



School for Advanced Therapies for Movement Disorders

Liverpool, United Kingdom | November 27-29, 2025



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Apomorphine: An overview of efficacy and selection criteria

Monty Silverdale

Professor of Neurology



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No disclosures relevant to this talk

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When to refer?



Levodopa Resistant Axial Problems



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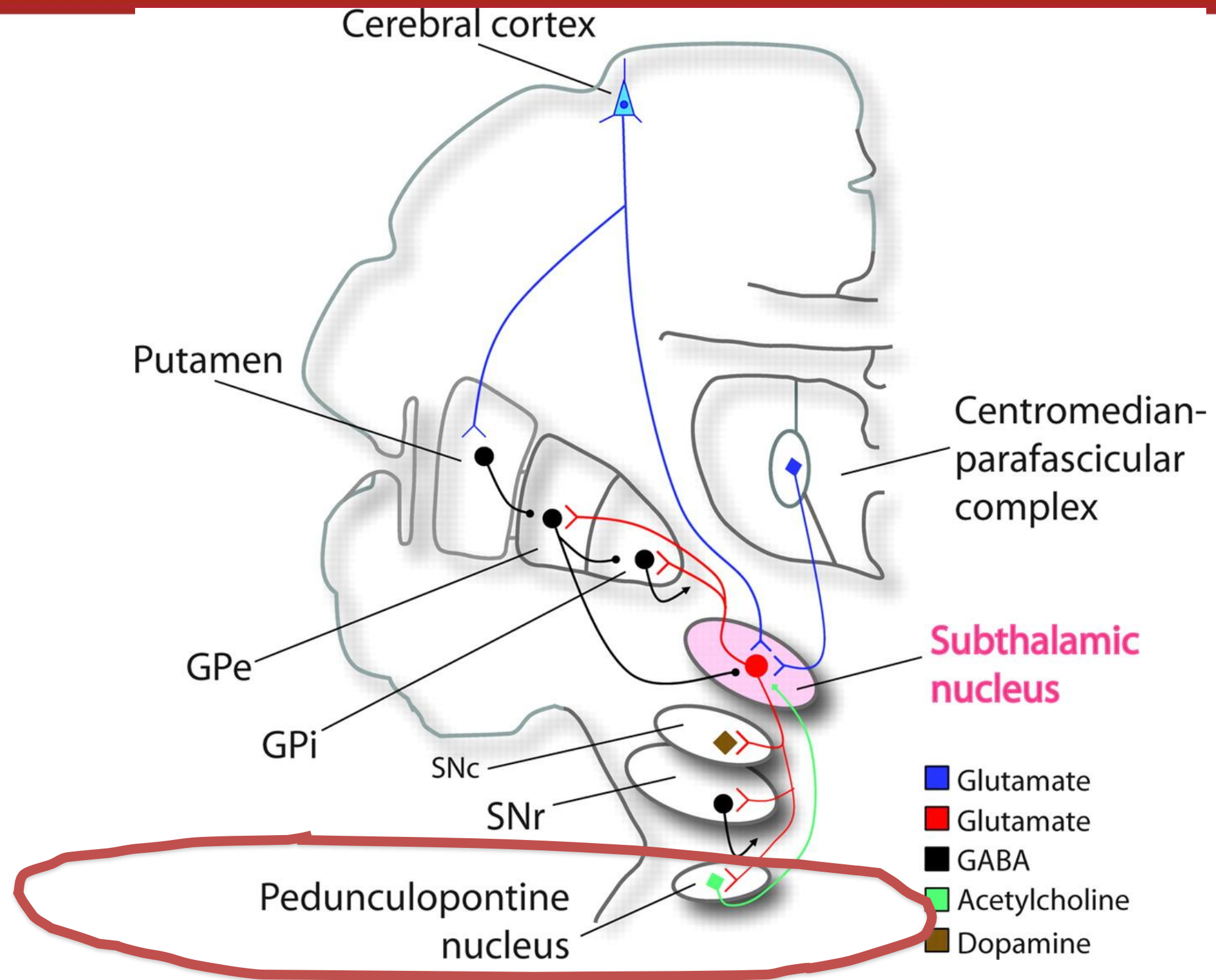
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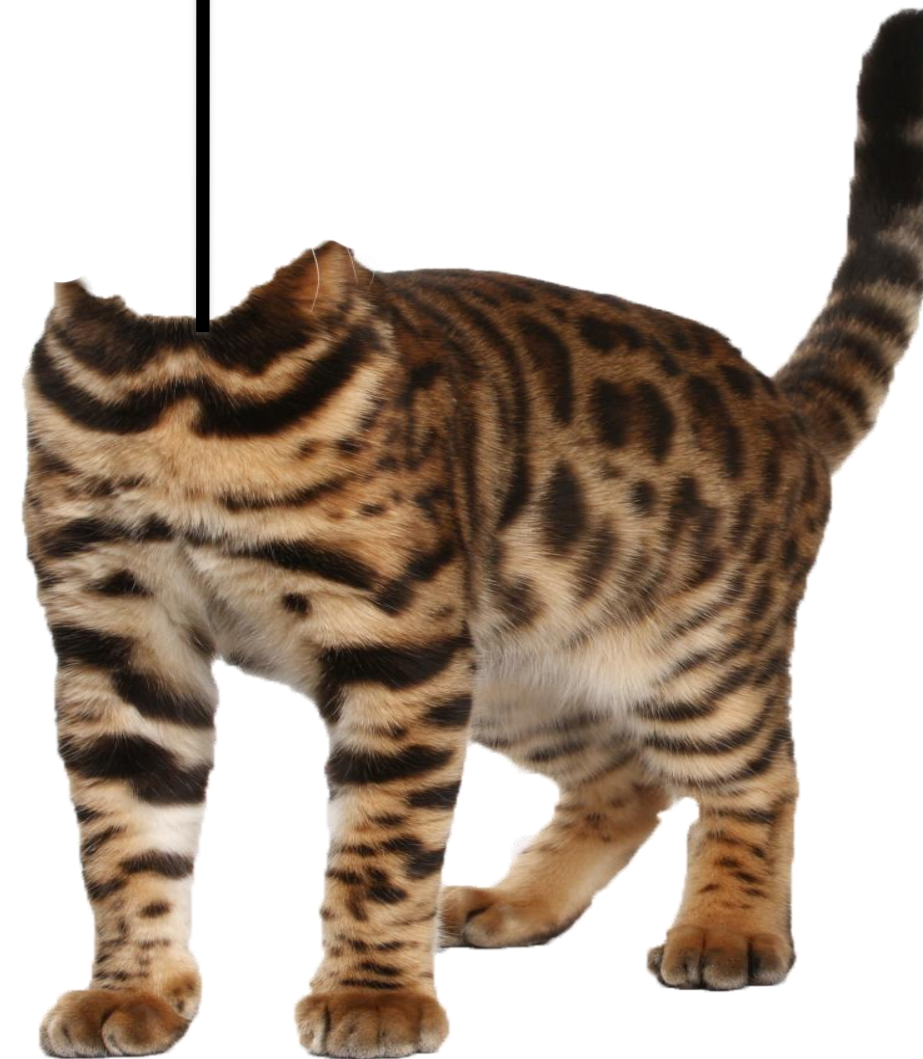
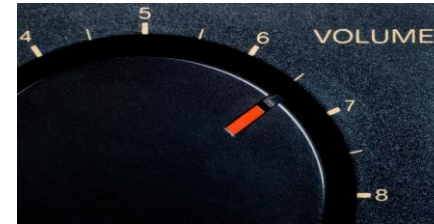


