Behavioral and cognitive changes in Parkinson disease

PARKINSON FOUNDATION
OF THE NATIONAL CAPITAL AREA

PFNCA Symposium - May 2022

Howard D. Weiss MD FAAN

adjunct **Associate Professor of Neurology**

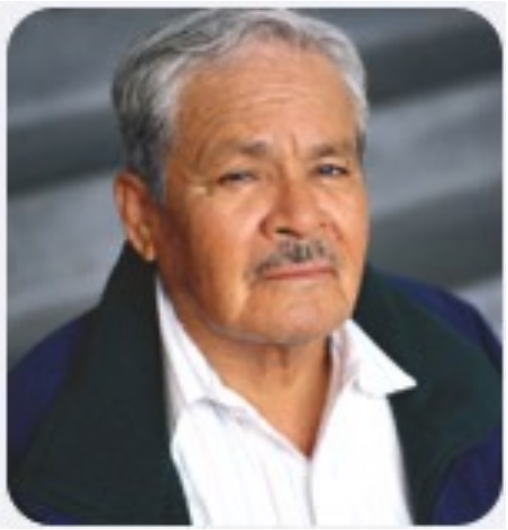
Johns Hopkins

No conflicts of interest to report

We have all heard the old saying

“if you’ve seen one, you’ve seen them all”

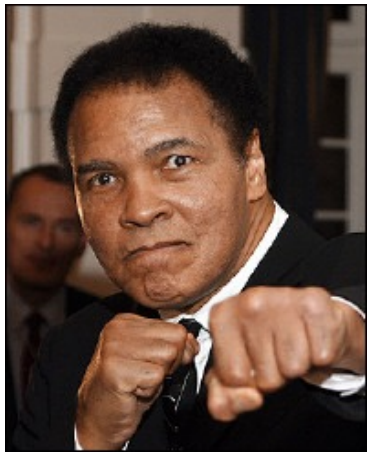
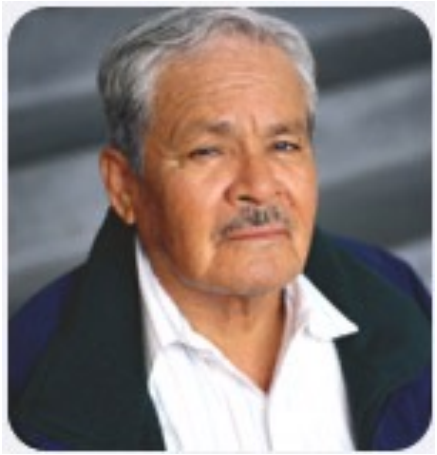
However, if you’ve seen <u>one</u>
person with Parkinson disease …

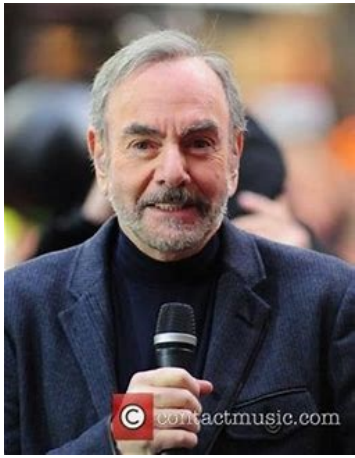


you've seen **one** person with Parkinson disease !

PD symptoms and problems vary widely,

and no two persons are exactly alike.





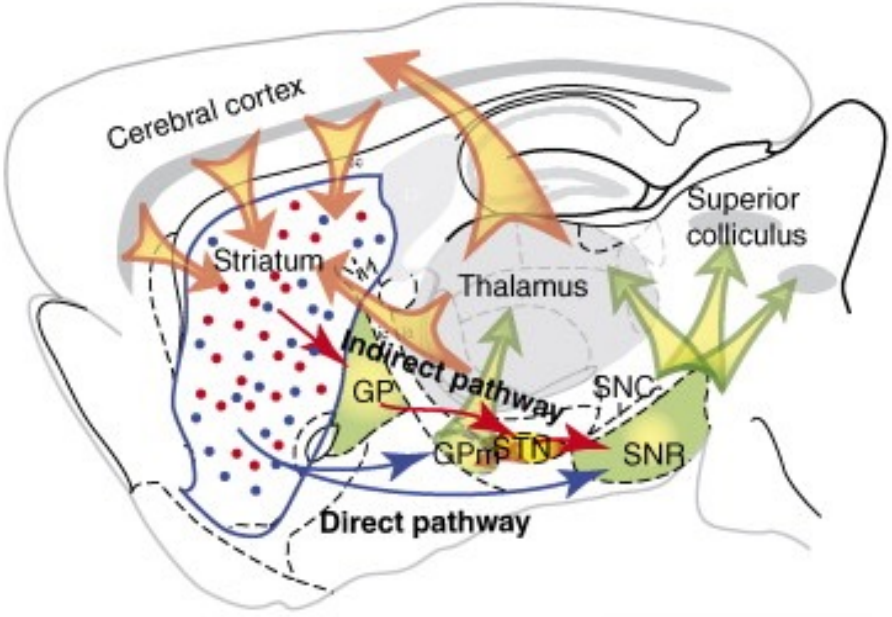
Parkinson's disease
versus
"Parkinson diseases"

