

Supplementary Tables

Table I: mRNA expression levels of genes encoding subunits of the mitochondrial complexes and energy metabolism-related enzymes in the frontal cortex MA, iPD, PD and PDD as determined with TaqMan PCR assays using *GUS-β* for normalization. Note marked differences in gene expression between MA and PD, mostly characterized by up-regulated gene expression, and between PD and PDD, with dramatic down-regulation of the majority of mitochondrial subunits assessed. Subunits are not limited to a single complex but members of all the mitochondrial complexes are affected in PDD. A more complex scenario occurs in the expression of other energy metabolism-related enzymes at different stages of disease. However, important decay in gene expression is also observed in PDD when compared with PD. Student's T-test **p* < 0.05, ***p* < 0.01, ****p* < 0.001. ^a No Gaussian distribution (Mann Whitney test **p* < 0.05, ***p* < 0.01, ****p* < 0.001).

		Frontal cortex									
		MA	iPD	PD	PDD	MAvsIPD	MAvsPD	iPDvsPD	MAvsPDD	iPDvsPD	PDvsPDD
Mitochondrial elements											
Complex I	<i>NDUFA2</i>	1.08 ± 0.46	0.75 ± 0.49	1.20 ± 0.44	0.60 ± 0.36	-	-	↑*	-	-	-
	<i>NDUFA7</i>	1.08 ± 0.38 ^a	0.94 ± 0.56	1.65 ± 0.44	0.62 ± 0.37	-	↑**	↑**	-	-	↓**
	<i>NDUFA10</i>	1.07 ± 0.36	1.09 ± 0.52	1.68 ± 0.53 ^b	0.81 ± 0.43	-	↑**	↑*	-	-	↓*
	<i>NDUFB3</i>	1.08 ± 0.42	0.67 ± 0.47	1.33 ± 0.46	0.95 ± 0.45	↓*	-	↑**	-	-	-
	<i>NDUFB7</i>	1.07 ± 0.40	1.15 ± 0.63	1.67 ± 0.76	0.60 ± 0.29	-	↑*	-	-	-	↓*
	<i>NDUFB10</i>	1.10 ± 0.45	1.14 ± 0.74	1.58 ± 0.42	0.74 ± 0.47	-	↑*	-	-	-	↓*
	<i>NDUFS7</i>	1.02 ± 0.19	0.98 ± 0.30	1.17 ± 0.41 ^b	0.75 ± 0.33	-	-	-	-	-	-
	<i>NDUFS8</i>	1.10 ± 0.45	1.16 ± 0.62	1.58 ± 0.49	0.82 ± 0.37	-	↑*	-	-	-	↓*
