What is PD?

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Will discuss:

1. Where PD starts & how it evolves
2. How is PD diagnosed
3. Search for new ways to diagnose it earlier
- ≈ 50% neuron loss in the substantia nigra (SN) at dx
- ≈ 80% striatal dopamine is lost by dx
REM-Sleep Behavior Disorder: Enactment of dreams

From the internet
Synuclein pathology in gut

- ≈50% neuron loss in the substantia nigra @ dx
- ≈80% striatal dopamine is lost by dx

Diagnosis 4 to ≥ 15 Years

Striatal dopamine

100%
80%
60%
40%
20%
0%

Stages I-II
Stages III-IV
Stages V-VI

α-SYNUCLEIN

TRENDS in Neurosciences
Non-Motor PD Symptoms

Are important

- Olfactory loss
- Constipation
- Enacting dreams
- Depression/Anxiety
- Cognitive disturbances
- Insomnia
- Decrease in blood pressure when standing

May be more bothersome than the motor problems!
Previous estimates based on:

• age,
• sex &
• environmental risk factors

+  

• Diagnostic Markers
  • Olfactory loss
  • Enacting dreams
  • Depression ± Anxiety
  • Constipation
  • Neuroimaging
PD Stages

Preclinical
- Abnormal Imaging
- Other Biomarkers?
- Genetic Factors?

Prodromal
- +
- Hyposmia
- iRBD
- Constipation
- Depression

PD Early
- +
- Slowness
- Stiffness
- Tremor

PD Advanced
- +
- Dyskinesia
- Cognitive Problems
- Autonomic Problems
Relevance: Gut Microbiome
How does PD spreads?

Information is transmitted as a template that changes the configuration of normal proteins in preserved cells.

From Marc Diamond
How PD spreads?

Propagation of Abnormal Configuration

From Marc Diamond
Definition of Parkinsonism

- Slowness and:
  - Tremor
  - Stiffness

No longer Postural Instability
Supportive Criteria

1. Dramatic response to dopaminergic therapy
2. Rest tremor
3. L-dopa induced dyskinesia
4. Olfactory loss or cardiac sympathetic denervation on MIBG
Need to exclude:
Drug Induced Parkinsonism

Dopamine blockers
Neuroleptics
Antiemetics

Medications that lower L-dopa)
Rapid progression: wheelchair sign
What investigations?

- Olfaction
- Neuropsychological testing
- Other problems
- Imaging
- Genetics
Biomarkers can help us make an earlier diagnosis:

Deposits of alpha-synuclein

Colon biopsies?

Submandibular gland biopsies?

Figure 1. Needle biopsy of the submandibular gland
Conclusion

1. PD starts in the **gut and olfactory bulb**—not in the substantia nigra, spreads following neuronal pathways explaining **initial Non-Motor symptoms** and possible new therapeutic approaches

2. Changed in how PD is defined—**Prodromal PD**

3. Search for new ways to diagnose it earlier: biopsies of the colon, submandibular gland, etc

4. New prospects for treatment: antibodies against synuclein
UCSD NPF COE Staff
Thank you!

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