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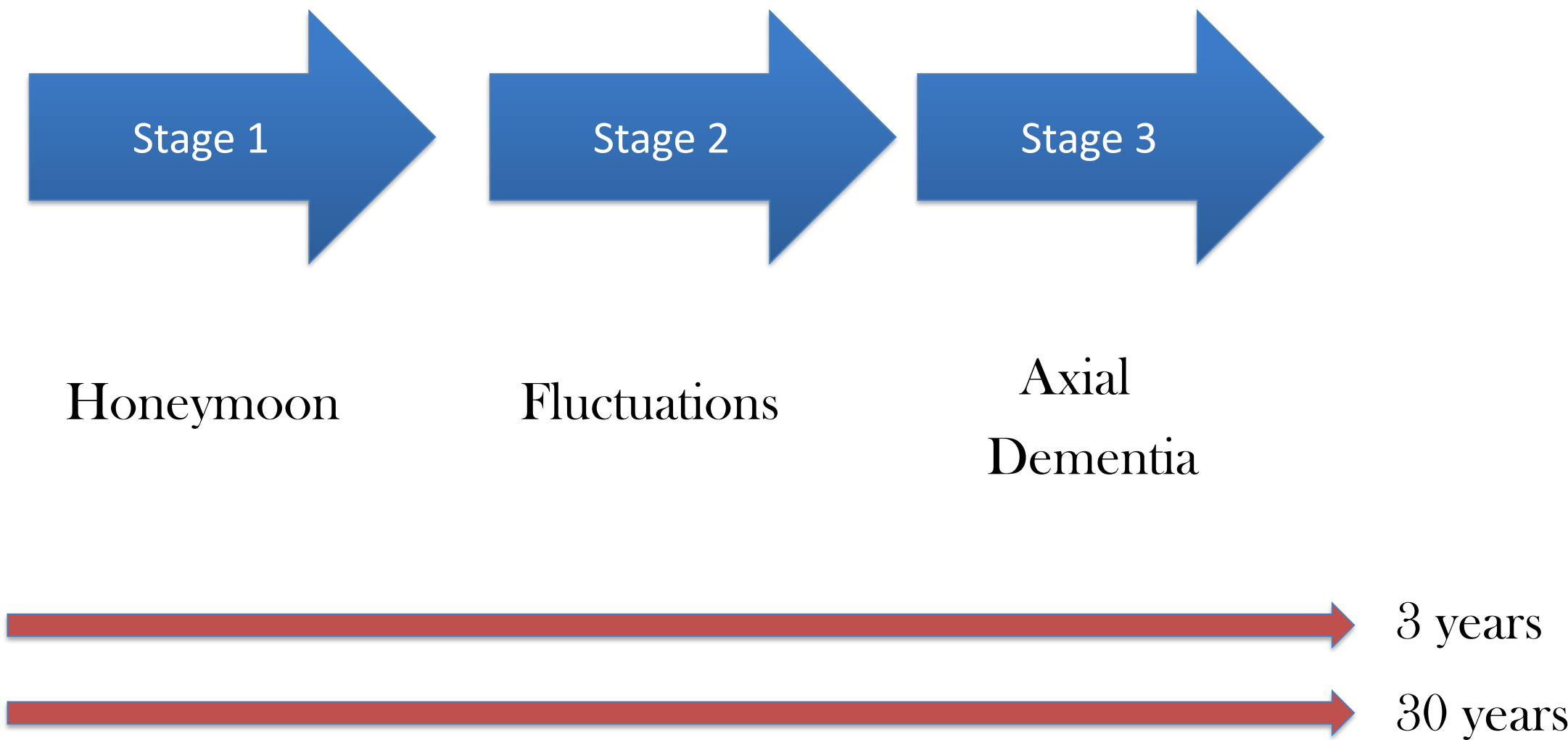


