



**Behavioral aspects of Parkinson's disease**  
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# Disclosures

- No relevant financial relationships with commercial interests.
- Advisor for Acadia Pharmaceuticals
- The following talk includes unlabeled/unapproved use of medications.

## Objectives:

- 1.To become familiar with behavioral disturbances in Parkinson's disease (PD) including: anxiety, apathy, depression, impulse control disorders, and mild cognitive impairment
- 2.Discuss how the physical/biological aspects of PD and its treatments may be associated with behavioral symptoms
- 3.Review examples of specific behavioral disturbances in PD

**I. Overview of Parkinson's as a 'disease' model for behavioral symptoms**

**II. Anxiety, depression, and apathy in PD**

**III. Unusual behaviors in PD**





***Essay on the Shaking Palsy***

**“...the senses and intellects being uninjured.”**

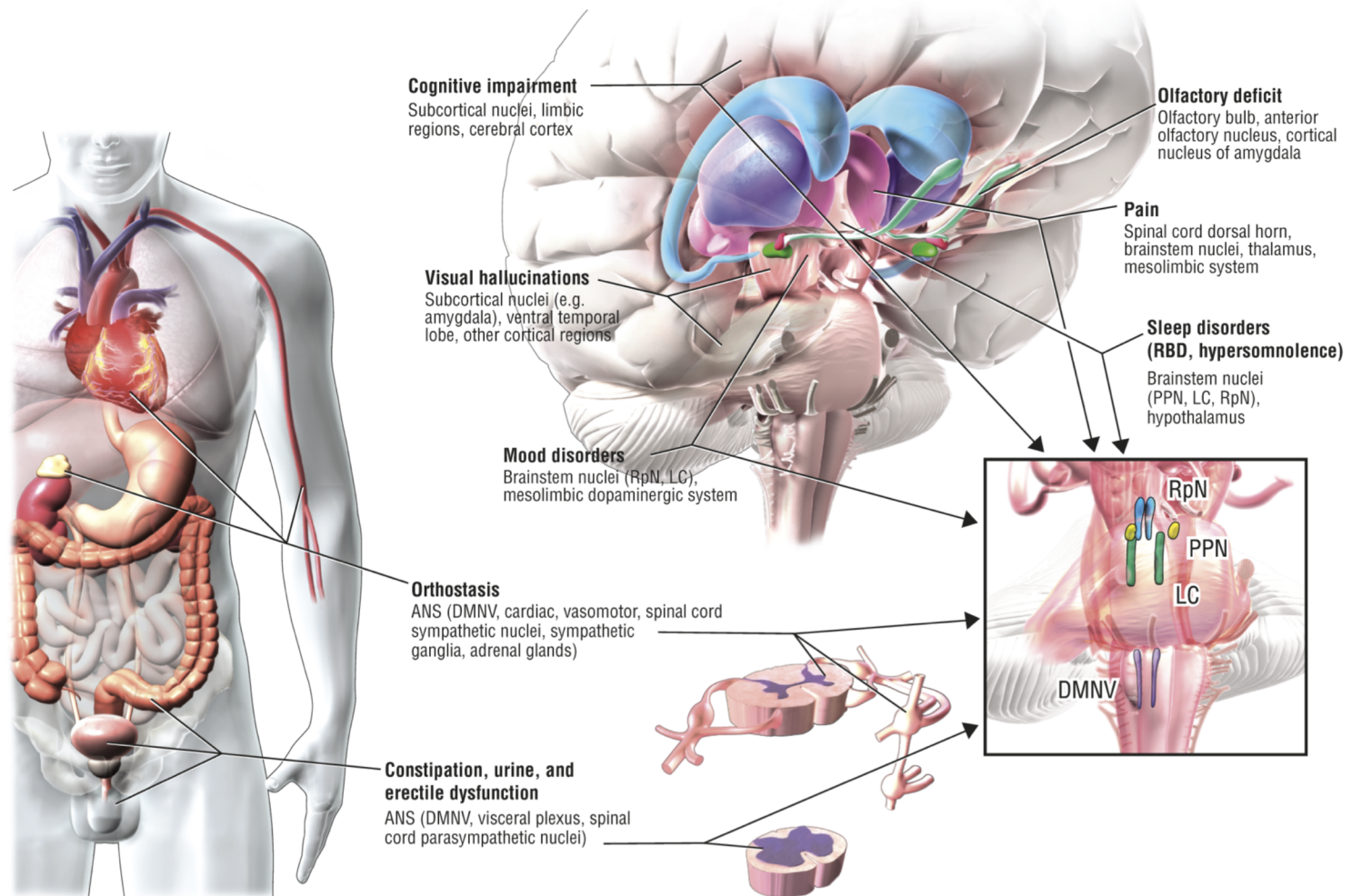
**James Parkinson, 1817**

# Non-motor symptoms of Parkinson's disease

- Olfactory loss, up to 90% of PD
- Dysautonomia, up to 70% of PD (constipation, gastroparesis, erectile dysfunction, orthostatic hypotension)
- Neuropsychiatric symptoms: mood and anxiety disorders, at least 40-50%
- Impulse control disorders >15%
- Sleep disturbances >30%(e.g. RBD)
- Cognitive impairment, up to 40% have selective deficits at diagnosis (mild cognitive impairment)

