

Supplementary information

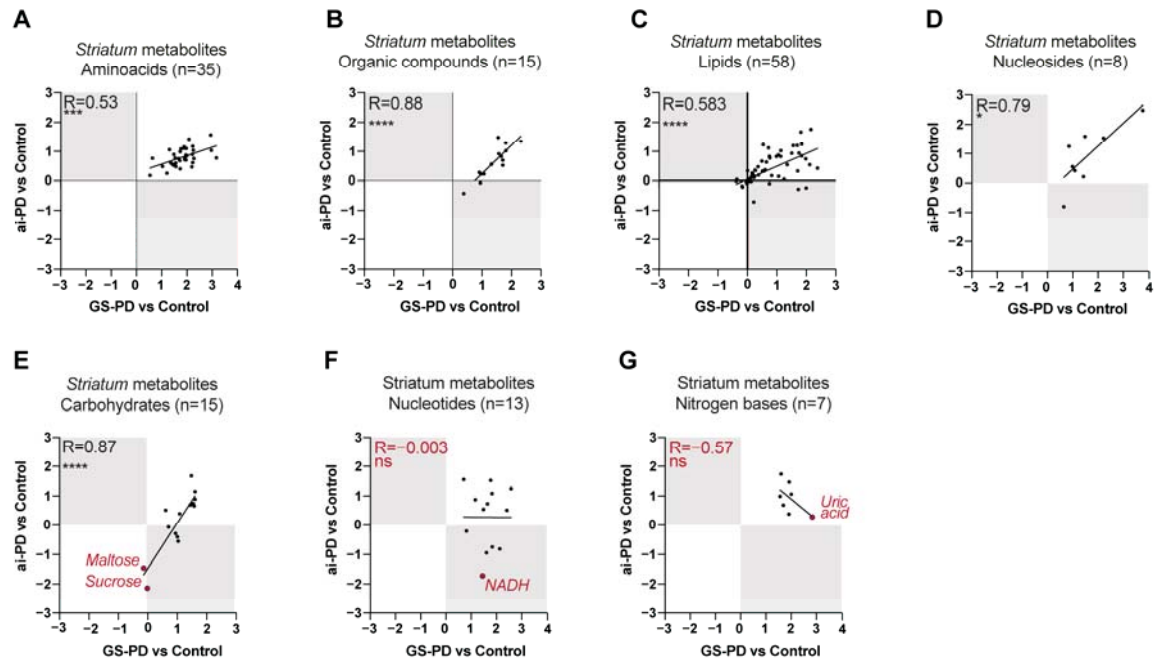


Figure S1: Correlation analysis between the changes observed in striatal neurons of the genetic model of PD (GS-PD) and acute intoxication (ai-PD) compared to healthy mice (Control). Striatum metabolites were analyzed by divisions into metabolic routes: amino acids (A), organic compounds (B), lipids (C), nucleosides (D), carbohydrates (E), nucleotides (F) and nitrogen bases (G). Statistical analysis was performed by obtaining p values (ns: non-significant; *** ($p<0.001$), **** ($p<0.0001$)), and Pearson's correlation coefficients (R) between the observed changes.

