

FATIGUE AND SLEEP DISORDERS

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Overview

Sleep disorders

- What changes in PD
- Insomnia
- Dream enactment
- Restlessness
- Daytime sleepiness
- Troubleshooting

Fatigue

- What is it?
- How common?
- General causes
- PD specific causes
- Approach

Why does this matter?



Fatigue



Sleepiness



Sleep benefit

Worst problem: 33%



Top 3 problem: 50%



Sleep may have an impact on neurodegeneration

What affects sleep (and vice versa)?



Time awake and circadian rhythm

Accumulation of adenosine
Protein phosphorylation



“I’m a night owl”

Multiple genetic factors



Hormones



Caffeine and stimulants



Exercise



Natural light exposure



Artificial light exposure

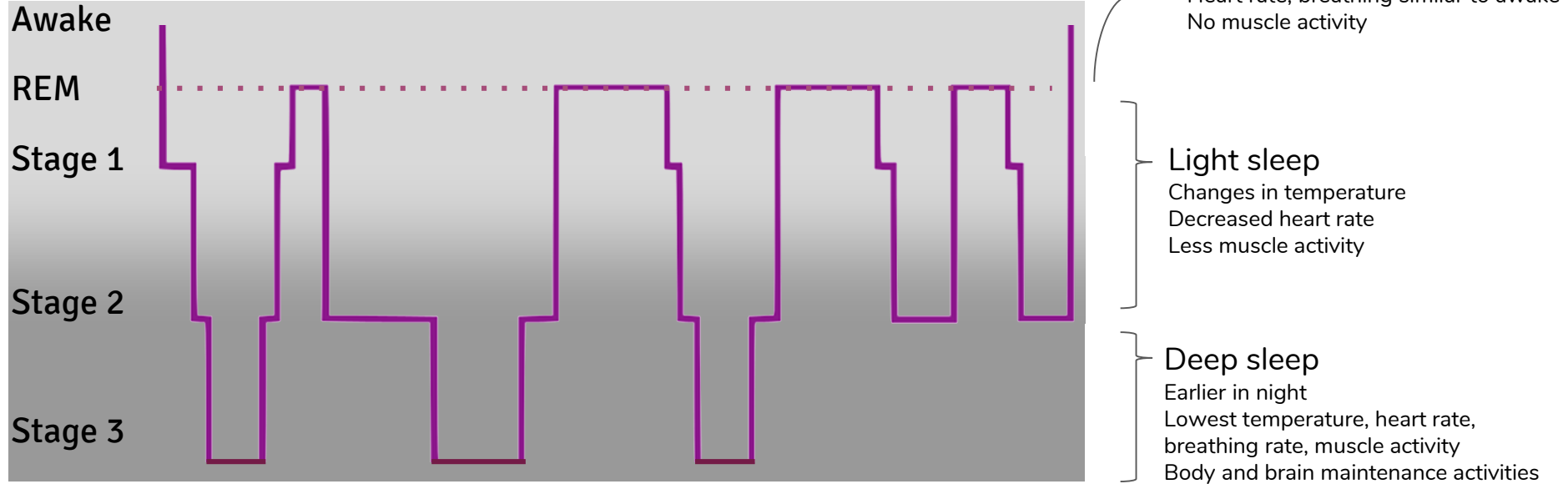
“Awake” hormones

Cortisol
Adrenaline / noradrenaline

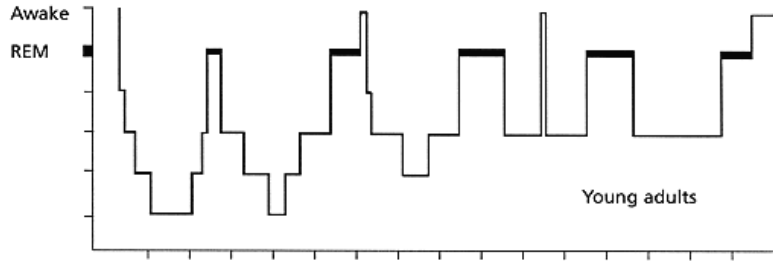
“Asleep” hormones

Melatonin
Testosterone
Growth hormone
Erythropoietin
Leptin

Normal sleep stages



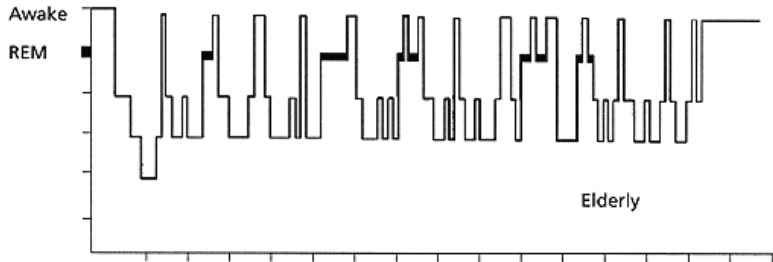
Sleep changes with aging



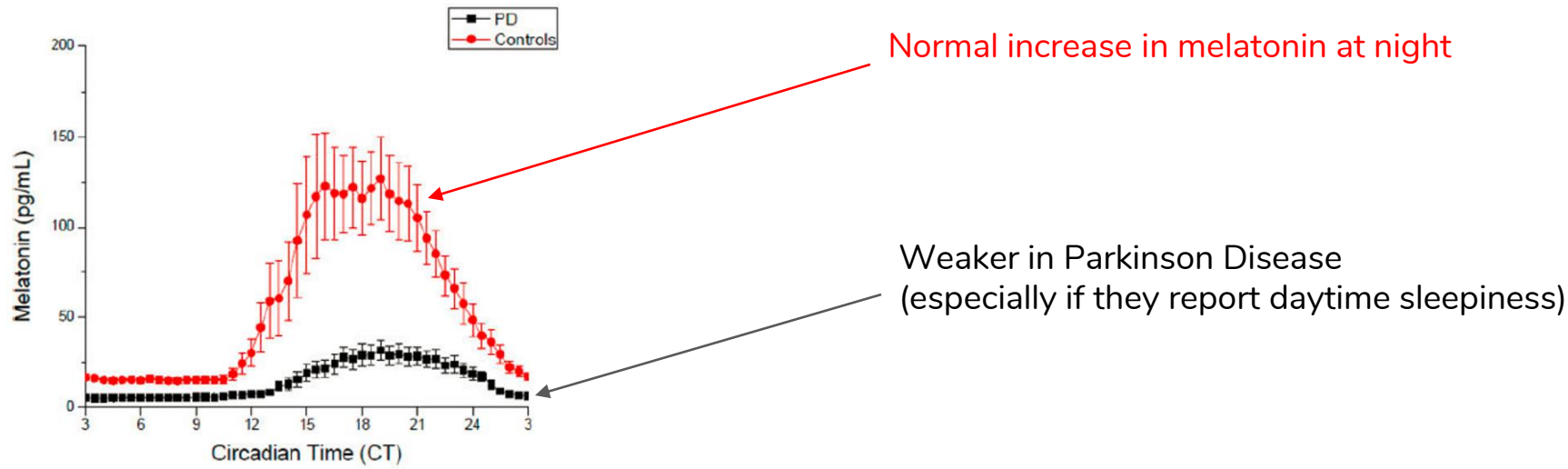
Less overall sleep time

Shorter time in each stage

More time awake while in bed



Why is sleep affected in Parkinson Disease?



Disruption of the circadian rhythm
Changes in the brain's sleep system