# Extranigral Aspects of Parkinson's disease

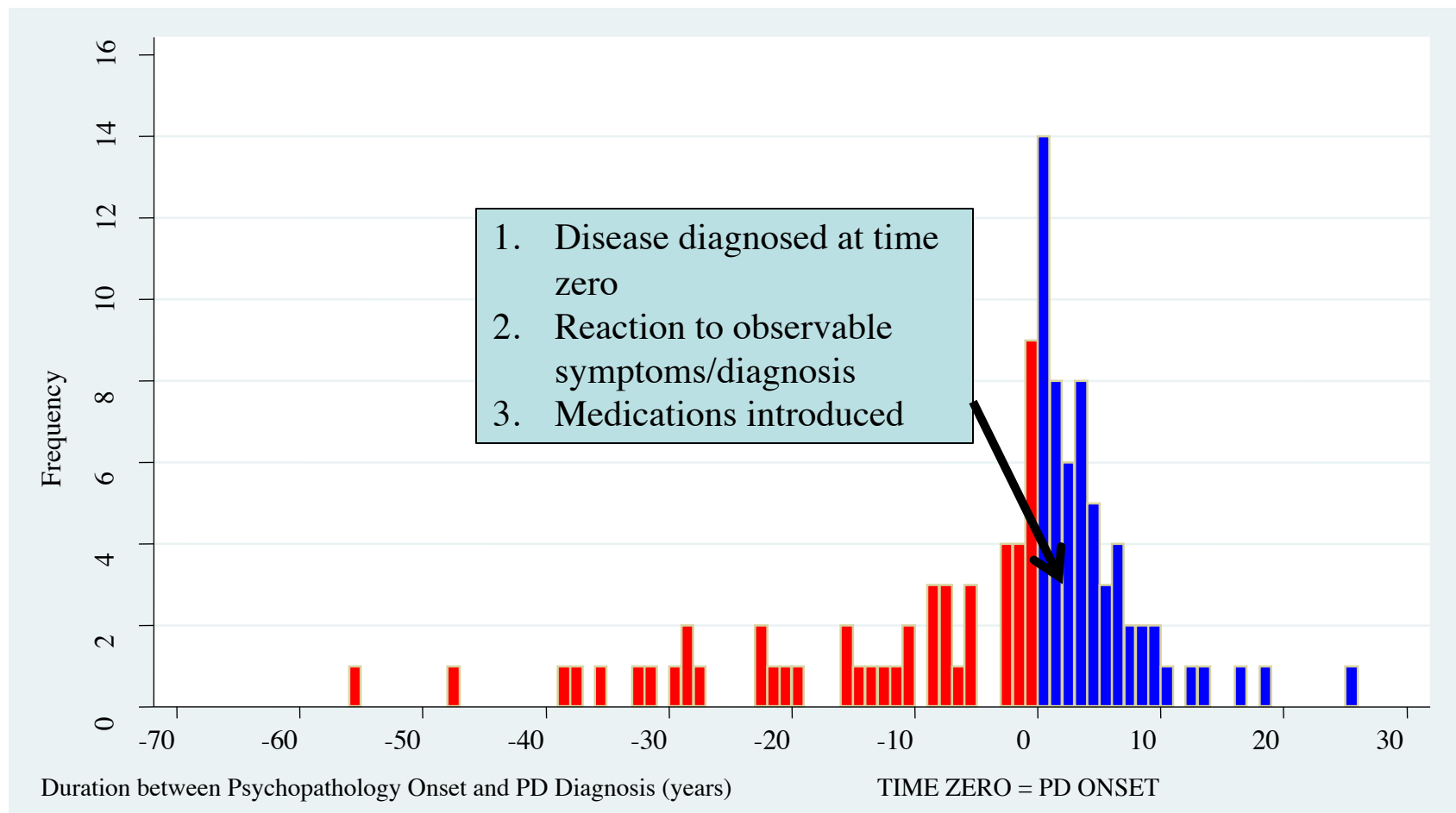
(Arch. Neurol 2009, Lim et al)



# What causes behavioral changes in PD?

1. Reaction to the diagnosis - altered interpersonal roles, disability, and other psychosocial features
2. Related to the disease process
3. Interaction between the disease and dopaminergic medications

