PARKINSON'S DISEASE AND NEUROPSYCHIATRIC COMPLICATIONS

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Fraser Health Movement Disorder Clinic

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DISCLOSURES

- I **DO NOT** have an affiliation (financial or otherwise) with any for-profit or not-for-profit organizations

LEARNING OBJECTIVES

- Be able to describe common non-motor neuropsychiatric complications of Parkinson's disease.
- Understand the importance of addressing the following issues in Parkinson's disease and have an approach to treatment for them:
  - sleep disorders
  - cognition
  - psychosis
  - mood

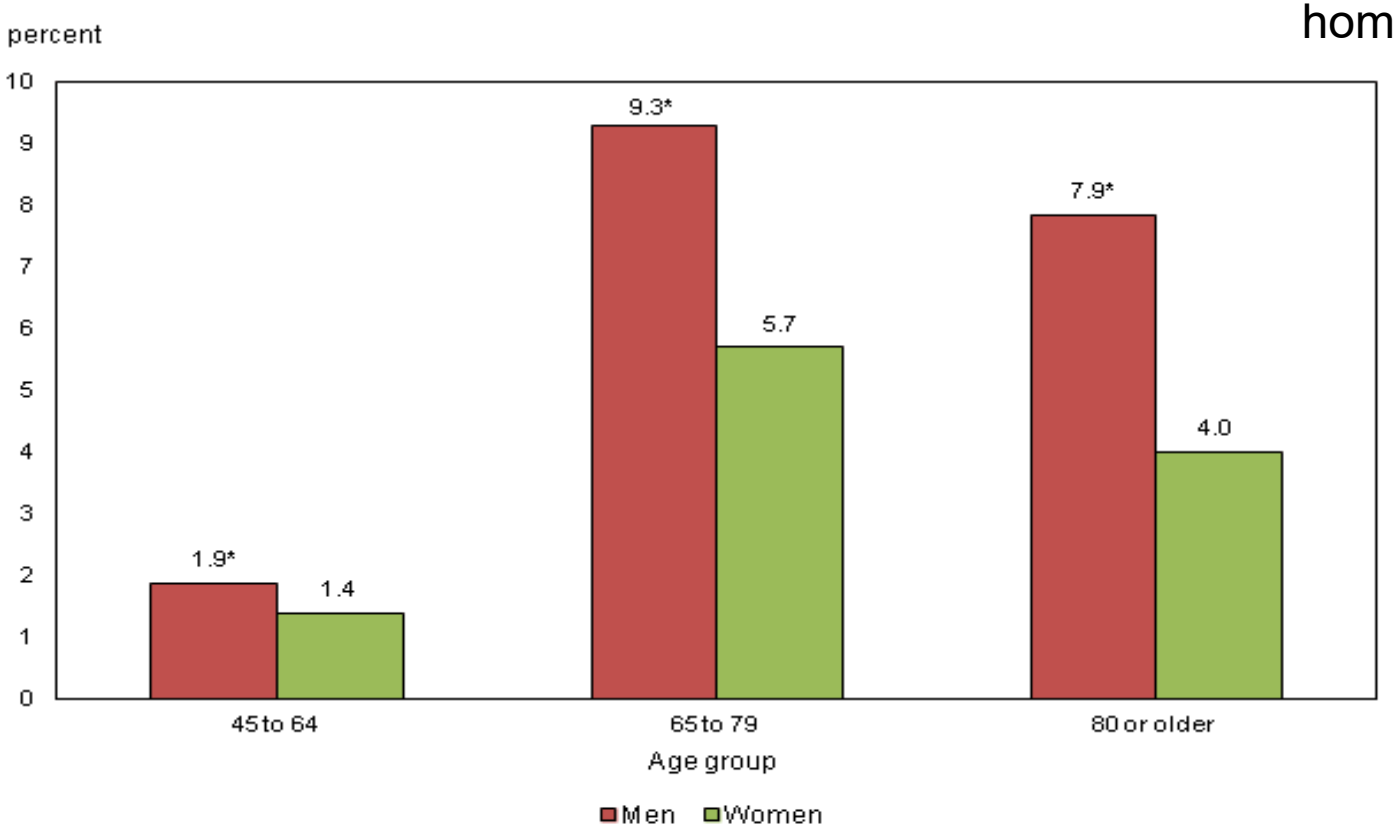
IMPACT OF PD

Canada

100,000 (0.2% of adults in private households)

12500 residents of LTC homes have PD (4.9%)

Figure 2
Prevalence of Parkinson's disease in institutional population, by age group and sex, population aged 45 or older, Canada excluding territories, 2011/2012



* significantly different from women ($p < 0.05$)
Source: Statistics Canada, CANSIM Table 105-1305.

OUTLINE

- Sleep
- Cognition
- Psychosis
- Mood

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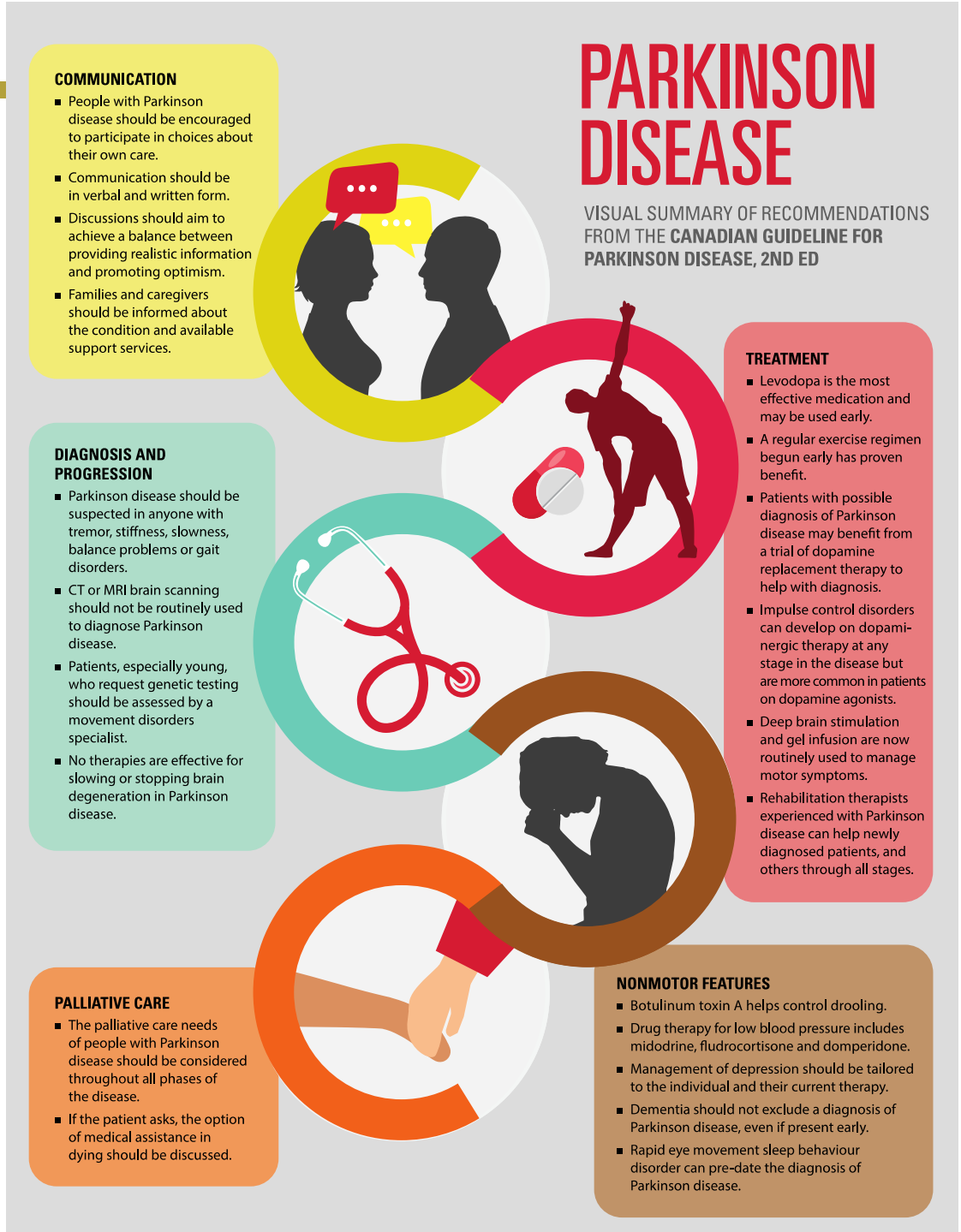


PD SYMPTOMS

NON-MOTOR SYMPTOMS

Autonomic

- orthostatic hypotension
- urinary urgency/frequency
- constipation
- erectile dysfunction
- temperature dysregulation

