PARKINSON'S DISEASE IN THE RESIDENTIAL CARE SETTING

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Disclosures

- I have participated in clinical trials sponsored by Roche, Boehringer Ingelheim, TauRx, Lilly, and AstraZeneca
  - None are related to Parkinson's disease
- I am on the volunteer Board of Directors of Headway (Victoria Epilepsy and Parkinson Centre)
- I will be discussing off-label use of medication

Desired Learning Outcomes

- By the end of this presentation you will be able to:
  - Describe the estimated prevalence of PD in residential care centres
  - List many of the symptoms of PD
  - Provide a systematic approach for evaluating patients with PD in the residential care setting
- Format: 45 min. didactic presentation; 15 min. Q&A

Parkinson's Disease in LTC Facilities

- 25% of US patients with PD reside in LTC facilities

  Safarpour *et al. Neurology* 2015: 85(5); 413-419

  - Only 1/3 still have any contact with outpatient neurology

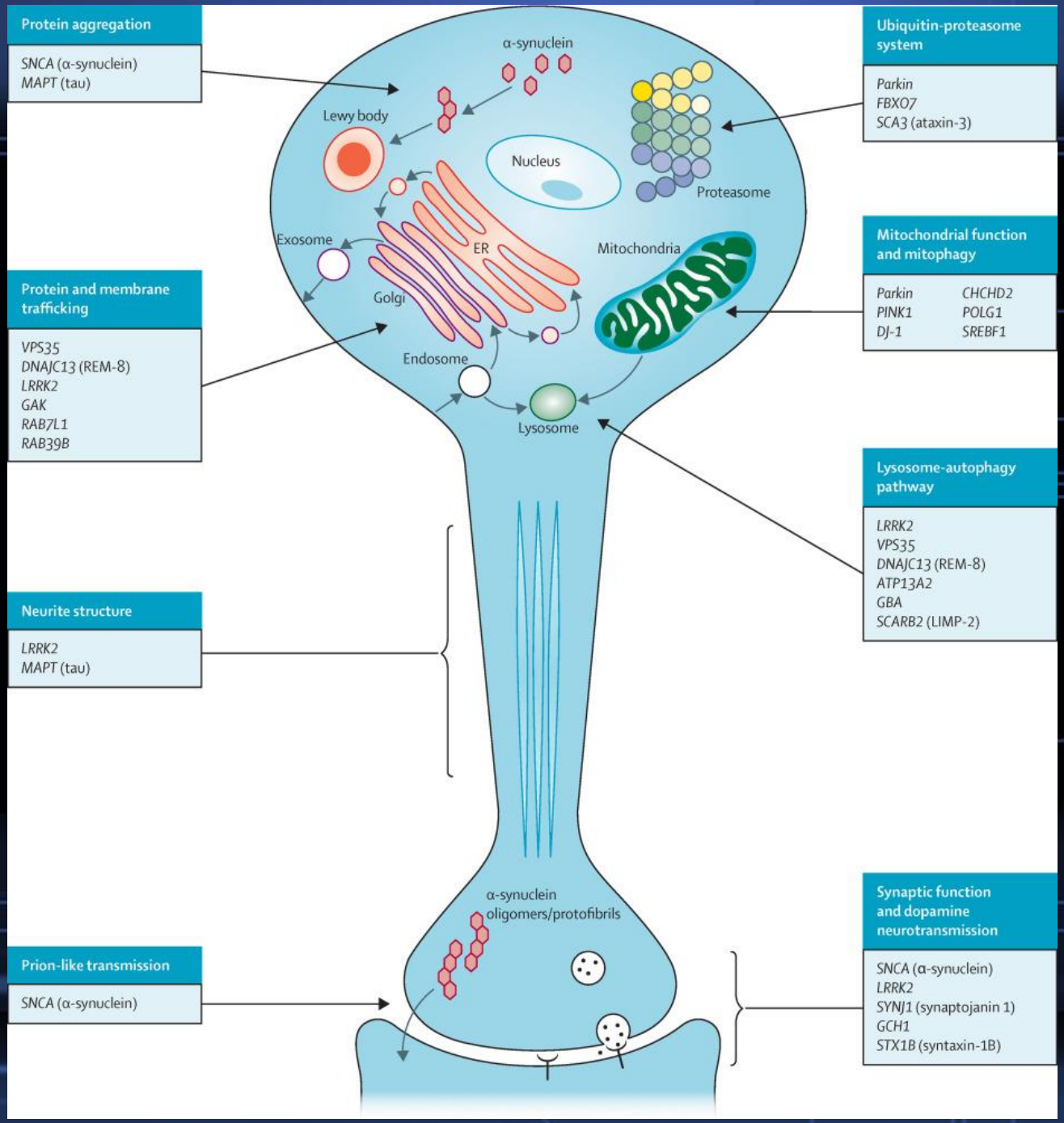
- Presence of dementia and hip fracture predispose to LTC

