APPENDIX 1: Kinetic model of myocardial catecholaminergic neurodegeneration in Lewy body diseases

We are given reaction rates as follows:

$$r^0 = (r_1^0, \ldots, r_{17}^0)^T.$$

The problem is to find reaction rates $r = (r_1, \ldots, r_{17})^T$ that satisfy exactly the equilibrium system and are as close as possible to the vector r^0.

Consider the following equilibrium system:

$$Ar = 0, \quad A \in \mathbb{R}^{m \times n}, r = (r_1, \ldots, r_n)^T \in R^n, m = 9, n = 17,$$

where *r* is the vector of unknown equilibrium reaction rates.

The singular value decomposition of *A* is:

(1) $$A = U\Sigma V^T, \; U \in \mathbb{R}^{m \times m}, \; \Sigma \in \mathbb{R}^{m \times n}, \; V \in \mathbb{R}^{n \times n},$$

where U and V are orthogonal and Σ is diagonal. This gives rank$(A) = m$ (the number of non-zero elements in the matrix Σ).

Using the fact that:

$$x \in N(A) \Rightarrow x = \sum_{i=m+1}^{n} c_i v_i, \text{ where } V = [v_1 \ldots v_n],$$

the general solution of (1) is:

(2) $$r = \sum_{i=m+1}^{n} c_{i-m} v_i$$

for arbitrary constants $c_1, \ldots, c_{n-m}$

To find $c_1, \ldots, c_{n-m}$, we solve the system,

$$\sum_{i=m+1}^{n} c_{i-m} v_i = r^0$$

or, in the matrix form,

(3) $$Bc = r^0, r^0 = [r_1^0, \ldots, r_n^0)^T, B = [b_1 \ldots b_{n-m}] \equiv [v_{m+1} \ldots v_n], c = (c_1, \ldots, c_{n-m})^T.$$

Since there are $n - m = 8$ unknowns and $n = 17$ equations, we use the least squares method for the solution:

(4) $$\min_c \|Bc - r^0\|_2.$$

The equilibrium reaction rates are given by:

(5) $$r = Bc$$

To get the best % accuracy (equilibrating the % error for all the rates, we replace (3) by a scaled problem:

(6) $$B_s c_s = r_s^0, \quad B_s = \begin{bmatrix} b_{1,1}/r_1^0 & \dots & b_{1,n-m}/r_1^0 \\ \dots & \dots & \dots \\ b_{n,1}/r_n^0 & \dots & b_{n,n-m}/r_n^0 \end{bmatrix}, \; r_s^0 = (1, \dots 1)^T \in \mathbb{R}^n$$

We use the least squares method for the solution.

(7) $$\min_{c_s} \|B_s c_s - r_s^0\|_2.$$

Then the optimal equilibrium reaction rates are given by:

(8) $$r = B_s c_{ss}, \;\; \text{where } c_{ss} = \begin{bmatrix} (c_s)_1 \cdot r_1^0 \\ \dots \\ (c_s)_n \cdot r_n^0 \end{bmatrix}.$$

APPENDIX 2: Model Assumptions and Calculations

Reaction rates

(1) TYR_Uptake: Uptake of tyrosine into the cytoplasm of the neurons was the input into the model. TYR_Uptake was assumed to occur at a constant rate—i.e., a zero-order kinetic process. TYR_Uptake was estimated from the literature, as follows. It was assumed that the compared groups had the same coronary sinus plasma flow (95 mL/min) and the same plasma tyrosine concentration (65 nmol/mL) (45), so that the tyrosine delivery rate to the myocardium was 6,175 nmol/min. It was also assumed that 1% of the myocardium is nerves and that 90% of the nerves is cytoplasm, so that the tyrosine delivery rate to the cytoplasm was estimated to be 55.6 nmol/min in the control group.

The amounts of catechols in myocardial tissue were assumed to reflect some combination of loss of innervation and functional abnormalities in the residual myocardial sympathetic noradrenergic nerves. Across 6 studies the left ventricular concentration of immunoreactive TH, an index of innervation, has been reported to be decreased by a mean of 74.4% in PD compared to controls (12-16). TYR_Uptake in the Lewy body disease group therefore was set at 0.256 times that in the control group.

(2) TYR_Loss: The rate of loss of cytoplasmic tyrosine from the nerves was calculated from TYR_Uptake – TH.

(3) TH: The rate of conversion of cytoplasmic tyrosine to cytoplasmic 3,4-dihydroxyphenylalanine (DOPA) via TH was calculated from the sum of LAAAD + DOPAc_Loss.

(4) LAAAD: The rate of cytoplasmic dopamine (DA) from cytoplasmic DOPA via LAAAD was calculated from the sum of MAO_DA + MAO_NE + NE_Release.

(5) DOPAc_Loss: Empirical spillover rates of DOPA were determined, according to the equation

$$Q * ([DOPAv] - [DOPAa])) + 0.08 * Q * [DOPAa]$$

where [DOPAv]=coronary sinus plasma concentration of DOPA and [DOPAa]=arterial plasma concentration of DOPA (46). Extraneuronal loss of DOPA by metabolism was assumed to be negligible.

(6) VMAT_DA: The rate of vesicular uptake of cytoplasmic DA via the vesicular monoamine transporter (VMAT) was calculated from LAAAD – MAO_DA + DA_Leak.

(7) MAO_DA: The rate of conversion of cytoplasmic DA to cytoplasmic 3,4-dihydroxyphenylacetic acid (DOPAC) via monoamine oxidase (MAO) was determined empirically from the DOPAC spillover rate, according to the equation

$$Q * ([DOPACv] - [DOPACa]).$$

where [DOPACv]=coronary sinus venous DOPAC concentration and [DOPACa]= arterial DOPAC concentration.

(8) DOPACc_Loss: The rate of loss of cytoplasmic DOPAC from the nerves was assumed to be the same as MAO_DA.

(9) DBH: The rate of production of vesicular norepinephrine (NE) from vesicular DA was calculated from NE_Leak + NE_Release -VMAT_NE.

(10) DA_Leak: In the control group the rate of loss of vesicular DA to the cytoplasm via leakage was calculated as 1.14% per minute * the vesicular DA amount (DAv) (28). When septal ^{18}F-dopamine-derived radioactivity is tracked over time between the peak value (about 8') and the midpoint of the 10' frame ending at 30' from the start of ^{18}F-DA injection, the mono-exponential slope of decline (k8'-25') is greater in Lewy body patients than in controls.(36) In controls k8'-25' averages 0.01819 ± (SEM) 0.00133 min^{-1} and in Lewy body 0.03711 ± 0.00341 min^{-1} (unpublished updated data). This means k8'-25' in Lewy body disease patients is 0.03711 / 0.01819 = 2.04 times control. We used 2.04 * 1.14% = 2.33% as the leakage percent of vesicular DA per minute for the Lewy body disease group.

(11) VMAT_NE: The NEc vesicular uptake rate was calculated from U1 + NE_Leak – MAO_NE.

(12) MAO_NE: The rate of 3,4-dihydroxyphenylglycol (DHPG) spillover was calculated from the empirical arteriovenous production rates of DHPG, by the equation

$$Q * ([DHPGv] - [DHPGa]), + 0.7 * Q * [DHPGa]$$

where [DHPGv]=coronary sinus plasma DHPG concentration and [DHPGa]=arterial plasma DHPG concentration (46). The rate of extraneuronal DHPG loss from metabolism was assumed to be 57.89% of DHPG (28). The DHPG production rate, MAO_NE, was then taken as the sum of the DHPG spillover rate and the estimated rate of extraneuronal DHPG loss from metabolism, or 1.5789 * the DHPG spillover rate.

(13) Leak_NE: The rate of leakage rate of vesicular NE to the cytoplasm was calculated as the same percent of the vesicular NE amount (NEv) as for DAv_Leak above.

(14) NE_Release: The rate of NE release from the vesicles into the extracellular fluid was calculated from U1 + NEe_Loss.

(15) U1: The rate of neuronal uptake of NE via the cell membrane norepinephrine transporter (NET) was obtained empirically from (1 - E) * [NEa] (47).

(16) DHPGc_Loss: The rate of loss of cytoplasmic DHPG from the nerves was assumed to be equal to MAO_NE.

(17) NEe_Loss: The rate of loss of extracellular fluid NE from the model was calculated based on empirical values for the rate of appearance of endogenous NE in the coronary sinus plasma (NE spillover), which is the sum of the arteriovenous production rate between the arterial and coronary sinus plasma plus the arterial plasma NE removal rate, i.e.,

$$Q * ([NEv] - [NEa]) + Q * E *[NEa] =$$

$$Q * (([NEv] - [NEa]) + E *[NEa]) =$$

$$Q * (([NEv] + (1 - E) * [NEa])$$

where Q = coronary sinus plasma flow, in mL/min, [NEv]= coronary sinus plasma NE concentration, [NEa]=arterial plasma NE concentration, and E= extraction fraction of ^{3}H- NE during systemic intravenous infusion of a tracer amount of ^{3}H- NE. NEe_Loss was taken from

the sum of NE spillover and the amount of extraneuronal NE lost from metabolism, or 2.135 ∗ NE spillover (28).

For the reactants and reactions depicted in Figure 1, differential equations were produced, as follows.

