Supplementary Table 1. Detailed statistic results.

Table 1-A. Two-way measure repeated ANOVA for **Figure 1**B, D.

Test	Time*Injury	Time*Treatment	Time*Injury*Treatment
von Frey	$F_{(5,135)} = 1.99$, P=0.084	$F_{(5,135)} = 4.122$, P=0.002	$F_{(5,135)} = 4.122$, P=0.002
Pin	$F_{(5,135)} = 10.967$, P<0.001	$F_{(5,135)} = 6.938$, P<0.001	$F_{(5,135)} = 6.938$, P<0.001

Table 1-B. Two-way ANOVA for **Figure 1**C, E.

Test	Vehicle vs WIN	Sham vs SNI	Interaction
Pin test	$F_{(1, 27)} = 4.851$, P=0.0383	$F_{(1, 27)} = 222.4$, P<0.0001	$F_{(1, 27)} = 4.745$, P=0.0383
von Frey	$F_{(1, 27)} = 4.523$, P=0.0427	$F_{(1, 27)} = 75.7$, P<0.0001	$F_{(1, 27)} = 4.523$, P=0.0427

Table 1-C. Two-way ANOVA for **Figure 2**D.

	Vehicle vs WIN	Sham vs SNI	Interaction
DH SA	$F_{(1, 17)} = 7.574$, P=0.0136	$F_{(1, 17)} = 13.35$, P=0.002	$F_{(1, 17)} = 9.372$, P=0.00071

Table 1-D. Two-way ANOVA for **Figure 3**D, E, F, G, and H.

Figure 3.C	Vehicle vs WIN	Sham vs SNI	Interaction
	$F_{(1, 96)} = 108.3$, P<0.0001	$F_{(1, 96)} = 153$, P<0.0001	$F_{(1, 96)} = 71.01$, P<0.0001
Figure 3.D	Vehicle vs WIN	Sham vs SNI	Interaction
	$F_{(1, 87)} = 28.79$, P<0.0001	$F_{(1, 87)} = 0.1093$, P=0.7418	$F_{(1, 87)} = 12.29$, P=0.0007
Figure 3.E	Vehicle vs WIN	Sham vs SNI	Interaction
	$F_{(1, 73)} = 11$, P=0.0014	$F_{(1, 73)} = 1.761$, P=0.1886	$F_{(1, 73)} = 4.73$, P=0.0329
Figure 3.F	Vehicle vs WIN	Sham vs SNI	Interaction
	$F_{(1, 66)} = 12.05$, P=0.0009	$F_{(1, 66)} = 1.863$, P=0.1769	$F_{(1, 66)} = 1.097$, P=0.2987
Figure 3.G	Vehicle vs WIN	Sham vs SNI	Interaction
	$F_{(1, 91)} = 31$, P<0.0001	$F_{(1, 91)} = 8.025$, P=0.0057	$F_{(1, 91)} = 17.55$, P<0.0001

Table 1-E. Two-way repeated ANOVA for **Figure 4**B, D, F, H.

Test	Time	Treatment	Interaction
Pin test	$F_{(4.002, 164.1)} = 83.44$, P<0.0001	$F_{(3, 41)} = 122$, P<0.0001	$F_{(15, 205)} = 32.54$, P<0.0001
von Frey	$F_{(2.418, 99.14)} = 16.69$, P<0.0001	$F_{(3, 41)} = 49.28$, P<0.0001	$F_{(3, 41)} = 49.28$, P<0.0001
Brush	$F_{(2.927, 120)} = 17.07$, P<0.0001	$F_{(3, 41)} = 107.3$, P<0.0001	$F_{(15, 205)} = 11.32$, P<0.0001

Acetone	$F_{(3.857, 158.1)} = 21.10$, P<0.0001	$F_{(3, 41)} = 61.08$, P<0.0001	$F_{(15, 205)} = 8.634$, P<0.0001

Table 1-F. Two-way repeated ANOVA for **Figure 4**C, E, G, I.

