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NEURO-PSYCHIATRIE

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UZ GENT

Evolving concepts Parkinson's Disease

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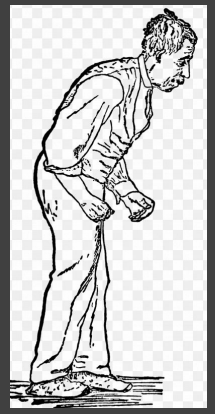


Evolving concepts

- Non-motor symptoms as important determinants of QoL
- Early and premotor signs
- More than just dopamine
- Away from the brain ?

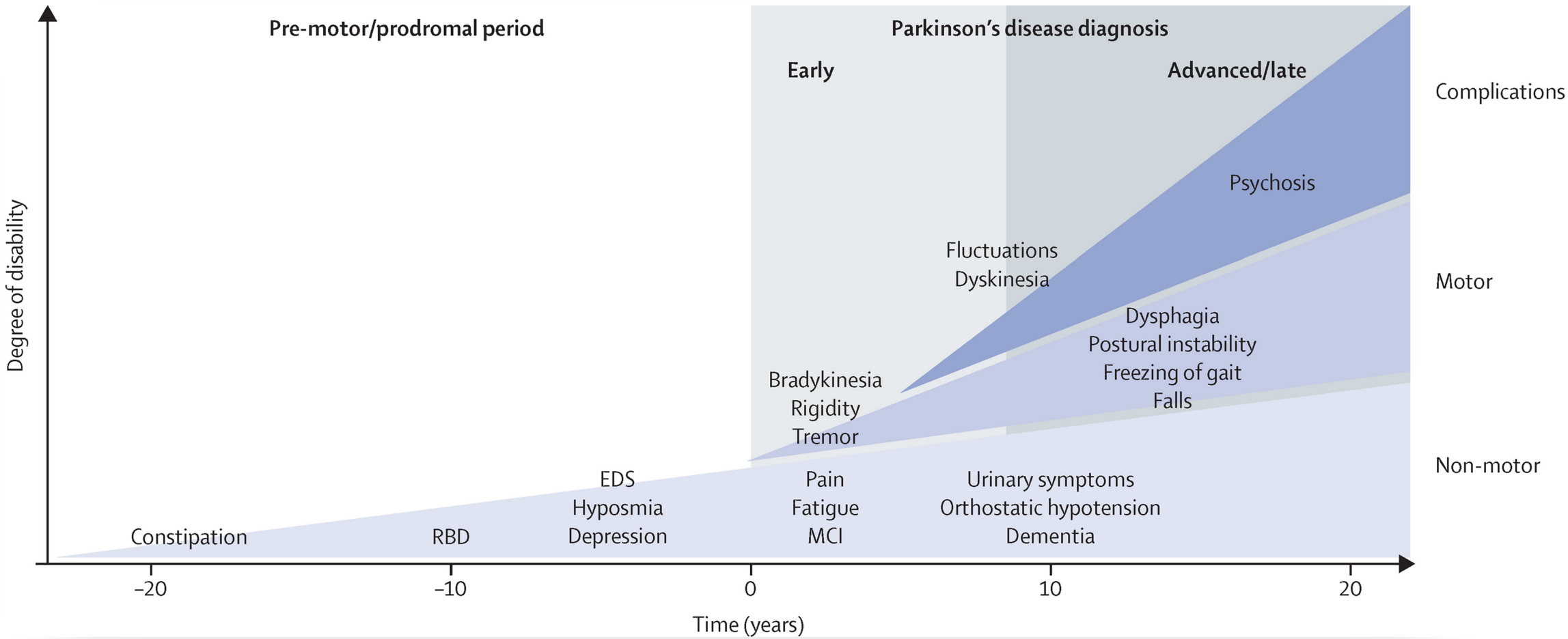
Motor symptoms

- Hypokinesia/bradykinesia/akinesia
- Cogwheel rigidity
- Resting tremor
- Postural changes

