Impulsivity versus apathy in PD: a comparison of clinical, psychiatric and behavioural correlates

Iracema Leroi [1,2], Michelle Andrews[1], Rebecca Elliot[2], Inês Sousa[3], E. Jane Byrne,[2] Alistair Burns[2]
[1]Lancashire Care Foundation Trust; [2]University of Manchester, Dept of Psychiatry & Behavioural Science; [3]Lancaster University

BACKGROUND

- Disorders of motivation and reward processing in PD range from the "impulse control and compulsive disorders" (ICCDs) to apathy and amotivation.
- Risk factors and clinical and behavioural correlates of these disorders are not well understood.
- ICCDs in PD include pathological gambling, hypersexuality, binge eating, compulsive shopping and the dopamine dysregulation syndrome.
- Apathy in PD is characterised by diminished drive and loss of motivation in various spheres of functioning and occurs in >50% of PD sufferers

We hypothesize that:
(1) Distinct demographic, psychiatric and cognitive factors exist in PD sufferers with ICCD ("PD-ICCD") vs apathy ("PD-A") vs neither complication ("PD-C")
(2) Level of motivation, as measured by the Apathy Evaluation Scale (AES-C) is a key factor in predicting behavioural outcome in PD sufferers

Objective:
To compare the clinical and behavioural correlates of 3 groups of PD sufferers: those with impulse control disorders, those with apathy and those with neither.

METHODS

This is a cross-sectional, descriptive study comparing three groups of PD sufferers on various clinical and behavioural factors. Current descriptive and univariate analysis compares a preliminary subgroup of this sample (total n=90), divided clinically into 3 groups by behavioural diagnosis:

- **Inclusion criteria for the 3 behavioural diagnostic groups:**
  - **(1) PD-ICCD:** ≥ 1 ICCD as per defined by Voon et al, 2007[1]
  - **(2) PD-A:** ≥14 on the modified Apathy Scale (AS)[2]
  - **(3) PD-C:** neither ICCD or Apathy

- **Assessment tools ("on" medication only):**

(1)Demographic, disability & PD-disease-related variables (UPDRS, Hoehn-Yahr)
(2) Psychiatric assessment: SCID-NP, rating scales (HADS, NPI)
(3) Motivation: Apathy Eval. Scale (AES); Barrett Impulsiveness Scale (BIS-II)
(4) Cognitive screen: Mini-Mental State Exam (MMSE); "FAS" task; Trails A&B
(5) Personality profile: NEO-FFI

RESULTS: *This is a preliminary descriptive analysis of the first 61 participants:*

Demographic and Clinical Variables of Entire Sample

Mean age (SD): 63.1 (9.8), range 35-86 years
Mean (SD) duration motor symptoms: 101.4 (72.0) months
Gender and work: 71% male; 18% working
PD subtype: 36% akinetic-rigid; 31% tremor dom; 33% mixed

Comparison of variables on 3 groups by clinical diagnosis:

PD-C: n=23 **PD-A:** n=14 **PD-ICCD:** n= 24

Breakdown of ICCD Subtype	n (%)
Pathological Gamblers	8 (42%)
Hypersexuality	6 (32%)
Binge Eating	6 (32%)
Compulsive Shopping	4 (21%)
Dopamine Dysregulation	2 (11%)
Other (transvestism, hobbyism, punding)	10(53%)

- **There were no differences among the 3 groups in the following variables:**
  - **Demographic:** % male, years education, premorbid IQ (NART)
  - **PD Disease Factors:** Hoen-Yahr stage; PD-motor subtype; PD-A had slightly longer duration PD, but this did not meet statistical significance
  - **DRT:** Total LEDD; LEDD-dopamine agonist only
  - **Psychiatric Diagnosis:** % DSM-IV diagnosis current & since onset PD; NPI score, current

- **Significant differences existed between the 3 groups in the following variables:**