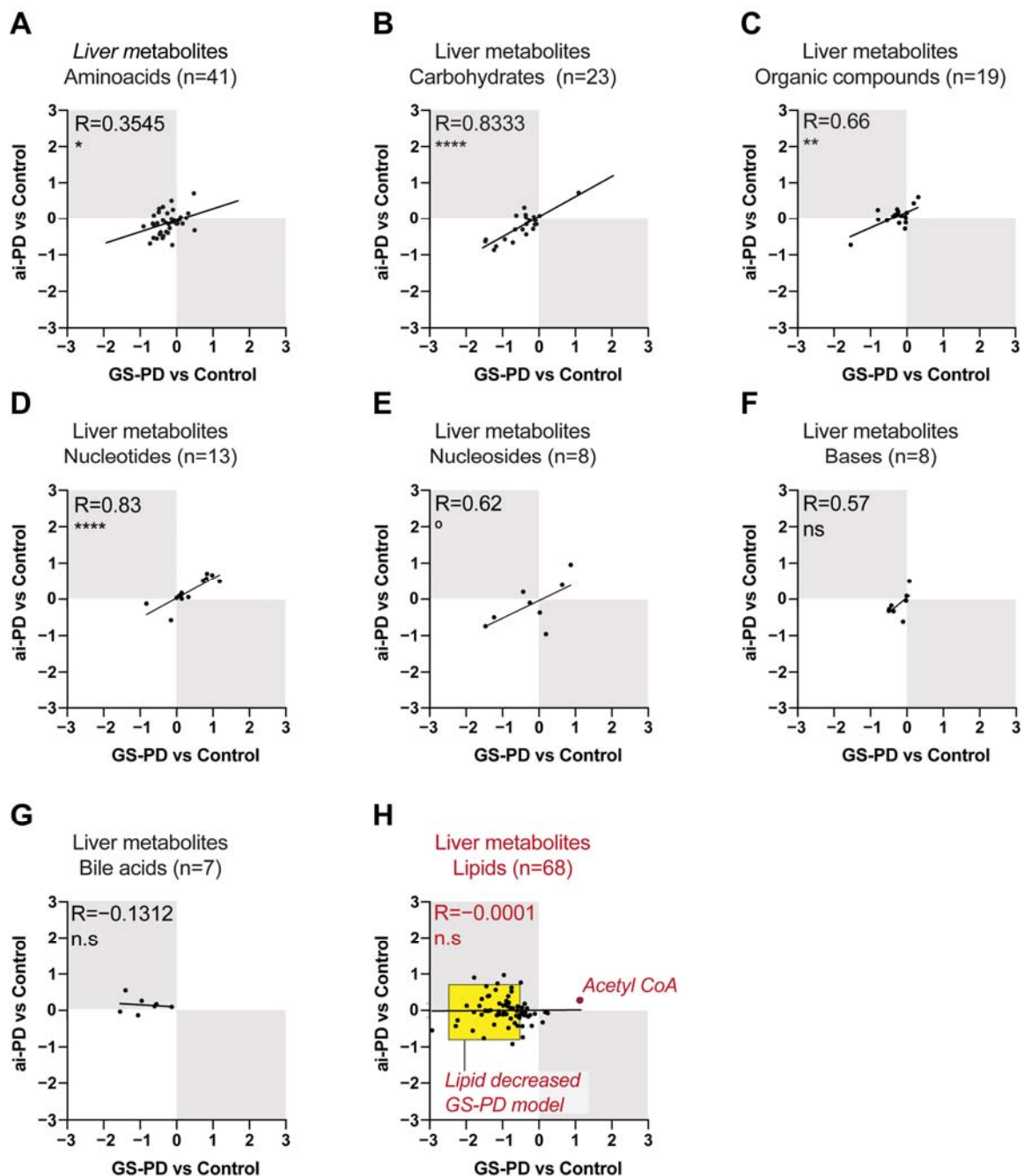


Figure S2: Correlation analysis between the changes observed in hepatic cells of the genetic model of PD (GS-PD) and acute intoxication (ai-PD) compared to healthy mice (Control). Metabolites were analyzed by divisions into metabolic routes: amino acids (A), carbohydrates (B), organic compounds (C), nucleotides (D), nucleosides (E), nitrogenous bases (F), bile acids (G) and lipids (H). Statistical analysis was performed by obtaining p values (n.s: non-significant; ° ($p<0.1$), * ($p<0.05$), ** ($p<0.01$), **** ($p<0.0001$)), and Pearson's correlation coefficients (R) between the observed changes.


 Liver	WT-LRRK2 (Untreated)	GS-PD (Untreated)	ai-PD (6-OHDA treated)
	Control	Genetic PD	acute intoxicic. PD
ATP and NADP	—	↑	↑
Acetyl CoA	—	↑	—
Maltose/Ribose Ribitol/Xilitol Hypotaurine	—	↓	↓
Saturated long chain-FA Monounsatur. long chain-FA Polyunsaturated-FA Phosphatidylcholine Phosphatidylethanolamine	—	↓	—

Figure S3: Summary with the models used and the main metabolic results obtained in this work. Green arrows indicate an increase and red arrows indicate a decrease in levels compared to the untreated control mice. 6-OHDA, 6-hydroxydopamine; ai, acute intoxication; ATP, adenosine triphosphate; FA, fatty acids; GS, *LRRK2* G2019S mutation; NADH, nicotinic amide adenine dinucleotide; NADP, Nicotinamide adenine dinucleotide phosphate; PD, Parkinson disease.

