**Supplemental Material**

**Supplementary Method:**

**LC-MS/MS measurement of transmission of ibudilast through lactation.** Lactating mothers were injected with 30mg/Kg ibudilast daily for 2 weeks starting one day after parturition. Five hours after the last injection, blood and brain were collected from the offspring. The blood was allowed to clot for 30 min after which it was centrifuged at 15,000 rpm for 15 min and serum was collected and frozen. Brains were homogenized in lysis buffer containing protease inhibitors, carried out with 3 cycles of sonication and centrifuged at 14,000 rpm for 20 minutes at 4°C. The protein concentration was determined using a BCA assay (Pierce, Thermo Scientific). Liquid chromatography/tandem mass spectrometry (LC-MS/MS) was used for ibudilast serum and brain sample analysis. A Waters ACQUITY UPLC system (Waters, Milford, MA) coupled to an Applied Biosystem 4000 Q TRAP®quadrupole linear ion trap hybrid mass spectrometer with an electrospray ionization (ESI) source (Applied Biosystems/MDS Sciex, Foster City, CA) was used. MS/MS analyses were performed in positive electrospray ionization mode; specific detection of ibudilast was performed by monitoring the transition 231.1→161.1 m/z. UPLC separation was carried out using an ACQUITY UPLC®BEH Shield RP 18 column with a isocratic mobile phase of 0.1% formic acid: acetonitrile (1:1, v/v) at a flow rate of 0.25 mL/min. For sample preparation, 1 mL of ice-cold acetonitrile was added to 50 µL serum or 100 µL brain homogenate samples. Samples were then vortexed and centrifuged at 16,000 g for 10 minutes. The supernatant was aspirated, evaporated under vacuum, and reconstituted in a 100 µL 50% acetonitrile. After centrifugation at 16,000 g for 10 minutes, 10 µL of each sample was used for LC-MS/MS analysis.

**Supplemental Table 1:** Dendritic parameters for the various experiments.

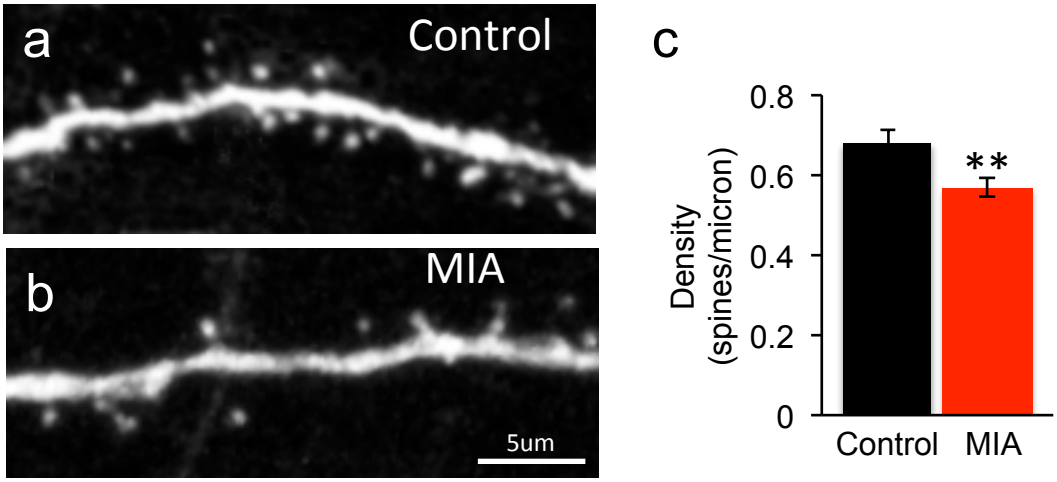
mean±sem

| **P17 Protrusion (Fig. 1)** | **Con** | **MIA** |
|---|---|---|
| Total dendrite length (um) | 1341 | 2500 |
| Mean dendrite length (um) | 37.4±3.5 | 35.8±2.4 |
| Mean dendrite diameter (um) | 1.1±0.04 | 1.07±0.02 |
| Total number of spines | 1338 | 1935 |