there is a spectrum of potential

- **"motor symptoms"** and
- **"non-motor symptoms**

that is quite variable from case to case

Parkinson disease affects networks that facilitate brain function

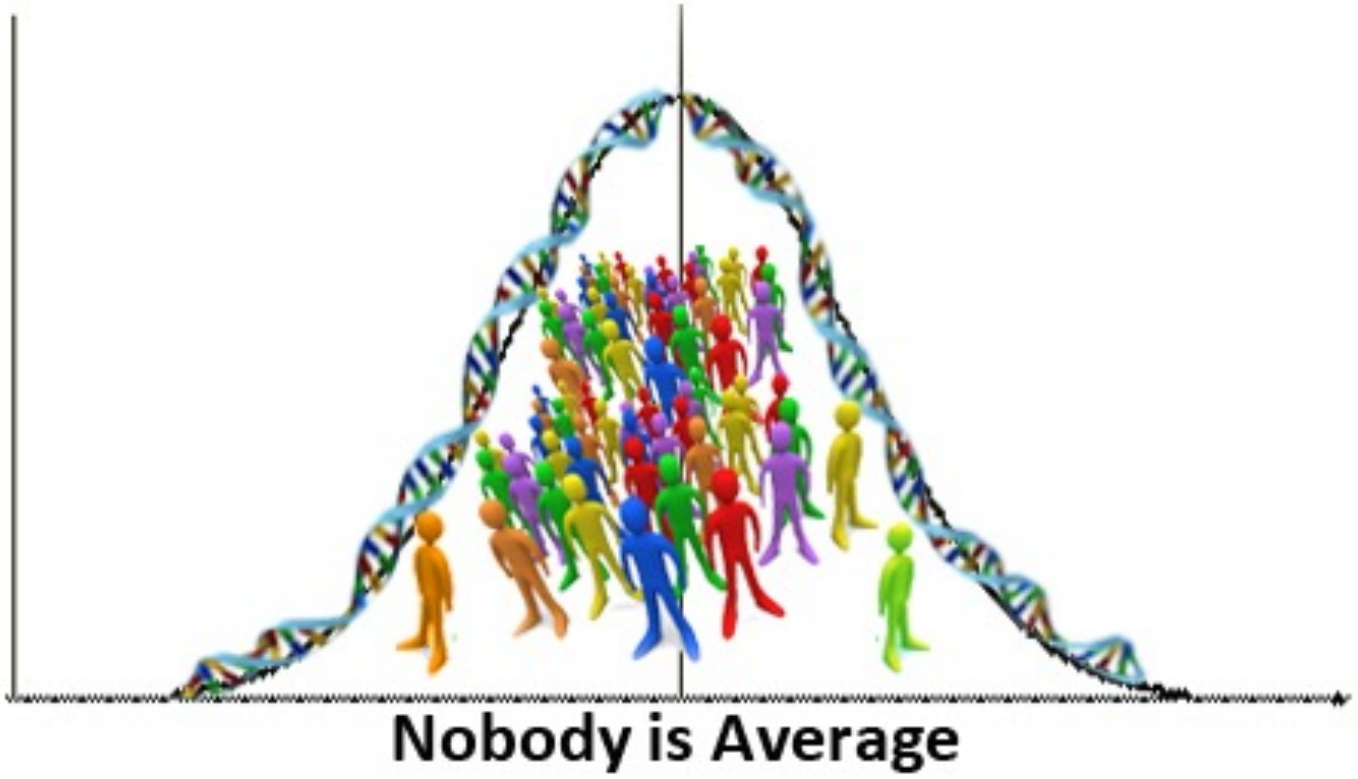


Loss of dopamine in PD is a major factor (but not the only factor) **altering the brain networks that facilitate movement.**

Networks that affect behavior and cognitive processing can also be involved in PD.

Every person is unique!

Information at the population level does not necessarily apply to the individual patient.



Case # 1

Mrs. Smith brings Jack to the office:

"he's not the same"

"he's very quiet and doesn't say much"

"he doesn't get anything started or finished"

"no motivation"

"he doesn't seem to be concerned"

"he shows no interest or enthusiasm"

"if left alone he does nothing"

"he's become a couch potato, just watching TV all day"

Jack says

“I’m all right”

Mrs. Smith says

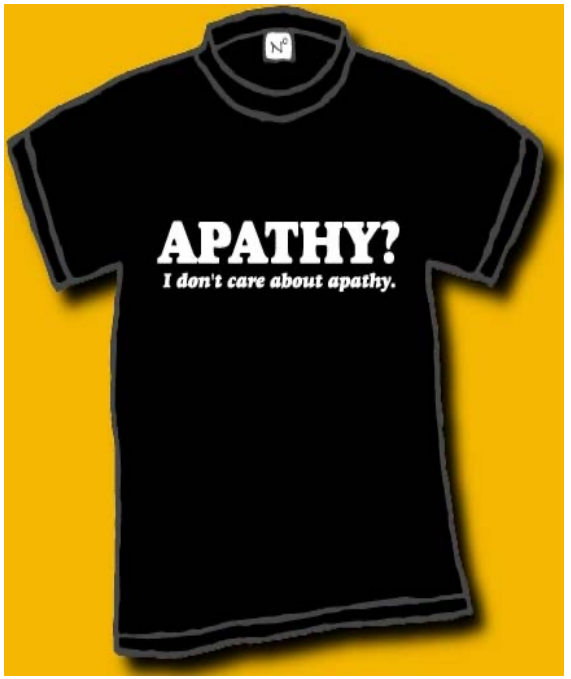
“Jack must be depressed”

Does she know “Jack”?

Is she a good diagnostician ?

Clinical manifestations of ***apathy***:

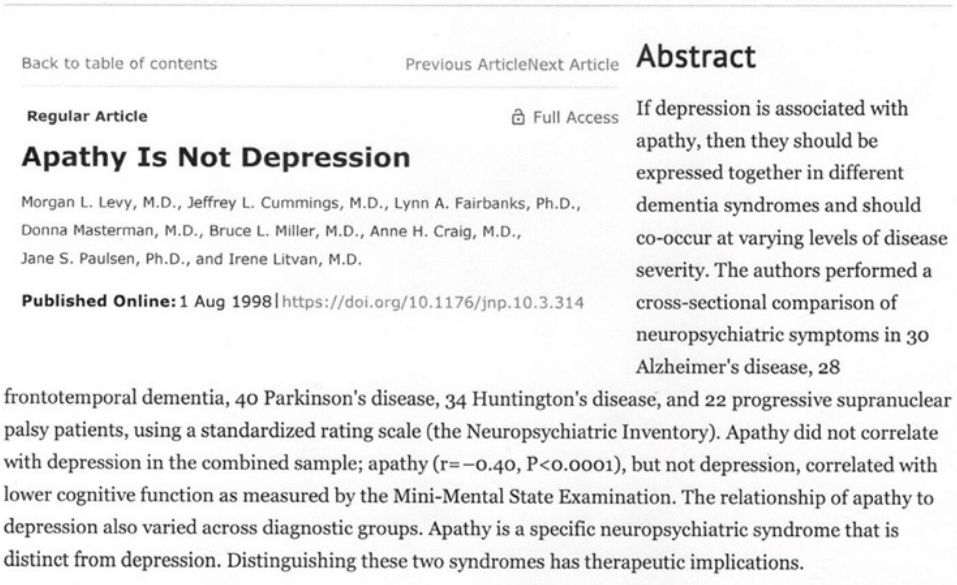
- Reduced interest
- Reduced participation
- Problems initiating activities
- Problems completing activities
- Slowed thought processes
- Lack of motivation
- Lack of ideas or conversation
- Loss of curiosity
- Lack of concern / indifference
- Lack of pleasure
- Flat affect



Loss of motivation and **lack of concern** are core symptoms of **APATHY:**

APATHY
can be a symptom in some persons with
DEPRESSION
but can occur as a problem for some persons who are **not** depressed.

Apathy and depression can occur together



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Apathy Is Not Depression

Morgan L. Levy, M.D., Jeffrey L. Cummings, M.D., Lynn A. Fairbanks, Ph.D., Donna Masterman, M.D., Bruce L. Miller, M.D., Anne H. Craig, M.D., Jane S. Paulsen, Ph.D., and Irene Litvan, M.D.

Published Online: 1 Aug 1998 | https://doi.org/10.1176/jnp.10.3.314

Abstract

If depression is associated with apathy, then they should be expressed together in different dementia syndromes and should co-occur at varying levels of disease severity. The authors performed a cross-sectional comparison of neuropsychiatric symptoms in 30 Alzheimer's disease, 28 frontotemporal dementia, 40 Parkinson's disease, 34 Huntington's disease, and 22 progressive supranuclear palsy patients, using a standardized rating scale (the Neuropsychiatric Inventory). Apathy did not correlate with depression in the combined sample; apathy ($r=-0.40$, $P<0.0001$), but not depression, correlated with lower cognitive function as measured by the Mini-Mental State Examination. The relationship of apathy to depression also varied across diagnostic groups. Apathy is a specific neuropsychiatric syndrome that is distinct from depression. Distinguishing these two syndromes has therapeutic implications.

