



Mood and Emotional Regulation in Parkinson's Disease

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Disclosures

- No relevant financial relationships with commercial interests.
- Consultant for Acadia Pharmaceuticals Inc

Psychiatric Issues and Management in Parkinson's Disease

Objectives:

1. Become familiar with the presentation of mood issues in Parkinson's disease (PD)
2. Discuss how the physical/biological aspects of PD may be associated with mood issues
3. Recommend strategies for managing mood issues in PD

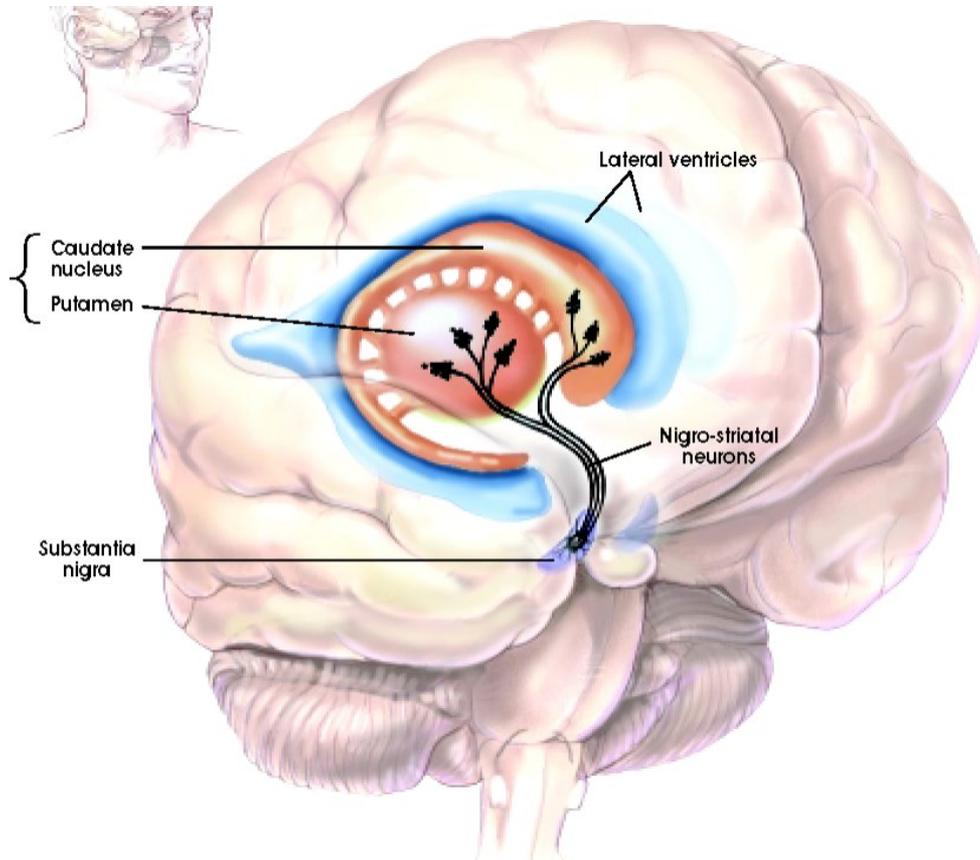


I. Overview of mood issues in Parkinson's

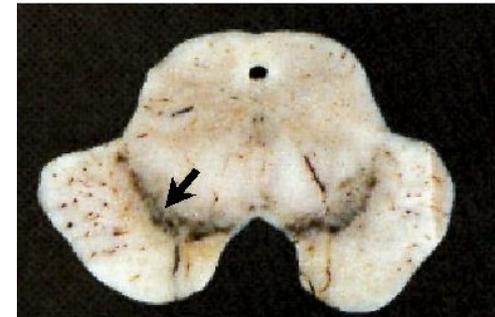
II. Depression in Parkinson's

III. Other mood and emotional disturbances in Parkinson's

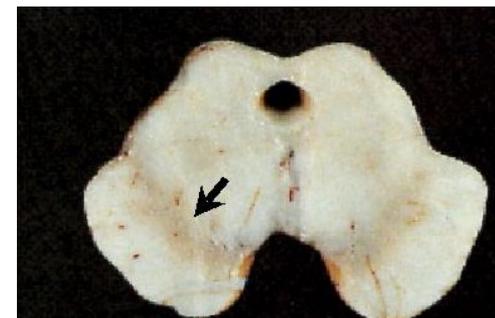
Gross Pathology of Parkinson's Disease



Normal

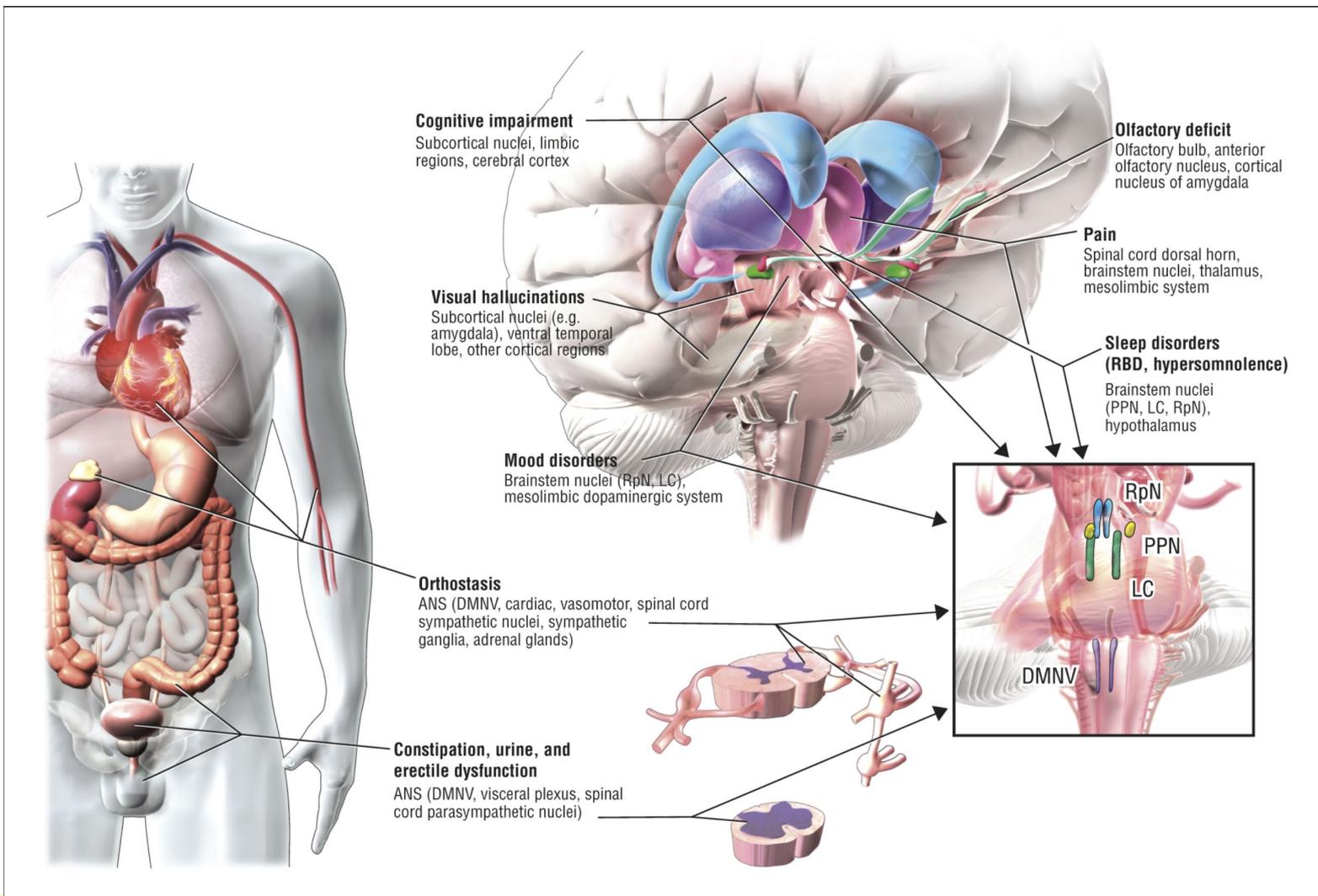


Parkinson's



Extranigral Aspects of Parkinson's disease

