Loss of dopaminergic function mediates speech difficulties in early *de novo* Parkinson's disease

Sotirios Polychronis,[1], Gennaro Pagano,[1] Rosa De Micco,[1] Flavia Niccolini,[1] and Marios Politis,[1]

[1]Neurodegeneration Imaging Group, Institute of Psychiatry, Psychology & Neuroscience (IoPPN), King's College London, UK.

OBJECTIVE

To investigate whether speech difficulties are mediated by loss of dopaminergic function in early *de novo* PD patients with and without speech difficulties.

BACKGROUND

In Parkinson's disease, the major neuropathological feature is degeneration of dopaminergic nigrostriatal pathways [1]. Dopamine transporter is a crucial protein regulating dopamine neurotransmission [2]. PD patients show lower level of dopamine transporter in striatum [3]. As a result, the motor cortical areas are disturbed and parkinsonian motor symptoms appear, including changes in speech [4]. Nearly 90% of PD patients develop speech difficulties during the course of their disease [5]. However, the role of speech difficulties as a factor associated with the nature and/or the progression of PD is still poorly understood.

Table 1. Demographic Characteristics of PD patients with and without speech difficulties

Demographic Characteristics	PD with speech difficulties (n=169)	PD without speech difficulties (n=229)	p value*
Age, mean ± SD	63.9±8.7	59.9±10.1	<0.0001
Gender male, % (n)	72.8% (123)	59.8% (137)	**0.049**
PD duration (months), mean ± SD	6.6±6.1	6.4±6.6	>0.1
Family history of PD, % (n)	23.1% (39)	26.6% (61)	>0.1
Year of Education, mean ± SD	15.2±2.9	15.8±2.9	>0.1

METHODS

We performed a cross-sectional study using the Parkinson's Progression Markers Initiative database, where we assessed and compared semi-quantified [^{123}I]FP-CIT single photon emission computed tomography (SPECT), and motor and non-motor features in PD patients with and without speech difficulties. Speech difficulties were evaluated using MDS-UPDRS Part-III, Item 18 (Speech) ≥ 1 and correlated with [^{123}I]FP-CIT SPECT, motor and non-motor symptoms.

RESULTS

The prevalence of speech difficulties in the population of early de novo PD patients was 42.4% (169/398). Demographic characteristics, motor and non-motor symptoms of PD patients with and without speech difficulties are shown in Table 2 and 3.

[^{123}I]FP-CIT SPECT binding within Putamen and Caudate were lower in PD with speech difficulties when compared with PD patients without speech difficulties (Figure 1). Greater speech difficulties correlated with lower [^{123}I]FP-CIT SPECT binding within Putamen (r=-0.255, p<0.0001) and Caudate (r=-0.206, p<0.0001) (Figure 2).

Table 2. Motor symptoms of PD patients with and without speech difficulties

Motor Symptoms	PD with speech difficulties (n=169)	PD without speech difficulties (n=229)	p value*
Hoehn and Yahr scale, mean ± SD	1.67±0.47	1.48±0.518	**<0.0001**
Motor Subtypes, % (n)	AR: 69.8% (118) Mixed: 10.7% (18) TD: 19.5% (33)	AR: 53.7% (123) Mixed: 23% (23) TD: 36.2% (83)	**0.007**
MDS-UPDRS Part III	23.48±8.30	17.88±8.01	**<0.0001**
MDS-UPDRS Part-III No Speech	22.4±8.242	17.88±8.01	**<0.0001**
Rigidity subscore, mean ± SD	4.28±2.7	3.38±2.4	**0.006**
Bradykinesia subscore, mean ± SD	11.78±5.3	8.87±5.28	**<0.0001**
Postural instability subscore, mean ± SD	1.01±1.02	0.72±0.895	**0.018**
Global Tremor subscore, mean ± SD	4.22±3.35	4.51±3.04	>0.1

Table 3. Non-motor symptoms of PD patients with and without speech difficulties

Non-motor Symptoms	PD with speech difficulties (n=169)	PD without speech difficulties (n=229)	p value*
MoCA, mean ± SD	26.9±2.29	27.26±2.34	>0.1
SCOPA-AUT°, mean ± SD	11.14±6.63	8.45±5.7	**<0.0001**
Epworth Sleeping Scale, mean ± SD	6.47±3.77	5.32±3.09	**0.008**
RBDQ Score, mean ± SD	4.33±2.86	3.96±2.4	>0.1
MDS-UPDRS			
Depressed mood, mean ± SD	0.3±0.61	0.25±0.48	>0.1
Anxious mood, mean ± SD	0.39±0.66	0.45±0.61	>0.1
Apathy, mean ± SD	0.25±0.56	0.16±0.42	>0.1
Constipation, mean ± SD	0.54±0.71	0.33±0.6	**0.024**
Fatigue, mean ± SD	0.70±0.77	0.61±0.8	>0.1