# Intersection of mental and physical health in PD



# Anxiety in Parkinson's disease JOHNS HOPKINS MEDICINE

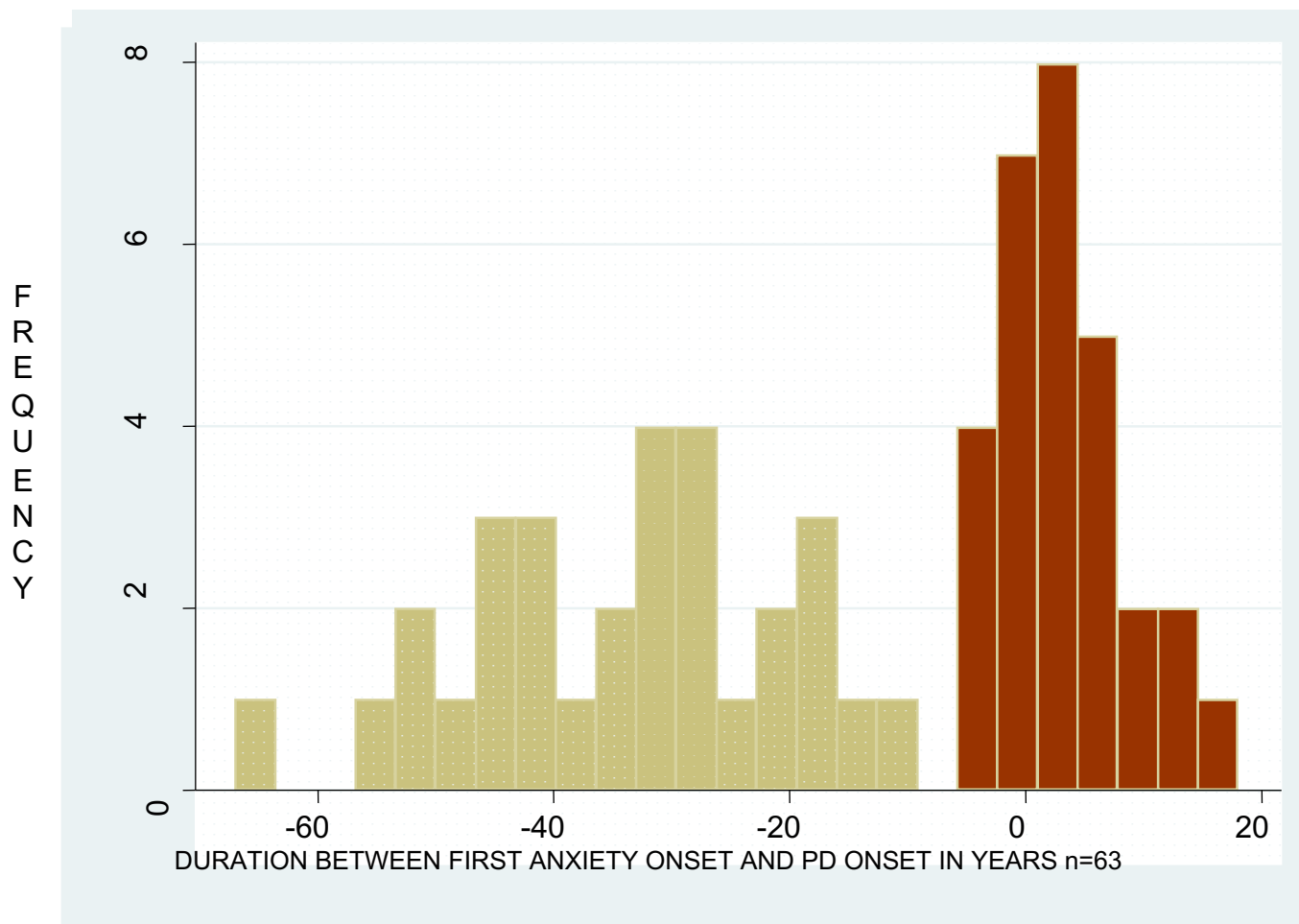


# Prevalence of anxiety and anxiety disorders in PD

- Up to 55% have clinically significant anxiety symptoms
- 31% have an anxiety disorder (e.g. DSM)