Neuropsychiatric

- sleep
- RBD
- depression, anxiety
- apathy
- cognitive impairment
- psychosis

NEUROPSYCHIATRIC COMPLICATIONS OF PD

Intrinsic to PD

- depression
- anxiety
- apathy
- impaired executive function
- subcortical dementia
- RBD
- akathisia
- anhedonia

Associated with dopaminergic therapy

- hallucinations
- paranoia
- delusions
- ICD
- compulsive behaviours
- delirium
- dopamine dysregulation syndrome

MAJOR MEDICATION CLASSES

****DOPAMINE****

Levodopa-carbidopa

Levodopa-benserazide

DOPAMINE AGONISTS

Pramipexole

Ropinirole

Rotigotine patch

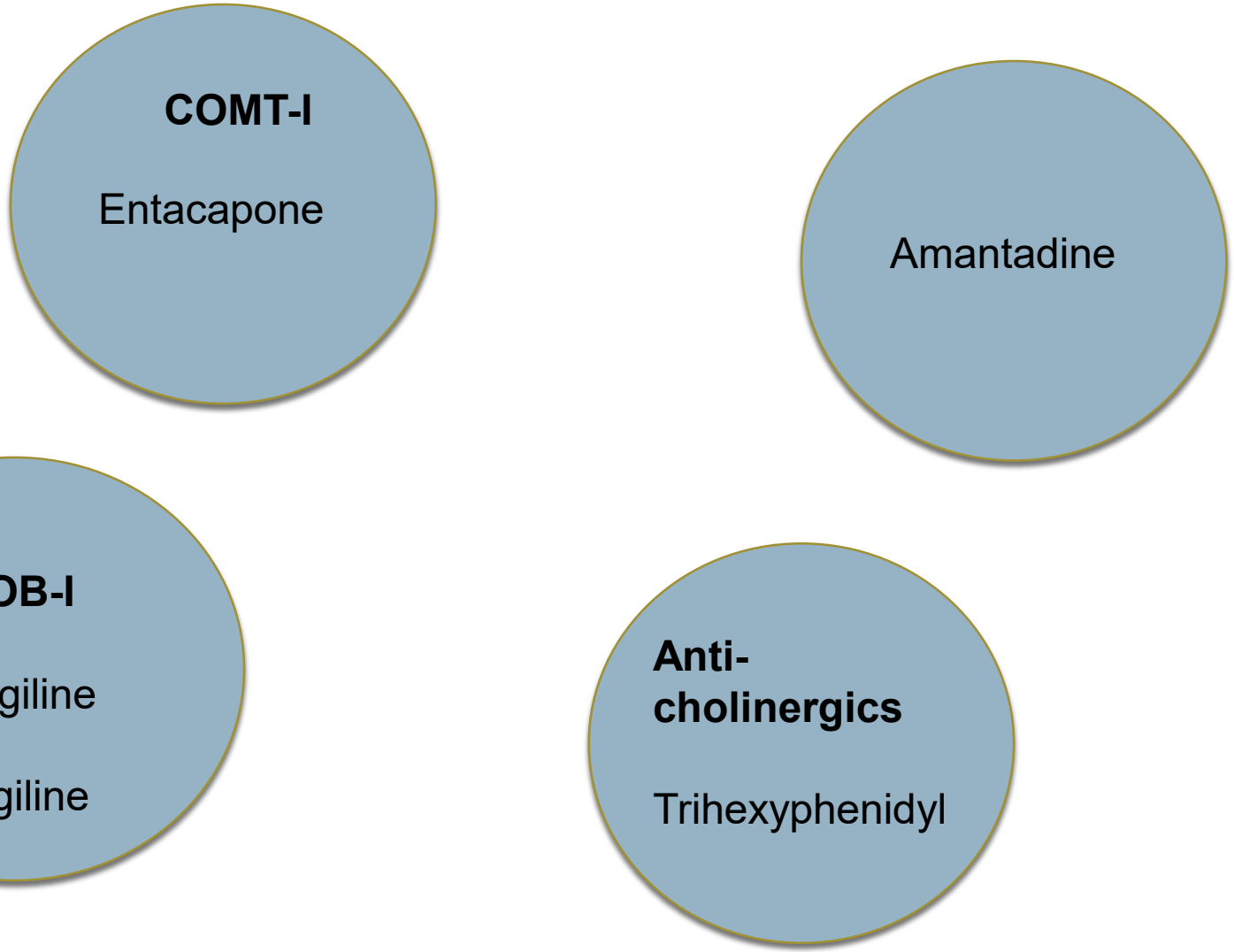
Bromocriptine

MAOB-I

Rasagiline

Selegiline

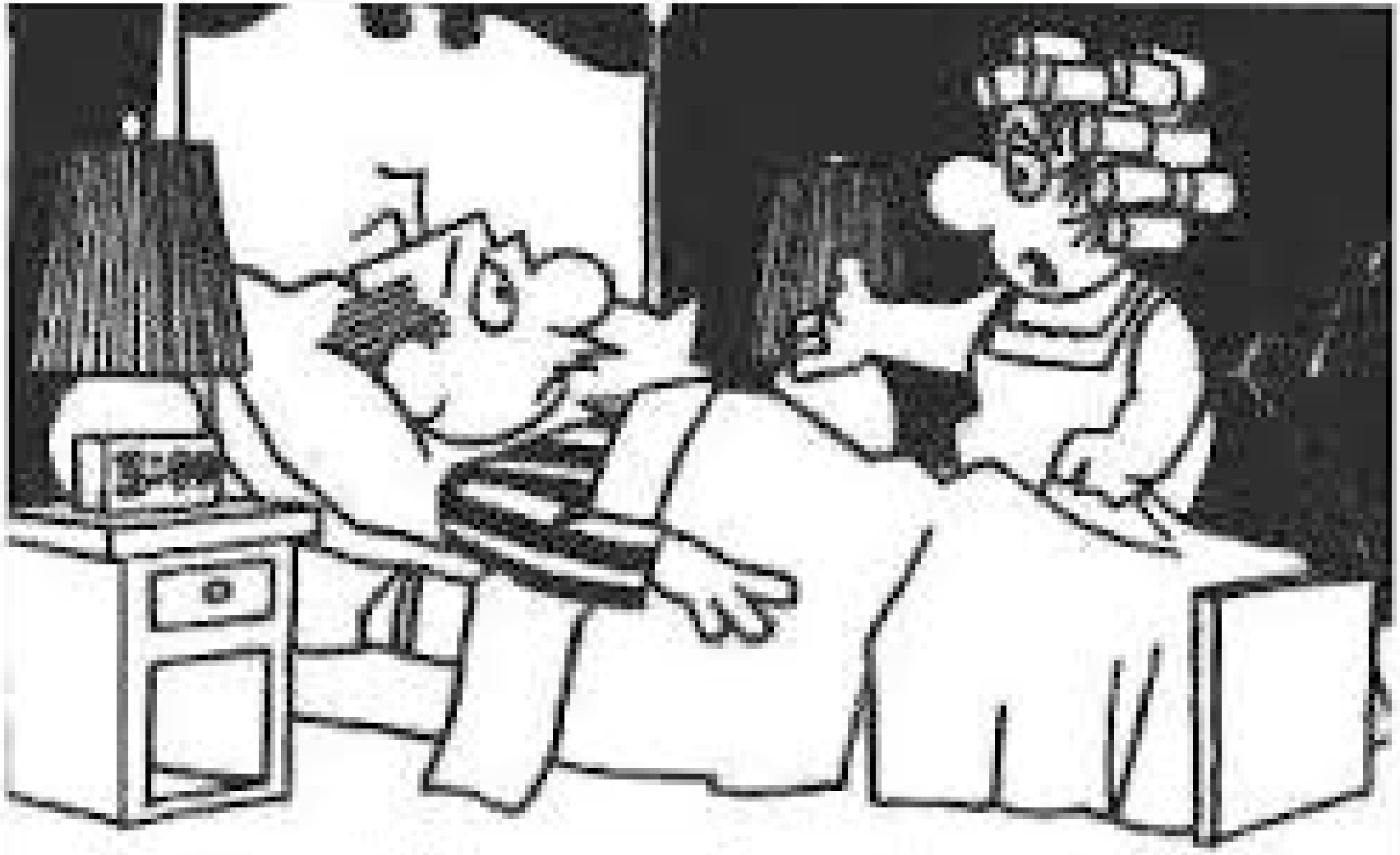
ADD-ON MEDICATIONS




YOU'VE GOT A LOT OF NERVE.
Neurologist
STAHLER 6/28
www.gocomics.com

PD MEDS – TIMING IS EVERYTHING

- routine is key
- missed or delayed doses have significant deleterious effects on patient in that moment and rest of the day
- not acceptable to delay or miss (eg: patient napping)
  - if meds interfere with sleep regularly, we can adjust schedule
- acceptable window is maximum 15 minutes
- requires policy change for nursing staff
- allow patients to administer if appropriate



"No wonder you have insomnia . . . lying there awake all night."

