

**Table S1.** Differentially expressed genes in SN from mice with MPTP+CBE compared to mice with CBE

<b>DEGs</b>	<b>p-value</b>	<b>Log2FoldChange</b>
<i>Mirg</i>	5.87*10 <sup>-6</sup>	0.59399156
<i>Arap2</i>	1.66*10 <sup>-5</sup>	-0.64772314
<i>Pcgf2</i>	5.94*10 <sup>-5</sup>	0.64560150
<i>Klhl11</i>	1.42*10 <sup>-4</sup>	-1.97081617
<i>Dbn1</i>	3.47*10 <sup>-4</sup>	0.61752537
<i>Ryr1</i>	3.52*10 <sup>-4</sup>	1.30517771
<i>Slc24a2</i>	4.68*10 <sup>-4</sup>	-0.84869852
<i>Ankrd63</i>	4.84*10 <sup>-4</sup>	4.26887775
<i>Tbx2</i>	4.97*10 <sup>-4</sup>	1.17503584
<i>Zc3h12c</i>	5.89*10 <sup>-4</sup>	-0.60031129
<i>Kif5b</i>	6.15*10 <sup>-4</sup>	-0.63478363
<i>Zfp831</i>	6.75*10 <sup>-4</sup>	2.89086435
<i>Atp13a5</i>	6.95*10 <sup>-4</sup>	0.73688808
<i>Mef2c</i>	0.00118040	1.07138316
<i>Neto2</i>	0.00121295	-0.65772502
<i>Syne4</i>	0.00136080	0.72538958
<i>Crocc</i>	0.00213178	0.76535787
<i>Adam8</i>	0.00264611	0.80238999
<i>Prmt8</i>	0.00264718	0.60765600
<i>Cdk3</i>	0.00323735	1.30858203
<i>Hecw1</i>	0.00341241	-0.62433392
<i>Tnfrsf25</i>	0.00406376	1.07777881
<i>Thbs3</i>	0.00469813	0.58576518

SN – substantia nigra; MPTP - 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; CBE - conduritol B epoxide; DEGs - differentially expressed genes

**Table S2.** Differentially expressed genes in SN from mice with MPTP+CBE compared to mice with vehicle

<b>DEGs</b>	<b>p-value</b>	<b>Log2FoldChange</b>
<i>Arl4d</i>	1.91*10 <sup>-7</sup>	-1.83005951
<i>Pdk4</i>	8.24*10 <sup>-7</sup>	-1.01097351
<i>St18</i>	5.00*10 <sup>-6</sup>	-0.81759584
<i>Sgk1</i>	5.53*10 <sup>-6</sup>	-1.66604096
<i>Arrdc3</i>	1.54*10 <sup>-5</sup>	-0.70916389
<i>Neto2</i>	7.91*10 <sup>-5</sup>	-0.91135940
<i>Ddit4</i>	8.26*10 <sup>-5</sup>	-0.72050667
<i>Rcor2</i>	1.91*10 <sup>-4</sup>	0.75428811
<i>Zfp831</i>	1.88*10 <sup>-4</sup>	3.47671204
<i>Ciart</i>	2.93*10 <sup>-4</sup>	-0.58955761
<i>Idi1</i>	3.14*10 <sup>-4</sup>	-0.61682728
<i>Ldb2</i>	3.26*10 <sup>-4</sup>	0.67938838
<i>Tlcd4</i>	3.51*10 <sup>-4</sup>	-0.59426052
<i>Islr2</i>	4.61*10 <sup>-4</sup>	1.55549782
<i>Till3</i>	5.13*10 <sup>-4</sup>	0.70661232
<i>Ankrd63</i>	7.55*10 <sup>-4</sup>	3.69671419
<i>Lrrn1</i>	9.82*10 <sup>-4</sup>	-0.60061231
<i>Npy2r</i>	0.00103964	1.70016592
<i>Slc24a2</i>	0.00104371	-0.74572326
<i>Nsun7</i>	0.00105934	0.89010552
<i>Rhpn2</i>	0.00108437	-0.60907209
<i>Crocc</i>	0.00115782	0.86478225
<i>Tiam1</i>	0.00134855	0.66832341
<i>Aldh3b2</i>	0.00142340	1.63789228
<i>Prmt8</i>	0.00149763	0.69218137
<i>Hsd17b7</i>	0.00158508	-0.92862897
<i>Armh4</i>	0.00162667	-0.69704755
<i>Got1l1</i>	0.00169645	2.02327625
<i>Foxo6</i>	0.00182587	0.89747095
<i>Tmc4</i>	0.00241028	0.61771605
<i>Lmo1</i>	0.00261155	0.59388295
<i>Drc1</i>	0.00266271	1.09400153
<i>Cdh4</i>	0.00293771	0.88816271
<i>Mef2c</i>	0.00299999	0.85976461
<i>Akap5</i>	0.00305353	0.71494285
<i>Ecel1</i>	0.00350562	0.89207296
<i>Adora1</i>	0.00372698	-0.58899960