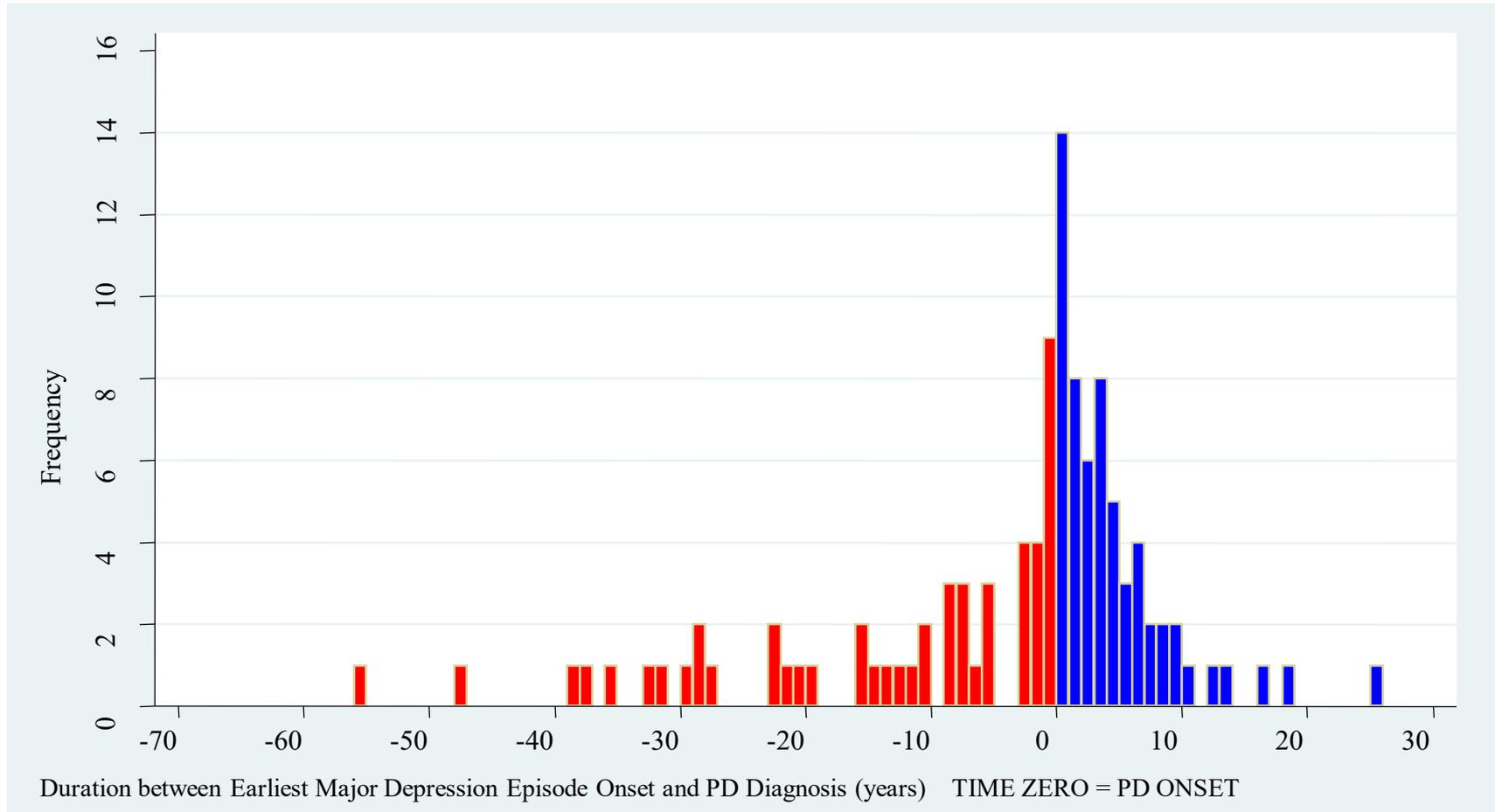
(Arch. Neurol 2009, Lim et al)



Mechanistic Theories of Depression: Monoamine theory

- Major depression is mechanistically complex and likely heterogeneous
- Monoamine theory: depression is due to a deficiency of monoamine neurotransmitters (NE, SE, DA)
- Antidepressants that modulate monoaminergic neurotransmission induce a therapeutic response in just 50% of patients, with only 30% achieving remission