	PD-ICCD (n=24)	PD-Apathy (n=14)	PD-Control (n=23)
Demographic (mean (SD)):			
Assessment age	58.5 (8.6) yrs	70.3(7.3) yrs: A vs ICCD**	63.1(9.7) yrs
Age at onset PD	50.2 (7.5)	**59.1 (10.6):** A vs ICCD*	54.8 (12.7)
PD-disease:			
Age onset PD, yrs	50.2 (7.5)	59.1 (10.6): A vs ICCD*	56.8 (12.7)
UPDRS total	44.2 (14.9)	**62.4 (15.9):** A vs ICCD*, A vs C***	39.8 (16.0)
UPDRS motor	24.6 (2.0)	**36.3 (12.5):** A vs ICCD**, A vs C**	23.5 (10.8)
PD Medication:			
% on DA (dopamine agonists)	**75:** ICCD vs A*	33	64
Cognitive Functioning:			
MMSE total	28.9 (1.2)	**27.0 (2.5):** A vs ICCD*, A vs C*	29.0 (1.3)
MMSE serial 7's	4.5 (0.8)	**3.2 (1.7):** A vs ICCD**, A vs C**	4.4 (0.7)
TMT-A (time sec, mean, SD)	50.0 (28.4)	**114.0 (98.9):** A vs ICCD*, A vs C*	49.0 (15.4)
TMT-B (time sec, mean, SD)	117.6 (82.2)	**225.7 (87.5):** A vs ICCD**, A vs C**	123.5 (68.2)
TMT-B (mean , score, SD)	20.5 (7.0)	**10.0 (12.0):** A vs ICCD*, A vs C*	20.2 (8.1)
Phonemic fluency (FAS)	48.2 (14.3)	**36.5 (9.4):** A vs ICCD*	41.7 (16.0)
Psychiatric Measures:			
HADs (Anxiety)	**8.1 (5.1):** ICCD vs C*	7.2 (3.8)	3.9 (3.3)
Premorbid Personality: NEO-FFI			
Neuroticism	58.0 (11.6)	59.6 (13.3)	**48.1 (9.6):** C vs ICCD*, C vs A*
Extraversion	53.1 (10.7) ICCD vs A (trend)	43.8 (9.4)	46.8 (12.5)
Agreeableness	47.0 (9.1) ICCD vs C (trend)	54.6 (9.7)	54.5 (12.8)

*p<0.05
**p=0.001
***p<0.001

- **Significant differences are seen when comparing 3 behavioural diagnostic groups on degree of impulsiveness and motivation:**

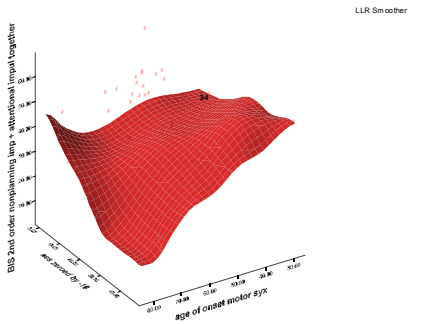
	PD-ICCD (n=24)	PD-Apathy (n=14)	PD-Control (n=23)
Impulsiveness (Barrett Impulsiveness Scale-II) (mean SD):			
BIS total	**62.1 (19.9)** ICCD v C*	57.1 (10.1)	48.7 (17.7)
BIS non-planning impulsivity	**25.8 (5.8)** ICCD v A* ICCD v C*	19.3 (9.0)	18.2 (6.7)
BIS attentional impulsivity	**12.2 (3.3)** ICCD v C**	**11.7 (2.9)** A v C*	8.6 (2.7)
BIS motor impulsivity	**15.6 (5.4)** ICCD v A**	9.7 (5.6)	12.5 (4.0)
Motivation (Apathy Evaluation Scale-Clinician Version (mean SD):			
	28.6 (14.6)	**47.1 (11.7)** A v ICCD*** A v C***	20.8 (6.6)

*p<0.05
**p=0.001
***p<0.001

SUMMARY OF COMPARISONS

- **Compared to PD-ICCD, PD-A have LOWER:**
global and specific cognitive functioning
And, later onset PD
- **Compared to both PD-ICCD & PD-C, PD-A have LOWER**:
motor functioning, overall functional ability and **HIGHER** motivation
- **Compared to PD-C & PD-A, PD-ICCD have GREATER:**
non-planning and attentional impulsivity, anxiety, premorbid extraversion and disagreeableness
- **Compared to both PD-A & PD-ICCD, PD-C have LESS**:
premorbid neuroticism

3-D scatterplot of degree of impulsiveness (Barrett Impulsiveness Scale-II) vs degree of motivation (Apathy Evaluation Scale AES-C) and age of onset:



- **If:**

	Young onset (<55 yrs)	Older onset PD (≥ 55 yrs)
Low AES	High impulsivity drives behaviour	No difference in impulsivity or motivation
High AES	Low motivation drives behaviour	No difference in impulsive behaviour and motivation remains low

CONCLUSION:

- There appears to be distinct behavioural subgroups, with different associated risk factors, of those presenting as ICD or apathy in PD
- Degree of motivation in PD is associated with different demographic, disease-related and medication factors
- In young onset PD, there appears to be a greater risk of behavioural disturbance, depending on whether one presents with either low or high levels of apathy.

FUTURE WORK:

- Based on these preliminary descriptions, logistical (according to behavioural diagnostic grouping) & linear regression models (according to degree of motivation) will be created to clarify direction and magnitude of associations of variables and behavioural phenotype
- Full sample (n=90) will be recruited and assessed
- Laboratory-based behavioural testing (risk-taking & decision-making tasks) in the groups will be reported, when both ON and OFF anti-PD medications
- Genotyping (COMT Val-Met) in the groups will be reported

KEY REFERENCES:

[1] Voon et al. Curr Opin Neurol. 2007: 20:484-492
[2]Starkstein et al. Journal of Neuropsychiatry. 2006: Vol 4(2); 134-139

ACKNOWLEDGEMENTS:

The authors would like to express their appreciation to the Parkinson's Disease Society, who is funding this study and **DeNDRoN**, whose help with this study has been invaluable.