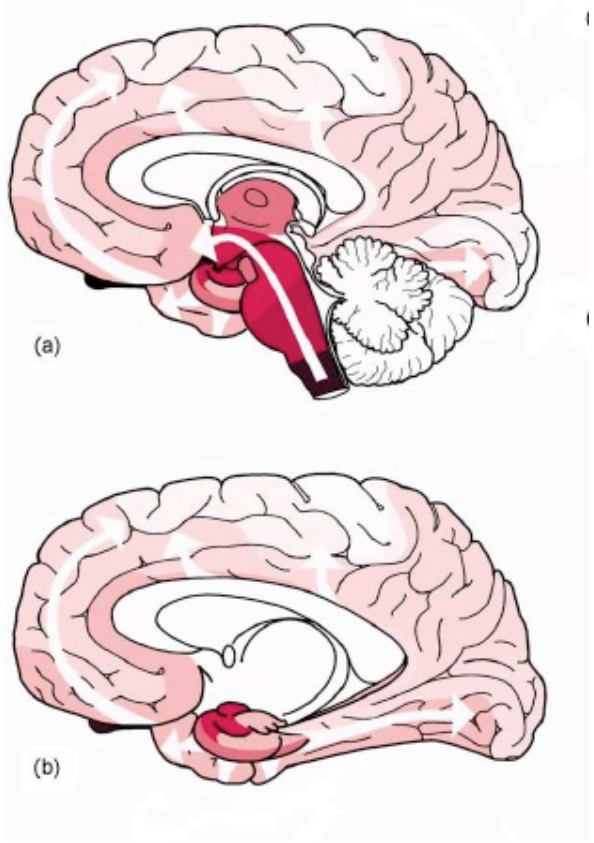
Non-motor symptoms

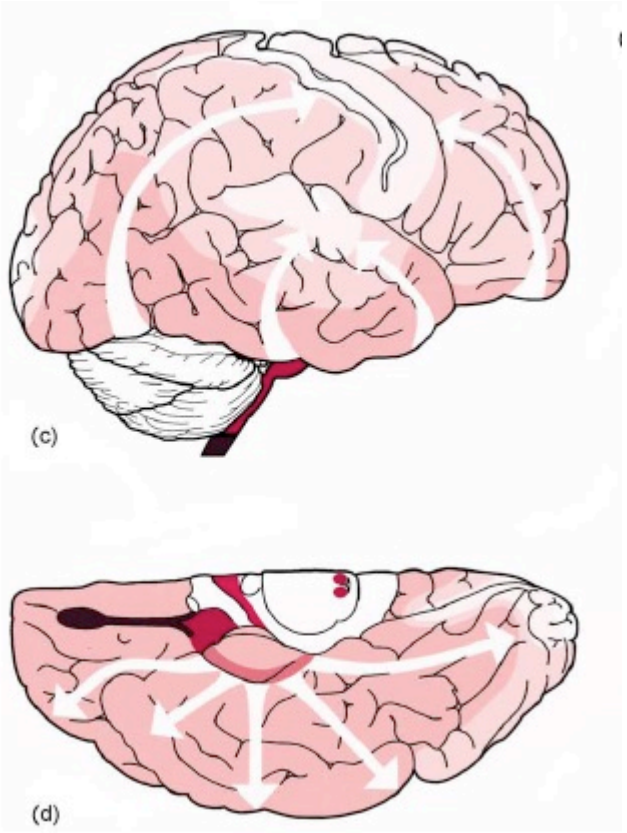
- Autonomous dysfunction: constipation, genito-urinary problems, hypotension, sweating
- Cognitive and behavioral disorders: depression, apathy, memory problems, executive dysfunction,…
- Sensory problems: paresthesia, pain, cramps
- Sleeping disorders: sleep fractionation, REM sleep behaviour disorder, fatigue and somnolence

