PARKINSON DISEASE: LATEST DEVELOPMENTS

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February 13, 2025

UAB HEERSINK SCHOOL OF MEDICINE
The University of Alabama at Birmingham

DISCLOSURES

- Dr. Standaert has served as a paid consultant to these companies within the last 12 months:
  - Abbvie Inc.
  - Curium Pharma
  - CVS/Pharmacy
  - Eli Lilly
  - F. Hoffman La Roche
  - Sanofi-Aventis Research and Development (DSMB member)
  - Alnylam Pharmaceuticals (DSMB member)
  - Theravance, Inc. (DSMB member)

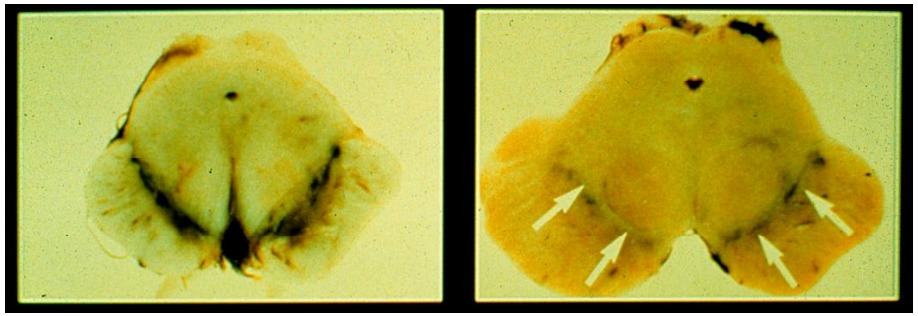
HOT TOPICS IN PD

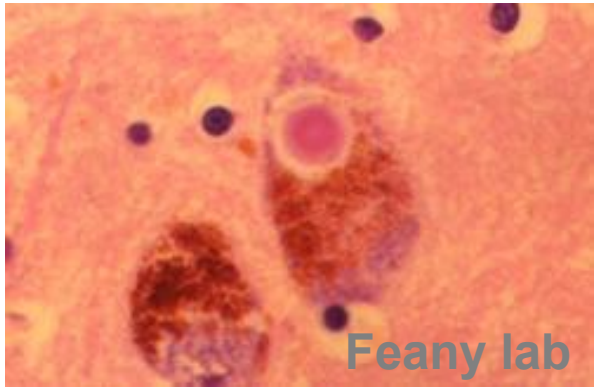
- Diagnosing PD
  - Seeding assays
  - Imaging
  - Staging
- Preventing PD – environmental toxins
- Search for neuroprotection from PD
- New approaches for treating PD symptoms

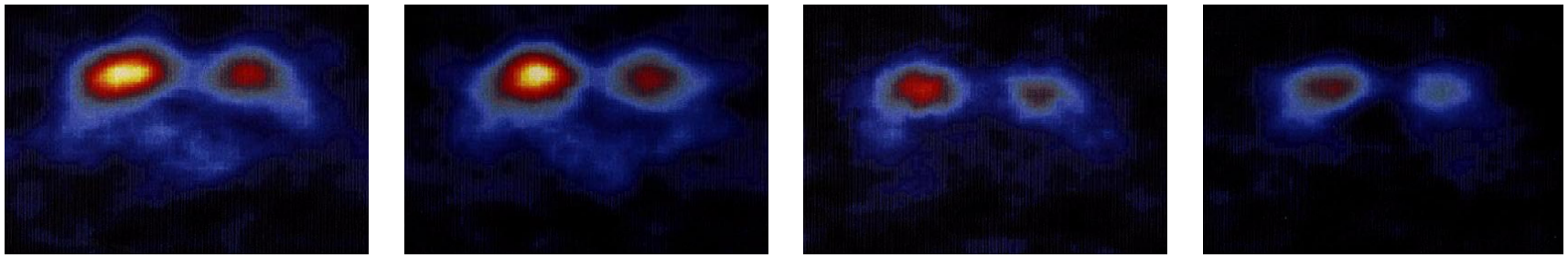
PARKINSON'S:
A QUICK PRIMER

CLASSICAL FEATURES OF PARKINSON DISEASE

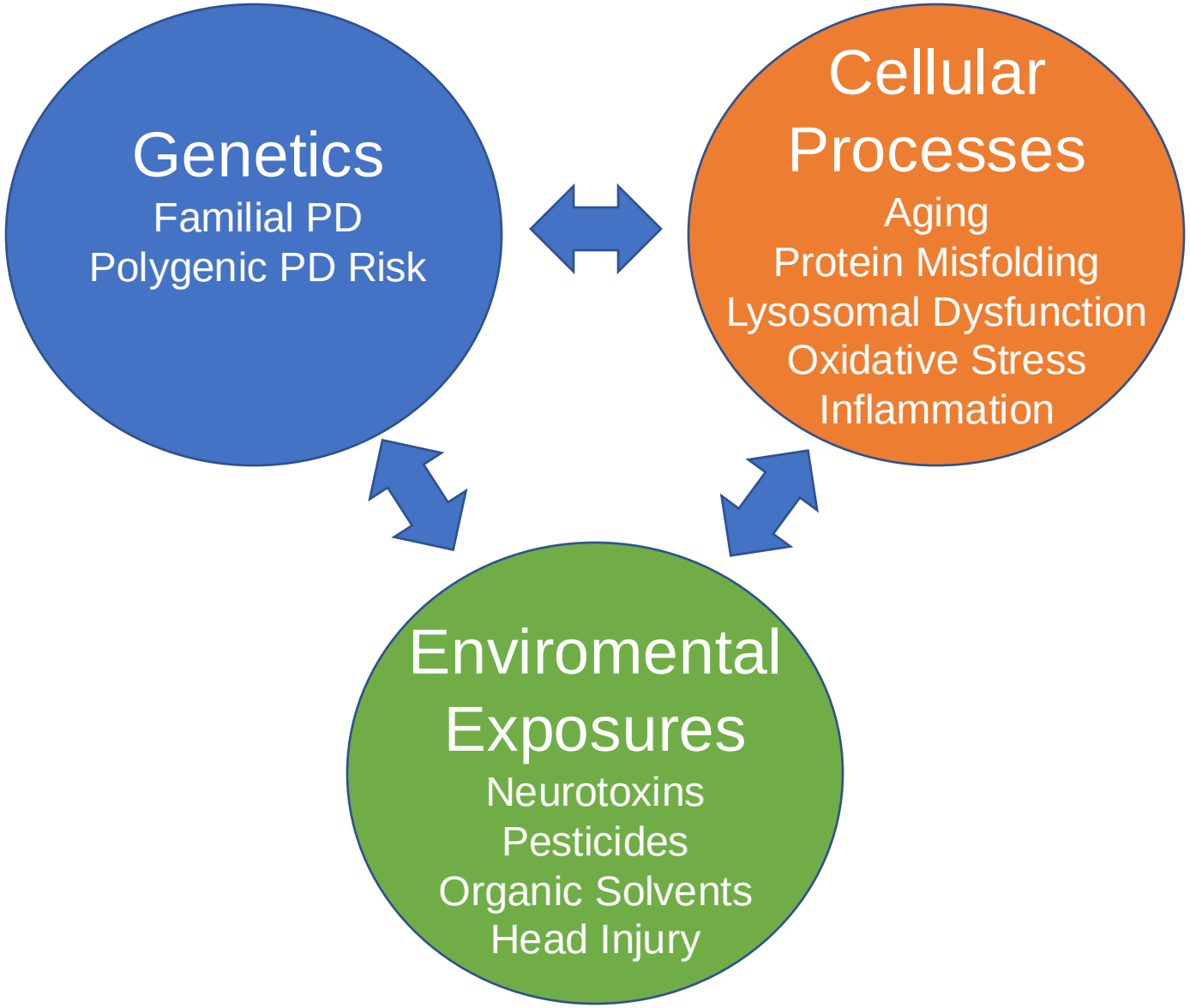
- Rest Tremor
- Bradykinesia
- Rigidity
- Postural Imbalance







WHAT CAUSES PARKINSON DISEASE?

