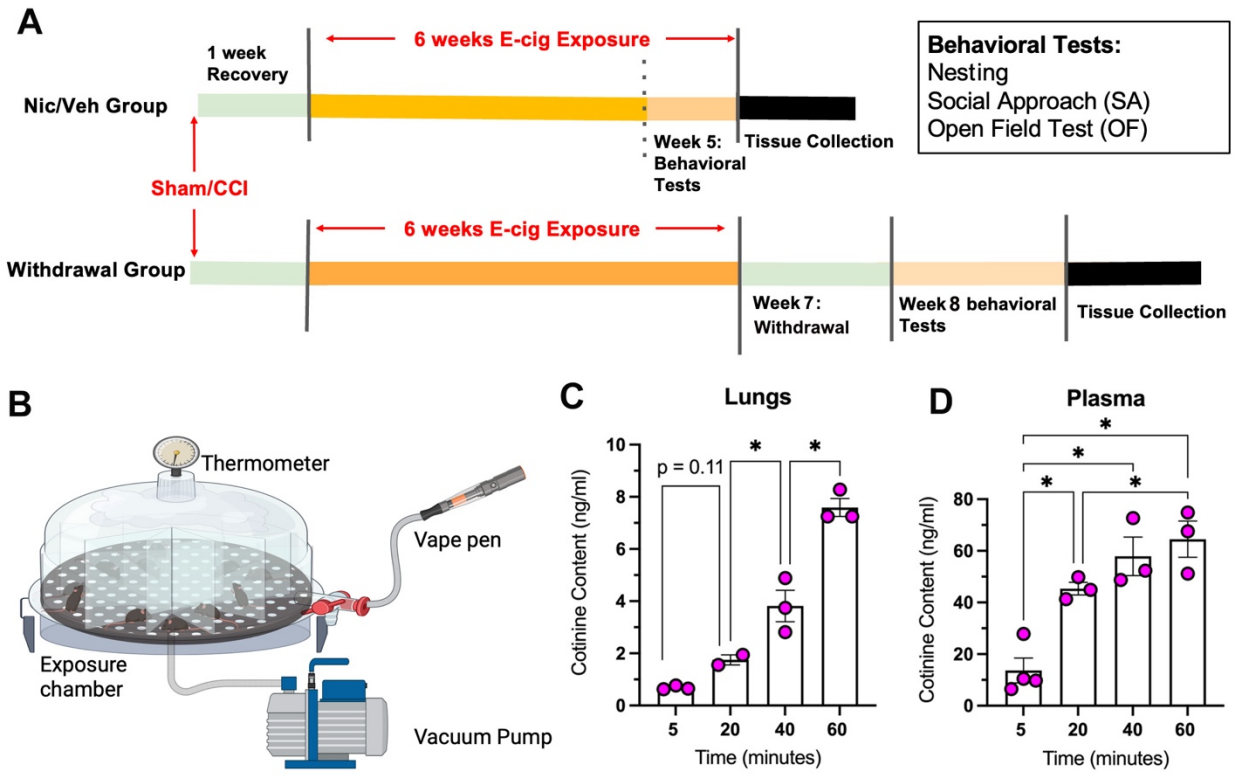


Figure 1. Confirmation of nicotine delivery efficacy via a new E-cigarette vapor exposure chamber. (**A)** Experiment timeline**.** (**B)** Illustration of the E-cig vapor exposure chamber. **(C-D)** Cotinine concentrations in lung tissue homogenates and blood plasma. Cotinine concentrations were analyzed using a one-way ANOVA followed by post hoc Fisher's LSD test. Data are presented as mean ± SEM, n=2-4 per group. Significance was assumed when $p < 0.05$.