(1) $$d[TYRc]/dt = kTYR\_Uptake - (kTH + kTYR\_Loss) * [TYRc]$$

(2) $$d[DOPAc]/dt = kTH * [TYRc] - (kDOPA\_Loss + kLAAAD) * [DOPAc]$$

(3) $$d[DAv]/dt = kVMAT\_DA * [DAc] - (kLeak\_DA + kDBH) * [DAv]$$

(4) $$d[DAc]/dt = kLAAAD * [DOPAc] + kLeak\_DA * [DAv] - (kMAO\_DA + kVMAT\_DA) * [DAc]$$

(5) $$d[DOPACc]/dt = kMAO\_DA * [DAc] - kDOPAC\_Loss * [DOPACc]$$

(6) $$d[NEv]/dt = kDBH * [DAv] + kVMAT\_NE * [NEc] - (kLeak\_NE + kNE\_Release) * [NEv]$$

(7) $$d[NEc]/dt = kLeak\_NE * [NEv] + kU1 * [NEe] - (kVMAT\_NE + kMAO\_NE) * [NEc]$$

(8) $$d[DHPGc]/dt = kMAO\_NE * [NEc] - kDHPG\_Loss * [DHPGc]$$

(9) $$d[NEe]/dt = kNE\_Release * [NEv] - kU1 * [NEe]$$

where the reactant abbreviations were:

(1) TYRc=cytoplasmic tyrosine, (2) DOPAc=cytoplasmic 3,4-dihydroxyphenylalanine, (3) DAv=vesicular dopamine, (4) DAc=cytoplasmic dopamine, (5) DOPACc=cytoplasmic 3,4-dihydroxyphenylacetic acid; (6) NEv=vesicular norepinephrine, (7) NEc=cytoplasmic norepinephrine, (8) DHPGc=cytoplasmic 3,4-dihydroxyphenylglycol; and (9) NEe=norepinephrine in the extracellular fluid

and the reaction abbreviations were: (1) TYR_Uptake=neuronal uptake of tyrosine, (2) TYR_Loss=loss of tyrosine from the nerves, (3) TH=tyrosine hydroxylase, (4) LAAAD=L-aromatic-amino-acid decarboxylase, (5) DOPA_Loss=loss of DOPAC from the nerves, (6) VMAT_DA=vesicular uptake of cytoplasmic DA via the VMAT, (7) MAO_DA=MAO acting on cytoplasmic DA, (8) DOPAC_Loss=loss of DOPAC from the nerves, (9) DBH=DA-beta-

hydroxylase acting on vesicular DA to form vesicular NE, (10) Leak_DA=leakage of vesicular DA into the cytoplasm, (11) VMAT_NE=vesicular uptake of cytoplasmic NE via the VMAT, (12) MAO_NE=monoamine oxidase acting on cytoplasmic norepinephrine to form DHPG, (13) Leak_NE=leakage of vesicular NE into the cytoplasm, (14) NE_Release=NE release by vesicular exocytosis, (15) U1=neuronal uptake of NE via the cell membrane norepinephrine transporter (NET), (16) DHPG_Loss=loss of DHPG from the nerves, and (17) NE_Loss=loss of extracellular NE from the nerves.

Rate constants for the 17 reactions were obtained via the above equations, assuming equilibrium conditions (i.e., d[Reactant]/dt = 0). Graphs of predicted effects of altering values for rate constants were generated using software we developed (48).

Reactant amounts

Amounts of NE and DA in the vesicles (NEv and DAv) were obtained empirically from the myocardial tissue concentrations of NE and DA, with the presumptions that all of myocardial tissue NE and DA was in the vesicles, myocardial mass was 545 grams, and myocardial tissue density was 1.0 g/mL.

Amounts of DOPA, DOPAC, and DHPG in the cytoplasm (DOPAc, DOPACc, and DHPGc) were obtained empirically from the myocardial tissue concentrations. It was assumed that all of myocardial tissue DOPA, DOPAC, and DHPG was in nerves.

It was difficult to estimate cytoplasmic DA (DAc) and cytoplasmic NE (NEc) amounts because of the lack of empirical data. A method for estimating DAc and NEc was based on the myocardial tissue concentration of 5-S-cysteinyldopamine (Cys-DA) (33, 49). Cys-DA is a product of the spontaneous oxidation of cytoplasmic DA (50). Empirical data for myocardial Cys-DA were compared with those for DOPAC in the same samples, and the ratio of Cys-DA / DOPAC was found to be about 1/10. Previous literature indicated that DA is a somewhat better substrate than is NE for the VMAT, by a factor of 1.23,(51) and the k_VMAT for ^{18}F-DA is 2.50 min^{-1} (31). The avidity of ^{18}F-DA for the VMAT was assumed to be the same as that of

cytoplasmic NE, so that the value for k_VMAT DA was 2.50 ∗ 1.23 = 3.08 min^{-1}. From the equation

DAc = DA vesicular uptake rate / kVMAT_DA

In the control group DAc = 1.86 nmol/min / 3.08 min^{-1} = 0.60 nmoles = DOPACc / 41.6.
In the Lewy body group DAc therefore was estimated to be 2 / 41.6 = 0.05 nmoles.

Analogously, NEc was taken to be equal to DHPGc / 33.8, for NEc values of 2.1 nmoles in controls and 0.27 nmoles in Lewy body patients.

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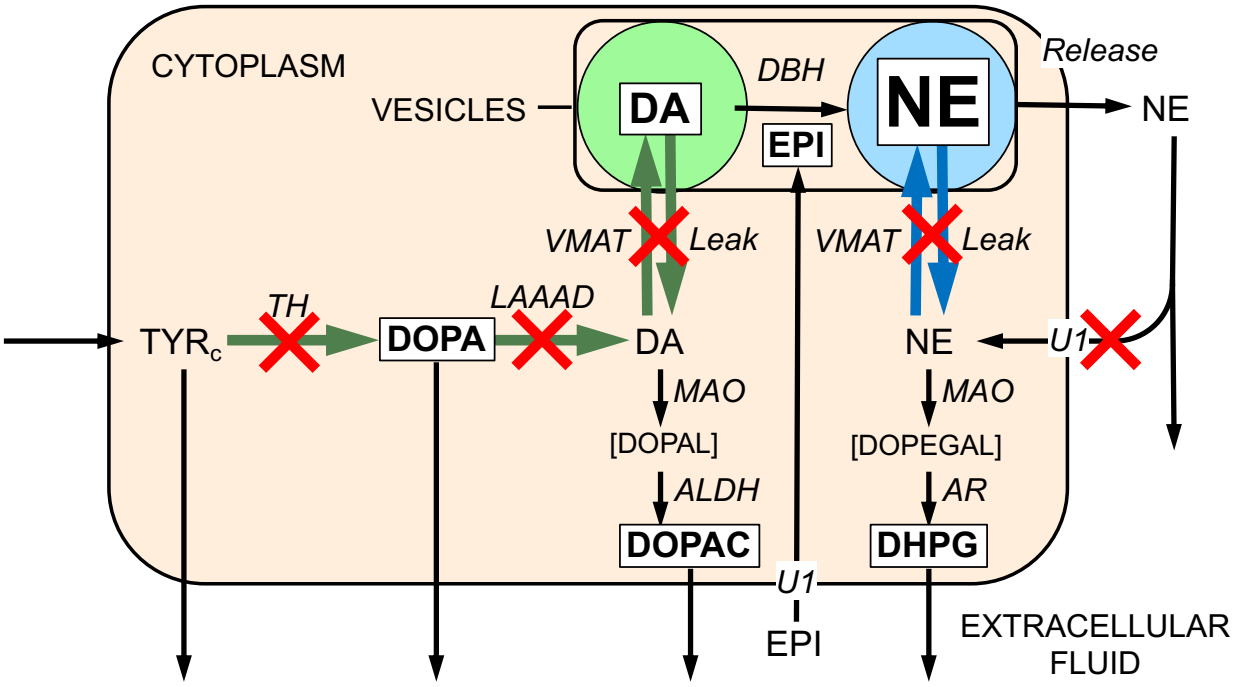
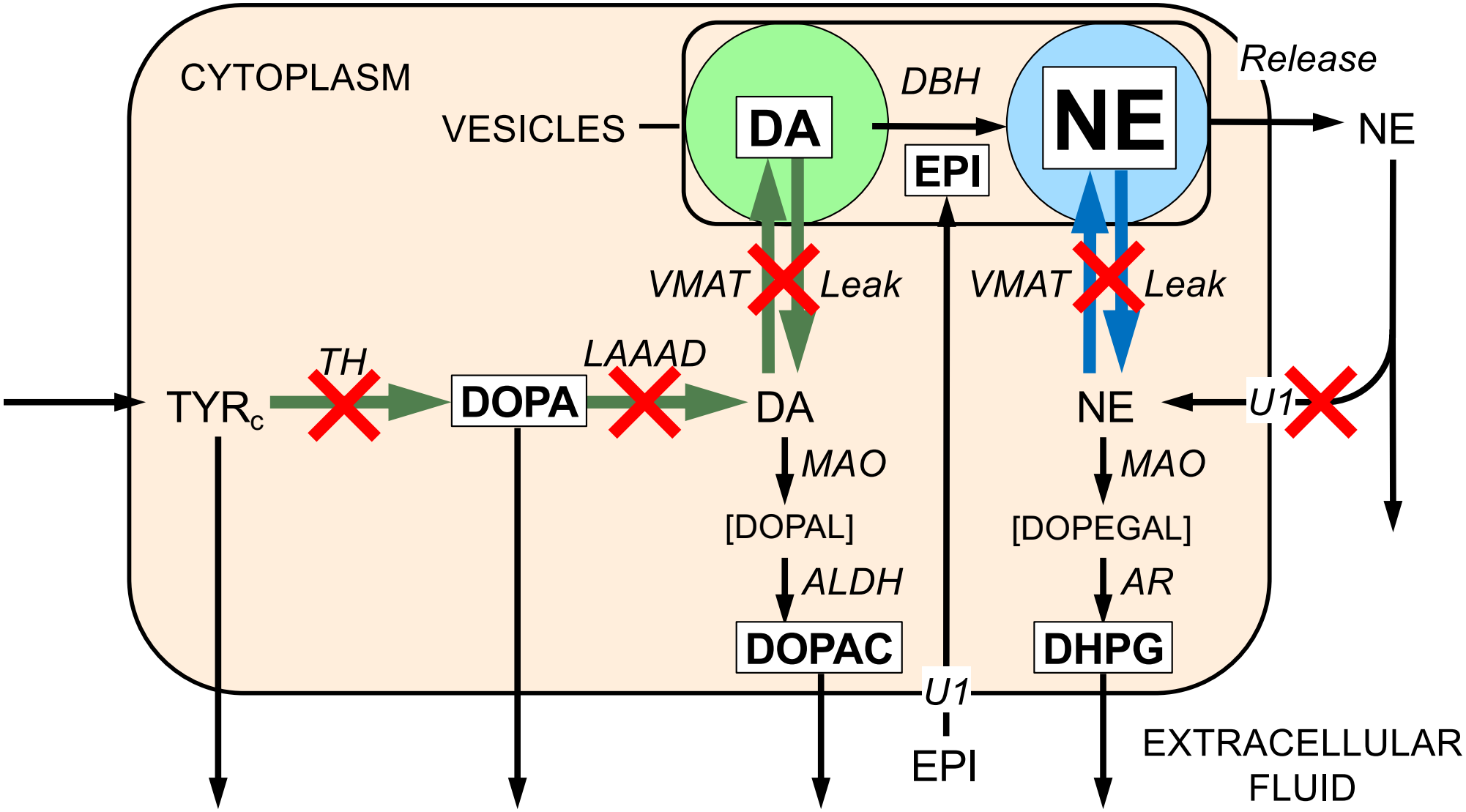
GRAPHICAL ABSTRACT

