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Integrated Care in Parkinson Disease: Neuropsychiatric Issues in Parkinson Disease

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Disclosures

- No relevant financial relationships with commercial interests
- The following talk may include unlabeled/unapproved use of medications
- Dr. Pontone has consulted for Acadia Pharmaceuticals Inc

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I. Overview of Parkinson's as a 'diseaso' model for neuropsychiatric symptoms

II. Anxiety in PD

III. Depression and apathy in PD

IV. Psychosis in PD

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PARKINSON'S DISEASE – A COMPLEX NEUROPSYCHIATRIC CONDITION

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Essay on the Shaking Palsy
"…the senses and intellects being uninjured."
James Parkinson, 1817

Parkinson's as a disease model for neuropsychiatric symptoms

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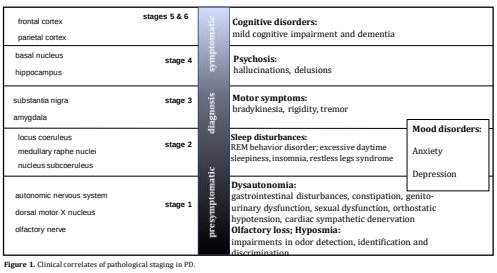

Figure 1. Clinical correlates of pathological staging in PD.

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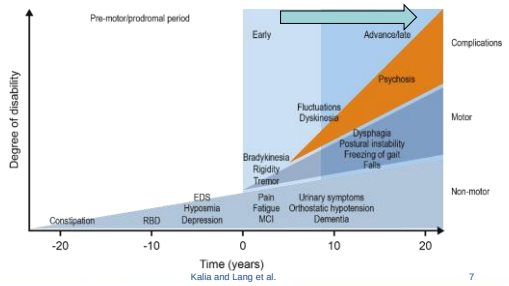
Parkinson's as a disease model for neuropsychiatric symptoms



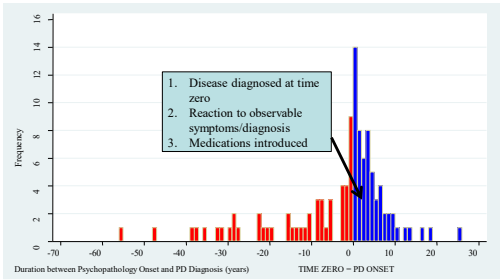
Kalia and Lang et al.

Meta-analysis of anxiety and depression as risk factors for PD

- 11 Case-control studies OR 1.90 (95% CI 1.62-2.22)
- 2 Cohort studies OR 1.79 (95% CI 1.72-1.86)
- Combined OR 1.86 (95% CI 1.64-2.11)

Noyce AJ et al. Ann Neurol 2012;72:893-901

Intersection of mental and physical health in PD



Ishihara and Brayne 2006

Anxiety in Parkinson's disease

Prevalence of anxiety and anxiety disorders in PD

- 31% have an anxiety disorder (e.g. DSM)

  ~30% had more than one anxiety disorder

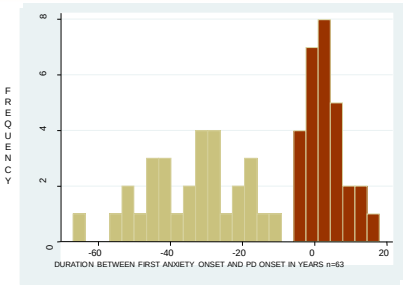
Yamanishi et al 2013, Broen M et al 2016

Anxiety as a 'premotor' symptom of Parkinson's disease

- Anxiety **disorders** are associated with later development of PD: OR 2.2 (95% CI 1.4-3.4; p=0.0003) up to 20 years before PD onset
- **Symptoms** of phobic anxiety are associated with increased risk of PD: RR 1.5 (95% CI 1.0-2.1; p=0.01)
- Anxious **personality** (from MMPI) was associated with increased risk of PD: HR 1.63 (95% CI 1.16-2.27; p=0.004)

Shiba et al 2000, Weisskopf et al 2003, Bower et al 2010

First Anxiety Disorder Onset Relative to Parkinson's Onset



Bimodal distribution of anxiety disorder onset compared to PD onset

Pontone et al 2009 13

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"

