

Revised Supplementary Files

Revised supplementary file1: revised supplementary figures 1-4

Revised supplementary file2: revised supplementary dataset

**Mirtazapine exerts astrocyte-mediated dopaminergic neuroprotection**

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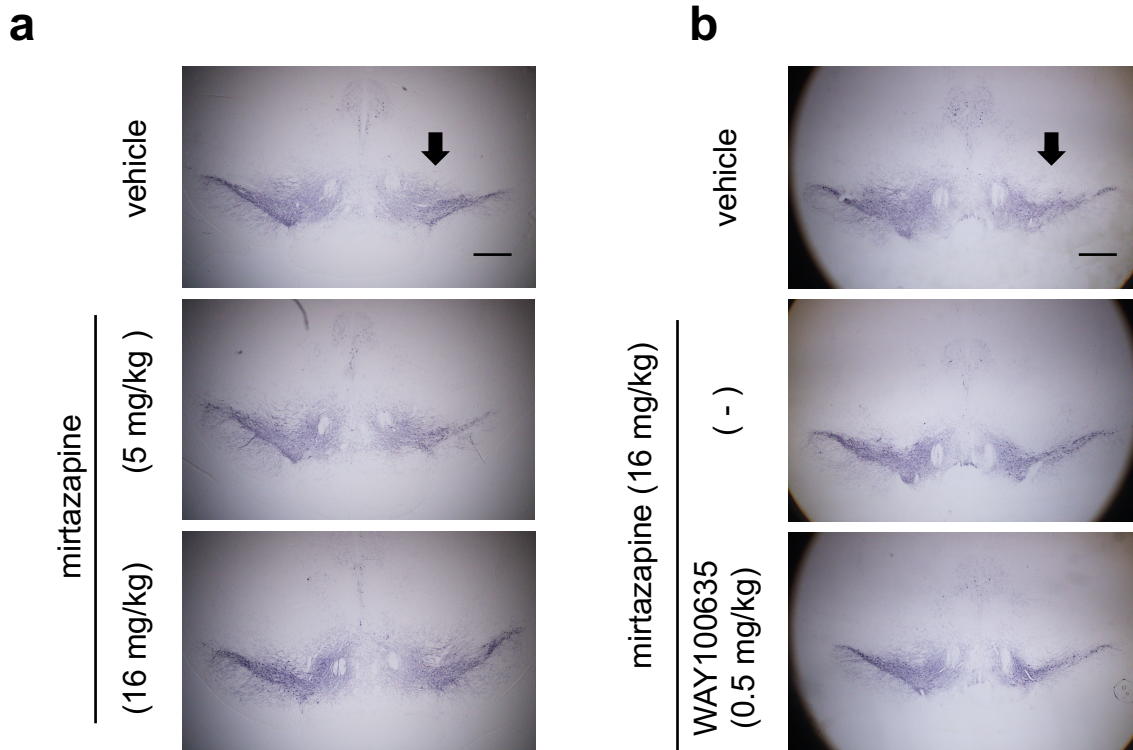
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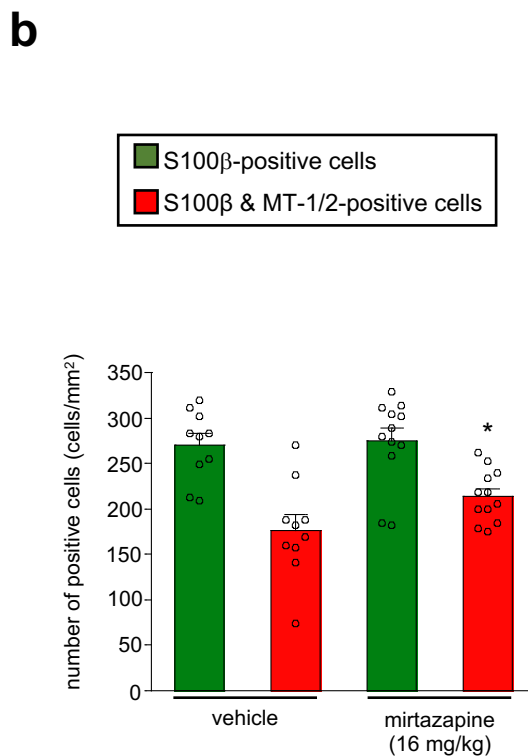
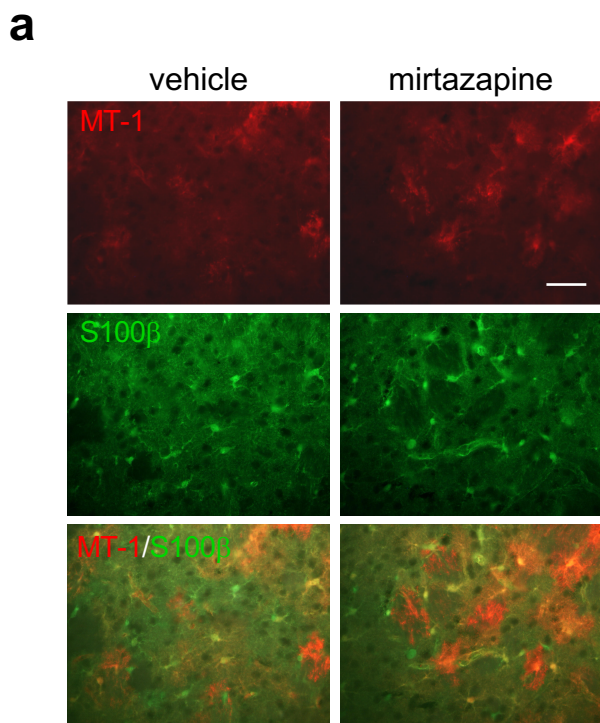