Therapists are the
only treatment for
levodopa-
resistant axial
problems



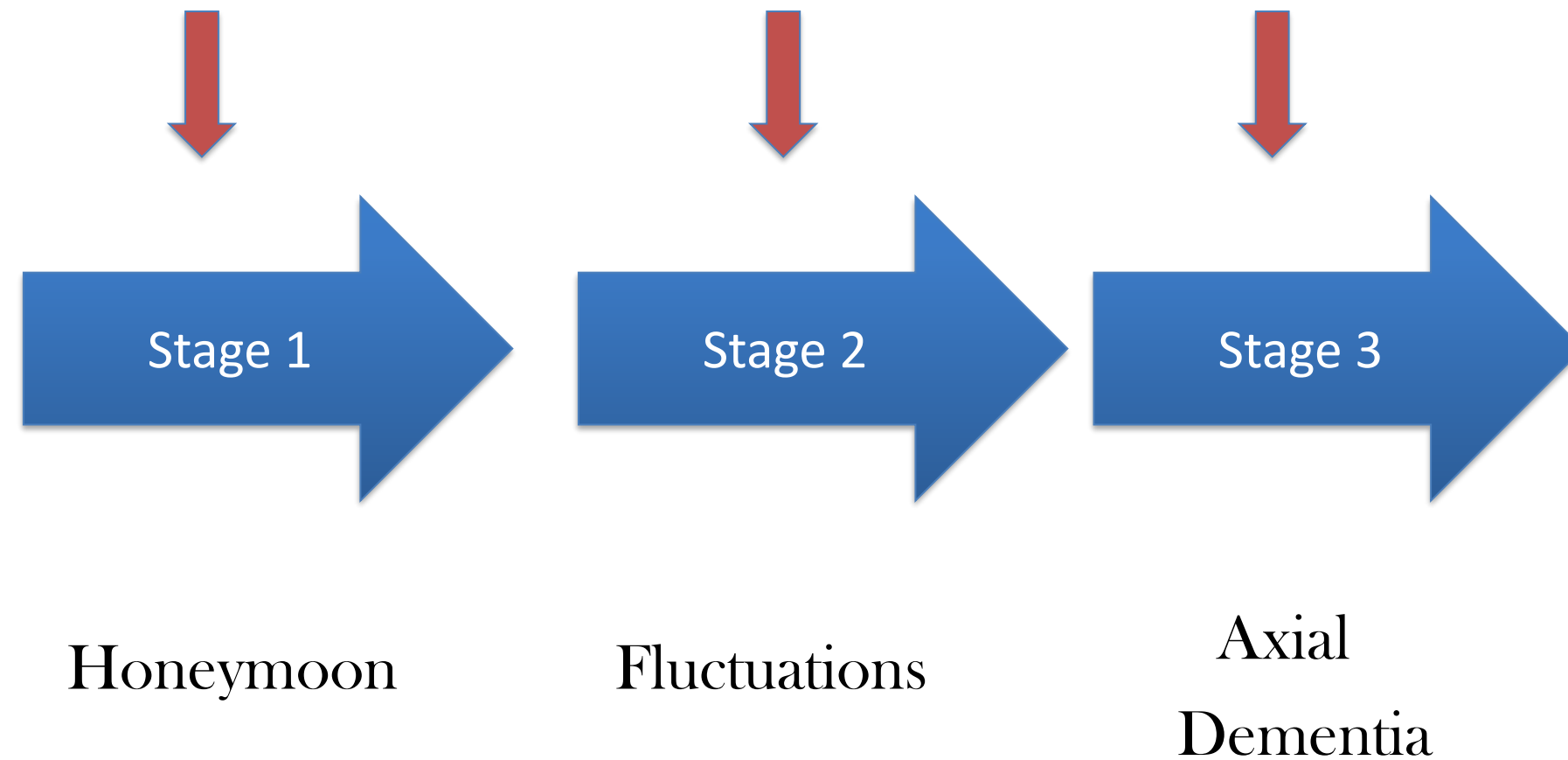


3 stages of Parkinson's disease



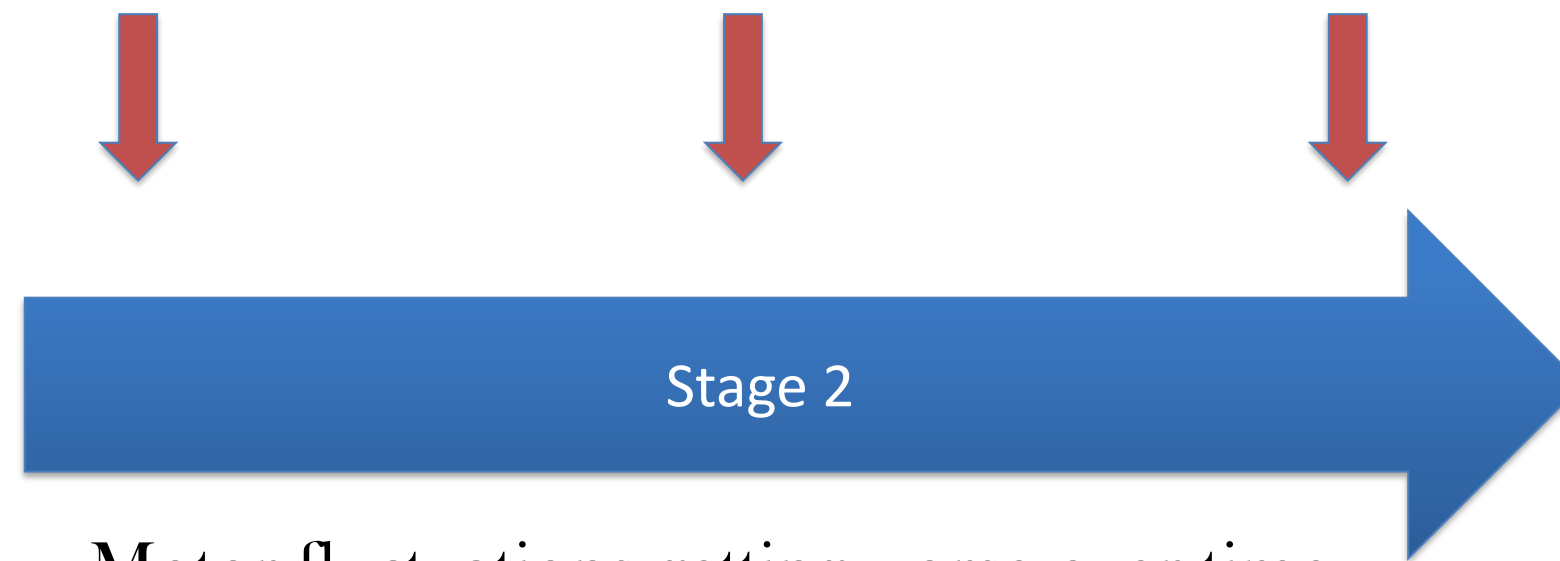


When to consider advanced therapies





When to consider advanced therapies