- Up to 10% of LTC patients may have PD

  Weerkamp *et al.* JAMDA 2014: 15(2); 90-94

What is PD?

- Neurodegenerative disease
- Hallmarks:
  - Lewy bodies
  - Loss of DA neurons in SNpc



Kalia and Lang. *Lancet* 2015: 386 (9996); 896-912

What are the Symptoms of PD?

Motor

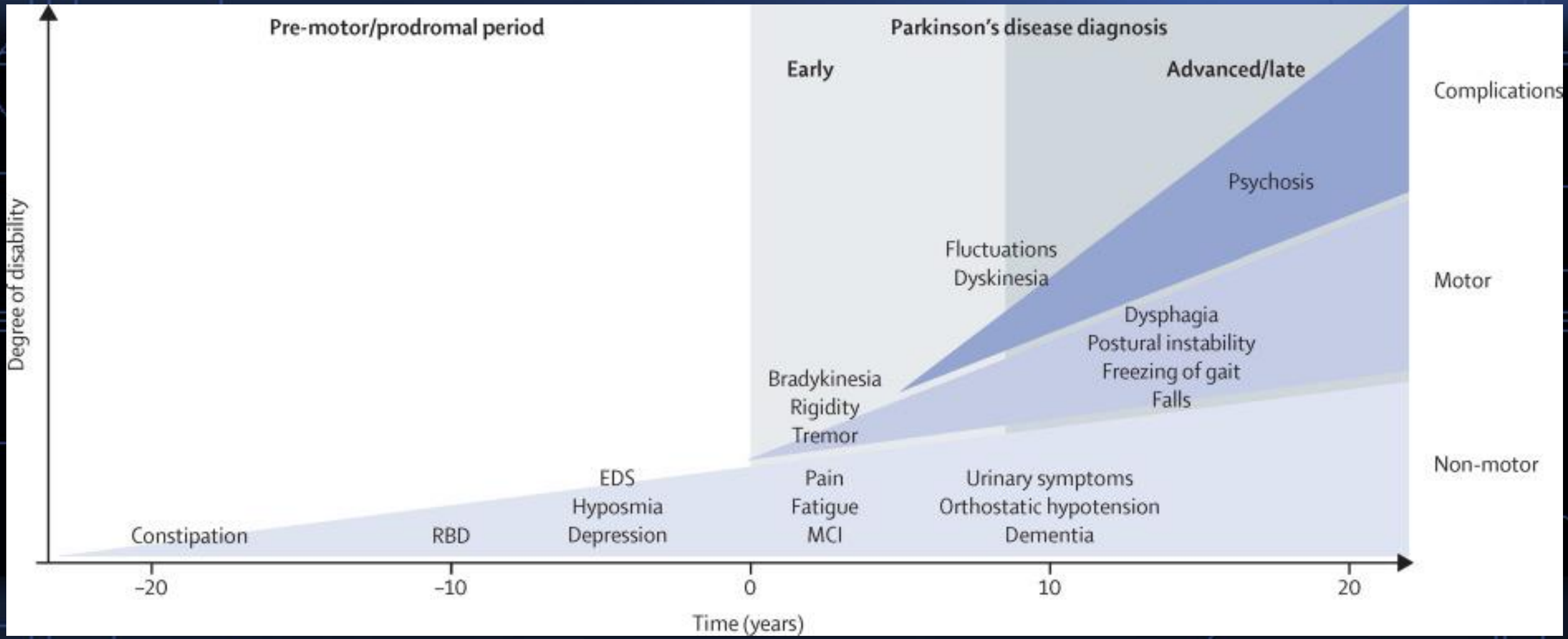
- Tremor
- Rigidity
- Akinesia
- Gait impairment