However:

- **Everyone who is depressed is not necessarily apathetic**
- **Everyone who is apathetic is not necessarily depressed**

What are the symptoms of depression ?

- Persistent sadness
- Lack of interests
- Lack of enjoyment
- Pessimism
- Hopelessness
- Negative ruminations
- Negative view of self
- Guilt
- Morbid thoughts
- Inability to cope
- Overwhelmed / anxious
- Irritability

Anhedonia in Parkinson disease

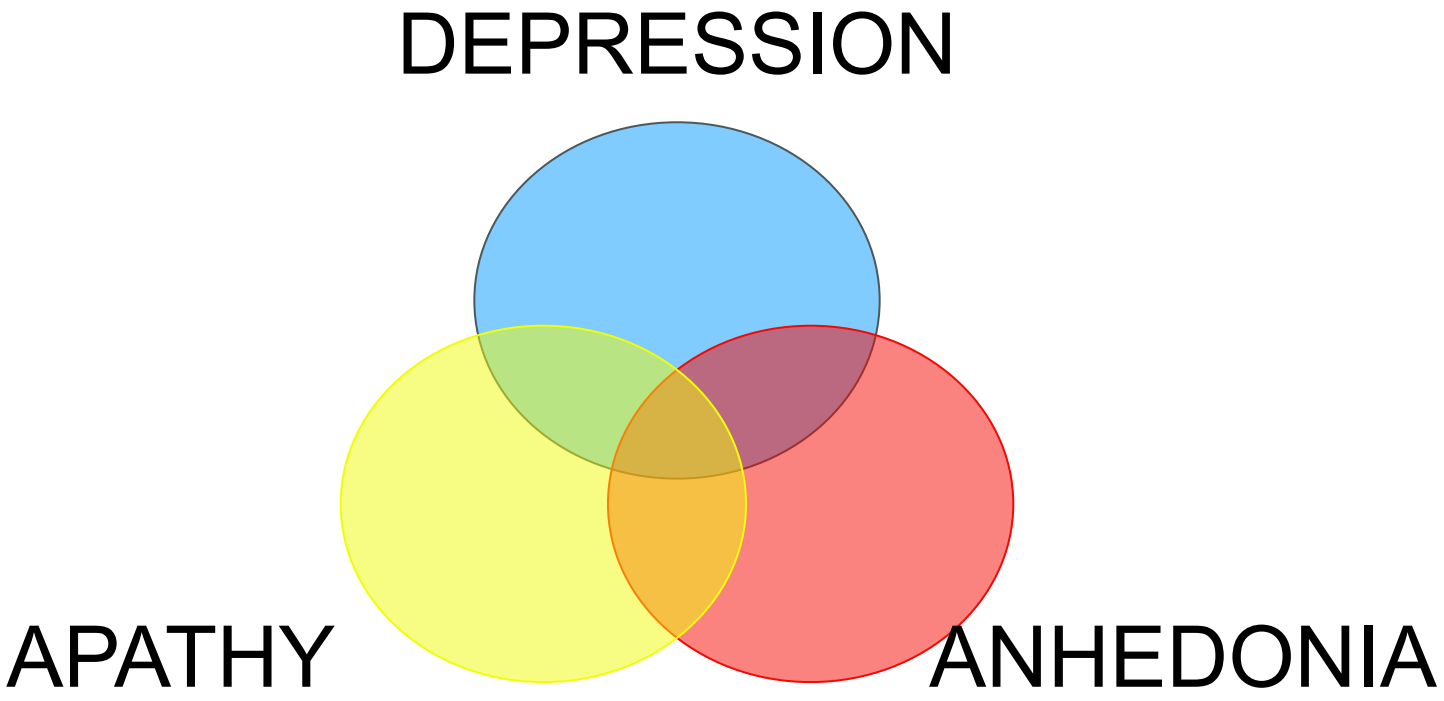
Anhedonia: inability to experience pleasure from activities previously found to be enjoyable

Many depressed persons have anhedonia,

but

persons with anhedonia are not all depressed

Depression is common in PD, but is often under-diagnosed or over-diagnosed



Distinguishing “apathy” from “depression”

Diagnosing **“depression”**
requires **emotional features**:

- **Persistent sadness**
- **Inability to cope**
- **Guilt**
- **Diminished self esteem**
- **Negativity**
- **Anxiety**
- **Morbid thoughts**

"Portrait of Patience Escallier"
by Vincent van Gough

Is it depression apathy or both?

The major criterion for diagnosis of **DEPRESSION** in a patient with profound apathy is the patient's **MOOD**:

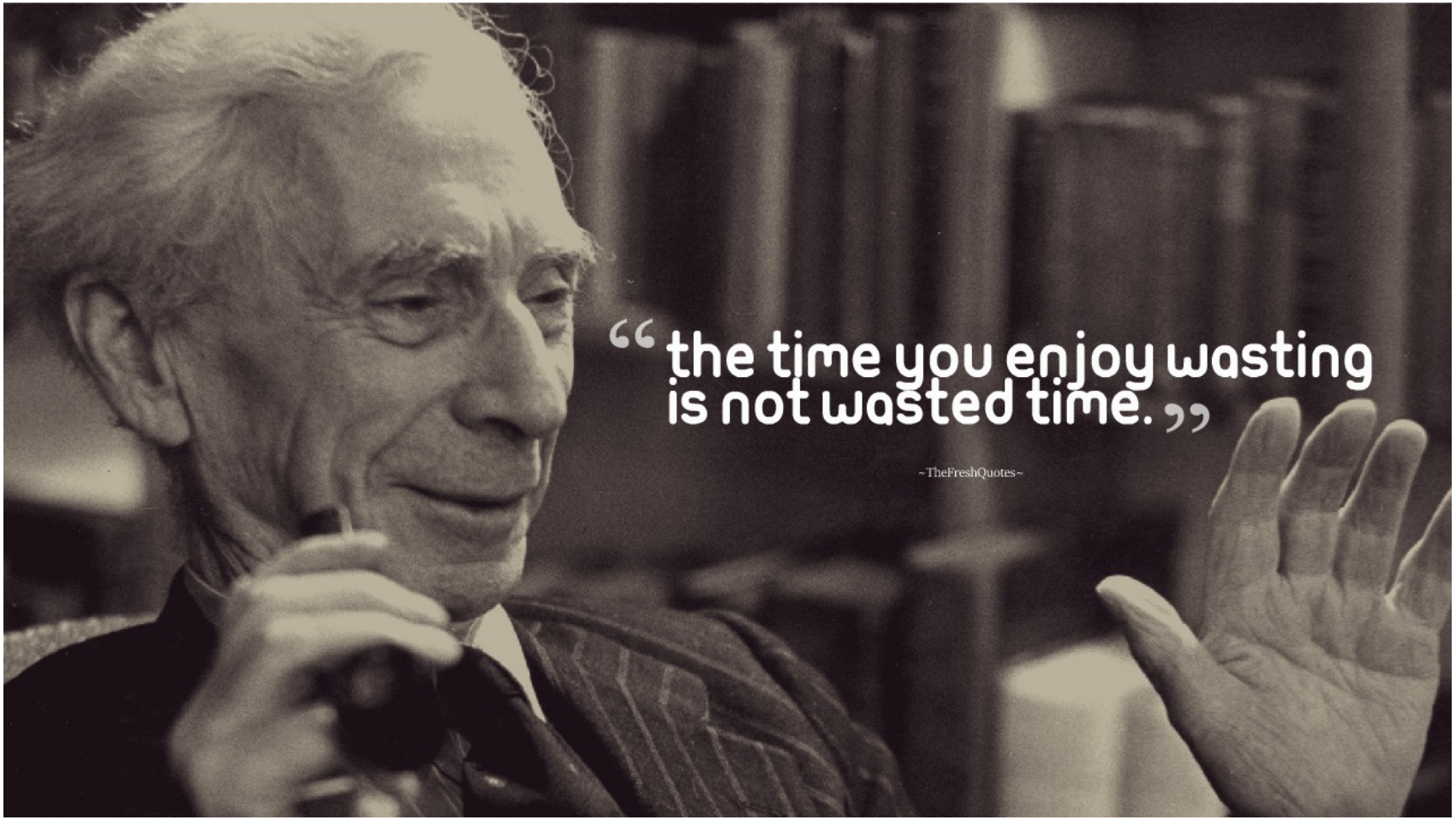
- **Depressed patient**:

