

Inhibition of p38 MAPK after repetitive mTBI ameliorates immune signaling and functional deficits

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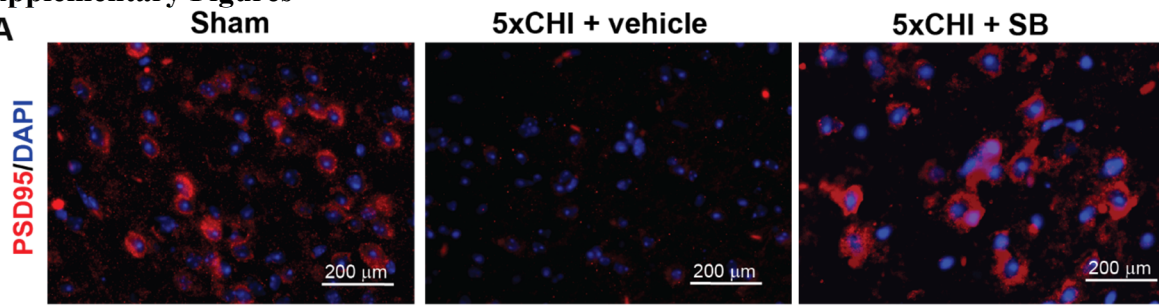


Fig. S1. IHC for PSD95 in frontal cortex 4-weeks post final CHI in females. A. Additional IHC images in the cortex showing PSD95 stain (red) and DAPI (blue) (scale bar: 200 μm, representative sections from n=3-4 mice/group).

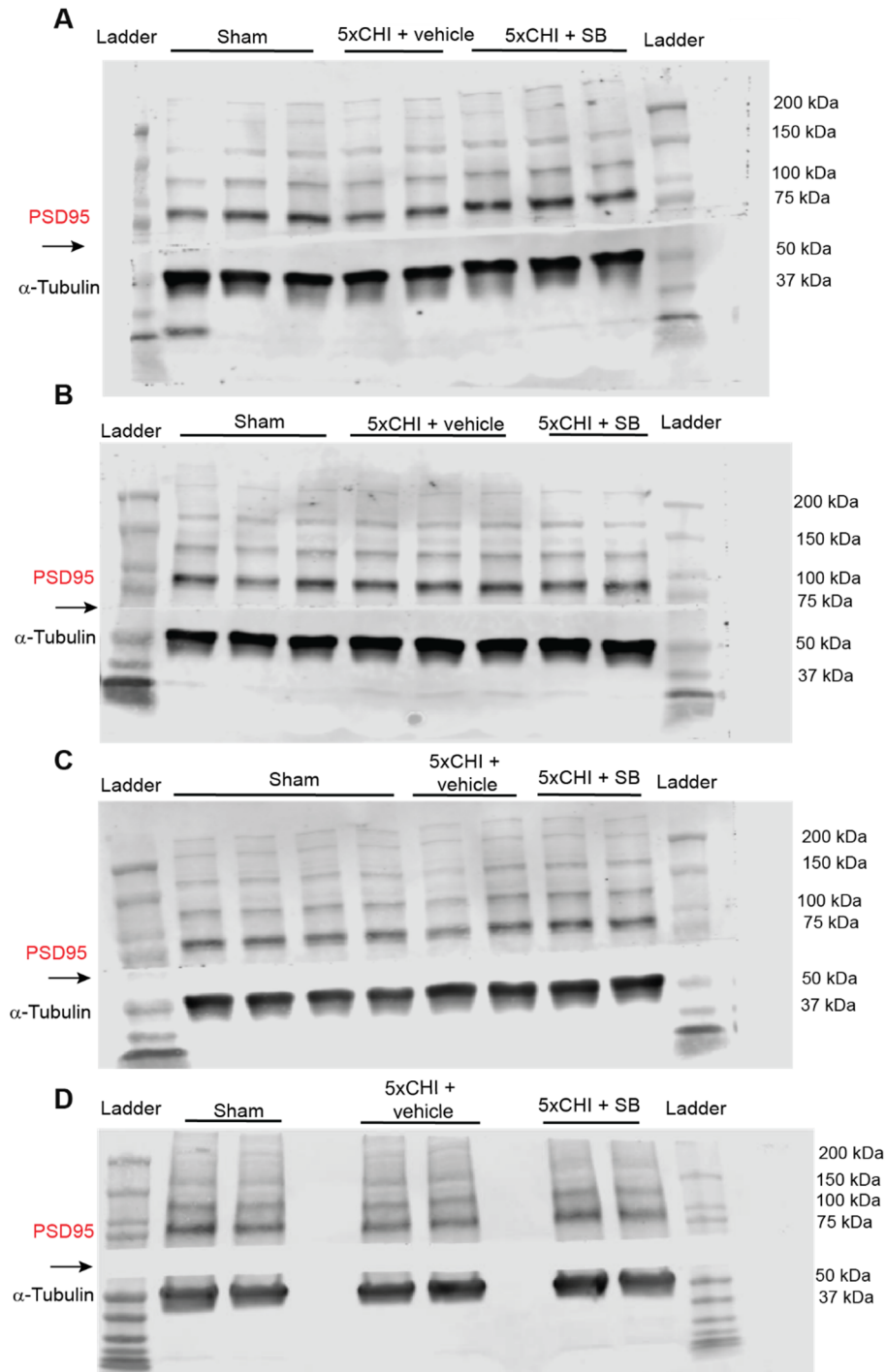


Fig. S2. PSD95 Western blot for females at 4-weeks post-injury. A. Complete blot for **Fig. 2B. B-D.** Western blot results for PSD95 and α-Tubulin. The arrows on the left side of the blots mark the location where the blots were cut. Data points from these blots were included in the Western blot quantification plot in **Fig. 2C**.

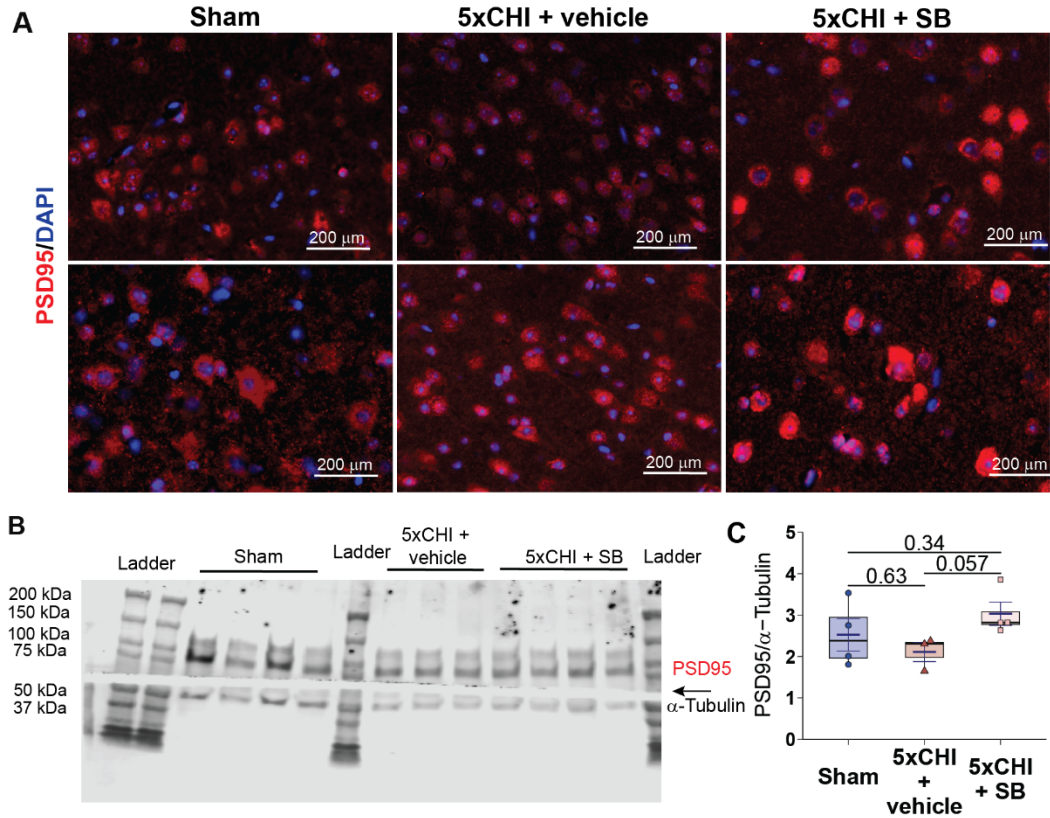


Fig. S3. 5xCHI and SB have limited effect on PSD95 level 4-hours post final CHI in females. **A.** IHC images in the cortex showing PSD95 stain (red) and DAPI (blue) (scale bar: 200 μ m, representative sections from n=3-4 mice/group). **B.** Western blot for PSD95 and α -Tubulin. The arrow on the right side of the blot marks the location where the blot was cut. **C.** Boxplot of quantification of Western blot for PSD95 expression normalized to α -Tubulin (n=3-4). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons.

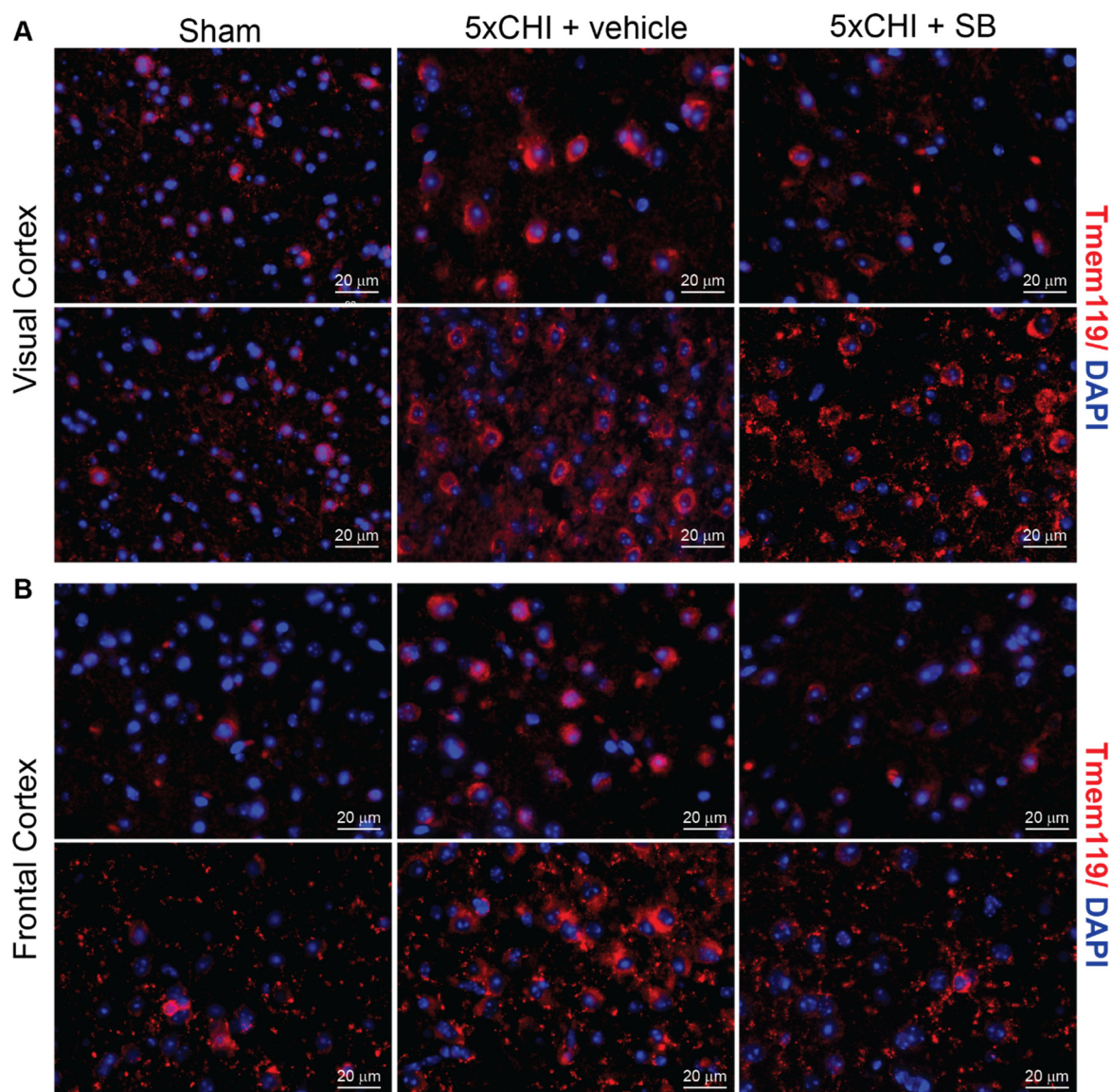


Fig. S4. IHC for Tmem119 in visual and frontal cortex 4-hours post final CHI in females.
A. Additional histological images for marker of Tmem119 for visual cortex (scale bar: 20 μ m). Counts for Tmem119-positive cells in these images were included in the statistical analysis of cell counts in **3C**. **B.** Histological images for marker of Tmem119 for frontal cortex. Red: Tmem119; Blue: DAPI.