SN – substantia nigra; MPTP - 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; CBE - conduritol B epoxide; DEGs - differentially expressed genes

**Table S3.** Differentially expressed genes in SN from mice with MPTP+CBE compared to compared to mice with MPTP

<b>DEGs</b>	<b>p-value</b>	<b>Log2FoldChange</b>
<i>Sgk1</i>	7.34*10 <sup>-5</sup>	-1.39303692
<i>Ucn</i>	3.72*10 <sup>-4</sup>	5.10126015
<i>Arl4d</i>	4.55*10 <sup>-4</sup>	-1.06955067
<i>Prmt8</i>	0.00140147	0.69323273
<i>Popdc3</i>	0.00250220	0.83564281
<i>Ankrd63</i>	0.00258946	2.58085457
<i>Pik3r6</i>	0.00336224	1.20161688
<i>Nkx6-1</i>	0.00418106	0.90280976

*SN* – substantia nigra; *MPTP* - 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; *CBE* - conduritol B epoxide; *DEGs* - differentially expressed genes

**Table S4.** Differentially expressed genes in SN from mice with MPTP compared to compared to mice with CBE

<b>DEGs</b>	<b>p-value</b>	<b>Log2FoldChange</b>
<i>Parpbbp</i>	7.15*10 <sup>-9</sup>	7.75728016
<i>Pmch</i>	1.32*10 <sup>-8</sup>	6.89975245
<i>Hcrt</i>	2.15*10 <sup>-6</sup>	10.2272463
<i>Ldb2</i>	4.73*10 <sup>-5</sup>	0.80732283
<i>Vangl1</i>	1.00*10 <sup>-4</sup>	0.75320020
<i>H2-Q2</i>	3.15*10 <sup>-4</sup>	1.75304129
<i>Syne4</i>	4.42*10 <sup>-4</sup>	0.85847611
<i>Tox</i>	4.56*10 <sup>-4</sup>	0.94608529
<i>Galr1</i>	7.17*10 <sup>-4</sup>	1.98777749
<i>Calcr</i>	0.00123451	1.91549766
<i>L3mbtl1</i>	0.00178669	0.67146595
<i>Nkd2</i>	0.00180863	0.80701645
<i>Tmem114</i>	0.00217489	1.87679603
<i>Slc24a2</i>	0.00257441	-0.62294054
<i>Prlhr</i>	0.00287968	1.74111262
<i>Gabre</i>	0.00294519	1.37213337
<i>Papln</i>	0.00308649	0.99136525
<i>Rrad</i>	0.00386851	1.04071978
<i>Adamts15</i>	0.00417637	0.61223298
<i>Gabrg3</i>	0.00420713	0.78473896
<i>Plkl1</i>	0.00421446	0.74063491
<i>Ngb</i>	0.00429757	0.93952362
<i>Irx6</i>	0.00440310	1.05900092

SN – substantia nigra; MPTP - 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; CBE - conduritol B epoxide; DEGs - differentially expressed genes