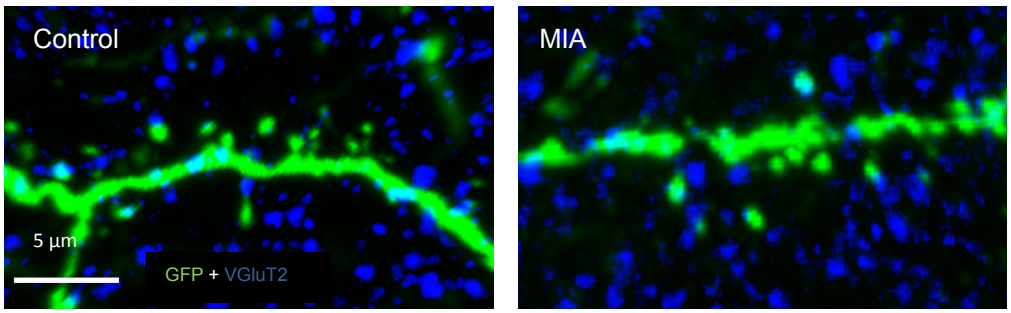
| **Colocalization (Fig. 3)** | **Con** | **MIA** |
|---|---|---|
| Total dendrite length (um) | 690 | 805 |
| Mean dendrite length (um) | 31.4±2.7 | 32.4±1.8 |
| Mean dendrite diameter (um) | 1.16±0.03 | 1.23±0.05 |
| Total number of spines | 661 | 574 |

| **P17 spines (Fig. 5)** | **Con+Veh** | **MIA+Veh** | **Con+Ibud** | **MIA+Ibud** |
|---|---|---|---|---|
| Total dendrite length (um) | 836.6 | 1078. | 622.7 | 792.7 |
| Mean dendrite length (um) | 41.6±2.5 | 40.17±3.3 | 39.3±1.9 | 35.4±3.7 |
| Mean dendrite diameter (um) | 1.16±0.06 | 1.22±0.03 | 1.23±0.06 | 1.26±0.04 |
| Total number of spines | 751 | 825 | 559 | 727 |

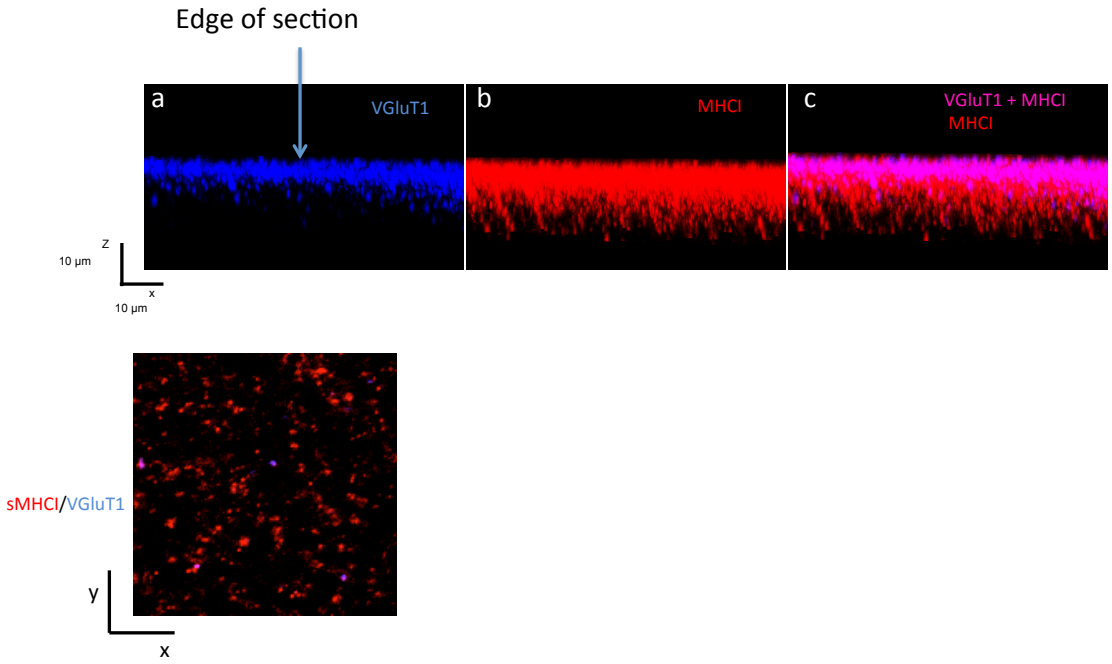
| **Adult spines (Fig. 7)** | **Con+Veh** | **MIA+Veh** | **Con+Ibud** | **MIA+Ibud** |
|---|---|---|---|---|
| Total dendrite length (um) | 1446.4 | 1357.4 | 700.7 | 1153 |
| Mean dendrite length (um) | 43.26±1.4 | 44.6±1.9 | 38.2±3 | 45.74±3.1 |
| Mean dendrite diameter (um) | 1.08±0.02 | 1.07±0.014 | 1.2±0.07 | 1.17±0.05 |
| Total number of spines | 1226 | 794 | 517 | 869 |