\*Anxiety disorder not otherwise specified 13.3%

# First Anxiety Disorder Onset Relative to PD Onset



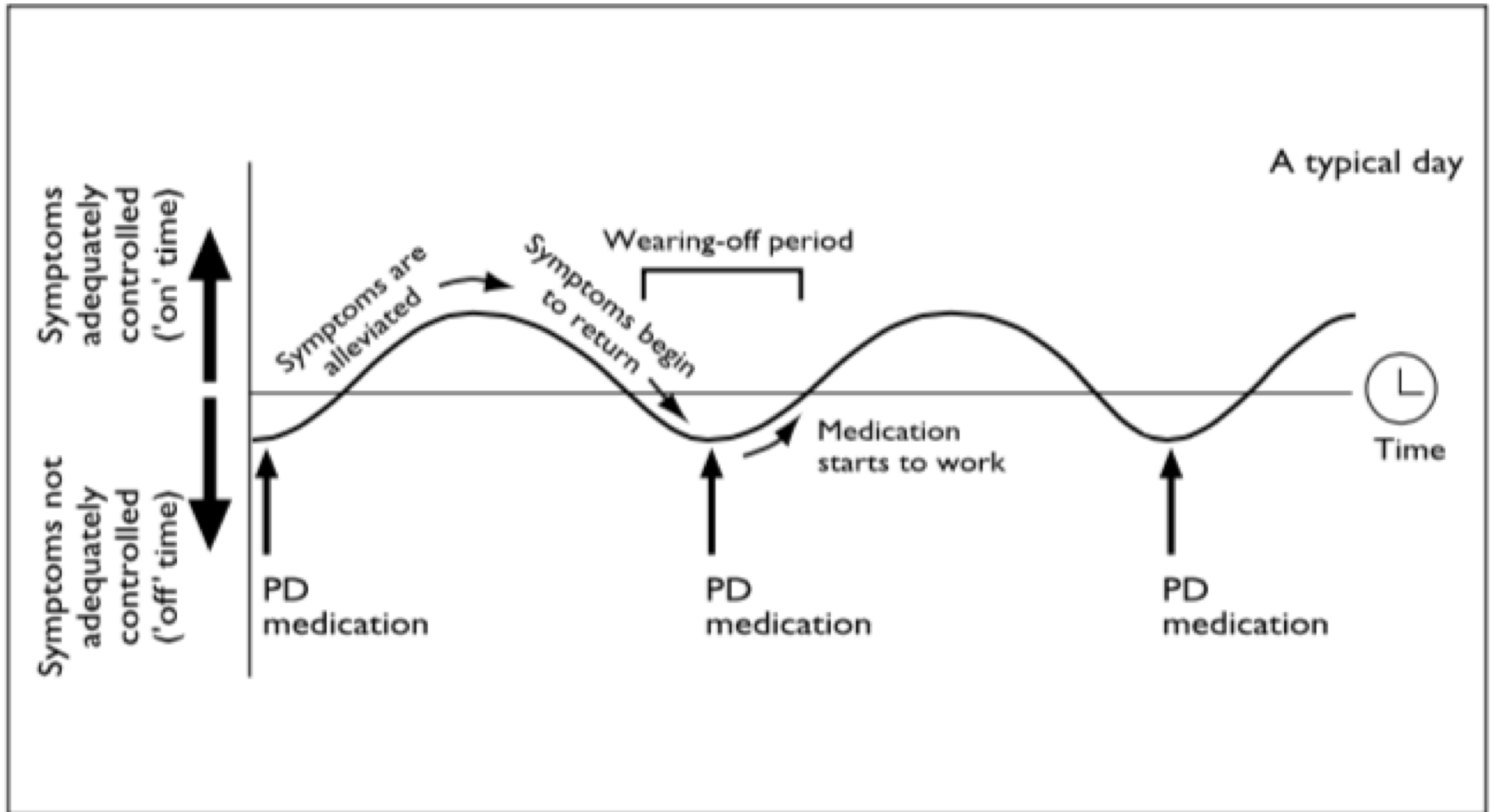
Bimodal distribution of anxiety disorder onset compared to PD onset



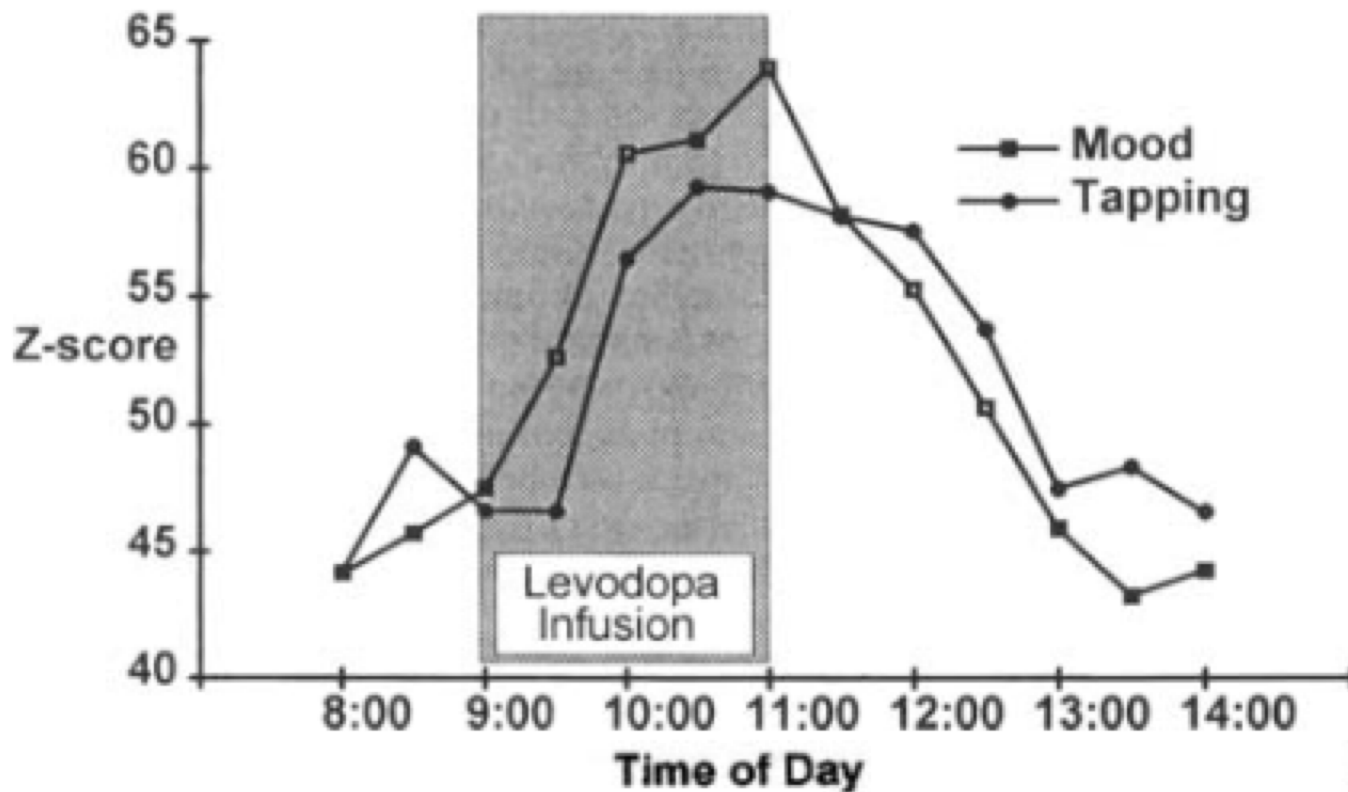
# Dopaminergic on-off motor fluctuations