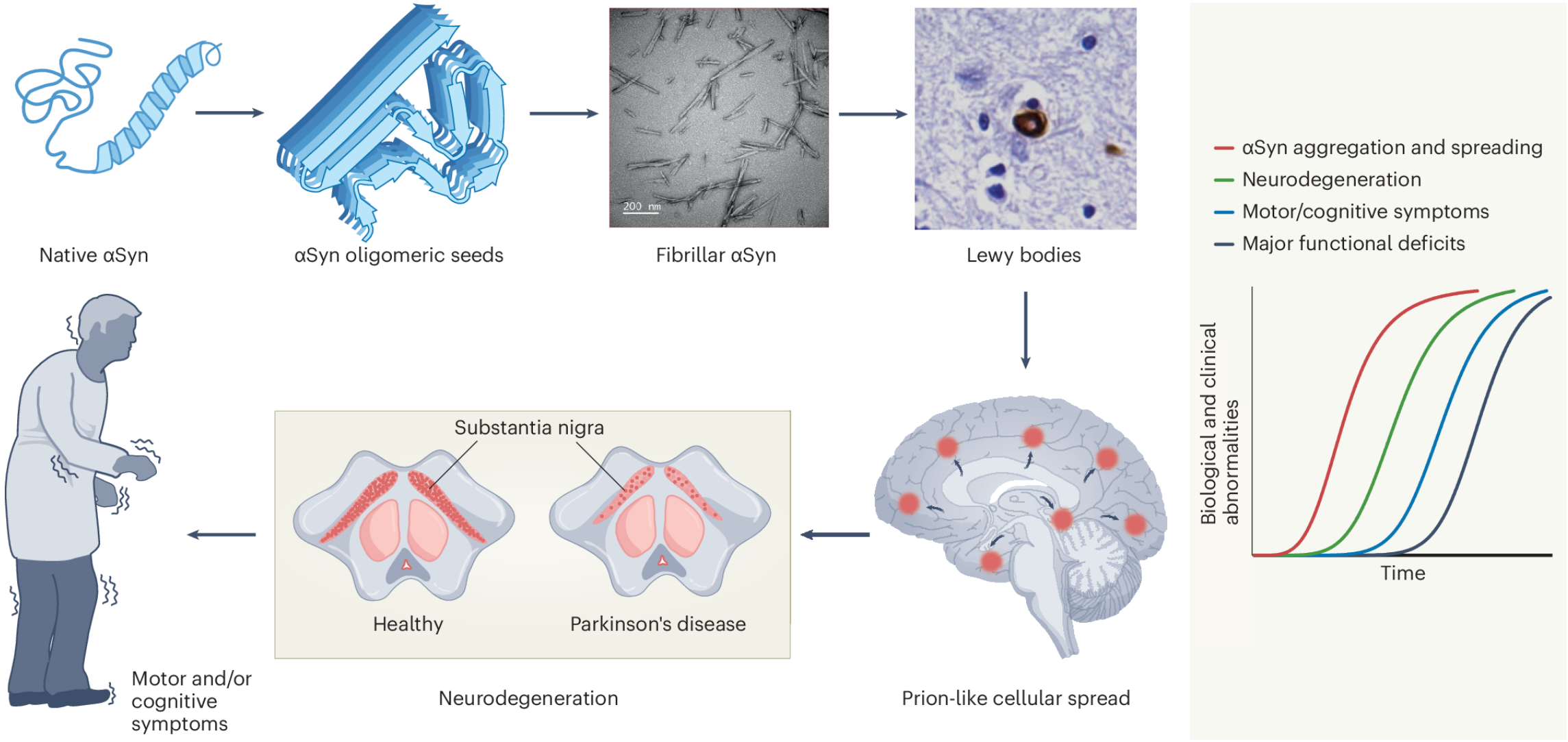


STATES OF PARKINSON DISEASE

At Risk	Prodromal	Early PD	Advanced PD
▪ No symptoms ▪ Genetic risk factors	▪ Hyposmia – loss of the sense of smell ▪ REM Behavior Disorder – “acting out dreams” ▪ Constipation	▪ Tremor ▪ Bradykinesia ▪ Rigidity ▪ Fatigue	▪ Impaired balance ▪ Wearing off ▪ Dyskinesia ▪ Memory problems ▪ Hallucinations