Depressive disorders can occur at any stage of PD



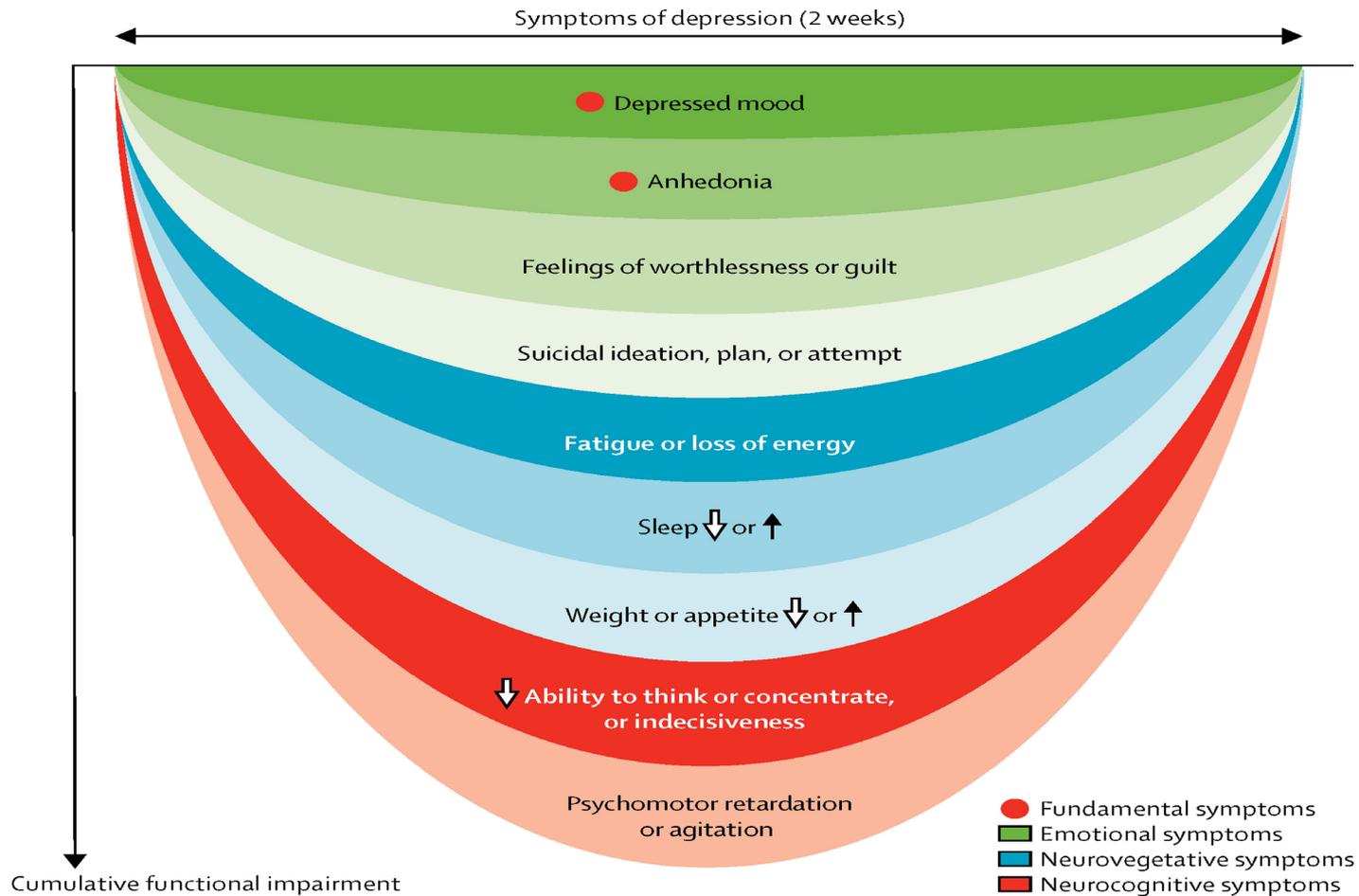


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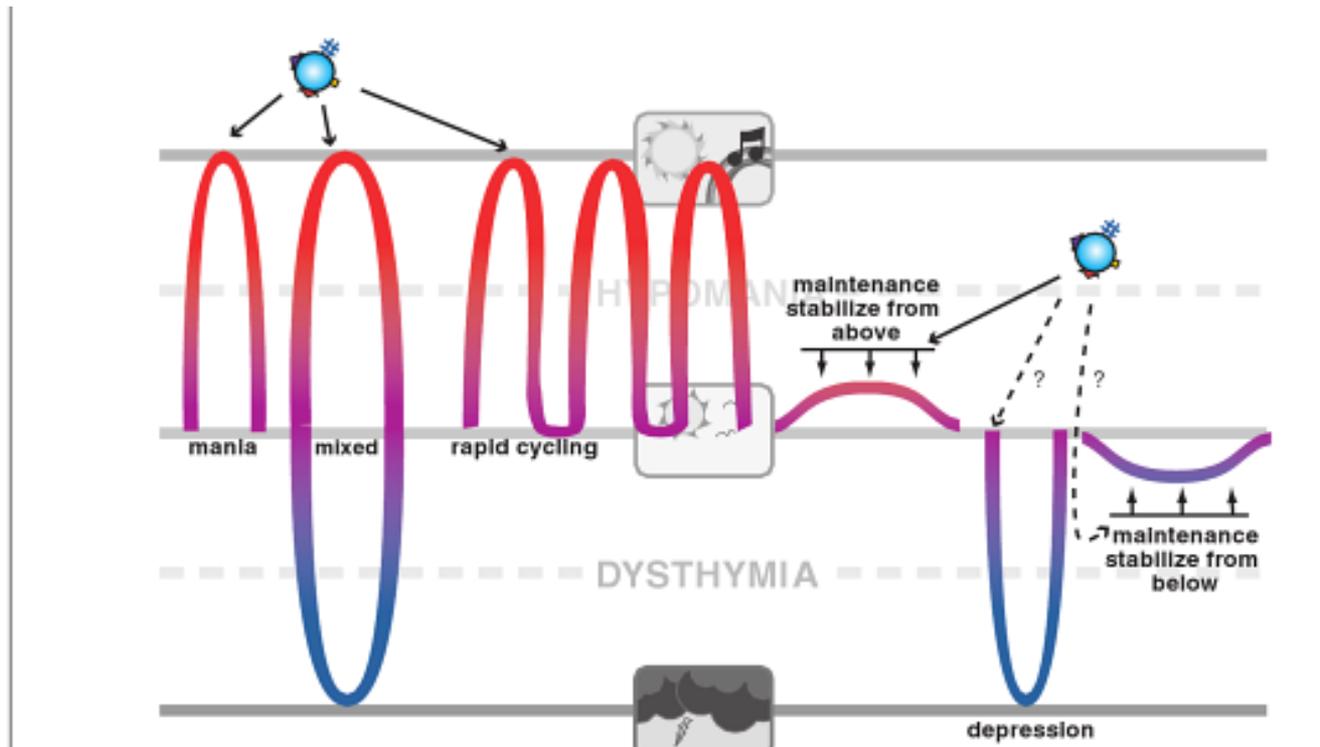
Major depression



Parkinson's disease symptoms that could mimic symptoms of major depressive disorder

Core depressive symptoms in Major Depressive Disorder	Parkinson's symptoms that may mimic depressive symptoms
Depressed mood	Masked facies, adjustment disorder to diagnosis
Lack of interest of participation in usual activities	PD-related apathy
Weight loss or decrease in or increase in appetite	Wasting of advanced PD, levodopa-induced nausea, dysphagia
Insomnia or hypersomnia	Sleep fragmentation, medication-induced somnolence
Psychomotor agitation or retardation	Levodopa-induced dyskinesia, bradykinesia
Low energy	PD-related fatigue
Diminished ability to think or concentrate	PD-related cognitive impairment with prominent executive deficits
Feelings of inappropriate guilt or worthlessness or hopelessness	Core depressive symptom, no PD mimic
Suicidal ideation or plan	Core depressive symptom, no PD mimic

Bipolar Disorder: Mood Cycling



Bipolar disorder and the risk of Parkinson's

- Bipolar disorder is associated with an increased risk of later Parkinson's disease
- PWP with bipolar disorder are at increased risk of impulse control disorders, delusions, dementia, and early mortality
- PWP with bipolar disorder are more like than PWP without bipolar to have a family history of PD

1. Onofrj M, Di Iorio A, Carrarini C, et al. Preexisting Bipolar Disorder Influences the Subsequent Phenotype of Parkinson's Disease. *Mov Disord.* 2021 Dec;36(12):2840-2852. Epub 2021 Aug 24. PMID: 34427338
2. Faustino PR, Duarte GS, Chendo I, Castro Caldas A, Reimão S, Fernandes RM, Vale J, Tinazzi M, Bhatia K, Ferreira JJ. Risk of Developing Parkinson Disease in Bipolar Disorder: A Systematic Review and Meta-analysis. *JAMA Neurol.* 2020 Feb 1;77(2):192-198. PMID: 31609378