  inner sadness

- **Apathetic patient**:

  emotional dullness

"Portrait of Patience Escallier" by Vincent van Gough


“the time you enjoy wasting is not wasted time.”
~TheFreshQuotes~

How do you spend your day ?

Wife: **“He watches television all day!”**

Patient: **“I don’t watch TV all day”**

“When I sit in my chair and doze off, the television watches me!”

Apathy in early untreated Parkinson disease

95 newly diagnosed persons with Parkinson disease:

- **18 were apathetic (19%)**
- **5 of these 18 were also depressed**

The apathetic patients:

- **Had more motor symptoms**
- **Lower cognitive function**
- **More fatigue**
- **More anhedonia**

than non-apathetic patients

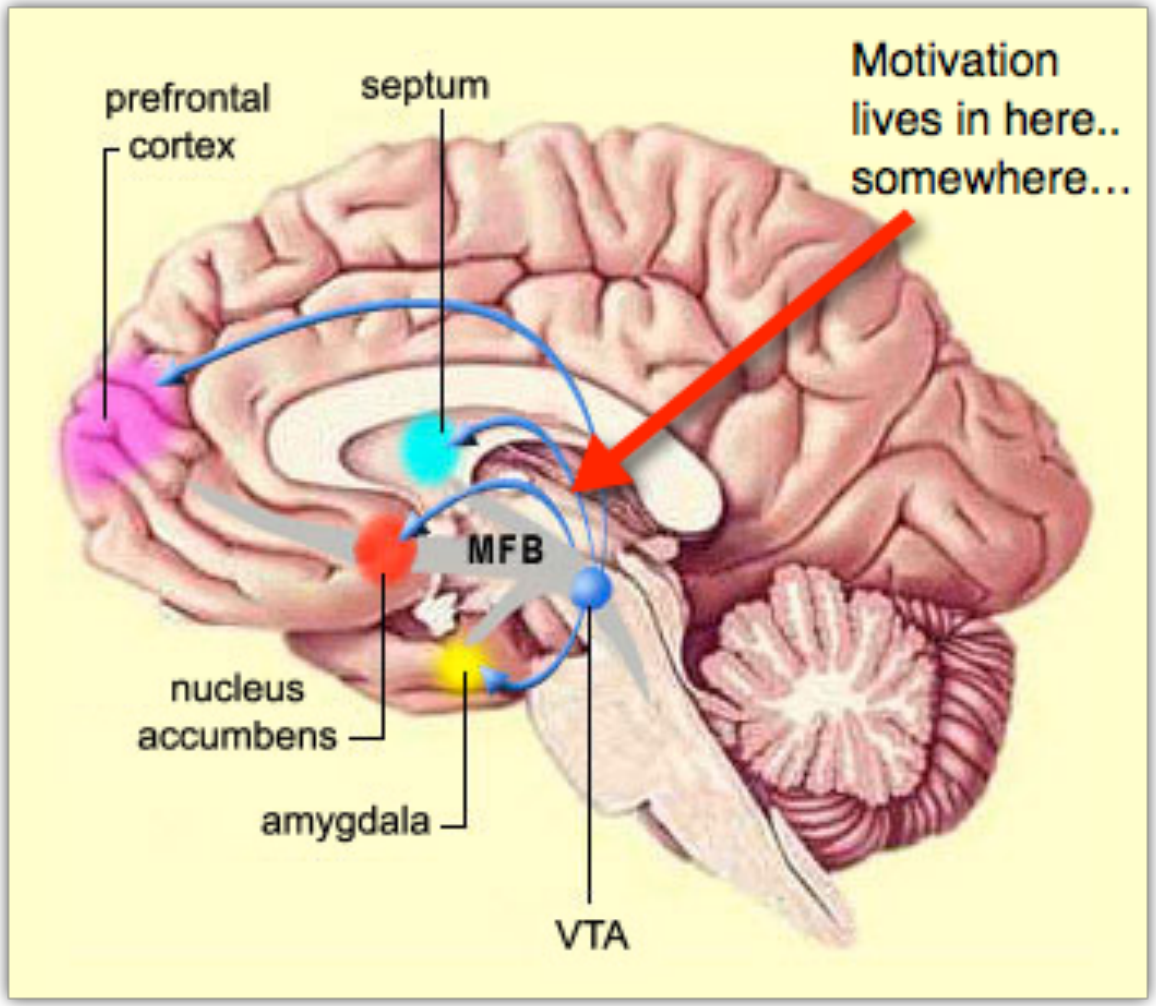
What causes “apathy” in PD ?

APATHY is caused by the parkinsonian disease process and **not** a psychological response to physical impairment or associated disability.