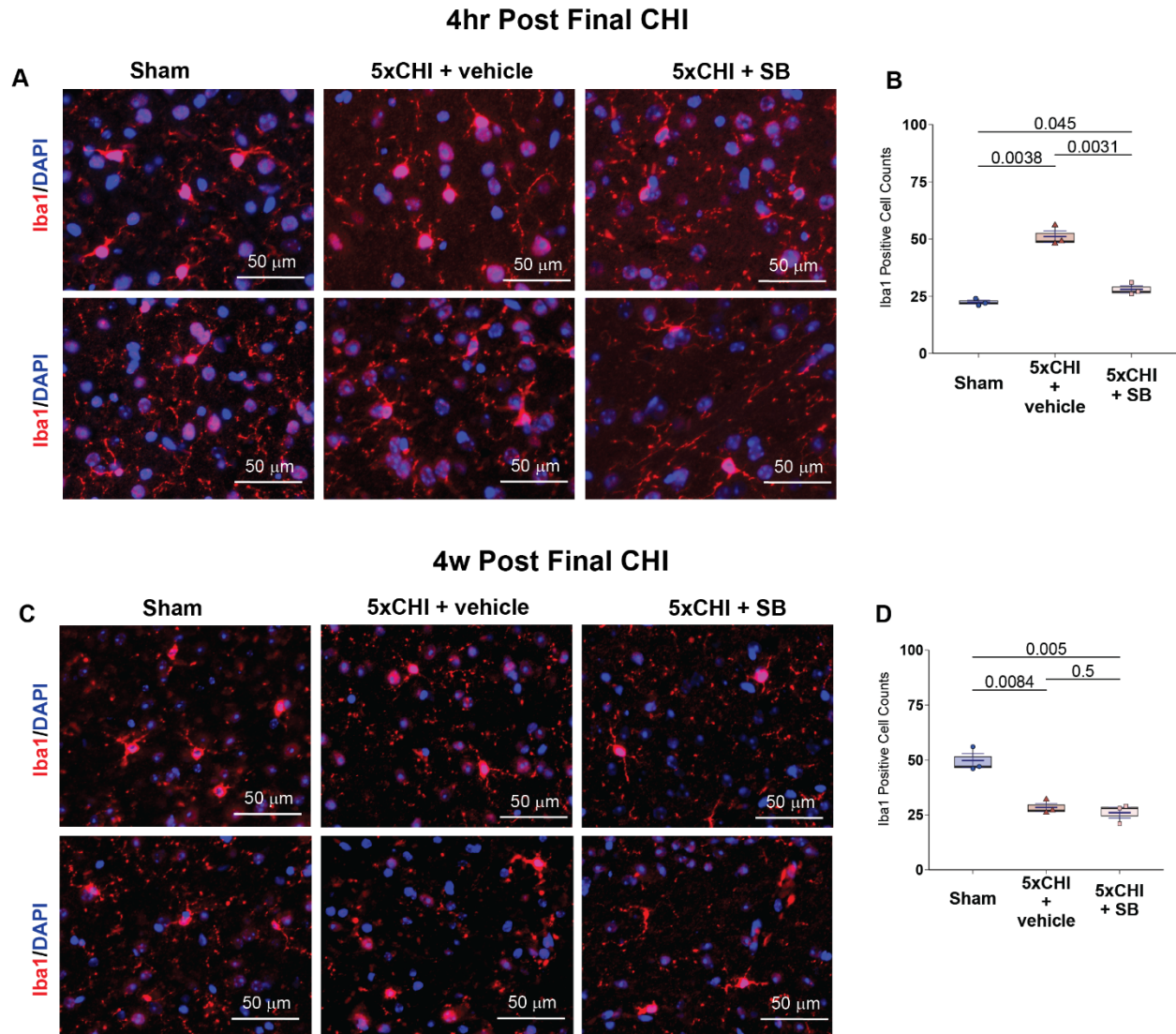


Fig. S5. IHC for Iba1 in visual cortex 4-hours and 4-weeks post final CHI in females. A. The top panels (A-B) represent data from tissues collected 4-hours post injury and the bottom panels (C-D) represent data from tissues collected 4-weeks post injury. A. Representative images of immunohistochemistry for marker of Iba1 stain (red) and DAPI (blue) (scale bar: 50 μ m, representative sections from n=3-4 mice/group). B. Boxplot of Iba1 positive cells count from immunohistochemistry. C. Representative images of immunohistochemistry for marker of Iba1 stain (red) and DAPI (blue) (scale bar: 50 μ m, representative sections from n=3 mice/group). D. Boxplot of Iba1 positive cells count from immunohistochemistry. In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons.

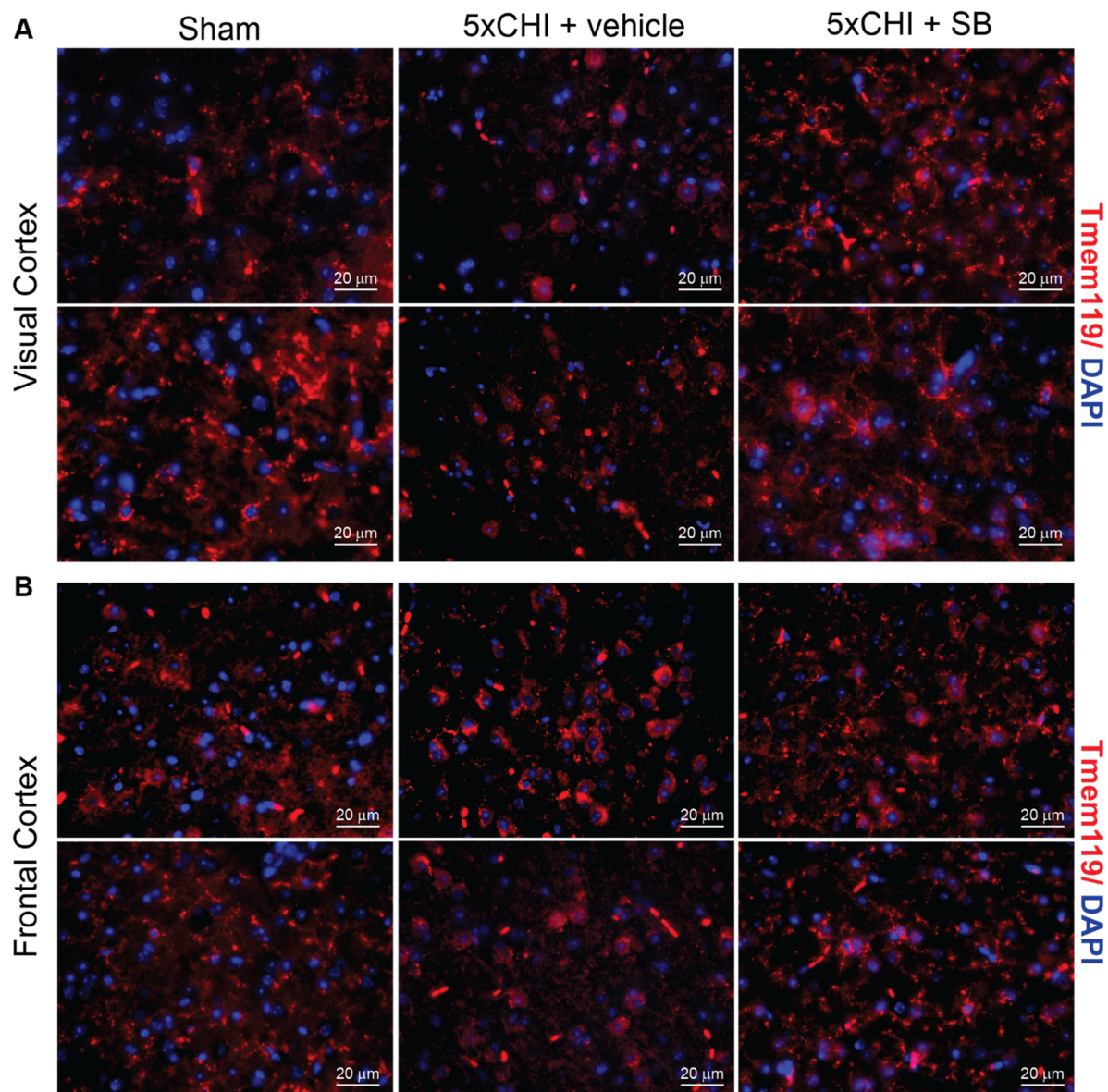


Fig. S6. IHC for Tmem119 in visual and frontal cortex 4-weeks post final CHI in females.
A. Additional histological images for marker of Tmem119 for visual cortex (scale bar: 20 μm). Counts for Tmem119-positive cells in these images were included in the statistical analysis of cell counts in **3G**. **B.** Histological images for marker of Tmem119 for frontal cortex. Red: Tmem119; Blue: DAPI.

