

Continuous dopaminergic stimulation minimizes levodopa-induced motor complications

Jeff Bronstein MD, PhD

Director, UCLA Movement Disorders
Program and Veterans Administration
SW PADRECC



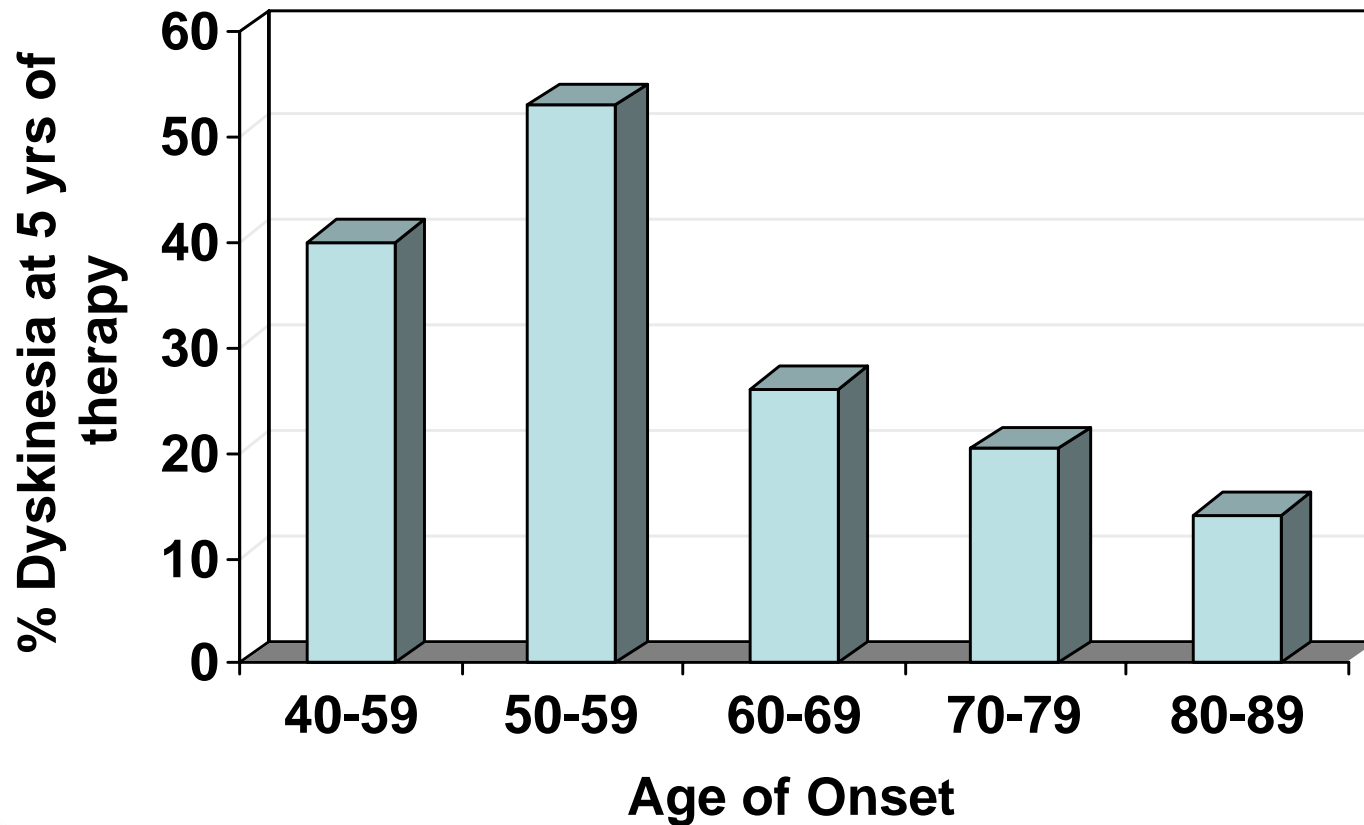
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Prevalence of Motor Fluctuations

