

Supplementary Materials for  
**Inhibition of mTOR Signaling in Parkinson's Disease Prevents L-DOPA-Induced Dyskinesia**

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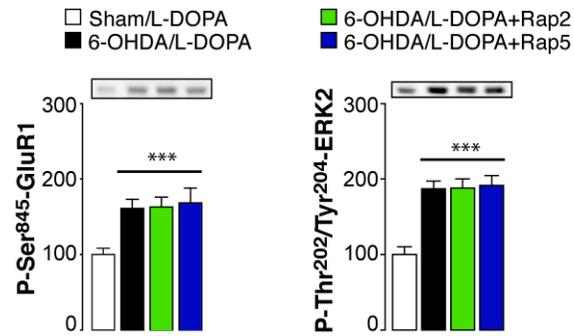
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Fig. S1. Rapamycin does not affect L-DOPA-induced phosphorylation of GluR1 and ERK2.

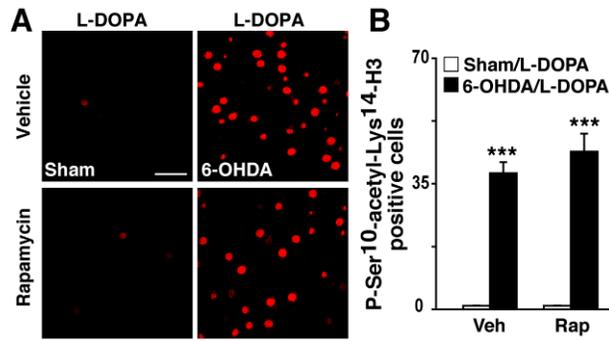
Fig. S2. Rapamycin does not affect L-DOPA-induced phosphorylation of Lys<sup>14</sup>-acetylated histone H3.

Fig. S3. Evaluation of the degree of DA denervation after striatal 6-OHDA injection.

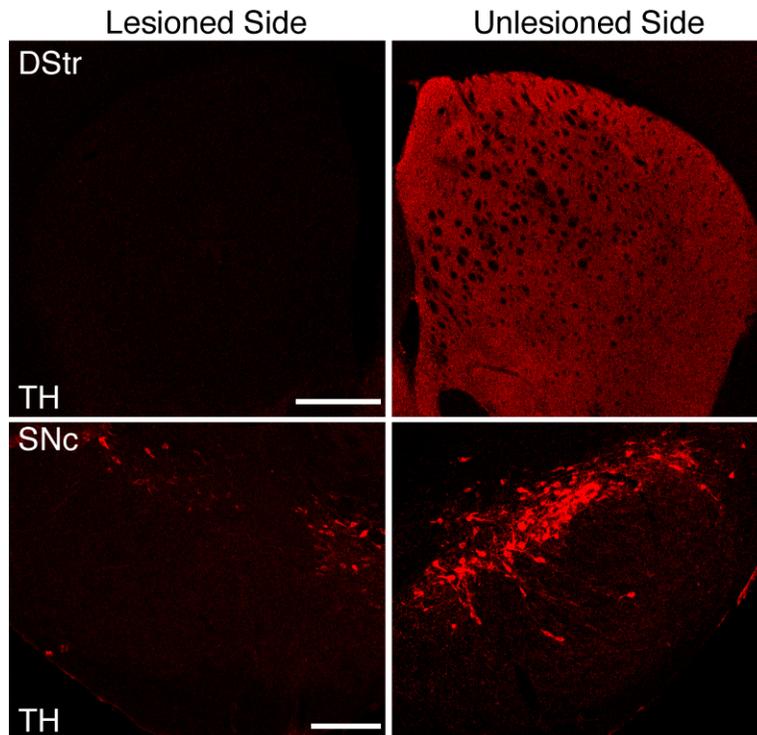
Table S1. Effect of 6-OHDA and L-DOPA on selected proteins involved in mTOR signaling.