Evolution of symptoms

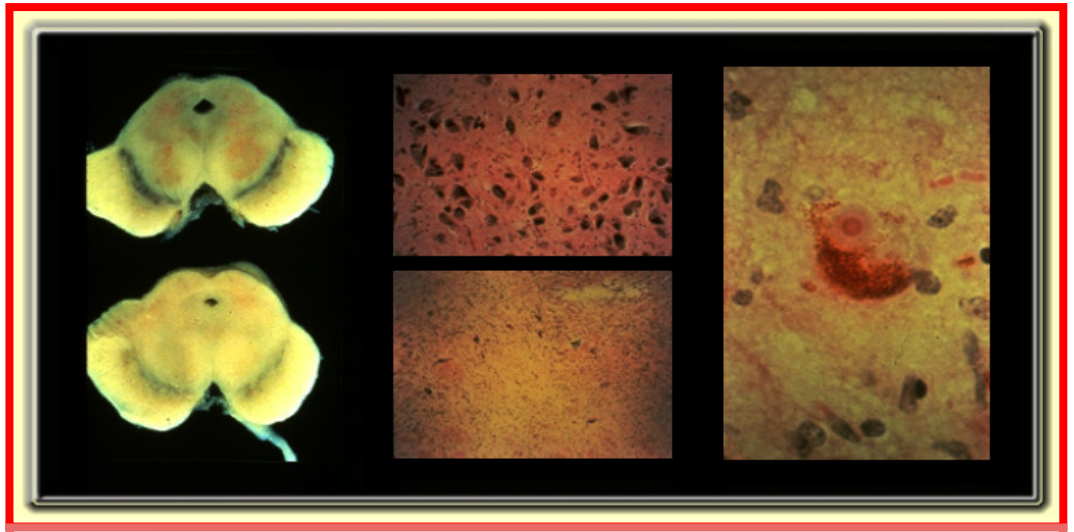


Evolution of synuclein pathology of PD





Substantia nigra degeneration



Progressive degeneration

Origin in extracerebral organs

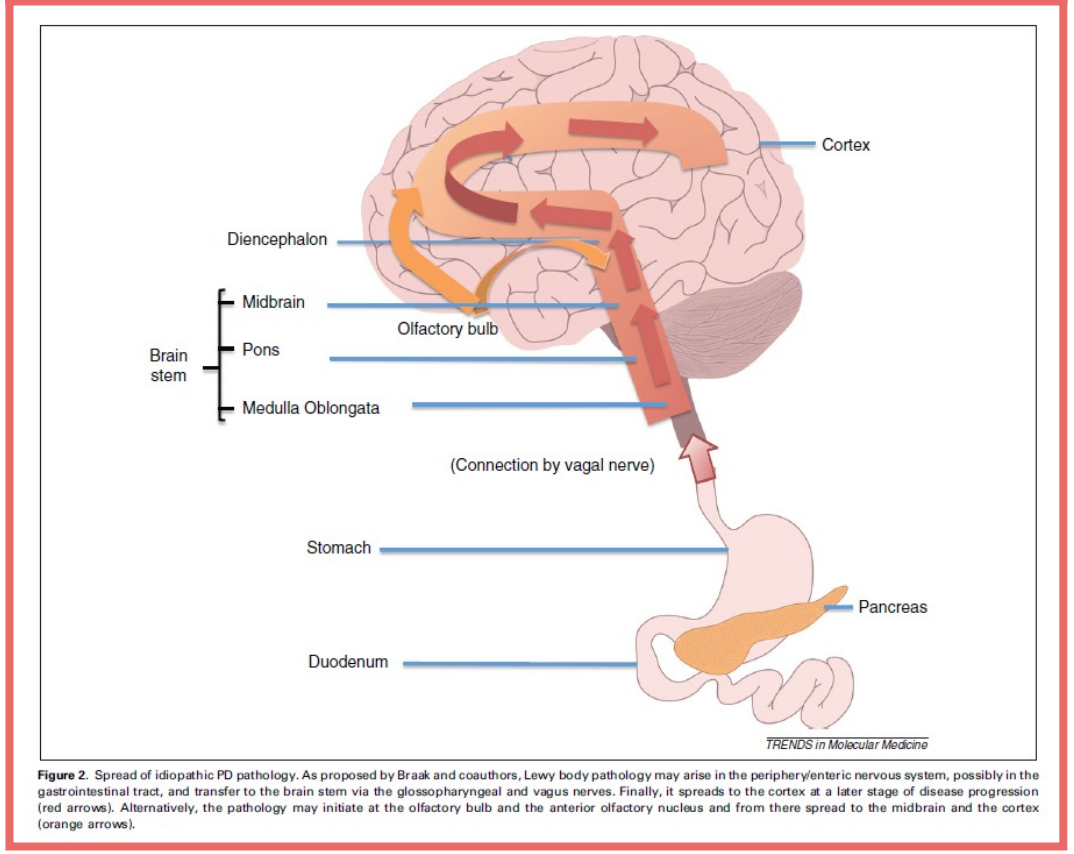
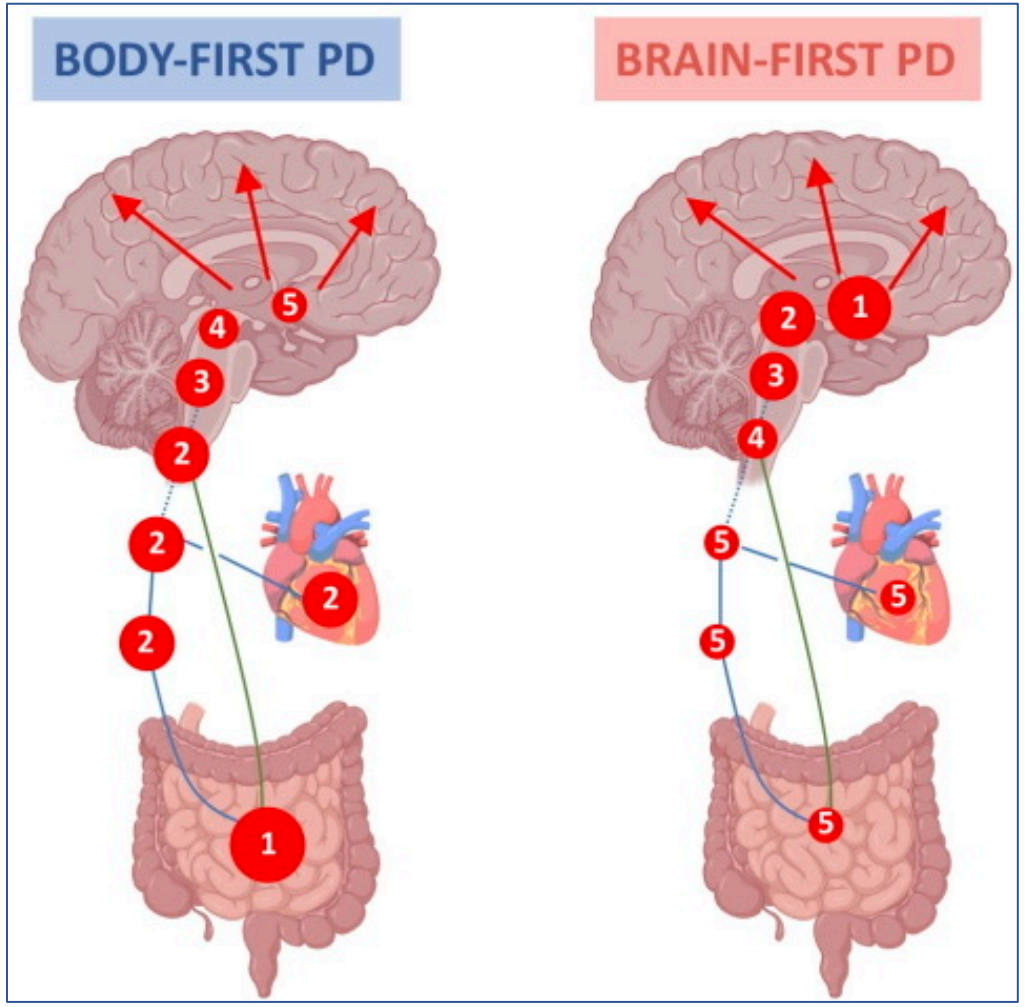
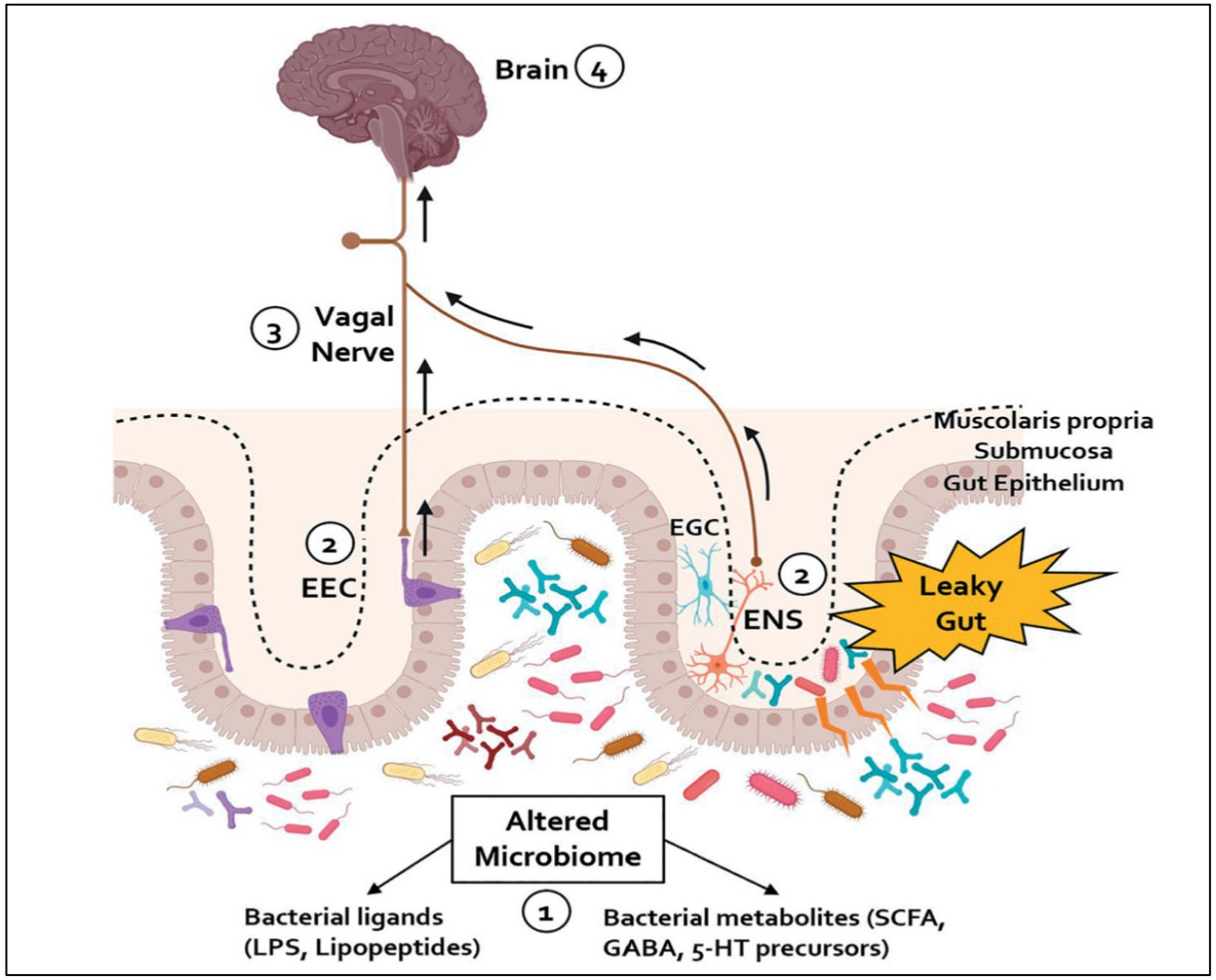
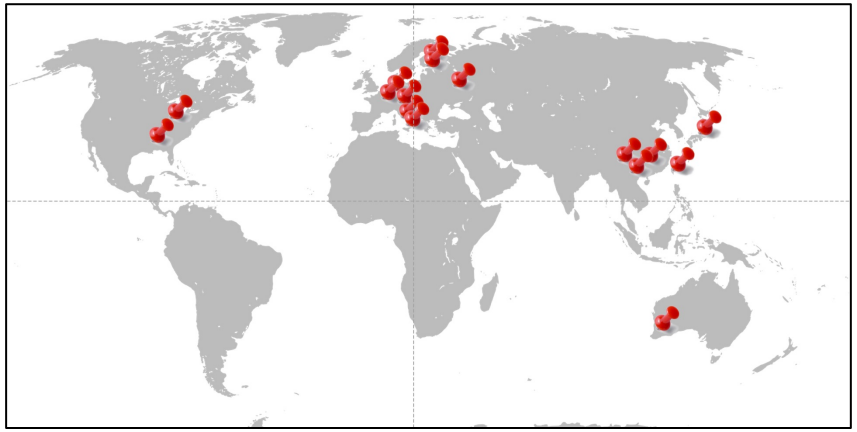


