

# Prodromal – Very Early Symptoms of PD

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PATIENT EDUCATION SERIES 10/14/2021

# Prodromal PD

- ▶ Definition: The stage at which individual does not meet criteria for PD diagnosis (pre-diagnosis), with higher than normal risk for developing PD, and has non-motor symptoms that are impactful to quality of life. This is also referred to as the long latent phase of PD.
- ▶ Does not fulfill diagnostic criteria – bradykinesia + 1 other motor sign
  - ▶ Motor features: Bradykinesia (slowness of movement), rigidity, tremor, and postural instability.

# Clinical non-motor markers of prodromal PD

The list of prodromal markers have now been expanded:

- ▶ Hyposmia (diminished or loss of sense of smell)
- ▶ Constipation
- ▶ REM sleep behavior disorder (RBD) (active dreams)
- ▶ Mood disorders (anxiety/depression)
- ▶ Erectile dysfunction
- ▶ Somnolence
- ▶ Orthostatic hypotension
- ▶ Urinary dysfunction
- ▶ Abnormal DAT/SPECT imaging study
- ▶ Cognitive dysfunction

# Hyposmia

- ▶ Anosmia - Loss of smell;  
Hyposmia – impaired sense of smell.
- ▶ Most common, best characterized non-motor feature.
- ▶ 80% of patients with Hyposmia have Lewy body pathology.
- ▶ Standard tests such as 12-item Brief Smell Identification Test (B-SIT).
- ▶ Affects taste, weight loss.



# Constipation

- ▶ Defined as infrequent stools, difficulty with stool passage.
- ▶ First and most common disabling non-motor symptom during prodromal phase.
- ▶ Pathological alpha-synuclein inclusions can be detected in the GI tract up to 20 years before diagnosis.
- ▶ Disabling non-motor symptom because it causes bloating, discomfort, and nausea.
- ▶ Honolulu – Asia Aging Study – symptoms to development of PD symptoms ~ 10 years, diagnosis ~ 12 years.

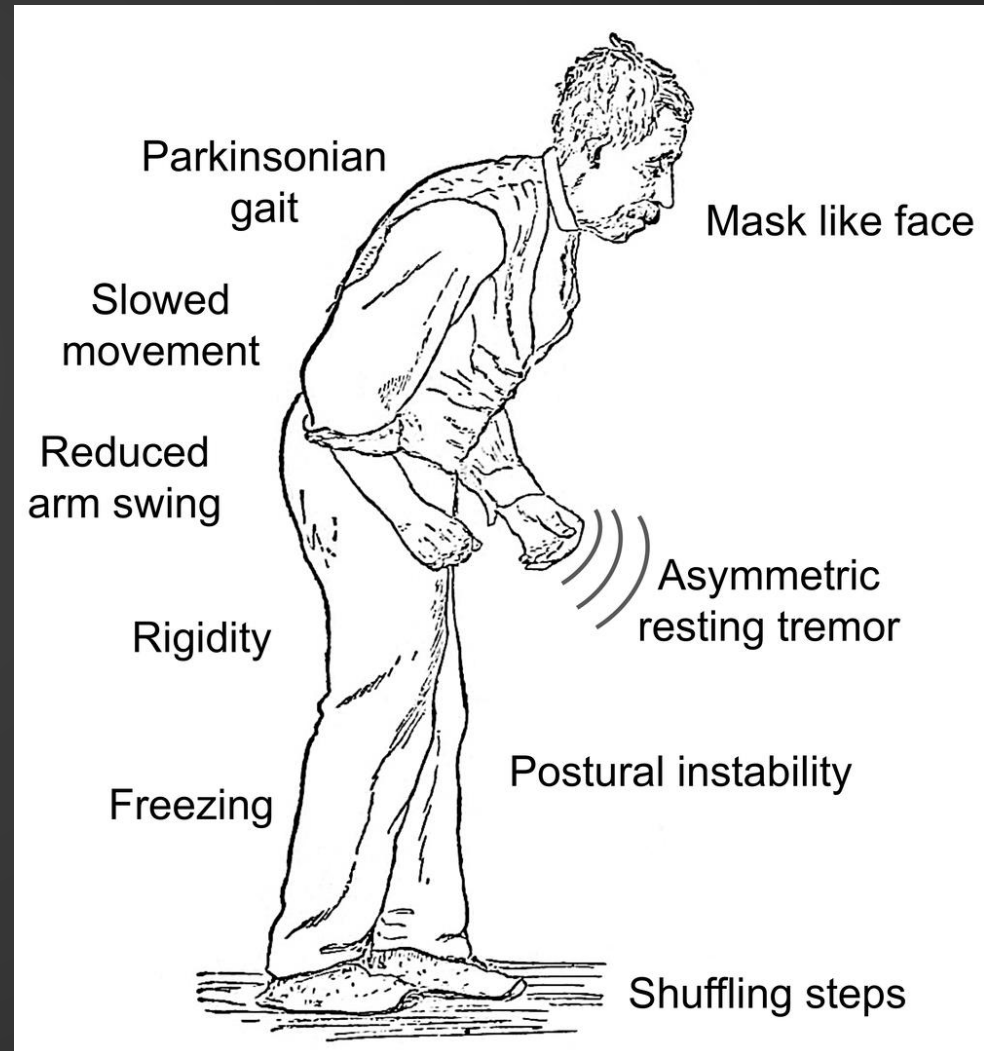
# Rem Behavior Disorder (RBD)