BENEFIT OF GOOD SLEEP IN PD

- better quality of life ratings
- improved mood
- clearer cognition
- reduced severity of daytime parkinsonism
- reduced daytime sleepiness

SLEEP IN THE OLDER PERSON

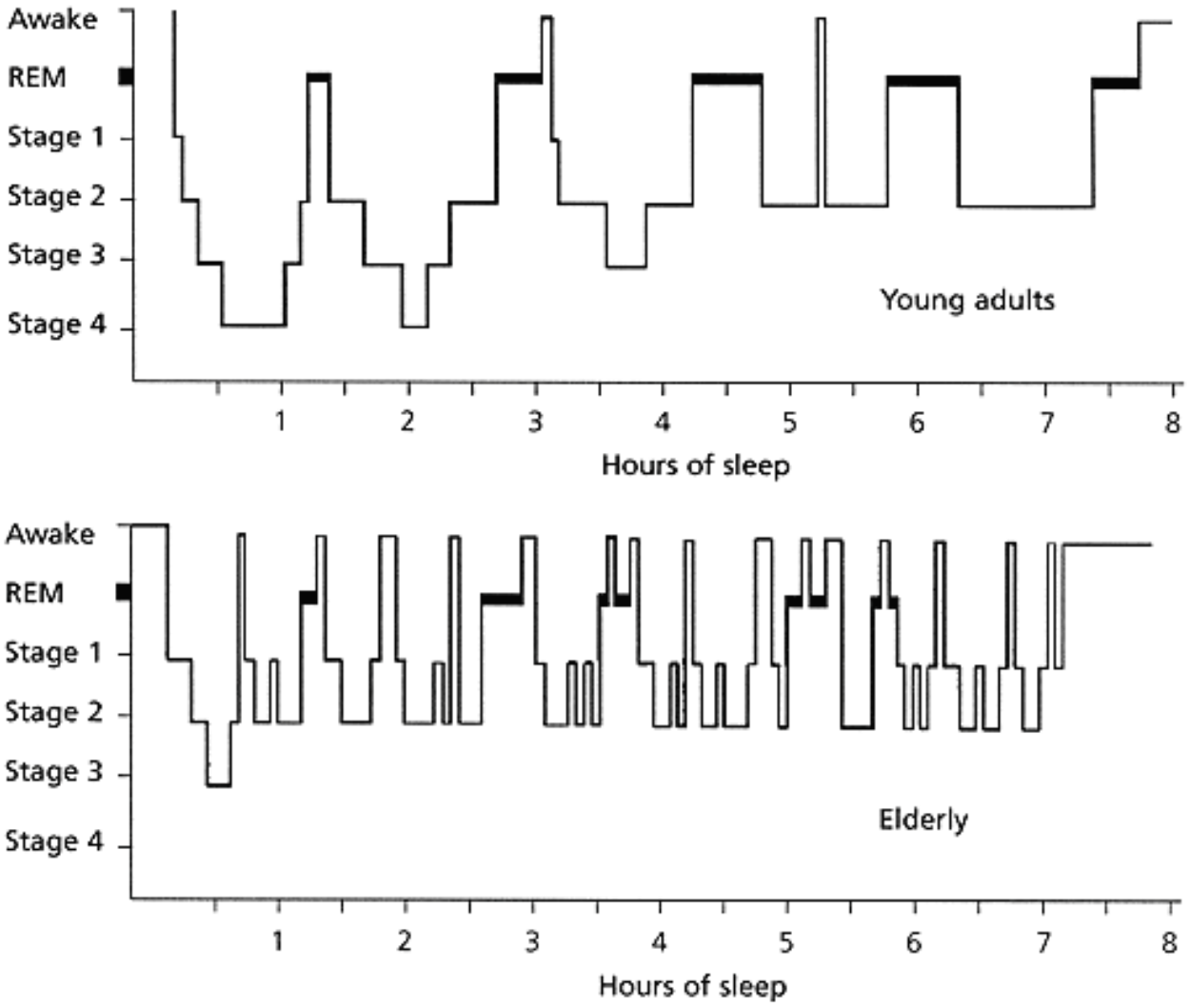


image from http://www.aafp.org/afp/1999/0501/p2551.html

SLEEP PROBLEMS IN PD

- more fragmented than in same age without PD
- difficulty sleeping through the night
- difficulty getting back to sleep
- may get to sleep but wake after a few hours
- can get reversal of sleep-wake cycle with sundowning

PATIENT EXPERIENCE

- 75 yo gentleman reported trouble sleeping
- his legs started bothering him later in the evening and he had to walk around for 20-30 minutes til they felt better and he could finally get to sleep
- he woke up several times a night and had trouble getting back to sleep
- he woke up unrefreshed in the morning and struggled through til mid morning when he finally ‘got going’
- he had a nap in the later afternoon as he couldn’t make it til bedtime
- he was becoming more irritable and having problems with his short term memory

Causes of Sleep Problems

- Parkinson's related
- Not Parkinson's related
  - caffeine, alcohol, drugs s/e
  - foods
  - timing of exercise
  - behavioural (late night TV)

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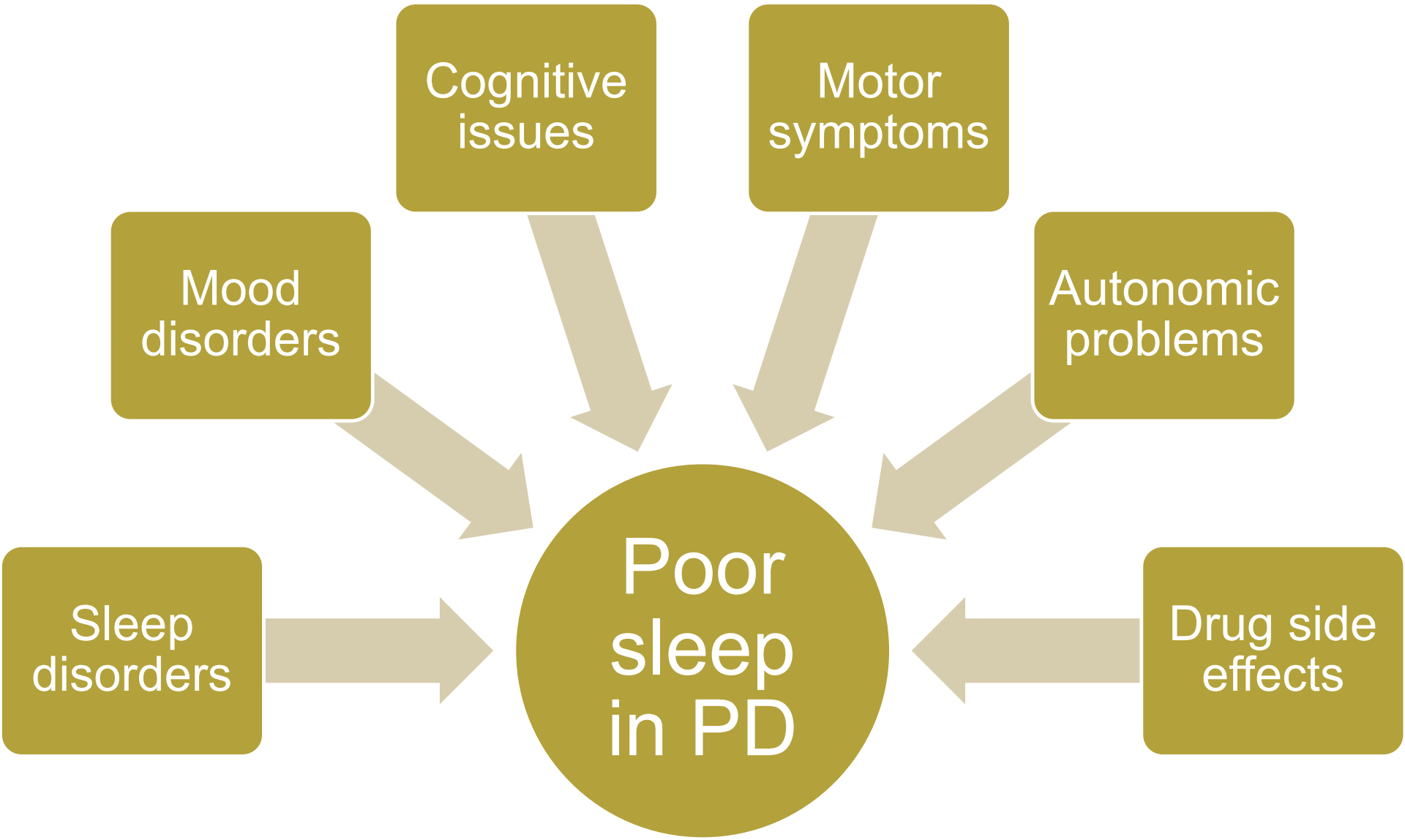
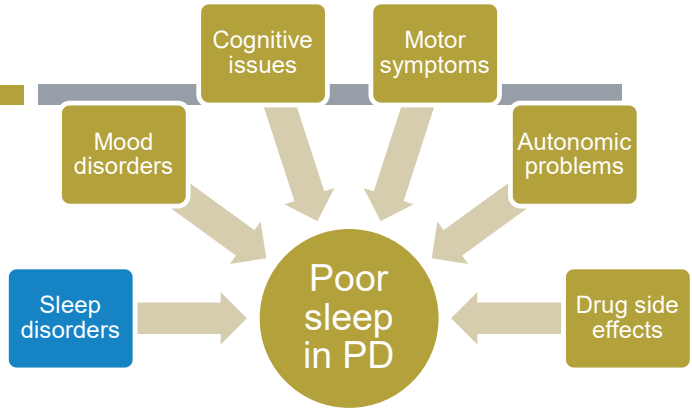
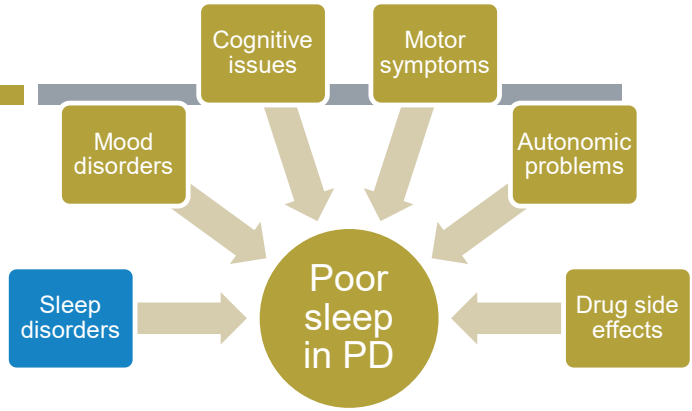