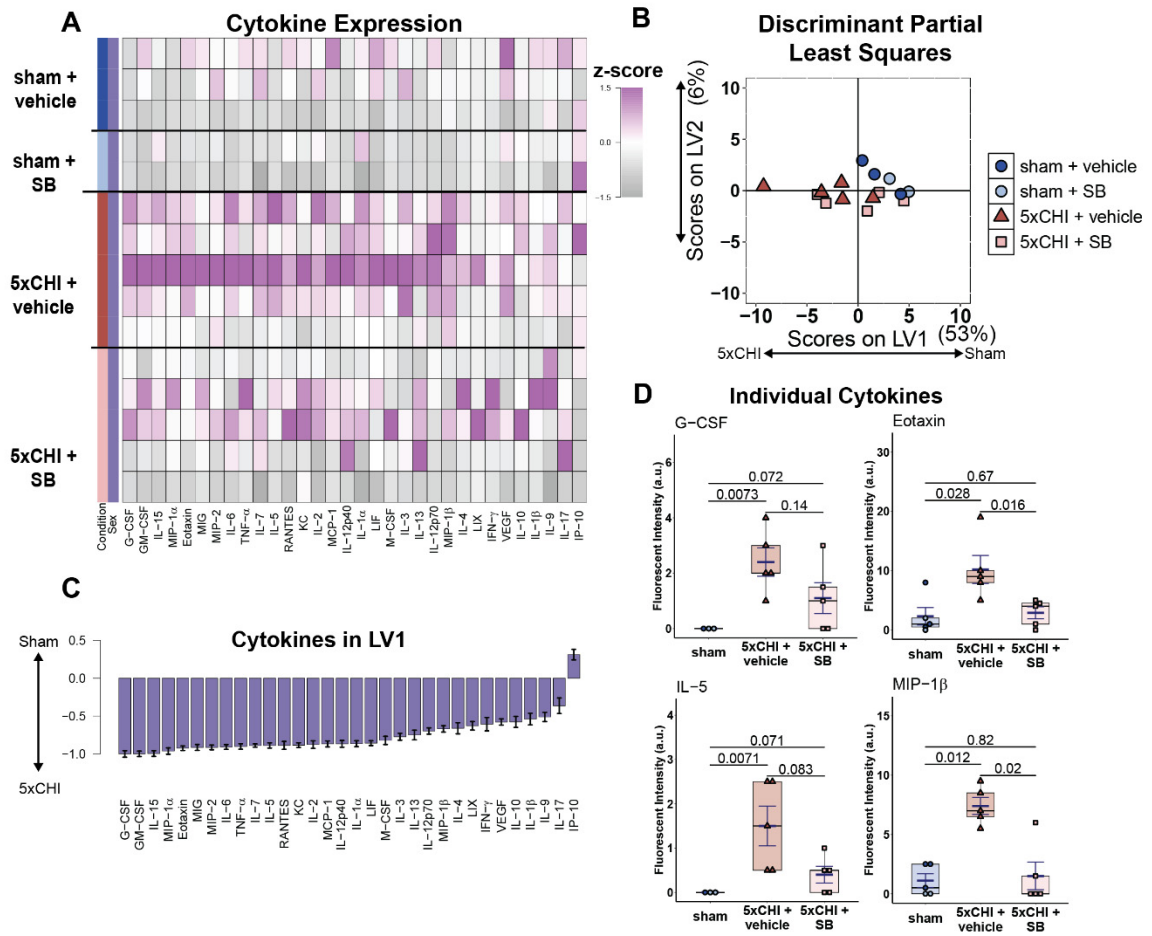


Fig. S7. Acute Inhibition of p38 phosphorylation suppressed 5xCHI induced changes in cortical cytokine expression 4-hours post final CHI in females. **A.** Multiplexed Luminex analysis of thirty-two cytokines (columns) expressed in the visual cortex 4-hours after 5xCHI (n=5) and sham-injury (n=5). Each row in the z-scored heat map denotes an individual animal from either the sham (bottom rows) or injured (top rows) group. **B.** Scores plot of discriminant partial least square regression. **C.** Discriminant partial least squares regression identified a variable, LV1, that separated samples by experimental group. LV1 consists of a weighted profile of cytokines that were up regulated in either 5xCHI (negative weights) or sham-injured controls (positive weights) (mean $\pm$ SD across LV1 generated for all models in a leave one out cross validation). **D.** Box plots for individual cytokines. In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. Light blue circle from sham group denoted samples treated with sham procedure and SB treatment; dark blue circle denoted samples treated with sham procedure and vehicle. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons.

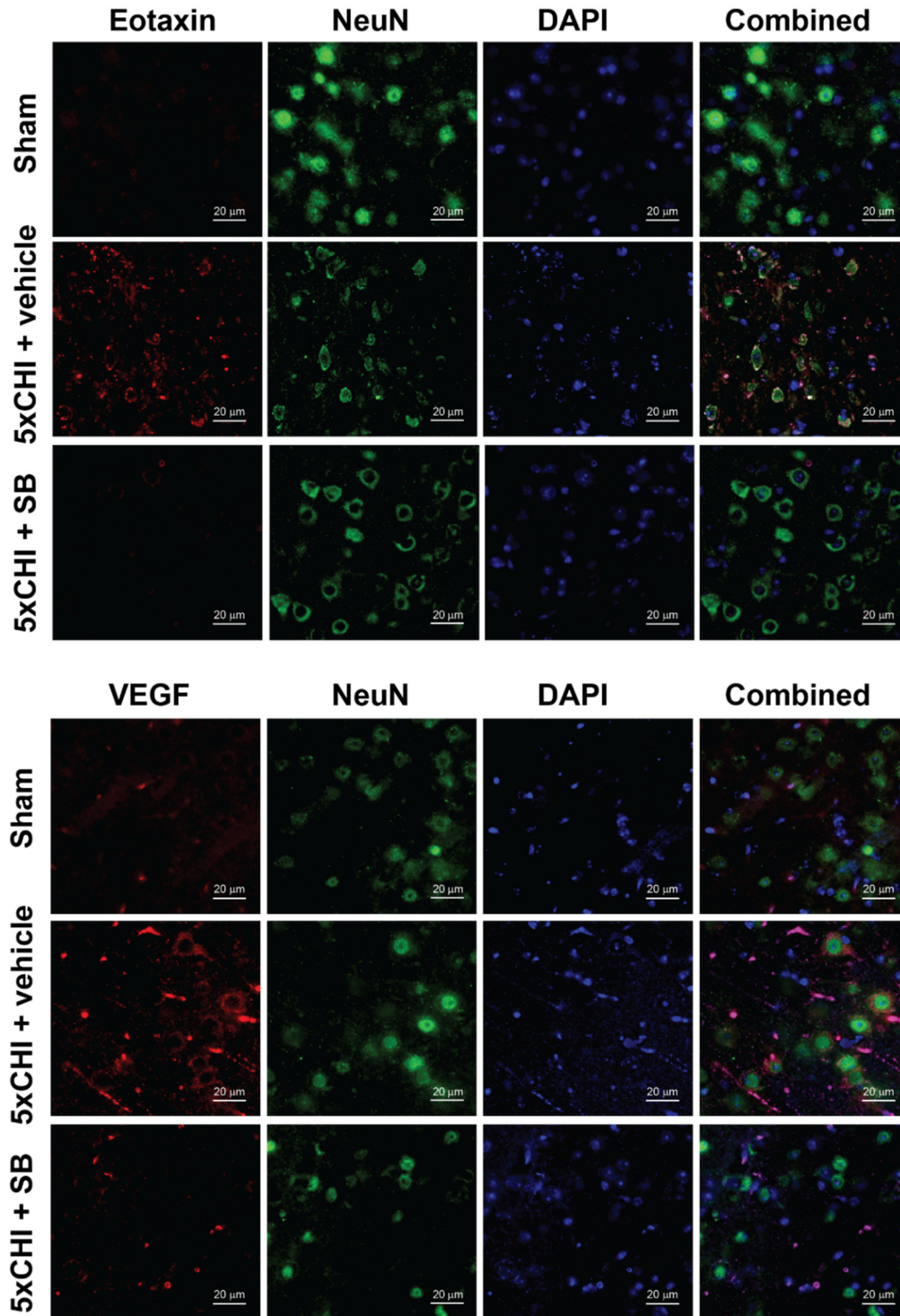


Fig. S8. Additional histological images co-labeling cytokines and NeuN in females. Cytokines upregulated with 5xCHI and normalized with SB (Eotaxin, VEGF) (red) co-stained with NeuN (green) and DAPI (blue) show neuronal co-labeling at 4-hours post injury in females (scale bar: 20 μm, additional sections).

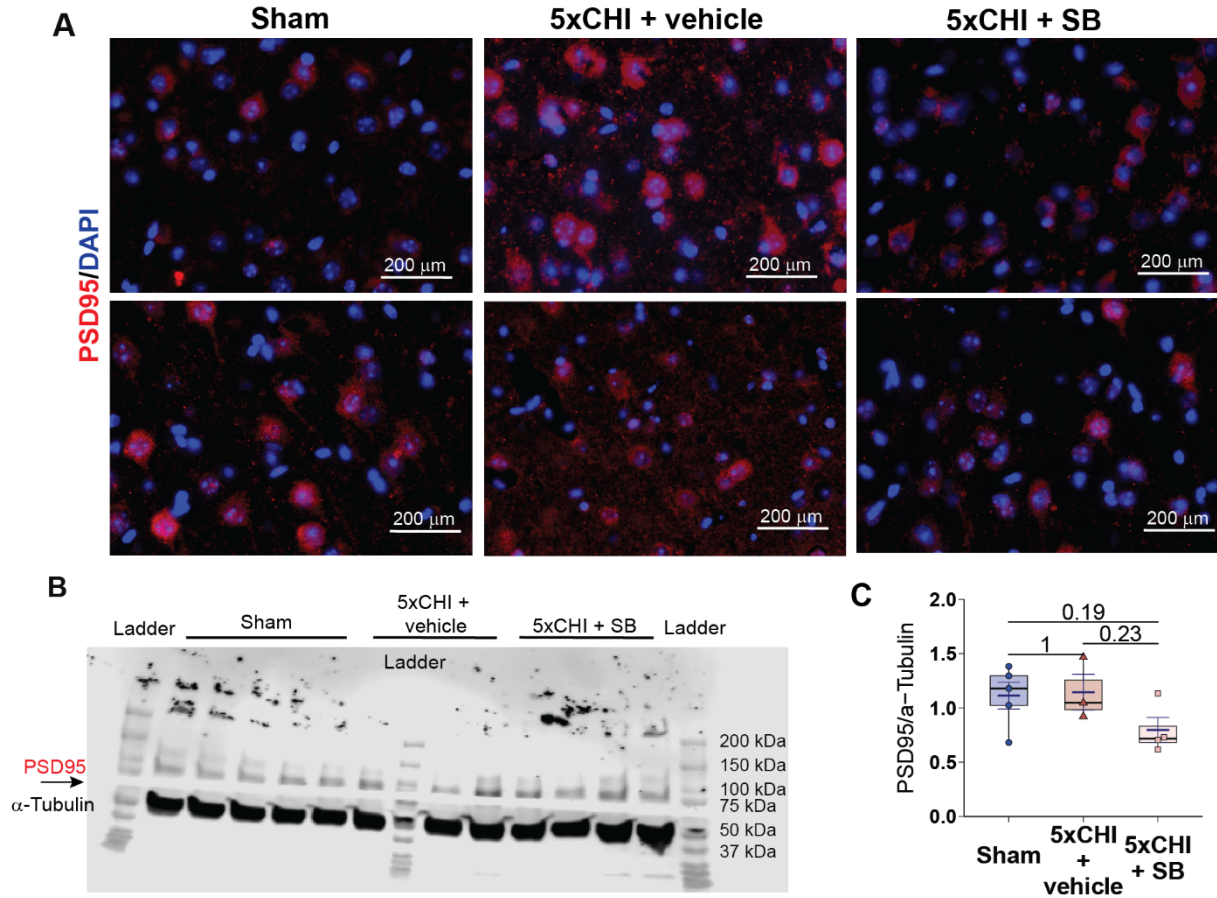


Fig. S9. 5xCHI and SB have limited effect on PSD95 level 4-hours post final CHI in males.
A. IHC images in the cortex showing PSD95 stain (red) and DAPI (blue). **B.** Western blot results blotted for PSD95 and α -Tubulin (scale bar: 200 μ m, representative sections from n=4 mice/group). The arrow on the left side of the blot marks the location where the blot was cut. **C.** Quantification of Western blot for PSD95 expression normalized to α -Tubulin (n=3-5). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons. PSD95 = post synaptic density marker 95.