May start even before movement problems

Insomnia: Other factors in Parkinson disease



Rigidity

*



Tremor

*



Dyskinesia

*



Pain

*

*



Anxiety / Racing thoughts

*

*



Restlessness

*

*



Nighttime urination

*



Temperature changes

*

Some aspects can relate to medication wearing off

Others can relate to overtreatment

Parkinson disease is an around-the-clock condition

How should we approach insomnia?

Address sleep behaviors / sleep hygiene



Address issues suspected to relate to dopamine medications



Look for other common sleep issues in Parkinson Disease



Troubleshoot if you suspect an additional sleep problem
(like sleep apnea)

Insomnia and restlessness - medical approaches

- Restlessness / fragmentation may respond to dopamine treatment changes
 - Controlled release levodopa at bedtime
 - Dopamine agonists (oral / rotigotine)
 - Addition of entacapone
 - Duodopa
- Check dose times of medications that can interfere with sleep
 - Amantadine
 - Selegiline
 - Some antidepressants (e.g. bupropion, venlafaxine)
- Other approaches
 - Zopiclone (insufficient evidence)
 - Melatonin 3-5 mg insufficient evidence, may help dream enactment
 - Doxepin, amitriptyline (can cause dry mouth, other side effects)
 - Restlessness can respond to gabapentin, other treatments