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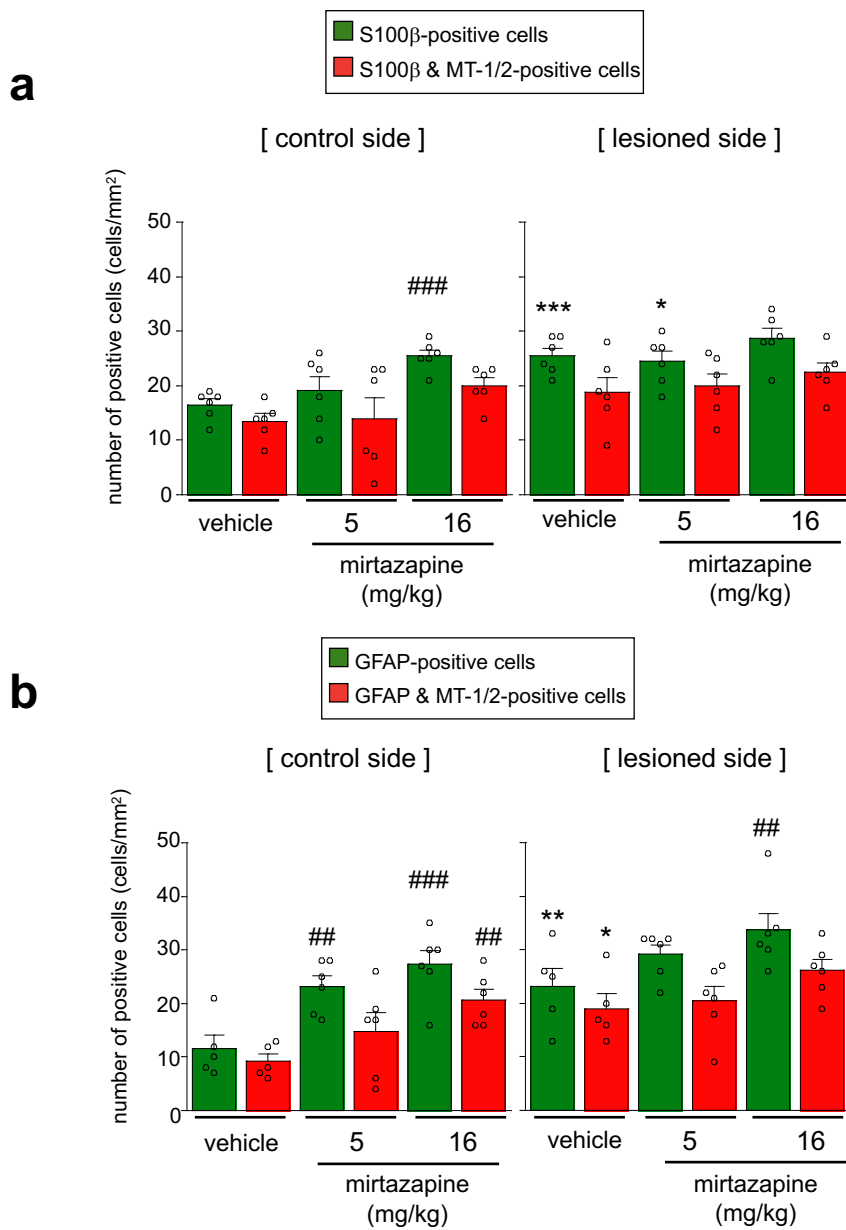
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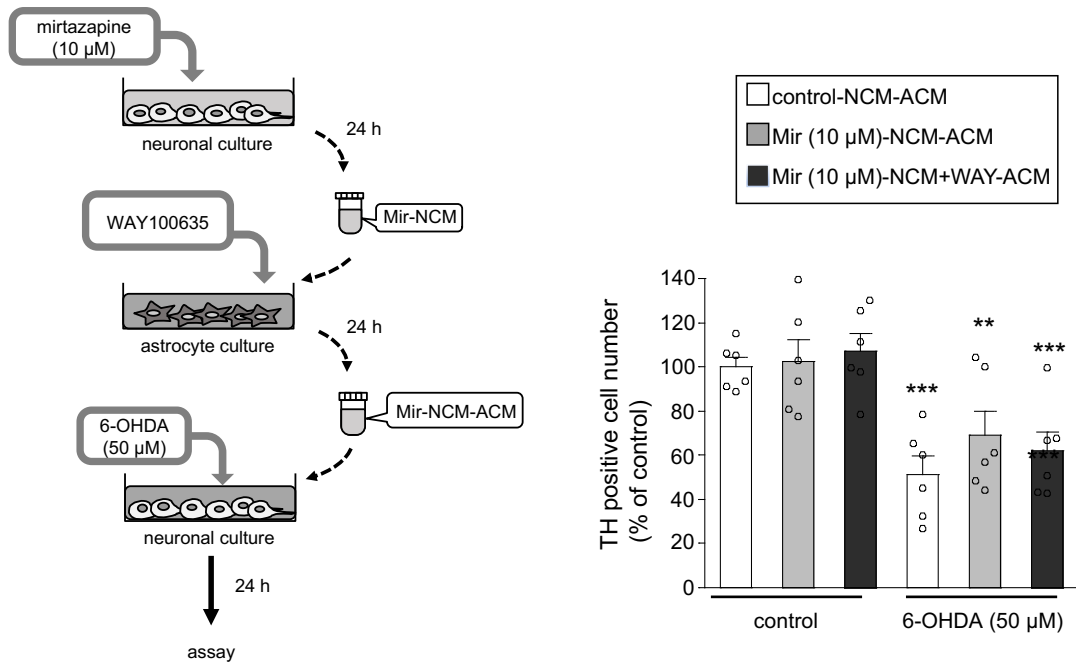
**Supplemental Figure 1.** Representative microphotographs of immunohistochemistry for TH in the SNpc of hemi-PD. (a) Mirtazapine (5-16 mg/kg)-treated mice. (b) Mirtazapine (16 mg/kg) with or without WAY 100635 (0.5 mg/kg)-treated mice. Right side is the 6-OHDA-injected lesioned side (arrow). Scale bar = 500  $\mu$ m.