Table S1: Metabolite changes in striatum cells from control and PD mouse models (GS-PD or ai-PD). N: number of mice/groups detected for each metabolite; Average: Average log2area; SEM: standard error of the mean; Log2FC: Log2 fold change between two groups and statistical analysis was performed by obtaining *p* values (GS-PD vs control, first column Log2FC; ai-PD vs control second column Log2FC). PCae (phosphatidylcholine); PCee (phosphatidylethanolamine).

Metabolites	Name	Control					N	AVERAGE	SEM	GS-PO					N	AVERAGE	SEM	al-PO					N	AVERAGE	SEM	sigFC vs Control		al-PO vs Control	
		Control 1	Control 2	Control 3	Control 4	Control 5				GS-PO 1	GS-PO 2	GS-PO 3	GS-PO 4	al-PO 1				al-PO 2	al-PO 3	al-PO 4	sigFC	sigFC				al-PO vs Control	TTEST		
Amino acids	3-methylcrotonic acid	1.35	3.99	4.39	1.24	1.82	5	2.56	0.68	3.61	1.21	0.99	1.52	4	1.98	0.39	1.26	4.61	1.67	0.08	0.27	5	2.38	0.84	0.62	0.32	0.11	0.872	
	4-guanidinobutyrate	-0.62	4.42	0.39	0.39	0.17	5	1.73	0.56	0.36	0.08	0.88	1.16	3	1.36	1.16	0.75	0.29	-1.84	-2.46	-1.09	5	1.67	1.56	0.37	0.861	0.05	0.881	
	4-hydroxyproline	-0.86	-0.58	-0.52	-1.14	-0.22	5	-0.66	0.16	-1.46	-1.26	-0.34	1.07	4	-0.50	0.38	-0.02	0.69	-1.46	-2.09	-1.15	5	0.80	0.50	0.17	0.764	0.14	0.797	
	5-aminomethyl acid	0.17	-0.07	-0.49	0.16	0.36	5	-0.04	0.17	-0.29	-0.06	0.19	0.48	4	-0.14	0.04	0.25	0.09	0.16	0.33	0.07	5	0.12	0.08	0.02	0.246	0.16	0.406	
	5-isopropyl	-0.55	-0.63	-0.58	-0.57	0.04	5	-0.46	0.13	-0.95	-0.65	-0.22	0.35	4	-0.54	0.16	-0.40	-0.16	-0.76	-0.74	-0.38	5	-0.49	0.11	0.09	0.676	0.03	0.862	
	Alanine	-0.23	-0.36	-0.80	-0.16	0.03	5	-0.30	0.14	-0.79	-0.50	-0.09	0.10	4	-0.27	0.22	-0.38	-0.32	-0.45	-0.60	-0.46	5	0.44	0.05	0.03	0.910	0.14	0.376	
	Arginine	1.96	3.97	4.43	1.47	1.06	5	3.12	0.65	3.12	1.43	0.23	0.96	4	1.37	0.66	1.51	3.94	3.32	4.25	0.19	5	2.44	0.76	0.38	0.329	0.19	0.429	
	Asparagine	-0.05	-0.13	-0.27	-0.23	0.59	5	0.00	0.16	-0.07	-1.06	0.17	0.45	4	-0.38	0.40	-0.26	0.06	-0.68	-0.80	-1.01	5	0.54	0.19	0.38	0.366	0.54	0.060	
	Aspartic acid	-0.62	-0.60	-0.84	-0.44	0.46	5	-0.41	0.23	-0.96	-0.32	-0.09	0.80	4	-0.14	0.37	-0.28	0.34	-0.62	-1.19	-1.10	5	-0.39	0.24	0.27	0.538	0.02	0.959	
	Beta-alanine	1.10	-0.01	0.13	0.11	0.09	5	0.23	0.22	0.08	0.30	-0.81	0.06	4	0.15	0.62	0.36	1.00	1.47	0.21	5	0.12	0.08	0.02	0.167	0.28	0.489		
	Betaine/Valine	2.34	2.86	4.00	2.16	2.59	5	2.79	0.33	2.85	1.25	1.73	2.41	4	2.06	0.35	2.06	3.68	2.00	2.64	0.11	5	2.10	0.58	0.73	0.175	0.69	0.327	