**NOW WITH
"LIMITED
EVIDENCE"!**

Sleep hygiene



- Get into bed only when ready to sleep

Get back out if you are awake after 15 minutes



- Nonstimulating activities before bed or if unable to sleep



- Pre-sleep rituals like meditation help some people



- Journal / externalize your worries or thoughts



- Limit alcohol, avoid coffee past noon



- Avoid screens at least 1 hour before bed

Difficulty repositioning

More common with axial (mid-body) stiffness

May depend on dopamine medication

Silk or satin sheets and bedclothes

Bedrails (occupational therapy)

Softer mattresses may be more difficult



Troubleshooting nighttime bladder function

Avoid fluid 2 hours before bed

Empty bladder before bed

Assess the problem



- Urgency / “overactive”
- Short notice
- Can occur as part of Parkinson Disease
- Might depend on dopamine medication in part
- Some other medications may help



- Hesitant / slow to start
- Slow stream
- Incomplete emptying
- Can be from low bladder tone / obstruction
- Different treatment approach

Unclear pattern / mixed symptoms - may need further testing / urologist

Nighttime awakenings affect sleep quality, and can ↑ fall risk

Troubleshooting: other sleep disorders

Sleep apnea

- 5 pauses per hour lasting 10 seconds or longer
- ↓ oxygen level in the blood
- Shallower, fragmented sleep and sleepiness in the day
- ~20% in Parkinson Disease / 5% in general population
- Treatments: weight reduction, ↓ alcohol
- Air pressure (masks), position...



UNSCRAMBLE THE EGG

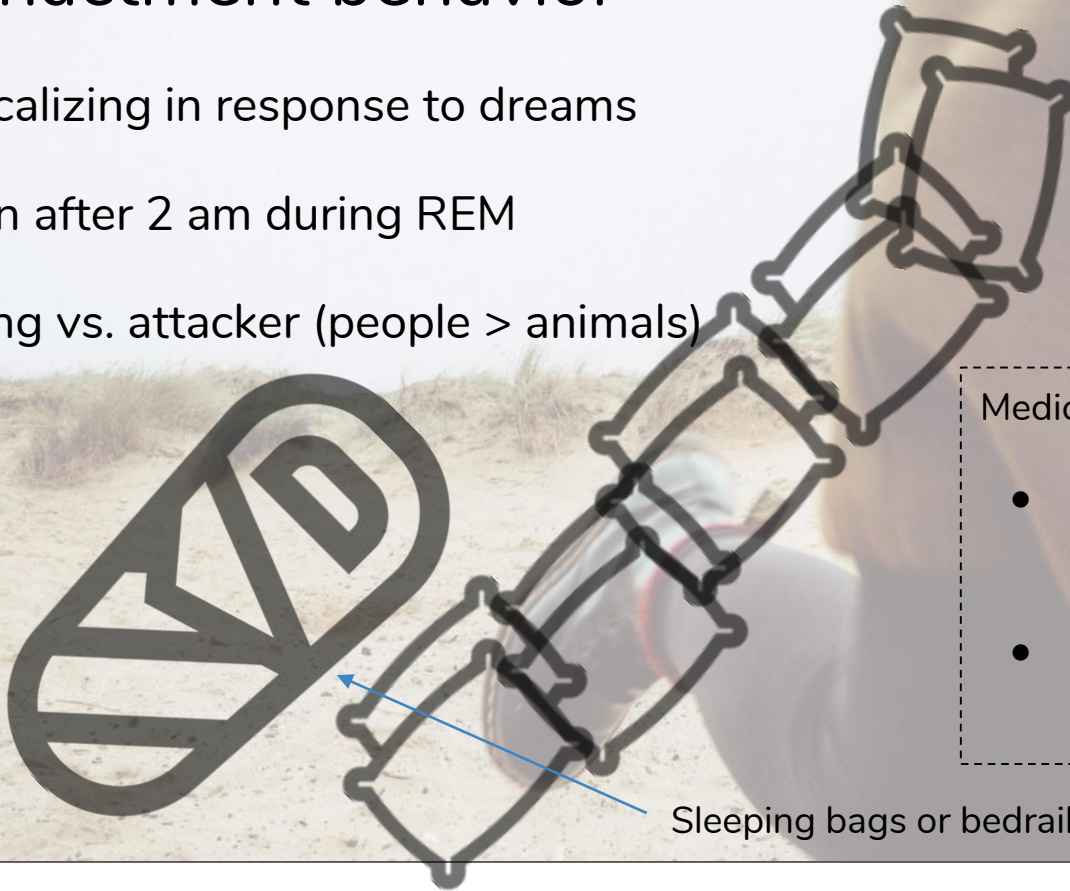
Sleep studies can help when the sleep problem is not clear