Cognitive issues
Motor symptoms
Mood disorders
Autonomic problems
Sleep disorders
Poor sleep in PD
Drug side effects

SLEEP DISORDERS



- REM sleep disorder
- Sleep apnea
- Periodic limb movements
- Restless leg syndrome

SLEEP DISORDERS



melatonin

REM sleep disorder

CPAP

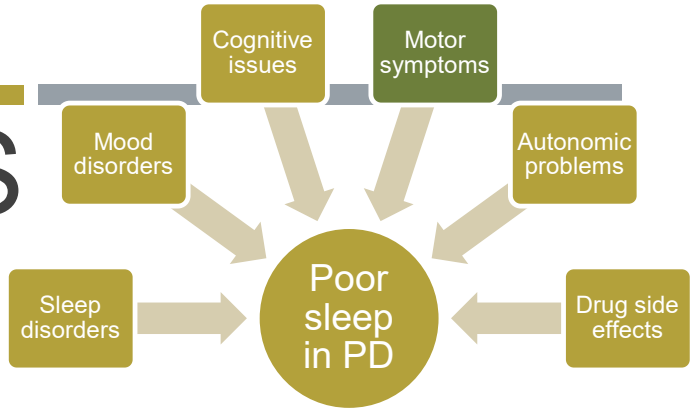
Sleep apnea

Periodic limb movements

Restless leg syndrome

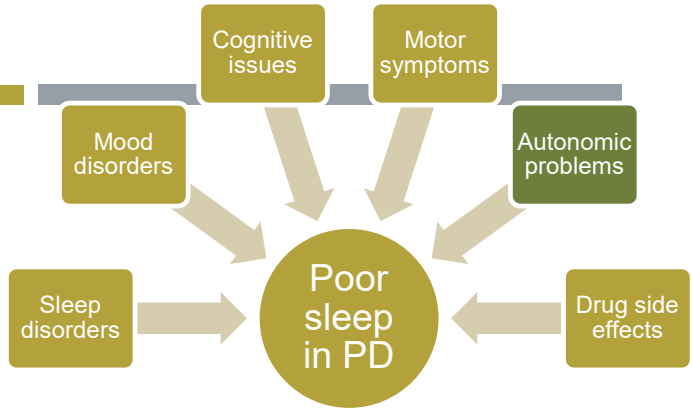
gabapentin
pregabalin
dopamine agonists
low potency opioids

MOTOR SYMPTOMS



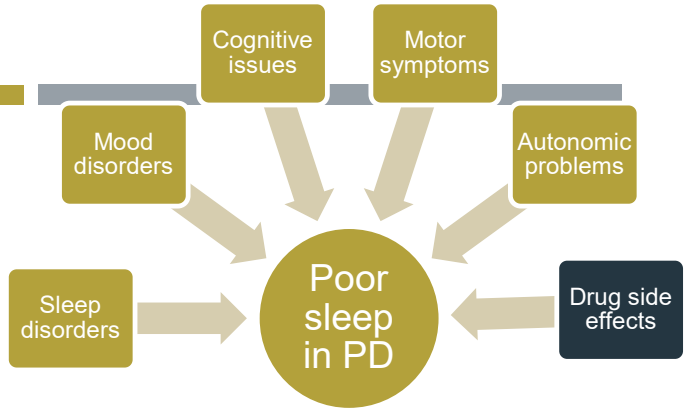
- cramps
- stiffness, difficulty rolling
- akathisia, restless
- treatment
  - bedtime levodopa (CR)
  - overnight levodopa
  - cautiously rotigotine patch (but not if any cog issues)

AUTONOMIC PROBLEMS



- Urination issues
  - minimize drinking liquids x 3 hours before bed
  - go to bathroom right before sleep
  - commode or urinal (reduce effort, arousal, light)
  - condom catheter
  - medications to reduce frequency (solifenacin, mirabegron)
    - avoid centrally acting anticholinergics
  - urologist referral
- Temperature dysregulation
  - behavioural (change sheets, frequent baths, light clothing/bedding)

DRUG SIDE EFFECTS



- Levodopa-carbidopa and dopamine agonists
  - sleep attacks
  - daytime sleepiness
  - can be alerting at bedtime
  - provoke vivid dreams
- Medication review
  - mirtazapine, SSRIs can worsen RBD

DAYTIME SLEEPINESS

- excessive daytime somnolence
  - Parkinson's disease itself (more in advanced PD and those with cognitive impairment)
  - sleep disturbance at night
  - drug side effects – dopamine, anti-depressants, sedatives
- stimulants
  - careful in elderly
  - controversial

PATIENT EXPERIENCE

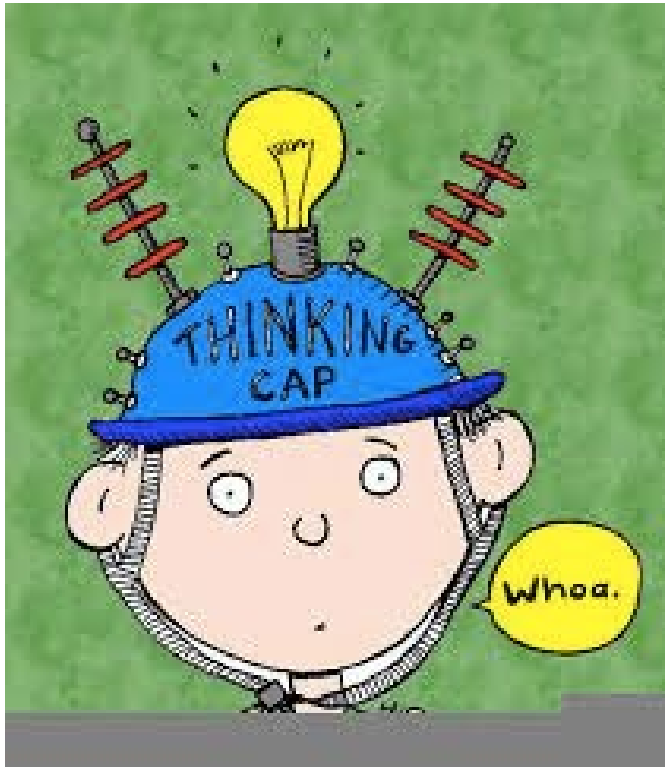
- his legs started bothering him in the evening, had to walk around for 20-30 minutes
  - **RESTLESS LEGS** – started low dose gabapentin cautiously
- he woke up several times a night and had trouble getting back to sleep
  - **URINARY FREQUENCY -** reduced fluid intake, had prostate checked, tried solifenacin
  - **ANXIETY** mindfulness exercises before bed
- awoke unrefreshed and struggled through til mid morning when he finally 'got going'
  - **DRUG SIDE EFFECT (eg: taking high dose of mirtazapine at bedtime)** reduced bedtime dose of mirtazapine
  - **RBD -** tried melatonin
- he had a nap the later afternoon as he couldn't make it til bedtime
  - **BEHAVIOURAL-** moved nap earlier and made it shorter
- he was becoming more irritable and have problems with his short term memory
  - **CAUSED MOOD AND COGNITIVE SYMPTOMS**
- Overall improvement in sleep and physical symptoms

TIPS AND TRICKS

- satin sheets and pjs to make moving in bed easier
- keep regular sleep schedule
- bedtime routine – keep same
- get outside everyday and exercise, in morning, avoid evening
- if nap, same time every day, < 1 hr, not after 3pm
- avoid stimulants
- alcohol can disrupt sleep
- avoid heavy evening meals
- sleep in cool dark room
- bed for sleep and sexual activity only
- avoid screen time later in evening

SUMMARY

- Sleep is a common problem in Parkinson’s disease
- Untreated it can significantly affect quality of life
- Detective work is needed to break the problem down to find the contributing causes that can be treated


THINKING
CAP
Whoa.