Prevalence of Depression in Parkinson's disease

- 25% for major depression up to 50% for 'minor' depression/dysthymia
- Anxiety disorders often co-occur

Parkinson Foundation



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

The longitudinal impact of depression on disability in Parkinson disease

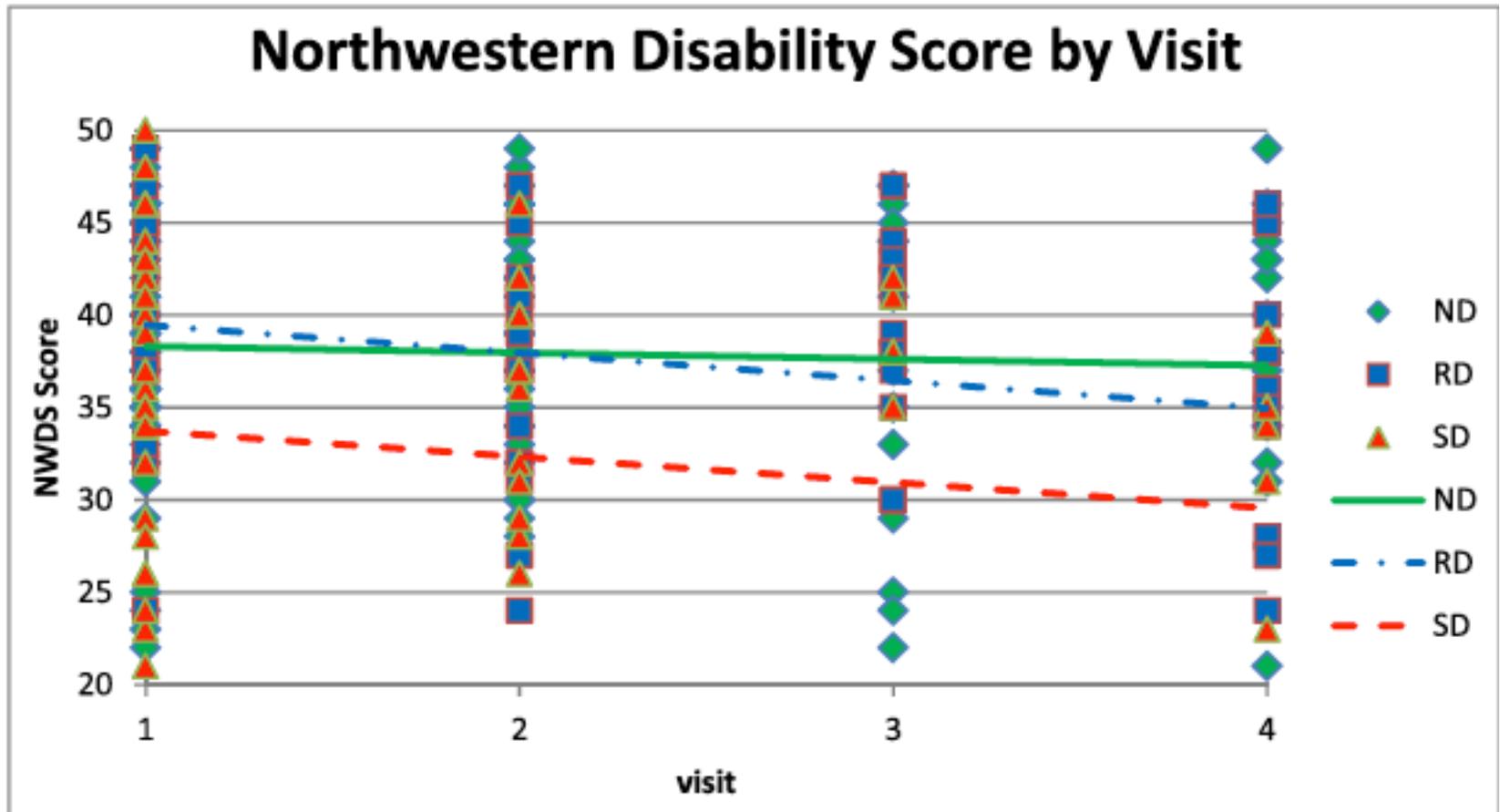
Gregory M. Pontone^{1,2}, Catherine C. Bakker^{1,2}, Shaojie Chen³, Zoltan Mari^{2,4}, Laura Marsh^{1,2†,‡}, Peter V. Rabins^{2,1}, James R. Williams^{1§} and Susan S Bassett^{1,2}