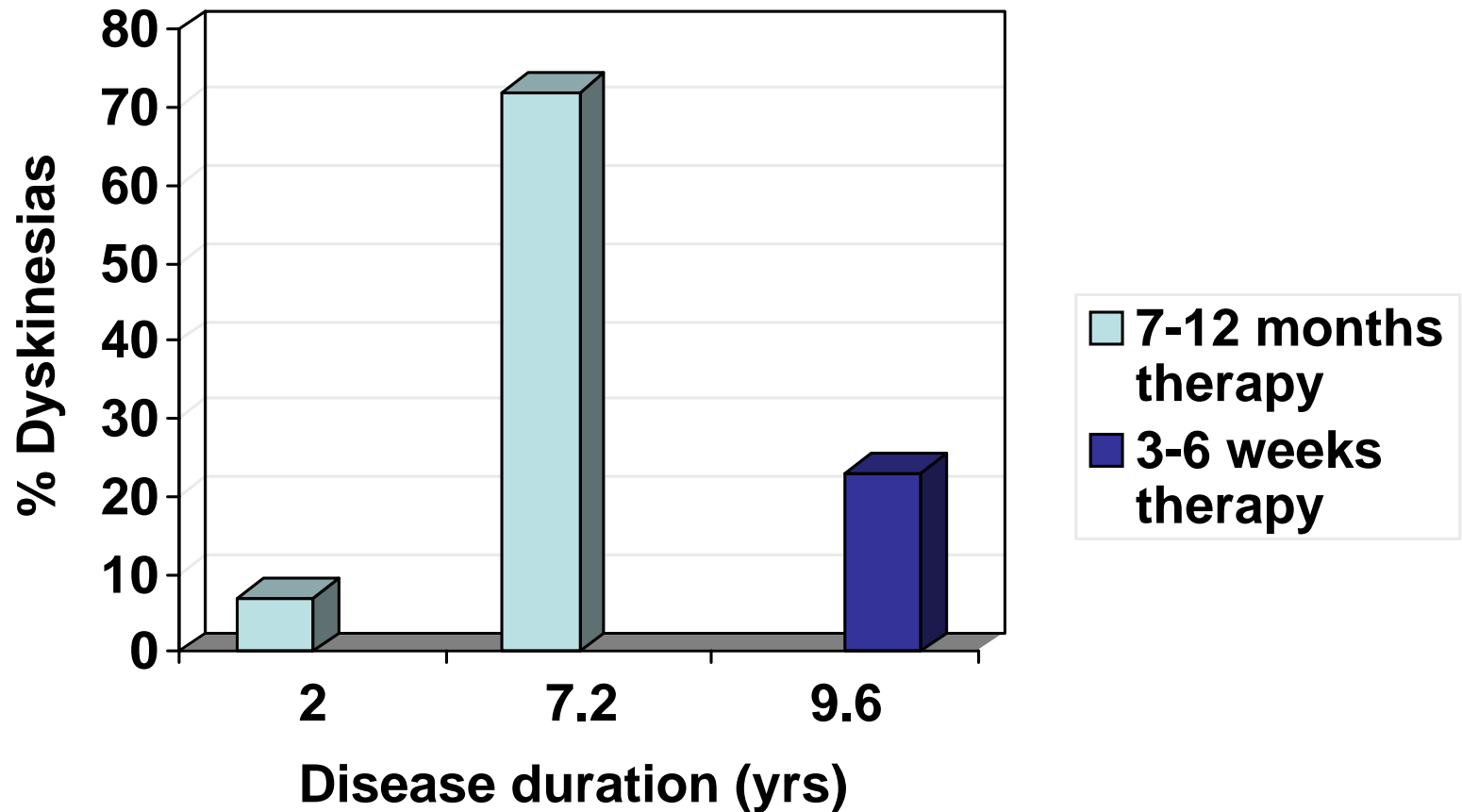
- Varies with
 - age of patient
 - duration of disease
 - type of therapy