- Improvement in motor symptoms after L-dopa administration = “on”
- Return of parkinsonian movement symptoms at the end of the dosing effect = “off”

# Dopaminergic medication on-off fluctuations in PD

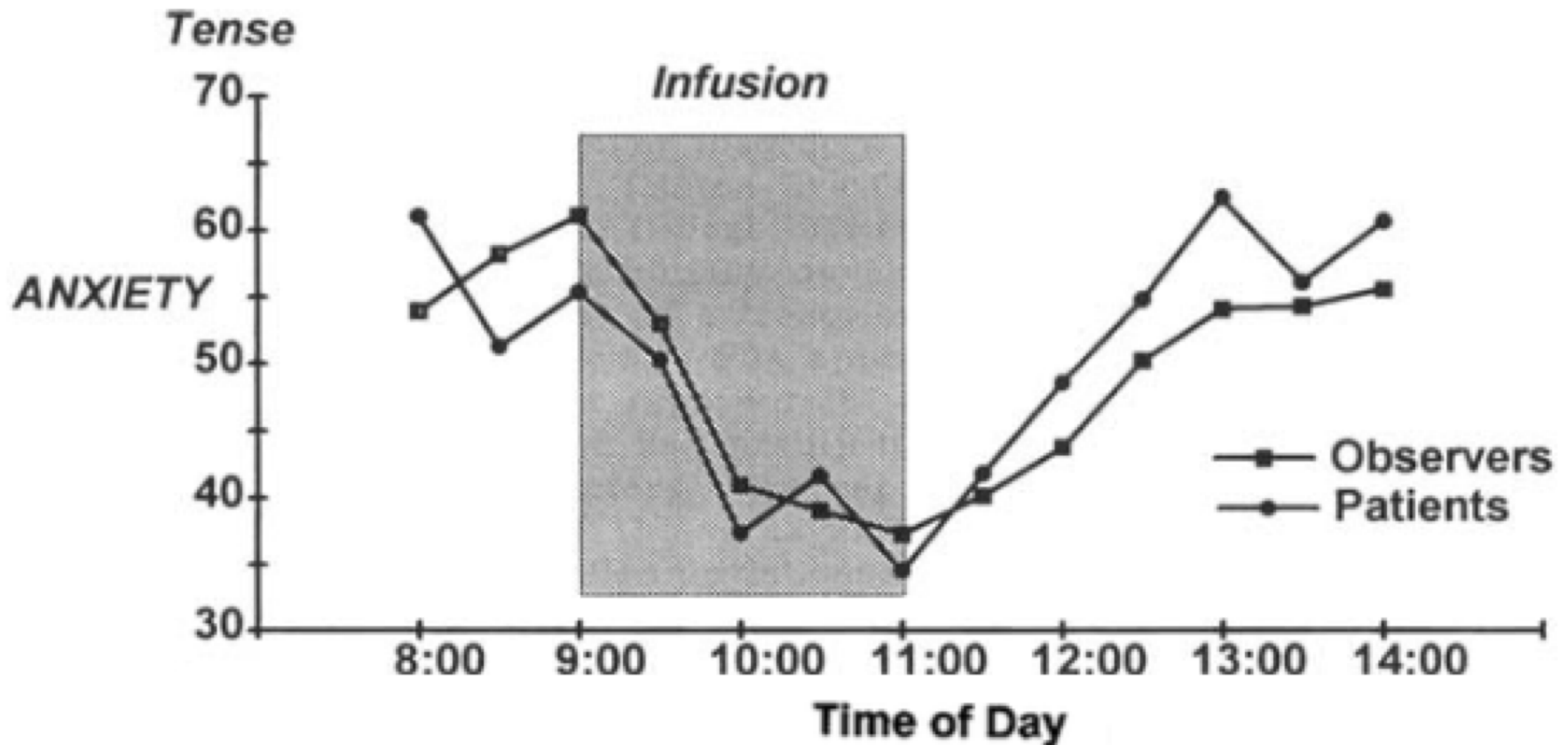


# Mood and motor fluctuation with levodopa infusion



**FIG. 3.** Relationship of mood change and motor change.

# Anxiety fluctuation with levodopa infusion



# Evidence based treatments for JOHNS HOPKINS MEDICINE anxiety in PD

- Cognitive Behavioral Therapy (CBT) for anxiety in PD
- MDS Task Force on Evidenced Based Medicine and the American Academy of Neurology conclude that “the evidence to support or refute specific treatments for anxiety is insufficient”