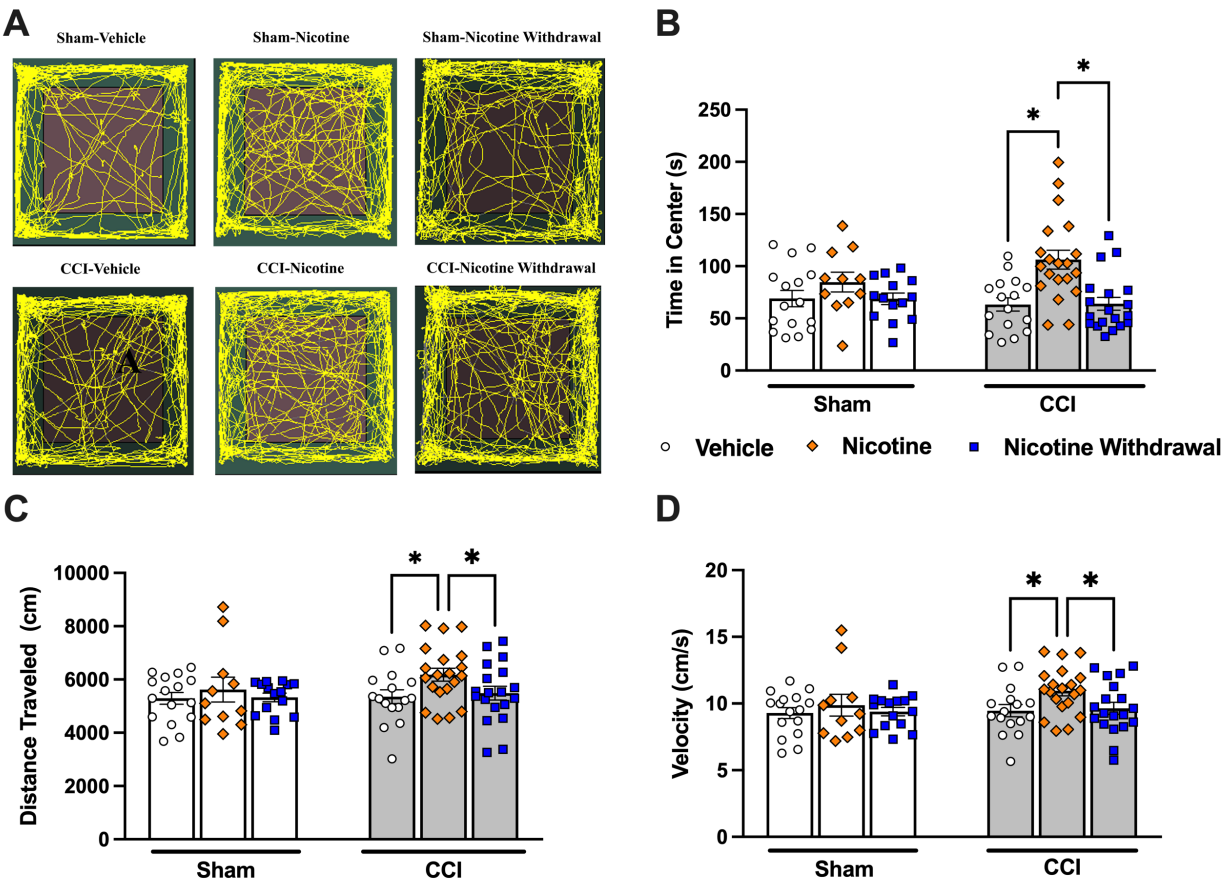


Figure 2. Chronic nicotine exposure induces transient hyperactivity and anxiolytic effects in CCI mice. (**A**) Representative OF track visualization. (**B**)Time in the center of the OF arena at the end of post-exposure week 5. (**C-D**) Total distance traveled and velocity of animals in the OF arena. B-D are analyzed using two-way ANOVA followed by post hoc Fisher's LSD comparison test. Data are presented as mean ± SEM, n= 11-20 per group. *$p < 0.05$, significantly different from vehicle within Sham and CCI groups.