Test	Time*Injury	Time*Treatment	Time*Injury*Treatment
von Frey	$F_{(5,205)} = 16.744$, P<0.001	$F_{(5,205)} = 5.853$, P<0.001	$F_{(5,205)} = 5.658$, P<0.001
Pin	$F_{(5,205)} = 81.098$, P<0.001	$F_{(5,205)} = 8.584$, P<0.001	$F_{(5,205)} = 11.283$, P<0.001
Brush	$F_{(5,205)} = 16.72$, P<0.001	$F_{(5,205)} = 7.748$, P<0.001	$F_{(5,205)} = 8.368$, P<0.001
Acetone	$F_{(5,205)} = 21.582$, P<0.001	$F_{(5,205)} = 1.913$, P=0.093	$F_{(5,205)} = 1.909$, P=0.094

Table 1-G. Two-way ANOVA for **Figure 5**C.

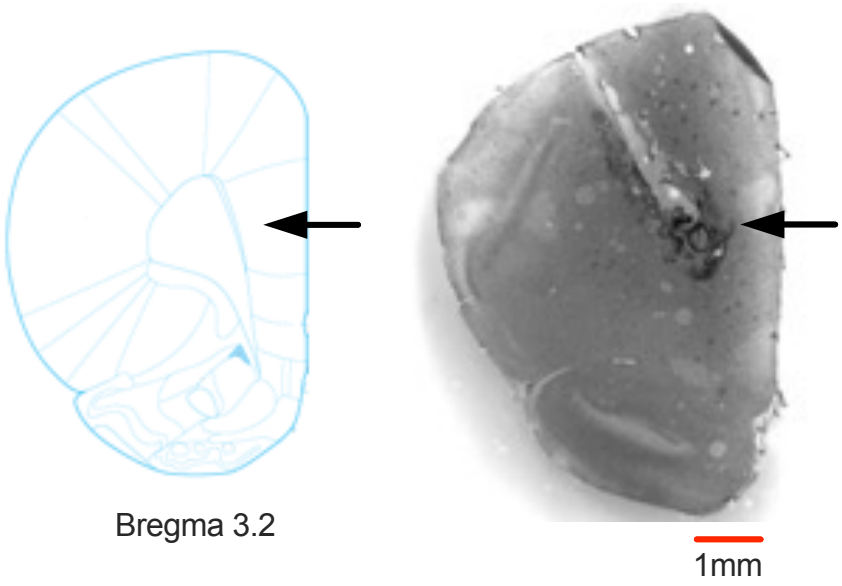
	Vehicle vs WIN	Sham vs SNI	Interaction
DH SA	$F_{(1, 18)} = 7.204$, P=0.0152	$F_{(1, 18)} = 19.01$, P=0.0004	$F_{(1, 18)} = 2.706$, P=0.1173

Table 1-H. Two-way ANOVA for **Figure 6**C, D, E, F, and G.