NEUROPSYCHIATRIC COMPLICATIONS OF PD

Intrinsic to PD

- depression
- anxiety
- apathy
- **impaired executive function**
- **subcortical dementia**
- RBD
- akathisia
- anhedonia

Associated with dopaminergic therapy

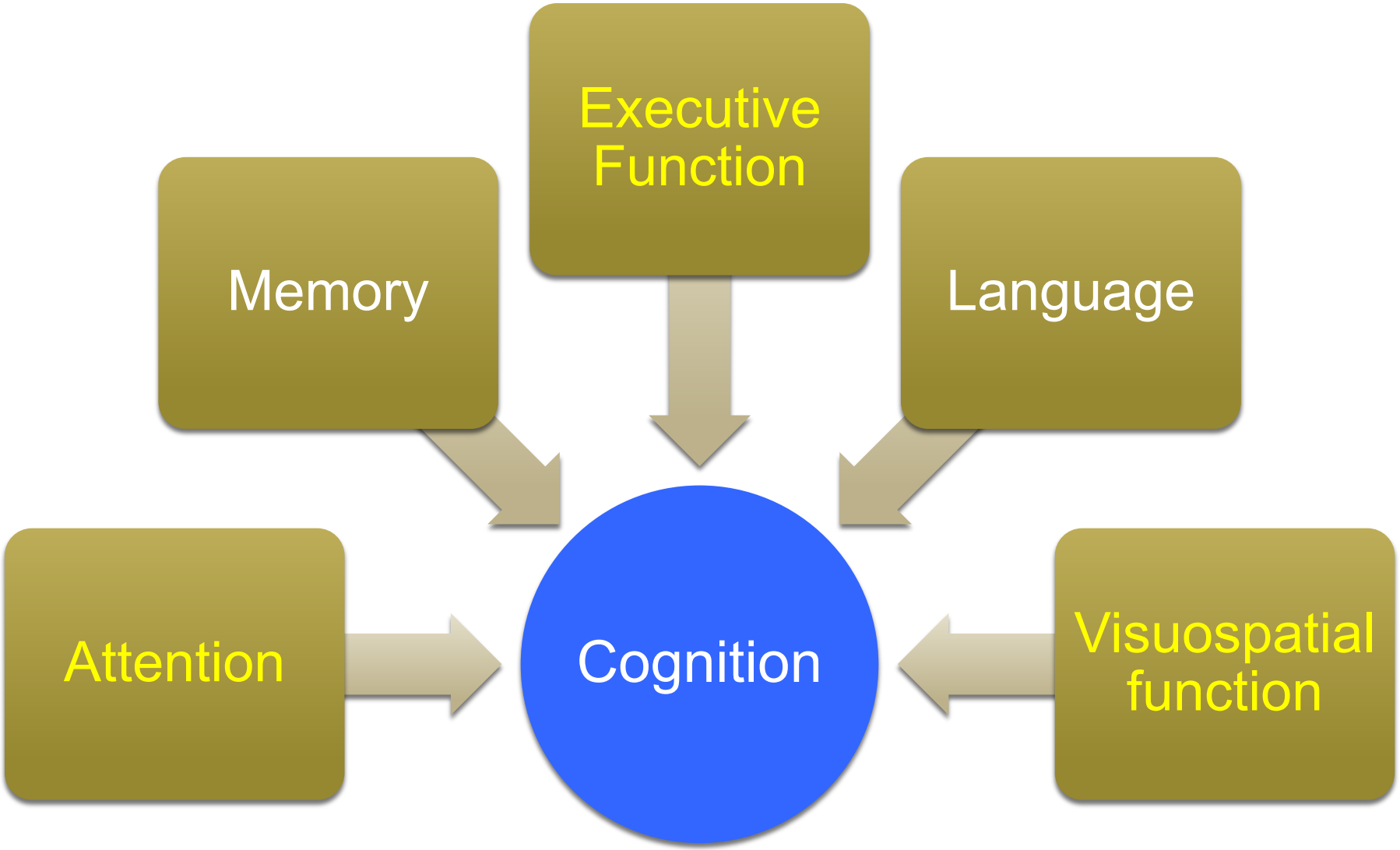
- hallucinations
- paranoia
- delusions
- ICD
- compulsive behaviours
- delirium
- dopamine dysregulation syndrome

COGNITION IN PD

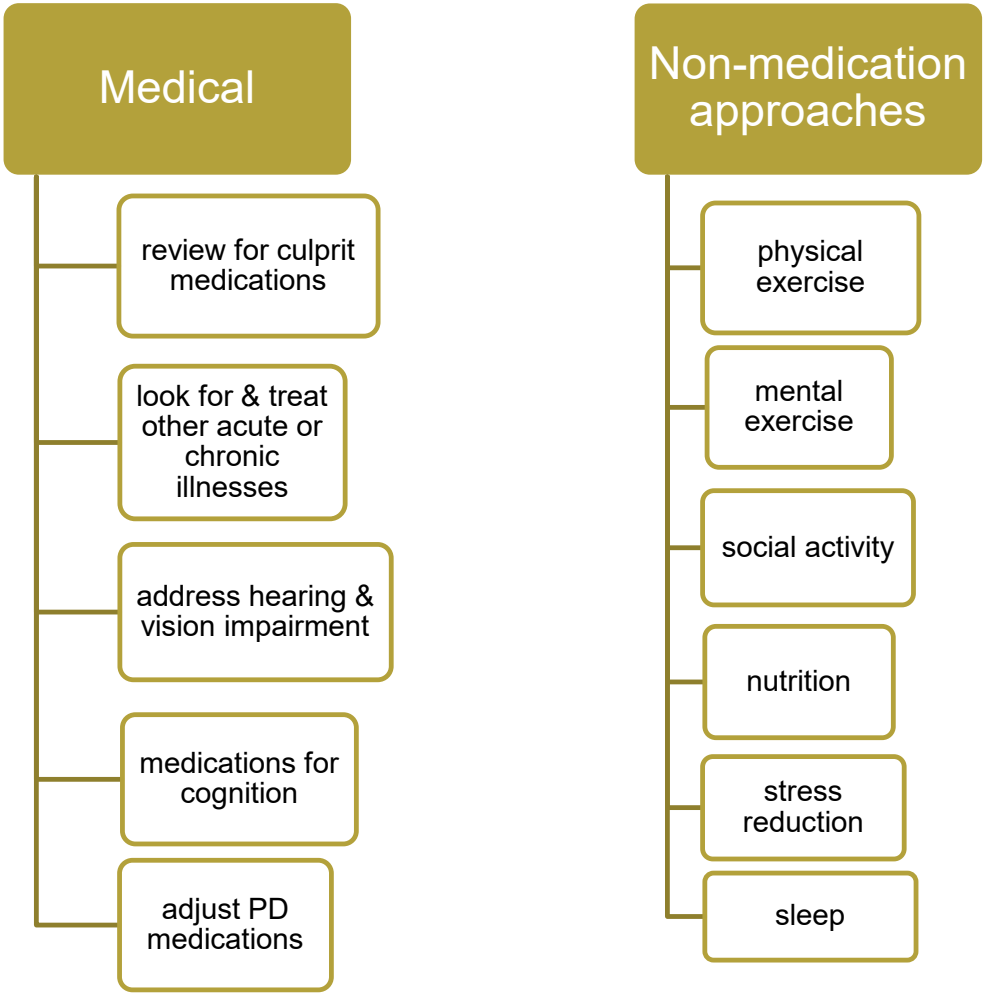
- at time of diagnosis, 30% have mild cognitive impairment
- about 40-80% of people with PD develop dementia
- not everyone with PD experiences dementia
- slow ≠ cognitively impaired
- DO NOT diagnosis patient with new onset cognitive symptoms as dementia – very likely delirium = REVERSIBLE condition