**Table S5.** Differentially expressed genes in SN from mice with MPTP compared to vehicle mice

<b>DEGs</b>	<b>p-value</b>	<b>Log2FoldChange</b>
<i>Marchf11</i>	6.12*10 <sup>-6</sup>	-1.39441538
<i>Ldb2</i>	6.97*10 <sup>-6</sup>	0.92570483
<i>Pmch</i>	1.08*10 <sup>-5</sup>	4.90803528
<i>Parpbp</i>	2.51*10 <sup>-5</sup>	4.87574422
<i>Prlhr</i>	4.25*10 <sup>-5</sup>	4.16288499
<i>Gm5535</i>	6.13*10 <sup>-5</sup>	-2.07723070
<i>Plagl2</i>	8.40*10 <sup>-5</sup>	0.79668247
<i>Il11ra1</i>	1.27*10 <sup>-4</sup>	-0.73338837
<i>Till3</i>	1.47*10 <sup>-4</sup>	0.81263952
<i>Hcrt</i>	3.27*10 <sup>-4</sup>	5.42990022
<i>Naa38</i>	3.52*10 <sup>-4</sup>	-0.59561024
<i>Zfp367</i>	3.89*10 <sup>-4</sup>	-0.61555647
<i>Hr</i>	4.01*10 <sup>-4</sup>	0.90706627
<i>Mybl1</i>	4.25*10 <sup>-4</sup>	-1.10023703
<i>Tox</i>	4.28*10 <sup>-4</sup>	0.95559851
<i>Galr1</i>	4.33*10 <sup>-4</sup>	2.14210920
<i>Islr2</i>	4.74*10 <sup>-4</sup>	1.55262315
<i>Rxrg</i>	4.75*10 <sup>-4</sup>	1.44305501
<i>Mreg</i>	5.17*10 <sup>-4</sup>	-0.90997493
<i>Pradcl</i>	5.29*10 <sup>-4</sup>	-0.60925737
<i>Aldh3b2</i>	6.37*10 <sup>-4</sup>	1.86049836
<i>Tead1</i>	6.46*10 <sup>-4</sup>	0.60220973
<i>Gck</i>	6.71*10 <sup>-4</sup>	1.67727679
<i>Gm5805</i>	7.07*10 <sup>-4</sup>	-0.97674700
<i>Npsr1</i>	8.36*10 <sup>-4</sup>	1.60982807
<i>Mgst3</i>	8.66*10 <sup>-4</sup>	-0.86363937
<i>Cast</i>	9.96*10 <sup>-4</sup>	-0.73852800
<i>Pdyn</i>	0.00105191	1.84914286
<i>Smc4</i>	0.00123026	-0.72789888
<i>Tbc1d4</i>	0.00131115	-0.61766263
<i>Gm10925</i>	0.00140480	-0.64665629
<i>Mapk15</i>	0.00141277	2.70633496
<i>Armh4</i>	0.00149456	-0.71556109
<i>Cox14</i>	0.00154585	-0.59853593
<i>Inhbb</i>	0.00154993	-0.68488490
<i>Cdh7</i>	0.00156830	-0.67298463
<i>Syne4</i>	0.00175996	0.68369976
<i>Kif6</i>	0.00180070	0.86067353
<i>Gabre</i>	0.00185505	1.56838404
<i>Kcna5</i>	0.00200873	0.99216274
<i>Cfap54</i>	0.00201416	1.32978322
<i>Tac2</i>	0.00237660	2.69816659
<i>Sv2b</i>	0.00239419	-0.88481644
<i>Apod</i>	0.00250002	-0.81569282
<i>Gabrg3</i>	0.00258473	0.94540467
<i>4933427D14Rik</i>	0.00261159	0.91296547
<i>Amigo2</i>	0.00263749	0.74983049

<i>Plxdc1</i>	0.00268039	0.64568630
<i>Parp3</i>	0.00274272	-0.67492838
<i>Gm17833</i>	0.00286693	2.48960962
<i>Rtl5</i>	0.00291866	0.61842218
<i>Myo18b</i>	0.00297219	0.71620205
<i>Hsd17b7</i>	0.00300901	-0.79940140
<i>Rskr</i>	0.00308534	0.81083439
<i>Ngb</i>	0.00322447	1.11465781
<i>Vamp8</i>	0.00349565	-0.86815506
<i>1700095J03Rik</i>	0.00395746	1.20447328
<i>Krt90</i>	0.00400068	1.46304392
<i>Rsph4a</i>	0.00456301	1.20006114
<i>Mycl</i>	0.00458642	0.62218277
<i>Crocc</i>	0.00472544	0.60208596
<i>Drc1</i>	0.00486860	0.83598210
<i>Fbxw7</i>	0.00508217	-0.59395953
<i>Itih3</i>	0.00528863	0.65943353

*SN* – substantia nigra; *MPTP* - 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; *DEGs* - differentially expressed genes

**Table S6.** Differentially expressed genes in SN from mice with CBE compared to mice with vehicle

DEGs	p-value	Log2FoldChange
<i>Pomc</i>	0.00027706	-2.64777546

*SN – substantia nigra; CBE - conduritol B epoxide; DEGs - differentially expressed genes*

