Predicting Impulsivity in Parkinson's Disease: A Descriptive Analysis

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Introduction

Parkinson's Disease

- PD: movement disorder due to loss of dopaminergic neurons in the substantia nigra[1]
- Cardinal symptoms include tremors, bradykinesia, rigidity, and postural instability[2]
- Dopamine agonists (DA), a common treatment for PD, increases the risk of developing an impulse control disorder (ICD)

Impulse Control Disorder

- ICD: characterized by behaviors performed excessively and compulsively, causing impairment in social or occupation function
- Previously, Penn researchers created a clinical-genetic model to predict ICD risk in PD patients

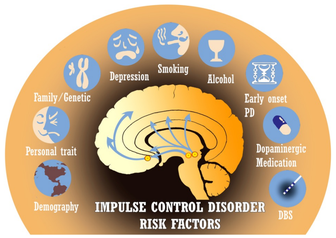

FIG. 1. This diagram shows the risk factors associated with ICDs in PD patients. Figure from Frontiers. (2019).

Objective: We sought to characterize DA, levodopa and other PD medication exposure in people with PD using descriptive statistics. We then identified study instruments to evaluate different domains of impulsivity in groups of high versus low ICD risk.

Methods

- Extracted electronic medical records (EMRs) with keywords: ICD, impulsiveness, sexual impulsiveness, or impulse disorder
- Summarized demographics and medication usage using Counts and Percentages

$$\begin{aligned}\text{ICD} - \text{RS} &= \ln\left(\frac{p_{\text{ICD}}}{1-p_{\text{ICD}}}\right)\\ &= 0.365 + 1.408 \times (\text{cohort}) - 0.823 \times (\text{Sex})\\ &\quad -0.037 \times (\text{age at test}) + 0.590 \times (\text{DA use})\\ &\quad -0.729 \times (\text{levodopa use}) - 0.096\\ &\quad \times (\text{PD duration}) - 0.96 \times (\text{Ethnicity}) + 0.429\\ &\quad \times (\text{rs } 1800497 : \text{G}) + 0.465 \times (\text{rs } 1799971 : \text{A})\end{aligned}$$

FIG 2. Clinical-genetic risk score calculator for ICD in PD patients. Figure from Weintraub et al. (2022).

Methods

- Identified past literature testing impulsivity and consulted with Penn psychiatrists and psychologists to determine the appropriate tests
  - Built the questionnaires on REDCap, a web based application for data capture
  - Created a testing module for the tasks on Inquisit Lab, a psychological testing platform

Results

- Majority of patients (79.4% of total cohort) were not taking a dopamine agonist at time of enrollment, but were taking levodopa (87.3%)
- 36% of participants were taking both dopamine agonists and levodopa simultaneously
- Among the DA medications, Pramipexole was prescribed at the highest frequency of 46.31%

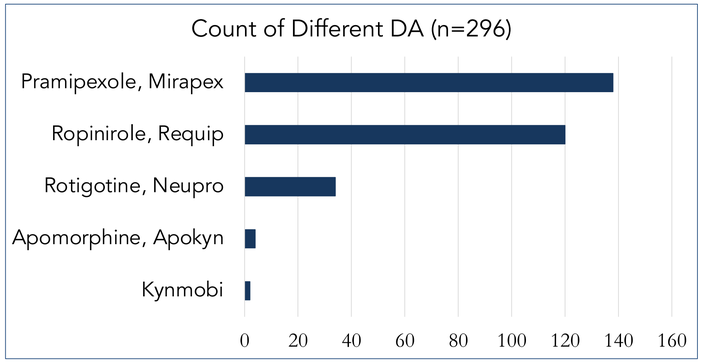

FIG 3. At test point, 296 individuals were recorded to be on various DA medications. Majority of patients (46.31%) were on Pramipexole.

- Demographic breakdown:
  - Average age of 68 years old (SD = 9)
  - 1343 (91% of total cohort) were White
  - 950 (64%) were male and 525 (36%) were female
- Only 4.36% of participants had an ICD diagnosis in their medical records
  - Compared to self-reported frequency of 17.46% for ICD symptoms in the molecular integration in neurological diagnosis (MIND) cohort

Impulsivity Testing

Study Instrument	Description
Questionnaire for ICD in PD Rating Scale (QUIP-RS)	Rating scale to measure **severity of ICD symptoms** in PD
Barratt Impulsivity Scale-11 (BIS-11)	30 self-report questions to measure **trait impulsivity**
Ten Item Personality Inventory (TIPI)	10 questions to measure **Big 5 personality domains**
Balloon Analogue Risk Task (BART)	Computerized measure of **risk-taking behavior**
Delayed Discounting Task (DDT)	Assessment of **delayed gratification**
Stop Signal Task (SST)	Measures **motor response inhibition**

TABLE 1. Summary of the study instruments chosen to assess the different domains of impulsivity.

Conclusion

- Identified the necessary information to fit into the parameters of the predictor model
- Generated a impulsivity testing paradigm, which will be pilot tested by 3 healthy individuals
- ICD diagnosis captured in EMRs is lower than the self-reported frequency by the MIND cohort
  - May be because the diagnosis must be entered by the physician at the visit, which occurs infrequently
- Next step involves assigning ICD-RS with genetic information and recruiting individuals for clinical impulsivity testing
- Validation of the the predictive model will enable future translation into a precision medicine treatment approach for PD patients

References

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