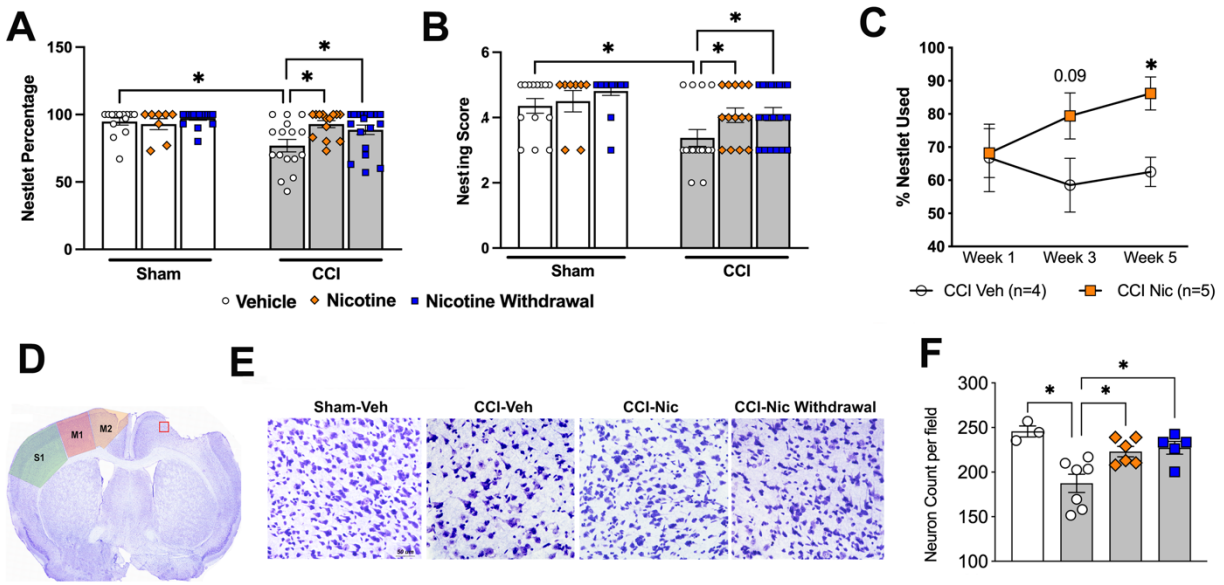


Figure 3. Chronic nicotine exposure facilitates sensorimotor function recovery in CCI mice. (**A-B)** Percentage of total nestlet used and nesting score after 6 weeks exposure, n= 8-19 per group. (**C**) Biweekly nesting result over 5 weeks, n=4 -5 per group. (**D**) Representative image of Nissl staining showing lesion in the motor and sensory cortex. Red box represents the zoomed in area for neuronal count analysis. (**E-F**) Representative image of zoomed in Nissl staining in the perilesion motor cortex and the quantification, n=3-7 per group. A, B, C are analyzed using two-way ANOVA followed by post hoc Fisher's LSD comparison test. F are analyzed using one-way ANOVA followed by post hoc Fisher's LSD comparison test. Data are presented as mean ± SEM. Significance was assumed when *p < 0.05.