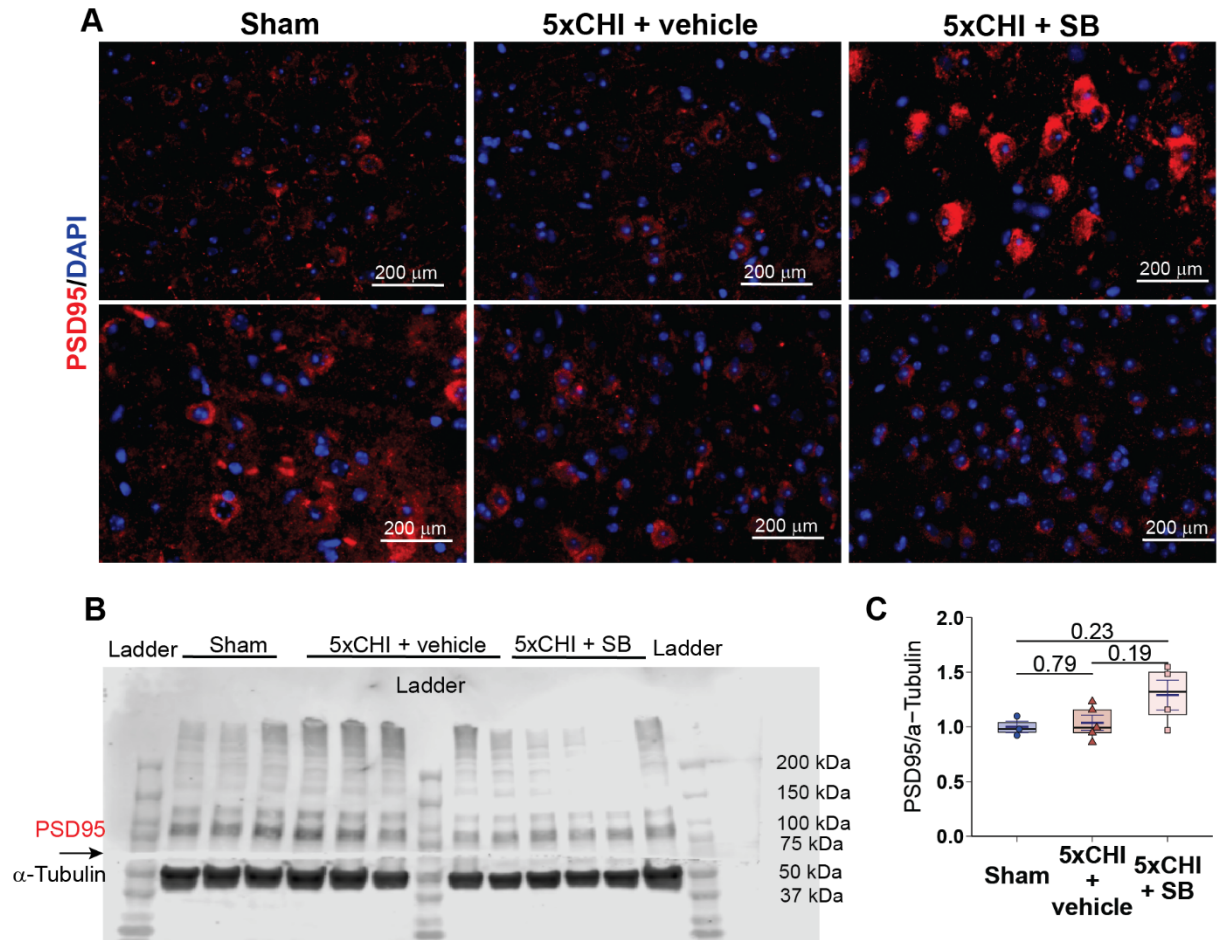


Fig. S10. 5xCHI and SB have limited effect on PSD95 level 4-weeks post final CHI in males. **A.** IHC images in the cortex showing PSD95 stain (red) and DAPI (blue). **B.** Western blot results blotted for PSD95 and α -Tubulin (scale bar: 200 μ m, representative sections from n=4 mice/group). The arrow on the left side of the blot marks the location where the blot was cut. **C.** Quantification of Western blot for PSD95 expression normalized to α -Tubulin (n=3-5). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons. PSD95 = post synaptic density marker 95.

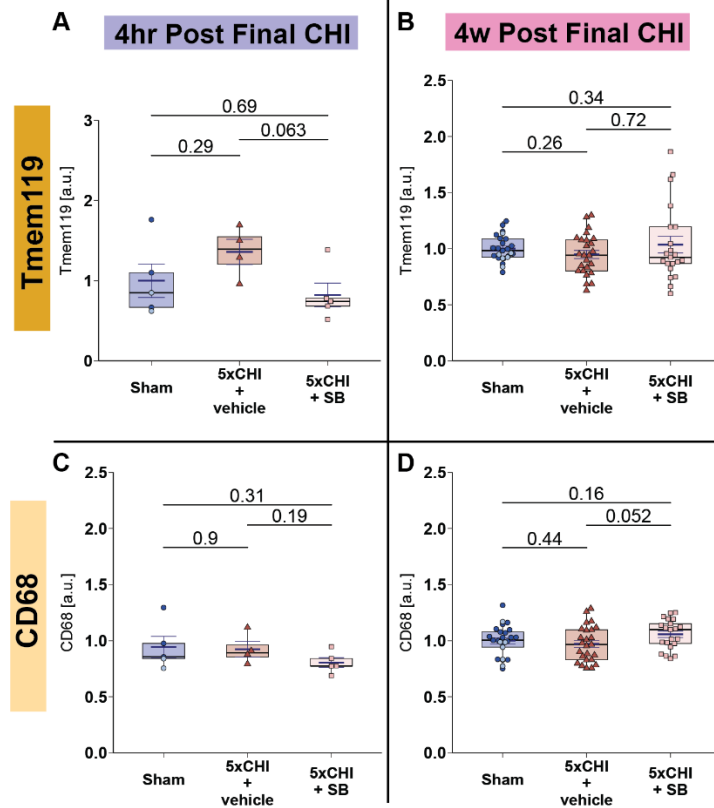


Fig. S11. Acute Inhibition of p38 phosphorylation and 5xCHI have limited effects on cortical microglial marker in males. The left panels (A, C) represent data from tissues collected 4-hours post injury and the right panels (B, D) represent data from tissues collected 4-weeks post injury. **A.** Box plot of cortical Tmem119 expression at 4-hours post-injury (n=4-5). **B.** Box plot of cortical Tmem119 expression at 4-weeks post-injury (n=20-25). **C.** Box plot of cortical CD68 expression at 4-hours post-injury (n=4-5). **D.** Box plot of cortical CD68 expression at 4-weeks post-injury (n=20-25). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Light blue circles from sham group denoted sham + SB; dark blue denotes sham + vehicle. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons. a.u.= arbitrary units. Tmem119 = transmembrane protein 119. CD68 = cluster of differentiation 68.

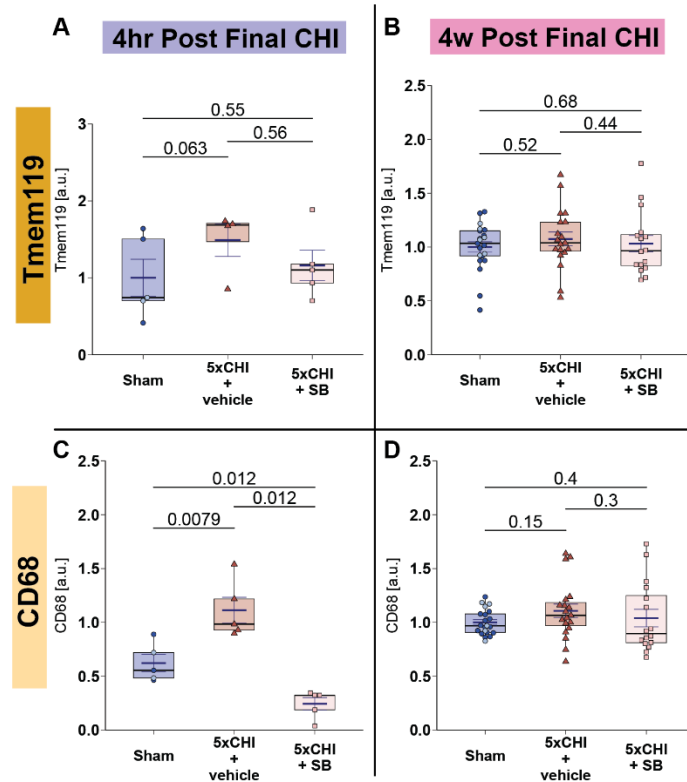


Fig. S12. Acute Inhibition of p38 phosphorylation attenuated injury-induced changes in hippocampal microglial marker in males. The left panels (A, C) represent data from tissues collected 4-hours post injury and the right panels (B, D) represent data from tissues collected 4-weeks post injury. **A.** Box plot of hippocampal Tmem119 expression at 4-hours post-injury (n=4-5). **B.** Box plot of hippocampal Tmem119 expression at 4-weeks post-injury (n=16-21). **C.** Box plot of hippocampal CD68 expression at 4-hours post-injury (n=4-5). **D.** Box plot of hippocampal CD68 expression at 4-weeks post-injury (n=16-22). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Light blue circles from sham group denoted sham + SB; dark blue denotes sham + vehicle. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons. a.u.= arbitrary units. Tmem119 = transmembrane protein 119. CD68 = cluster of differentiation 68.

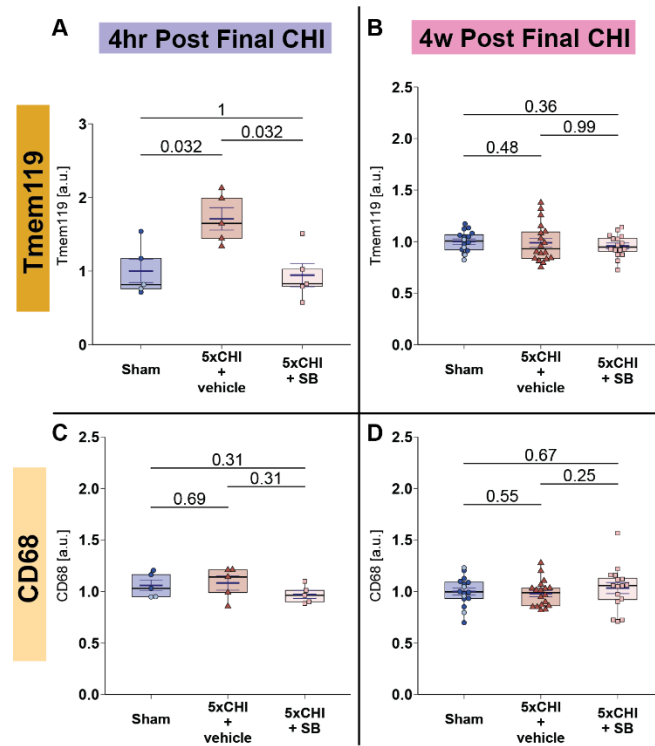


Fig. S13. Acute Inhibition of p38 phosphorylation and 5xCHI have limited effects on hippocampal microglial markers at post final CHI in females. The left panels (A, C) represent data from tissues collected 4-hours post injury and the right panels (B, D) represent data from tissues collected 4-weeks post injury. **A.** Box plot of hippocampal Tmem119 expression at 4-hours post-injury (n=2-5). **B.** Box plot of hippocampal Tmem119 expression at 4-weeks post-injury (n=16-18). **C.** Box plot of hippocampal CD68 expression at 4-hours post-injury (n=2-5). **D.** Box plot of hippocampal CD68 expression at 4-weeks post-injury (n=16-18). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Light blue circles from sham group denoted sham + SB; dark blue denotes sham + vehicle. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons. a.u.= arbitrary units. Tmem119 = transmembrane protein 119. CD68 = cluster of differentiation 68.