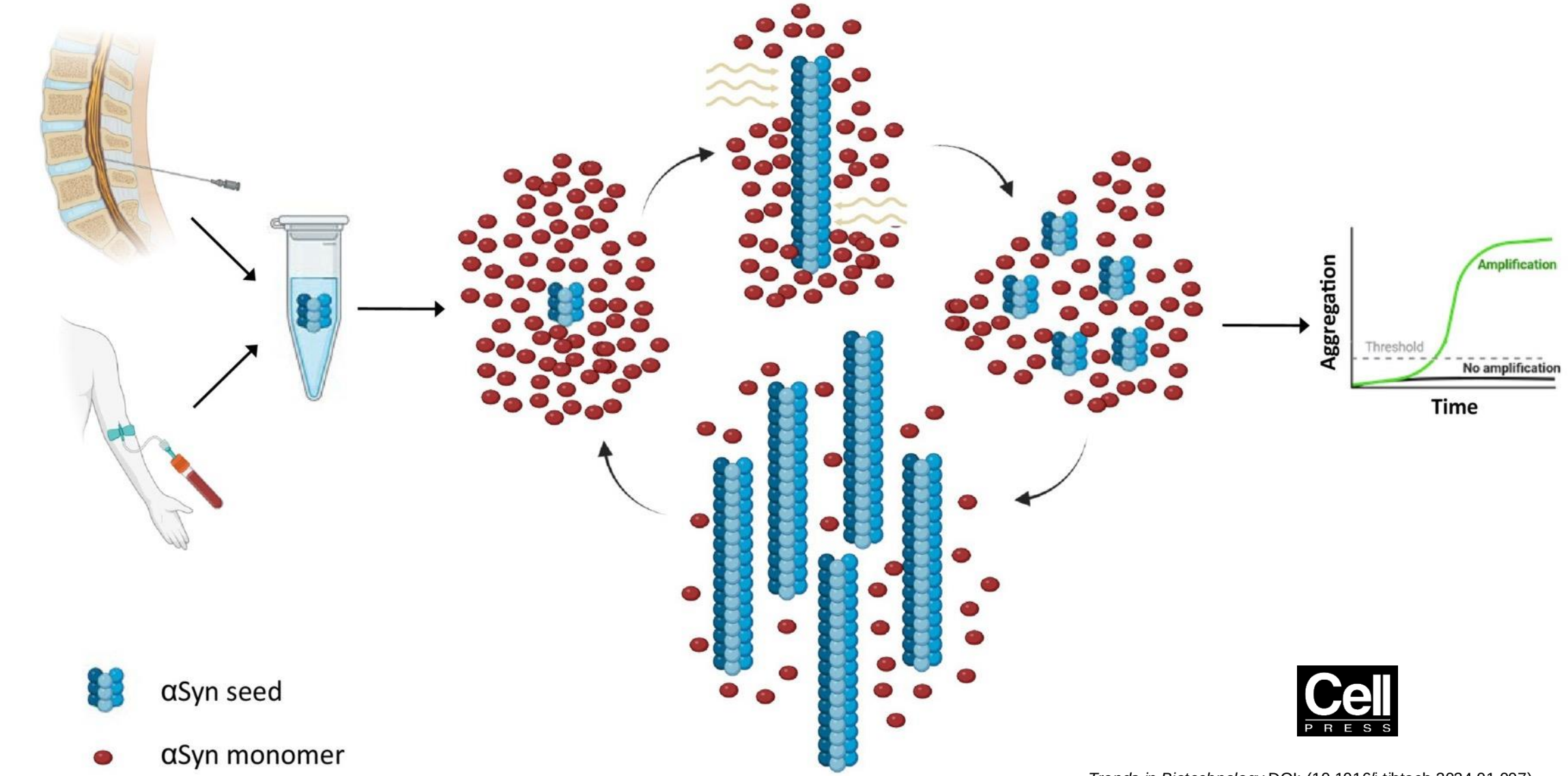
DETECTING AND DIAGNOSING PD

FROM SYNUCLEIN TO PARKINSON DISEASE



Nature Med. 2025 Jan 30. doi: 10.1038/s41591-024-03469-7.

SYNUCLEIN SEEDING ASSAYS



Trends in Biotechnology DOI: (10.1016/j.tibtech.2024.01.007)

Trends in Biotechnology

IMAGING BRAIN ALPHA-SYNUCLEIN

Neuron

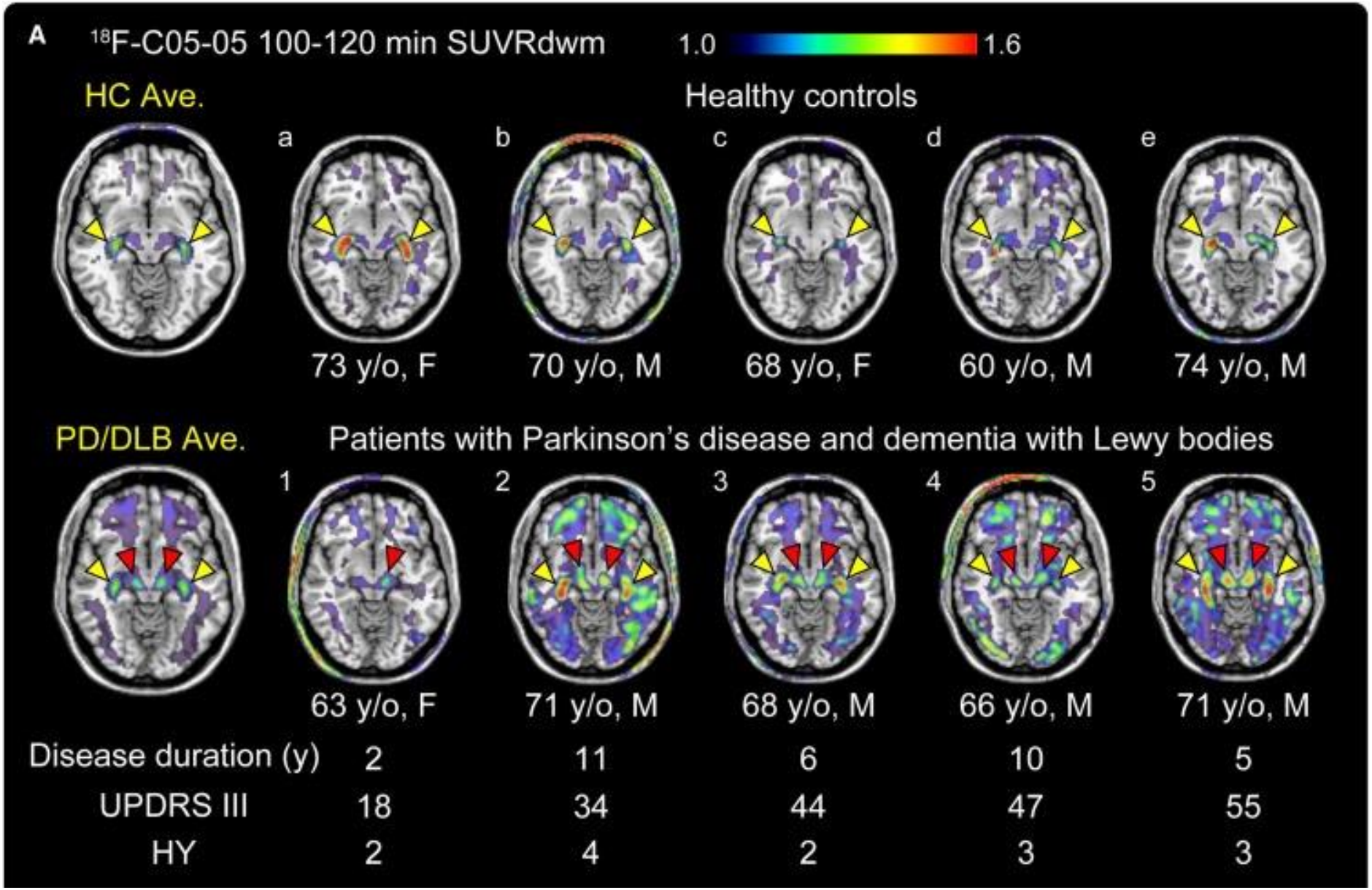
Volume 112, Issue 15, 7 August 2024, Pages 2540-2557.e8