Figure 2. Spread of idiopathic PD pathology. As proposed by Braak and coauthors, Lewy body pathology may arise in the periphery/enteric nervous system, possibly in the gastrointestinal tract, and transfer to the brain stem via the glossopharyngeal and vagus nerves. Finally, it spreads to the cortex at a later stage of disease progression (red arrows). Alternatively, the pathology may initiate at the olfactory bulb and the anterior olfactory nucleus and from there spread to the midbrain and the cortex (orange arrows).

The gut-brain inflammatory hypothesis of PD







The gut microbiome and PD

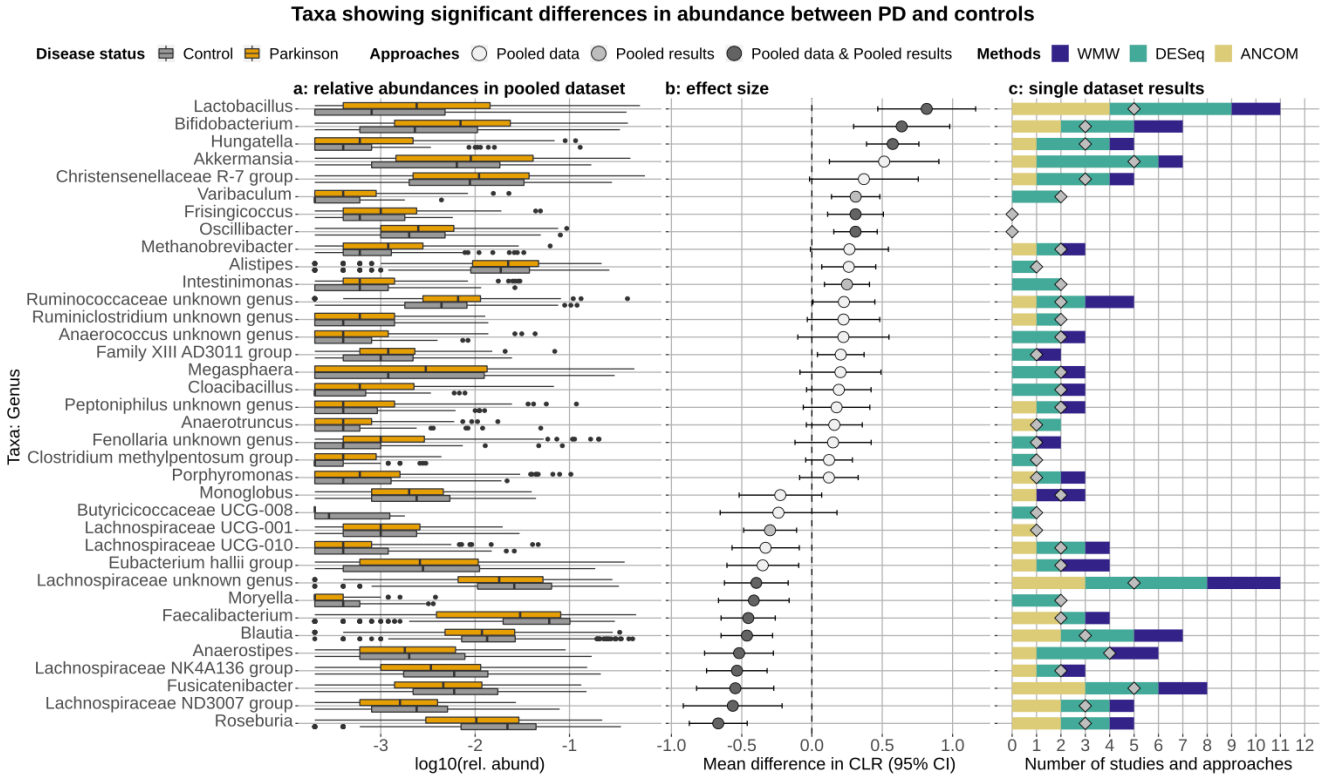


Fig. 5 Genera showing a significant difference in abundance between PD patients and controls. The relative abundances of the genera retrieved from the rarefied pooled data are reported in panel **a**. Effect sizes were estimated via the mean difference in CLR (panel **b**) using a random-effect meta-analysis approach (Pooled results approach). This was calculated for all taxa resulting differentially abundant in the Pooled results or Pooled data approaches. The color of the dots indicates which of the two above approaches detected the taxa differentially abundant. Taxa more abundant in controls have an effect size shifted to the left, whereas taxa more abundant in PD have an effect size shifted to the right. Panel **c** shows the number of times each genus was detected differentially abundant between PD patients and control samples across studies (diamonds) and approaches (bars). We used ten studies and three approaches, hence the maximum number of times a taxon can be detected differentially abundant is 30.