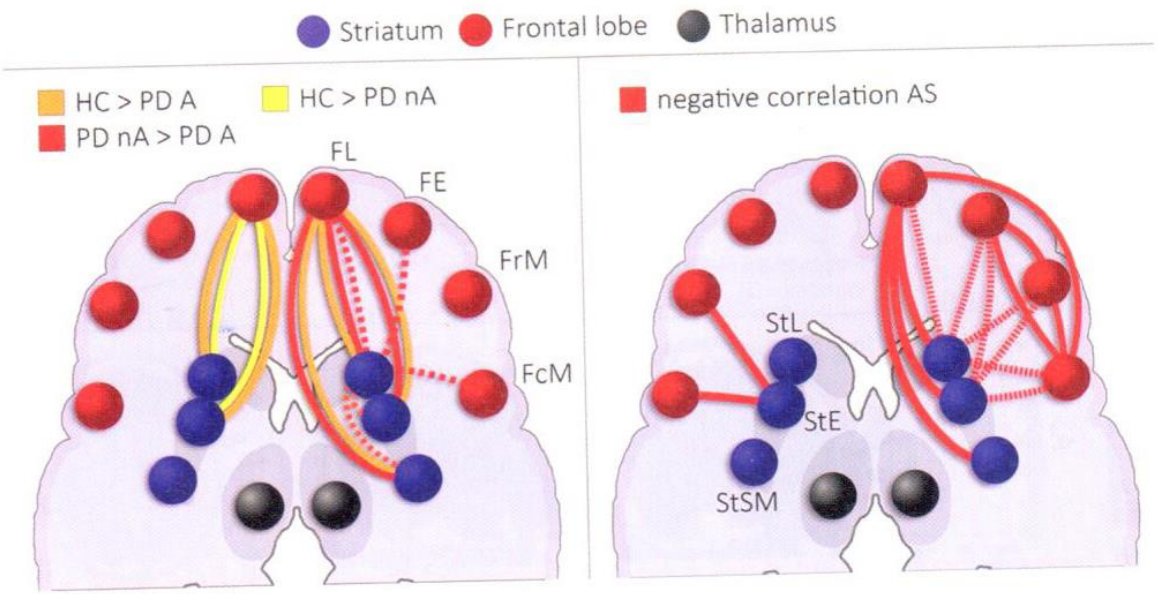
It is not *voluntary* or due to being *stubborn* or *lazy*.

JNNP 73: 636-642, 2002

Apathy: caused by impairment of fronto-striatal connectivity ?



Functional MRI studies of apathy in PD



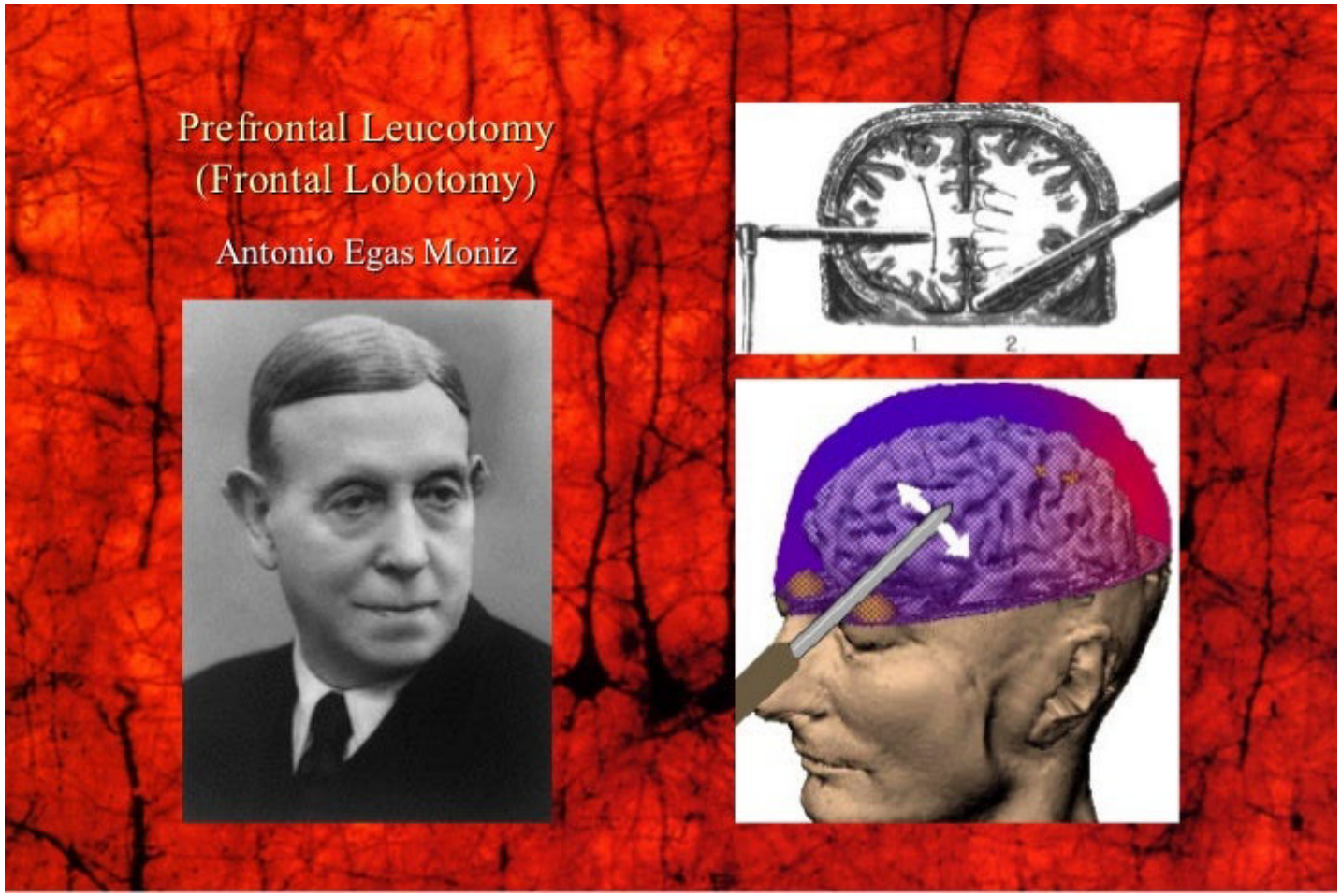
Apathetic PD patients were found to have reduced connectivity in fronto-striatal circuits compared to controls

Movt Dis 2015; 30: 671

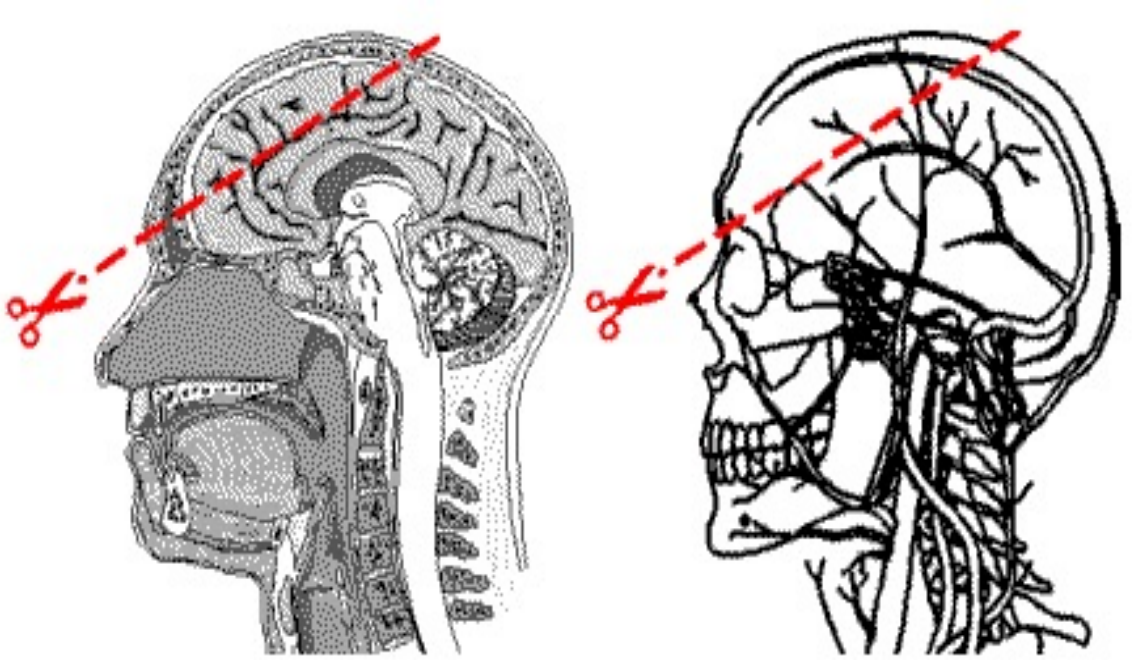
“apathy” is common in brain disorders affecting limbic-frontal-subcortical circuits