	Citrulline	-0.07	-0.11	-0.39	-0.44	0.01	5	-0.28	0.10	-1.04	-0.76	0.05	0.46	4	-0.29	0.20	0.13	-0.09	-0.55	-0.40	-0.30	5	0.38	0.18	0.02	0.796	0.10	0.644	
	Creatine	0.68	-0.07	-0.36	-0.03	0.67	5	0.18	0.21	-0.64	0.05	0.08	0.67	4	0.04	0.27	0.92	0.23	1.34	0.08	0.83	5	0.68	0.23	0.14	0.691	0.50	0.148	
	Creatinine	1.63	2.50	2.39	1.56	1.48	5	2.02	0.29	2.38	1.09	1.18	1.95	4	1.64	0.31	1.63	3.68	2.48	3.17	0.78	5	2.35	0.52	0.37	0.413	0.33	0.595	
	Cystine/Cystanone	0.66	-0.57	-0.68	-0.57	0.08	5	-0.04	0.33	-1.64	-0.87	-0.34	0.47	4	-0.67	0.39	0.19	0.07	-0.54	-0.10	-0.15	5	0.05	0.22	0.02	0.253	0.09	0.822	
	Dimethylglycine	2.38	2.99	3.49	2.33	2.23	5	2.73	0.23	2.86	1.63	1.30	2.50	4	2.07	0.37	1.78	4.11	2.86	3.70	0.39	5	2.58	0.68	0.65	0.154	0.44	0.848	
	Dimethyllysine	2.20	2.90	3.72	2.38	1.76	5	2.59	0.34	3.15	1.77	2.20	2.20	4	2.23	0.36	1.82	4.15	1.63	3.48	-0.04	5	2.11	0.76	0.36	0.488	0.49	0.574	
	GABA	0.34	-0.54	-0.49	-1.00	-0.31	5	-0.49	0.20	-1.31	-1.08	-0.41	0.81	4	-0.50	0.48	0.00	0.46	-0.55	-0.08	-0.73	5	0.15	0.27	0.30	0.851	0.25	0.455	
	Glutamic acid	-0.59	-0.77	0.05	-0.77	0.99	5	-0.12	0.31	-1.45	-0.88	-0.46	1.37	4	-0.35	0.61	-0.29	0.31	-1.27	-1.18	-0.15	5	-0.52	0.31	0.24	0.724	0.40	0.389	
	Glutamine	-0.22	0.39	0.45	-0.07	1.14	5	0.34	0.24	0.45	-0.06	1.26	1.01	4	0.38	0.50	0.55	0.01	0.14	0.75	0.11	5	0.49	0.14	0.12	0.414	0.15	0.591	
	Glycine	0.59	-0.25	0.25	-0.36	0.06	5	-0.04	0.17	-0.22	0.33	-0.40	0.23	4	-0.30	0.04	0.25	-0.09	0.16	0.33	0.07	5	0.12	0.08	0.02	0.246	0.16	0.406	
	Homocysteine	0.23	0.11	-0.15	-0.31	0.33	5	0.04	0.12	-0.08	-0.07	0.52	0.75	4	0.05	0.38	0.05	0.30	-0.50	-0.34	-0.27	5	0.04	0.15	0.01	0.975	0.08	0.696	
	Isoleucine	0.10	-0.60	-0.89	-0.84	-0.32	5	-0.53	0.15	-1.30	-0.93	-0.46	-0.51	4	-0.42	0.36	-0.10	-1.30	-0.09	0.12	-0.07	5	-0.49	0.29	0.11	0.767	0.04	0.904	
	Isoleucine	-0.17	-0.60	-0.73	-0.82	-0.39	5	-0.54	0.12	-1.38	-0.76	-0.40	0.58	4	-0.68	0.29	0.01	-1.09	-0.28	-0.22	-1.17	5	-0.55	0.24	0.14	0.663	0.01	0.971	
	Lysine	0.03	-0.20	-0.20	-0.13	0.27	5	-0.16	0.34	-0.30	-1.59	0.35	0.84	4	-0.67	0.44	-0.06	0.07	-0.24	0.13	-0.83	5	0.19	0.17	0.08	0.848	0.07	0.888	
	Methionine	0.25	-0.44	-0.56	-0.27	0.40	5	-0.12	0.19	-1.72	-1.03	-0.30	0.02	4	-0.76	0.39	-0.72	-0.17	-0.16	-1.02	-1.26	5	-0.66	0.22	0.63	0.181	0.54	0.102	
	N-acetylglutamic acid	2.63	4.01	0.34	0.74	2.89	5	2.56	0.36	4.71	1.85	2.35	3.24	4	1.04	0.63	3.23	6.05	2.69	4.41	0.81	5	3.27	0.94	0.48	0.598	0.71	0.534	