# Depression in Parkinson's disease



- **Parkinson's Outcomes Project**, a longitudinal look at which treatments produce the best health outcomes in PD n=12,000+
- **The impact of depression on quality of life is almost twice that of the motor impairments**

# Prevalence of Depression in Parkinson's disease

- up to 50% (major and minor depression or dysthymia)
- Rates of recurrence or treatment resistance unclear
- Anxiety disorders often co-occur



# NET-PD Study/Neuroprotective Treatment Trials



- Mild depressive symptoms predicted development of more severe depressive symptoms (RR=6.16 [95%CI 2.14.17.73])
- Depressive symptom severity, older age, longer PD duration predicted failure to remit (HR 0.83-0.92)

# NET-PD Study/Neuroprotective Treatment Trials



Depressive symptoms predicted

- Increased need for symptomatic PD therapy (HR 1.86; 95% CI 1.29-2.68)
- Increased impairment in activities of daily living ( $p < 0.0001$ )

RESEARCH ARTICLE

# The longitudinal impact of depression on disability in Parkinson disease

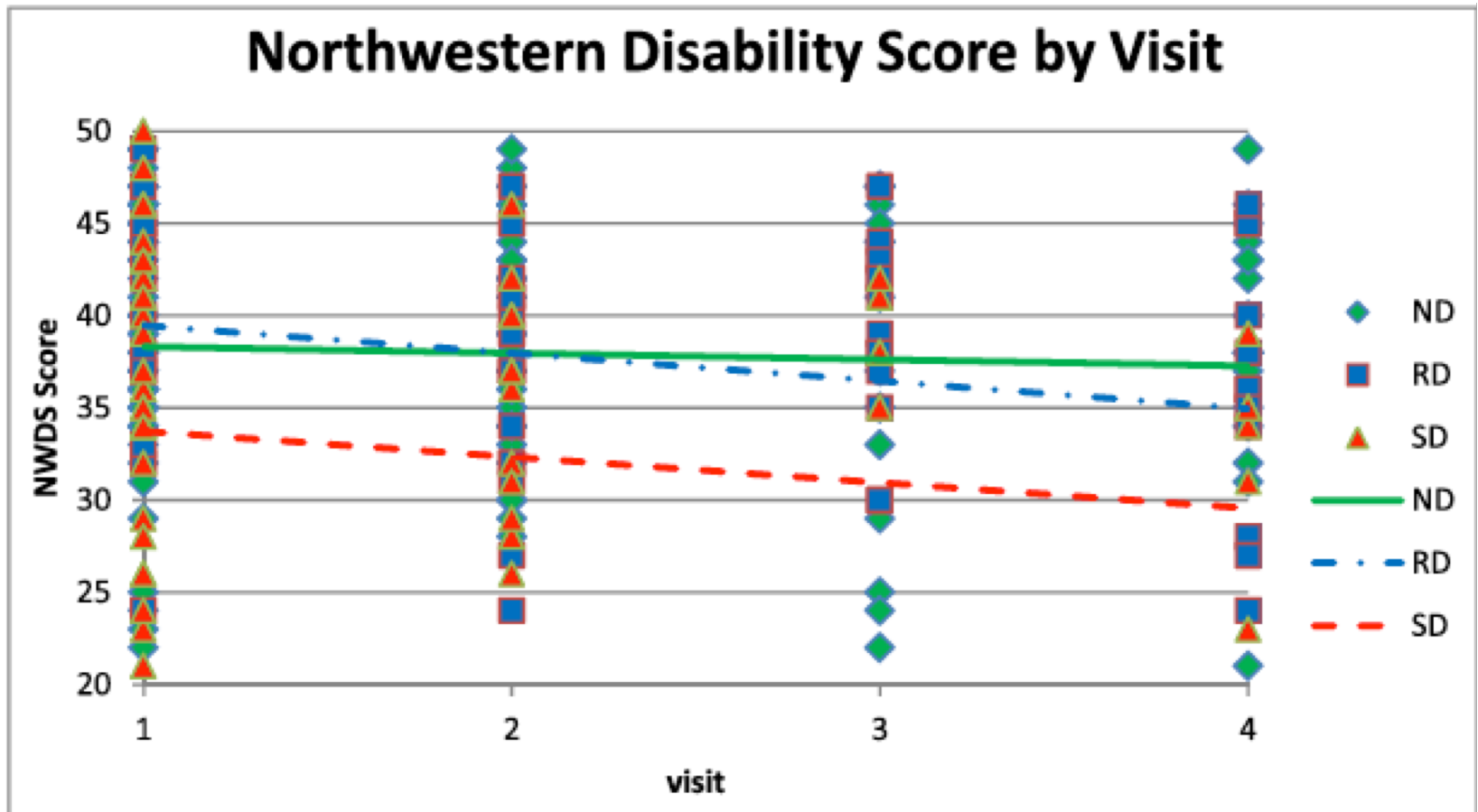
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**Objective:** This study examined the association between physical disability and DSM-IV-TR depression status across six years

**Methods:** 137 adults with idiopathic PD. A generalized linear mixed model with Northwestern Disability Scale score as dependent variable to determine the effect of baseline depression status on disability

**Results:** 43 depressed at baseline vs 94 without depression. Symptomatic depression predicted greater disability compared to both never depressed ( $p=0.0133$ ) and remitted depression ( $p=0.0009$ ) after controlling for sex, education, dopamine agonist use, and motor fluctuations.