Effect of Age on Motor Fluctuations



Effect of Disease Duration on Motor Fluctuations



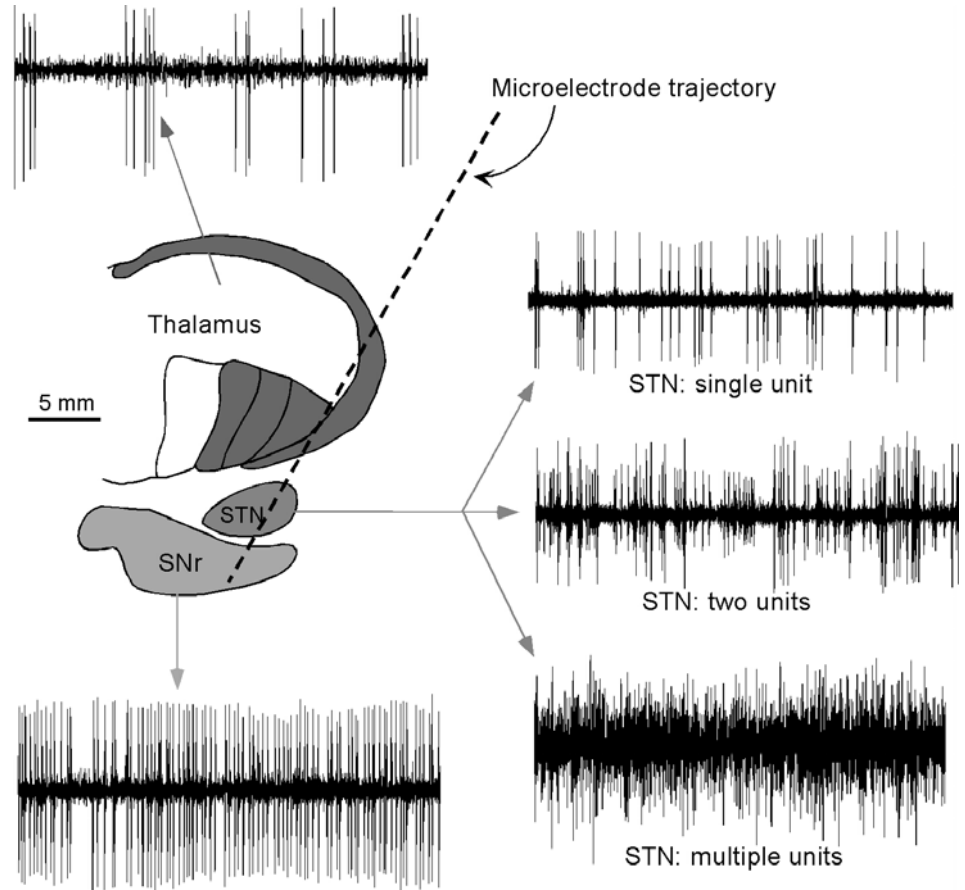
Effect of Therapy on Motor Fluctuations

- Continuous dopamine stimulation (CDS)
 - Physiological
 - Reduces priming
 - Reduces fluctuations once primed



CDS is Physiological

QuickTime™ and a
TIFF (LZW) decompressor
are needed to see this picture.



Grace and Bunney, 1984



Dopamine is tonically released

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Keefe, Zigmond, Abercombie, 1992

Etiology of Fluctuations

- Presynaptic mechanisms
 - Loss of DA buffering capacity
 - Extraneuronal DA synthesis from levodopa
- Postsynaptic
 - Alterations in DA receptors (unlikely)
 - Plasticity
 - Increased PPE in indirect pathway
 - Altered glutamate receptors



Priming with Postsynaptic Pulsatile Stimulation



Maybe COMT-I will help.