COGNITIVE IMPAIRMENT

- does NOT mean patient has DLB
  - Fluctuations in cognition with pronounced changes in attention/alertness
  - Recurrent visual hallucinations
  - REM behavior disorder
  - ≥ 1 spontaneous features of parkinsonism
  - different Dx and prognosis
  - neuroleptic sensitivity
- if develop cog issues at same time as parkinsonism – think DLB (< 1 year)
- if develop parkinsonism and then some time later start to develop dementia – think PDD (mean 10 years)
- DO NOT diagnosis hospitalized patient with new cognitive symptoms as dementia – very likely delirium = REVERSIBLE condition


Executive Function
Memory
Language
Attention
Cognition
Visuospatial function

APPROACH TO COGNITIVE IMPAIRMENT IN PD



SPECIFIC MEDICATION TX OF COGNITION

- medications – play a small role overall
- indicated for mild to moderate dementia
- rivastigmine is the only one FDA-approved to treat PDD
- Canadian guidelines:
  - can use rivastigmine or donepezil for PD dementia
  - can consider using galantamine for PD dementia (if not responding or side effects on the others)
  - s/e: nausea, diarrhea, orthostasis
  - not recommended if heart block, syncope or significant bradycardia
  - memantine can be added or substituted if cholinesterase inhibitors are not tolerated or lack efficacy

COGNITIVE IMPAIRMENT

The diagnoses of dementia associated with PD and of mild cognitive impairment in PD can be made using the Movement Disorder Society Clinical Diagnostic Criteria. These require reports of subjective cognitive decline and difficulties on psychometric testing.	CAN	GPP
For PD dementia, cholinesterase inhibitors could be added: rivastigmine (grade: A), donepezil (grade: A), or galantamine (grade: C). There may be idiosyncrasy in clinical response and adverse effects, so it is worth trying an alternative agent (grade: GPP). Memantine can be added or substituted if cholinesterase inhibitors are not tolerated or lack efficacy (grade: C).	EFNS[14]	Varied
No interventions have been proven to reduce the risk of progression of PD from mild cognitive impairment to dementia but lifestyle modifications, such as engaging in cognitive and social activities and physical exercise, are encouraged.	CAN	GPP

cholinesterase inhibitor

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- ICD
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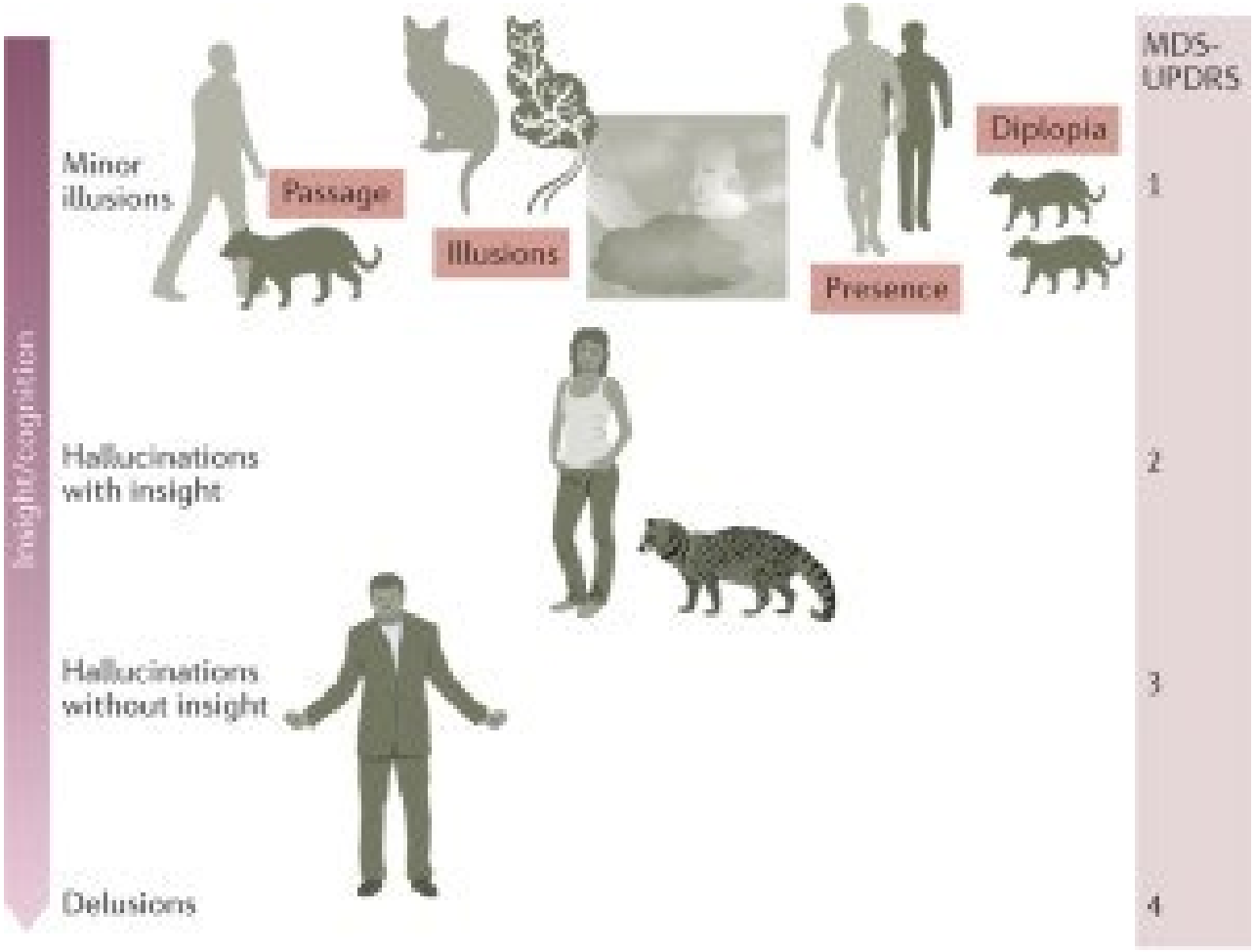
PSYCHOSIS IN PD



PSYCHOSIS - CAUSES

Patient factors

- cognitive decline
- sleep deprivation
- other medical condition (delirium)
- depression
- advanced age

Due to med side effect

- dopaminergic medications
- use of adjuntive PD tx
- multiple PD meds
- concomitant use of other psychoactive meds

PSYCHOSIS APPROACH

Non-medication

- lighting
- redirect
- sleep
- safety – weapons etc.

Medication

- review polypharmacy
- consider taper and stop, in order:
  - anti-cholinergics
  - amantadine
  - dopamine agonists
  - entacapone
  - MAOB inhibitors (rasagiline, selegiline)
- adjust levocarb-cautious, consult

PSYCHOSIS

- Treatments:
  - Cholinesterase inhibitors
  - Quetiapine
  - Clozapine – FDA approved in PD
  - Pimavanserin – FDA approved in PD (not in Canada yet)