Motor fluctuations getting worse over time

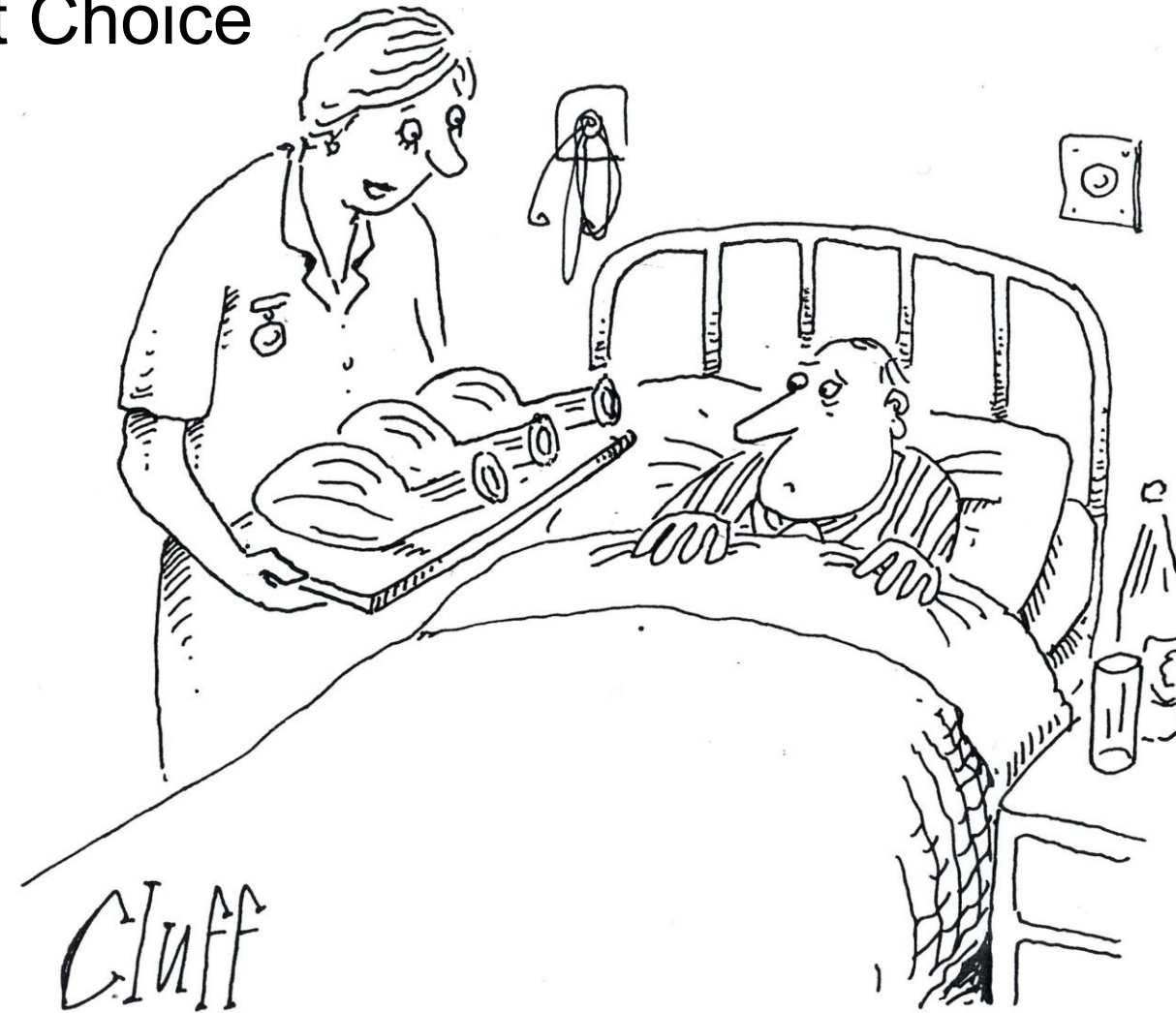
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Patient Choice



' IT'S THE HEALTH TRUSTS' POLICY TO OFFER
THE PATIENT CHOICE, WHENEVER POSSIBLE,
MR. LUMB '



Advanced Therapies – who to refer and when?