Complex II	<i>SDHB</i>	1.04 ± 0.30	1.05 ± 0.67	1.40 ± 0.46	0.49 ± 0.43	-	↑*	-	↓*	-	↓*
Complex III	<i>UQCRCB</i>	1.07 ± 0.41	0.94 ± 0.66	1.33 ± 0.49	0.55 ± 0.42	-	-	-	-	-	↓*
	<i>UQCRC11</i>	1.04 ± 0.31	1.00 ± 0.70	1.44 ± 0.51	0.73 ± 0.40	-	↑*	-	-	-	-
Complex IV	<i>COX7A2L</i>	1.17 ± 0.53	1.19 ± 0.87	1.76 ± 0.49	0.70 ± 0.44	-	↑*	-	-	-	↓**
	<i>COX7C</i>	1.10 ± 0.46	0.77 ± 0.59	1.12 ± 0.42	0.50 ± 0.31	-	-	-	↓*	-	↓*
Complex V	<i>ATP5D</i>	1.12 ± 0.55	0.91 ± 0.63	1.26 ± 0.62	0.84 ± 0.47	-	-	-	-	-	-
	<i>ATP5G2</i>	1.04 ± 0.28	1.02 ± 0.41	1.37 ± 0.31 ^b	0.60 ± 0.43	-	↑*	↑*	↓*	-	↓**
	<i>ATP5H</i>	1.08 ± 0.43	0.64 ± 0.34	1.14 ± 0.41	0.59 ± 0.40	↓**	-	↑**	-	-	-
	<i>ATP5L</i>	1.12 ± 0.66	1.24 ± 0.72	1.66 ± 0.44	0.66 ± 0.36	-	-	↑*	-	-	↓**
	<i>ATP5O</i>	1.06 ± 0.40	0.91 ± 0.52	1.19 ± 0.37	0.60 ± 0.39	-	-	-	-	-	↓*
Energy metabolism-related molecules											
	<i>ATP2B3</i>	1.09 ± 0.43	0.85 ± 0.62	1.30 ± 0.58	0.76 ± 0.49	-	-	-	-	-	-
	<i>ATP2B4</i>	1.06 ± 0.35	0.70 ± 0.39	1.39 ± 0.55	0.59 ± 0.32	↓*	-	↑**	↓*	-	↓*
	<i>ATP4A</i>	1.14 ± 0.78	1.94 ± 0.99	3.04 ± 2.15	0.68 ± 0.24	↑*	-	↑**	-	-	-
	<i>ATP6V0A1</i>	1.10 ± 0.44	0.82 ± 0.42	1.52 ± 0.54	0.65 ± 0.38	-	-	↑**	-	-	↓*
	<i>ATP6V0B</i>	1.10 ± 0.14	0.81 ± 0.20	1.52 ± 0.56	0.72 ± 0.42	↓**	-	↑**	↓**	-	↓*
	<i>ATP6V1H</i>	1.33 ± 0.73	1.34 ± 1.09	1.98 ± 0.72	0.50 ± 0.40	-	-	-	-	-	↓**
	<i>FAM82A2</i>	1.07 ± 0.38	1.05 ± 0.43	1.42 ± 0.70	0.51 ± 0.25	-	-	-	↓*	-	-
	<i>LHPP</i>	1.04 ± 0.31 ^b	1.06 ± 0.43	1.15 ± 0.52	0.60 ± 0.23	-	-	-	↓*	-	-
	<i>SLC6A6</i>	1.05 ± 0.45	1.38 ± 0.48	1.15 ± 0.60	0.90 ± 0.31	-	-	-	-	-	-
	<i>SLC25A31</i>	1.11 ± 0.51	1.06 ± 0.49	1.04 ± 0.39	0.73 ± 0.24	-	-	-	-	-	-
	<i>TOMM40</i>	1.09 ± 0.45	0.67 ± 0.36	1.04 ± 0.34	0.60 ± 0.45	↓*	-	↑*	-	-	-
	<i>ZNF642</i>	1.02 ± 0.43	1.94 ± 1.12	1.95 ± 0.53	0.75 ± 0.33	-	↑**	↑**	-	-	↓**

