Comorbid Impulse Control Disorders in Parkinson's disease: an ^{11}C-Raclopride Positron Emission Tomography study of Reward-Cue Evoked Striatal Dopamine Release

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Background:

Impulse control disorders (ICDs) are reported in Parkinson's disease (PD) in association with dopaminergic treatment. Approximately 25% of patients with ICDs have comorbid ICDs (i.e. more than one diagnosed ICD). The extent to which dopaminergic neurotransmission in PD patients with comorbid ICDs differs from those with only one diagnosed ICD is unknown.

Aims:

1. To investigate dopamine neurotransmission in PD patients diagnosed with comorbid ICDs, single ICDs and non-ICD controls in response to reward-related visual cues using positron emission tomography with ^{11}C-raclopride.
2. 2. To compare clinical features of the above three groups.

Methods:

PD subjects with comorbid ICDs (n=10), single ICD (n=7) and controls (n=9) (Table 1) underwent two positron emission tomography scans with ^{11}C-raclopride: one where they viewed neutral visual cues and the other where they viewed a range of visual cues related to different rewards.

Results:

Subjects with both comorbid ICDs and single ICDs showed significantly greater ventral striatal dopamine release compared to non-ICD subjects in response to reward cues (Table 2, Figure 1). Subjects with comorbid ICDs were significantly more depressed, and were marginally higher on impulsive sensation seeking compared to subjects with single ICDs and controls (Table 1); but did not evidence significantly greater ventral striatal dopamine release.

Table 1. Clinico-behavioural details of participants.

	Comorbid ICDs	Single ICD	Non-ICD controls	P value
Frequency	10	7	9	-
Age (yrs)	58.1 (2.8)	62.3 (3.9)	60.2 (3.2)	0.668
Disease duration (yrs)	14.3 (11.2)	10.6 (2.0)	9.9 (2.1)	0.478
UPDRS(III) 'off' meds	41.0 (3.5)	42.1 (3.8)	32.8 (3.0)	0.133
Total LEDD(mg/day)	724.0 (99.0)	782.3 (83.5)	831.9 (119.2)	0.751
L-dopa (mg/day)	268.5(84.9)	538.0 (83.4)	666.3 (129.0)	0.483
LEU DA (mg/day)	244.0 (55.4)	244.3 (51.4)	165.6(48.9)	0.485
BDI (II)	8.4 (5.6)	6.1 (1.1)	5.0 (0.9)	0.018**
BSS	8.4 (5.6)	6.1 (1.1)	5.0 (0.9)	0.097

All values are given as mean (SEM). [a]Comparisons made with one-way ANOVA corrected with Fisher's Least Significant Difference, where ** denotes statistical difference (p<0.05). Abbreviations: LEU DA = Levodopa Equivalent Units of Dopamine Agonists; LEDD = L-Dopa Equivalent Daily Dose; BDI(II) = Beck Depression Inventory, version II; BSS = Brief Sensation Seeking.

Table 2. Percentage reduction in regional 11C-raclopride binding potentials (RAC BPND) comparing scan with reward cues to scan with neutral cues.

Region-of-Interest	Comorbid ICDs	Single ICD	Non-ICD controls	P value
Caudate	7.9 (2.7)	4.0 (4.9)	6.0 (3.4)	0.754
Putamen	6.0 (2.9)	10.5 (4.8)	5.8 (2.4)	0.563
Ventral striatum	17.5 (2.8)[ab]	17.2 (6.8)[ac]	6.7 (2.2)[bc]	0.050** [a]0.051 [b]0.028** [c]0.920

Omnibus comparisons made with one-way ANOVA. Values given are % change (SEM) in BP_{ND} values comparing scan with reward cues to scan with neutral cues. [a]Post-hoc comparison (Least Significant Difference) between controls and single ICD groups. [b]Post-hoc comparison between controls and >1 ICD group. [c]Post-hoc comparison between single and >1ICD group. ** denotes statistical significance.

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Figures 1a-c. Scatter plots of regional RAC BP_{ND} during the scan showing neutral cues. Figures 1d-f. Percentage reduction in regional RAC BP_{ND} comparing scan with reward cues to scan with neutral cues (please see Table 2 for values).

Fig 1a. Caudate

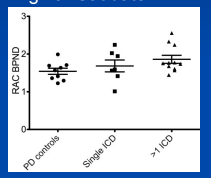

Fig 1b. Putamen

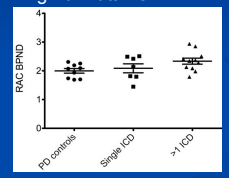

Fig 1c. Ventral Striatum

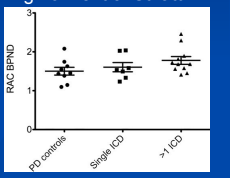

Fig 1d. Caudate % change in RAC BP_{ND}

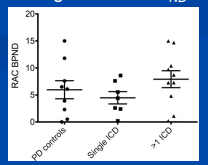

Fig 1e. Putamen % change in RAC BP_{ND}

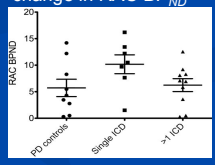

Fig 1f. Ventral Str % change in RAC BP_{ND}

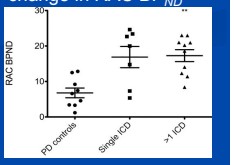

Figure 1a. Caudate (PD controls: 1.542±0.243; single ICD: 1.684±0.417; >1 ICD: 1.860±0.354; p=0.134). Figure 1b. Putamen (PD controls: 11.998±0.242; single ICD: 2.087±0.413; >1 ICD: 2.335±0.436; p=0.0854). Figure 1c. Ventral striatum (PD controls: 1.502±0.300; single ICD: 1.606±0.314; >1 ICD: 1.779±0.331; p=0.164). ** Denotes statistical significance.

Discussion:

This is the first study to compare dopamine neurotransmission using positron emission tomography neuroimaging in PD subjects with comorbid vs. non-comorbid ICDs. Our results suggest that striatal dopamine neurotransmission is not directly related to the severity of ICDs in PD, implicating non-dopaminergic mechanisms in comorbidity. Clinically, these results are supported by other larger clinical studies [1,2] and those from the general psychiatric populations where comorbidity is associated with more severe psychopathology, and greater psychosocial functioning impairments [3,4].

References:

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[2] Joutsa J et al. Parkinsonism Relat. Disord. 2012;**18**(2):155-60
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[4] Krueger RF, Bezdjian S. World psychiatry : 2009;**8**(1):3-6