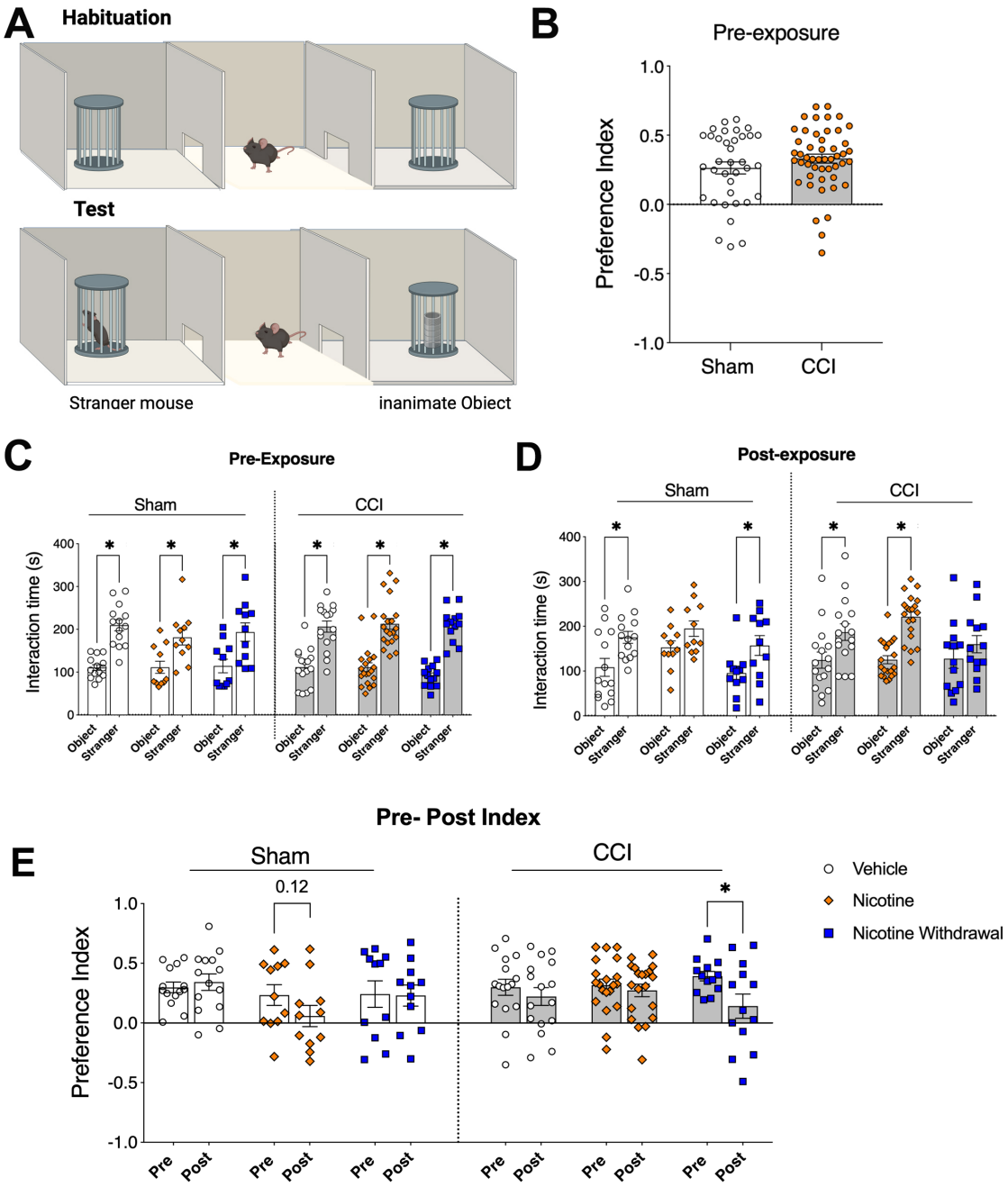


Figure 4. Chronic nicotine exposure inhibits social approach behavior. (A) Schematic diagram of the three-chambered social approach test. (**B**) Pre-exposure baseline social preference of Sham and CCI mice. (**C**) Interaction time with object and strange before exposure (after Sham or CCI surgery). (**D**) Interaction time with object and strange after 30-day exposure. (**E**) Social preference changes from pre-exposure to post-exposure time point. B is analyzed using unpaired t-test. C-E are analyzed using two-way ANOVA followed by post hoc Fisher LSD's comparison test. Data are presented as mean ± SEM. Significance was assumed when *p < 0.05.