Article

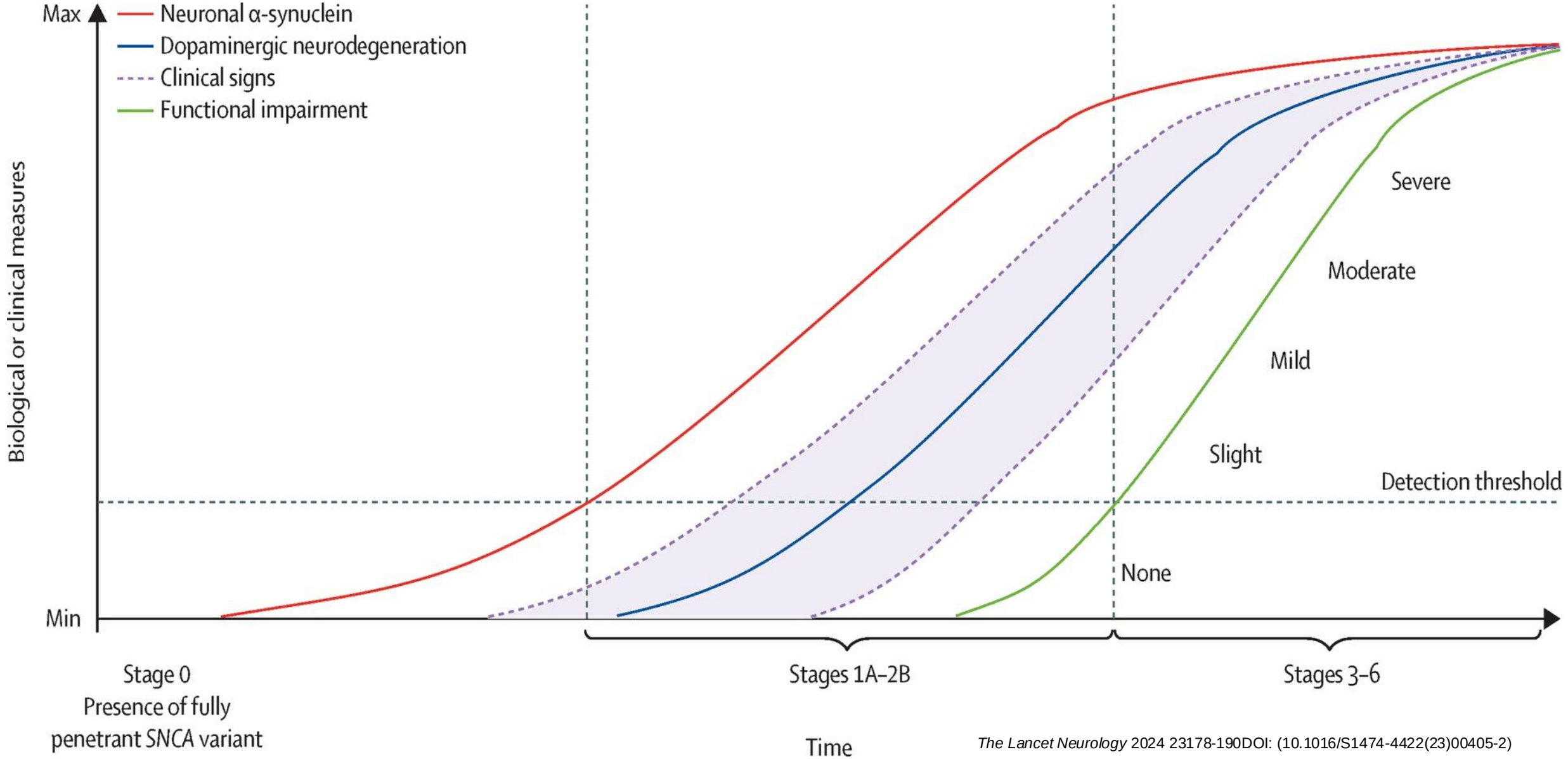
Imaging α-synuclein pathologies in animal models and patients with Parkinson's and related diseases

Hironobu Endo [1 19 20], Maiko Ono [2 19], Yuhei Takado [2], Kiwamu Matsuoka [1 3], Manami Takahashi [4], Kenji Tagai [1 5], Yuko Kataoka [1], Kosei Hirata [1 6], Keisuke Takahata [1 7], Chie Seki [1], Naomi Kokubo [1], Masayuki Fujinaga [8], Wakana Mori [8], Yuji Nagai [1], Koki Mimura [1 9], Katsushi Kumata [8], Tatsuya Kikuchi [8], Aki Shimozawa [10], Sushil K. Mishra [11], Yoshiki Yamaguchi [12], Makoto Higuchi [1 18]

- Brain imaging with C05-05
- Shows alpha-synuclein in the brain in PD



THE LONG VIEW: A NEW WAY TO LOOK AT PD



The Lancet Neurology 2024 23178-190DOI: (10.1016/S1474-4422(23)00405-2)