Somatic Non-Motor

- Sleep disturbances incl. RBD
- Olfactory dysfunction
- Visual disturbances
- Constipation
- Excessive daytime somnolence
- Dysphagia
- Autonomic dysfunction
  - Orthostasis, urinary symptoms, sialorrhoea, hyperhidrosis
- Pain
- Appetite & weight changes

Psychiatric

- Cognitive dysfunction
- Dementia
- Hallucinations
- Anxiety
- Depression
- Apathy
- Delusions
- Impulse control disorders



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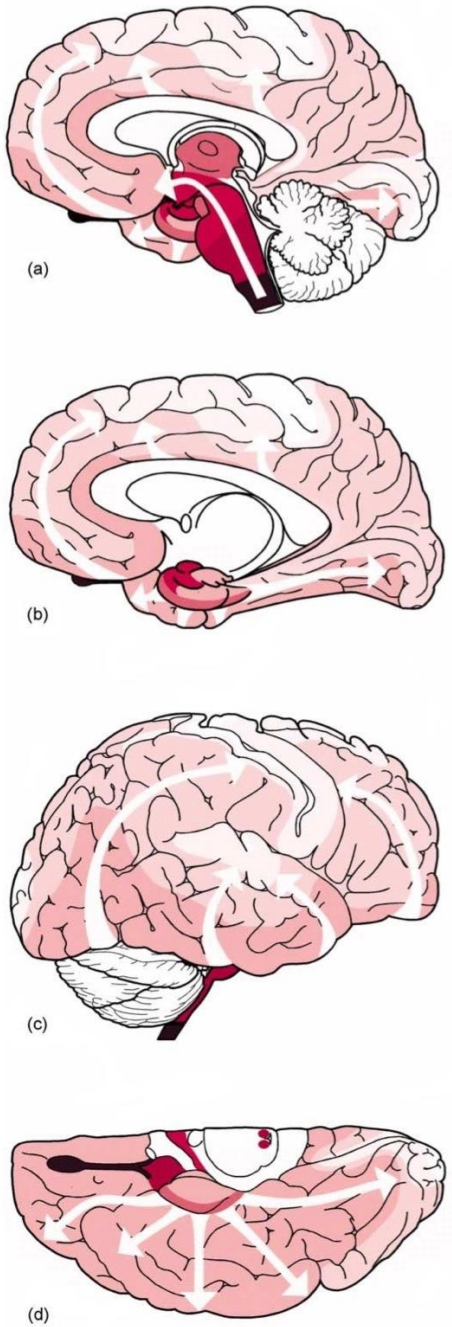
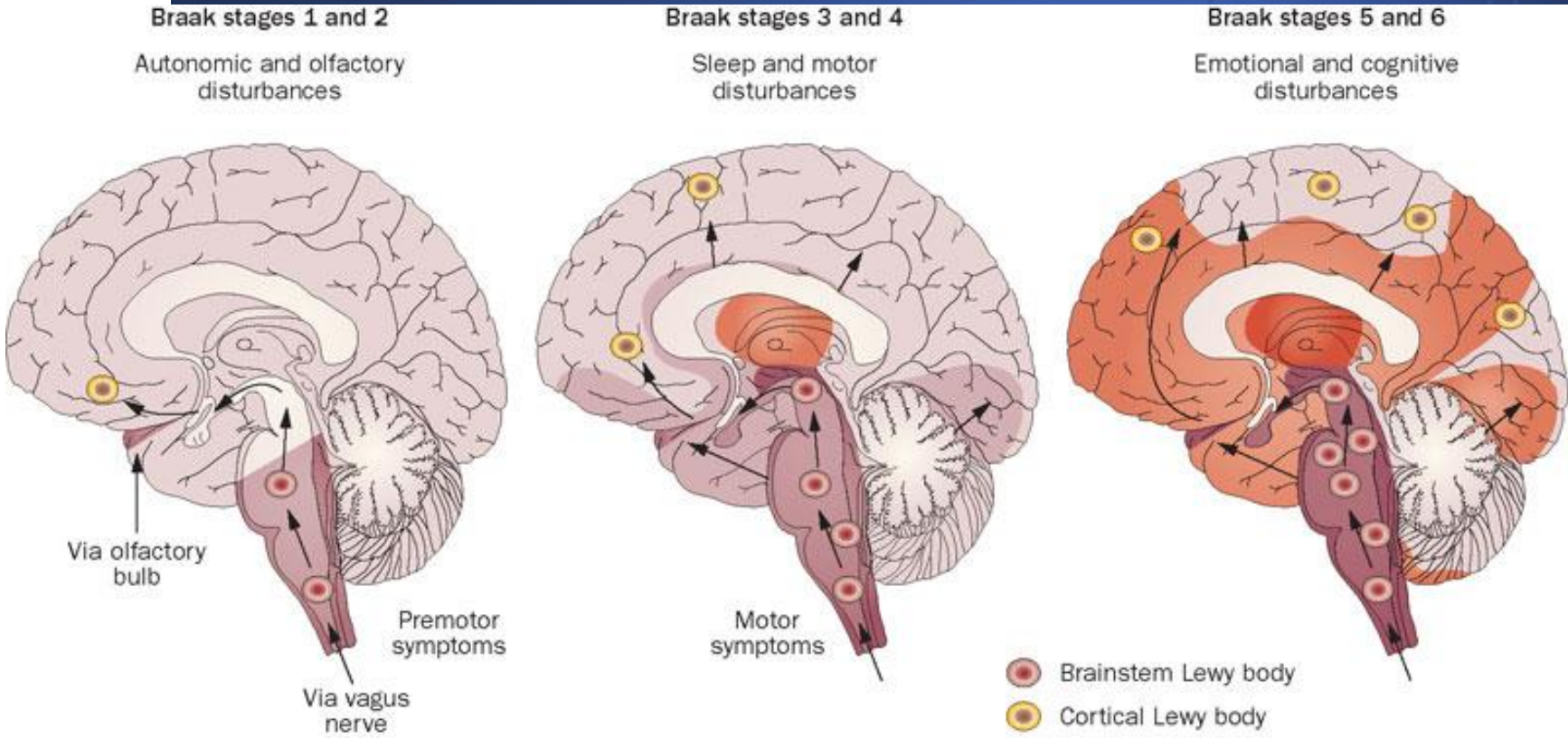
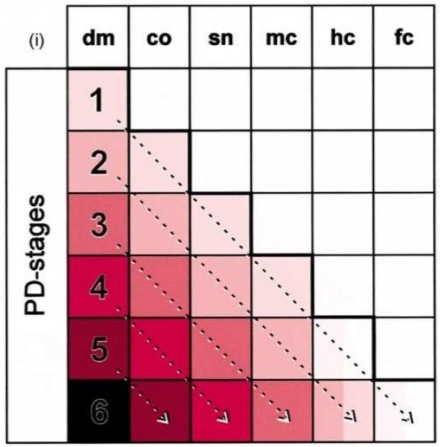
Progression of PD-related intraneuronal pathology





Halliday *et al. Mov. Disord.* 2011; 26: 1015–1021.



Braak *et al*. *Neurobiol Aging.* 2003; 24(2):197-211.

PD as a Highly Protean Illness

- Some patients complain mainly of motor symptoms that are successfully treated for years
- Others have early and debilitating non-motor symptoms including psychiatric symptoms

Question / Discussion

What are some challenges you have had treating motor symptoms of PD patients in a residential care setting?