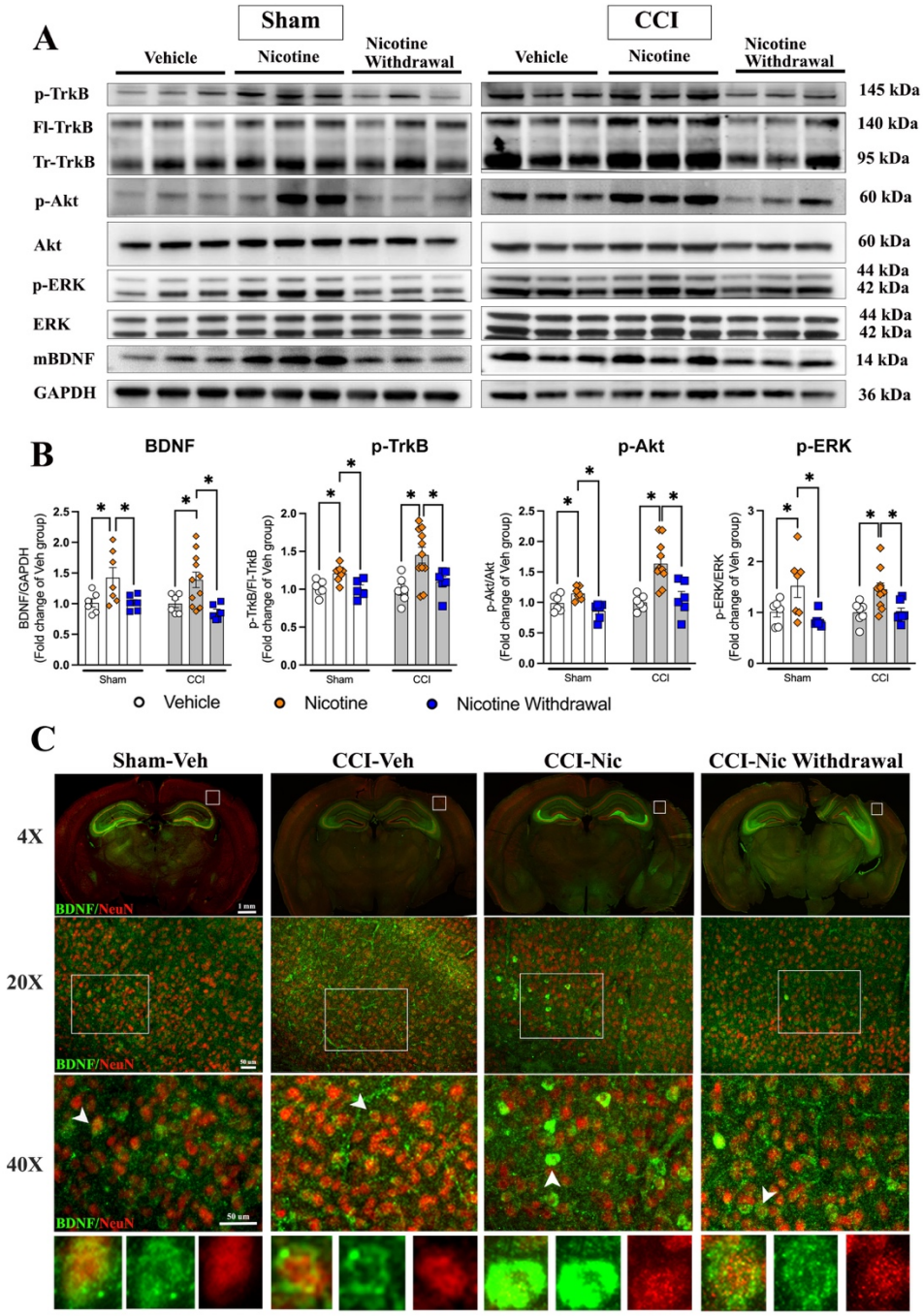


Figure 5. Chronic nicotine exposure increases mBDNF expression and upregulates BDNF-TrkB signaling in the ipsilateral cortex. (A) Immunoblot analyses of the expression of p-TrkB, TrkB, p-Akt, Akt, p-ERK, ERK, mBDNF, and GAPDH in the ipsilateral cortex of Sham (**A**) and CCI mice. (**B)** Quantification of above blots in (**A**), n= 6-11 per group. (**C**) Representative immunofluorescence images of BDNF (green) and neuronal marker NeuN (red). Images in the lower row show higher magnification images of the box region in the respective upper row. Bottom panel shows zoomed in views as indicated by arrowhead in 40x image. Data are analyzed using one-way ANOVA followed by Fisher's LSD tests. Data are presented as mean ± SEM. Significance was assumed when *$p < 0.05$.