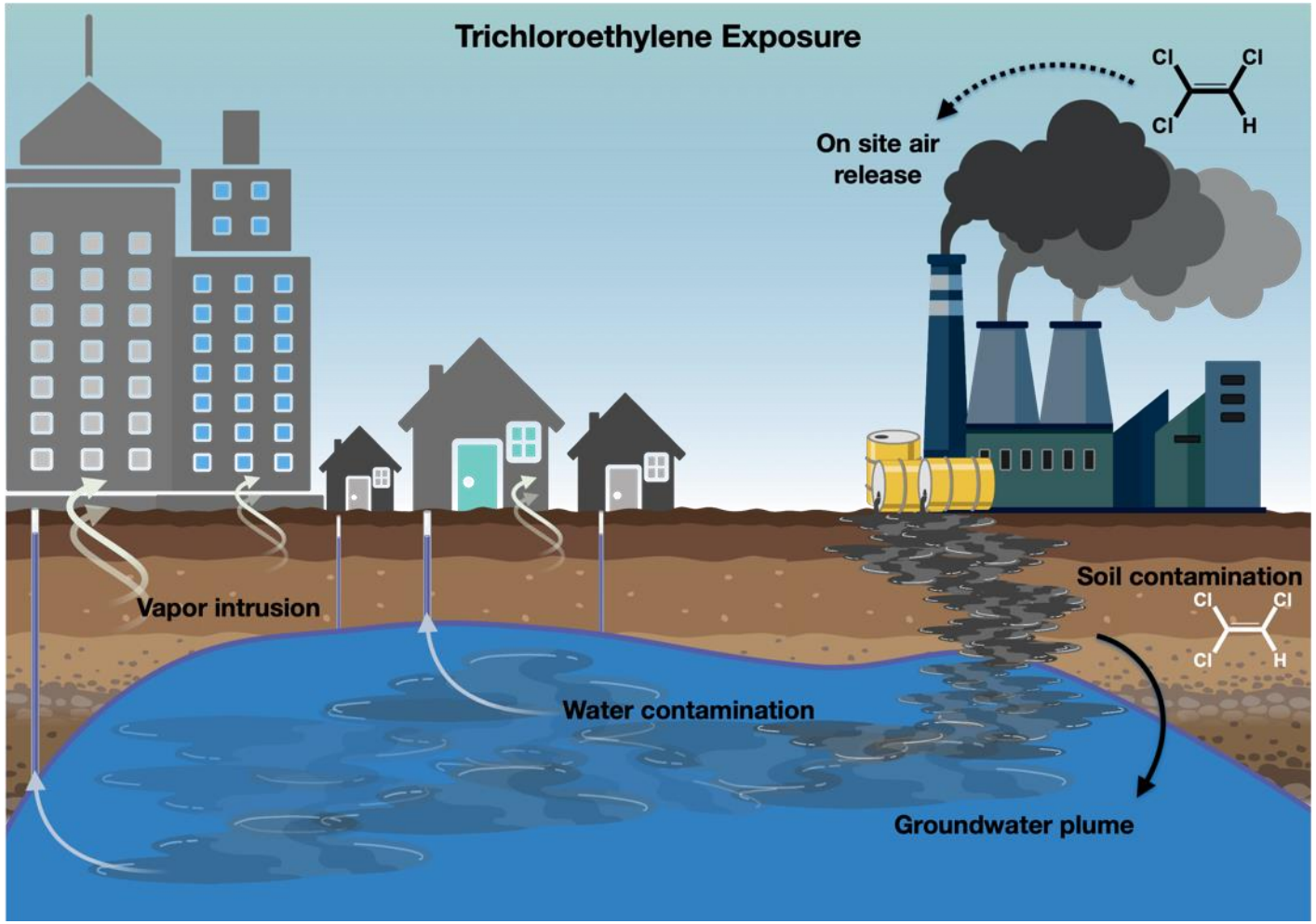
PREVENTING PARKINSON DISEASE

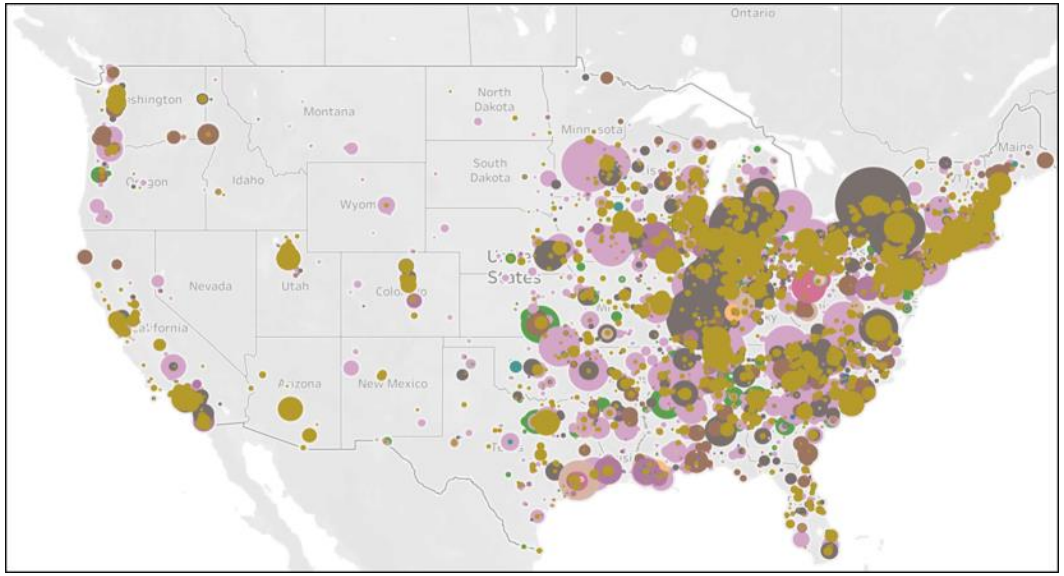
ENVIRONMENTAL TOXINS AND PD

- Growing evidence for a role of environmental toxins in triggering PD
- Pesticides
  - Paraquat
  - Rotenone
- Chemicals
  - TCE

https://www.youtube.com/watch?v=HnWJW4F3XP8

TCE EXPOSURE LINKED TO PD





May 15, 2023

Risk of Parkinson Disease Among Service Members at Marine Corps Base Camp Lejeune

Samuel M. Goldman, MD, MPH[1,2]; Frances M. Weaver, PhD[3,4]; Kevin T. Stroupe, PhD[3,4]; et al

» Author Affiliations | Article Information

JAMA Neurol. Published online May 15, 2023. doi:10.1001/jamaneurol.2023.1168

OR 1.68 (95%CI: 1.37-2.06)

TCE USED BANNED IN US

Updates from Washington Save for later

A Landmark Victory for the Parkinson's Community: EPA Bans Trichloroethylene

December 9, 2024

THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

SLOWING THE PROGRESSION OF PARKINSON DISEASE

GLP-1 AGONISTS (OZEMPIC®, WEGOVY®, ETC.)

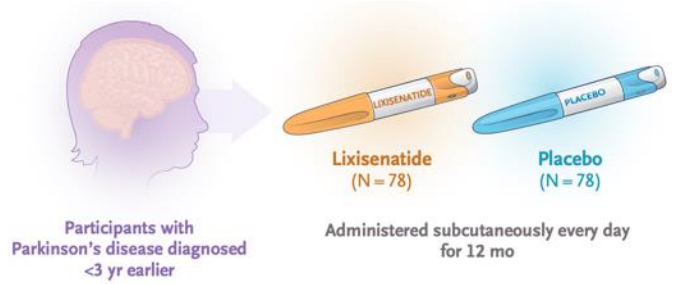
The NEW ENGLAND JOURNAL of MEDICINE

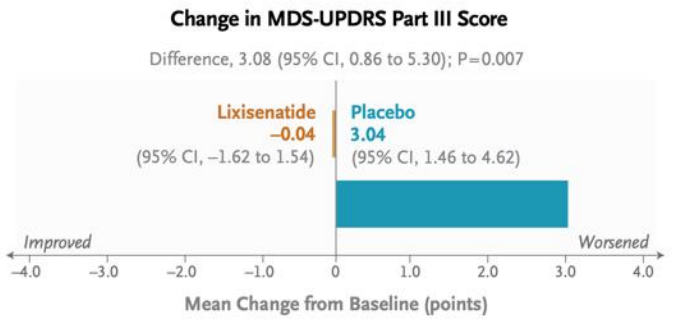
EDITORIAL

GLP-1, Parkinson's Disease, and Neuroprotection

Author: David G. Standaert, M.D., Ph.D. Author Info & Affiliations

Published April 3, 2024 | N Engl J Med 2024;390:1233-1234 | DOI: 10.1056/NEJMe2401743
VOL. 390 NO. 13 | Copyright © 2024





Exenatide once a week versus placebo as a potential disease-modifying treatment for people with Parkinson's disease in the UK: a phase 3, multicentre, double-blind, parallel-group, randomised, placebo-controlled trial

Nirosen Vijiaratnam, Christine Girges, Grace Auld, Rachel McComish, Alexa King, Simon S Skene, Steve Hibbert, Alan Wong, Sabina Melander, Rachel Gibson, Helen Matthews, John Dickson, Camille Carroll, Abigail Patrick, Jemma Inches, Monty Silverdale, Bethan Blackledge, Jessica Whiston, Michele Hu, Jessica Welch, Gordon Duncan, Katie Power, Sarah Gallen, Jacqueline Kerr, K Ray Chaudhuri, Lucia Batzu, Silvia Rota, Edwin Jabbari, Huw Morris, Patricia Limousin, Nigel Greig, Yazhou Li, Vincenzo Libri, Sonia Gandhi, Dilan Athauda, Kashfia Chowdhury, Tom Foltynie