**Table S7.** Venn diagram of DEGs in compared study groups

Groups	Number of DEGs	DEGs
Common		
MPTP+CBE vs CBE MPTP+CBE vs MPTP MPTP+CBE vs vehicle	2	<i>Ankrd63, Prmt8</i>
MPTP vs CBE MPTP+CBE vs CBE MPTP+CBE vs vehicle	1	<i>Slc24a2</i>
MPTP vs vehicle MPTP+CBE vs CBE MPTP+CBE vs vehicle	1	<i>Crocc</i>
MPTP vs CBE MPTP vs vehicle MPTP+CBE vs CB	1	<i>Syne4</i>
MPTP vs CBE MPTP vs vehicle MPTP+CBE vs vehicle	1	<i>Ldb2</i>
MPTP+CBE vs CBE MPTP+CBE vs vehicle	3	<i>Zfp831, Neto2, Mef2c</i>
MPTP+CBE vs MPTP MPTP+CBE vs vehicle	2	<i>Sgk1, Arl4d</i>
MPTP vs vehicle MPTP+CBE vs vehicle	6	<i>Ttll3, Armh4, Hsd17b7, Islr2, Aldh3b2, Drc1</i>
MPTP vs CBE MPTP vs vehicle	9	<i>Hcrt, Pmch, Gabre, Prlhr, Tox, Parpbp, Ngf, Gabrg3, Galr1</i>
Unique		
MPTP+CBE vs CBE	15	<i>Hecwl, Klhl11, Mirg, Dbn1, Ryr1, Pcgf2, Kif5b, Thbs3, Adam8, Cdk3, Atp13a5, Tnfrsf25, Arap2, Tbx2, Zc3h12c</i>
MPTP+CBE vs vehicle	21	<i>Adora1, Ddit4, Nsun7, Akap5, Rcor2, Foxo6, Tlcd4, Lmo1, Arrdc3, Pdk4, Npy2r, Stl8, Ciart, Idi1, Tiam1, Tmc4, Lrrn1, Rhpn2, Cdh4, Got111, Ecell</i>
MPTP+CBE vs MPTP	4	<i>Popdc3 Nkx6-1 Pik3r6 Ucn</i>
MPTP vs vehicle	46	<i>Itih3, Mreg, Smc4, Mgst3, Cast, Npsr1, Cfap54, Marchf11, Gm5805, Zfp367, Gm5535, Sv2b, Gm10925, Mycl, Vamp8, Fbxw7, Kif6, Mybl1, Apod, Naa38, Plxdc1, Tbc1d4, Amigo2, Pdyn, Tead1, Gck, Inhbb, Rtl5, Mapk15, Rsph4a, Rskr, Hr, 4933427D14Rik, Cox14, Pradc1, Myo18b, Plagl2,</i>



		<i>Irf103, Krt90, Il11ra1, Rxrg, Parp3, Gm17833, Kcna5, Tac2, Cdh7</i>
MPTP vs CBE	11	<i>H2-Q2, Vangl1, Tmem114, Plk1, Calcr, Nkd2, L3mbtl1, Adamts15, Papln, Irx6, Rrad</i>
CBE vs vehicle	1	<i>Pomc</i>

*MPTP - 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; CBE - conduritol B epoxide; DEGs - differentially expressed genes*

**Table S8.** DEGs of SN of mice with MPTP+CBE vs vehicle mice involved in PI3K/AKT/mTOR pathway based on literature analysis

Genes	Number from list of DEGs	p-value	Log2FoldChange	Association with PI3K/AKT/mTOR pathway	References
<i>Arl4d</i>	1	$1.91 \times 10^{-7}$	-1.8301	The expression of ARL4D was found to be post-transcriptionally regulated by the AKT/mTOR pathway and linked to the status of PTEN in human glioma.	[86]
<i>Pdk4</i>	2	$8.24 \times 10^{-7}$	-1.0110	Knockdown of PDK4 suppressed the tumor development of cancer cells with activated mTORC1. The abundance of PDK4 dictated the responsiveness of cells to the mTOR inhibitor, rapamycin.	[58]
<i>Sgk1</i>	4	$5.53 \times 10^{-6}$	-1.6660	mTOR, specifically mTORC2, is the hydrophobic motif-kinase for SGK1. Activated SGK1 contributes to the maintenance of residual mTORC1 activity through direct phosphorylation and inhibition of TSC2.	[57,87]
<i>Ddit4</i>	7	$8.26 \times 10^{-5}$	-0.7205	DDIT4 is an inhibitor of mTORC1	[88]

**Table S9.** DEGs of PBMC-derived macrophages of GBA-PD (L444P/N) vs controls involved in PI3K/AKT/mTOR pathway based on literature

DEGs	Number from list of DEGs	p-value	Log2FoldChange	Association with PI3K/AKT/mTOR pathway	References
<i>EGR1</i>	3	$3.17 \times 10^{-6}$	-4.1878	mTORC2 inhibition increases expression of EGR1	[89,90]

				Stimulation of mTORC1 increase expression of Egr1 regardless of its mRNA levels.	
<i>DUSP1</i>	4	$3.95 \times 10^{-6}$	-3.2510	The activity of ULK1 is negatively regulated by MTOR, and inhibition of MTOR activates ULK, leading to autophagy induction. ULK1 phosphorylates BECN1 at Ser15 and promotes PIK3C3-BECN1-ATG14 complex formation and activation in <i>dusp1</i> <sup>-/-</sup> cells.	[91]
<i>IL6</i>	5	$3.95 \times 10^{-6}$	-3.4155	IL-6 is a strong activator of mTOR	[92]
<i>ARL4C</i>	6	$5.06 \times 10^{-6}$	-2.1475	AKT/mTOR inhibits ARL4C ubiquitination	[64]
<i>NR4A2</i>	7	$2.94 \times 10^{-4}$	-3.0012	Nr4a2 Expression Is Induced by the PI3K-Akt-mTOR Pathway	[93]