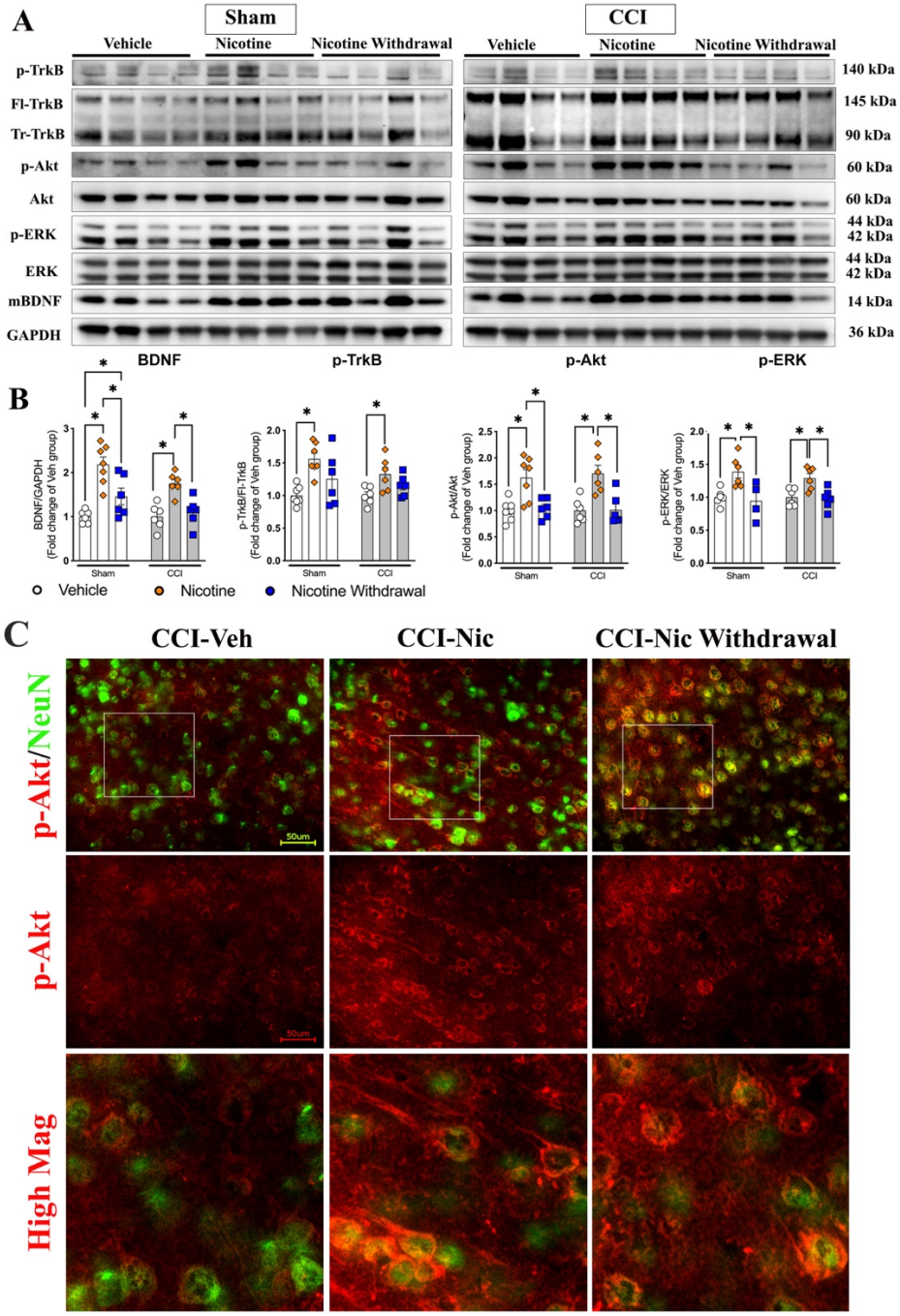


Figure 6. Chronic nicotine exposure increases mBDNF expression and upregulates BDNF-TrkB signaling in the contralateral cortex. (A) Immunoblot analyses of the expression of p-TrkB, TrkB, p-Akt, Akt, p-ERK, ERK, mBDNF, and GAPDH in contralateral cortex of Sham (A) and CCI mice. **(B)** Quantification of above blots in (A), n= 6-7 per group. **(C)** Representative immunofluorescence images of p-Akt (red) and neuronal marker NeuN (green). Scale bar, 500 μm. Data are analyzed using one-way ANOVA followed post hoc Fisher's LSD tests. Data are presented as mean ± SEM. Significance was assumed when *p < 0.05.

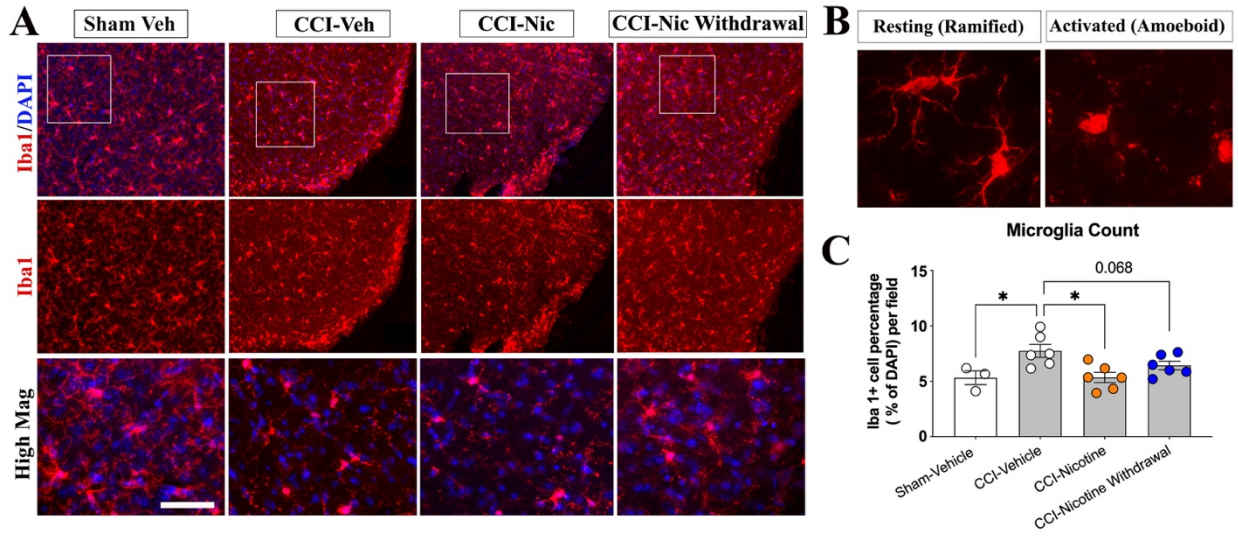
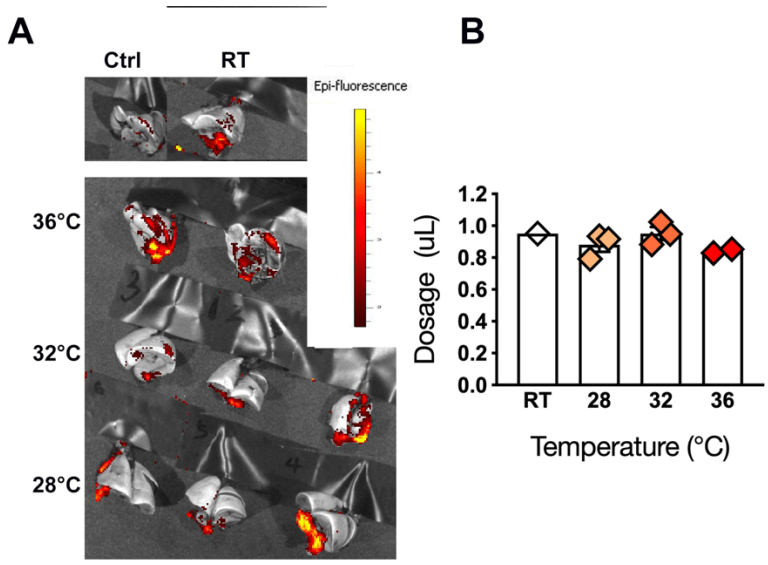
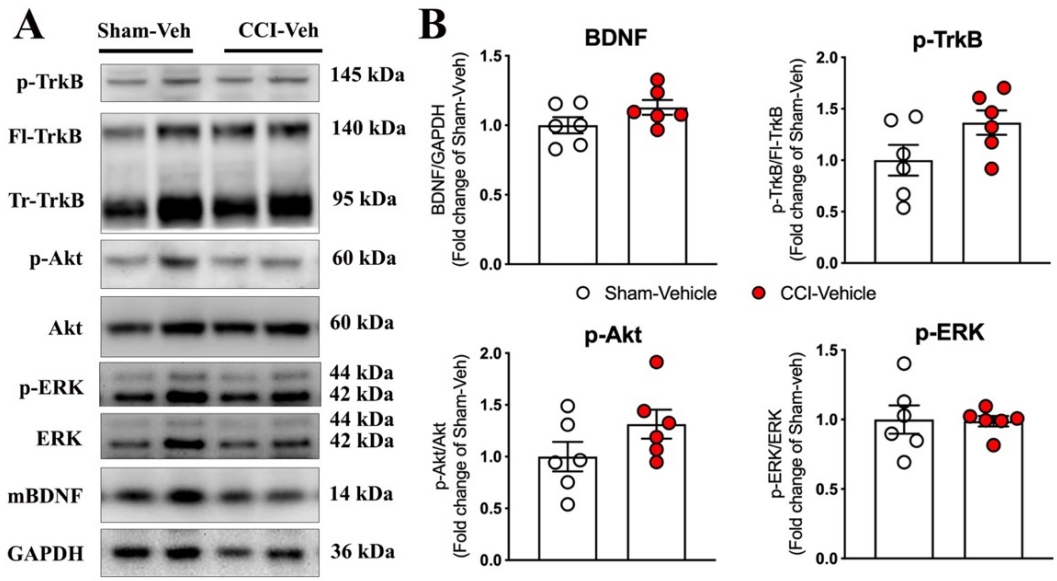


