

Impulse Control Disorders in Parkinson's Disease: A 20-year Odyssey

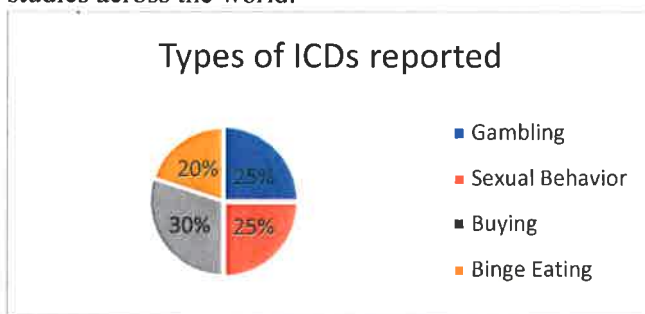
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Impulse Control Disorders (ICDs) are behavioral problems resulting from a person's difficulty with or inability to resist the drive to behave in ways that result in distress or significant negative impact on mental and physical health, quality of life and relationships. In Parkinson's disease (PD), ICDs are closely related to use of dopaminergic medications, and most commonly include pathological gambling (PG), excessive spending, hypersexuality, over-eating and compulsive medication use. Individuals can have more than one ICD concurrently (American Parkinson's Disease Association).

- In the last 20 years, ICDs have become more widespread with the introduction of newer dopaminergic medications for PD, such as Pramipexole and Ropinirole.
- Similar to addictive disorders, PD patients who discontinue dopaminergic treatment can experience dopamine withdrawal syndrome, which can have similar psychiatric and physical symptoms as withdrawal symptoms in addiction.

Research findings:

- One study (DOMINION) identified ICDs in 14% of PD patients, with 29% of these PD patients, who have such symptoms, demonstrating at least 2 ICDs. Similar rates were reported in other studies across the world.



- Another study found that 17% of PD patients starting dopaminergic medication for the first time reported ICD symptoms during a 2 year period.
- Another study reported that 39% of patients without ICDs before starting medications, went on to develop ICDs during a 4 year period after starting dopaminergic medication.
- Another study found that 9% of PD patients using a dopamine patch reported ICDs, which usually developed 4 to 5 years after starting the medication.

Primary Etiology of ICDs:

- ICDs are more common in patients treated with dopaminergic medication, and increased risk has been associated with higher doses as well as increased receptor binding to dopamine receptors in the brain.

- Longer acting medications with continuous delivery systems, such as oral, patch or pump administrations have been associated with decreased risk for ICD.
- Other medications have been associated with ICDs, such as Amantadine and Rasagiline, which impact the dopamine system in the brain indirectly.
- Dopaminergic medication use has also been linked to ICDs in other populations, including restless leg syndrome, fibromyalgia and pituitary adenomas, suggesting that ICDs are not simply a manifestation of PD symptoms.

Risk factors associated with ICDs:

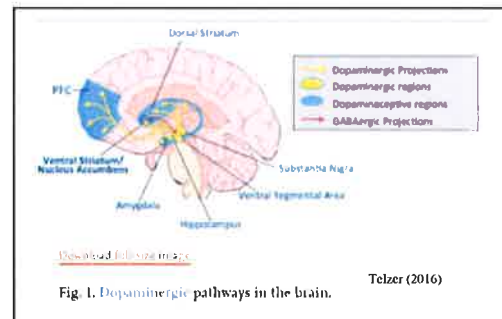
- Personal or familial history of alcoholism, gambling or impulsive personality traits
- Younger age or age of PD onset
- Being unmarried
- Past or current cigarette smoking
- Mood disorders including rapid cycling as in bipolar disorder
- Various genes have also been associated with ICDs (e.g., Taq1A, ANKK1)
- Men show more compulsive sexual behaviors while woman show more compulsive buying and binge eating

Brain Structures involved in ICDs:

- Ventral Striatum
- Prefrontal cortex (PFC)
- Anterior cingulate
- Subthalamic nucleus

Cognitive changes in PD at risk for ICDs:

- Executive abilities (e.g., inhibition, control)
- Punishment and reward learning
- Decisional impulsivity



Advances in Assessment and Management of ICDs

- ICD behaviors in PD continue to be underrecognized and undermanaged
- Routine screening is uncommon and patients may not always report symptoms
- Assessment instruments have been developed and validated, including
 - o Questionnaire for Impulsive-Compulsive Disorders in PD
 - o Questionnaire for ICDs in PD Rating Scale
 - o Ardouin Scale of Behavior in PD
 - o Parkinson's Impulse-Control Scale
- Prompt identification and treatment of the symptoms is imperative
- ICDs often resolve after reduction or discontinuation of dopaminergic medication, with increase in other PD medications
- Medications used for addiction (e.g., Naltrexone) have shown benefit in reducing ICD severity
- Cognitive Behavioral Therapy has also shown benefit in treating ICDs

- Research on DBS and ICDs remains controversial

Conclusions: Twenty Years in Hindsight

- PD medications are associated with development of ICDs
 - Up to 20% of PD patients may experience at least 1 ICD at some point
 - ICDs are declining as a result of changes in prescribing practices
 - ICDs in PD have significant overlap with addictive disorders in general
 - Despite advances in assessment, we still need to identify individuals who are at great risk of developing ICDs and develop better treatments for those affected
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