Sites of functional abnormalities of catecholamine synthesis, storage, release, recycling, and metabolism in myocardial sympathetic nerves in Lewy body disease.



Reactions are in italics and amounts of reactants in plain text. Font sizes correspond roughly to amounts of reactants. Green arrows indicate dopamine (DA) synthesis and blue arrows norepinephrine (NE) vesicular uptake and leakage. Red X marks placed to indicate sites of abnormalities in residual sympathetic nerves in Lewy body diseases. Application of a kinetic model to previously published data revealed 3 types of abnormal intra-neuronal processes in the Lewy body disease group—(a) attenuated catecholamine biosynthesis via tyrosine hydroxylase and L-aromatic-amino-acid decarboxylase, (b) impaired vesicular sequestration of cytoplasmic catecholamines, reflecting the balance of vesicular uptake vs. leakage, and (c) inefficient recycling of released NE by reuptake through the cell membrane NE transporter. Predictions from the model were tested in coded samples of post-mortem myocardial tissue from PD patients and controls, and the results confirmed the model-generated abnormal "triple hit" pattern. Other abbreviations: ALDH=aldehyde dehydrogenase; AR=aldehyde/aldose reductase; Cys-DA=5-S-cysteinylDA; Cys-DOPA= 5-S-cysteinylDOPA; DAc=cytoplasmic DA; DBH=dopamine-beta-hydroxylase; DHPG=3,4-dihydroxyphenylglycol; DOPAc=cytoplasmic DOPA; DOPAC=3,4-dihydroxyphenylacetic acid; DOPEGAL=3,4-dihydroxyphenylglycolaldehyde; DOPAL =3,4-dihydroxyphenylacetaldehyde; DOPET=3,4-dihydroxyphenylethanol; EPI=epinephrine; LAAAD=L-aromatic-amino-acid decarboxylase; MAO=monoamine oxidase; NEc=cytoplasmic NE; NEe=NE in the extracellular fluid ; NESO=NE entering the cardiac venous drainage; TH=tyrosine hydroxylase; TYR=tyrosine; TYRc=cytoplasmic TYR; U1=Uptake-1=neuronal uptake; U2=Uptake-2=extraneuronal uptake; VMAT=vesicular monoamine transporter.


CYTOPLASM
VESICLES
DA
DBH
NE
Release
NE
EPI
VMAT
Leak
VMAT
Leak
TH
LAAAD
TYRc
DOPA
DA
NE
U1
MAO
MAO
[DOPAL]
[DOPEGAL]
ALDH
AR
DOPAC
DHPG
U1
EPI
EXTRACELLULAR
FLUID

Patient	Diagnosis	DHPG	NE	DOPA	DA	DOPAC	LOG DHPG	LOG NE	LOG DOPA	LOG DA	LOG DOPAC
		pmol/mg	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg wet*	*pmol/mg wet*	*pmol/mg wet*	*pmol/mg wet*	*pmol/mg wet*
1	Control	0.02875	0.59224	0.16196	0.11818	0.05921	-1.54143	-0.22750	-0.79060	-0.92747	-1.22758
2	Control	0.37610	4.81572	0.22736	0.09682	0.08572	-0.42469	0.68266	-0.64329	-1.01406	-1.06692
3	Control	0.04440	0.63669	0.47845	0.01799		-1.35262	-0.19607	-0.32016	-1.74491	
4	Control	0.21222	2.77304	0.28807	0.04117	0.00163	-0.67321	0.44296	-0.54050	-1.38539	-2.78707
5	Control	0.00883	2.43192	0.48217	0.01604	0.00197	-2.05388	0.38595	-0.31680		-2.70540
6	Control	0.02088	2.62714	0.82561	0.00805	0.01058	-1.68017	0.41948	-0.08323	-2.09434	-1.97541
7	Control	0.03924	1.64858	0.23193	0.03248	0.01006	-1.40632	0.21711	-0.63465	-1.48834	-1.99742
8	Control	0.12059	1.01065	0.15127	0.02026	0.02798	-0.91870	0.00460	-0.82025	-1.69333	-1.55321
9	Control	0.04013	1.51657	0.14751	0.26384	0.05938	-1.39657	0.18086	-0.83118	-0.57866	-1.22635
10	Control	0.13529	1.96154	0.22538	0.06275	0.03393	-0.86872	0.29260	-0.64708	-1.20242	-1.46943
11	Control	0.04941	1.61893	0.17208	0.12418	0.06369	-1.30617	0.20923	-0.76427	-0.90594	-1.19593
12	Control	0.87250	5.22308	0.13936	0.14572	0.19316	-0.05923	0.71793	-0.85587	-0.83648	-0.71409
13	Control	0.09235	3.22840	0.13807	0.28039	0.10536	-1.03455	0.50899	-0.85990	-0.55223	-0.97734
14	Control	0.08676	1.15325	0.10794	0.02086	0.01345	-1.06167	0.06193	-0.96683	-1.68071	-1.87137
15	Control	0.21568	1.20296	0.14473	0.08250	0.10193	-0.66620	0.08025	-0.83945	-1.08354	-0.99170
16	Control	0.23168	2.62899	0.17160	0.08848	0.08381	-0.63511	0.41979	-0.76548	-1.05314	-1.07669
17	Control	0.04319	1.37633	0.07896	0.06228	0.01539	-1.36465	0.13872	-1.10262	-1.20564	-1.81289
18	Control	0.03666	1.60237	0.16696	0.03468	0.01357	-1.43580	0.20476	-0.77738	-1.45991	-1.86734
19	Control	0.03821	2.28806	0.09226	0.10157	0.01131	-1.41786	0.35947	-1.03497	-0.99323	-1.94641
20	Control	0.01904	0.56190	0.11727	0.47344	0.11811	-1.72028	-0.25034	-0.93083	-0.32473	-0.92771
21	Control	0.03021	4.23257	0.09192	0.64554	0.03670	-1.51982	0.62660	-1.03657	-0.19008	-1.43528
22	Control	0.06272	3.15547	0.11641	0.58668	0.08477	-1.20259	0.49906	-0.93400	-0.23160	-1.07175
23	Control	0.03423	1.45721	0.10712	0.11380	0.01067	-1.46554	0.16352	-0.97014	-0.94384	-1.97171
24	Control	0.02647	2.09231	0.23198	0.11895	0.00536	-1.57724	0.32063	-0.63455	-0.92462	-2.27107
25	Control	0.03059	1.75740	0.25178	0.02680	0.00655	-1.51445	0.24487	-0.59898	-1.57191	-2.18392
26	Control	0.00000	1.28107	1.43096	0.06732	0.00595		0.10757	0.15563	-1.17185	-2.22531
MEAN	**Control**	**0.11139**	**2.11055**	**0.26073**	**0.14041**	**0.04641**	**-1.21190**	**0.25445**	**-0.71323**	**-1.09033**	**-1.62197**
SEM	**Control**	**0.03499**	**0.24068**	**0.05644**	**0.03400**	**0.00966**	**0.09149**	**0.05054**	**0.05834**	**0.09722**	**0.11452**
N	**Control**	**26**	**26**	**26**	**26**	**25**	**25**	**26**	**26**	**25**	**25**
Patient	**Diagnosis**	**DHPG**	**NE**	**DOPA**	**DA**	**DOPAC**	**LOG DHPG**	**LOG NE**	**LOG DOPA**	**LOG DA**	**LOG DOPAC**
		pmol/mg	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg wet*	*pmol/mg wet*	*pmol/mg wet*	*pmol/mg wet*	*pmol/mg wet*
1	Lewy	0.07671	0.03428	0.12886	0.00701	0.00327	-1.11517	-1.46493	-0.88989	-2.15403	-2.48504
2	Lewy	0.00000	0.00742	0.00502	0.00000	0.00000		-2.12940	-2.29971		
3	Lewy		0.00000	0.07646	0.00276	0.00000			-1.11659		
4	Lewy	0.00108	0.00573	0.10412	0.00250	L-DOPA?	-2.96540	-2.24166	-0.98245	-2.60257	
5	Lewy	0.00103	0.01850	0.39130	0.00000	0.00330	-2.98871	-1.73275	-0.40749		-2.48190
6	Lewy	0.34751	0.01313	0.32092	0.00207	0.06177	-0.45903	-1.88189	-0.49360	-2.68489	-1.20922
7	Lewy	0.00186	0.04812	0.12585	0.00204		-2.73004	-1.31770	-0.90013	-2.68956	
8	Lewy	0.00000	0.03557	0.12265	0.00192	0.00683		-1.44898	-0.91132		-2.16544
9	Lewy	0.00678	0.00769	0.36254		0.00438	-2.16882	-2.11433	-0.44064		-2.35818
10	Lewy	0.00200	0.00221	0.12940	0.00000	0.00354	-2.69929	-2.65529	-0.88807		-2.45156
11	Lewy	0.00394	0.00839	0.34575		0.00390	-2.40420	-2.07642	-0.46124		-2.40856
12	Lewy	0.01296	0.00467	0.46139	0.00261	0.02307	-1.88725	-2.33099	-0.33593	-2.58349	-1.63702
13	Lewy	0.01156	0.00828	0.22139	0.00096	0.01899	-1.93709	-2.08187	-0.65484	-3.01775	-1.72146
14	Lewy	0.01195	0.29658	0.20192	0.00579	0.04042	-1.92252	-0.52786	-0.69481	-2.23741	-1.39344
15	Lewy	0.00486	0.18514	0.11315	0.00442	0.03419	-2.31358	-0.73251	-0.94636	-2.35487	-1.46605
16	Lewy	0.01765	0.08225	0.11015	0.00392	0.00536	-1.75333	-1.08487	-0.95801	-2.40654	-2.27107
17	Lewy		0.02012	0.16599	0.00392	0.00774		-1.69641	-0.77992	-2.40654	-2.11137
18	Lewy		0.07633	0.35178	0.00261	0.00655		-1.11730	-0.45373	-2.58263	-2.18392
19	Lewy		0.03964	0.41523	0.01373	0.00119		-1.40181	-0.38171	-1.86247	-2.92428
20	Lewy		0.17101	0.33249	0.00392	0.00357		-0.76699	-0.47822	-2.40654	-2.44716
21	Lewy	0.00635	0.10917	0.01336	0.00210	0.00422	-2.19717	-0.96191	-1.87410	-2.67731	-2.37500
22	Lewy	0.00000	0.00187	0.00000	0.00000	0.00869		-2.72747			-2.06095
23	Lewy	0.00109	0.02845	0.24586		0.00138	-2.96267	-1.54597	-0.60932		-2.85985
24	Lewy	0.00066	0.00925	0.35158		0.00350	-3.18294	-2.03396	-0.45397		-2.45649
25	Lewy		0.01000	0.30965		0.00414		-1.99998	-0.50913		-2.38298
26	Lewy		0.02196	0.23981		0.00268		-1.65830	-0.62014		-2.57112
27	Lewy	0.00471	0.00828	0.24112	0.00261	0.00952	-2.32736	-2.08176	-0.61777		-2.02119
28	Lewy	0.00358	0.00771	0.05376	0.00212	0.00202	-2.44660	-2.11268	-1.26951		-2.69425
MEAN	**Lewy**	**0.02458**	**0.04506**	**0.21220**	**0.00305**	**0.01016**	**-2.24784**	**-1.70096**	**-0.79365**	**-2.47619**	**-2.21406**
SEM	**Lewy**	**0.01654**	**0.01303**	**0.02540**	**0.00064**	**0.00286**	**0.16198**	**0.11118**	**0.08676**	**0.07517**	**0.09132**
N	**Lewy**	**21**	**28**	**28**	**22**	**26**	**18**	**27**	**27**	**14**	**24**
Lewy % of Control		22.1%	2.1%	*81.4%*	2.2%	21.9%					
p Lewy vs Control							*5.3E-07*	*2.7E-21*	*0.44874*	*8.9E-12*	*0.00021*