# Longitudinal impact of depression on disability in PD (Pontone et al 2016)



ND=never depressed, RD=remitted depression, SD=symptomatically depressed

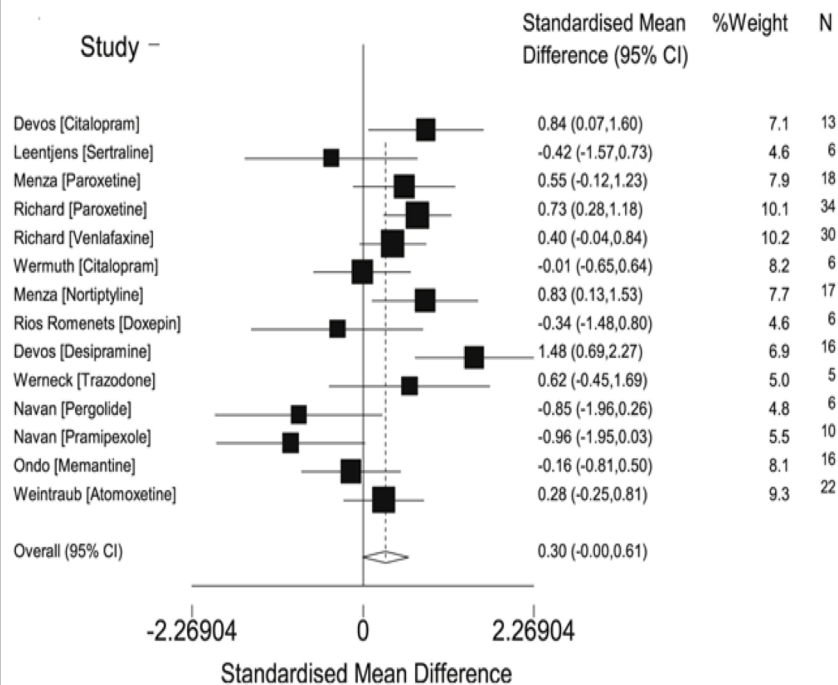
# Antidepressive Treatment for PD

## Systematic Review & Meta-analysis

N=893, 20 RCTs (13 meds, 4 CBT, Alexander Tech, 2 rTMS)

### ALL INTERVENTIONS

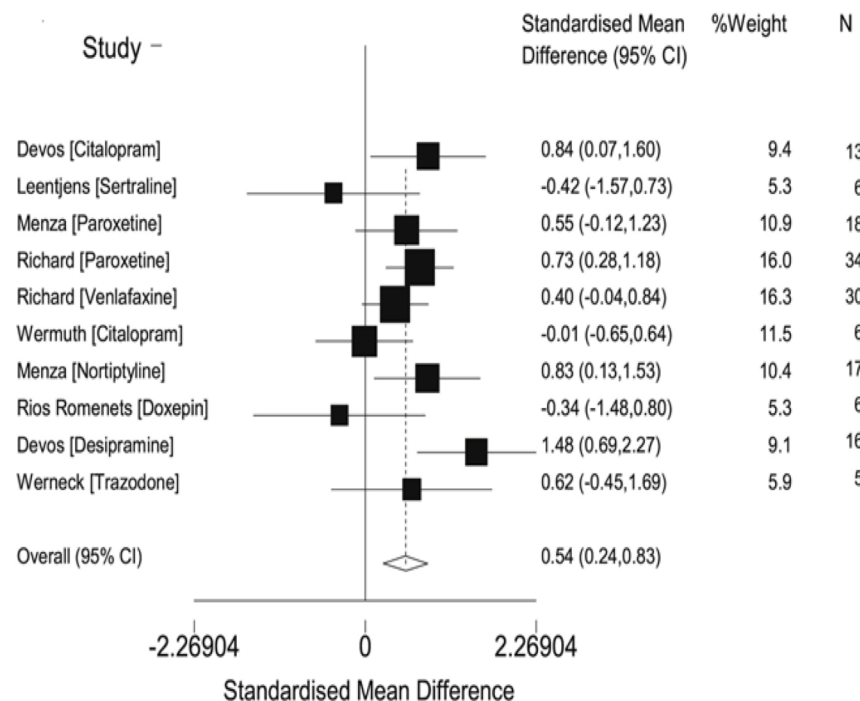
SMD=.30



Test of SMD = 0 : z = 1.93 p = 0.054

### ANTIDEPRESSANTS

SMD=.56



Test of SMD = 0 : z = 3.56 p = 0.000

# APATHY IN PARKINSON'S DISEASE



# Apathy in Parkinson's disease JOHNS HOPKINS MEDICINE

- May affect more than 1/3 of persons with PD
- Associated with more severe motor symptoms and cognitive impairment; more likely to be men and older age