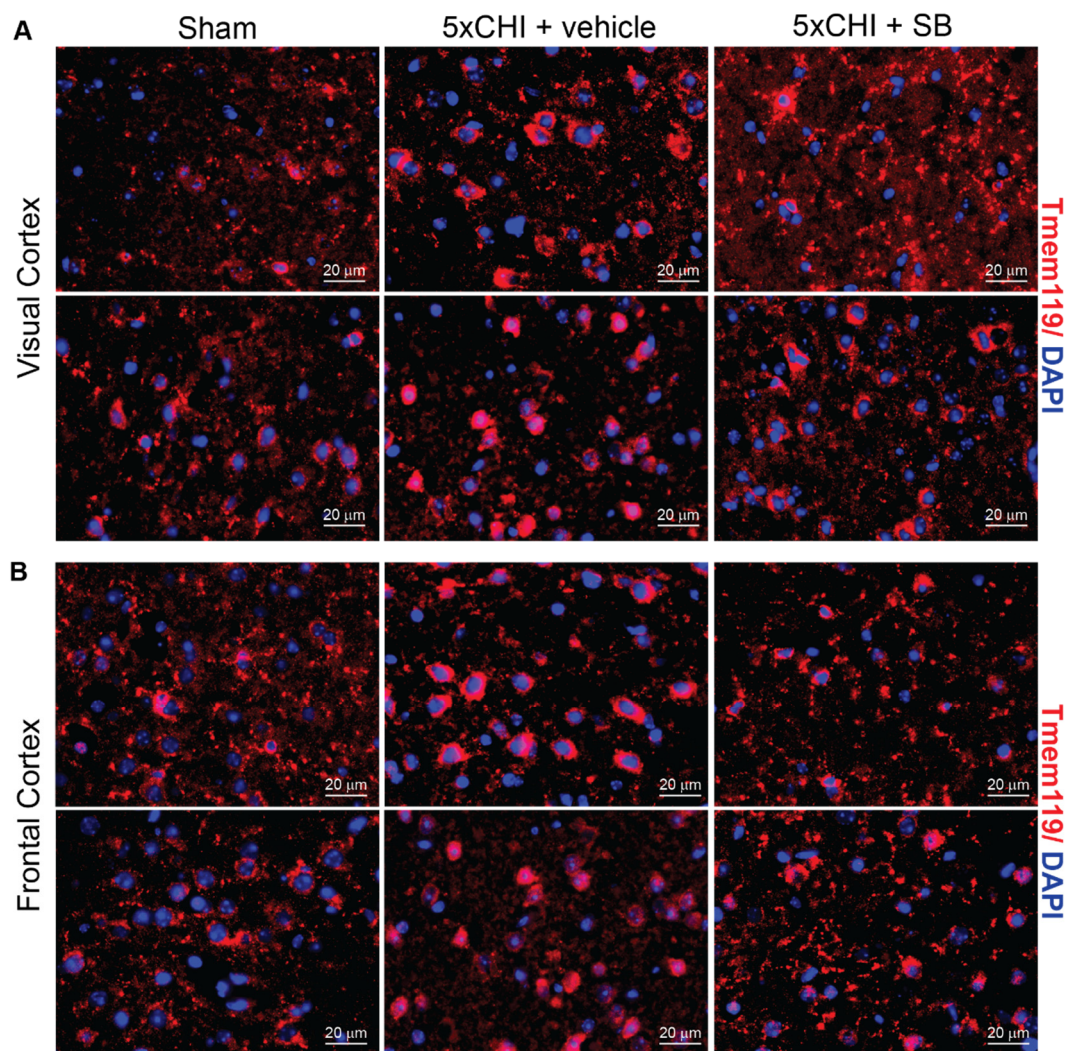


Fig. S14. IHC images for visual and frontal cortex 4-hours post final CHI in males. A. Histological images for marker of Tmem119 for visual cortex. **B.** Histological images for marker of Tmem119 for frontal cortex. Red: Tmem119; Blue: DAPI.

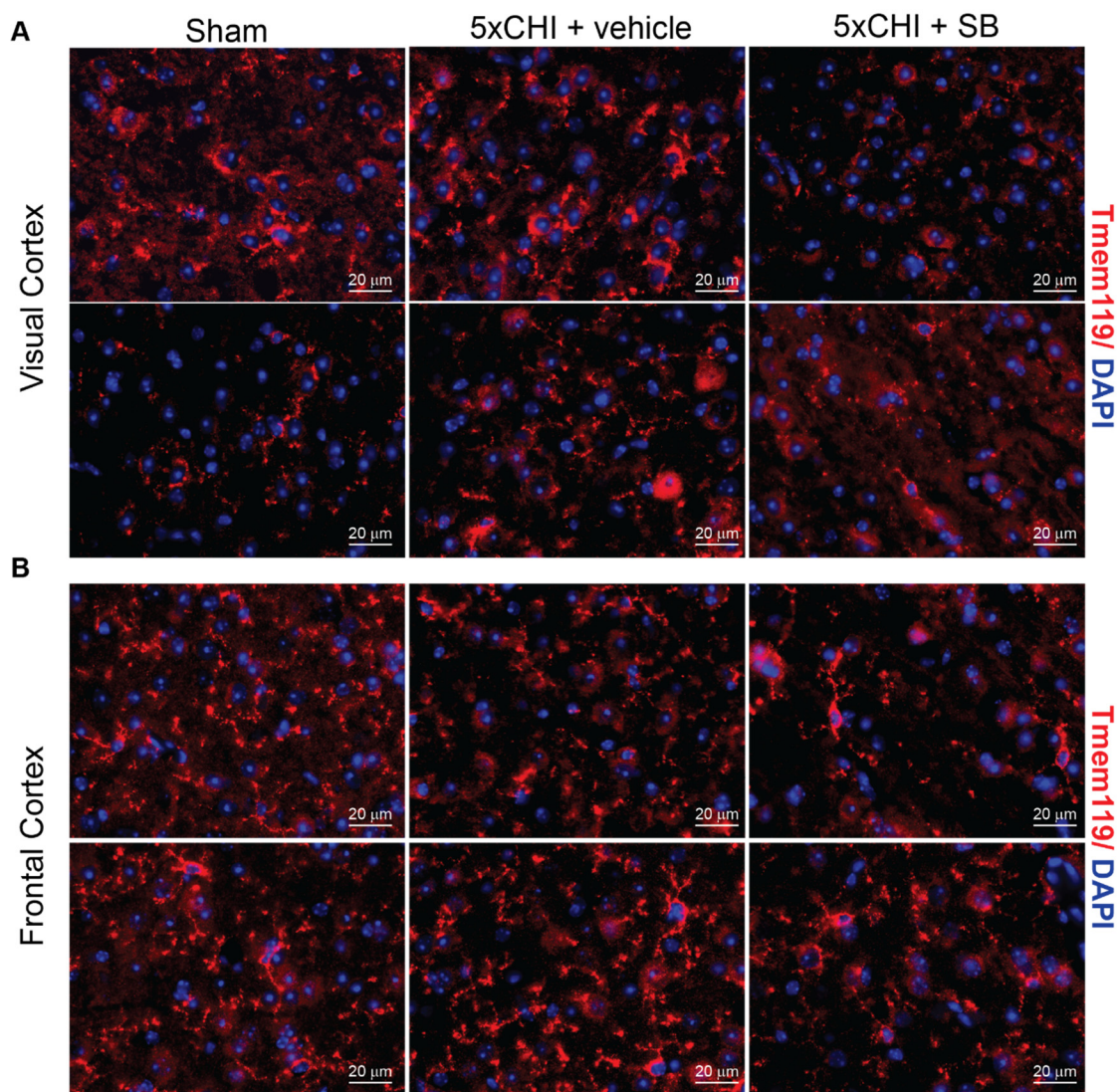


Fig. S15. IHC for visual and frontal cortex 4-weeks post final CHI in males. A. Histological images for maker of Tmem119 for visual cortex. **B.** Histological images for maker of Tmem119 for frontal cortex. Red: Tmem119; Blue: DAPI

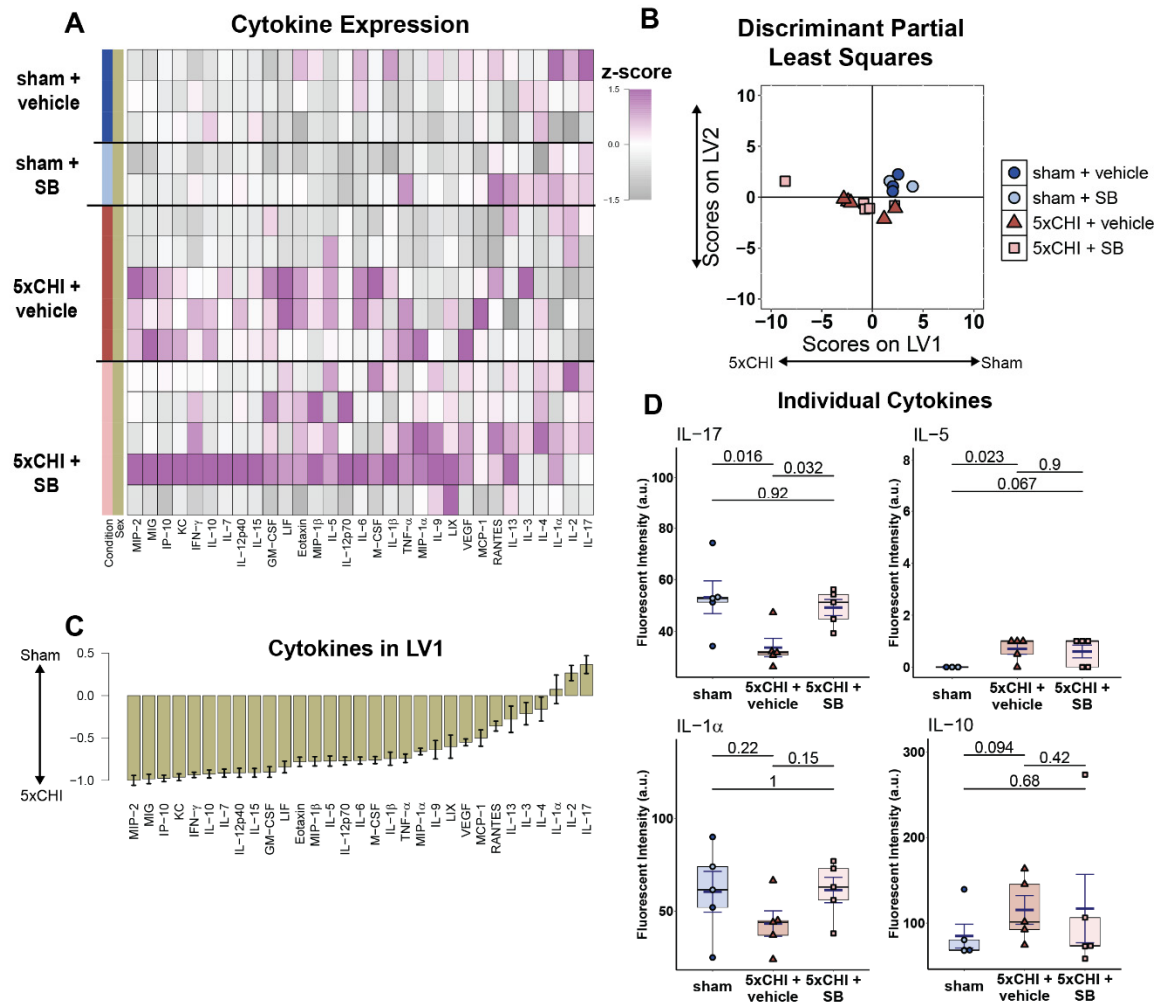


Fig. S16. Acute Inhibition of p38 phosphorylation partially suppressed 5xCHI induced changes in hippocampal cytokine expression 4-hours post final CHI in males. A. Multiplexed Luminex analysis of thirty-one cytokines (columns) expressed in the hippocampus 4-hours after 5xCHI (n=5) and sham-injury (n=2-3). Each row in the z-scored heat map denotes an individual animal from either the sham (bottom rows) or injured (top rows) group. **B.** Scores plot of discriminant partial least square regression. **C.** Discriminant partial least squares regression identified a variable, LV1, that separated samples by experimental group. LV1 consists of a weighted profile of cytokines that were up regulated in either 5xCHI (negative weights) or sham-injured controls (positive weights) (mean $\pm$ SD across LV1 generated for all models in a leave one out cross validation). **D.** Box plots for individual cytokines (mean $\pm$ SEM, Wilcoxon rank sum test). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Light blue circles from sham group denoted sham + SB; dark blue denotes sham + vehicle. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons. a.u.= arbitrary units.