Dream enactment behavior

Moving or vocalizing in response to dreams

More common after 2 am during REM

80% defending vs. attacker (people > animals)



Pillow barricade

Medical approaches:

- Clonazepam
Suppresses dreaming and ↓ movement
Tolerance / dependance
- Melatonin
Less potent, can suppress movement

Sleeping bags or bedrails can prevent injury

Daytime sleepiness

Bright light therapy

Compared in clinical trial to sham light therapy (Videnovic et al. JAMA Neurology 2017;74:411-418)

Improved sleepiness, sleep quality, measures of daytime activity

Caffeine: slight benefit vs. placebo

(Postuma RB, Lang AE, Munhoz RP, et al. Caffeine for treatment of Parkinson disease: a randomized controlled trial. Neurology 2012;79:651-658.)

Dopamine medications can contribute (dopamine agonists > levodopa) to sleepiness / sleep attacks

Insufficient evidence / may help in some cases

Modafinil (usually used in narcolepsy)

Rasagiline

Selegiline

Amantadine



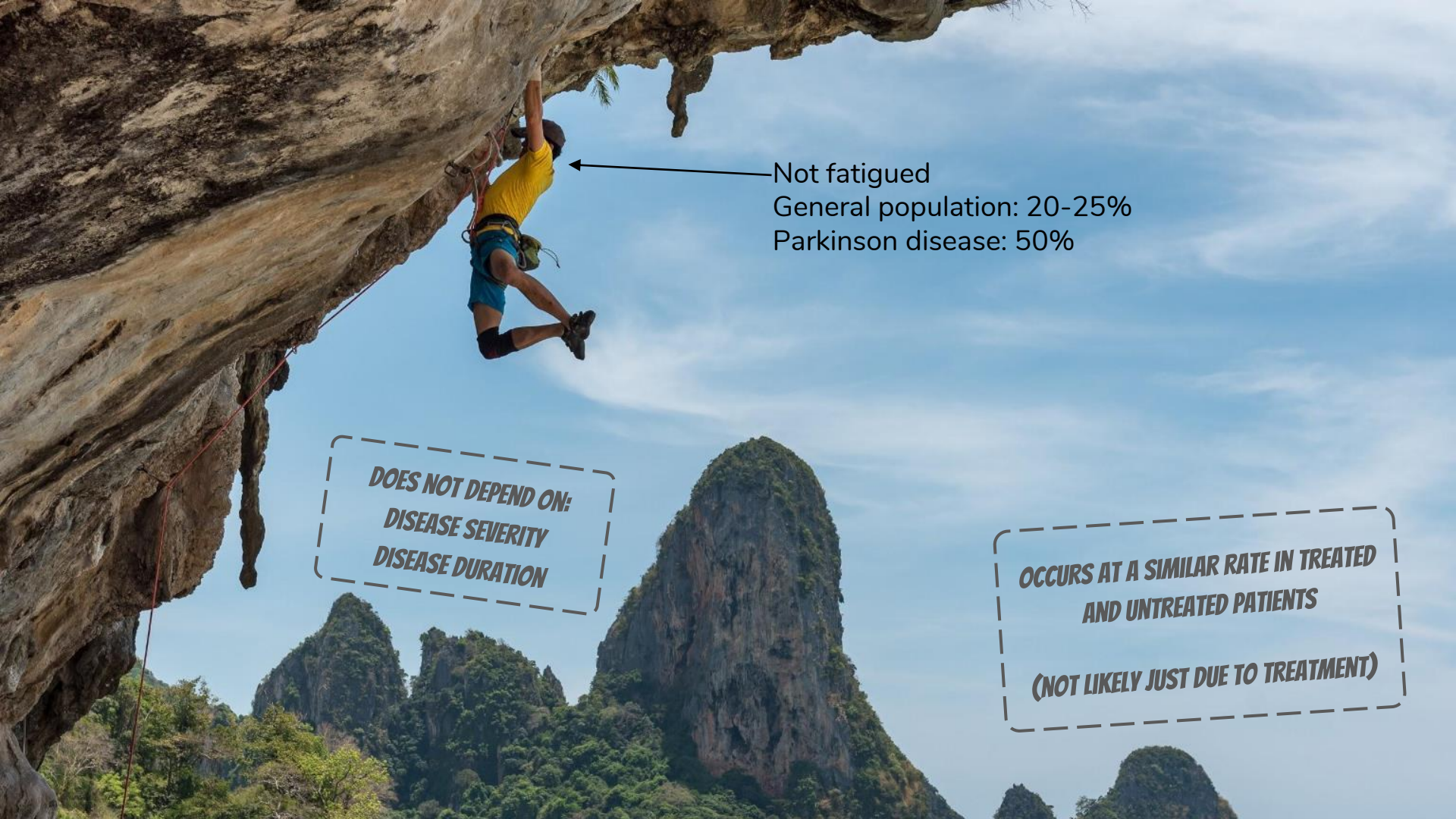
What is fatigue?

