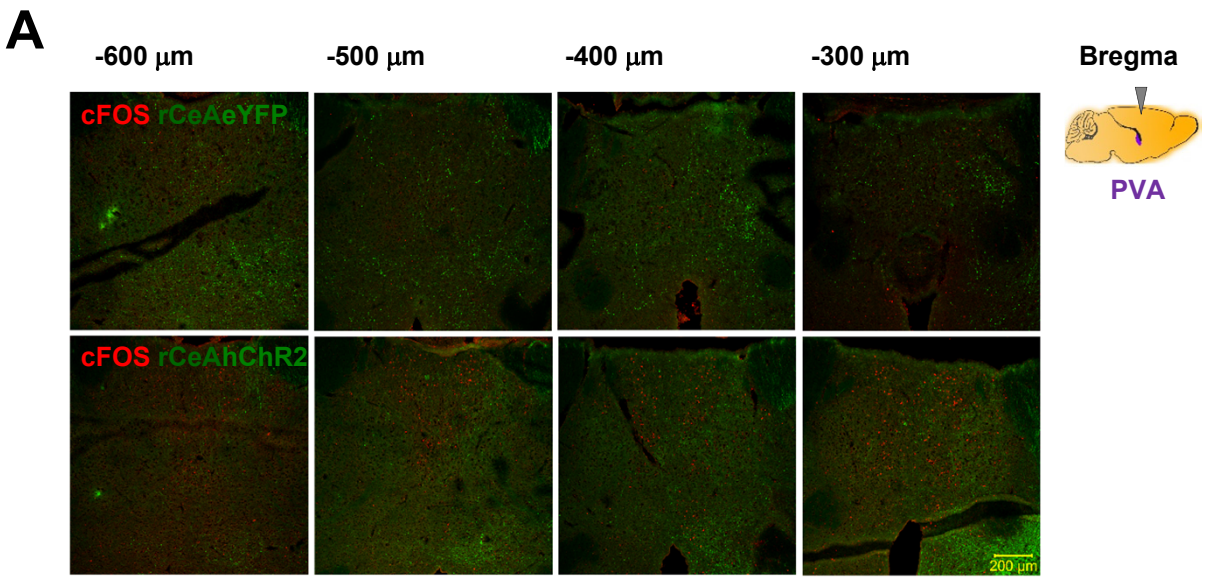
Supplementary Fig. 6 The offsite control of intra-PVA PDBu and U0126 infusion has no effect on SNI-induced mechanical hyperalgesia. Effect of infusion of 5mM U0124 or U0126 in 50% DMSO, the same dose with intra-PVA infusion,, in **A.** the dorsal third ventricle (D3V) or **B.** somatosensory cortex of barrel field (S1BF) at 3 days after SNI surgery. Effect of infusion of U0126 or U0124 into D3V as a leakage control or S1BF as an off-target control on SNI-induced mechanical hyperalgesia. **C.** Effect of 20 pmol PDBu in 50%DMSO into CA1 region of hippocampus on D1 and D2 in naïve mice as an off-target control. (Data are mean±SEM. * $p<0.05$ compared to the contralateral hind limb; sample size is shown in brackets.)



Supplementary Fig. 7 AAV viral infection in PVA has no effect on basal mechanical response. Mechanical withdrawal frequency of hind paws to 1-g von-Frey monofilament in **A.** mice infected with rAAV5/CaMKII-hChR2(H134R)-eYFP-EPRE and rAAV5/CaMKII-eYFP in PVA and **B.** mice infected with rAAV8/CamKII-hM4D-mCherry and rAAV5/CaMKII-eYFP in PVA. Effect of PVA viral infected with 0.2μl AAV on the withdrawal ratio to 1-g force compared to the basal response detected before the viral infection. (Data are mean±SEM. Sample size is shown in parenthesis.)



Supplementary Fig. 8 Diagrammatic representation of coronal sections of mouse brain showing the location of PDBu infusion site inside, AAV viral injection sites and optical fiber insertion sites. **A**. The red line indicates rAAV8/CamKII-hM4D-mCherry injection site. **B.** The red line indicates PDBU osmotic pump infusion site. **C.** The green line indicates rAAV5/CaMKII-hChR2(H134R)-eYFP-EPRE injection site and the blue square indicates the location the tip of optical fiber. **D.** The green line indicates rAAV5/CaMKII-hChR2(H134R)-eYFP-EPRE injection site in the right CeA region and the blue square indicates the location of the tip of optical fiber in PVA region.



Supplementary Fig. 9 Immunoactivity of c-FOS in PVA after light stimulation on the hChR2-expressing rCeA terminals. 6-wk after AAV infection of the rCeA neurons, the rCeA-eYFP- and rCeA-hChR2- expressing mice were subjected to a 4-day protocol of light stimulation, 5 min of 10Hz blue light each day. At 90-min after the fourth blue light stimulation, the brain slices containing PVA were processed and stained with antibody against c-FOS (red) and eYFP- or hChR2-expresssing rCeA nerve endings (green) were also examined. Immunofluorescent staining of c-Fos signals at the same rostrocaudal level, 600 to 300 μm posterior to bregma, were examined in the rCeA-eYFP and rCeA-hChR2 groups.