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Smith et al., 1995

Fluctuations are Dependent on Levodopa Levels

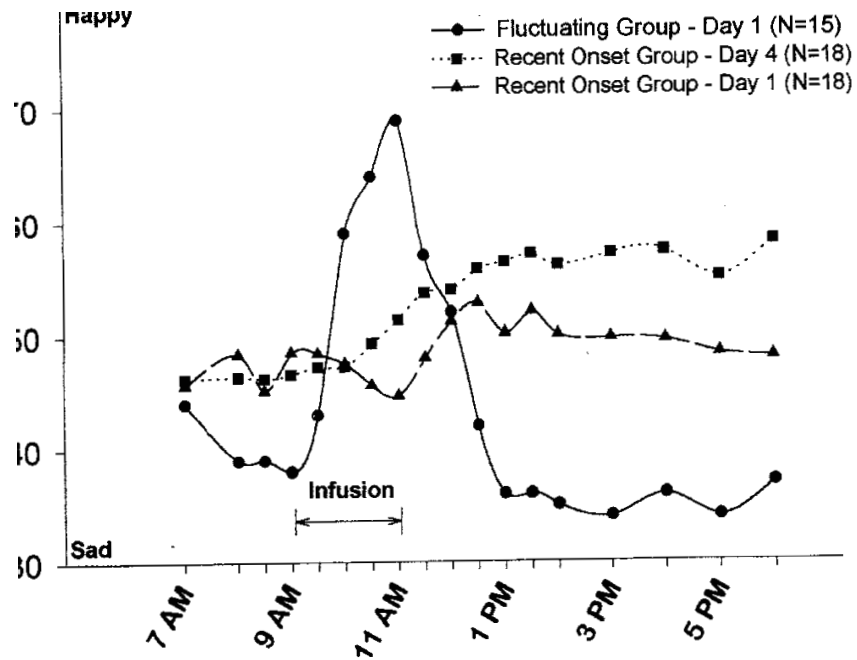
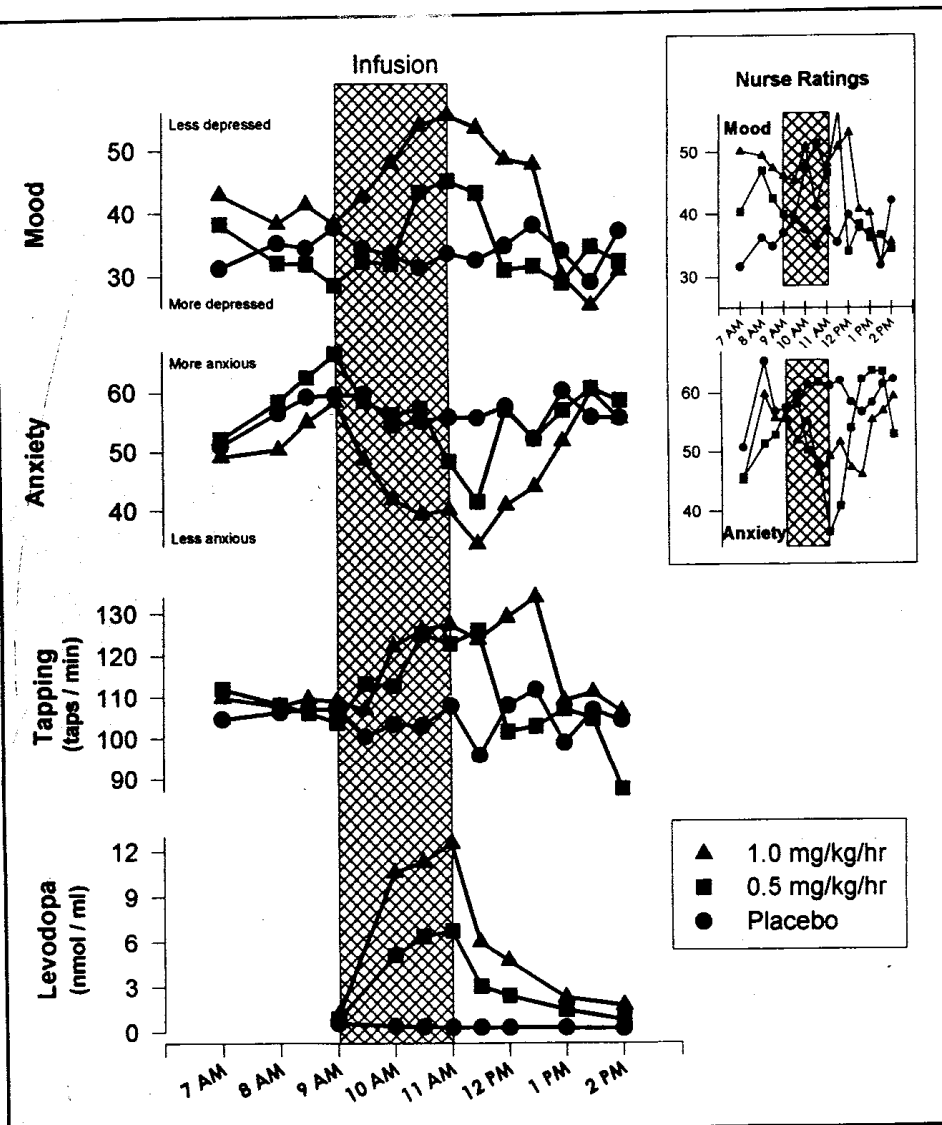