ARTICLE OPEN

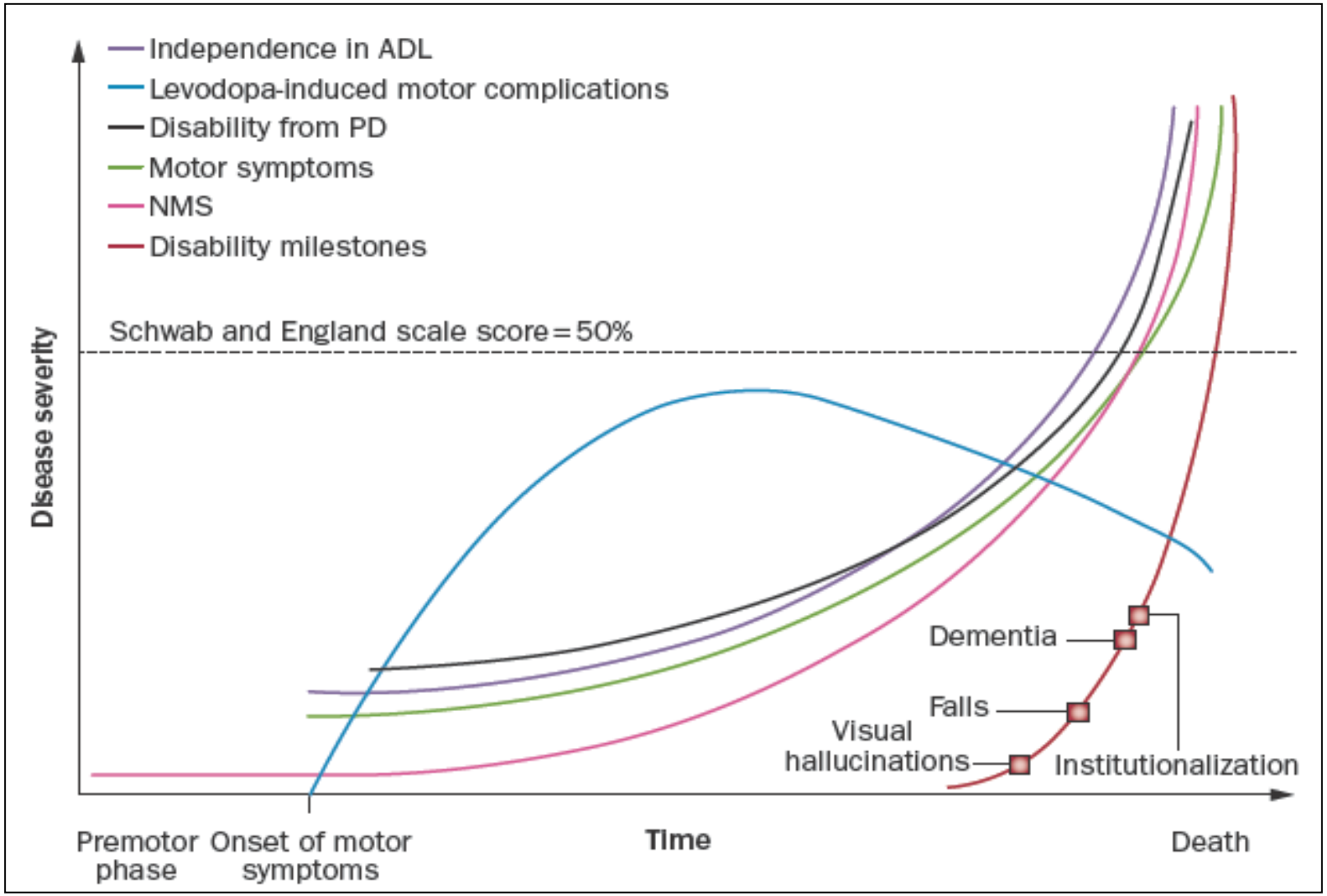
Check for updates

Meta-analysis of the Parkinson's disease gut microbiome suggests alterations linked to intestinal inflammation

Stefano Romano[1]✉, George M. Savva[1], Janis R. Bedarf[1,2], Ian G. Charles[1,3], Falk Hildebrand[1,4]✉ and Arjan Narbad[1]

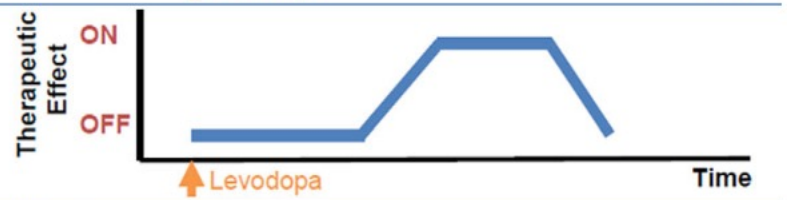
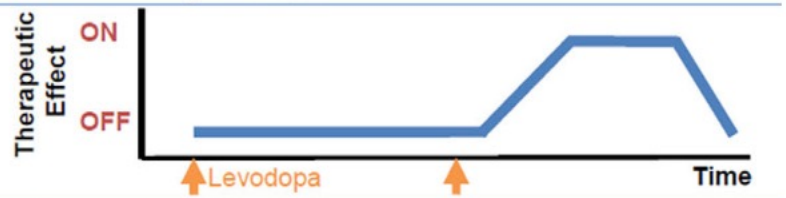
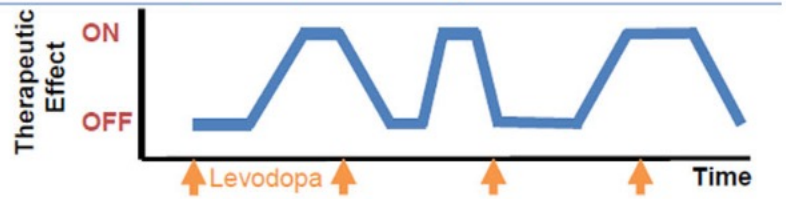
npj Parkinson's Disease (2021)7:27 ; https://doi.org/10.1038/s41531-021-00156-z