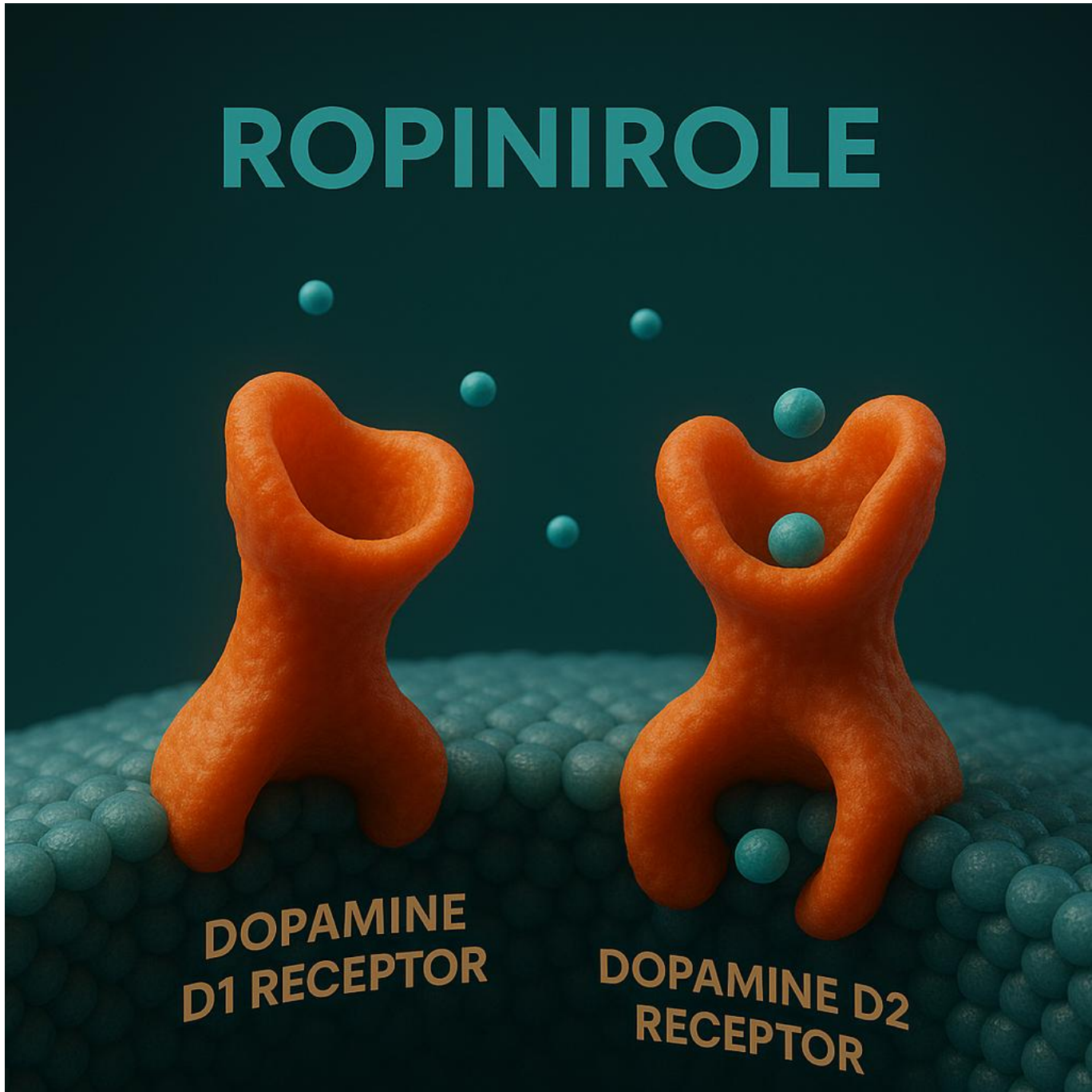
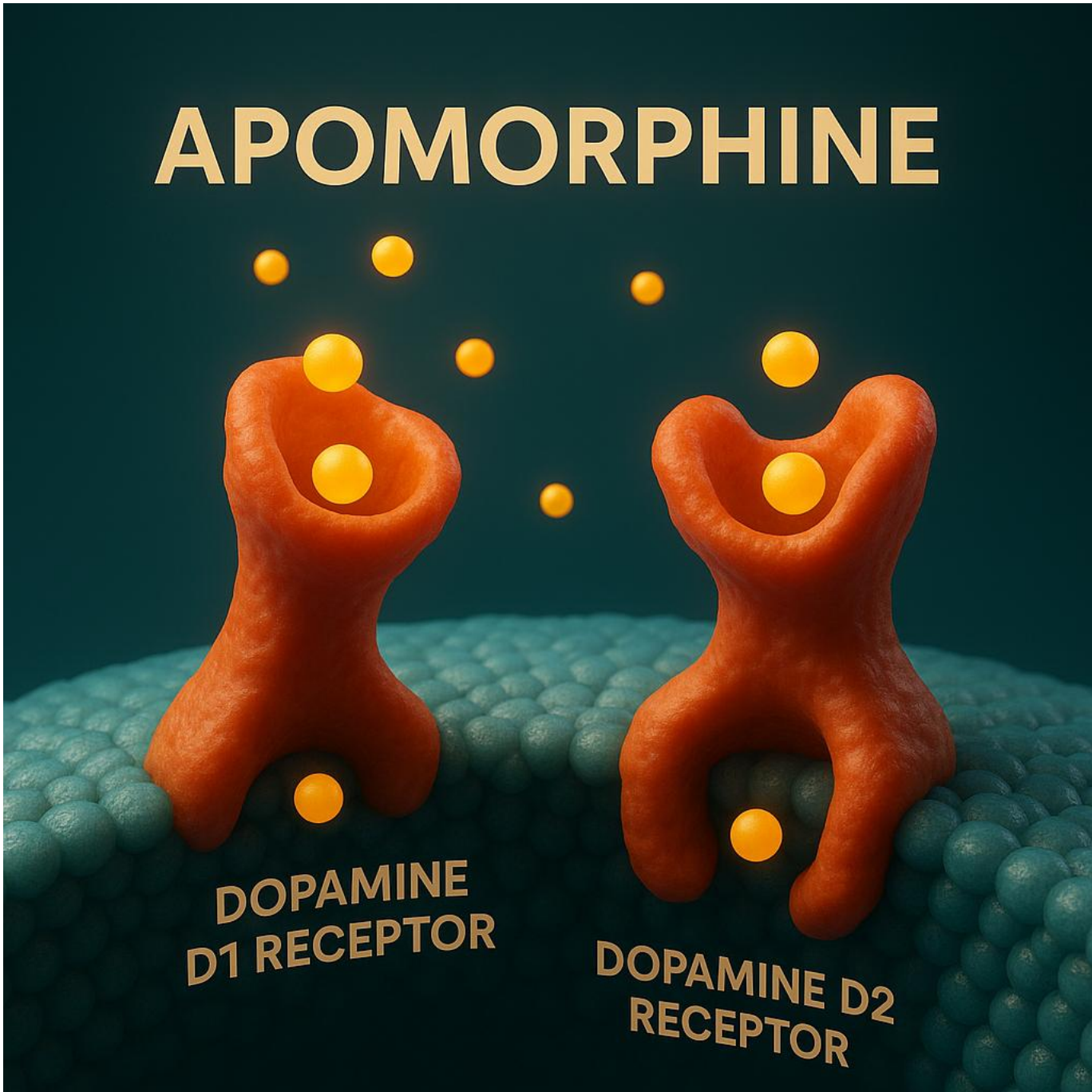
- Maximum age around 75ish for DBS, possibly a bit older for infusion therapies
- Motor fluctuations (can be mild)
- Good response to levodopa – good ON
- Good gait when on – no major axial problems
- Not significantly demented