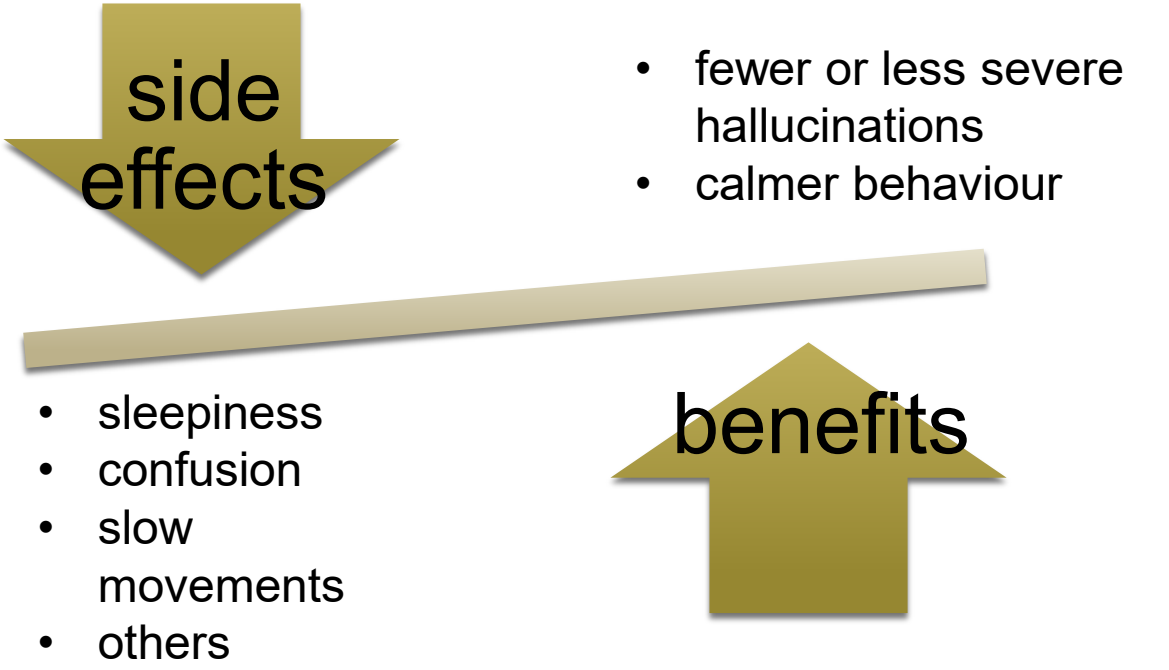


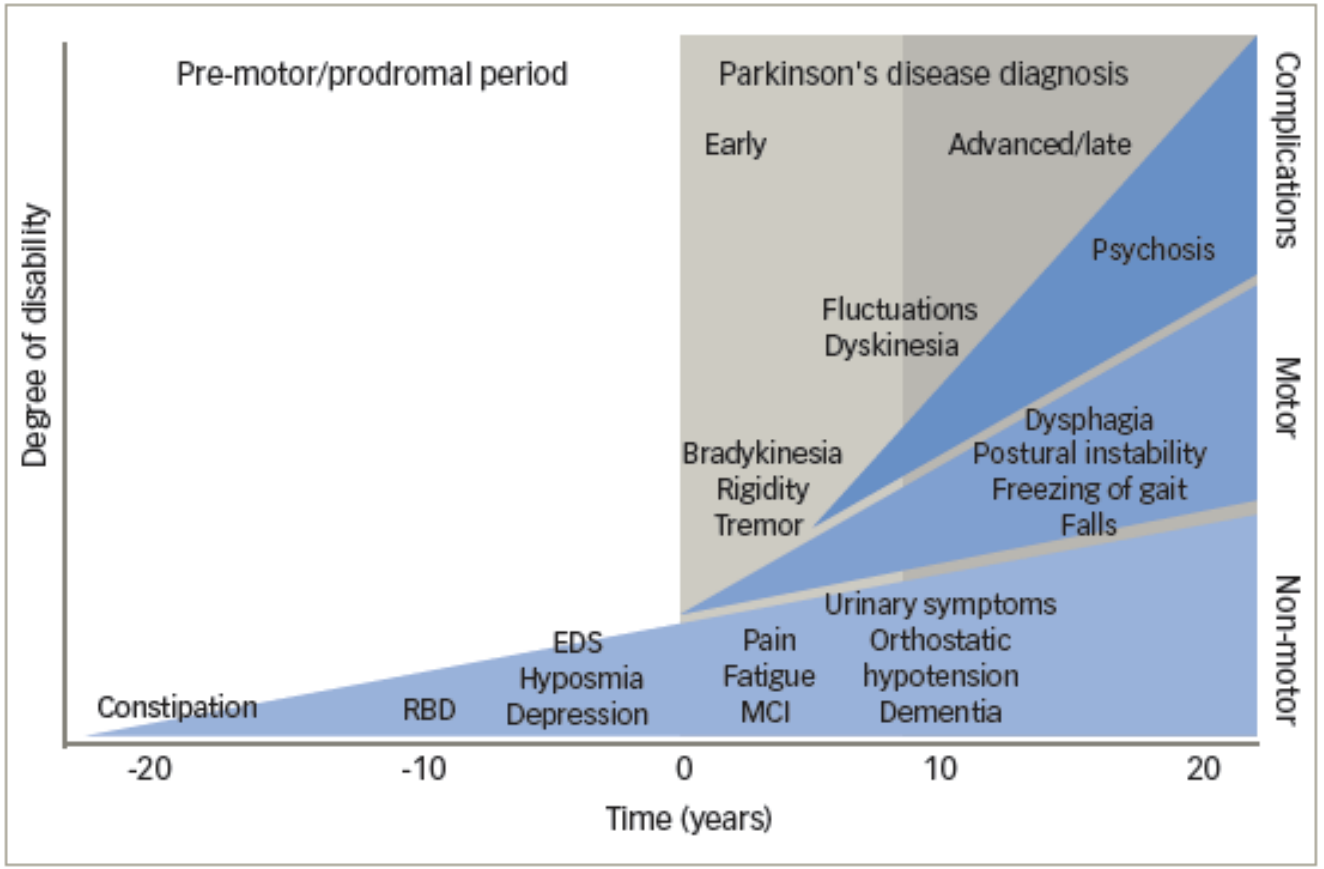
Table 1: Parkinson's disease psychosis and antipsychotic use

Commonly Used in PDP	
Clozapine	Improves psychosis without worsening PD symptoms; may cause agranulocytosis therefore requires specialized monitoring[38–40]
Quetiapine	Most commonly used, inconsistent efficacy but no worsening of PD symptoms[40,42–45]
Should Not Be Used in PDP	
All typical antipsychotics	Significant worsening of PD symptoms[24]
Aripiprazole	Inconsistent efficacy and worsening of PD symptoms[25–27]
Olanzapine	No efficacy and worsening of PD symptoms[28–30]
Risperidone	Some efficacy but worsening of PD symptoms[31–35]
Ziprasidone	Insufficient evidence for efficacy and tolerability, but has limited use due to cardiac side effects and should be avoided[36,37]

PD = Parkinson's disease; PDP = Parkinson's disease psychosis

All people with PD and psychosis should receive a general medical evaluation and treatment for any precipitating condition.	NICE[7]	D GPP
For patients with PD and psychosis, polypharmacy should be reduced. • Anticholinergic antidepressants should be reduced or stopped; anxiolytics or sedatives should be reduced or stopped. • Antiparkinsonian drugs should be reduced. Anticholinergics should be stopped, amantadine should be stopped, dopamine agonists should be reduced or stopped, MAO-B and COMT inhibitors should be reduced or stopped and, lastly, levodopa should be reduced.	EFNS[14]	GPP
Hallucinations and delusions should not be treated if they are well tolerated by the person with PD and their family members and caregivers (as appropriate). Even minor hallucinations or delusions should be considered a marker of disease progression, and should warrant a general medical evaluation and treatment for any precipitating factors.	NICE[8]	GPP
For patients with PD and psychosis needing treatment: • Quetiapine is possibly useful. • Clozapine is useful but requires monitoring.	 EFNS[14] EFNS[14]	 GPP A
With the exception of quetiapine and clozapine as described in recommendation C90, all other antipsychotics should be avoided in PD psychosis (grade: GPP). Olanzapine (grade: A), risperidone (grade: C) and aripiprazole (grade: GPP) can worsen parkinsonism (harmful).	EFNS[14]	Varied
Pimavanserin could be considered as a treatment for PD psychosis.	CAN	B

Figure 1. Clinical symptoms and time course of Parkinson's disease[3]



EDS = excessive daytime sleepiness; MCI = mild cognitive impairment; RBD = rapid eye movement sleep behavior disorder. Reproduced with permission from Kalia et al., 2015.[3]


BANANAS AGAIN? YOU PRESCRIBE BANANAS FOR EVERYTHING!

NEUROPSYCHIATRIC COMPLICATIONS OF PD

Intrinsic to PD

- **depression**
- **anxiety**
- **apathy**
- **anhedonia**
- impaired executive function
- subcortical dementia
- RBD
- akathisia

Associated with dopaminergic therapy

- hallucinations
- paranoia
- delusions
- ICD
- compulsive behaviours
- delirium
- dopamine dysregulation syndrome