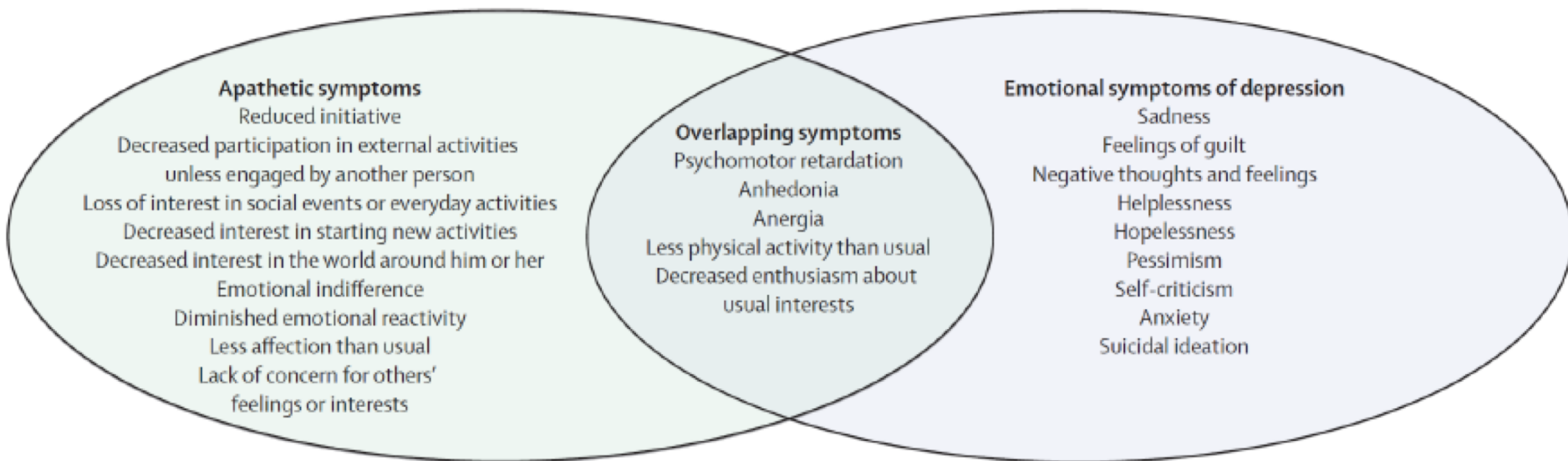
# Apathy in Parkinson's disease

3+ symptoms lasting more than one month and impacting function

- Reduced initiative and decreased self-driven ideas
- Decreased curiosity and spontaneity
- Difficulty continuing activities to completion
- Indifference or blunted emotional reactions
- Lack of concern about personal problems
- Lack of affectionate behavior



# Apathy vs depression in PD



# Management of apathy in PD

- Non-pharmacological interventions
  - scheduled activities (social and physical)
  - establish clear and achievable goals
  - rewards conditional on completion of goals
  - recruit social support for activities
- Dopamine agonists and acetylcholinesterase inhibitors (Seppi et al. 2019)



# **Impulse control disorders in Parkinson's disease**

# Impulse control disorders (ICDs) in PD

- “An assortment of behaviors performed repetitively, excessively, and with a ***lack of self-control*** to an extent that interferes with life functioning”
- **Associated with dopamine agonist medications** and other dopamine replacement therapies

# Impulse control disorders in PD

- Pathological gambling
- Compulsive buying/shopping
- Hypersexual behaviors
- Binge eating

# Dopamine dysregulation syndrome

- Drug addiction-like state marked by self-medication with inappropriately high doses of dopaminergic medications
- May be more common in early onset PD and males—prevalence 3%-4%
- Co-occurs with ICDs, psychosis, panic attacks

- Repetitive, purposeless behaviors, characterized by an intense preoccupation with specific items or activities – collecting, arranging, or taking apart objects
- Hobbyism – higher level repetitive behaviors, e.g. excessive internet use, reading, art work, work on projects

# **EXECUTIVE DYSFUNCTION: MENTAL AND PHYSICAL DISEASE INTERACTION IN PD**



# Executive Dysfunction

- Deficits in initiation, sequencing, planning, and set shifting; impaired mental speed (bradyphrenia)
- One of the earliest detectable cognitive changes

# Influence of Task Demands

- “Let’s have tea!” Study (Rochester et al, Arch Phys Med Rehab, 2004)
  - Looked at how attentional demands during an everyday functional activity contributes to functional performance and gait disturbances
- Study
  - 20 mild to moderate PD, 10 Controls
  - 4 Tasks
    - Simple walking: Walk to kitchen
    - Dual-motor: Walk and carry tray
    - Dual-cognitive: Walk and recall a memory
    - Multiple motor-cognitive task: Walk, carry tray, and recall a memory
- Results
  - Increased task complexity → ↓ gait speed

# Questions?