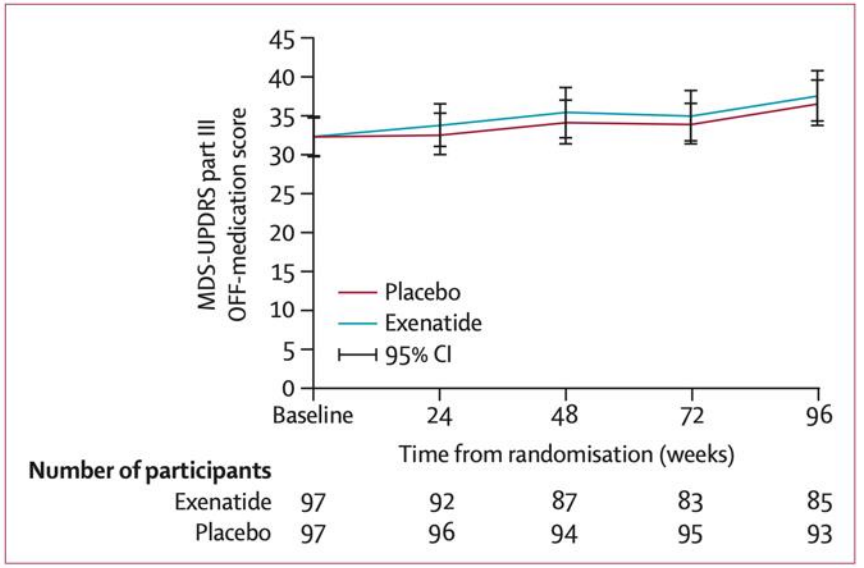
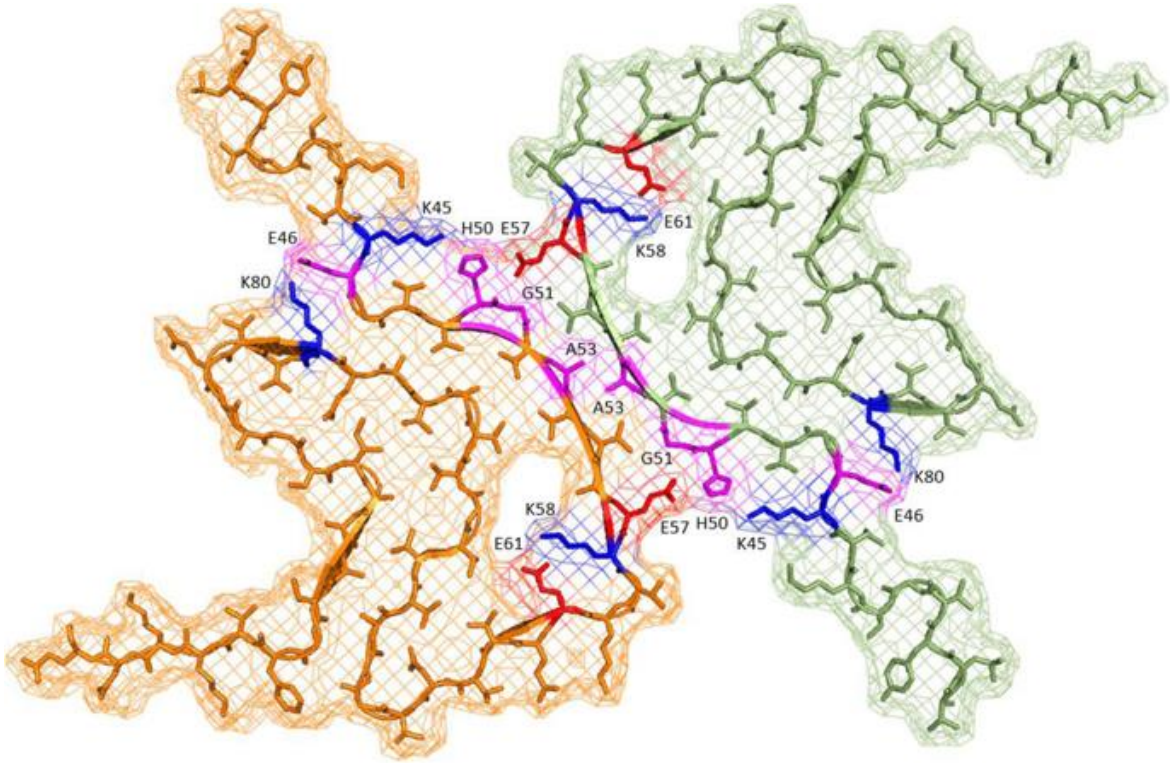


Figure 2: **Mean MDS-UPDRS part III OFF-medication score by group over 96 weeks**
MDS-UPDRS=Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale.

CAN WE TARGET ALPHA-SYNUCLEIN FOR PD?

- **Reducing synuclein production**
  - Antisense strategies
  - Transcriptional Inhibitors
- **Enhancing synuclein removal**
  - Enhances of autophagy and lysosomal
  - Antibody mediated clearance
- **Targeting abnormal forms**
  - Anti-aggregation strategies
  - Antibodies specific for misfolded forms



Meade et al., *Mol Neurodegeneration* **14,** 29 (2019)

CURRENT TRIALS TARGETING ALPHA-SYNUCLEIN

Drug Name	Sponsor	Modality	Status	ClinicalTrials.gov Number
UB-312	Vaxxinity, Inc	Vaccine	Phase I-completed	NCT04075318
			Phase Ib-active	NCT05634876
AFFITOPE PD01A,	AFFiRiS	Vaccine	Phase I-completed	NCT02618941
			Phase I-completed	NCT02216188
			Phase I-completed	NCT01568099
			Phase I-completed	NCT01885494
			Phase I-withdrawn	NCT02758730
PD03A	AFFiRiS	Vaccine	Phase I-completed	NCT02267434
ACI-7104.056	AC Immune	Vaccine	Phase II-recruiting	NCT06015841
Prasinezumab	Hoffmann-La Roche	Antibody	Phase I-completed	NCT02095171
			Phase I-completed	NCT02157714
			Phase II-active	NCT03100149
			Phase IIb-active	NCT04777331
Cinpanemab	Biogen	Antibody	Phase I-completed	NCT02459886
			Phase I-terminated	NCT03716570
			Phase II-terminated	NCT03318523
MEDI1341	AstraZeneca	Antibody	Phase I-completed	NCT03272165
			Phase I-completed	NCT04449484
Lu AF82422	Lundbeck A/S	Antibody	Phase I-completed	NCT03611569
			Phase I-active	NCT06258720

Journal of Neurology (2025) 272:21
https://doi.org/10.1007/s00415-024-12770-x

INFLAMMATION IN PD

- Increasing evidence for activation of the immune system in PD
- Signs of inflammation both in the brain and in the blood
- PD as a systemic inflammatory disease?