PD Treatment – Motor Symptoms

- Levodopa + carbidopa / benserazide
  - The mainstay of treatment; still the most effective
- Dopamine agonists
  - Pramipexole, ropinirole, rotigotine patch
  - Bromocriptine rarely used due to adverse effects
- MAO B inhibitors: rasagiline, selegiline
- COMT inhibitors: entacapone
- Anticholinergics
- Amantadine

Treatment of Motor Symptoms in LTC Settings

- Patients often have co-morbid psychiatric or other symptoms that are aggravated by medications used to treat motor symptoms
- Principle of treatment: reduce medications trying to compromise motor function as little as possible
- GO SLOW! Reassess frequently

PD Treatment – Motor Symptoms

- Dopamine agonists: used to minimize levodopa-related fluctuations or to augment therapy
  - Generally less effective than levodopa
  - Can often start by cutting down here!
- Anticholinergics: worsen cognitive impairment
  - Should usually be minimized / eliminated
  - Are no longer routinely used anyway
- Amantadine: can worsen cognitive impairment

What types of motor fluctuations exist in patients with PD?

Treatment of Motor Fluctuations

- Wearing off:
  - End-of-dose wearing off:
    - More frequent dosing
    - Add MAOB inhibitor (e.g., rasagiline 5mg OD)
      - Beware drug interactions
    - Add COMT inhibitor
      - May need to decrease levodopa doses
      - Diarrhoea
  - Unpredictable and “missed dose” phenomenon
    - Avoid protein with levodopa
    - Use “rescue dose” of levodopa
      - Crushed with soda works best

Treatment of Motor Fluctuations

- Freezing
  - Use rescue doses
  - Have clear nursing plan to avoid falls
- Dyskinesias
  - Unpredictable
    - Decrease total dopaminergic drug burden
    - May try adding amantadine but not if cognitive impairment
  - Peak-dose
    - Give smaller doses more frequently

Treatment of Motor Fluctuations

- Are these really motor fluctuations or are they something else?
  - Non-motor symptoms, esp. anxiety
  - Behavioural
- Need behavioural charting, with specific attention to PD symptoms to really determine what is going on!

Question / Discussion

What are some challenges you have had treating psychiatric symptoms of PD patients in a LTC setting?

Treatment – Cognitive Impairment

- 2 Patterns of cognitive impairment
  - Subcortical – slow thought processing, concentration difficulties, executive dysfunction
    - Same pathophysiology as motor symptoms
    - May fluctuate with motor function and treatment
  - Cortical – visuospatial and memory dysfunction
    - More often associated with psychosis
    - Due to cortical Lewy body pathology
- Remove anticholinergic medication
- Cholinesterase inhibitors
- May be worsened by orthostatic hypoperfusion