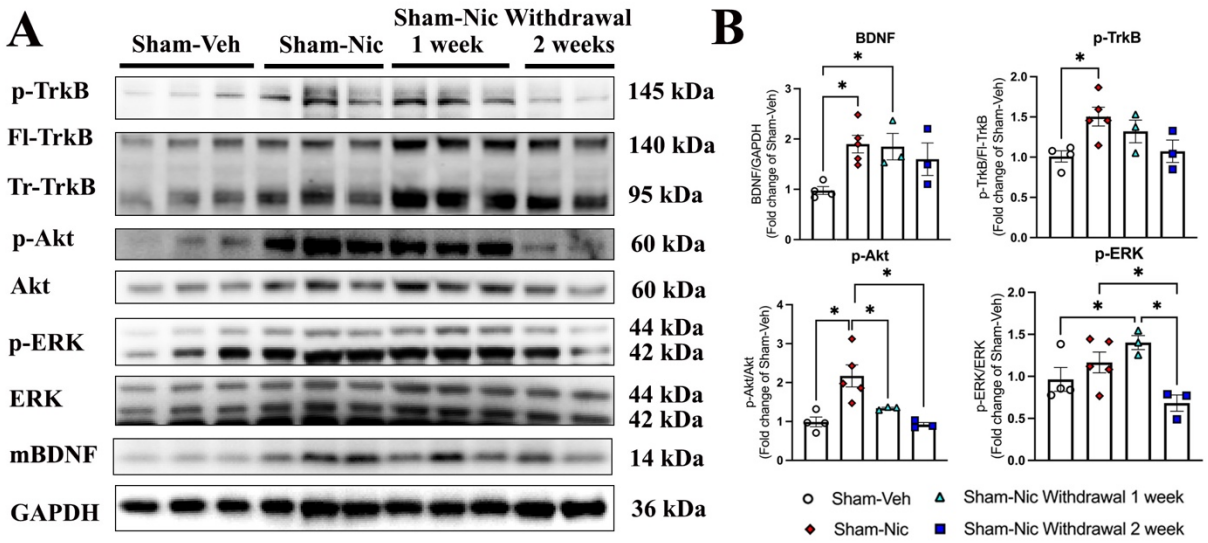
Figure 7. Chronic nicotine exposure mitigates microglia-mediated neuroinflammation in CCI mice. (A) Representative images of Iba1(red) staining in the perilesional cortex. DAPI (blue) indicates the nucleus. The bottom row shows the higher magnification images of white box region in top row, scale bar, 500 μm. **(B)** Representative images of homeostatic (ramified) vs. activated (amoeboid-like) microglial morphology**. (C)** Percentage of microglia in the counting field (n=3 for Sham-Vehicle group, n=6 for all CCI groups). Data are analyzed using one-way ANOVA followed by post hoc Fisher's LSD tests. Data are presented as mean ± SEM. Significance was assumed when *$p < 0.05$.