Complex

Hard to describe

Lack of energy

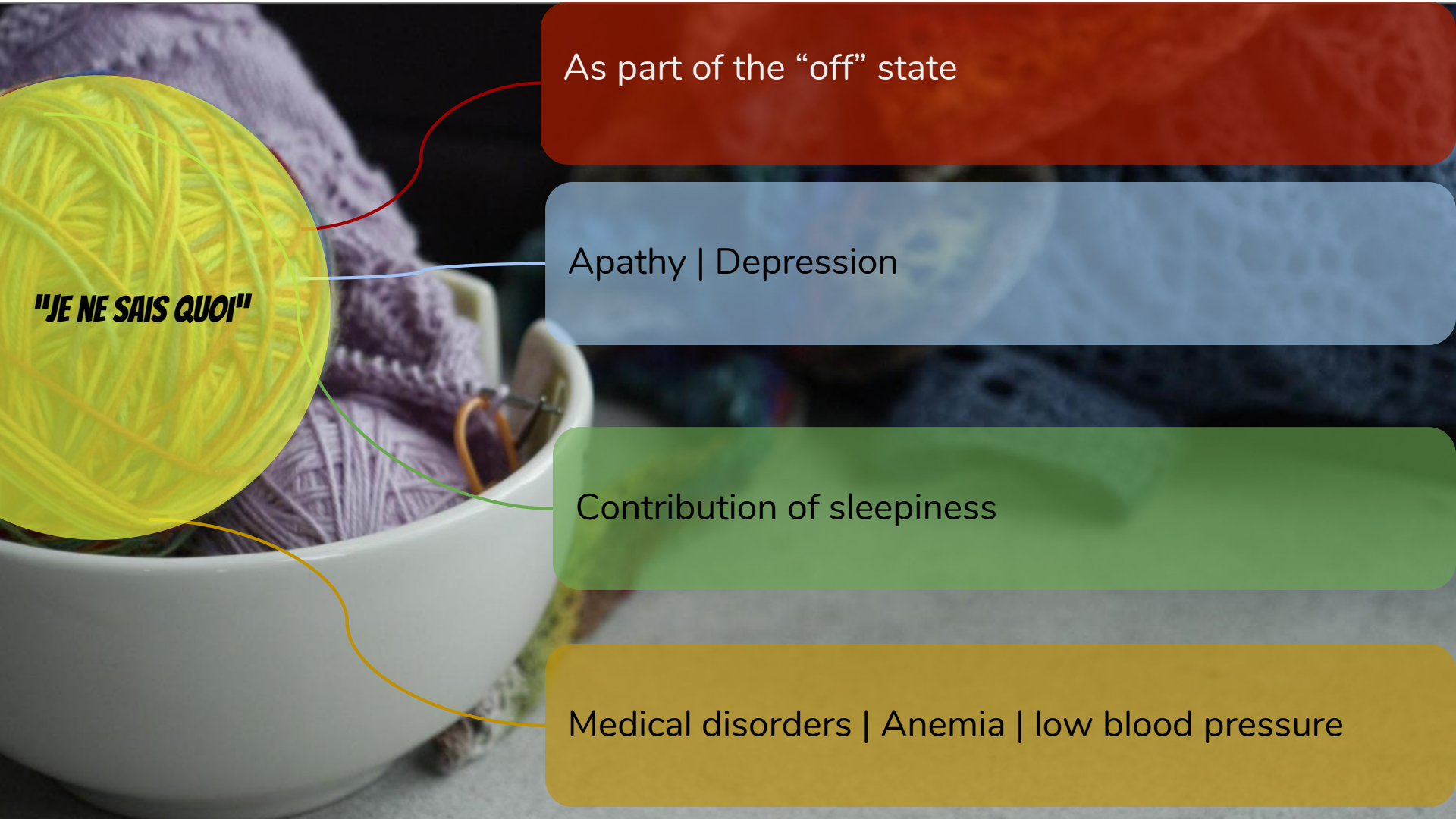
More perceived effort



Not fatigued
General population: 20-25%
Parkinson disease: 50%

**DOES NOT DEPEND ON:
DISEASE SEVERITY
DISEASE DURATION**

**OCCURS AT A SIMILAR RATE IN TREATED
AND UNTREATED PATIENTS
(NOT LIKELY JUST DUE TO TREATMENT)**



As part of the “off” state

Apathy | Depression

Contribution of sleepiness

Medical disorders | Anemia | low blood pressure

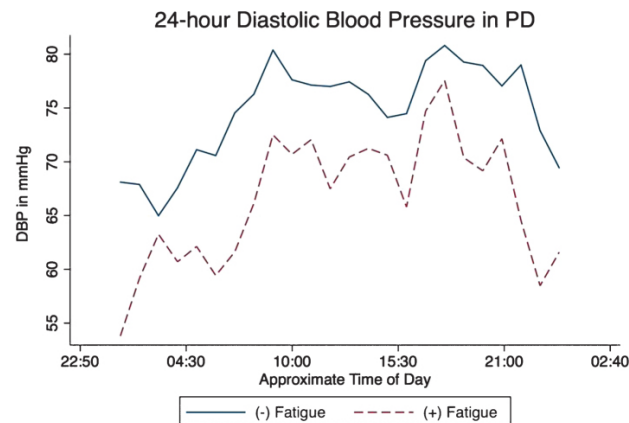