Subject	Diagnosis	Age	Sex	Fx Ext *NE	Cardiac NESOcs	Cardiac NESOcs p COMT	Adj. DHPG SO	Adj. DHPG SO p COMT	ΔDOPA	Adj. DOPA SO	DOPAC SO
		years	*M=1, F=0*		*pmole/min*	*nmol/min*	*nmol/min*	*nmol/min*	*pmole/ml*	*nmol/min*	*nmol/min*
1	Control	69	1	0.73	122.0	0.26	0.64	1.00	1.99	0.21	0.19
2	Control	61	1	0.90	130.8	0.28	0.75	1.18	8.16	1.16	1.20
3	Control	67	1	0.79	192.8	0.41	0.69	1.09	2.03	0.27	0.21
4	Control	68	1	0.71	228.5	0.49	0.74	1.17	0.44	0.14	0.04
5	Control	61	1	0.76	212.2	0.45	0.98	1.54	0.97	0.36	0.14
6	Control	18	1	0.78	62.6	0.13	0.55	0.88	0.41	0.15	0.07
7	Control	26	1	0.81	101.7	0.22	0.61	0.97	2.60	0.24	0.23
8	Control	62	1	0.85	102.3	0.22	0.59	0.93	1.63	0.19	0.12
9	Control	68	1	0.80	50.0	0.11	0.36	0.56	0.42	0.04	0.02
10	Control	64	0	0.76	248.3	0.53	1.16	1.83	0.38	0.21	0.09
11	Control	41	1	0.33	50.0	0.11	0.40	0.63	1.47	0.16	0.13
12	Control	65	1	0.83	154.8	0.33	1.32	2.09	3.73	0.68	0.68
13	Control	19	1	0.83	31.7	0.07	0.42	0.66	0.64	0.10	0.05
14	Control	25	1	0.84	112.8	0.24	0.58	0.92	2.35	0.28	0.21
15	Control	20	1	0.66	141.2	0.30	1.51	2.39	0.50	0.27	0.14
16	Control	65	1	0.86	71.7	0.15	0.50	0.79	2.57	0.18	0.17
17	Control	19	1	0.92	30.0	0.06	0.92	1.46	1.51	0.16	0.13
18	Control	20	1	0.80	69.0	0.15	1.49	2.35	1.02	0.38	0.23
19	Control	63	1	0.77	103.1	0.22	0.24	0.37	0.70	0.12	0.08
20	Control	49	1	0.81	171.1	0.37	1.18	1.86	1.58	0.21	0.20
21	Control	23	1	0.82	31.1	0.07	0.54	0.85	2.99	0.35	0.32
22	Control	39	1	0.84	97.9	0.21	0.76	1.20	1.15	0.17	0.14
23	Control	34	1	0.87	63.4	0.14	0.66	1.04	0.77	0.10	0.07
24	Control	39	1	0.88	60.0	0.13	0.51	0.81	1.67	0.12	0.12
25	Control	39	1	0.86	143.9	0.31	1.16	1.83	1.46	0.27	0.23
26	Control	29	1	0.92	42.0	0.09	0.37	0.59	2.11	0.08	0.08
27	Control	26	1	0.87	28.2	0.06	0.41	0.65	1.88	0.13	0.13
28	Control	36	1	0.87	138.9	0.30	1.30	2.06	2.51	0.39	0.38
29	Control	38	1	0.91	57.5	0.12	0.85	1.34	1.16	0.15	0.13
30	Control	23	1	0.86	44.7	0.10	0.53	0.84	0.11	0.04	0.01
31	Control	50	1	0.87	103.8	0.22	1.06	1.67	1.26	0.25	0.21
32	Control	41	1	0.87	75.8	0.16	0.91	1.44	1.70	0.20	0.20
33	Control	26	0	0.78	170.2	0.36	1.22	1.93	1.49	0.30	
34	Control	27	0	0.77	178.7	0.38	1.08	1.71	1.56	0.34	
35	Control	28	0	0.88	106.3	0.23	1.11	1.76	2.07	0.27	
36	Control	55	0	0.84	80.7	0.17	0.56	0.88	1.91	0.23	
37	Control	43	0	0.89	51.1	0.11	0.78	1.23	1.64	0.18	
38	Control	38	0	0.77	105.2	0.22	0.72	1.13	1.39	0.17	
39	Control	41	0	0.83	67.9	0.15	0.42	0.66	0.83	0.07	
40	Control	32	1	0.91	15.1	0.03	0.29	0.46	0.73	0.06	0.05
41	Control	23	0	0.81	42.7	0.09	0.41	0.65	1.15	0.07	0.05
42	Control	30	0	0.83	61.2	0.13	0.51	0.81	1.23	0.13	0.12
43	Control	58	1	0.89	149.9	0.32	0.40	0.64	0.99	0.07	0.12
44	Control	25	0	0.89	44.0	0.09	0.42	0.66	1.32	0.07	0.07
45	Control	44	0	0.80	114.2	0.24	0.35	0.55	1.74	0.09	0.10
Mean Overall	**Control**	**41**	**33**	**0.82**	**99.1**	**0.21**	**0.73**	**1.2**	**1.60**	**0.22**	**0.18**
SEM		**2**	**12**	**0.01**	**8.6**	**0.02**	**0.05**	**0.1**	**0.19**	**0.03**	**0.03**
N		**45**	**45**	**45**	**45**	**45**	**45**	**45**	**45**	**45**	**38**
QUARTILE 1					15.1	0.109		0.661		0.120	0.077
MEDIAN					75.8	0.209		1.003		0.180	0.127
QUARTILE 3					138.9	0.297		1.544		0.269	0.204
QUARTILE 4					248.3	0.530		2.389		1.161	1.199
ARTILE (2)-MEDIAN)/MEDIAN %						52%		66%		67%	61%
ARTILE (3)-MEDIAN)/MEDIAN %						142%		154%		150%	161%
Subject	**Diagnosis**	**Age**	**Sex**	**Fx Ext *NE**	**Cardiac NESOcs**	**Cardiac NESOcs p COMT**	**Adj. DHPG SO**	**Adj. DHPG SO p COMT**	**ΔDOPA**	**Adj. DOPA SO**	**DOPAC SO**
		years	*M=1, F=0*		*pmole/min*	*nmol/min*	*nmol/min*	*nmol/min*	*pmole/ml*	*nmol/min*	*nmol/min*
1	Lewy Body	64	0	0.10	2.5	0.005	0.01	0.021	0.43	0.077	-0.023
2	Lewy Body	76	1	0.00	-2.4	-0.005	0.00	-0.003	-0.16	0.040	-0.033
3	Lewy Body	72	1	0.09	1.7	0.004	-0.01	-0.020	-0.16	0.009	0.087
4	Lewy Body	71	1	0.33	13.4	0.029	0.11	0.168	-0.11	0.027	0.023
5	Lewy Body	65	1	0.20	24.9	0.053	0.01	0.008	-0.16	0.011	-0.013
6	Lewy Body	45	1	0.76	27.0	0.058	0.31	0.482	0.41	0.061	0.108
7	Lewy Body	30	0	0.51	38.5	0.082	0.03	0.053	-0.13	0.006	-0.036
8	Lewy Body	65	1	0.08	42.2	0.090	0.04	0.056	On L-DOPA		
9	Lewy Body	67	1	0.16	30.3	0.065	0.03	0.052	-0.05	0.044	-0.005
10	Lewy Body	71	1	0.22	20.1	0.043	-0.07	-0.118	On L-DOPA		
11	Lewy Body	70	0	0.05	11.6	0.025	0.00	0.006	-0.25	0.021	-0.034
12	Lewy Body	57	1	0.17	7.7	0.016	0.02	0.034	-0.03	0.040	0.005
13	Lewy Body	78	0	0.06	22.4	0.048	0.03	0.043	-0.12	0.047	-0.038
MEAN	**Lewy Body**	**64**	**9**	**0.21**	**18.5**	**0.039**	**0.038**	**0.060**	**-0.03**	**0.035**	**0.004**
SEM	**Lewy Body**	**4**	**4**	**0.06**	**3.9**	**0.008**	**0.025**	**0.039**	**0.07**	**0.007**	**0.015**
N	**Lewy Body**	**13**	**13**	**13**	**13**	**13**	**13**	**13**	**11**	**11**	**11**
QUARTILE 1				0.079		0.016		0.006		0.016	-0.033
MEDIAN						0.043		0.034		0.040	-0.013
QUARTILE 3				0.225		0.058		0.053		0.046	0.014
QUARTILE 4				0.763		0.090		0.482		0.077	0.108
ARTILE (2)-MEDIAN)/MEDIAN %				50%		38%		19%		40%	-57%
ARTILE (3)-MEDIAN)/MEDIAN %				142%		134%		159%		114%	305%
p vs. Control				*3.5E-21*	*0.00001*	*0.00001*	*1.5E-09*	*1.5E-09*	*0.00008*	*0.00210*	*0.00773*