Treatment – Psychosis

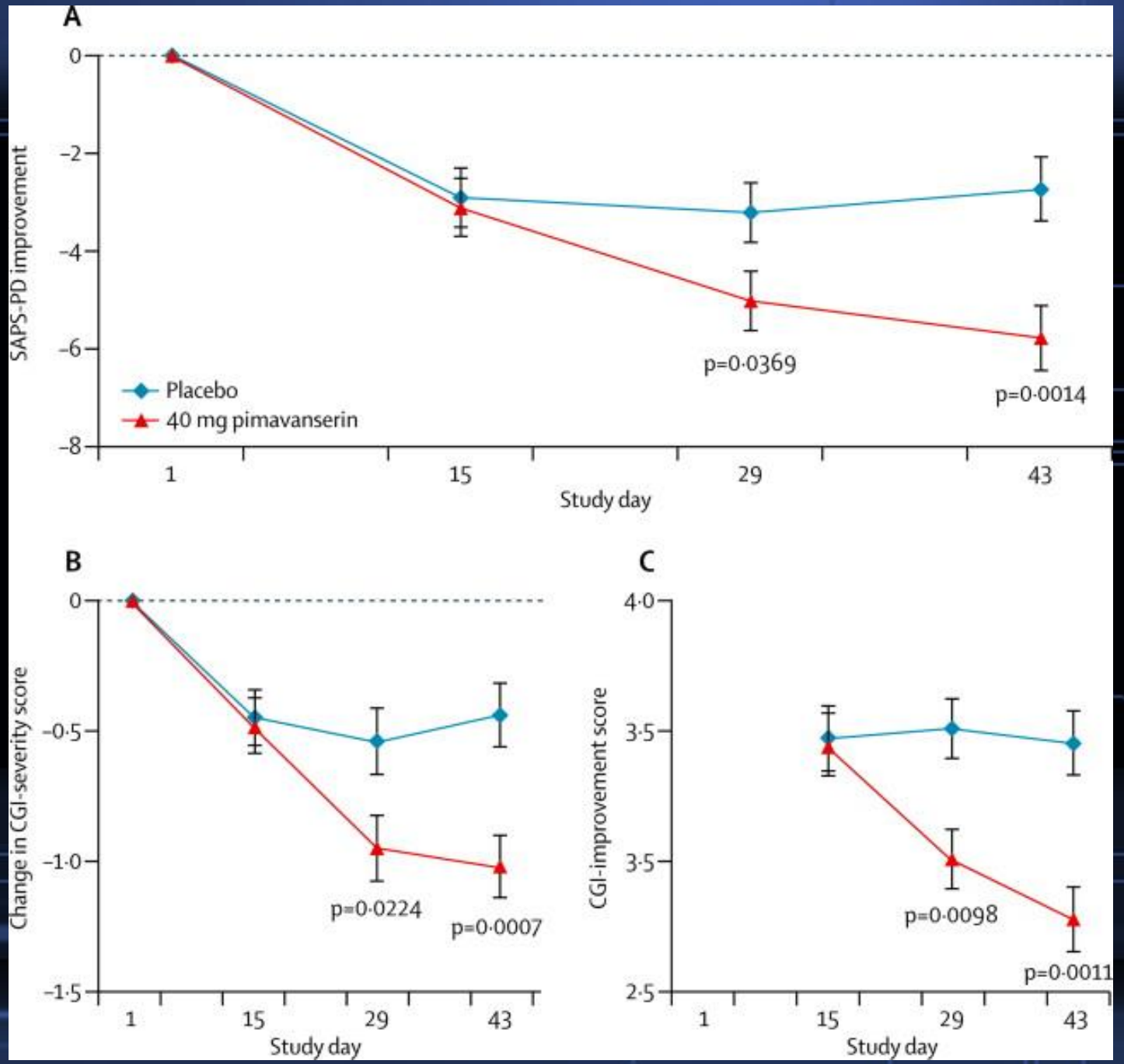
- If sudden in onset, look for delirium
- Behavioural charting: Look for triggers
- Ask if the symptoms really need to be treated: are they bothersome?
- First, slowly reduce dopaminergic medication as tolerated

Treatment – Psychosis

- Consider trial of cholinesterase inhibitor and memantine
  - Beware paradoxical reaction with memantine
- Mixed evidence for quetiapine
  - BUT safest and easiest to use, generally first-line
- Best evidence for clozapine: Need frequent monitoring
- Evidence that the following do **NOT** work and make symptoms worse: **olanzapine, risperidone, aripiprazole**

Treatment – Psychosis

- Pimavanserin (Nuplazid)
- 5HT2A inverse agonist
- No dopaminergic receptor antagonism
- Not yet approved in Canada (not even submitted to CDR)



Cummings *et al*. *Lancet* 2014: 383 (9916); 533-540

Treatment - Anxiety

- Episodic anxiety may or may not be directly due to motor fluctuations
- Behavioural charting! With concomitant note of motor and psychological symptoms
- Chronic anxiety is very common in PD (40%)
  - Less ruminative and more paralytic
  - If concomitant depression, try SSRI
  - Use benzodiazepines judiciously and reassess frequently
    - Falls, confusion

Treatment - Apathy

- Very difficult to treat
- Ensure no co-morbid depression
- Increasing dopaminergic medication may help
- Stimulants can be tried
  - Methylphenidate – side effects
  - Modafinil - expensive

Treatment - Insomnia

- Review sleep hygiene
- Night-time motor symptoms: give levodopa at HS or throughout night
- Treat urinary symptoms
- Melatonin up to 10mg HS
- Doxepin 5-10mg ac HS (anticholinergic)
- Zopiclone, trazodone

Treatment – REM Behaviour Disorder

- May not need treatment
- If severe, patient can injure self
- Antidepressants may worsen
- Melatonin 3-12mg QHS
- Clonazepam 0.25 – 2mg QHS (beware)

Question / Discussion

What are some challenges you have had treating other non-motor symptoms of PD patients in a residential care setting?