Evolution of symptoms requires a multi- or rather interdisciplinary approach



Coelho et al 2012 *Nat. Rev. Neurol.* 8, 435–442

Classification of levodopa-related motor fluctuations in PD

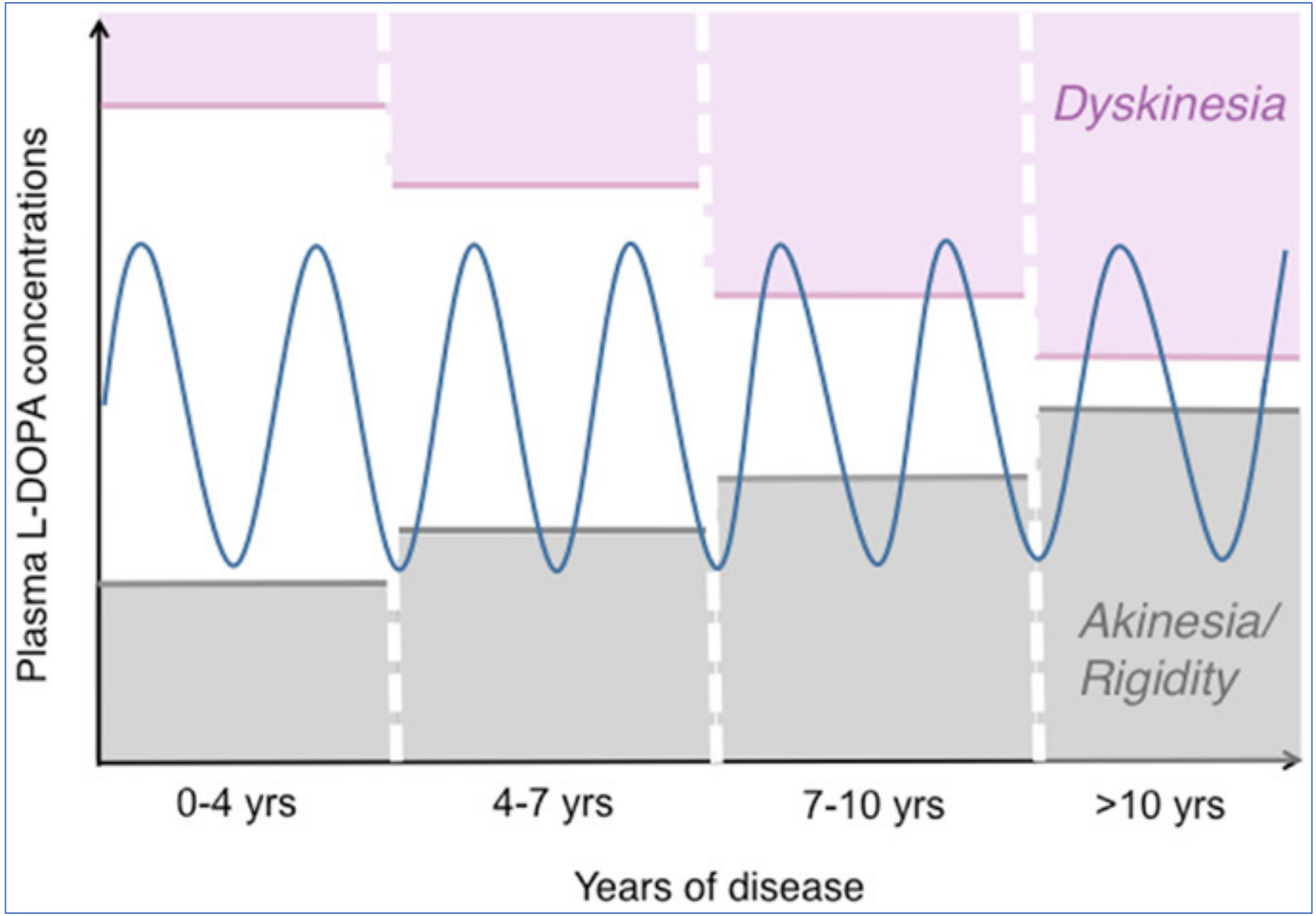
Clinical pattern	Mechanism	
Wearing-off	Levodopa – half-life Pre-synaptic storage	
Delayed-on	Gastric emptying Intestinal absorption	
Dose-failures (No-ON)	Gastric emptying Intestinal absorption Blood–brain barrier transport	
Random ON-OFF	Striatal Pharmacodynamic Changes	

REVIEW

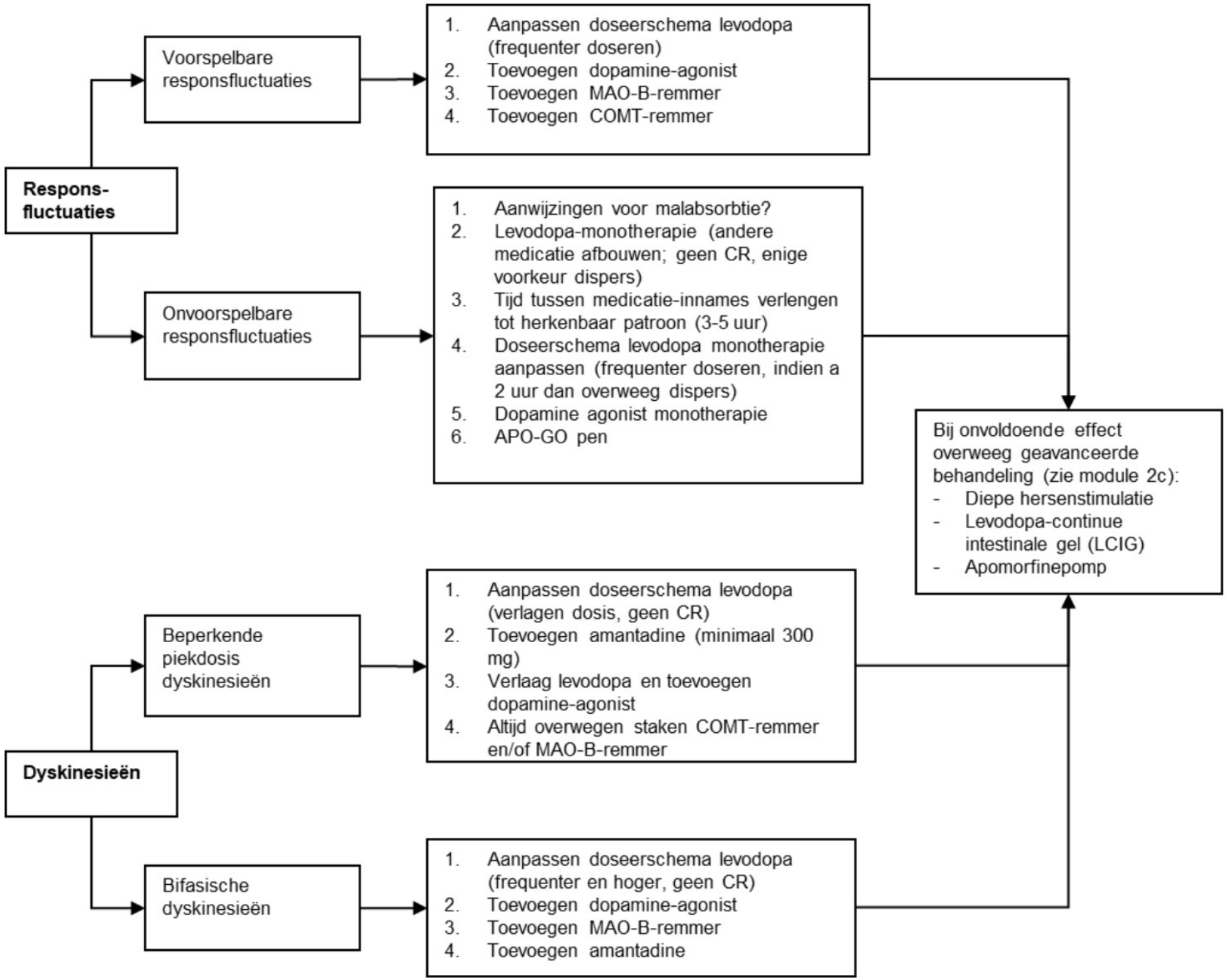
CME

Motor and Nonmotor Complications of Levodopa: Phenomenology, Risk Factors, and Imaging Features

