

GJBRC's Pioneering Research in Parkinson's Disease (PD)





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A brain disorder involving death/ damage to dopaminergic neurons, resulting in significant loss of dopamine release from the brain¹



Most common neurodegenerative disease, affecting 6 billion people globally



Every hour, 2 people in the UK are told by doctors that they have PD



Currently NO conclusive diagnostic test and NO cure

Investigate Non-motor Symptoms

Insomnia (Sleeping difficulty)²

• Caused by painful postures and sleep disturbed by the urge to urinate

Dysphagia (Swallowing difficulty)³

- Reduction in dopamine in the brain weakens nervous system functioning
- Result in a loss of normal muscles coordination along the oesophagus (food passageway)

Chronic pain⁴

- Caused by damages in muscle tissues and dysfunction of pain regulatory systems in the brain
- Electroencephalogram (a recording of brain's electrical activity) studies showed that PD patients have increased anticipation of pain
- Population-wide studies demonstrated a close link between pain and impulsive control behaviours, e.g. over-eating
- PD patients may develop depression and anxiety over time

Study Motor Impairments

Bradykinesia, Rigidity, & Postural instability⁵

- Damage in 2 major brain regions
 - Substantia Nigra of Basal Ganglia (Excitation centre)
 - **■** Reduce dopamine stimulation of cortex
 - Pedunculopontine Nucleus (Communication centre between Basal Ganglia & Cerebellum)
 - Reduce stimulation of cerebellum (motor control centre in the brain)
- When muscles don't receive adequate stimulation from the brain:
 - Longer response time from brain to muscle → Leads to bradykinesia (slowness of movement)
 - Reduced stimulation of muscle → Leads to rigidity
 - Increased time for brain to correct movements → Leads to postural instability (e.g. prone to fall when seated)

Improve Non-invasive Screening

Aims to detect PD before physical symptoms arise

• Allows earlier intervention, improved disease monitoring and treatment outcomes

Neuromelanin-magnetic resonance imaging (NM-MRI)⁶

- Neuromelanin: Pigmented by-product of dopamine metabolism, which accumulates over time in the brainstems of healthy people
- In PD patients, the loss of neurons in the brain leads to loss of neuromelanin

Skin swab test⁷

- Developed after Joy Milne who has a condition that makes her extremely sensitive to smell
- 1. Collect sebum (lipid-rich biofluid on the skin) from upper back and forehead of the individual
- 2. Identify compounds in the sebum with biochemical tools
- 3. Compare PD patients' sebum composition with that of undiseased people and develop it into diagnostic tools

Improve Treatments

Deep Brain Stimulation (DBS)⁸

- Surgical therapy where electric currents are passed into the subthalamic nucleus (a movement regulation region in the brain)
- Improves both motor and non-motor symptoms, thus enhances quality of life
- Effects proven by multiple clinical trials with over 6 months monitoring

Parkinson's KinetiGraph⁹

- A small watch-like device worn on the wrist to collect data on movements, daytime sleepiness and night-time sleep disturbances
- Help clinicians and research team evaluate how medications or DBS treatments affects symptoms → Better management of symptoms

Images from flaticon.com and storyset.com

(1) Parkinson's Disease [Internet]. NHS]. Available from: https://www.nhs.uk/conditions/parkinson's disease/. (2) Kharkar S, Ellenbogen JR, Samuel M, Rizos A, Silverdale M, Chaudhuri KR, et al. Changes in parkinson's disease sleep symptoms and daytime somnolence after bilateral subthalamic deep brain stimulation in parkinson's disease. np parkinson's disease. 2018;4(1). (3) Michou E, Kobylecki C, Hamdy S. Dysphagia in parkinson's disease. Dysphagia in parkinson's disease. European Journal of Neuroscience. 2019;51(2):611–27. (5) Jenkinson N, Nandi D, Muthusamy K, Ray NJ, Gregory R, Stein JF, et al. Anatomy, physiology, and pathophysiology of the Pedunculopontine nucleus. Movement Disorders. 2028;24(3):319–28. (6) Xing Y, Sapuan AH, Martín-Bastida A, Naidu S, Tench C, Evans J, et al. neuromelanin-mri to quantify and track nigral depigmantation in parkinson's disease: A Multicenter Longitudinal Study using template-based standardized analysis. Movement Disorders. 2022;37(5):1028–39. (7) Sinclair E, Trivedi DK, Sarkar D, Walton-Doyle C, Milne J, Kunath T, et al. Metabolomics of sebum reveals lipid dysregulation in parkinson's disease. Nature Communications. 2021;12(1). (8) Dafsari HS, Ray-Chaudhuri K, Ashkan K, Sachse L, Mahlstedt P, Silverdale M, et al. Beneficial effect of 24-month bilateral subthalamic stimulation on quality of sleep in parkinson's disease. Journal of Neurology. 2020;267(6):1830–41. (9) Noui Y, Silverdale MA, Evans J, Partington-Smith L, Kobylecki C. Parkinson's kinetigraph in the selection of levodopa-carbidopa intestinal gel for motor fluctuations refractory to deep brain stimulation. Journal of Movement Disorders. 2021;14(3):239–41. 10