HEART	PD/CON	DHPG	NE	DOPA	EPI	Cys_DOPA	DOPET	DA	DOPAC
		pmol/mg	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*
1	CON	0.01710	1.71455	0.22632	0.11428	0.03598	0.00215	0.12463	0.03643
2	CON	0.04542	1.70197	0.39994		0.02263	0.00160	0.09731	0.02877
3	CON	0.02647	2.09231	0.23198	0.04317	0.01171	0.00260	0.11895	0.00536
4	CON	0.00000	1.28107	1.43096	0.04809	0.13892	0.00000	0.06732	0.00595
5	CON	0.03059	1.75740	0.25178	0.09836	0.01709	0.00000	0.02680	0.00655
6	CON	0.06272	3.15547	0.11641	0.15174	0.00613	0.01300	0.58668	0.08477
7	CON	0.03423	1.45721	0.10712	0.03063	0.00325	0.00478	0.11380	0.01067
8	CON	0.03021	4.23257	0.09192	0.01079	0.00258	0.00970	0.64554	0.03670
9	CON	0.02391	1.21026	0.09096	0.02918	0.02426	0.00199	0.11324	0.02023
10	CON	0.05410	4.18356	0.15813	0.01386	0.00831	0.00463	0.29984	0.04153
11	CON	0.01904	0.56190	0.11727	0.04354	0.00695	0.02160	0.47344	0.11811
MEAN		**0.03126**	**2.12257**	**0.29298**	**0.05836**	**0.02526**	**0.00564**	**0.24250**	**0.03592**
SEM		**0.00533**	**0.36510**	**0.11725**	**0.01486**	**0.01179**	**0.00200**	**0.06730**	**0.01079**
N		**11**	**11**	**11**	**10**	**11**	**11**	**11**	**11**
MAX		**0.06272**	**4.23257**	**1.43096**	**0.15174**	**0.13892**	**0.02160**	**0.64554**	**0.11811**
QUARTILE 3		**0.03983**	**2.62389**	**0.24188**	**0.08579**	**0.02345**	**0.00724**	**0.38664**	**0.03912**
MEDIAN		**0.03021**	**1.71455**	**0.15813**	**0.04335**	**0.01171**	**0.00260**	**0.11895**	**0.02877**
QUARTILE 1		**0.02148**	**1.36914**	**0.11176**	**0.02954**	**0.00654**	**0.00180**	**0.10527**	**0.00861**
MIN		**0.00000**	**0.56190**	**0.09096**	**0.01079**	**0.00258**	**0.00000**	**0.02680**	**0.00536**
HEART	**PD/CON**	**DHPG**	**NE**	**DOPA**	**EPI**	**Cys_DOPA**	**DOPET**	**DA**	**DOPAC**
		pmol/mg	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*
1	PD		0.02196	0.23981	0.00259	0.02863	0.00000		0.00268
2	PD	0.00167	0.01376	0.15608	0.00171	0.02924	0.00000	0.00000	0.00570
3	PD	0.00066	0.00925	0.35158	0.00235	0.05207	0.00000		0.00350
4	PD	0.00471	0.00828	0.24112	0.00710	0.04968	0.00000	0.00261	0.00952
5	PD		0.08402	0.81269	0.00383	0.05696	0.00000	0.02418	0.00357
6	PD	0.00358	0.00771	0.05376	0.00431	0.01706	0.00000	0.00212	0.00202
7	PD		0.01845	1.87021	0.04703	0.02243	0.00000	0.00000	0.00174
8	PD	0.00109	0.02845	0.24586	0.00492	0.03746	0.00000		0.00138
9	PD		0.01000	0.30965	0.00193	0.02578	0.00000		0.00414
10	PD	0.00287	0.03442	0.33108	0.00620	0.02604	0.00000	0.00455	0.01260
11	PD	0.00782	0.02655	0.26356	0.00934	0.02612	0.00000	0.00217	0.01029
MEAN		**0.00320**	**0.02390**	**0.44322**	**0.00830**	**0.03377**	**0.00000**	**0.00509**	**0.00520**
SEM		**0.00094**	**0.00661**	**0.15372**	**0.00394**	**0.00402**	**0.00000**	**0.00324**	**0.00116**
N		**7**	**11**	**11**	**11**	**11**	**11**	**7**	**11**
MAX		**0.00782**	**0.08402**	**1.87021**	**0.04703**	**0.05696**	**0.00000**	**0.02418**	**0.01260**
QUARTILE 3		**0.00414**	**0.02750**	**0.34133**	**0.00665**	**0.04357**	**0.00000**	**0.00358**	**0.00761**
MEDIAN		**0.00287**	**0.01845**	**0.26356**	**0.00431**	**0.02863**	**0.00000**	**0.00217**	**0.00357**
QUARTILE 1		**0.00138**	**0.00962**	**0.24046**	**0.00247**	**0.02591**	**0.00000**	**0.00106**	**0.00235**
MIN		**0.00066**	**0.00771**	**0.05376**	**0.00171**	**0.01706**	**0.00000**	**0.00000**	**0.00138**
PD % of CON		*10.2%*	*1.1%*	*151.3%*	*14.2%*	*133.7%*	*0.0%*	*2.1%*	*14.5%*
p PD vs. CON									