Orthostatic hypotension

- Can be worsened by dopaminergic medication
  - Consider slow monitored reduction
- Eliminate anti-hypertensives
- Increase salt and water intake
- Domperidone antagonizes peripheral action of dopamine
  - 10mg TID
- If concomitant constipation, consider physostigmine 30-60mg QID (start low, go slow)
- Midodrine 2.5-10mg TID; fludrocortisone 0.1-0.3mg / day
  - Supine hypertension

Constipation

- Hydrate, exercise routine
- Fiber, usual stool softeners, laxatives (PEG)
- Domperidone, physostigmine

Urinary symptoms

- Look for typical causes first (e.g., BPH in men)
- Usually due to detrusor-sphincter dissynergy
- May be aggravated by dopaminergic medication
- Mainstay used to be anticholinergic but these worse cognition
- Mirabegron 25-50mg OD increasingly used

Sialorrhoea

- Many patients will have success with gum chewing!
- May improve with increasing dopaminergic therapy
- Consider sublingual atropine drops
- Botulinum toxin for severe cases

Pain

- What is the cause:
  - Is it related to freezing / wearing off, dystonia?
    - Need careful symptom charting!
  - Orthostatic hypotension: coat hanger headache
  - Central neuropathic pain is common
    - Pregabalin, gabapentin, antidepressants can be used

Table 5. Treatment of Nonmotor Symptoms of Parkinson Disease

Nonmotor Symptom	Medication	Dosage	Level of Recommendation[a]	Adverse Effects
Nausea	Domperidone[b]	10 mg thrice daily; max, 20 mg 4 times daily	U	Cardiac arrhythmia, sudden cardiac death, breast pain, drowsiness, dry mouth, headache, hot flashes, and nausea
RBD	Clonazepam	0.25-2 mg at bedtime	U	Sedation and confusion
	Melatonin	3-15 mg at bedtime	U	Daytime sleepiness, dizziness, and headache
Depression	Citalopram	10-20 mg once daily	U	Akathisia, anorexia, nausea, drowsiness, and sexual dysfunction
	Fluoxetine	10-50 mg once daily	C	Same as citalopram
	Paroxetine	20-40 mg once daily	U	Same as citalopram
	Sertraline	25-200 mg once daily (rarely >100 mg)	U	Same as citalopram
	Venlafaxine extended release	37.5-225 mg once daily	B	Drowsiness, insomnia, sexual dysfunction, and gastrointestinal symptoms
	Nortriptyline	25-150 mg/d single or divided	C	Anticholinergic effects[d], orthostatic hypotension, ventricular arrhythmias, heart block, drowsiness, sexual dysfunction, and weight gain
	Desipramine	25-150 mg/d single or divided	B	Same as nortriptyline
Hallucinations	Clozapine	6.25-150 mg at bedtime or divided (often effective in very low doses)	B	Agranulocytosis, seizure, myocarditis, cardiomyopathy, and sedation
	Quetiapine	12.5-400 mg at bedtime or divided	C	Extrapyramidal symptoms and sedation
	Rivastigmine[c]	1.5-6 mg twice daily; transdermal patch, 4.5-9.8 mg/24 h	C	Gastrointestinal symptoms, bradycardia, vivid dreams, and exacerbation of rest tremor
PD-MCI	Atomoxetine	Target dose, 80 mg once daily	U	Alopecia, dry mouth, sexual dysfunction, gastrointestinal symptoms, dizziness, and increased heart rate and blood pressure
PDD	Rivastigmine	1.5-6 mg twice daily; transdermal patch, 4.5-9.8 mg/24 h	B	Same as rivastigmine
	Donepezil	5-10 mg once daily	B	Same as rivastigmine
	Galantamine	4-12 mg twice daily	U	Same as rivastigmine
Orthostatic Hypotension	Fludrocortisone	0.05-0.1 mg once or twice daily	C	Hypertension, metabolic abnormalities (including hypokalemia), gastrointestinal symptoms, and myopathy
	Domperidone[b]	10 mg thrice daily; max, 20 mg 4 times daily	C	Same as domperidone
	Midodrine	2.5-10 mg thrice daily	U	Hypertension, nausea, weakness, heartburn, headache, scalp tingling, and chills
	Pyridostigmine	50 mg thrice daily	U	Hypertension, gastrointestinal symptoms, sweating, and increased salivation/bronchial secretions
	Indomethacin	50 mg thrice daily	U	Hypertension, edema, metabolic abnormalities, gastrointestinal symptoms, headache, and renal damage
	Yohimbine	2 mg thrice daily	U	Blood pressure changes, sexual dysfunction, hallucinations, seizure, and renal failure
	Droxidopa	300 mg thrice daily	U	Hypertension, tachycardia, nausea, vomiting, and headache
Sialorrhea	Glycopyrrolate	1 mg thrice daily	B	Anticholinergic effects[d]
	Atropine	1-2 drops of 1% concentration up to 4 times daily	U	Same as glycopyrrolate
	Ipratropium bromide	1-2 sprays (21 µg); max, 4 times daily	U	Same as glycopyrrolate
	BTA	Varies by formulation	B	Dysphagia, dry mouth, and injection-associated discomfort
	BTB	Varies by formulation	B	Same as BTA