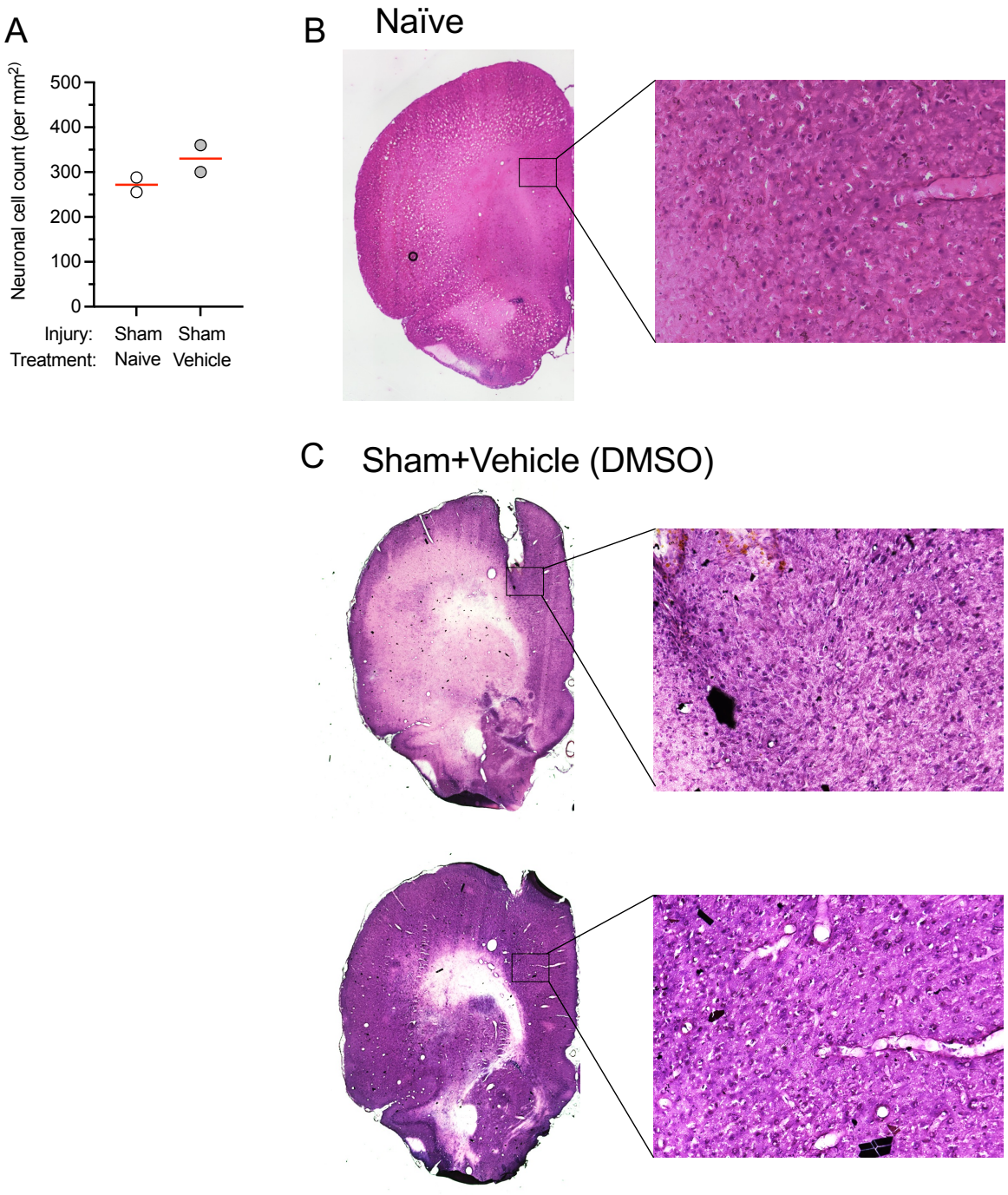
Figure 6.B	Vehicle vs AM4113	Sham vs SNI	Interaction
	$F_{(1, 91)} = 23.02$, P<0.0001	$F_{(1, 91)} = 120.9$, P<0.0001	$F_{(1, 91)} = 71.83$, P<0.0001
Figure 6.C	Vehicle vs AM4113	Sham vs SNI	Interaction
	$F_{(1, 91)} = 12.44$, P<0.3856	$F_{(1, 91)} = 5.958$, P=0.0166	$F_{(1, 91)} = 12.44$, P=0.0007
Figure 6.D	Vehicle vs AM4113	Sham vs SNI	Interaction
	$F_{(1, 77)} = 2.523$, P=0.1163	$F_{(1, 77)} = 0.07366$, P=0.7868	$F_{(1, 77)} = 13.1$, P=0.0005
Figure 6.E	Vehicle vs AM4113	Sham vs SNI	Interaction
	$F_{(1, 91)} = 0.6612$, P=0.4183	$F_{(1, 91)} = 1.953$, P=0.1657	$F_{(1, 91)} = 11.42$, P=0.0011
Figure 6.F	Vehicle vs AM4113	Sham vs SNI	Interaction
	$F_{(1, 93)} = 1.875$, P=0.1742	$F_{(1, 93)} = 0.4209$, P=0.5181	$F_{(1, 93)} = 111.51$, P=0.001

Table 1-I. One-way ANOVA for **Figure 7**C and E.