K. Ray Chaudhuri, DSc,[1]* Werner Poewe, PhD,[2] and David Brooks, DSc[3]


Plasma L-DOPA concentrations
Dyskinesia
Akinesia/
Rigidity
0-4 yrs
4-7 yrs
7-10 yrs
>10 yrs
Years of disease

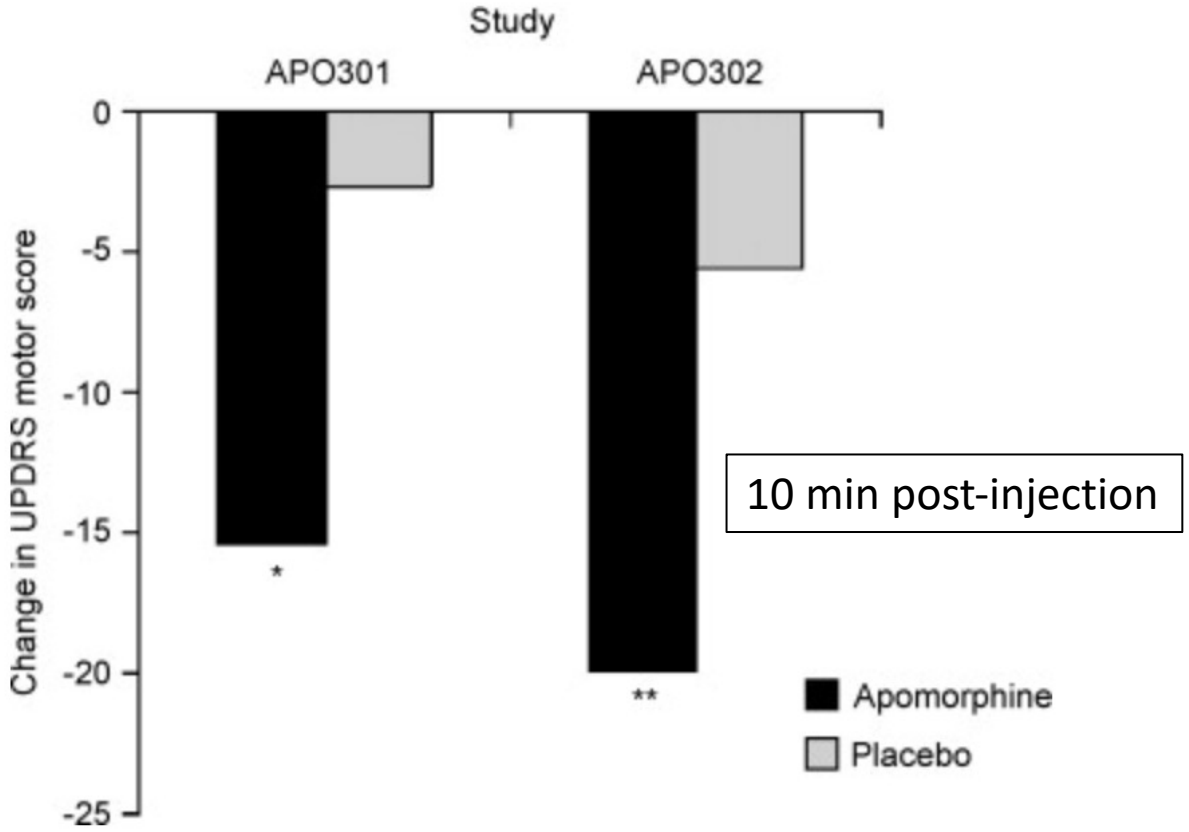
Flowchart


Respons-fluctuaties
Voorspelbare responsfluctuaties
1. Aanpassen doseerschema levodopa (frequenter doseren)
2. Toevoegen dopamine-agonist
3. Toevoegen MAO-B-remmer
4. Toevoegen COMT-remmer
Onvoorspelbare responsfluctuaties
1. Aanwijzingen voor malabsorbtie?
2. Levodopa-monotherapie (andere medicatie afbouwen; geen CR, enige voorkeur dispers)
3. Tijd tussen medicatie-innames verlengen tot herkenbaar patroon (3-5 uur)
4. Doseerschema levodopa monotherapie aanpassen (frequenter doseren, indien a 2 uur dan overweeg dispers)
5. Dopamine agonist monotherapie
6. APO-GO pen
Dyskinesieën
Beperkende piekdosis dyskinesieën
1. Aanpassen doseerschema levodopa (verlagen dosis, geen CR)
2. Toevoegen amantadine (minimaal 300 mg)
3. Verlaag levodopa en toevoegen dopamine-agonist
4. Altijd overwegen staken COMT-remmer en/of MAO-B-remmer
Bifasische dyskinesieën
1. Aanpassen doseerschema levodopa (frequenter en hoger, geen CR)
2. Toevoegen dopamine-agonist
3. Toevoegen MAO-B-remmer
4. Toevoegen amantadine
Bij onvoldoende effect overweeg geavanceerde behandeling (zie module 2c):
- Diepe hersenstimulatie
- Levodopa-continue intestinale gel (LCIG)
- Apomorfinepomp

”invasive” approaches to advanced PD

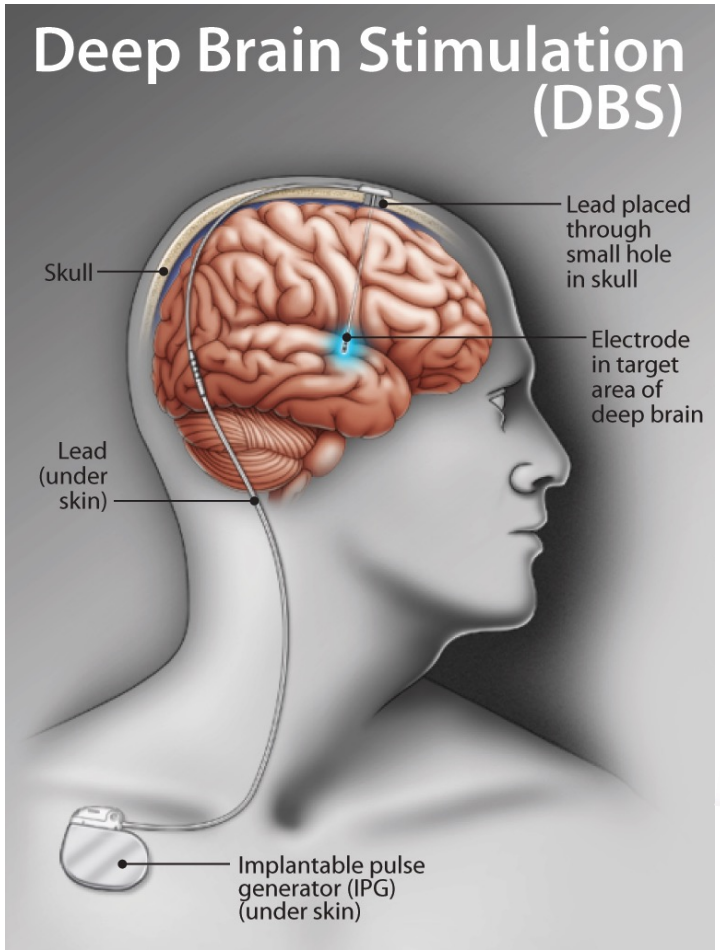
- Subcutaneous apomorphine as a rescue treatment for off-episodes
- Deep brain stimulation
- Continuous intraduodenal administration of levodopa (Duodopa/Lecigimon)

