Parkinson's disease progression is associated with increased putaminal serotonin to dopamine transporter ratio: relevance for dyskinesias

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Background:

•Presynaptic dopaminergic mechanisms in LIDs

In advanced PD: buffer capacity of dopaminergic terminals is lost ⟶ L-dopa derived DA is immediately released in synaptic cleft ⟶ peak dose LIDs

•Serotonergic hypothesis in LIDs

5-HT terminals play a role in LIDs by mishandling exogenous L-dopa and releasing DA as a false neurotransmitter

Objective:

- To assess the role of both **dopaminergic** and **serotonergic** mechanisms in the development of LIDs

⟶ by calculating SERT/DAT ratio in the striatum of PD patients with and without LIDs

Subjects/Methods:

28 patients with idiopathic PD recruited from our movement disorders clinic:

- **11 PD patients without LIDs**
- **17 PD patients with LIDs**

12 age–matched healthy controls

- on levodopa treatment for at least 2 years
- no history of depression and cognitive impairment
- none of the participants on any 5-HT drugs

SPECT Imaging of Dopamine Transporter (DAT) with 123I-Ioflupane

PET Imaging of Serotonin Transporter (SERT) with 11C-DASB

$\frac{SERT}{DAT}$ ratios

Demographics and clinical characteristics

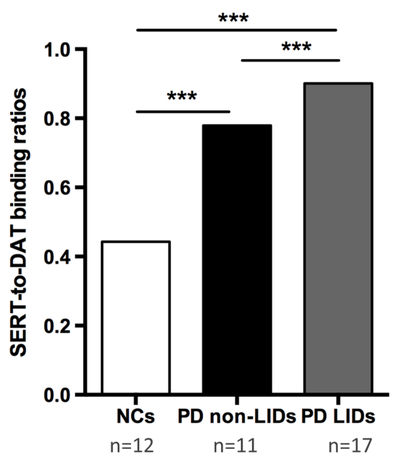
	Normal controls	PD all	non-LIDs	LIDs
Number of subjects	12	28	11	17
Age at the time of the scan (years)	61.4±8.7	64.9±8.2	69.3±4.7	**61.7±8.9***
Disease duration from diagnosis (years)	-	7.9±5.0	5.8±4.9	**9.6±5.5***
Disease duration from onset (years)		9.8±4.9	7.8±3.7	**11.1±5.4***
H&Y "off"	-	2.3±0.6	2.3±0.5	2.4±0.6
UPDRS-III "off"	-	27.6±8.3	26.7±7.3	28.1±9.1
UPDRS total "off"	-	45.0±10.9	40.6±10.3	47.8±10.6
AIMS	-	-	0	8.1±4.3
Duration on DA medication (years)	-	6.7±4.7	4.4±2.1	**8.4±5.1***
Time from diagnosis to initiation of DA meds			1.45±1.1	1.03±1.3
Daily LED_{Total} (mg)	-		537.5±199.9	**826.6±350.7***

Results:

Mean caudate and putamen SERT-to-DAT ratios in normal controls and PD patients with and without LIDs

Regions of interest	Normal controls	non-LIDs	LIDs
No. of subjects	12	11	17
11C-DASB BP			
Caudate	1.31±0.1	0.62±0.2	0.56±0.2
Putamen	1.36±0.1	0.86±0.2	0.94±0.2
123I-Ioflupane uptake			
Caudate	3.42±0.4	2.10±0.5	1.90±0.5
Putamen	3.07±0.3	1.51±0.4	1.15±0.3
SERT-to-DAT binding ratios			
Caudate	0.383	0.301	0.306
Putamen	0.443	0.779	0.901***

Bar graph of mean putaminal SERT-to-DAT ratios in normal controls and PD patients with and without LIDs



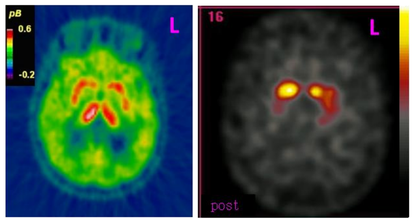
***p<0.001

•PD without LIDS: 76 % of normal ratio

•PD with LIDS: 103 % of normal ratio

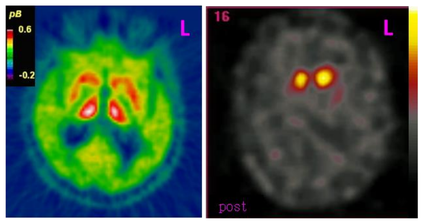
PET and SPECT images: subjects 003 and 016 (transverse plane)

PD patient without LIDs
DD: 7.1 years

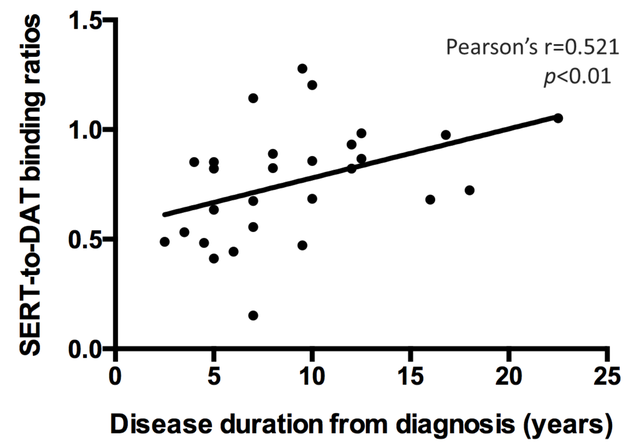


11C-DASB 123I-Ioflupane

PD patient with LIDs
DD: 10.2 years



Correlation between disease duration and SERT-to-DAT ratios in the putamen of all PD patients



Conclusions:

As Parkinson's progresses, the putaminal SERT–to–DAT ratio, as reflected by the ^{11}C-DASB BP to ^{123}I-Ioflupane uptake ratio, increases and patients experience dyskinesias.

This study indicates that it is the divergent ratio rather than the single DAT, SERT components of it that may be important for the development of LIDs.

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