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)

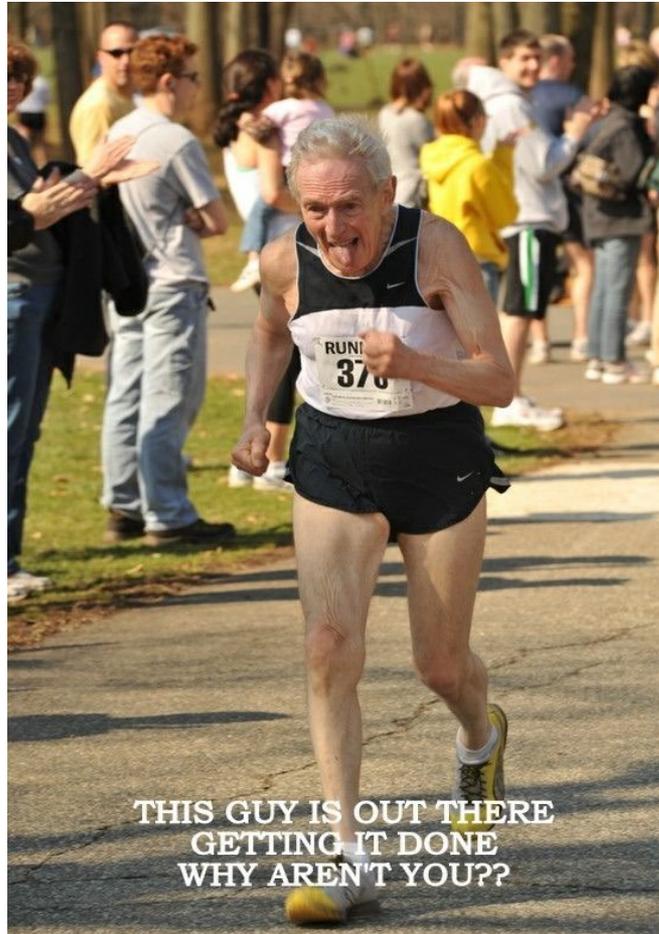


ND=never depressed, RD=remitted depression, SD=symptomatically depressed

Action items - strategies for depression in Parkinson's

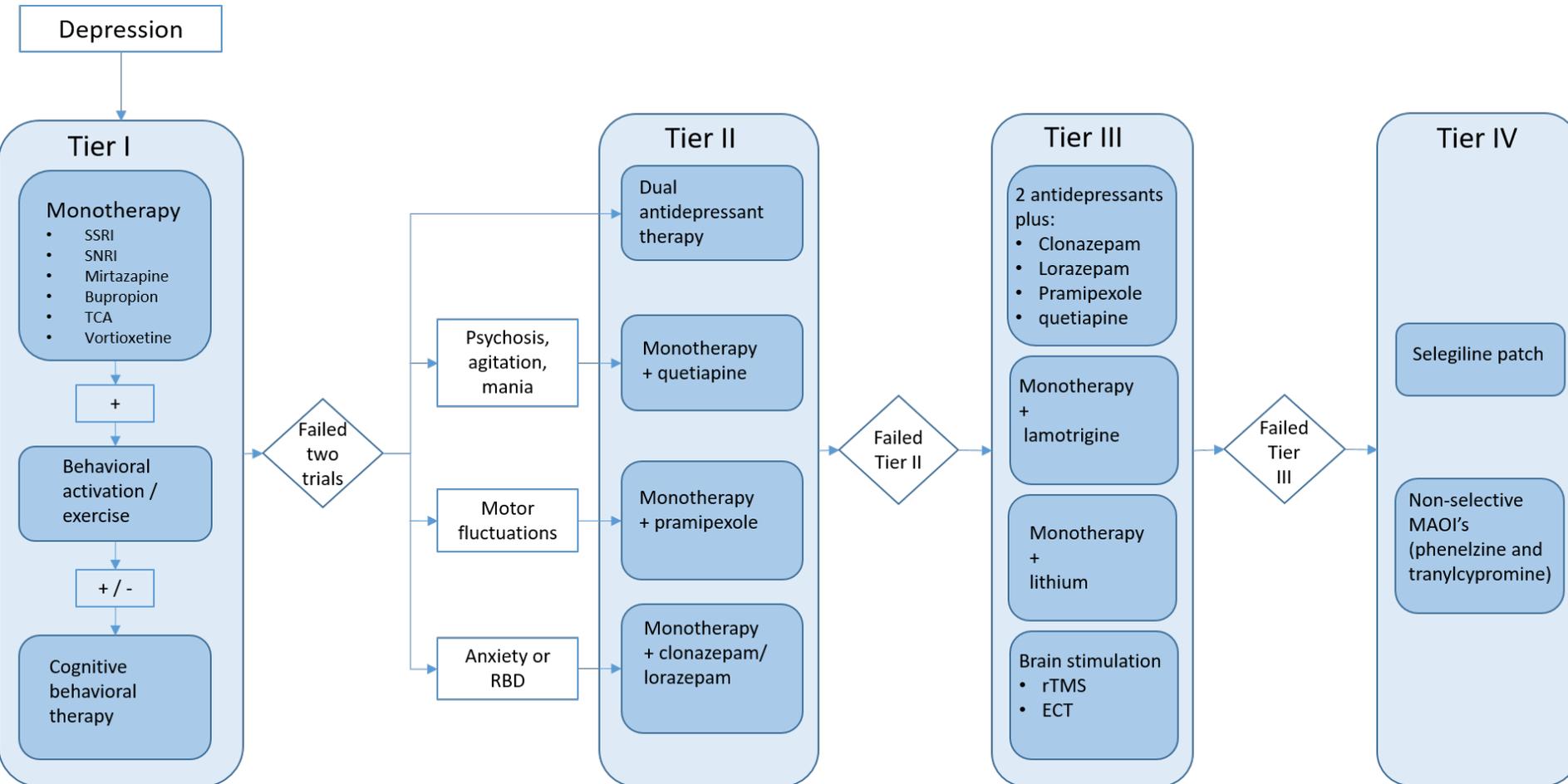
- Stay connected: Social isolation and loneliness are equivalent to smoking, HTN, or obesity for health
- Stay engaged, participating in structured activities is exercise for the mind
- Sleep well, poor sleep is both a risk factor for and symptom of depression
- Exercise, physical activity has been shown to benefit mental health by lifting mood and decreasing stress and tension

Aerobic exercise in Parkinson's



- Review of 18 articles: aerobic exercise improved, attention, processing speed, reaction time, executive function, and language
- Treadmill, walking, stationary bike were the most common aerobic exercises studied
- Reduces severity of depression

PD depression treatment algorithm





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APATHY IN PARKINSON'S DISEASE



Apathy vs depression in PD

Apathetic symptoms
Reduced initiative
Decreased participation in external activities
unless engaged by another person
Loss of interest in social events or everyday activities
Decreased interest in starting new activities