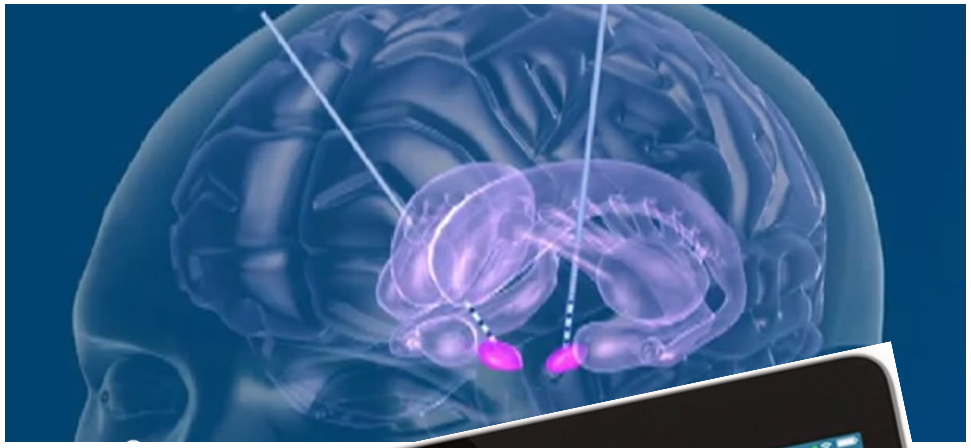
Apomorphine pen (Apo-Go)



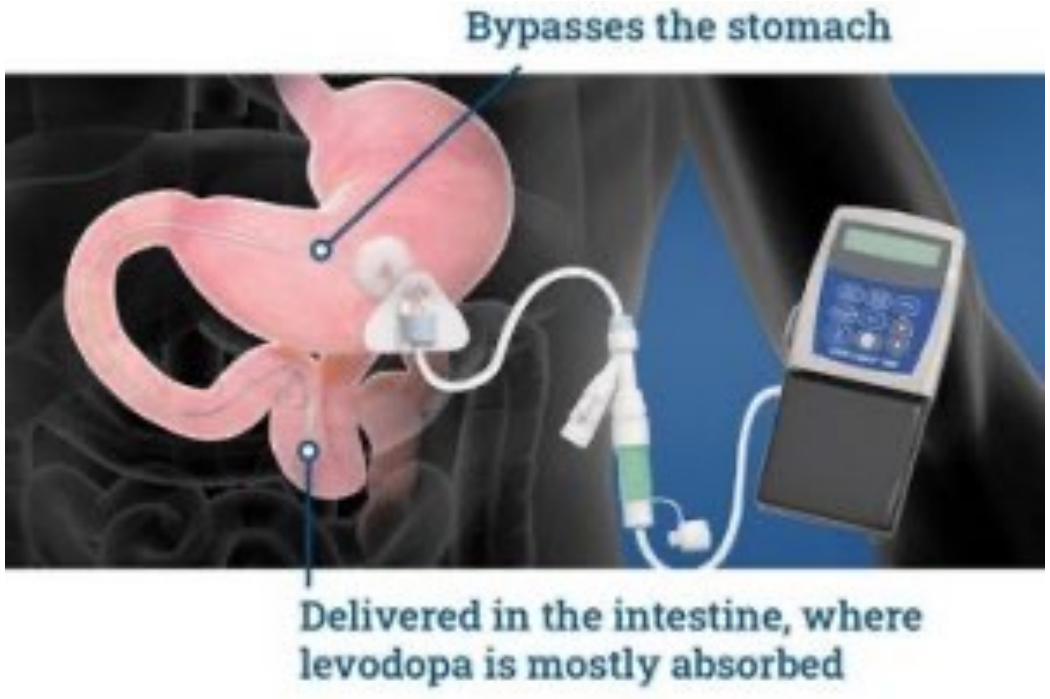
10 min post-injection

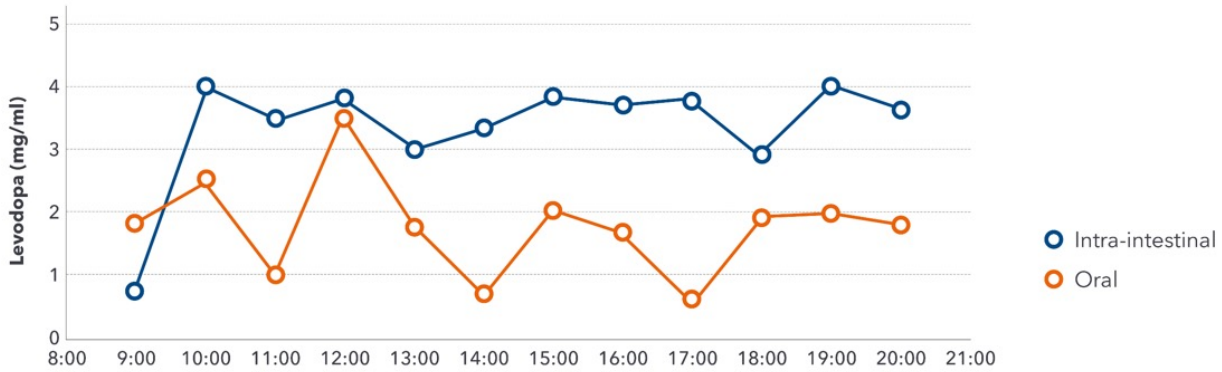
Deep Brain Stimulation





Duodopa/Lecigimon





Any questions ?