- Post-anoxic brain injury
- Frontal lobotomy
- Traumatic brain injury
- Alzheimer’s disease
- Multi-infarct states
- HIV dementia
- Parkinson disease
- “parkinson plus” syndromes (PSP, CBD, etc)
- Dementia with Lewy bodies
- Huntington’s disease
- Normal pressure hydrocephalus

Dr. Egas Moniz won the Nobel Prize in Medicine in 1949 by popularizing FRONTAL LOBOTOMY



I’d rather have a bottle in front of me



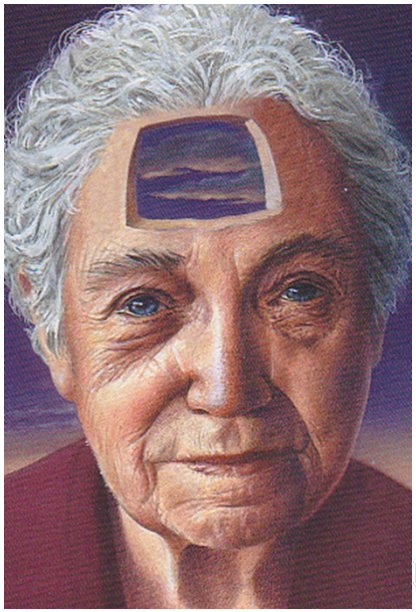
than a frontal lobotomy !

Why care about apathy ?

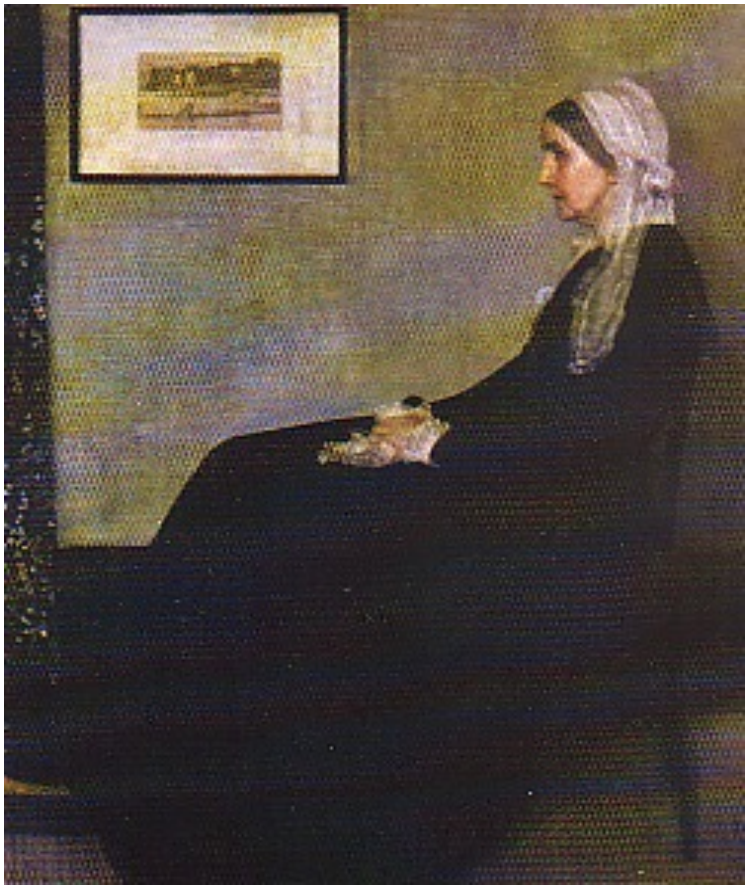
- Often **misinterpreted** or **misdiagnosed**
- Increases overall level of disability and handicap
- Reduces participation in daily activities
- Associated with worse outcomes and recovery
- **Increases care-giver burden and distress**

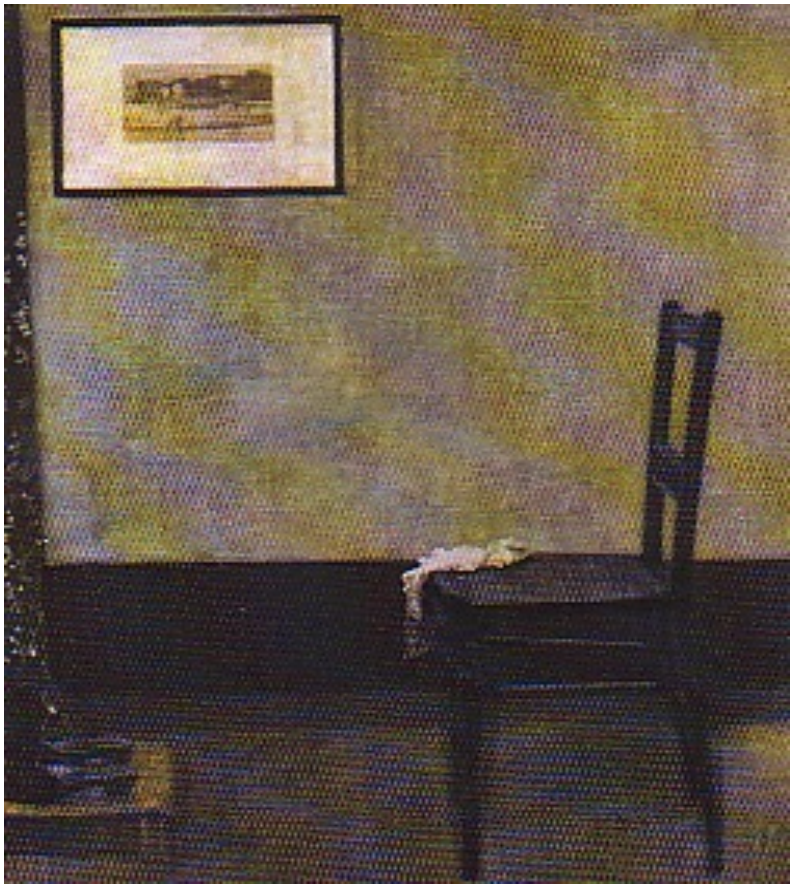
Importance of identifying apathy

- Apathy is often misinterpreted as ***willful*** or due to ***laziness*** *(*which can make the caregiver angry with the patient)
- Identifying “apathy” helps family understand and cope with the ambiguities and frustrations that arise from seeing previously competent active individuals fail to accomplish anything