MOOD IN PARKINSON'S

- Depression - up to 60%
- Anxiety - 25-45%
- Apathy

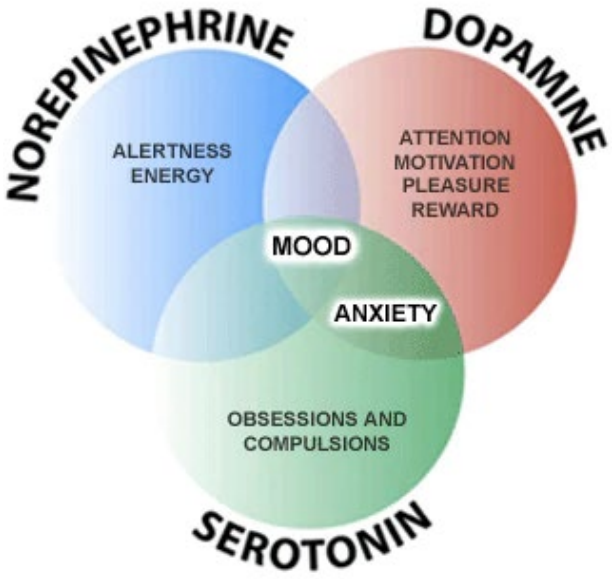
- Premotor for some patients

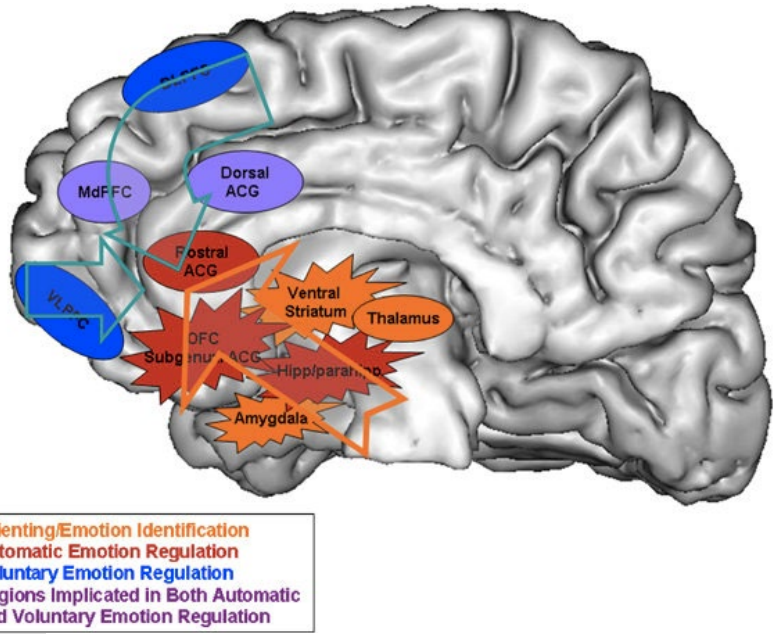
- Increased risk:
  - Women > men
  - Advanced stage of PD
  - Patients with cognitive problems

- **PD symptom most correlated with poor quality of life

- Can affect long-term outcomes by causing social withdrawal, lack of exercise, more reluctant to seek care

MOOD IN PARKINSON'S





MOOD IN PARKINSON'S

Depression

- Persistent sad, anxious, or "empty" mood
- Feelings of hopelessness or pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies or activities, especially those which were previously enjoyable
- Decreased energy or fatigue
- Difficulty concentrating, remembering, and making decisions
- Difficulty sleeping, early-morning awakening or oversleeping
- Appetite and/or weight changes
- Thoughts of death or suicide
- Restlessness, irritability
- Persistent physical symptoms

Anxiety

- Restlessness, feeling wound-up or on edge
- Fatigue
- Difficulty concentrating or having their minds go blank
- Irritability
- Muscle tension
- Difficulty controlling the worry
- Sleep problems, such as difficulty falling or staying asleep, or restless or unsatisfying sleep

MOOD- TREATMENT

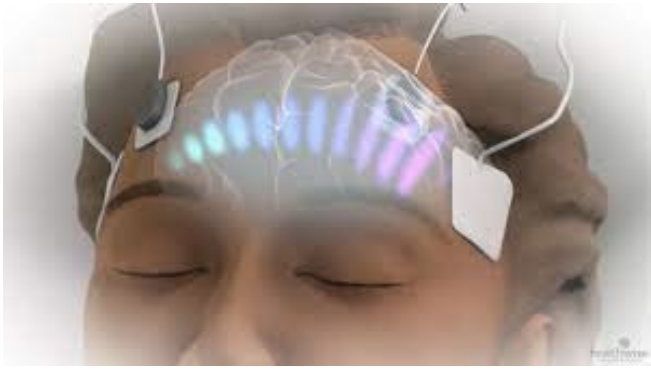
Medications

- SSRI
- SNRI
- TCA – generally avoid
- Other atypical antidepressants:
  - Bupropion (Wellbutrin) – increases norepinephrine and dopamine activity. Most activating antidepressant. Least likely to cause sexual side effects.
  - Mirtazepine (Remeron) – enhances release of norepinephrine and serotonin by different mechanism. Can stimulate appetite and improve sleep
- Others for anxiety
  - benzos – avoid – sedation, risk dementia
- MAOB-I interactions

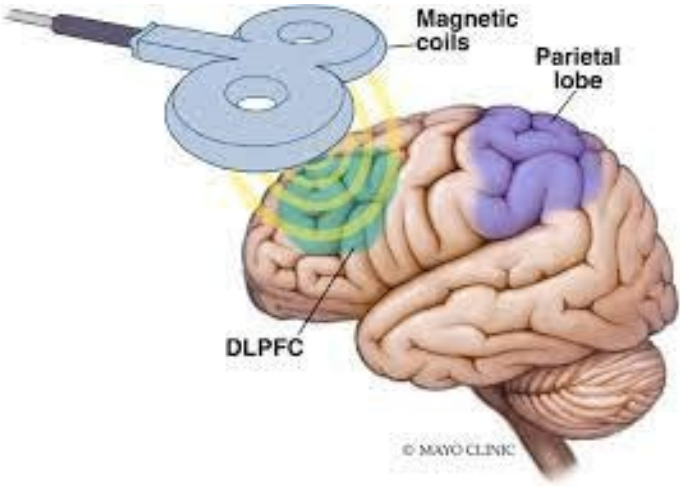
Non-medications

- exercise
- CBT
- social activities
- support groups
- review PD – can have ‘off’ anxiety
- Other interventions – relaxation techniques, biofeedback, meditation, massage, acupuncture, aromatherapy

INTERVENTIONS FOR MOOD



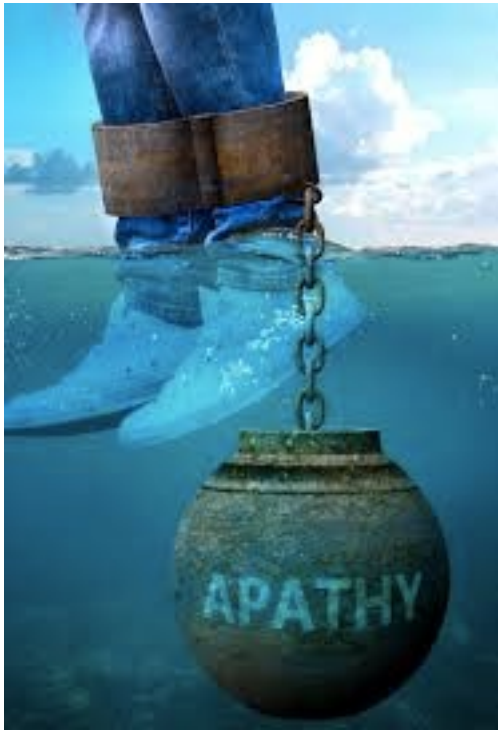
- Electroconvulsive Therapy:
  - Electric current applied through the scalp
  - Effective in severe or refractory depression
  - May also help motor symptoms
  - Drawbacks – requires general anesthesia, temporary confusion and/or short-term memory problems.
- Repetitive transcranial magnetic stimulation (rTMS)
  - Non-invasive coils to produce magnetic pulses that stimulate specific brain regions



PSEUDOBULBAR AFFECT

- brief episodes of emotional lability that do not match a person's feelings or situation
- uncontrollable or inappropriate laughing or crying
- frequently mistaken for depression
- due to damage to brain areas that control normal expression of emotion
- can cause stress or frustration or avoidance of social interaction
- Treatment:
  - education, understanding
  - SSRI

APATHY



- can occur by self or co-occur with depression or cognitive impairment
- Cognitive/Behavioral:
  - Little or no-goal directed behavior, inability to “get up and go”
  - Trouble initiating activities/tasks, needs to be prompted
  - Loss of curiosity in learning new things
- Emotional:
  - Emotional indifference or inability to express emotion
  - Lack of passion related to activities or situations that previously provoked emotion
  - Less empathy toward feelings of others
- Social:
  - Less interest in participating in social or leisure activities
  - Less interest in family or interest in meeting new people
  - Less participation in conversation
  - Reduced spontaneous interactions with others

APATHY - TREATMENT

- Treatment – no approved therapies
- Maintain a regular schedule of structured activities:
  - Focus on more relevant activities first – medical and therapy appointments
  - Chores, household duties
  - Keep a calendar and check tasks off as they are done
- Avoid isolation:
  - Schedule time with family and friends
  - Support groups
- Tips for caregivers:
  - Be patient
  - Provide positive feedback when goals are reached

TAKE HOME MESSAGES

- Medication
  - changes across the spectrum
  - watch for medication side effects that can can affect motor or non-motor aspects of PD
  - do NOT stop levocarb
  - *****medication timing*** - consider institutional policy**
- Sleep – multifactorial, need to be a detective
- As cognition declines and/or psychosis develops, review PD and non-PD medications
- Mood - #1 cause of poor quality of life in PD and is treatable
- If in doubt, please ask: movement disorder RACE app

THANK YOU