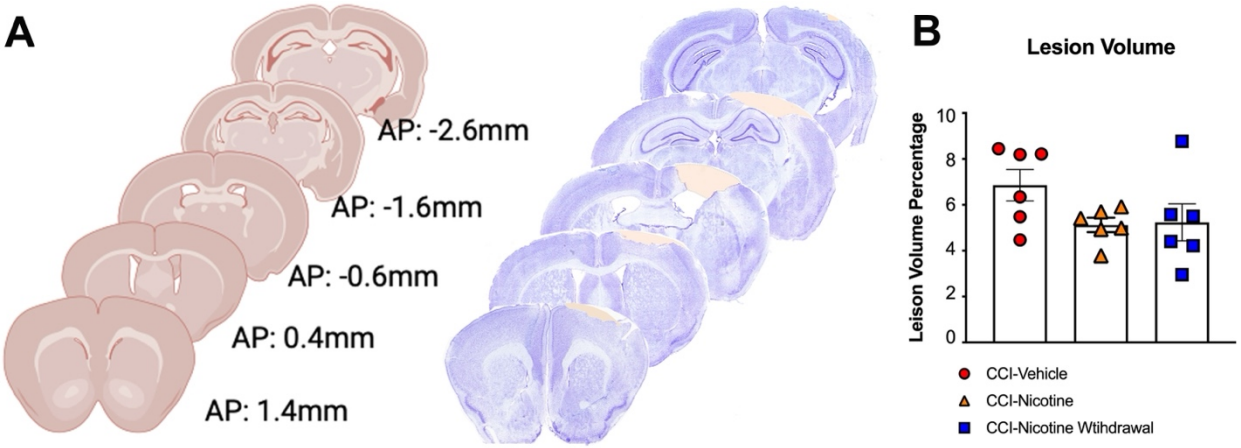
Supplemental Figure 1. Determination of optimal chamber exposure temperature. (**A**) Air-dried lungs from Evans Blue-exposed mice at room temperature (RT), 28°C, 32°C, 36°C. (**B**) Quantification of Evans Blue intensity in A, n=3 per group. Fluorescence intensity was analyzed using one-way ANOVA followed by post hoc Fisher's LSD test. Significance was assumed when *$p < 0.05$.



Supplemental Figure 2. CCI alone does not alter BDNF-TrkB signaling in the ipsilateral cortex. (A) Representative blots of p-TrkB, TrkB, p-Akt, Akt, p-ERK, ERK, mBDNF, and GAPDH in the ipsilateral cortex of Sham-Veh (A) and CCI-Veh mice. **(B)** Quantification of (A), n=6 per group. Data are analyzed using unpaired t-test. Data are presented as mean ± SEM. Significance was assumed when $p < 0.05$.



Supplemental Figure 3. Nicotine-induced activation of BDNF-TrkB signaling persists more than one week after cessation of nicotine exposure. (A) Representative blots of p-TrkB, TrkB, p-Akt, Akt, p-ERK, ERK, mBDNF, and GAPDH in the contralateral cortex. **(B)** Quantification of (A), n=3-5 per group. Data are analyzed using one-way ANOVA followed by Fisher's LSD test. Data are presented as mean ± SEM. Significance was assumed when $p < 0.05$.



Supplemental Figure 4. Chronic nicotine exposure did not affect lesion size. (**A)** Right: Cartoon image of slices analyzed for lesion size. Left: representative slices of Nissl staining showing lesion in the motor and sensory cortex. (**B**) Quantification of lesion volume, n = 6 per group. Data are presented as mean ± SEM and analyzed using one-way ANOVA followed by post hoc Bonferroni's comparison test. Significance was assumed when *$p < 0.05$.