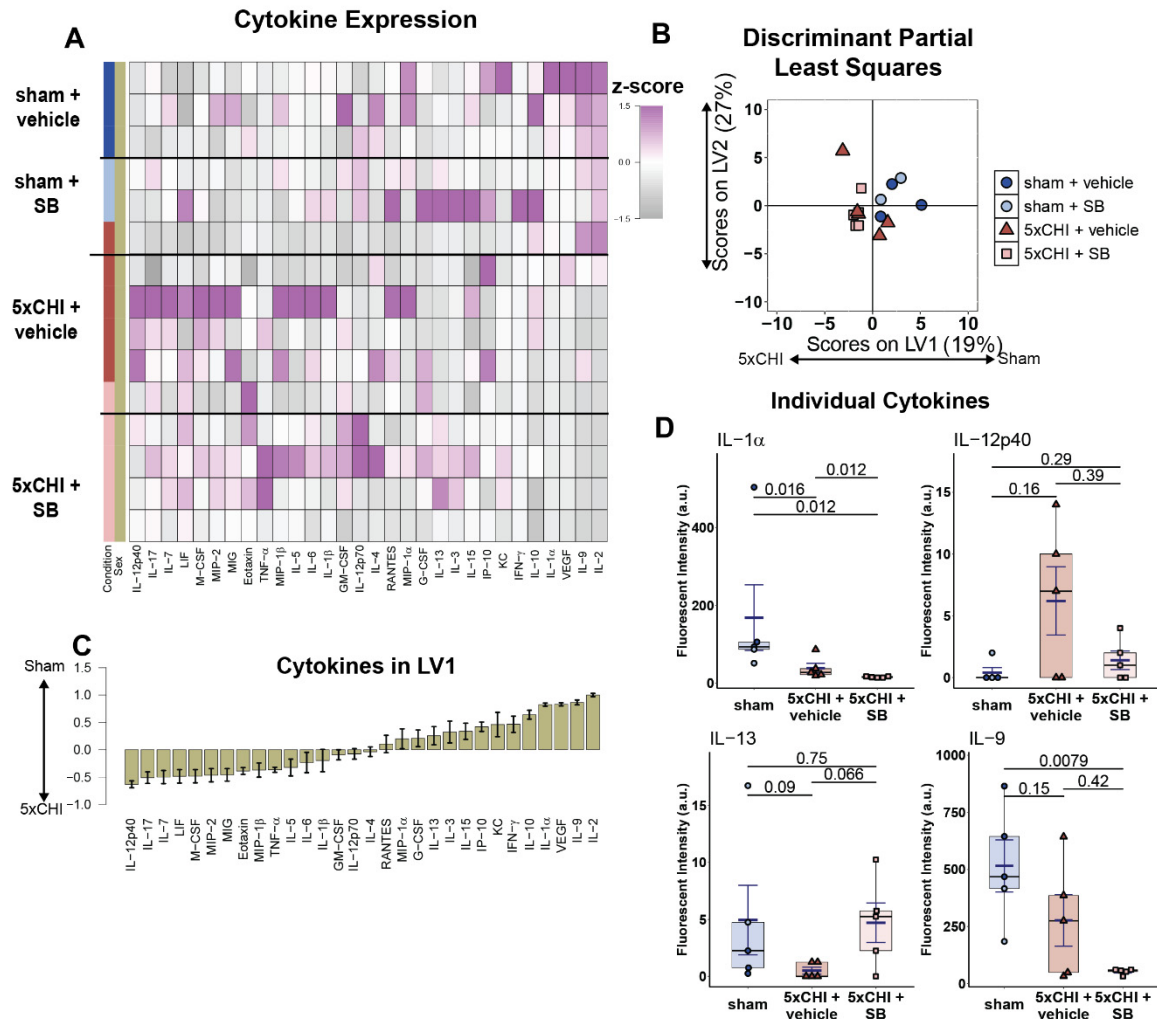


Fig. S17. Acute Inhibition of p38 phosphorylation partially suppressed 5xCHI induced changes in cortical cytokine expression 4-hours post final CHI in males. **A.** Multiplexed Luminex analysis of thirty-one cytokines (columns) expressed in the visual cortex 4-hours after 5xCHI (n=5) and sham-injury (n=5). Each row in the z-scored heat map denotes an individual animal from either the sham (bottom rows) or injured (top rows) group. **B.** Scores plot of discriminant partial least square regression. Each dot denotes one sample. **C.** Discriminant partial least squares regression identified a variable, LV1, that separated samples by experimental group. LV1 consists of a weighted profile of cytokines that were up regulated in either 5xCHI (negative weights) or sham-injured controls (positive weights) (mean $\pm$ SD across LV1 generated for all models in a leave one out cross validation). **D.** Box plots for individual cytokines (mean $\pm$ SEM, Wilcoxon rank sum test). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. Light blue circles from sham group denoted sham + SB; dark blue denotes sham + vehicle. mean $\pm$ SEM. All p-value reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons. a.u.= arbitrary units.

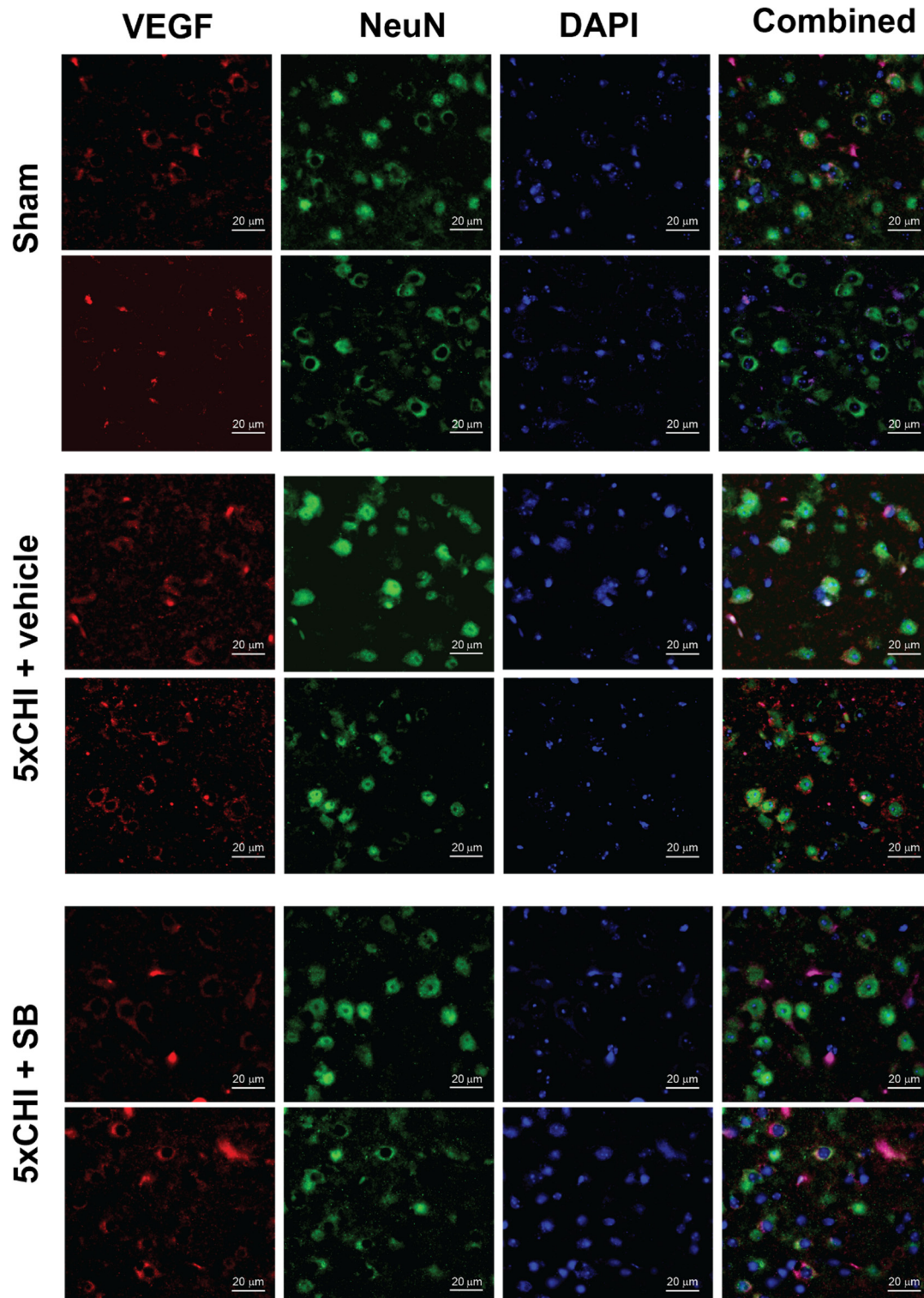


Fig. S18. IHC co-labelling for VEGF and NeuN 4-hours post final CHI in males. VEGF (red) co-stained with NeuN (green) and DAPI (blue) show neuronal co-labeling at 4-hours post injury in males (scale bar: 20 μ m).