**Fig. S1.** Rapamycin does not affect L-DOPA-induced phosphorylation of GluR1 and ERK2. Representative Western blots (top) and quantification (bottom). Error bars represent SEM (n = 8-16 mice per treatment) of data calculated as percent of Sham treated with L-DOPA. Statistical significance was determined by one-way ANOVA followed by the Bonferroni-Dunn test. \*\*\* p < 0.001 versus sham treated with L-DOPA.



**Fig. S2.** Rapamycin does not affect L-DOPA-induced phosphorylation of Lys<sup>14</sup>-acetylated histone H3. Immunofluorescent detection (A) and quantification (B) of cells positive for phospho-Ser<sup>10</sup>-acetyl-Lys<sup>14</sup>-H3 in the striata of sham- and 6-OHDA-lesioned mice treated with L-DOPA alone, or in combination with Rapamycin (Rap). Scale bar: 40  $\mu$ m. Error bars represent SEM (n = 3 mice per treatment). Statistical significance was determined by two-way ANOVA followed by the Bonferroni-Dunn test. \*\*\* p < 0.001 versus sham treated with L-DOPA.



**Fig. S3.** Evaluation of the degree of DA denervation following striatal 6-OHDA injection. Upper panels show lack of tyrosine hydroxylase (TH)-positive fibers in the dorsal striatum (DStr) of a mouse with unilateral lesion of nigrostriatal dopamine system (left) compared with a sham-lesioned mouse (right). Scale bar: 300  $\mu$ m. Lower panels, show the loss of dopaminergic neurons in the substantia nigra pars compacta (SNc) following striatal 6-OHDA lesion. Scale bar: 200  $\mu$ m.

	<b>Sham</b>	<b>6-OHDA/ Acute DOPA</b>	<b>High Dys (AIMs<math>\geq</math>35)</b>	<b>Low Dys (AIMs<math>\leq</math>20)</b>
<b>P-Thr<sup>389</sup>-S6K</b>	100 $\pm$ 24	220 $\pm$ 21 *	248 $\pm$ 11 *	165 $\pm$ 9 † <sup>o</sup>
<b>P-Thr<sup>421/424</sup>-S6K</b>	100 $\pm$ 4	150 $\pm$ 9 *	151 $\pm$ 6 *	110 $\pm$ 1 † <sup>o</sup>
<b>P-Ser<sup>240/244</sup>-S6</b>	100 $\pm$ 7	224 $\pm$ 28 *	270 $\pm$ 22 *	126 $\pm$ 6 † <sup>o</sup>
<b>P-Ser<sup>235/236</sup>-S6</b>	100 $\pm$ 4	281 $\pm$ 18 *	326 $\pm$ 22 *	138 $\pm$ 7 † <sup>o</sup>
<b>P-Thr<sup>197/202</sup>-Mnks</b>	100 $\pm$ 3	162 $\pm$ 8 *	163 $\pm$ 5 *	116 $\pm$ 3 † <sup>o</sup>
<b>P-Ser<sup>209</sup>-eIF4E</b>	100 $\pm$ 7	170 $\pm$ 15 *	160 $\pm$ 9 *	112 $\pm$ 2 † <sup>o</sup>
<b>P-Ser<sup>65</sup>-4E-BP</b>	100 $\pm$ 7	148 $\pm$ 13 *	164 $\pm$ 9 *	106 $\pm$ 2 † <sup>o</sup>

**Table S1.** Effect of 6-OHDA and L-DOPA on selected proteins involved in mTOR signaling. Determination of protein phosphorylation in the striata of sham-lesioned mice (Sham), 6-OHDA-lesioned mice treated acutely with L-DOPA (6-OHDA/Acute DOPA) and 6-OHDA-lesioned mice treated for 10 days with L-DOPA and displaying high (High Dys) or low dyskinesia (Low Dys). High Dys and Low Dys mice were selected based on a total AIMs score  $\geq$ 35 and  $\leq$ 20, respectively. Data are calculated as means  $\pm$  SEM (n = 6-18 mice per treatment). Statistical significance was determined by one-way ANOVA followed by the Bonferroni-Dunn test. \* p < 0.001 versus Sham group; † p < 0.001 versus 6-OHDA/Acute DOPA group; and <sup>o</sup> p < 0.001 versus High Dys group.