Decreased interest in the world around him or her
Emotional indifference
Diminished emotional reactivity
Less affection than usual
Lack of concern for others'
feelings or interests

Overlapping symptoms
Psychomotor retardation
Anhedonia
Anergia
Less physical activity than usual
Decreased enthusiasm about
usual interests

Emotional symptoms of depression
Sadness
Feelings of guilt
Negative thoughts and feelings
Helplessness
Hopelessness
Pessimism
Self-criticism
Anxiety
Suicidal ideation

Treatment of apathy in PD

- **Acetylcholinesterase inhibitors**
 - rivastigmine, efficacious, possibly useful
- **Dopamine agonists**
 - piribedil, likely efficacious, possibly useful following STN DBS
 - rotigotine, unlikely efficacious, investigational

Pseudobulbar affect aka emotional incontinence

Crying



Laughing



Pseudobulbar affect

- Neurological condition characterized by emotional lability that is often incongruent with emotional state
- Involuntary, sudden, uncontrollable episodes of laughing or crying
- Associated with social distress and embarrassment

Pseudobulbar affect treatment

- Dextromethorphan/quinidine (Nuedexta)
- Off label: antidepressants, SSRIs, SNRIs, TCAs (case reports)
- However, several studies have found that patients taking antidepressants have higher prevalence of PBA (confounding by indication)

Questions?