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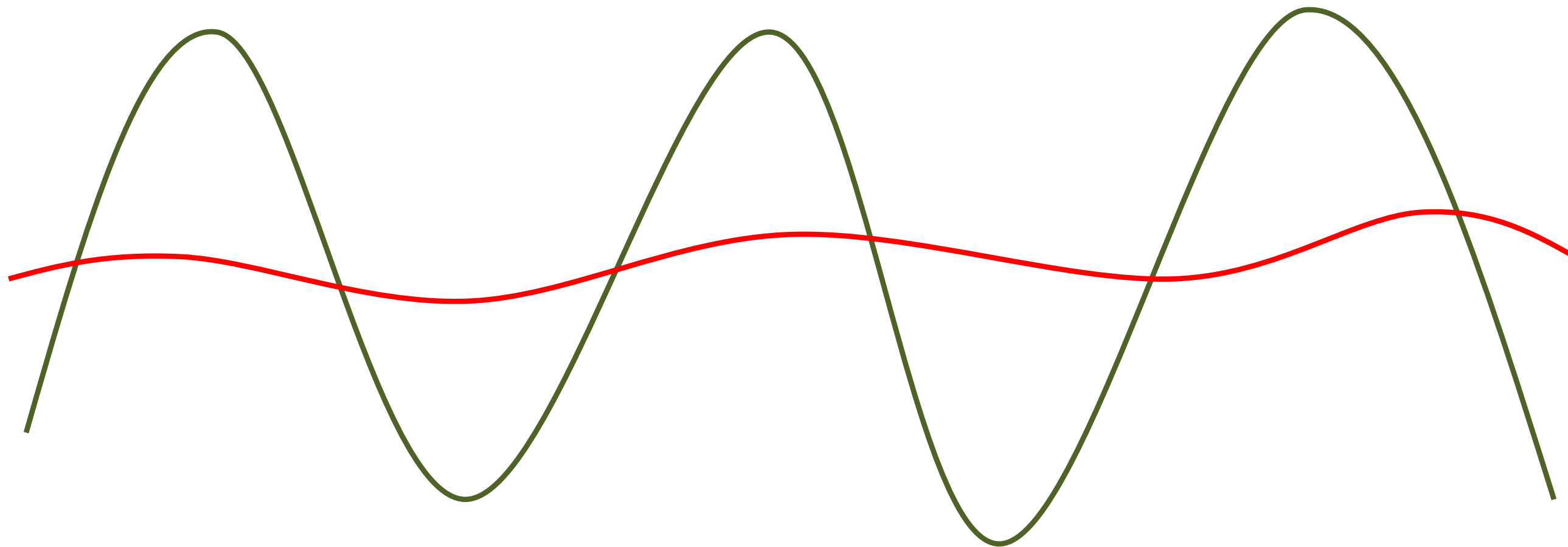


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Continuous Dopaminergic Stimulation