HEART	PD/CON	Cys-DA	Log DHPG	Log NE	Log DOPA	Log EPI	Log Cys_DOPA	Log DOPET
		pmol/mg	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*
1	CON	0.01486	-1.76699	0.23415	-0.64527	-0.94203		-2.66657
2	CON	0.00120	-1.34272	0.23095	-0.39801			-2.79598
3	CON	0.00000	-1.57724	0.32063	-0.63455	-1.36482	-1.93149	-2.58546
4	CON	0.00508		0.10757	0.15563	-1.31797	-0.85722	
5	CON	0.00000	-1.51445	0.24487	-0.59898	-1.00718	-1.76729	
6	CON	0.00631	-1.20259	0.49906	-0.93400	-0.81890	-2.21251	-1.88601
7	CON	0.00000	-1.46554	0.16352	-0.97014	-1.51379	-2.48868	-2.32080
8	CON	0.00501	-1.51982	0.62660	-1.03657	-1.96678	-2.58758	-2.01334
9	CON	0.00136	-1.62137	0.08288	-1.04113	-1.53489		-2.70064
10	CON	0.00379	-1.26676	0.62155	-0.80098	-1.85824		-2.33440
11	CON	0.00766	-1.72028	-0.25034	-0.93083	-1.36113	-2.15821	-1.66552
MEAN		**0.00411**	**-1.49978**	**0.26195**	**-0.71226**	**-1.36857**	**-2.00043**	**-2.32986**
SEM		**0.00135**	**0.05868**	**0.07699**	**0.10703**	**0.11849**	**0.21925**	**0.13292**
N		**11**	**10**	**11**	**11**	**10**	**7**	**9**
MAX		**0.01486**	**-1.20259**	**0.62660**	**0.15563**	**-0.81890**	**-0.85722**	**-1.66552**
QUARTILE 3		**0.00569**	**-1.37342**	**0.40984**	**-0.61677**	**-1.08488**	**-1.84939**	**-2.01334**
MEDIAN		**0.00379**	**-1.51713**	**0.23415**	**-0.80098**	**-1.36297**	**-2.15821**	**-2.33440**
QUARTILE 1		**0.00060**	**-1.61034**	**0.13555**	**-0.95207**	**-1.52962**	**-2.35060**	**-2.66657**
MIN		**0.00000**	**-1.76699**	**-0.25034**	**-1.04113**	**-1.96678**	**-2.58758**	**-2.79598**
HEART	**PD/CON**	**Cys-DA**	**Log DHPG**	**Log NE**	**Log DOPA**	**Log EPI**	**Log Cys_DOPA**	**Log DOPET**
		pmol/mg	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*	*pmol/mg*
1	PD	0.00000		-1.65830	-0.62014	-2.58679	-1.54317	
2	PD	0.00000	-2.77762	-1.86137	-0.80666	-2.76648	-1.53406	
3	PD	0.00000	-3.18294	-2.03396	-0.45397	-2.62952	-1.28338	
4	PD	0.00000	-2.32736	-2.08176	-0.61777	-2.14851	-1.30379	
5	PD	0.00000		-1.07560	-0.09007	-2.41735	-1.24441	
6	PD	0.00000	-2.44660	-2.11268	-1.26951	-2.36568	-1.76805	
7	PD	0.00000		-1.73395	0.27189	-1.32761	-1.64914	
8	PD	0.00000	-2.96267	-1.54597	-0.60932	-2.30836	-1.42643	
9	PD	0.00000		-1.99998	-0.50913	-2.71344	-1.58869	
10	PD	0.00000	-2.54155	-1.46317	-0.48007	-2.20790	-1.58432	
11	PD	0.00000	-2.10707	-1.57596	-0.57912	-2.02948	-1.58308	
MEAN		**0.00000**	**-2.62083**	**-1.74024**	**-0.52399**	**-2.31828**	**-1.50077**	**#DIV/0!**
SEM		**0.00000**	**0.14177**	**0.09600**	**0.11650**	**0.12225**	**0.05001**	**#DIV/0!**
N		**11**	**7**	**11**	**11**	**11**	**11**	**0**
MAX		**0.00000**	**-2.10707**	**-1.07560**	**0.27189**	**-1.32761**	**-1.24441**	**0.00000**
QUARTILE 3		**0.00000**	**-2.38698**	**-1.56096**	**-0.46702**	**-2.17820**	**-1.36511**	**#NUM!**
MEDIAN		**0.00000**	**-2.54155**	**-1.73395**	**-0.57912**	**-2.36568**	**-1.54317**	**#NUM!**
QUARTILE 1		**0.00000**	**-2.87014**	**-2.01697**	**-0.61896**	**-2.60815**	**-1.58651**	**#NUM!**
MIN		**0.00000**	**-3.18294**	**-2.11268**	**-1.26951**	**-2.76648**	**-1.76805**	**0.00000**
PD % of CON		*0.0%*						
p PD vs. CON			*6.3E-07*	*5.3E-13*	*0.24794*	*0.00002*	*0.01486*	*#DIV/0!*

HEART	PD/CON	Log DA	Log DOPAC	Log Cys-DA	DHPG/NE	Log DHPG/NE	DA/NE	Log DA/NE
		pmol/mg	*pmol/mg*	*pmol/mg*				
1	CON	-0.90437	-1.43857	-1.82812	0.00997	-2.00114	0.07269	-1.13852
2	CON	-1.01186	-1.54111	-2.92119	0.02669	-1.57367	0.05717	-1.24281
3	CON	-0.92462	-2.27107		0.01265	-1.89786	0.05685	-1.24525
4	CON	-1.17185	-2.22531	-2.29430	0.00000		0.05255	-1.27943
5	CON	-1.57191	-2.18392		0.01741	-1.75932	0.01525	-1.81678
6	CON	-0.23160	-1.07175	-2.19997	0.01988	-1.70166	0.18592	-0.73067
7	CON	-0.94384	-1.97171		0.02349	-1.62907	0.07810	-1.10736
8	CON	-0.19008	-1.43528	-2.30045	0.00714	-2.14643	0.15252	-0.81668
9	CON	-0.94601	-1.69403	-2.86597	0.01976	-1.70425	0.09356	-1.02889
10	CON	-0.52312	-1.38162	-2.42181	0.01293	-1.88831	0.07167	-1.14466
11	CON	-0.32473	-0.92771	-2.11581	0.03389	-1.46995	0.84257	-0.07439
MEAN		**-0.79491**	**-1.64928**	**-2.36845**	**0.01671**	**-1.77716**	**0.15262**	**-1.05686**
SEM		**0.12950**	**0.13941**	**0.13026**	**0.00287**	**0.06519**	**0.07047**	**0.12948**
N		**11**	**11**	**8**	**11**	**10**	**11**	**11**
MAX		**-0.19008**	**-0.92771**	**-1.82812**	**0.03389**	**-1.46995**	**0.84257**	**-0.07439**
QUARTILE 3		**-0.42393**	**-1.40845**	**-2.17893**	**0.02168**	**-1.64721**	**0.12304**	**-0.92279**
MEDIAN		**-0.92462**	**-1.54111**	**-2.29737**	**0.01741**	**-1.73178**	**0.07269**	**-1.13852**
QUARTILE 1		**-0.97894**	**-2.07781**	**-2.53285**	**0.01131**	**-1.89547**	**0.05701**	**-1.24403**
MIN		**-1.57191**	**-2.27107**	**-2.92119**	**0.00000**	**-2.14643**	**0.01525**	**-1.81678**
HEART	**PD/CON**	**Log DA**	**Log DOPAC**	**Log Cys-DA**	**DHPG/NE**	**Log DHPG/NE**	**DA/NE**	**Log DA/NE**
		pmol/mg	*pmol/mg*	*pmol/mg*				
1	PD		-2.57112		0.00000		0.00000	
2	PD		-2.24450		0.12127	-0.91625	0.00000	
3	PD		-2.45649		0.07096	-1.14898		
4	PD	-2.58263	-2.02119		0.56807	-0.24560	0.31559	-0.50087
5	PD	-1.61649	-2.44716		0.00000		0.28781	-0.54089
6	PD	-2.67332	-2.69425		0.46353	-0.33392	0.27501	-0.56064
7	PD		-2.75909		0.00000		0.00000	
8	PD		-2.85985		0.03831	-1.41670		
9	PD		-2.38298					
10	PD	-2.34185	-1.89971		0.08349	-1.07838	0.13223	-0.87868
11	PD	-2.66355	-1.98743		0.29437	-0.53111	0.08173	-1.08760
MEAN		**-2.37557**	**-2.39307**	**#DIV/0!**	**0.16400**	**-0.81014**	**0.13655**	**-0.71374**
SEM		**0.19897**	**0.09768**	**#DIV/0!**	**0.06527**	**0.16828**	**0.04875**	**0.11524**
N		**5**	**11**	**0**	**10**	**7**	**8**	**5**
MAX		**-1.61649**	**-1.89971**	**0.00000**	**0.56807**	**-0.24560**	**0.31559**	**-0.50087**
QUARTILE 3		**-2.34185**	**-2.13284**	**#NUM!**	**0.25109**	**-0.43252**	**0.27821**	**-0.54089**
MEDIAN		**-2.58263**	**-2.44716**	**#NUM!**	**0.07722**	**-0.91625**	**0.10698**	**-0.56064**
QUARTILE 1		**-2.66355**	**-2.63268**	**#NUM!**	**0.00958**	**-1.11368**	**0.00000**	**-0.87868**
MIN		**-2.67332**	**-2.85985**	**0.00000**	**0.00000**	**-1.41670**	**0.00000**	**-1.08760**
PD % of CON					*981.5%*		*89.5%*	
p PD vs. CON		*0.00001*	*0.00030*	*#DIV/0!*		*0.00002*		*0.12353*