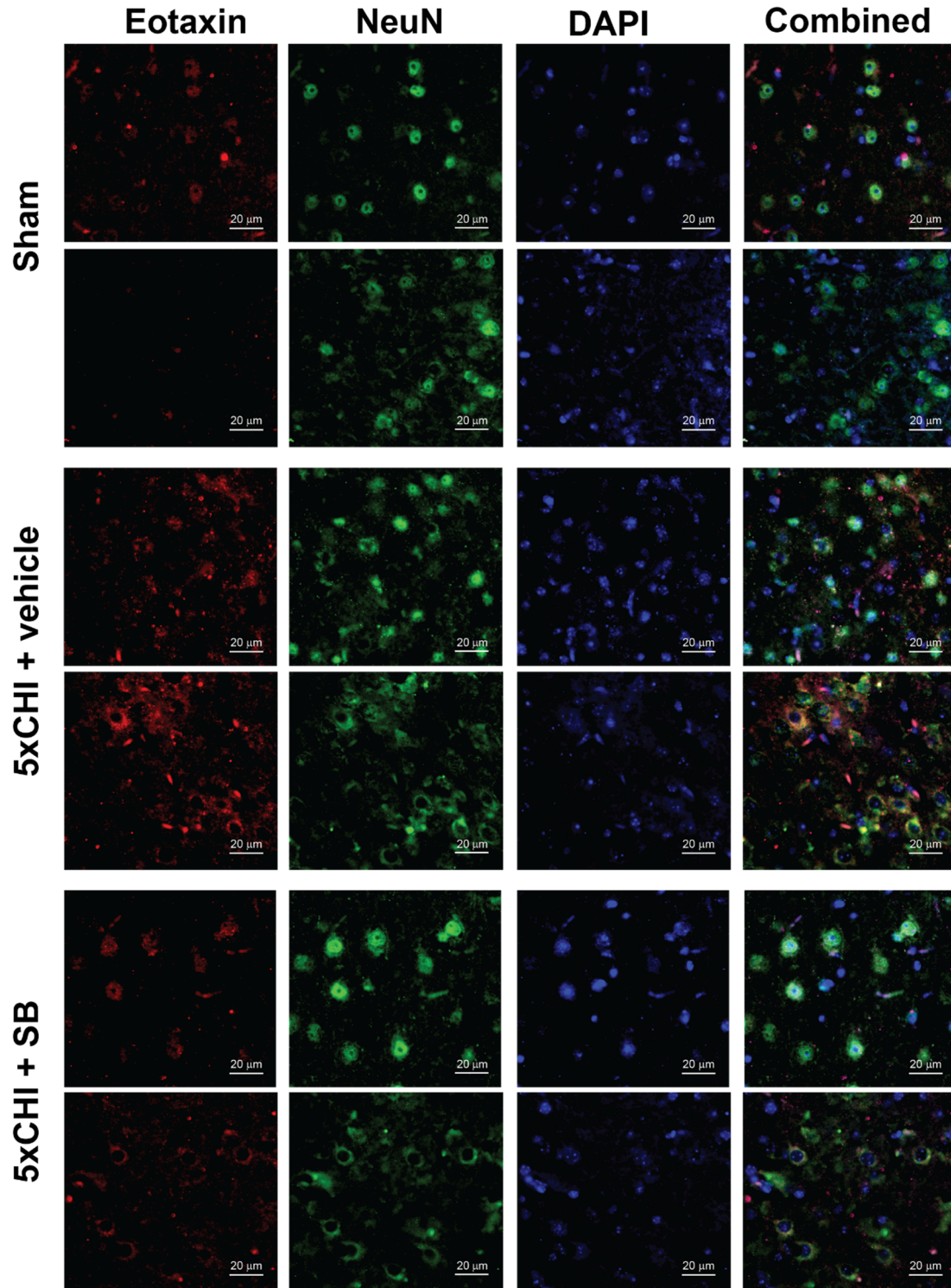


Fig S19. IHC co-labelling for Eotaxin and NeuN 4-hours post final CHI in males. Each row represents an individual mice. Eotaxin (red) co-stained with NeuN (green) and DAPI (blue) show neuronal co-labeling at 4-hours post injury in males (scale bar: 20 μ m).

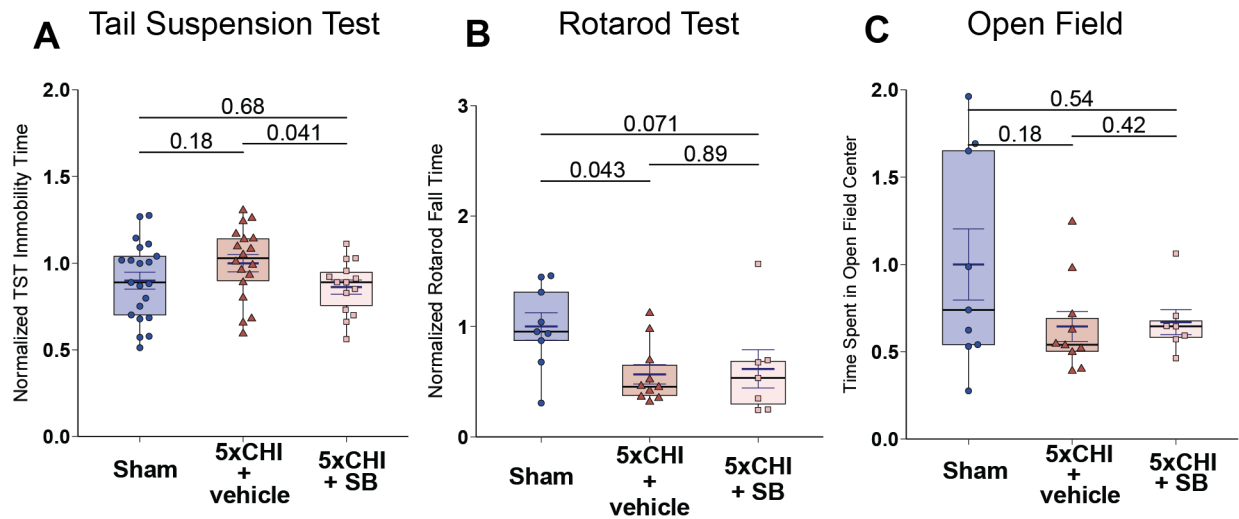


Fig S20. Acute inhibition of p38 MAPK ameliorated 5xCHI induced tail suspension test (TST) changes at 4-weeks post final CHI in males. Column A shows data from the TST, Column B from the rotarod, and Column C from the open field test. The top row represents female data, while the bottom row represents male data. **A.** Normalized TST immobility time for all groups. All TST immobility time was normalized by the mean immobility time from the sham group within each cohort (n=14-20/group). **B.** Rotarod fall time for all groups. All Rotarod fall time was normalized by the mean fall time from the sham group within each cohort (n=7-10/group). **C.** Box plot of normalized time spent in open field center for all groups (n=7-11/group). In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons.

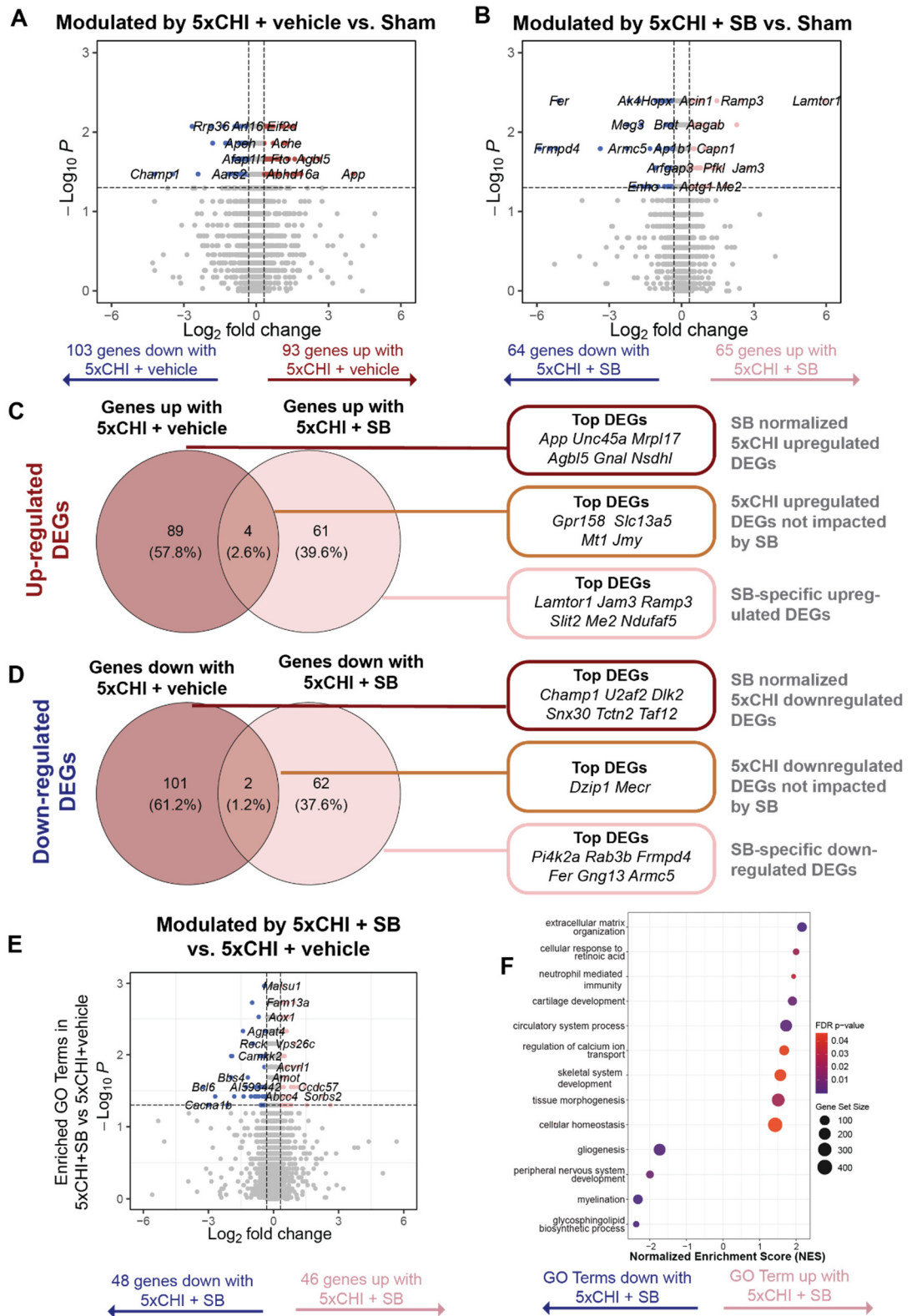


Fig. S21. SB activated protective genes and normalized injury-induced genes 4-weeks after 5xCHI. A. Volcano plot for differentially expressed genes (DEGs) between 5xCHI+vehicle and

sham-injured controls and **B.** between 5xCHI+SB and sham-injured controls. DEGs have p values ≤ 0.05 (above dashed horizontal line) and corresponding log2 fold change $|\log_2\text{FC}| \geq 0.32$. In the volcano plot, each dot represents a single differentially expressed gene (DEG); the x-axis indicates the log₂ fold change, and the y-axis represents the $-\log_{10}(\text{p-value})$. Venn diagrams highlight SB normalized (left most) and SB regulated (right most) DEGs. The red circle represents DEGs in the 5xCHI+vehicle vs. sham-injured control comparison, pink circle represents DEGs in the 5xCHI+SB vs. sham-injured control comparison. SB normalized DEGs are in the 5xCHI+vehicle vs. sham-injured control unique sections (darkest red) and SB-specific DEGs are in the 5xCHI+SB vs. sham-injured control unique sections for **C.** upregulated and **D.** downregulated. Top DEGs by highest $|\log_2\text{FC}|$ are listed on the right in corresponding color blots. **E.** Volcano plot for differentially expressed genes (DEGs) between 5xCHI+vehicle and 5xCHI+SB. **F.** Enriched Gene Ontology (GO) biological processes in 5xCHI+vehicle vs. 5xCHI+SB comparison. Each dot represents a significantly enriched GO term. The color gradient indicates the adjusted p-value, with darker colors representing greater statistical significance. Dot size corresponds to the number of genes associated with each GO term (gene set size), and the x-axis represents fold enrichment. DEG = differentially expressed gene. GO = gene ontology.