**Supplemental Figure 1: MIA results in a reduction in total dendritic spine density on basal dendrites.** Example images of basal dendrites from the somatosensory cortex in P30 **(a)** control and **(b)** MIA offspring. **c.** Spine densities in Control offspring 0.68±0.03 spines/μm, n= 48 images, 6 mice and MIA offspring 0.57±0.02, n= 58 images from 9 mice P=0.004, unpaired t-test.

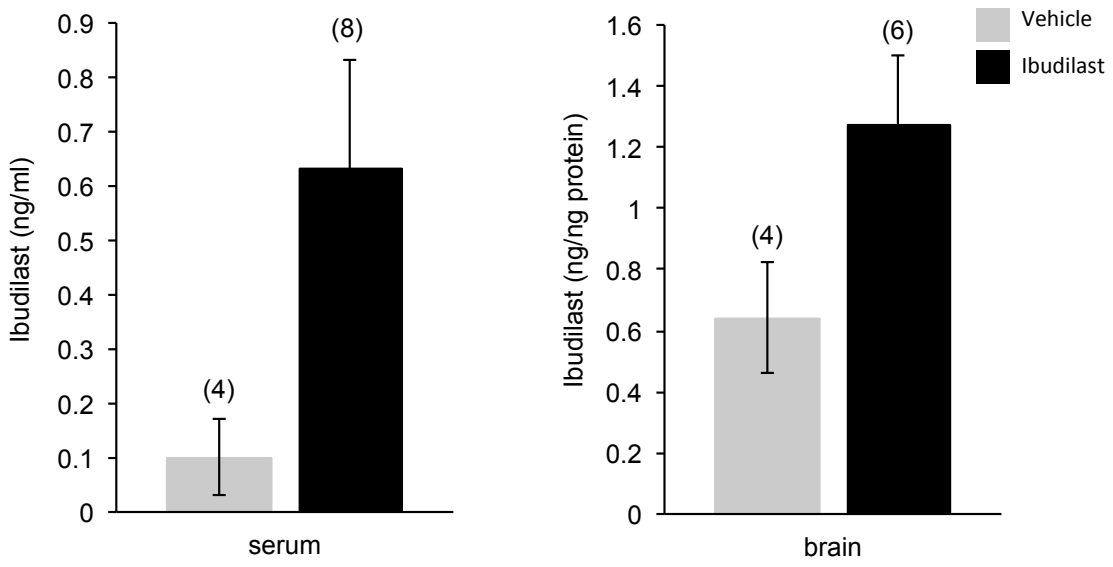



**Supplemental Figure 2: VGluT2 staining in the cortex.** Somatosensory sections from YFP-H P17 control and MIA offspring immunostained for VGluT2 and GAD-65.