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Evidence for apomorphine

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Beware Expert Opinion



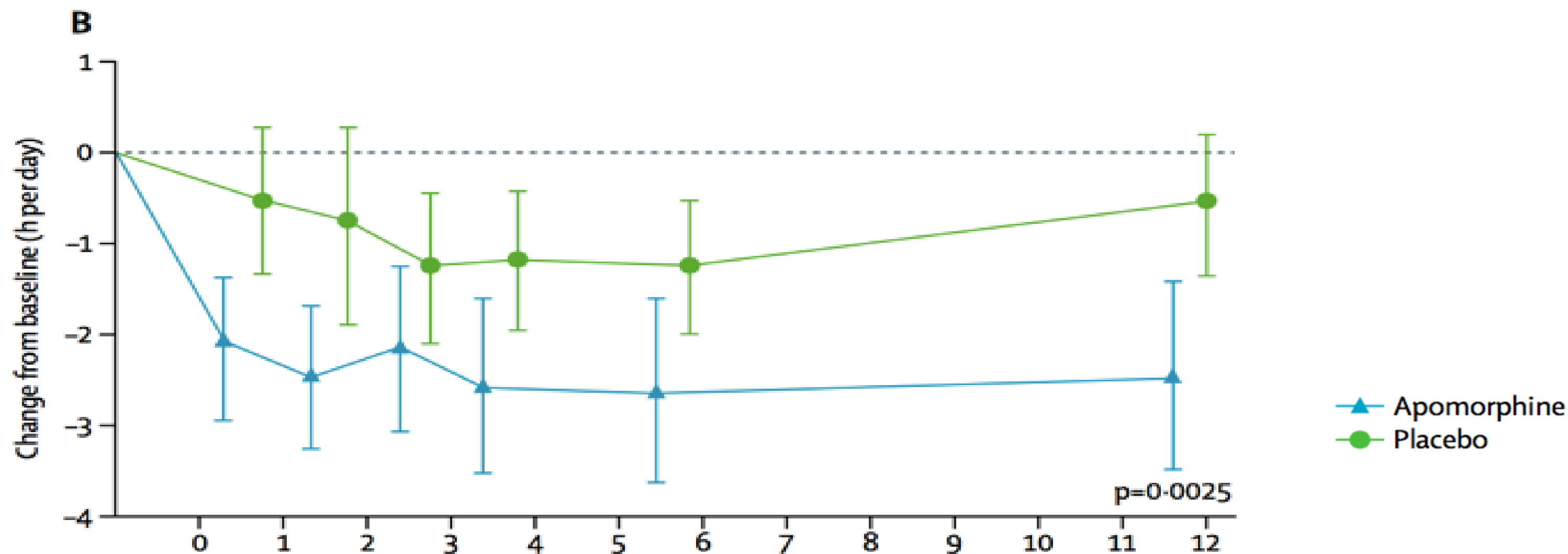


Toledo Study. Katzenschlager et al. 2018

- Double Blind Randomised Clinical Trial
- Apomorphine (3-8mg/hr) vs placebo (saline)
- Started in hospital
 - 5-10 day admission
 - Start at 1mg / hour
 - Reduce other PD medication
- 14-18 hours / day continuous infusion
- 12-week trial (adjustments in first 4 weeks)
- 107 participants



Toledo Study: reduction in OFF time



Number of patients
Apomorphine
Placebo

53	52	52	52	52	..	52	53
53	48	48	48	48	..	48	52

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	Apomorphine (n=54)	Placebo (n=53)
At least one treatment-emergent adverse event	50 (93%)	30 (57%)
Treatment-emergent adverse events*		
Skin nodules at infusion site	24 (44%)	0
Mild	20 (37%)	0
Moderate	4 (7%)	0
Nausea	12 (22%)	5 (9%)
Mild	10 (19%)	3 (6%)
Moderate	2 (4%)	2 (4%)
Somnolence	12 (22%)	2 (4%)
Mild	5 (9%)	1 (2%)
Moderate	6 (11%)	1 (2%)
Severe	1 (2%)	0
Infusion site erythema	9 (17%)	2 (4%)
Mild	8 (15%)	2 (4%)
Moderate	1 (2%)	0




Dyskinesia	8 (15%)	0
Mild	5 (9%)	0
Moderate	3 (6%)	0
Headache	7 (13%)	2 (4%)
Mild	6 (11%)	2 (4%)
Moderate	1 (2%)	0
Insomnia	6 (11%)	1 (2%)
Mild	2 (4%)	0
Moderate	4 (7%)	1 (2%)
At least one adverse event with local intolerability (skin changes at injection site)	32 (59%)	8 (15%)
Severe adverse events	8 (15%)	2 (4%)
Serious adverse events	5 (9%)	2 (4%)
Adverse events leading to study discontinuation	6 (11%)	0
Adverse events leading to dose modification	26 (48%)	6 (11%)

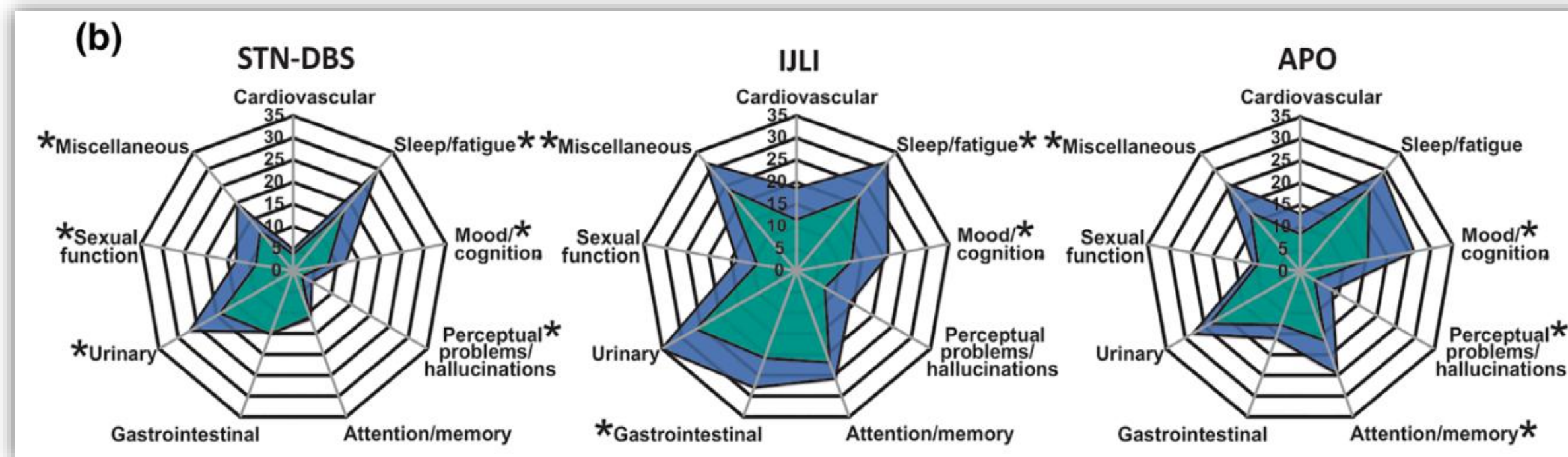


Non-Motor Symptoms

RESEARCH ARTICLE

EuroInf 2: Subthalamic Stimulation, Apomorphine, and Levodopa Infusion in Parkinson's Disease