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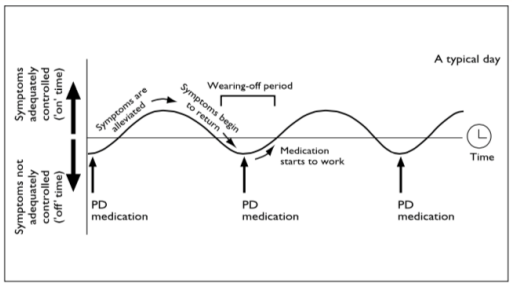
Dopaminergic medication on-off fluctuations in PD



Stacey M. and Hauser R. 2007 15

Mood and motor fluctuation with levodopa infusion

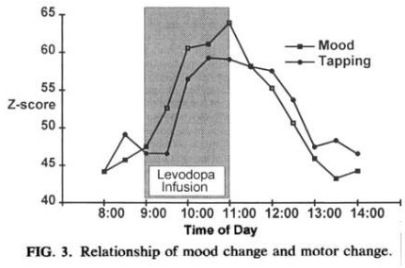
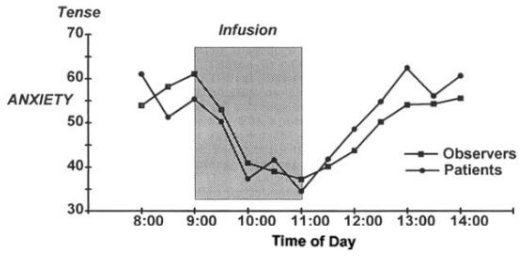


FIG. 3. Relationship of mood change and motor change.

Maricle RA et al 1995 16

Anxiety fluctuation with levodopa infusion



Maricle RA et al 1995 17

Integrated care for anxiety in PD

- Optimizing motor function and addressing motor fluctuations is likely important
- CBT has shown efficacy
- Mindfulness and relaxation therapy

Zesiewicz et al 2010, Seppi et al 2011, Seppi et al 2019 18

Depression in Parkinson's disease

National Parkinson Foundation

- **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

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

Reijnders 2008; Mayeux, 1981; Starkstein, 1992; Meara, 1999; Global PD Survey, 2002; Weintraub 2004; Even 2012; Shakeri 2015; Ghaddar 2016; Reidel 2016

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 symptoms increased need for symptomatic PD therapy (HR 1.86; 95% CI 1.29-2.68)

Ravina et al 2009

RESEARCH ARTICLE

International Journal of Geriatric Psychiatry

The longitudinal impact of depression on disability in Parkinson disease

Gregory M. Pontone[1,2], Catherine C. Bakker[1,2], Shaojie Chen[3], 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.

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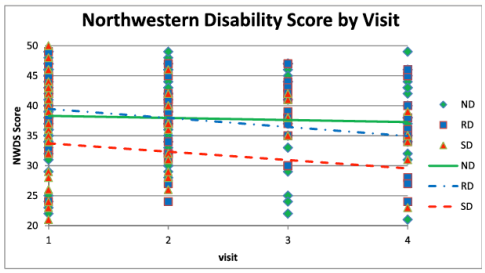
Longitudinal impact of depression on disability in PD (Pontone et al 2016)



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

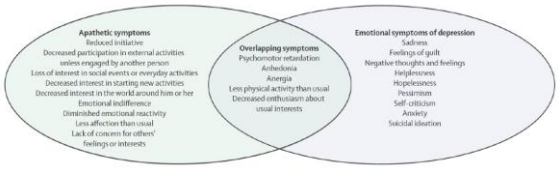
APATHY IN PARKINSON'S DISEASE

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



Pagonabarraga et al 2015

Psychosis in Parkinson's disease

Psychosis – phenomenology definitions

- **Hallucinations** – false sensory perceptions in the absence of external stimuli
- **Illusions** – misperception of actual stimuli
- **Passage hallucinations** – indefinite object passing through the peripheral visual field
- **Sense of presence hallucination** – a 'feeling' (or idea) of someone close by (leibhatige Bewussheit from Jaspers)
- **Delusions** – false, fixed, idiosyncratic belief

Management Strategies

- Screen for underlying medical illness
- Discontinuation of medications that may exacerbate psychosis (eg, pain, bladder, and CNS-acting medications)
- Reduction of PD medications
- Use of antipsychotic therapy
- Treatment with cholinesterase inhibitors
- Nonpharmacologic techniques to address PDP

Goldman JG, Holden S. *Curr Treat Options Neurol*. 2014;16(3):281.

Questions?