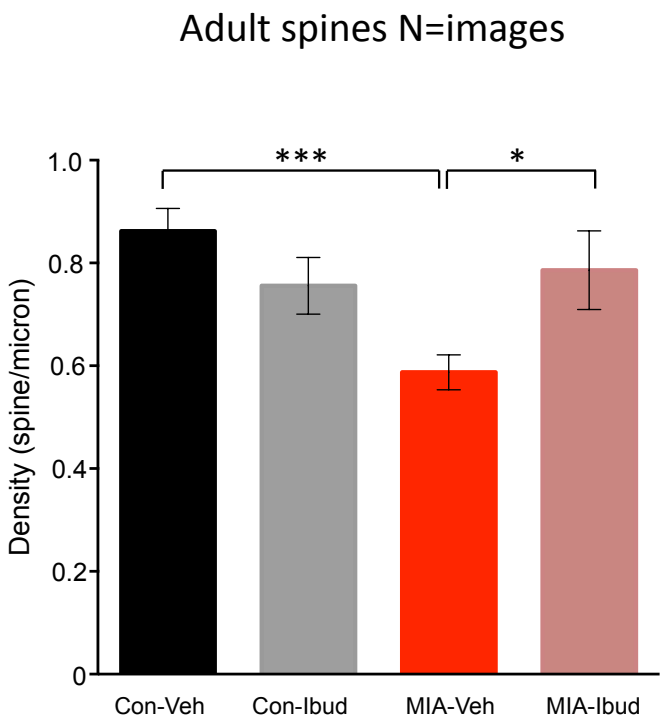



**Supplemental Figure 3: In vivo analysis of surface expression of MHCI.**

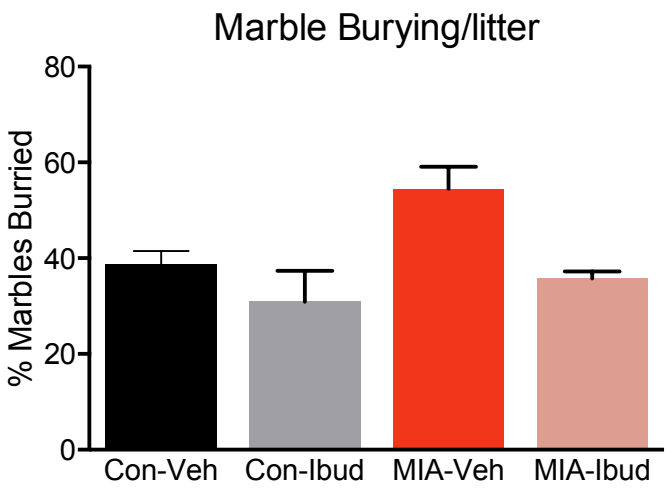
Side view (XZ) of VGluT1 (a) and MHCI (b) staining in unpermeabilized sections imaged on a confocal microscope. The top of the section is marked with an arrow. The portion of section in which VGluT1 and MHCI colocolized staining is detected (purple in c) is not considered for surface analysis. The MHCI staining found in focal planes immediately below the colocolized signal (as in the white box) is considered surface MHCI staining and is used for analysis.




**Supplemental Figure 4: Ibudilast can be detected in serum (ng/mL) and brain (ng/ng protein) of offspring following transmission of ibudilast through lactation.** Mean ± SEM, number of pups used are indicated.




**Supplemental Figure 5: Postnatal treatment with an anti-inflammatory drug prevents dendritic spine deficits. Same data as in figure 7b was analyzed with N=images.** Two-way ANOVA was first used to test for the presence of interaction between drug treatment and experimental groups. This revealed an interaction consistent with the observation that ibudilast increased dendritic spine density in the MIA offspring but had no effect on the controls $F(1, 103)=7.953$, $P=0.006$. *Post hoc* two-way ANOVA with Bonferroni's correction indicates that a reduction in spine density in MIA+Vehicle offspring persists into adulthood (control + vehicle: 0.86±0.04 spines/micron, n=34 images; MIA + vehicle: 0.58±0.03 spines/micron, n=30 images, $P=0.0006$,) but is prevented by postnatal treatment with the anti-inflammatory drug Ibudilast (MIA + Ibudilast: 0.78±0.07 ± spines/micron, n=25 images, MIA + vehicle: 0.58± 0.03 spines/micron, n=30 images, $P=0.04$). No changes in spines density in control+ibudilast offspring (control + vehicle: 0.86±0.04 spines/micron, n=34 images; control + ibudilast: 0.75±0.05 spines/micron, n=18 images, $P=0.45$).




**Supplemental Figure 6: Marble burying is increased in MIA offspring and is reduced by Ibudilast.** Because for the behavioral data 2-5 mice per litter were used the data presented in Figure 7c is compiled here while considering litters as independent variable. There was a main effect of prenatal treatment, $F(1,12)=5.84$, $P=0.03$, as well as a main effect of drug treatment, $F(1,12)=9.67$, $P=0.009$ on marble burying but no significant interaction $F(1,12)=1.63$, $P=0.22$. Marble burying increased in MIA offspring (con+veh: 38.73±2.76%, n= 4 litters; MIA+veh: 54.48±4.6%, n=4 litters). This increase is reduced in MIA offspring treated with ibudilast during the first 2 postnatal weeks (MIA+Ibud: 35.78±1.46%, n=4 litters). There was a mild effect of Ibudilast on control offspring (con+Ibud: 30.96±6.4%, n=4 litters).