Supplementary Table II: mRNA expression levels of genes encoding subunits of the mitochondrial complexes and energy metabolism-related enzymes in the angular gyrus in MA, iPD, PD and PDD as determined with TaqMan PCR assays using *GUS-β* for normalization. A transient increase in the mRNA expression of several genes encoding subunits of complexes I, IV and V, and encoding energy metabolism-related enzymes is observed in iPD when compared with MA. Although *NDUFA10* mRNA expression remains increased in PD when compared with MA, a significant decrease of several genes is found in PD when compared with iPD. A dramatic decrease is found in PDD when compared with iPD. *COX7A2L*, *ATP2B4*, *ATP6V1H* and *FAM82A2* mRNA expression is significantly decreased in PDD when compared with PD. Student's T-test *p < 0.05, **p < 0.01, ***p < 0.001. ^a No Gaussian distribution (Mann Whitney test) *p < 0.05, **p < 0.01, ***p < 0.001.

		Angular Gyrus									
		MA	iPD	PD	PDD	MAvsIPD	MAvsPD	iPDvsPD	MAvsPDD	iPDvsPDD	PDvsPDD
Mitochondrial elements											
Complex I	<i>NDUFA2</i>	1.07 ± 0.40	1.34 ± 0.48	1.01 ± 0.24	0.62 ± 0.36	-	-	-	-	↓*	-
	<i>NDUFA7</i>	1.06 ± 0.38	2.04 ± 0.66	1.02 ± 0.16	0.69 ± 0.50	↑**	-	↓***	-	↓**	-
	<i>NDUFA10</i>	1.14 ± 0.56	1.85 ± 0.53	1.98 ± 0.81	0.89 ± 0.49	↑*	↑*	-	-	↓*	-
	<i>NDUFB3</i>	1.10 ± 0.51	1.59 ± 0.74	1.03 ± 0.28	0.96 ± 0.37	-	-	-	-	-	-
	<i>NDUFB7</i>	1.05 ± 0.34	1.30 ± 0.46	1.01 ± 0.17	0.74 ± 0.42	-	-	-	-	-	-
	<i>NDUFB10</i>	1.39 ± 0.86	2.20 ± 0.65	1.36 ± 0.29	0.88 ± 0.60	↑*	-	↓**	-	↓**	-
	<i>NDUFS7</i>	1.11 ± 0.46	1.62 ± 0.42	1.08 ± 0.12	0.83 ± 0.30	↑*	-	↓**	-	↓**	-
	<i>NDUFS8</i>	1.03 ± 0.24	1.35 ± 0.45	0.97 ± 0.07	0.81 ± 0.24	-	-	↓*	-	-	-
Complex II	<i>SDHB</i>	1.09 ± 0.46	1.55 ± 0.66	1.05 ± 0.23	0.56 ± 0.34	-	-	-	-	↓*	-
Complex III	<i>UQCRCB</i>	1.06 ± 0.37	1.71 ± 0.79	1.16 ± 0.20	0.85 ± 0.48	↑*	-	-	-	-	-
	<i>UQCRC1</i>	1.10 ± 0.49	1.70 ± 0.66	1.08 ± 0.19	0.69 ± 0.60	↑*	-	-	-	↓*	-
Complex IV	<i>COX7A2L</i>	1.17 ± 0.73	2.06 ± 0.63	1.35 ± 0.16	0.71 ± 0.40	↑*	-	↓**	-	↓**	↓**
	<i>COX7C</i>	1.13 ± 0.58	1.72 ± 0.71	1.03 ± 0.25	0.72 ± 0.50	-	-	-	-	-	-
Complex V	<i>ATP5D</i>	1.06 ± 0.39	1.61 ± 0.55	1.15 ± 0.22	0.89 ± 0.49	↑*	-	-	-	-	-
	<i>ATP5G2</i>	1.01 ± 0.19	1.25 ± 0.20	1.06 ± 0.30	0.79 ± 0.62	↑*	-	-	-	↓*	-
	<i>ATP5H</i>	1.05 ± 0.35	1.23 ± 0.47	1.00 ± 0.35	0.77 ± 0.56	-	-	-	-	-	-
	<i>ATP5L</i>	1.08 ± 0.45	1.33 ± 0.47	1.08 ± 0.32	0.73 ± 0.44	-	-	-	-	-	-
	<i>ATP5O</i>	1.12 ± 0.56	1.68 ± 0.62	1.09 ± 0.20	0.68 ± 0.44	-	-	-	-	↓*	-
Energy metabolism-related molecules											
	<i>ATP2B3</i>	1.04 ± 0.31	1.17 ± 0.45	1.04 ± 0.50	0.94 ± 0.68	-	-	-	-	-	-
	<i>ATP2B4</i>	1.05 ± 0.34	0.82 ± 0.27	0.86 ± 0.03	0.46 ± 0.16	-	-	-	↓*	↓*	↓***
	<i>ATP4A</i>	1.16 ± 0.76 ^a	1.02 ± 0.78	0.92 ± 0.07	0.83 ± 0.24	-	-	-	-	-	-
	<i>ATP6V0A1</i>	1.04 ± 0.32	1.08 ± 0.38	1.03 ± 0.32	0.73 ± 0.39	-	-	-	-	-	-
	<i>ATP6V0B</i>	1.11 ± 0.49	2.32 ± 1.01	1.30 ± 0.30	0.82 ± 0.41	↑**	-	↓**	-	↓*	-
	<i>ATP6V1H</i>	1.28 ± 0.84	3.09 ± 0.72	1.54 ± 0.46	0.58 ± 0.43	↑***	-	↓***	-	↓***	↓**
	<i>FAM82A2</i>	1.02 ± 0.24	1.36 ± 0.90	1.03 ± 0.18	0.66 ± 0.32	-	-	-	↓*	-	↓**
	<i>LHPP</i>	1.03 ± 0.26	1.04 ± 0.39	1.23 ± 0.26	0.62 ± 0.20	-	-	-	↓*	-	↓**
	<i>SLC6A6</i>	1.04 ± 0.31	1.19 ± 0.24	1.10 ± 0.58	0.81 ± 0.25	-	-	-	-	↓*	-
	<i>SLC25A31</i>	1.17 ± 0.66	1.27 ± 0.82	1.22 ± 0.21	0.88 ± 0.43	-	-	-	-	-	-
	<i>TOMM40</i>	1.17 ± 0.75	1.72 ± 0.75	0.93 ± 0.16	0.70 ± 0.64	-	-	-	-	-	-
	<i>ZNF642</i>	1.11 ± 0.55 ^a	1.34 ± 0.32	1.01 ± 0.53	0.68 ± 0.34	-	-	-	-	↓**	-