Treatment of APATHY





Apathy

Apathy denotes a lack of concern and lack of emotional distress:

It would be illogical to say that the patient is *suffering* from apathy

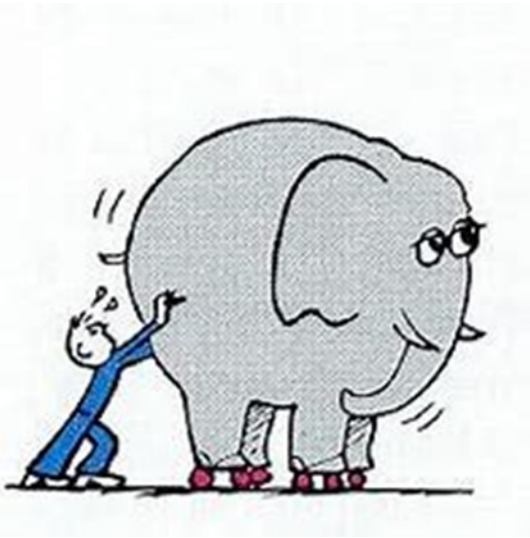
(however, the family often suffers from the patient's apathy)

Treating apathy

You can lead a horse to drink

But you can't make him water

Treating apathy in Parkinson disease



- Inertia is a powerful force: be a facilitator !
- Optimize dopaminergic treatments for PD
- Treat for depression only if also present
- Rivastigmine ?
- Methylphenidate ?

Case 2: Mr. Taylor is “seeing things”

Several years after being diagnosed with PD, Mr. Taylor began to occasionally experience a sensation that someone was standing behind him.

Three years later, after an increase in his PD meds, he would occasionally “see” a small animal in the bedroom at night, but realized nothing was there. He did not mention this to anyone.

However, the following year he often saw “small people” in his bedroom: “they looked so real”, but was aware that no-one was there. This began to frighten him, and Mr. Taylor told his wife who promptly called his physician.

Many of you have seen that frightening and misleading advertisement on television about hallucinations in Parkinson disease

What is the real story?

Definitions

Illusions-

misperception of actual stimuli

Hallucinations-

false sensory perceptions in the absence of external stimuli

Delusions –

false idiosyncratic beliefs

Minor hallucinatory phenomena in PD

“sense of presence”:

the feeling that someone is present when nobody is actually there

“passage hallucination”:

fleeting, vague imaging in the periphery of vision

“illusions”

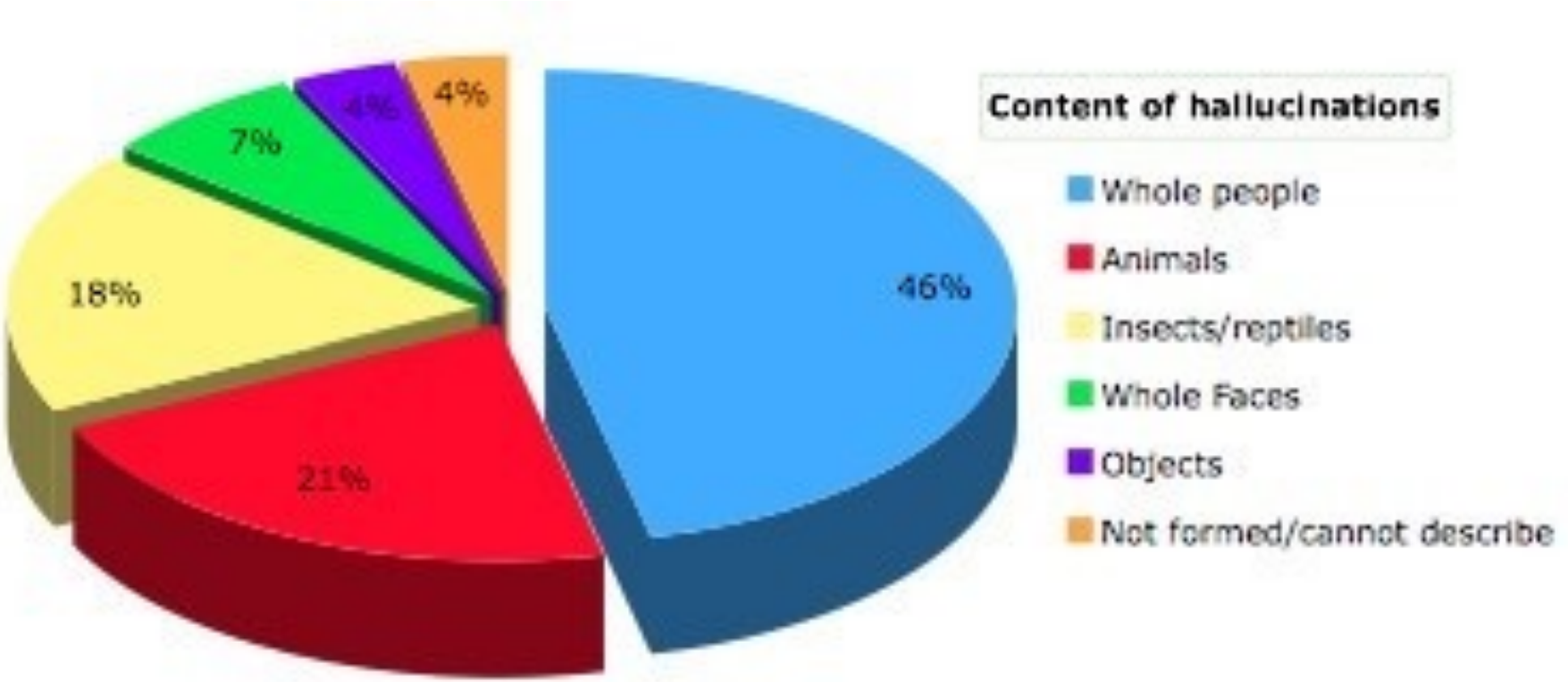
Formed hallucinations in PD

(visual hallucinations are much more common than auditory)