**Supplemental Figure 2.** Mirtazapine upregulated MT-1/2 expression in the striatal astrocytes of healthy ICR mice. (a) Representative microphotograph of immunohistochemistry for S100β (green) and MT-1/2 (red) in the striatum of mirtazapine (16 mg/kg)-treated mice. Scale bar = 50 μm. (b) Quantitation of the S100β- and MT-1/2-positive cells. Data are means ± SEM (n = 5-6). \*p < 0.05 vs. vehicle-treated control group.



**Supplemental Figure 3.** Effects of mirtazapine administration on MT-1/2 expression in astrocytes in the SNpc of parkinsonian mice. (a) Quantification of the S100β - and MT-1/2-positive cells. (b) Quantitation of the GFAP- and MT-1/2-positive cells. Data are means  $\pm$  SEM (n = 5-6). \*p < 0.05, \*\*p < 0.01 vs. control side of each group. ##p < 0.01, ###p < 0.001 vs. the same side of vehicle-treated group.



**Supplemental Figure 4.** Changes in the number of TH-positive cells in neuronal cultures after treatment with Mir (10  $\mu\text{M}$ )-NCM-ACM with or without WAY100635, followed by 6-OHDA exposure. To prepare Mir-NCM-ACM, astrocytes were treated with mirtazapine (10  $\mu\text{M}$ )-treated-NCM for 24 h. Mesencephalic neurons were pre-treated with Mir-NCM-ACM for 24 h, and then exposed to 6-OHDA (50  $\mu\text{M}$ ) for 24 h. Data are means  $\pm$  SEM (n = 6) expressed as percentage of control group. \*\*p < 0.01, \*\*\*p < 0.001 vs. each control groups.