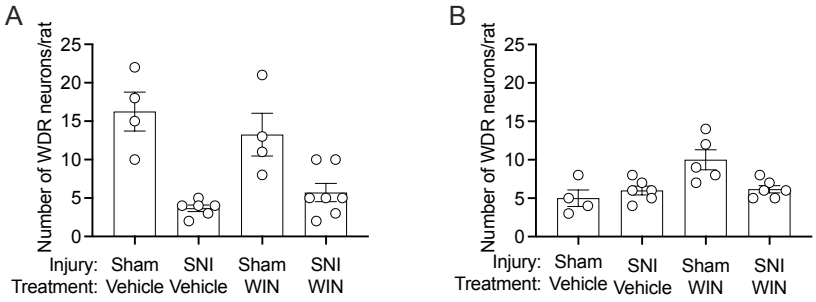
Figure 7.B	$F_{(3, 20)} = 46.52$, P<0.0001
Figure 7.E	$F_{(3, 20)} = 73.22$, P<0.0001



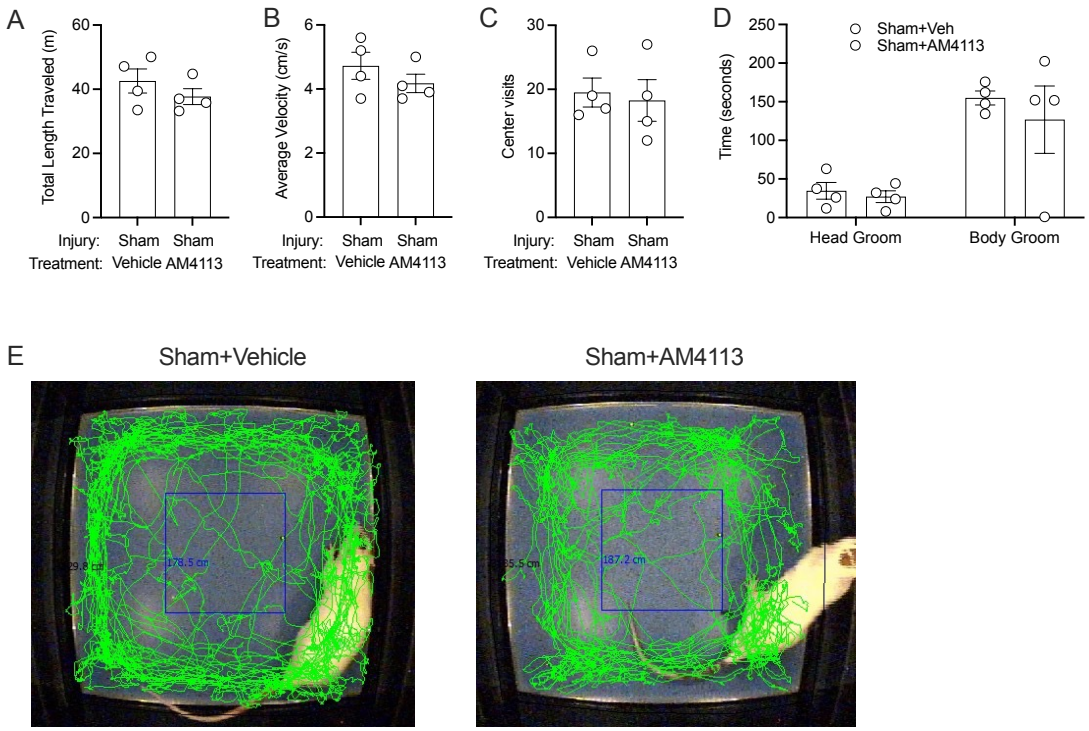
Supplementary Figure 1. Histological verification of intra-mPFC injection. The micrograph shows cresyl violet stained coronal section of typical intra-mPFC cannulae placement. Arrow indicates the cannula tip. Bar, 1mm.