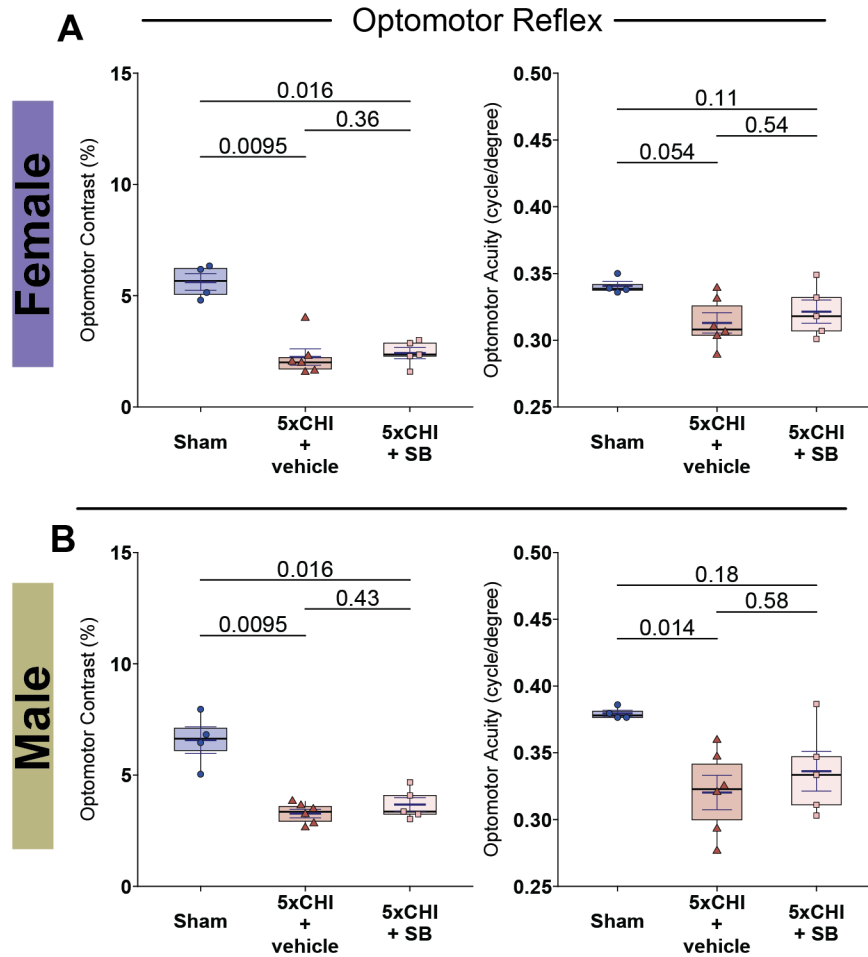


Fig. S22. 5xCHI led to visual impairment in male and female mice. A. Box plots of visual acuity (cycles/degree) and contrast (%) for all groups (Sham, 5xCHI + vehicle, 5xCHI + SB) measured in female and **B.** male animals, indicating decreases in contrast and visual acuity in 5xCHI + vehicle groups. In all plots, each dot denotes an individual animal: blue circles = sham, red triangles = 5xCHI + vehicle, pink squares = 5xCHI + SB. $\pm$ SEM. Navy bars denote mean $\pm$ SEM. All p-values reflect Wilcoxon rank sum tests with Bonferroni adjustment for multiple comparisons.

Supplementary Tables

Protein	Hippocampus 5xCHI+vehicle vs. Sham	Hippocampus 5xCHI+SB vs. Sham	Hippocampus 5xCHI + vehicle vs. 5xCHI + SB	Cortex 5xCHI+vehicle vs. Sham	Cortex 5xCHI+SB vs. Sham	Cortex 5xCHI + vehicle vs 5xCHI + SB
Eotaxin	**	ns	**	**	ns	**
G-CSF	ns	ns	ns	**	ns	ns
GM-CSF	**	ns	ns	ns	ns	ns
IFN- γ	**	ns	ns	**	ns	ns
IL-1 α	ns	ns	ns	ns	ns	ns
IL-1 β	ns	ns	**	ns	ns	ns
IL-2	ns	ns	ns	ns	ns	ns
IL-3	ns	ns	ns	ns	ns	ns
IL-4	ns	ns	ns	ns	ns	ns
IL-5	**	ns	ns	**	ns	ns
IL-6	**	ns	ns	**	ns	ns
IL-7	ns	ns	ns	ns	ns	ns
IL-9	ns	ns	ns	ns	ns	ns
IL-10	ns	ns	ns	ns	ns	ns
IL-12 p40	**	ns	ns	**	ns	ns
IL-12 p70	ns	ns	ns	ns	ns	ns
IL-13	**	ns	ns	**	ns	ns
IL-15	ns	ns	ns	**	ns	ns
IL-17	ns	ns	ns	ns	ns	ns
IP-10	ns	ns	ns	ns	**	ns
KC	ns	ns	ns	ns	ns	ns
LIF	ns	ns	ns	ns	ns	ns
LIX	**	**	ns	ns	ns	ns
MCP-1	ns	ns	ns	ns	ns	ns
M-CSF	ns	ns	ns	ns	ns	ns
MIG	ns	ns	ns	ns	ns	ns
MIP-1 α	ns	ns	ns	**	**	ns
MIP-1 β	**	ns	**	**	ns	**
MIP-2	ns	ns	ns	ns	ns	ns
RANTES	ns	ns	ns	ns	ns	ns
TNF- α	**	ns	ns	ns	ns	ns
VEGF	**	ns	**	ns	ns	ns

Table S1. Cytokine expression differences by protein within each brain region in females.
ns = not significant, **p<0.05. All p-values were calculated by Wilcoxon rank-sum test with Bonferroni adjustments for multiple comparisons.

TST	 Cohen's d 	Power
Sham vs. 5xCHI + vehicle	1.32	0.72
5xCHI + vehicle vs. 5xCHI + SB	0.58	0.2
Sham vs. 5xCHI + SB	0.48	0.15
Rotarod		
Sham vs. 5xCHI + vehicle	1.24	0.77
5xCHI + vehicle vs. 5xCHI + SB	0.73	0.32
Sham vs. 5xCHI + SB	0.39	0.13
Open Field		
Sham vs. 5xCHI + vehicle	0.69	0.3
5xCHI + vehicle vs. 5xCHI + SB	0.08	0.05
Sham vs. 5xCHI + SB	0.69	0.34

Table S2. Post hoc power analysis for functional measure in females. Cohen's d and post hoc power for pairwise contrasts were computed using a two-sample t-test based framework.

Protein	Hippocampus 5xCHI+vehicle vs. Sham	Hippocampus 5xCHI+SB vs. Sham	Hippocampus 5xCHI + vehicle vs. 5xCHI + SB	Cortex 5xCHI+vehicle vs. Sham	Cortex 5xCHI+SB vs. Sham	Cortex 5xCHI + vehicle vs 5xCHI + SB
Eotaxin	**	ns	**	**	ns	**
G-CSF	ns	ns	ns	**	ns	ns
GM-CSF	**	ns	ns	ns	ns	ns
IFN- γ	**	ns	ns	**	ns	ns
IL-1 α	ns	ns	ns	ns	ns	ns
IL-1 β	ns	ns	**	ns	ns	ns
IL-2	ns	ns	ns	ns	ns	ns
IL-3	ns	ns	ns	ns	ns	ns
IL-4	ns	ns	ns	ns	ns	ns
IL-5	**	ns	ns	**	ns	ns
IL-6	**	ns	ns	**	ns	ns
IL-7	ns	ns	ns	ns	ns	ns
IL-9	ns	ns	ns	ns	ns	ns
IL-10	ns	ns	ns	ns	ns	ns
IL-12 p40	**	ns	ns	**	ns	ns
IL-12 p70	ns	ns	ns	ns	ns	ns
IL-13	**	ns	ns	**	ns	ns
IL-15	ns	ns	ns	**	ns	ns
IL-17	ns	ns	ns	ns	ns	ns
IP-10	ns	ns	ns	ns	**	ns
KC	ns	ns	ns	ns	ns	ns
LIF	ns	ns	ns	ns	ns	ns
LIX	**	**	ns	ns	ns	ns
MCP-1	ns	ns	ns	ns	ns	ns
M-CSF	ns	ns	ns	ns	ns	ns
MIG	ns	ns	ns	ns	ns	ns
MIP-1 α	ns	ns	ns	**	**	ns
MIP-1 β	**	ns	**	**	ns	**
MIP-2	ns	ns	ns	ns	ns	ns
RANTES	ns	ns	ns	ns	ns	ns
TNF- α	**	ns	ns	ns	ns	ns

Table S3. Cytokine expression differences by protein within each brain region in males. NA = data not included, ns = not significant, **p<0.05. All p-values were calculated by Wilcoxon rank-sum test with Bonferroni adjustments for multiple comparisons.

TST	 Cohen's d 	Power
Sham vs. 5xCHI + vehicle	0.46	0.28
5xCHI + vehicle vs. 5xCHI + SB	0.19	0.08
Sham vs. 5xCHI + SB	0.73	0.51
Rotarod		
Sham vs. 5xCHI + vehicle	1.33	0.78
5xCHI + vehicle vs. 5xCHI + SB	0.14	0.06
Sham vs. 5xCHI + SB	0.93	0.41
Open Field		
Sham vs. 5xCHI + vehicle	0.77	0.35
5xCHI + vehicle vs. 5xCHI + SB	0.1	0.05
Sham vs. 5xCHI + SB	0.7	0.25

Table S4. Post hoc power analysis for functional measure in females. Cohen's d and post hoc power for pairwise contrasts were computed using a two-sample t-test based framework.

Resources	Catalog Number	Application	Dilution	Blocking Buffer	Brand
Anti-Tmem119	ab209064	IHC	1:500	5% BSA in 1X TBST	Abcam
Anti-NeuN	GTX00837	IHC	1:800	5% BSA in 1X TBST	GeneTex
Anti-VEGF	MA1-16629	IHC	1:100	5% BSA in 1X TBST	ThermoFisher
Anti-Eotaxin	AF-420-NA	IHC	1:100	5% BSA in 1X TBST	R&D Systems
Anti-Iba1	ab178846	IHC	1:500	5% BSA in 1X TBST	Abcam
Anti-PSD95	GTX133091	IHC	1:1000	5% BSA in 1X TBST	GeneTex
Anti-PSD95	GTX133091	Western blot	1:1000	5% BSA in 1X TBST	GeneTex
Anti- α - Tubulin	T6074	Western blot	1:10000	5% BSA in 1X TBST	Sigma Aldrich

Table S5: Antibody Information.

Sex	Injury	Treatment	OMR	TST	Rotarod	Open Field
Female	5xCHI	SB	5	8	9	10
		Vehicle	6	9	10	12
	sham	SB	0	2	0	0
		Vehicle	4	6	11	8
Male	5xCHI	SB	5	14	7	7
		Vehicle	6	18	10	10
	sham	SB	0	6	0	0
		Vehicle	4	15	9	9

Table S4: Experimental sample numbers for behavioral assays.

Supplementary Data (separate file)

Data S1: Differential gene expression analysis of the 5xCHI+vehicle vs. sham+vehicle comparison in female samples, calculated using Wilcoxon rank sum test. Found in Supplemental Excel file- Tab “Data S1”.

Data S2: Differential gene expression analysis of the 5xCHI+SB vs. sham+vehicle comparison in female samples, calculated using Wilcoxon rank sum test. Found in Supplemental Excel file- Tab “Data S2”.

Data S3: Differential gene expression analysis of the 5xCHI+SB vs. 5xCHI+vehicle comparison in female samples, calculated using Wilcoxon rank sum test. Found in Supplemental Excel file- Tab “Data S3”.

Data S4: GSEA analysis showing enriched GO biological processes 5xCHI+SB vs. 5xCHI+SB comparison in female samples. Found in Supplemental Excel file- Tab “Data S4”.

Data S5: Differential gene expression analysis of the 5xCHI+vehicle vs. sham+vehicle comparison in male samples, calculated using Wilcoxon rank sum test. Found in Supplemental Excel file- Tab “Data S5”.

Data S6: Differential gene expression analysis of the 5xCHI+SB vs. sham+vehicle comparison in male samples, calculated using Wilcoxon rank sum test. Found in Supplemental Excel file- Tab “Data S6”.

Data S7: Differential gene expression analysis of the 5xCHI+SB vs. 5xCHI+vehicle comparison in male samples, calculated using Wilcoxon rank sum test. Found in Supplemental Excel file- Tab “Data S7”.

Data S8: GSEA analysis showing enriched GO biological processes 5xCHI+SB vs. 5xCHI+SB comparison in male samples. Found in Supplemental Excel file- Tab “Data S8”.