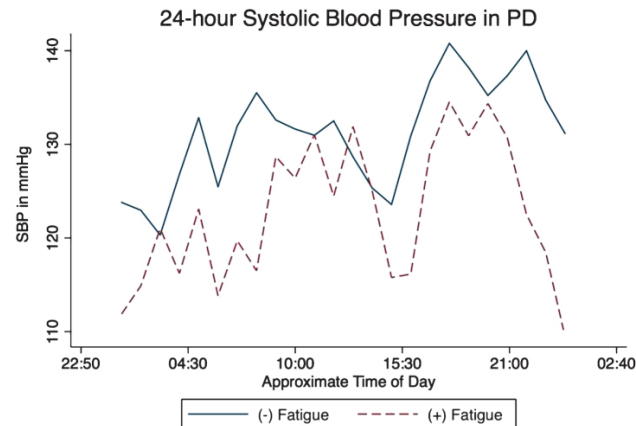
"JE NE SAIS QUOI"

Under pressure

Low blood pressure may cause fatigue before lightheadedness

Patients with low blood pressure have higher fatigue scores

The effects of low blood pressure are worse in some medical conditions (low blood counts / anemia / iron deficiency)



Check blood pressures
with your doctor

Careful when standing!

Apathy, mood and fatigue

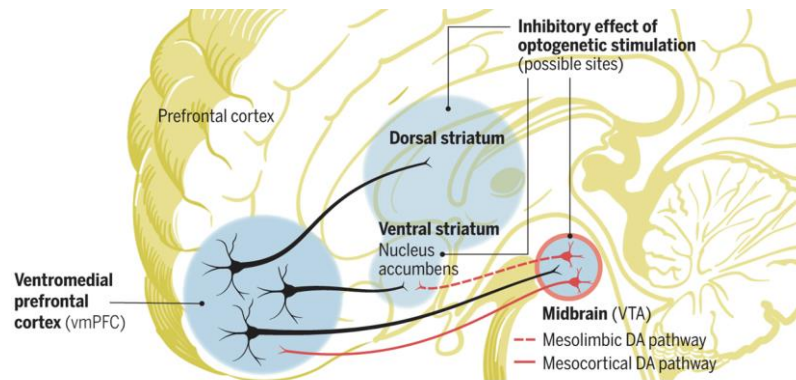
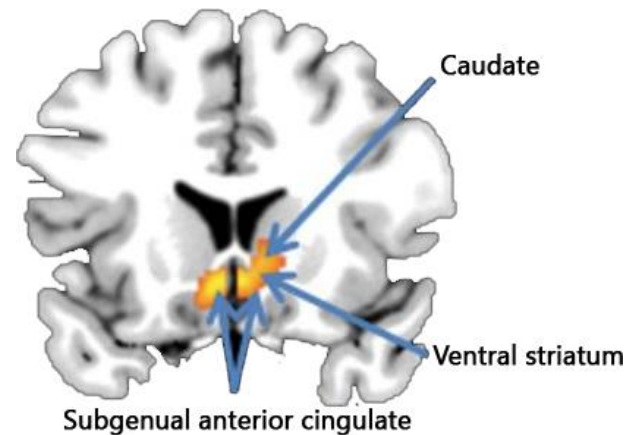
Fatigue, apathy, and depression often coexist