	N-acetylserine	1.13	-0.01	0.07	-0.15	0.76	5	-0.05	0.27	0.08	1.32	-0.36	0.44	4	-0.34	0.29	0.17	0.28	0.37	-0.31	-0.22	5	0.13	0.15	0.02	0.289	0.18	0.491	
	N-acetyltyrosine	2.12	3.05	3.73	1.75	1.76	5	2.48	0.39	2.71	1.98	2.35	1.76	4	1.95	0.28	1.45	4.26	2.18	3.61	0.24	5	2.35	0.72	0.53	0.333	0.13	0.877	
	Ornithine	0.38	-0.19	-0.27	-0.42	0.11	5	-0.13	0.22	-0.73	-0.42	-0.16	0.43	4	-0.12	0.26	-0.15	-0.22	-0.36	-0.15	-0.14	5	-0.23	0.26	0.15	0.486	0.08	0.645	
	Paranthanic acid	-0.98	-0.44	-0.11	-0.43	0.39	5	-0.31	0.22	-0.89	-1.16	-0.32	1.09	4	-0.32	0.50	0.21	-0.25	-0.69	-1.13	-0.43	5	-0.44	0.22	0.00	0.994	0.15	0.633	
	Phenylalanine	-0.12	-0.43	0.71	-0.43	0.35	5	-0.27	0.18	-1.08	-1.07	0.02	0.31	4	-0.46	0.36	-0.60	0.01	-0.52	-0.78	-0.79	5	0.54	0.15	0.19	0.686	0.27	0.281	
	Proline	0.71	-0.86	-1.32	-0.85	-0.49	5	-0.44	0.18	-1.58	-0.86	-0.21	0.61	4	-0.84	0.14	-0.56	-1.44	-0.46	-0.54	-0.54	5	0.46	0.15	0.19	0.686	0.27	0.281	
	Proline betaine	2.46	2.66	3.95	2.55	3.27	5	2.98	0.28	3.45	2.01	2.66	3.31	4	2.86	0.33	2.10	4.12	2.18	2.81	0.03	5	2.25	0.66	0.12	0.796	0.71	0.339	
Serine	0.14	-0.40	-0.34	-0.36	0.42	5	-0.11	0.16	-1.45	-0.34	-0.12	0.72	4	-0.17	0.34	-0.04	-0.97	-0.12	-0.39	-1.22	5	-0.35	0.23	0.46	0.229	0.44	0.144		
Threonine	0.04	-0.14	-0.04	-0.18	0.02	5	-0.16	0.21	-0.32	-0.16	-0.22	0.21	4	-0.17	0.34	-0.04	-0.97	-0.12	-0.39	-1.22	5	-0.35	0.23	0.46	0.229	0.44	0.144		
Trimethyllysine	1.79	4.12	4.47	1.39	2.09	5	2.77	0.63	4.03	1.48	1.18	1.81	4	2.12	0.65	1.49	4.49	3.23	4.53	0.20	5	2.61	0.85	0.60	0.503	0.16	0.882		
Tryptophan	0.15	-0.15	-0.17	-0.17	0.09	5	-0.15	0.22	-0.39	-0.46	-0.30	0.46	4	-0.15	0.22	-0.39	-0.46	-0.30	-0.46	-0.30	5	-0.15	0.22	0.31	0.179	0.18	0.779		
Tyrosine	0.13	-0.17	-0.47	-0.26	0.24	5	-0.11	0.13	-0.88	-1.11	0.06	0.46	4	-0.39	0.38	-0.43	-0.09	-0.31	-0.50	-1.07	5	-0.48	0.16	0.28	0.465	0.37	0.113		
Valine	0.09	-0.34	-0.99	-0.83	0.22	5	-0.37	0.24	-0.77	-0.84	-0.23	0.05	4	-0.46	0.21	-0.64	-0.62	-0.07	-0.45	-0.69	5	-0.46	0.14	0.09	0.788	0.09	0.744		
Bases	Adenosine	0.06	-0																										

Table S2: Metabolite changes in hepatic cells from control and PD mouse models (GS-PD or ai-PD). N: number of mice/groups detected for each metabolite; Average: Average log2area; SEM: standard error of the mean; Log2FC: Log2 fold change between two groups and statistical analysis was performed by obtaining *p* values (GS-PD vs control, first column Log2FC; ai-PD vs control second column Log2FC). PCae (phosphatidylcholine); PCee (phosphatidylethanolamine).