Figure 2. Changes in visual analog score mood ratings in

Fluctuations improve acutely with CDS

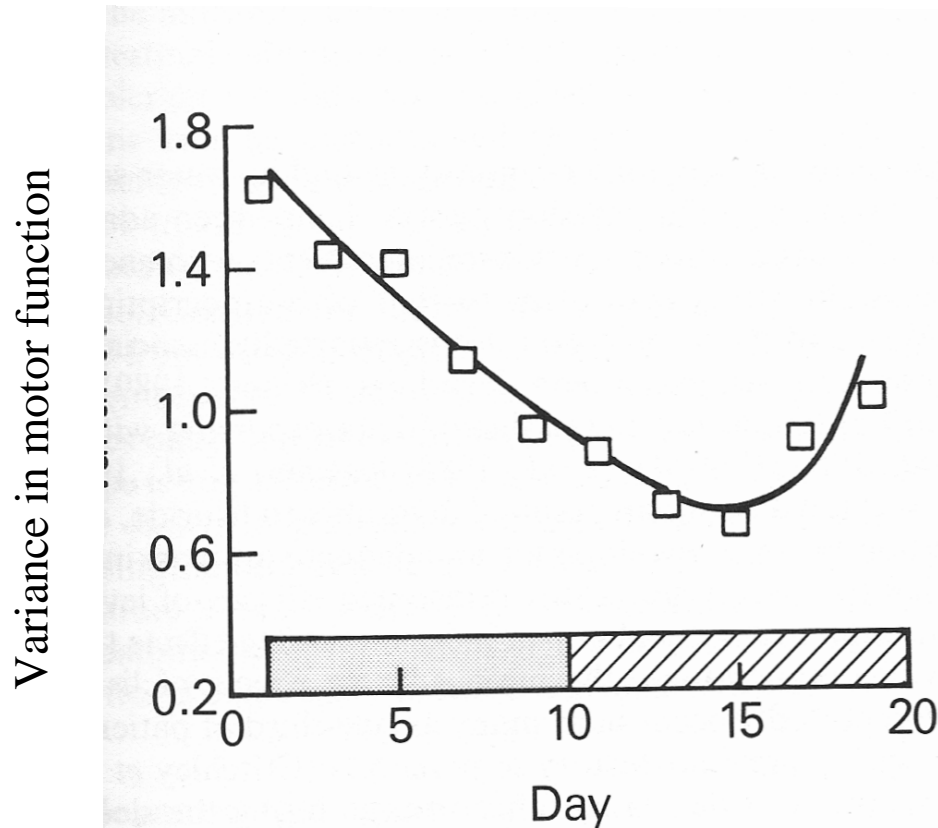


Figure 10.7 Gradual improvement of motor fluctuations during

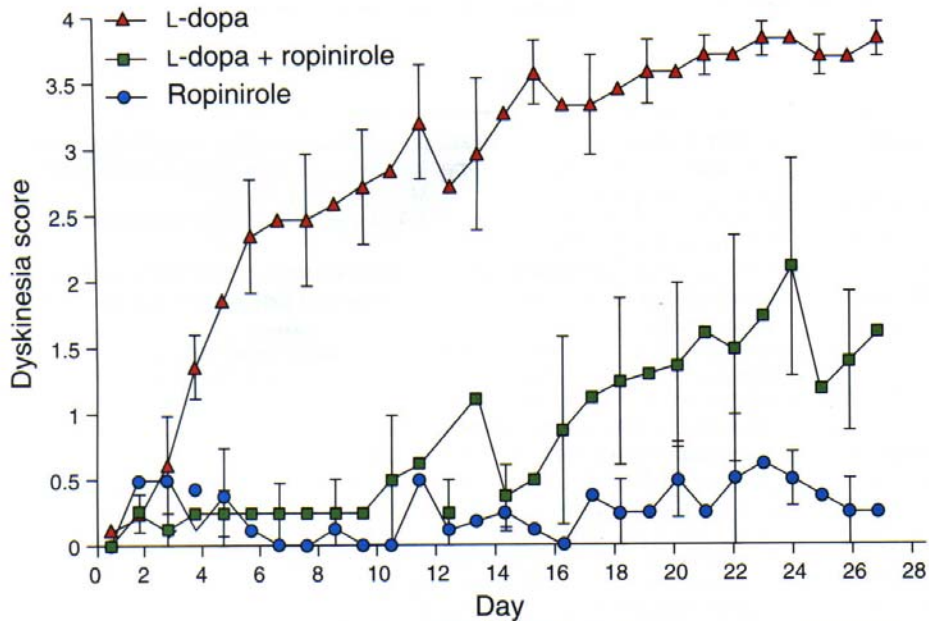
Levodopa infusion



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Mouradian et al. (1990)

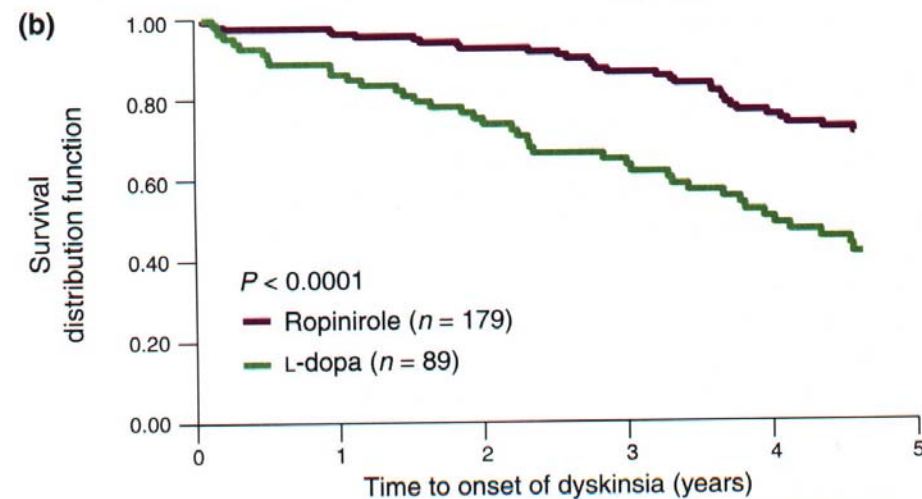
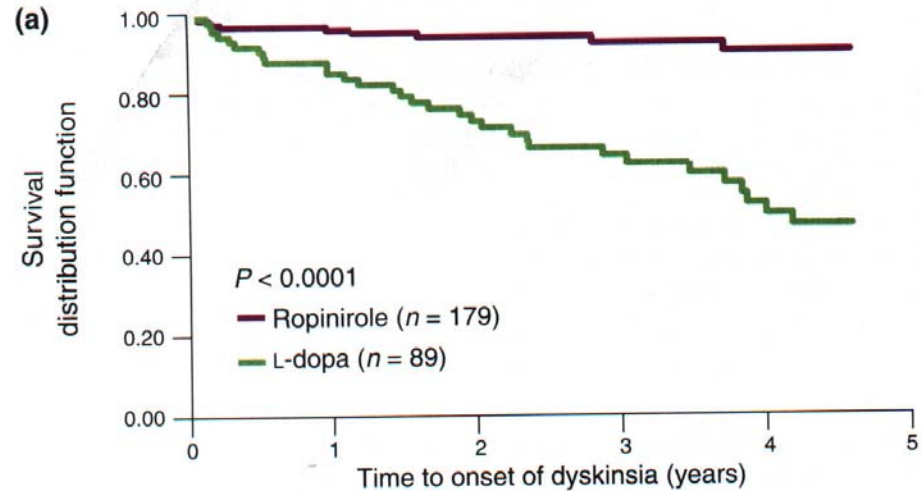
What's the evidence in clinical practice?



Basal ganglia, Parkinson's disease and levodopa therapy: TINS supplement

Fig. 1. Dyskinesias in MPTP monkeys. Frequency of dyskinesia in 1-methyl-4-phenyl-1,2,3,6-

Rascol et al (2000) NEJM



Basal ganglia, Parkinson's disease and levodopa therapy: TINS supplement



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CDS with Duodopa

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CDS with Continuous Apomorphine

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TIFF (LZW) decompressor
are needed to see this picture.

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Colzi, Turner, and Lees, 1998

Similarities to Kindling