HEART	PD/CON	DOPAC/DHPG	Log DOPAC/DHPG	DOPAC/NE	Log DOPAC/NE	DOPAC/DA
1	CON	2.13022	0.32842	0.02125	-1.67272	0.29229
2	CON	0.63329	-0.19840	0.01690	-1.77206	0.29563
3	CON	0.20238	-0.69383	0.00256	-2.59169	0.04504
4	CON			0.00465	-2.33288	0.08842
5	CON	0.21406	-0.66947	0.00373	-2.42879	0.24434
6	CON	1.35159	0.13085	0.02687	-1.57081	0.14450
7	CON	0.31177	-0.50616	0.00732	-2.13523	0.09379
8	CON	1.21492	0.08455	0.00867	-2.06188	0.05686
9	CON	0.84594	-0.07266	0.01671	-1.77691	0.17864
10	CON	0.76761	-0.11486	0.00993	-2.00317	0.13851
11	CON	6.20263	0.79258	0.21020	-0.67737	0.24947
MEAN		**1.38744**	**-0.09190**	**0.02989**	**-1.91123**	**0.16613**
SEM		**0.56719**	**0.14604**	**0.01818**	**0.15732**	**0.02780**
N		**10**	**10**	**11**	**11**	**11**
MAX		**6.20263**	**0.79258**	**0.21020**	**-0.67737**	**0.29563**
QUARTILE 3		**1.31742**	**0.11927**	**0.01907**	**-1.72239**	**0.24691**
MEDIAN		**0.80678**	**-0.09376**	**0.00993**	**-2.00317**	**0.14450**
QUARTILE 1		**0.39215**	**-0.42922**	**0.00599**	**-2.23405**	**0.09110**
MIN		**0.20238**	**-0.69383**	**0.00256**	**-2.59169**	**0.04504**
HEART	PD/CON	DOPAC/DHPG	Log DOPAC/DHPG	DOPAC/NE	Log DOPAC/NE	DOPAC/DA
1	PD			0.12223	-0.91282	
2	PD	3.41288	0.53312	0.41388	-0.38312	
3	PD	5.32671	0.72646	0.37799	-0.42253	
4	PD	2.02381	0.30617	1.14966	0.06057	3.64286
5	PD			0.04251	-1.37156	0.14768
6	PD	0.56539	-0.24765	0.26208	-0.58157	0.95296
7	PD			0.09437	-1.02515	
8	PD	1.26714	0.10282	0.04854	-1.31388	
9	PD			0.41400	-0.38300	
10	PD	4.38367	0.64184	0.36598	-0.43654	2.76781
11	PD	1.31717	0.11964	0.38773	-0.41147	4.74382
MEAN		**2.61382**	**0.31177**	**0.33445**	**-0.65283**	**2.45103**
SEM		**0.67559**	**0.13125**	**0.09331**	**0.13408**	**0.84638**
N		**7**	**7**	**11**	**11**	**5**
MAX		**5.32671**	**0.72646**	**1.14966**	**0.06057**	**4.74382**
QUARTILE 3		**3.89827**	**0.58748**	**0.40081**	**-0.39730**	**3.64286**
MEDIAN		**2.02381**	**0.30617**	**0.36598**	**-0.43654**	**2.76781**
QUARTILE 1		**1.29215**	**0.11123**	**0.10830**	**-0.96899**	**0.95296**
MIN		**0.56539**	**-0.24765**	**0.04251**	**-1.37156**	**0.14768**
PD % of CON		*188.4%*		*1119.0%*		*1475.3%*
p PD vs. CON			*0.06994*		*6.0E-06*	

HEART	PD/CON	Log DOPAC/DA	DOPET/DOPAC	Log DOPET/DOPAC	Cys-DA/DA	Log Cys-DA/DA
1	CON	-0.53419	0.05916	-1.22800	0.11919	-0.92375
2	CON	-0.52925	0.05561	-1.25487	0.01232	-1.90933
3	CON	-1.34645	0.48485	-0.31439		
4	CON	-1.05346	0.00000		0.07543	-1.12244
5	CON	-0.61201	0.00000			
6	CON	-0.84015	0.15337	-0.81427	0.01076	-1.96836
7	CON	-1.02787	0.44762	-0.34909		
8	CON	-1.24520	0.26420	-0.57806	0.00776	-2.11037
9	CON	-0.74802	0.09849	-1.00661	0.01202	-1.91995
10	CON	-0.85851	0.11149	-0.95277	0.01263	-1.89869
11	CON	-0.60297	0.18289	-0.73781	0.01618	-1.79108
MEAN		-0.85437	0.16888	-0.80399	0.03329	-1.70550
SEM		0.08562	0.05020	0.11477	0.01459	0.15331
N		11	11	9	8	8
MAX		-0.52925	0.48485	-0.31439	0.11919	-0.92375
QUARTILE 3		-0.60749	0.22355	-0.57806	0.03099	-1.62392
MEDIAN		-0.84015	0.11149	-0.81427	0.01247	-1.90401
QUARTILE 1		-1.04066	0.05738	-1.00661	0.01171	-1.93206
MIN		-1.34645	0.00000	-1.25487	0.00776	-2.11037
HEART	PD/CON	Log DOPAC/DA	DOPET/DOPAC	Log DOPET/DOPAC	Cys-DA/DA	Log Cys-DA/DA
1	PD		0.00000			
2	PD		0.00000			
3	PD		0.00000			
4	PD	0.56144	0.00000		0.00000	
5	PD	-0.83067	0.00000		0.00000	
6	PD	-0.02093	0.00000		0.00000	
7	PD		0.00000			
8	PD		0.00000			
9	PD		0.00000			
10	PD	0.44214	0.00000		0.00000	
11	PD	0.67613	0.00000		0.00000	
MEAN		0.16562	0.00000	#DIV/0!	0.00000	#DIV/0!
SEM		0.27578	0.00000	#DIV/0!	0.00000	#DIV/0!
N		5	11	0	5	0
MAX		0.67613	0.00000	0.00000	0.00000	0.00000
QUARTILE 3		0.56144	0.00000	#NUM!	0.00000	#NUM!
MEDIAN		0.44214	0.00000	#NUM!	0.00000	#NUM!
QUARTILE 1		-0.02093	0.00000	#NUM!	0.00000	#NUM!
MIN		-0.83067	0.00000	0.00000	0.00000	0.00000
PD % of CON			*0.0%*		*0.0%*	
p PD vs. CON		*0.00038*		*#DIV/0!*		*#DIV/0!*

HEART	PD/CON	Cys-DOPA/DOPA	Log Cys-DOPA/DOPA	Cys-DOPA/Cys-DA	Log Cys-DOPA/Cys-DA
1	CON	0.15900	-0.79861	2.42237	0.38424
2	CON	0.05659	-1.24724	18.87747	1.27594
3	CON	0.05047	-1.29694		
4	CON	0.09708	-1.01285	27.35735	1.43707
5	CON	0.06787	-1.16831		
6	CON	0.05266	-1.27851	0.97153	-0.01254
7	CON	0.03030	-1.51854		
8	CON	0.02812	-1.55101	0.51627	-0.28712
9	CON	0.26673	-0.57393	17.82004	1.25091
10	CON	0.05255	-1.27940	2.19495	0.34142
11	CON	0.05924	-1.22739	0.90698	-0.04240
MEAN		**0.08369**	**-1.17752**	**8.88337**	**0.54344**
SEM		**0.02130**	**0.08702**	**3.78847**	**0.24068**
N		**11**	**11**	**8**	**8**
MAX		**0.26673**	**-0.57393**	**27.35735**	**1.43707**
QUARTILE 3		**0.08248**	**-1.09058**	**18.08440**	**1.25717**
MEDIAN		**0.05659**	**-1.24724**	**2.30866**	**0.36283**
QUARTILE 1		**0.05151**	**-1.28817**	**0.95539**	**-0.02001**
MIN		**0.02812**	**-1.55101**	**0.51627**	**-0.28712**
HEART	PD/CON	Cys-DOPA/DOPA	Log Cys-DOPA/DOPA	Cys-DOPA/Cys-DA	Log Cys-DOPA/Cys-DA
1	PD	0.11939	-0.92302		
2	PD	0.18733	-0.72740		
3	PD	0.14811	-0.82941		
4	PD	0.20606	-0.68601		
5	PD	0.07009	-1.15434		
6	PD	0.31729	-0.49854		
7	PD	0.01199	-1.92103		
8	PD	0.15237	-0.81711		
9	PD	0.08326	-1.07956		
10	PD	0.07866	-1.10425		
11	PD	0.09909	-1.00396		
MEAN		**0.13397**	**-0.97678**	**#DIV/0!**	**#DIV/0!**
SEM		**0.02490**	**0.11185**	**#DIV/0!**	**#DIV/0!**
N		**11**	**11**	**0**	**0**
MAX		**0.31729**	**-0.49854**	**0.00000**	**0.00000**
QUARTILE 3		**0.16985**	**-0.77226**	**#NUM!**	**#NUM!**
MEDIAN		**0.11939**	**-0.92302**	**#NUM!**	**#NUM!**
QUARTILE 1		**0.08096**	**-1.09190**	**#NUM!**	**#NUM!**
MIN		**0.01199**	**-1.92103**	**0.00000**	**0.00000**
PD % of CON		*160.1%*		*#DIV/0!*	
p PD vs. CON			*0.17204*		*#DIV/0!*

HEART	PD/CON	DOPA/DOPAC	Log DOPA/DOPAC	Cys-DOPA/DOPAC	Log Cys-DOPA/DOPAC
1	CON	6.21293	0.79330	0.98783	-0.00532
2	CON	13.90280	1.14310	0.78679	-0.10414
3	CON	43.30288	1.63652	2.18565	0.33958
4	CON	240.40203	2.38094	23.33924	1.36809
5	CON	38.45316	1.58493	2.60990	0.41662
6	CON	1.37324	0.13775	0.07232	-1.14076
7	CON	10.03611	1.00157	0.30411	-0.51698
8	CON	2.50442	0.39871	0.07042	-1.15230
9	CON	4.49678	0.65290	1.19943	0.07897
10	CON	3.80751	0.58064	0.20010	-0.69876
11	CON	0.99285	-0.00312	0.05882	-1.23051
MEAN		**33.22588**	**0.93702**	**2.89224**	**-0.24050**
SEM		**21.18744**	**0.21493**	**2.06149**	**0.24197**
N		**11**	**11**	**11**	**11**
MAX		**240.40203**	**2.38094**	**23.33924**	**1.36809**
QUARTILE 3		**26.17798**	**1.36402**	**1.69254**	**0.20928**
MEDIAN		**6.21293**	**0.79330**	**0.78679**	**-0.10414**
QUARTILE 1		**3.15597**	**0.48967**	**0.13621**	**-0.91976**
MIN		**0.99285**	**-0.00312**	**0.05882**	**-1.23051**
HEART	PD/CON	DOPA/DOPAC	Log DOPA/DOPAC	Cys-DOPA/DOPAC	Log Cys-DOPA/DOPAC
1	PD	89.32687	1.95098	10.66493	1.02796
2	PD	27.40564	1.43784	5.13383	0.71044
3	PD	100.58081	2.00252	14.89737	1.17311
4	PD	25.31726	1.40342	5.21677	0.71740
5	PD	227.55330	2.35708	15.94937	1.20274
6	PD	26.59086	1.42473	8.43714	0.92620
7	PD	1073.95444	3.03099	12.88113	1.10995
8	PD	178.04510	2.25053	27.12787	1.43342
9	PD	74.79061	1.87385	6.22714	0.79429
10	PD	26.28087	1.41964	2.06724	0.31539
11	PD	25.60367	1.40830	2.53715	0.40435
MEAN		**170.49540**	**1.86908**	**10.10363**	**0.89230**
SEM		**92.64978**	**0.15877**	**2.22226**	**0.10354**
N		**11**	**11**	**11**	**11**
MAX		**1073.95444**	**3.03099**	**27.12787**	**1.43342**
QUARTILE 3		**139.31296**	**2.12652**	**13.88925**	**1.14153**
MEDIAN		**74.79061**	**1.87385**	**8.43714**	**0.92620**
QUARTILE 1		**26.43587**	**1.42219**	**5.17530**	**0.71392**
MIN		**25.31726**	**1.40342**	**2.06724**	**0.31539**
PD % of CON		*513.1%*		*349.3%*	
p PD vs. CON			*0.00232*		*0.00035*