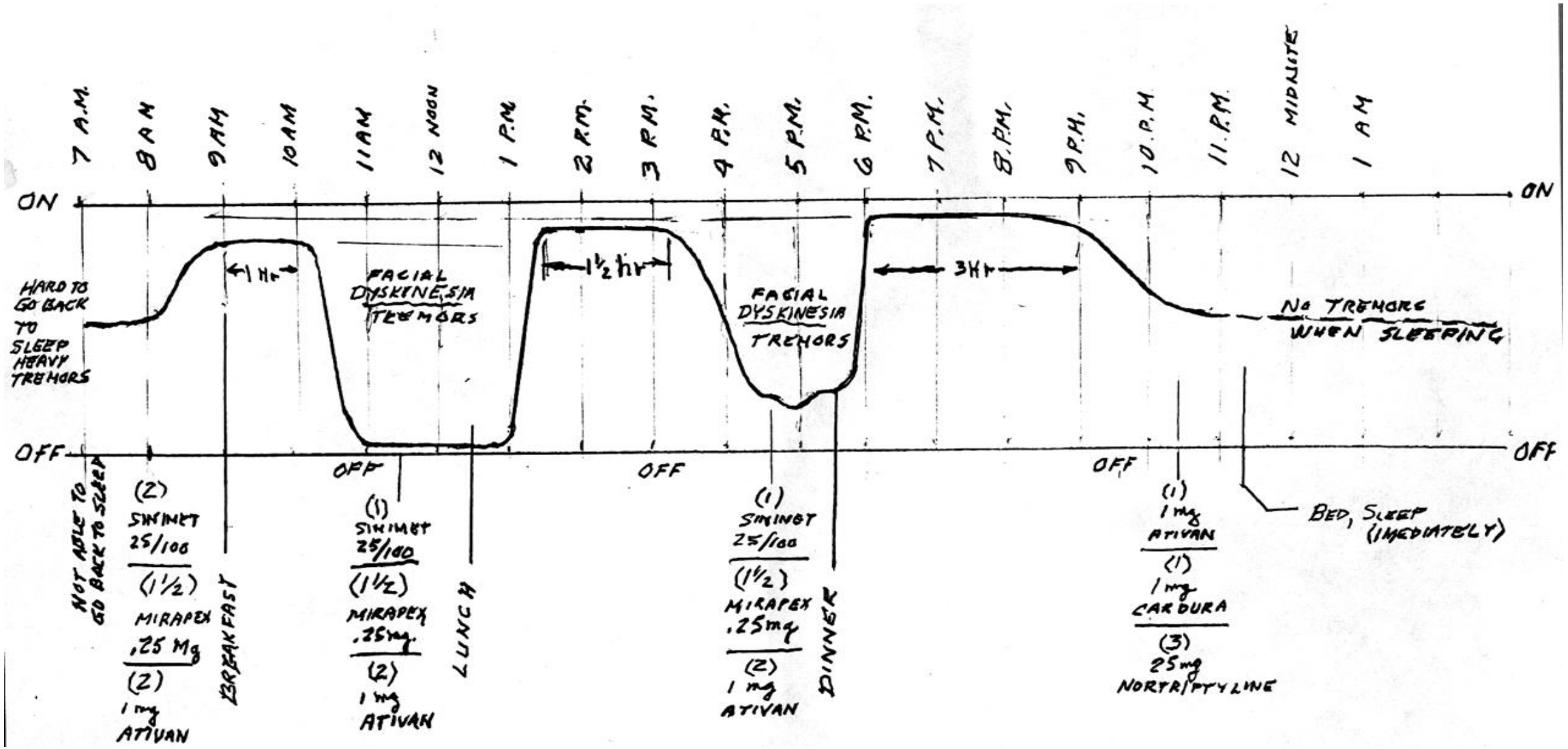
https://www.youtube.com/watch?v=Z4yswDDze1Q

TARGETING INFLAMMATION IN PD

- NLRP3 Inflammasome inhibitors
- Anti-microglial strategies
- Anti-TNF therapies
- T cell therapies

DOPAMINERGIC INFUSION THERAPIES FOR PD

MOTOR COMPLICATIONS IN PD



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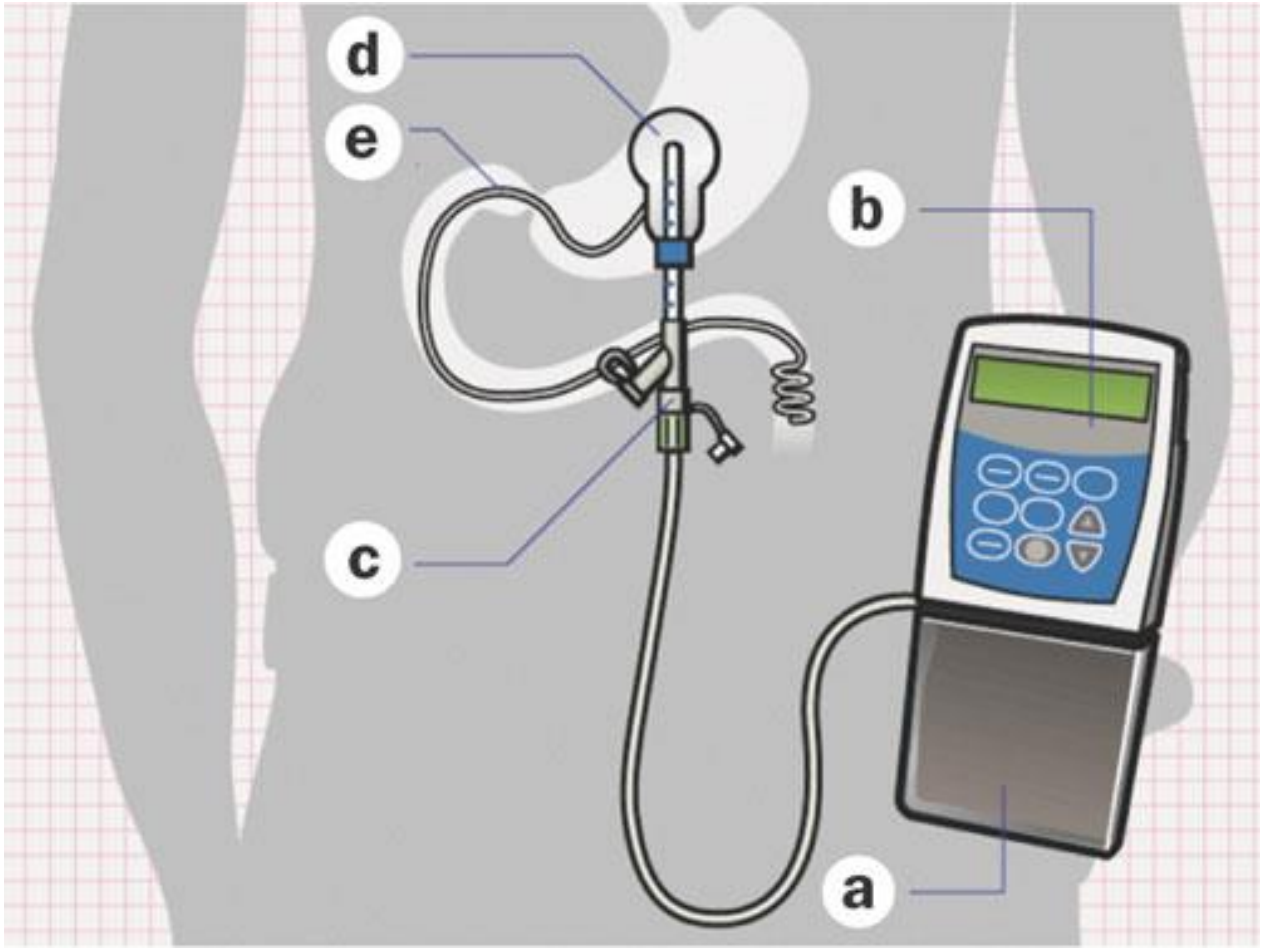
- Uses an external programmable pump