May relate to serotonin changes (upper figure)

Dopamine agonists are more likely than levodopa to affect reward experience

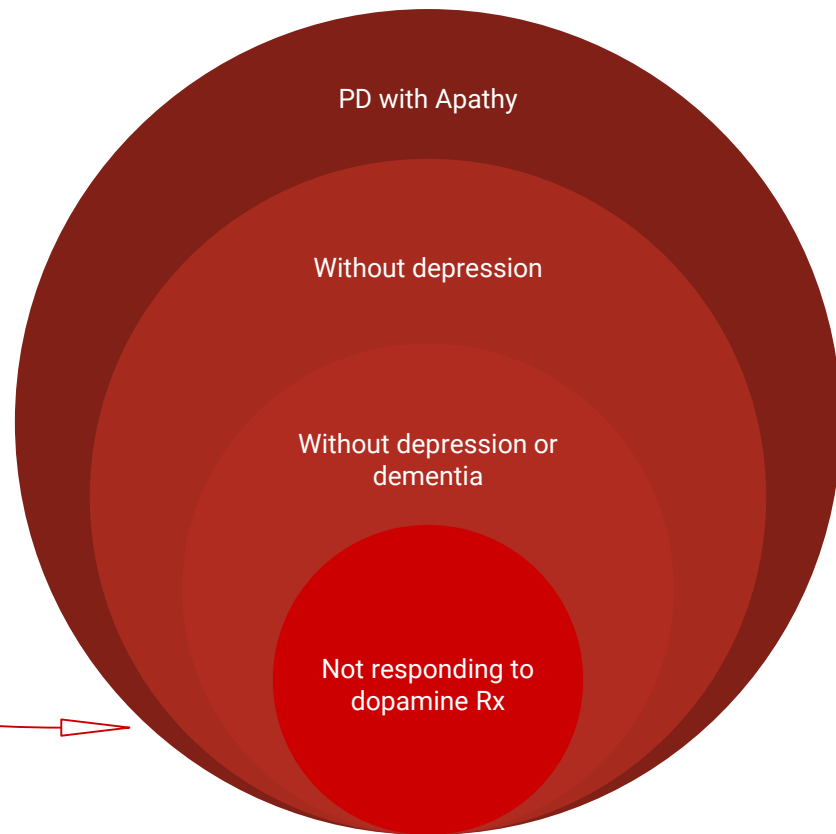
Also common when ↓ doses after deep brain stimulation

Relieved by dopamine agonist



Other brain changes in apathy

- Problems with acetylcholine in PD can relate to memory and balance problems
- Medicines used for these problems include rivastigmine, donepezil, galantamine
- Rivastigmine reduced apathy in some patients more than placebo
- May have effects on frontal lobe function



Fatigue treatments

General measures

Energy management

Anemia, blood pressure

Thyroid disease

Vitamin B12, D deficiency

Exercise

Depression



PD treatments

“Optimize” dopamine treatments

Selegiline or rasagiline

Amantadine (if appropriate)

Dopamine agonist (if appropriate)



Additional approaches

Modafinil (low quality evidence)

Methylphenidate (low quality evidence)

Complementary and alternative approaches

Qigong and Taichi may improve sleep but have not shown improvements in fatigue or quality of life

Tango and other dance therapy may improve fatigue severity

Yoga / mindfulness, music therapy, boxing may also help fatigue but evidence is lacking

Exercise usually is helpful unless anemia / cardiovascular causes are contributing

Q&A