**t*-test and Mann-Whitney U tests, Bonferroni corrected.

Figure 1 [^{123}I]FP-CIT SPECT binding within Putamen and Caudate in PD patients with and without speech difficulties

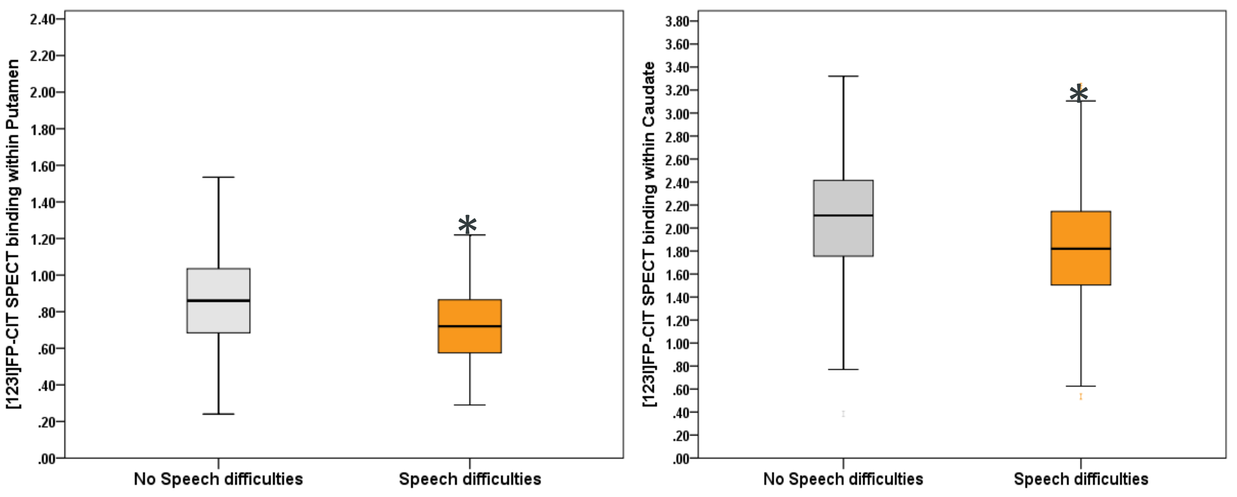
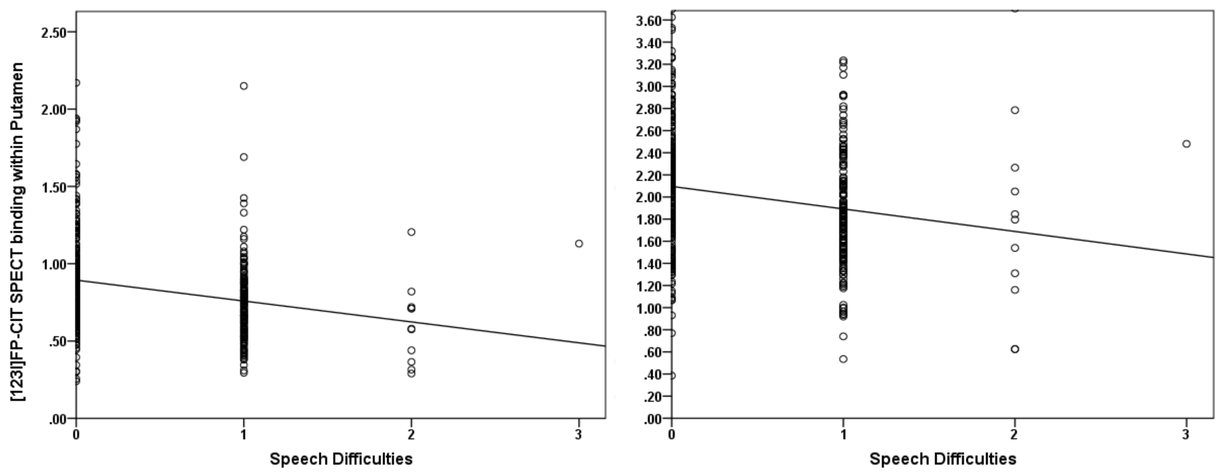


Figure 2. Correlation between [^{123}I]FP-CIT SPECT binding within Putamen and Caudate and degree of speech difficulties



CONCLUSION

Our findings demonstrate that loss of striatal dopaminergic function is associated with speech difficulties in patients with PD. This may be suggestive of a dopaminergic substrate underlying impairment of speech in PD. Speech could be a potential marker of disease severity.

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