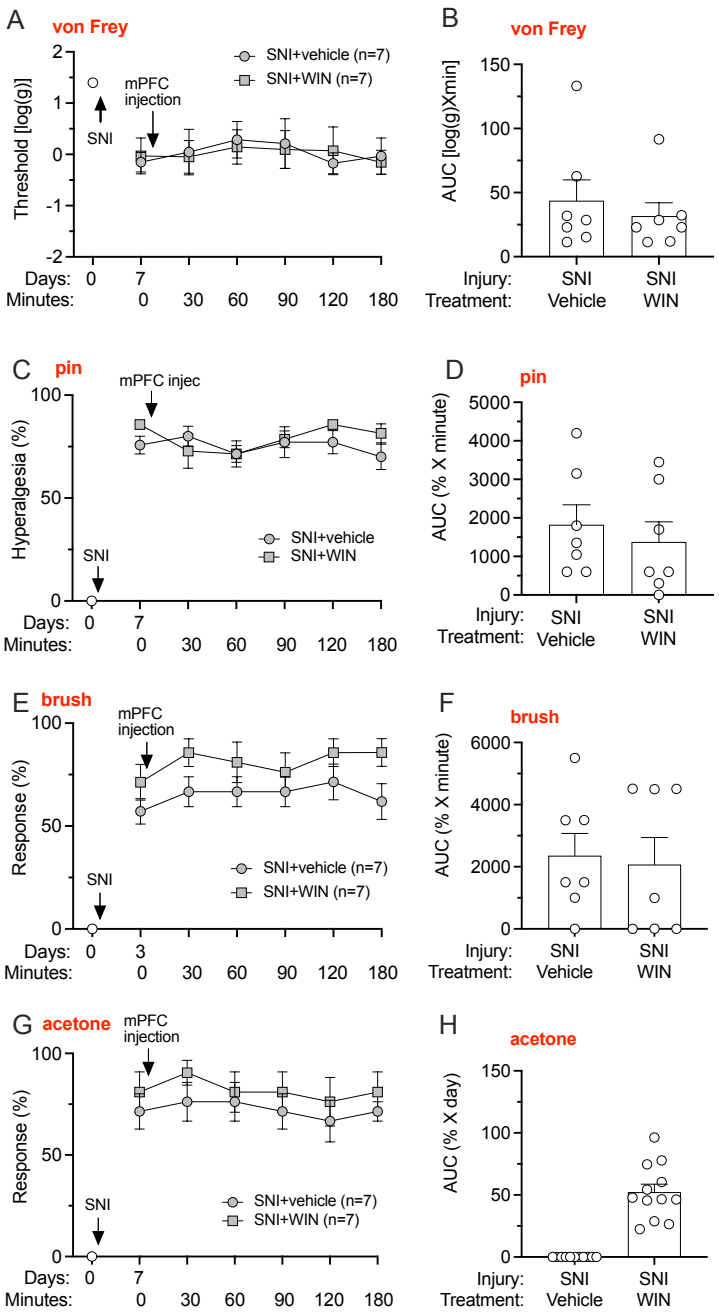
Supplementary Figure 2. The effect of DMSO on mPFC neurons was evaluated using histology with hematoxylin and eosin staining. The number of neurons was compared between rats with and without DMSO injection (**A**), and examples of mPFC histology from a control rat (**B**) and a rat with the chronic intra-mPFC injection of DMSO (**C**, top: the tip of the cannula; bottom: nearby brain area of the cannula) are shown. Each dot represents one rat in A.



Supplementary Figure 3. The recorded number of dorsal horn WDR neurons from each rat in experiments for Figure 2 (**A**) and Figure 5 (**B**).



Supplementary Figure 4. Effects of intra-mPFC injection of AM4113 in the early phase of neuropathic pain on locomotor activity (**A, B**) or anxiety levels (**C, D**) of rats. (**E**) Sample tracks recorded from ShamSNI rats with intra-mPFC injection of vehicle (left) and intra-mPFC injection of vehicle (right). Each dot represents one rat.



Supplementary Figure 5. Effects of intra-mPFC injection of CB1R agonist WIN-55,212-2 in the early phase of neuropathic pain on evoked pain-like behaviors. The time course of sensory behavior tests is shown in the left panels, and AUC analysis in the right panels of intra-mPFC injection of CB1R agonist, WIN-55,212-2 acutely alleviate hypersensitivity to mechanical stimuli (von Frey, **A**, **B**), noxious mechanical stimuli (pin, **C**, **D**), brush (**E**, **F**), and cold (acetone, **G**, **H**) after SNI (n=7 rats/group). Each dot represents one rat. Data represent means ± SEM.