- ▶ Characterized by dream enacting behavior, vocalizations, limb movements, usually related to unpleasant dreams.
- ▶ Loss of REM sleep muscle atonia
- ▶ Marker for prodromal degeneration or secondary to patients with PD.



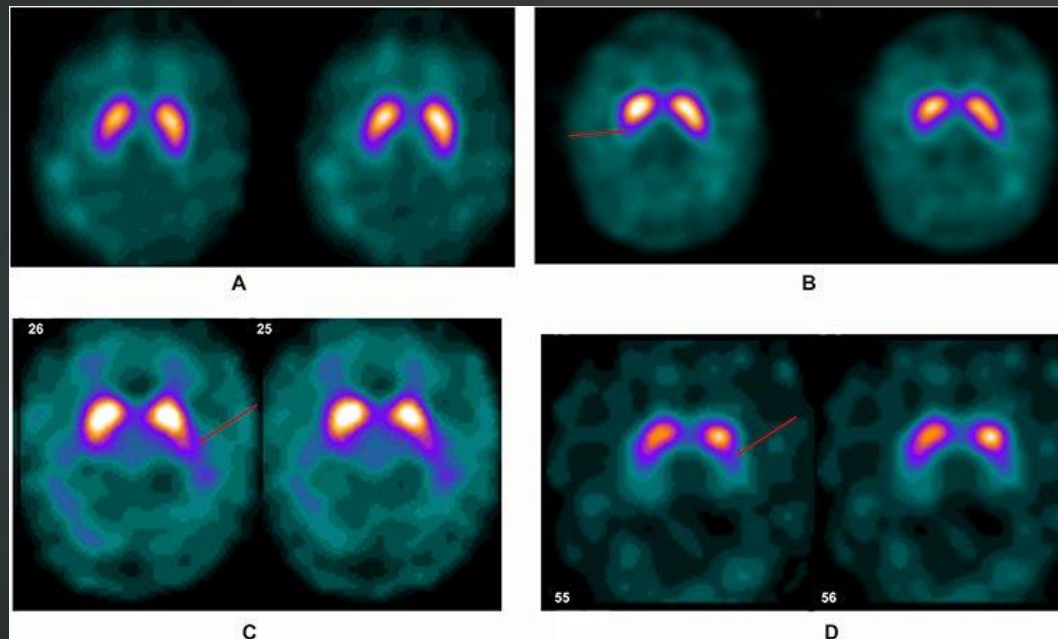
# Motor markers

- ▶ Unified Parkinson's disease Rating Scale
- ▶ Abnormal 4.5 years before diagnosis
- ▶ First signs – voice and face akinesia
- ▶ Later signs –
  - ▶ Rigidity
  - ▶ gait abnormalities
  - ▶ limb bradykinesia
  - ▶ tremor