HEART	PD/CON	(DOPA+Cys-DOPA)/DOPAC	Log (DOPA+Cys-DOPA)/DOPAC
1	CON	7.2	0.857
2	CON	14.7	1.167
3	CON	45.5	1.658
4	CON	263.7	2.421
5	CON	41.1	1.613
6	CON	1.4	0.160
7	CON	10.3	1.015
8	CON	2.6	0.411
9	CON	5.7	0.756
10	CON	4.0	0.603
11	CON	1.1	0.022
MEAN		**36.1**	**0.971**
SEM		**23.2**	**0.215**
N		**11**	**11**
MAX		**263.7**	**2.421**
QUARTILE 3		**27.9**	**1.390**
MEDIAN		**7.2**	**0.857**
QUARTILE 1		**3.3**	**0.507**
MIN		**1.1**	**0.022**
		100.0%	
HEART	**PD/CON**	**(DOPA+Cys-DOPA)/DOPAC**	**Log (DOPA+Cys-DOPA)/DOPAC**
1	PD	100.0	1.99996
2	PD	32.5	1.51241
3	PD	115.5	2.06250
4	PD	30.5	1.48478
5	PD	243.5	2.38650
6	PD	35.0	1.54442
7	PD	1086.8	3.03616
8	PD	205.2	2.31212
9	PD	81.0	1.90858
10	PD	28.3	1.45252
11	PD	28.1	1.44934
MEAN		**180.6**	**1.923**
SEM		**93.3**	**0.153**
N		**11**	**11**
MAX		**1086.8**	**3.036**
QUARTILE 3		**160.3**	**2.187**
MEDIAN		**81.0**	**1.909**
QUARTILE 1		**31.5**	**1.499**
MIN		**28.1**	**1.449**
PD % of CON		*500.0%*	
p PD vs. CON			*0.00178*

HEART	PD/CON	TH	Log TH	DOPA/DA	Log DOPA/DA
		(DOPA +Cys-DOPA adjusted for dec. LAAAD)			
1	CON	0.26231	-0.58119	1.81595	0.25910
2	CON	0.42257	-0.37410	4.11012	0.61385
3	CON	0.24369	-0.61316	1.95016	0.29007
4	CON	1.56989	0.19587	21.25607	1.32748
5	CON	0.26887	-0.57047	9.39557	0.97292
6	CON	0.12254	-0.91171	0.19843	-0.70240
7	CON	0.11036	-0.95718	0.94124	-0.02630
8	CON	0.09451	-1.02453	0.14240	-0.84649
9	CON	0.11523	-0.93845	0.80331	-0.09512
10	CON	0.16644	-0.77874	0.52739	-0.27786
11	CON	0.12421	-0.90583	0.24769	-0.60609
MEAN		**0.31824**	**-0.67813**	**3.76258**	**0.08265**
SEM		**0.12870**	**0.10718**	**1.93131**	**0.20946**
N		**11**	**11**	**11**	**11**
MAX		**1.56989**	**0.19587**	**21.25607**	**1.32748**
QUARTILE 3		**0.26559**	**-0.57583**	**3.03014**	**0.45196**
MEDIAN		**0.16644**	**-0.77874**	**0.94124**	**-0.02630**
QUARTILE 1		**0.11888**	**-0.92508**	**0.38754**	**-0.44198**
MIN		**0.09451**	**-1.02453**	**0.14240**	**-0.84649**
HEART	**PD/CON**	**TH**	**Log TH**	**DOPA/DA**	**Log DOPA/DA**
		(DOPA +Cys-DOPA adjusted for dec. LAAAD)			
1	PD	0.05368	-1.27015		
2	PD	0.03706	-1.43108		
3	PD	0.08073	-1.09298		
4	PD	0.05816	-1.23540	92.22716	1.96486
5	PD	0.17392	-0.75964	33.60584	1.52641
6	PD	0.01416	-1.84882	25.34002	1.40381
7	PD	0.37851	-0.42192		
8	PD	0.05666	-1.24672		
9	PD	0.06708	-1.17339		
10	PD	0.07142	-1.14618	72.74038	1.86178
11	PD	0.05793	-1.23708	121.45916	2.08443
MEAN		**0.09539**	**-1.16940**	**69.07451**	**1.76826**
SEM		**0.03074**	**0.10822**	**17.97827**	**0.13013**
N		**11**	**11**	**5**	**5**
MAX		**0.37851**	**-0.42192**	**121.45916**	**2.08443**
QUARTILE 3		**0.07607**	**-1.11958**	**92.22716**	**1.96486**
MEDIAN		**0.05816**	**-1.23540**	**72.74038**	**1.86178**
QUARTILE 1		**0.05517**	**-1.25843**	**33.60584**	**1.52641**
MIN		**0.01416**	**-1.84882**	**25.34002**	**1.40381**
PD % of CON		*30.0%*		*1835.8%*	
p PD vs. CON			*0.00424*		*0.00015*

HEART	PD/CON	Cys-DOPA/DA	Log Cys-DOPA/DA	(DOPA+Cys-DOPA)/(Sum of DA & Metabs.)
1	CON	0.28873	-0.53951	0.13735
2	CON	0.23260	-0.63339	0.22522
3	CON	0.09843	-1.00687	0.10851
4	CON	2.06363	0.31463	1.15483
5	CON	0.63770	-0.19539	0.14762
6	CON	0.01045	-1.98091	0.03135
7	CON	0.02852	-1.54484	0.06810
8	CON	0.00400	-2.39750	0.01906
9	CON	0.21427	-0.66904	0.08405
10	CON	0.02772	-1.55727	0.03628
11	CON	0.01467	-1.83348	0.10336
MEAN		**0.32916**	**-1.09487**	**0.19234**
SEM		**0.18262**	**0.25136**	**0.09793**
N		**11**	**11**	**11**
MAX		**2.06363**	**0.31463**	**1.15483**
QUARTILE 3		**0.26067**	**-0.58645**	**0.14249**
MEDIAN		**0.09843**	**-1.00687**	**0.10336**
QUARTILE 1		**0.02119**	**-1.69537**	**0.05219**
MIN		**0.00400**	**-2.39750**	**0.01906**
HEART	PD/CON	Cys-DOPA/DA	Log Cys-DOPA/DA	(DOPA+Cys-DOPA)/(Sum of DA & Metabs.)
1	PD			10.89077
2	PD			8.77273
3	PD			30.12468
4	PD	19.00396	1.27884	11.57272
5	PD	2.35546	0.37208	7.78017
6	PD	8.04026	0.90527	4.58860
7	PD			93.72375
8	PD			9.16370
9	PD			23.72078
10	PD	5.72173	0.75753	6.55932
11	PD	12.03576	1.08047	6.18599
MEAN		**9.43143**	**0.87884**	**19.37120**
SEM		**2.86516**	**0.15377**	**7.80617**
N		**5**	**5**	**11**
MAX		**19.00396**	**1.27884**	**93.72375**
QUARTILE 3		**12.03576**	**1.08047**	**17.64675**
MEDIAN		**8.04026**	**0.90527**	**9.16370**
QUARTILE 1		**5.72173**	**0.75753**	**7.16974**
MIN		**2.35546**	**0.37208**	**4.58860**
PD % of CON		*2865.3%*		*10071.4%*
p PD vs. CON			*0.00019*	

HEART	PD/CON	Log ((DOPA+Cys-DOPA)/(Sum of DA & Metabs.))
1	CON	-0.86216
2	CON	-0.64740
3	CON	-0.96451
4	CON	0.06252
5	CON	-0.83085
6	CON	-1.50377
7	CON	-1.16688
8	CON	-1.71998
9	CON	-1.07548
10	CON	-1.44031
11	CON	-0.98565
MEAN		**-1.01223**
SEM		**0.14461**
N		**11**
MAX		**0.06252**
QUARTILE 3		**-0.84651**
MEDIAN		**-0.98565**
QUARTILE 1		**-1.30359**
MIN		**-1.71998**
HEART	PD/CON	Log ((DOPA+Cys-DOPA)/(Sum of DA & Metabs.))
1	PD	1.03706
2	PD	0.94313
3	PD	1.47892
4	PD	1.06344
5	PD	0.89099
6	PD	0.66168
7	PD	1.97185
8	PD	0.96207
9	PD	1.37513
10	PD	0.81686
11	PD	0.79141
MEAN		**1.09023**
SEM		**0.11436**
N		**11**
MAX		**1.97185**
QUARTILE 3		**1.21928**
MEDIAN		**0.96207**
QUARTILE 1		**0.85392**
MIN		**0.66168**
PD % of CON		
p PD vs. CON		*3.3E-10*