Connolly and Lang. JAMA 2014: 311(16); 1670-1683

Approach to the PD Patient in RC

- Please take a history – does the patient have concerns?
  - Inadequately controlled motor symptoms?
  - Motor-fluctuations?
  - Psychiatric symptoms?
  - Other non-motor symptoms?
- Take inventory of non-motor symptoms
- http://www.parkinsonclinicalguidelines.ca/sites/default/files/PhysicianGuide_Non-motor_EN.pdf

Approach to the PD Patient in RC

- If problems, get your staff to implement hourly behavioural charting x 2-3 days
  - Fight for it, it is worth it!
- Motor symptoms:
  - Off (frozen) /on
  - Dyskinesias (“extra movements”): yes / no
  - Falls or gait / transfer difficulties?
- Psychiatric symptoms: hallucinations, agitation, anxiety

Approach to the PD Patient in RC

- Behavioural charting allows determination of:
  - Presence and frequency of motor fluctuations
  - Relationship of psychiatric symptoms to these

Approach to the PD Patient in RC

- While collecting information on PD symptoms, conduct thorough medication review, especially eliminating anti-dopaminergic or anti-cholinergic medication

Approach to the PD Patient in RC

- If residual problems are mainly due to motor fluctuations, treat them
- If excess dopamine (dysautonomia, psychosis, confusion):
  1. Reduce non-dopaminergic PD medication
  2. Reduce dopaminergic agonists
  3. Reduce levodopa
  - Always go slowly and constantly re-assess to allow patient to maintain maximum function

Approach to the PD Patient in RC

- Once dopaminergic medications decreased as low as possible, treat somatic non-motor symptoms
- If psychiatric symptoms:
  - If concomitant dementia, consider cholinesterase inhibitor
    - Sometimes depression or psychosis will improve considerably
    - Beware side-effects
  - Treat anxiety and depression
  - Only treat psychosis if bothersome or dangerous
    - Only use quetiapine or clozapine: start low and go slow!
- Consider re-increasing / reintroducing dopaminergic meds, esp. levodopa once psychiatric symptoms improved - slow

Approach to the PD Patient in LTC

- The most important principle is to make changes one at a time, in small increments, and to constantly re-assess
- Time consuming, but if done properly can lead to greatly improved function

Questions? Comments?

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