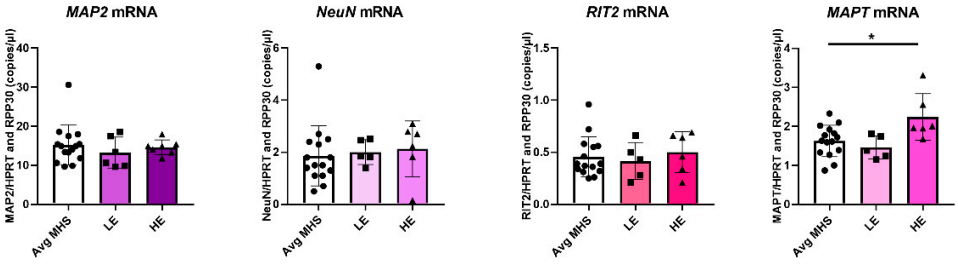
Droplet digital PCR (ddPCR)

To evaluate gene expression in the cortex, ddPCR experiments were performed using 0,2 ng of cDNA to amplify *MAPT* (HsPT5839989875, IDT, Tema Ricerca, Bologna, Italy) or 1ng of cDNA to amplify *RIT2* (HsPT58196183, IDT, Tema Ricerca, Bologna, Italy) *RFOX3* (HsPT582776427, IDT, Tema Ricerca, Bologna, Italy) and *MAP2* (HsPT5820103440, IDT, Tema Ricerca, Bologna, Italy). Primer sequences are reported in Table S1. Probe Supermix (No dUTP) (1863025; Bio-Rad Laboratories, Milan, Italy) was used for amplification using the following thermal profile: 10 minutes at 95°C, 40 cycles consisting of 30 seconds at 94°C followed by an annealing and extension step at 57°C for 1 minute, and a final step of 10 minutes at 98°C. Droplets were analyzed using Bio-Rad QX Manager v. 1.2 and transcript expression was quantified according to the software´s instructions.

Supplementary Figures



Supplementary Figure S1: Gene expression assessment of additional genes in the cortex from PD patients and matched healthy controls. ddPCR was used to quantify *MAP2*, *RBFOX3* (NeuN), *RIT2*and *MAPT* mRNA level in the RNA extracted from 11 PD Patients and 15 Matched Healthy controls. Patients were divided in two groups according to *SNCA* mRNA level. Patients whose *SNCA* level is >average *SNCA* level in MHS belong to „HE group" while those with *SNCA* level < average *SNCA* level in MHS belong to „LE group". Bar graphs show *MAP2, NeuN, RIT2* and *MAPT* mRNA levels. mRNA levels quantified in PD patients and healthy controls were compared between HE and LE groups and with the MHS. Mean ± s.e.m. (standard error of the mean) are shown. 1-way ANOVA with Bonferroni's correction for multiple comparison to calculate statistical significance. NS P>0.05, * P≤0.05.

Table S1: List of primers used for ddPCR experiments**.** Primer sequences for each assay are reported in the table. Assays for which this information was not available (NA), the sequence for assay´s amplicon is reported (MIQE).

Target gene	Assay name	Primer1 (5´→3´)	Primer2 (5´→3´)	Amplified sequence (MIQE)
ITPKB	HsPT584772564	ATGGACTGCAAGATGGGAATC	GTCCACCTCGATCATCTTCTG	-
MAPT	HsPT5839989875	AAGAGCCGCCTGCAGAC	AACTGGTTTGTAGACTATTTGCAC	-
RIT2	HsPT58196183	GCAGTTTATTAGTCATCAGTTCCC	AGCAGTGTCCAAGATGTCC	-
RFOX3	HsPT582776427	CGGTCGTGTATCAGGATGGA	GCCGTAACTGTCGCTGTAG	-
MAP2	HsPT5820103440	ACCTTCCTCCATTCTCCCT	ACCACTCTTCCCTGCTCT	-
RPP30	dHsaCPE5038241	NA	NA	TATTAATGTGGCGATTGACCG AGGCCTGGCTTTTGAACTTGTC TATAGCCCTGCTATCAAAGAC TCCACAATGAGAAGGTATACA ATTTCCAGTGCCCTCAATTTGA TGCAAATCTGCAAAG

HPRT	dHSaCPE5192872	NA	NA	ACTGGCAAAACAATGCAGAC TTTGCTTTCCTTGGTCAGGCAG TATAATCCAAAGATGGTCAAG GTCGCAAGCTTGCTGGTGAAA AGGACCCCACGAAGTGTTGGA TATAAGCCAGACTTTGTT