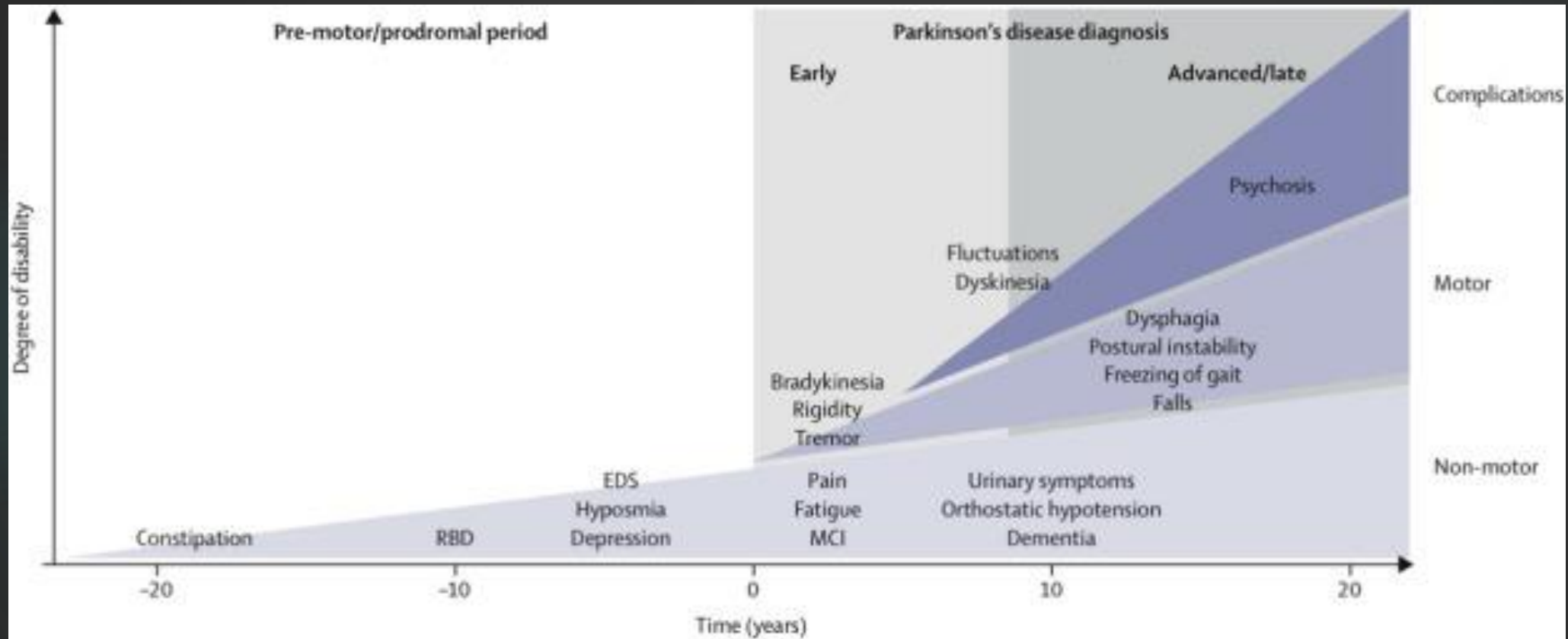
# Imaging markers – DAT/SPECT scan

- ▶ Dopamine transporter scan to assess for striatal dopaminergic uptake
- ▶ Decreased uptake in patients with PD