Haidar S. Dafsari, MD,^{1,2*}  Pablo Martinez-Martin, MD, PhD,³ Alexandra Rizos, MSc,² Maja Trost, MD,⁴ Maria Gabriela dos Santos Ghilardi, MD,⁵ Prashanth Reddy, MD/PhD,² Anna Sauerbier, MD,^{2,6} Jan Niklas Petry-Schmelzer, MD,¹ Milica Kramberger, MD,⁴ Robbert W. K. Borgemeester, MD,⁷ Michael T. Barbe, MD,¹ Keyoumars Ashkan, MD, PhD,² Monty Silverdale, MD, PhD,⁸ Julian Evans, MD, PhD,⁸ Per Odin, MD, PhD,^{9,10} Erich Talamoni Fonoff, MD, PhD,^{5,11} Gereon R. Fink, MD,^{1,12} Tove Henriksen, MD, PhD,¹³ Georg Ebersbach, MD,¹⁴ Zvezdan Pirtošek, MD, PhD,⁴ Veerle Visser-Vandewalle, MD, PhD,¹⁵ Angelo Antonini, MD, PhD,^{16,17}  Lars Timmermann, MD,^{1,18} and K. Ray Chaudhuri, MD, PhD,^{2,6*} 
on behalf of EUOPAR and the International Parkinson and Movement Disorders Society Non-Motor Parkinson's Disease Study Group





Impulse Control Disorder





Impulse Control Disorder

TOLEDO study

- No serious ICDs in double-blind phase
- Open-label phase – 8/84 patients reported ICB (3 resolved), all rated as mild in severity
- No discontinuation from open-label phase due to ICB

Barbosa 2020

- Brain bank study
- 24 CSAI patients on apo > 3months
- ICBs in 4 at baseline, partially improved after apomorphine
- 2 new onset cases of dopamine dysregulation after initiation

Todorova 2015

- 3 year observational study
- 41 apomorphine
- Mean 106mg / day
- Mean 16 hours per day
- 4 pre-existing ICB (1 resolved and other 3 reduced)
- 7 new ICD (only 1 required discontinuation)

References

Todorova A et al. Clin Neuropharm 2015;38:132-134.
Katzenschlager R et al. TOLEDO. Lancet Neurol 2018;17:749-759.
Katzenschlager R et al. TOLEDO. Parkinsonism Relat Disord 2021;83:79-85.
Barbosa P et al. Arq Neuropsychiatr 2020;80:56-61.

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Apomorphine and Sleep





Safety and efficacy of subcutaneous night-time only apomorphine infusion to treat insomnia in patients with Parkinson's disease (APOMORPHEE): a multicentre, randomised, controlled, double-blind crossover study

Valérie Cochen De Cock, Pauline Dodet, Smaranda Leu-Semenescu, Cécile Aerts, Giovanni Castelnovo, Beatriz Abril, Sophie Drapier, Hélène Olivet, Anne-Gaëlle Corbillé, Laurène Leclair-Visonneau, Magali Sallansonnet-Froment, Marie Lebouteux, Mathieu Anheim, Elisabeth Ruppert, Nicolas Vitello, Alexandre Eusebio, Isabelle Lambert, Ana Marques, Maria Livia Fantini, David Devos, Christelle Monaca, Nicolas Benard-Serre, Sandy Lacombe, Marie Vidailhet, Isabelle Arnulf, Mohamed Doulazmi, Emmanuel Roze

- Double-blind cross-over RCT
- 46 PD participants with insomnia
- Apomorphine max 5mg/hr vs placebo
- 10 nights
- PDSS better with apomorphine
- No increase in impulsivity or hallucinations



Managing Sudden OFF periods


- Madopar Dispersible
- Subcutaneous Apomorphine injections
- Sublingual apomorphine (Kynmobi)
- Inhaled levodopa (Inbrija)
- BUT
 - Remember priming and continuous dopaminergic stimulation

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Home initiation

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Journal of Neural Transmission
<https://doi.org/10.1007/s00702-023-02710-w>

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE

Home initiation of apomorphine infusion: lessons from the COVID-19 pandemic and implications for current clinical practice

Christopher Kobylecki^{1,2}  · Lucy Partington-Smith³

- 27 patients
- Median 4mg/hr (range 1-6mg/hr)
- 7/27 used night-time dose as well
- 21/27 = 78% achieved good therapeutic response.

- ECG
- Bloods - FBC, Retic, Coombs.
- BP - lying and standing
- Domperidone 10mg tds for at least 48 hours.
- Start at 1mg/hr (=0.2ml/hr).
- BP every 15 min 1hr then every 30min 2nd hour.
- Changes in flow typically made weekly. with med reductions.

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Journal of Neural Transmission

<https://doi.org/10.1007/s00702-023-02609-6>

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE



Feasibility and benefits of home initiation of subcutaneous apomorphine infusion for patients with Parkinson's disease: the APOKADO study

Fabien Zagnoli¹ · Amélie Leblanc² · Irina Viakhireva-Dovganyuk² · Jean-Philippe Delabrousse-Mayoux³ ·
Alain Pouyet⁴ · Marc Ziegler⁵ · Laura Sogni⁶ · Marie Patat⁶ · Régis Bouillot⁶ · Marc Vérin^{7,8,9}  · The APOKADO Group

- 145 patients, 29 centres
- 106 home initiation, 38 hospital initiation
- Similar benefit without all the hassle
- QOL improved more quickly in home initiation group



Conclusions

- Consider CSAI in patients with motor fluctuations
- Caution with significant axial symptoms
- Probable improvement in non-motor symptoms as well
- Caution with ICDs but studies reassuring
- Often good for sleep problems
- Home initiation works well



Apomorphine: An overview of efficacy and selection criteria: The End

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Professor of Neurology



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