Richards, L. (2009) Intrajejunal duodopa improves nonmotor symptoms *Nat. Rev. Neurol.* doi:10.1038/nrneurol.2009.84

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https://www.vyalevhcp.com/

https://pharmaphorum.com/news/abbvie-gets-continuous-parkinsons-drug-over-line-us

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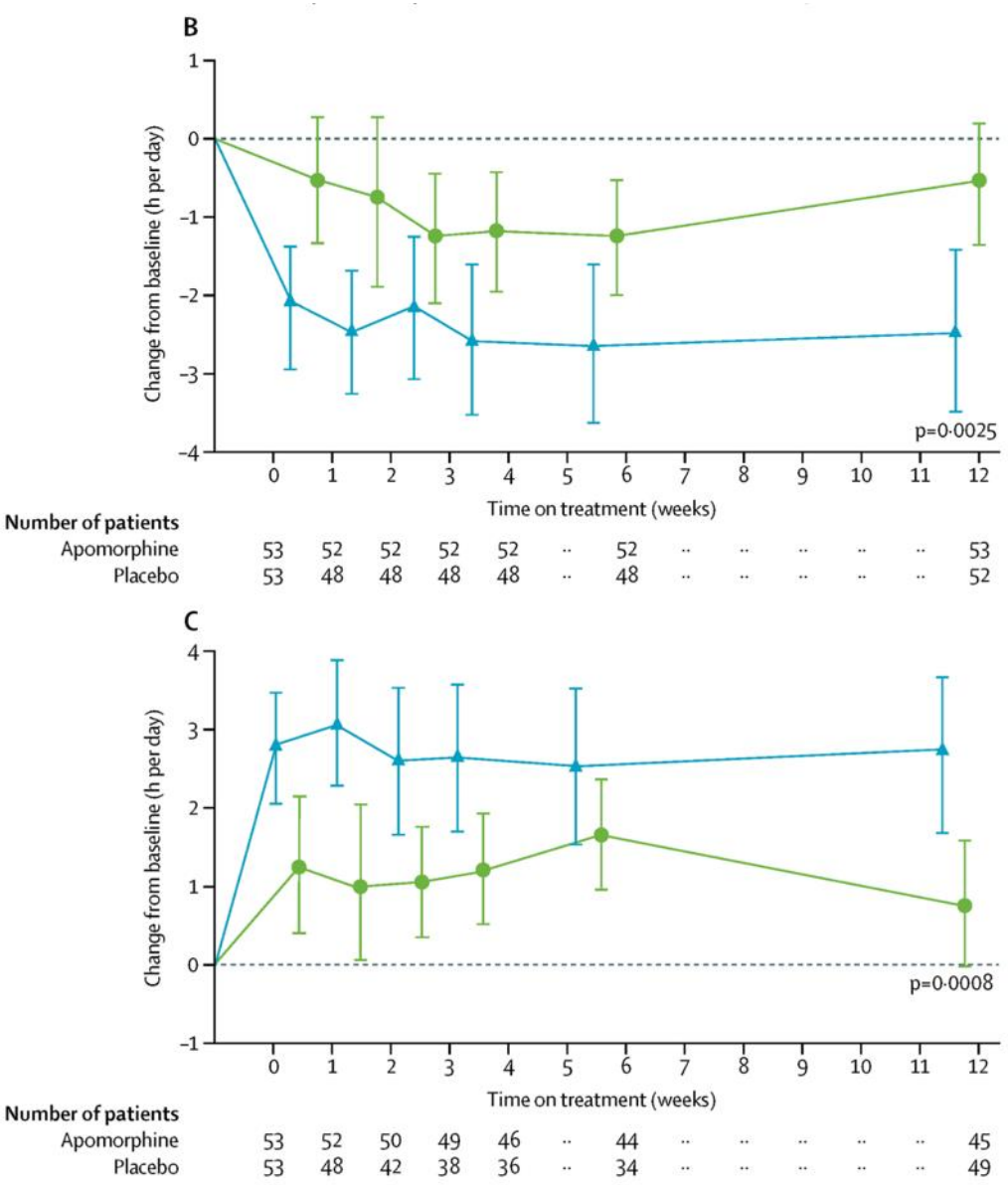
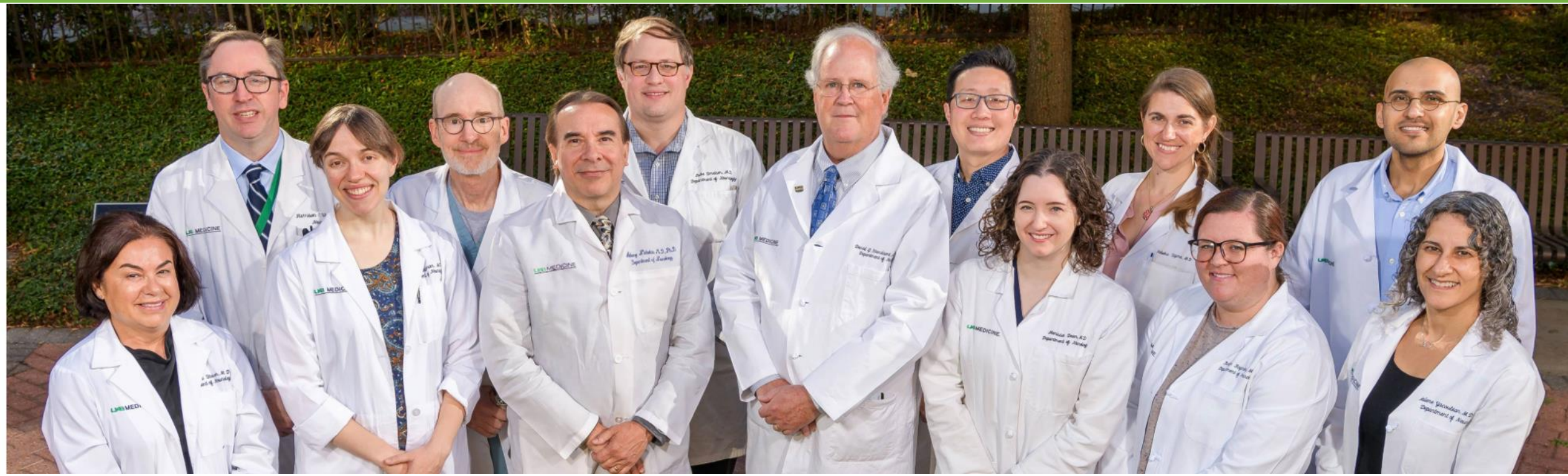
Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial

Katzenschlager, Regina et al. The Lancet Neurology, Volume 17, Issue 9, 749 - 759



UAB DIVISION OF MOVEMENT DISORDERS



- Physicians
  - Paul Atchinson
  - Juliana Coleman
  - Marissa Dean
  - Anthony Nicholas
  - Rebecca Sipma
  - David Standaert
  - Natividad Stover
  - Victor Sung
  - Harrison Walker
  - Ray Watts
  - Talene Yacoubian
- Fellows
  - Katlyn Roginsky
  - Mohamed Kandil
- Advanced Practice Providers
  - Stephanie Guthie
  - Laura Lieb
  - Melissa Wade
  - Bradleigh Pfitzer

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