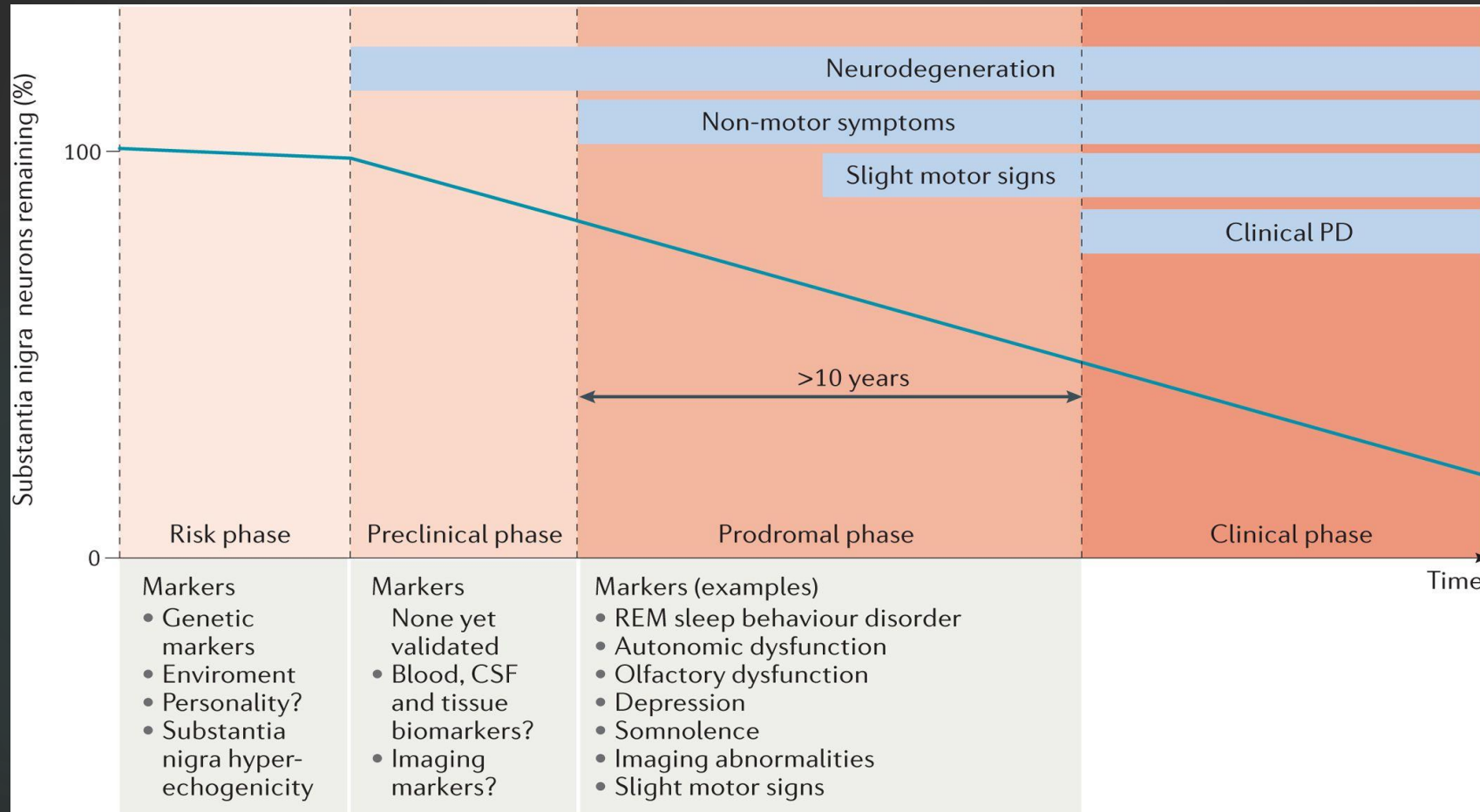


# Clinical PD Pathway and Determinant of Risks

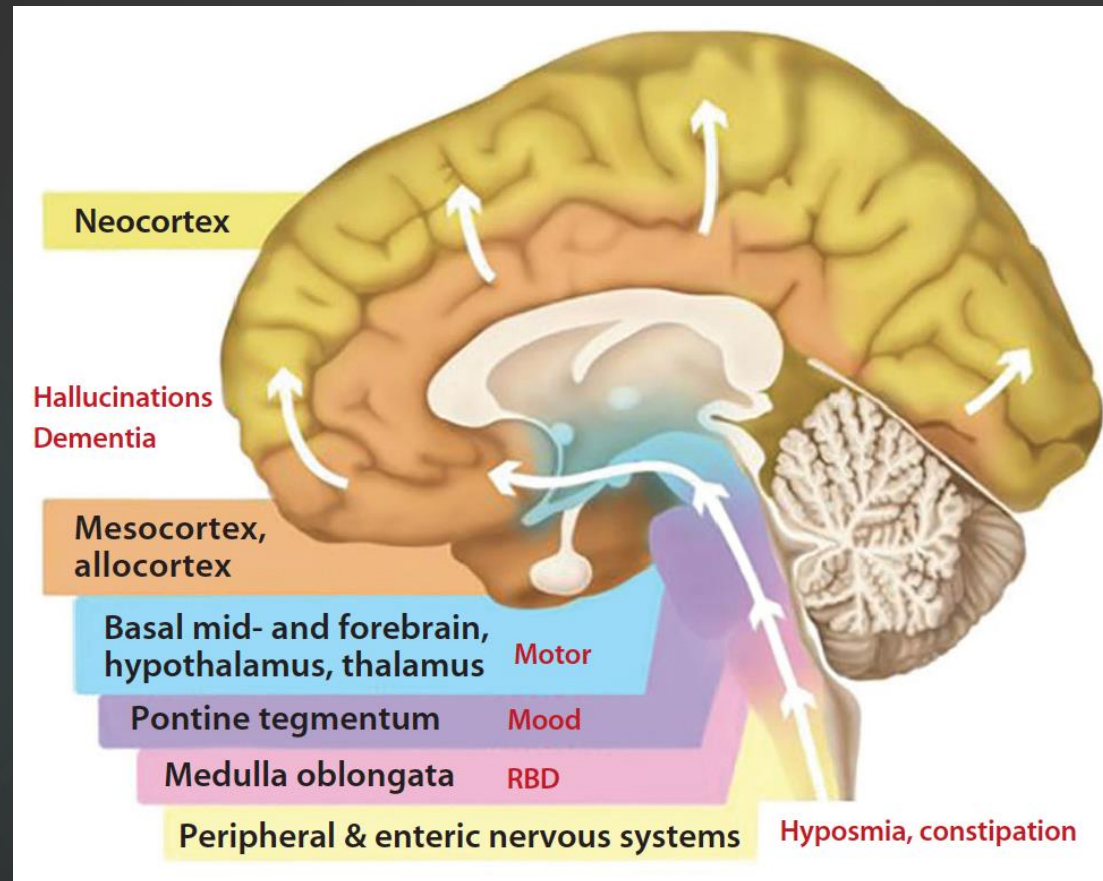


(Di Virgilio, 2016)

# Pre-diagnostic phase of PD



# Course of progression and Impact



(Mantri & Morley , 2016)

# What does all this mean to you?

- ▶ Early recognition helps identify patients for clinical trials for neuroprotective therapies.
- ▶ Wide therapeutic index window
- ▶ No symptomatic medications
- ▶ Improves prognosis counseling
- ▶ Clinical trials for drug therapy with hope to preserve neuronal tissue (possible interventions for disease modifying therapy)
  - ▶ [Clinicaltrials.gov](http://Clinicaltrials.gov)
- ▶ Consideration for dopaminergic therapy
- ▶ Neuro-rehabilitation services (PT,OT,ST) is valuable in preservation of motor function and independence

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