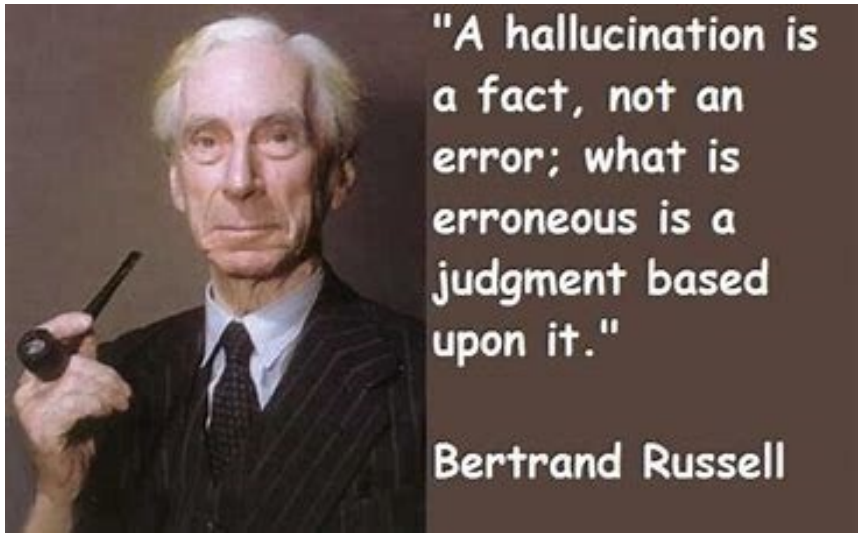
Mild / moderate: person retains awareness than the phenomenon is unreal

- I often “see” my late mother, but I know it is unreal
- The little children I occasionally “see” are cute, but I know they are not there

Content of formed hallucinations in PD



Severe hallucinations and psychosis in PD:



In severe cases the person is convinced that the hallucinations are "real" and acts accordingly:

- The person "sees" an intruder and calls the police
- The person becomes angry and argues when spouse does not "see" the animals in their house

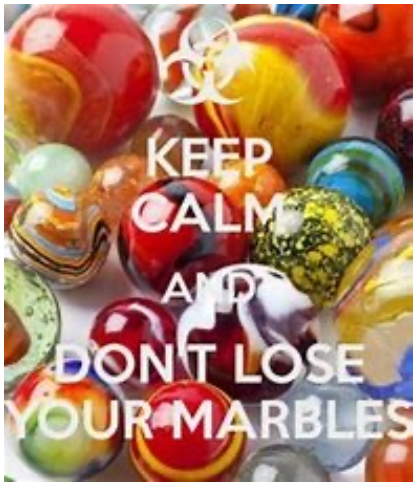
This is often accompanied by delusions. (full blown "psychosis")

Hallucinations in Parkinson disease

Prevalence of hallucinations varies in relation to duration of Parkinson disease

- **< 5 years: 9%**
- **5-10 years: 18%**
- **> 10 years: 38%**

Hallucinations in Parkinson disease



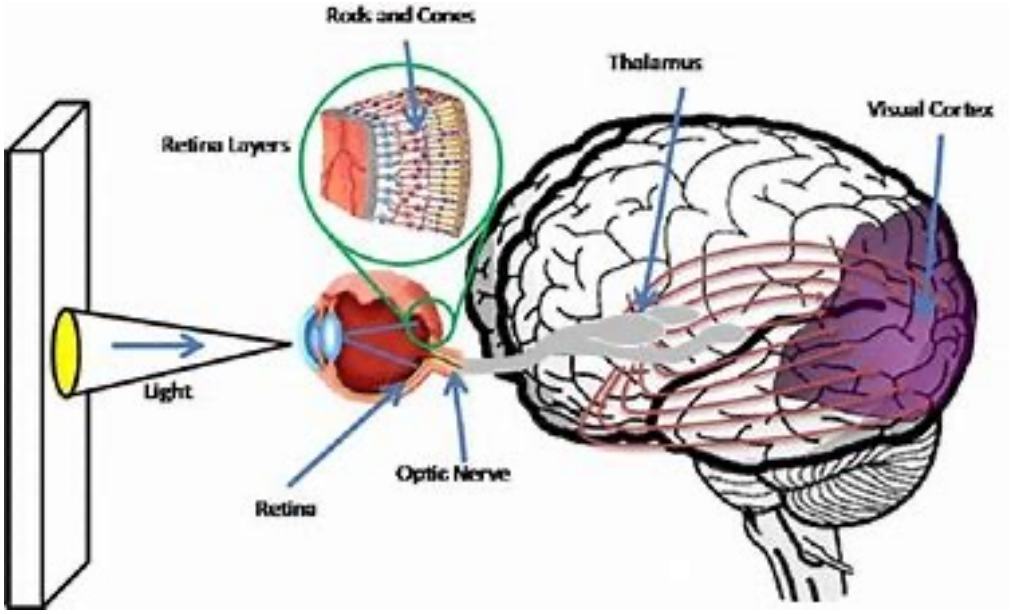
Visual hallucinations are noted in:

- **10% of patients with no cognitive decline**
- **50% with mild cognitive decline**

  (these are more likely “minor” or mild hallucinations)
- **>70% of patients with dementia**

  (these are more likely to be “major” hallucinations)

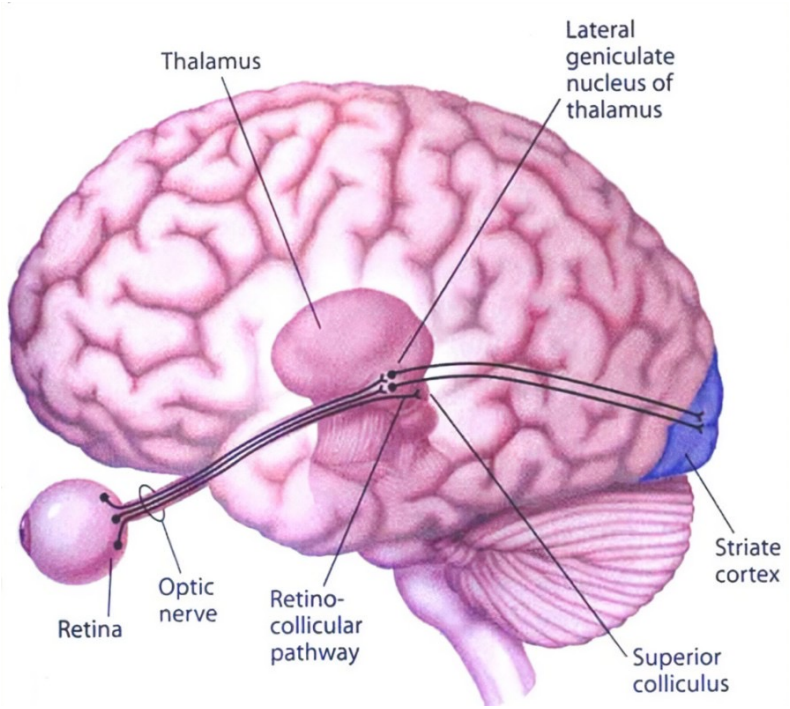
Impaired visual processing in PD



Compared to age matched controls, persons with Parkinson disease might have

- **Deficits of spatial and motion detection**
- **Impairments in visual attention**
- **Diminished speed of visual processing**

The role of dopamine in visual processing



- Neurons producing dopamine play a critical role in processing information in pathways that maintain visual attention
- Dopamine modifies behavior to visual cues

Hallucinations in Parkinson disease

Predisposing factors:

- Altered central visual processing
- Dysregulation of sleep-wake cycle
- Dream imagery intrusion into wakefulness (and REM sleep behavioral disorder)
- Influence of dopaminergic drugs
- Cognitive decline

Medications used to treat PD might cause or exacerbate hallucinations !

Likelihood of causing hallucinations:

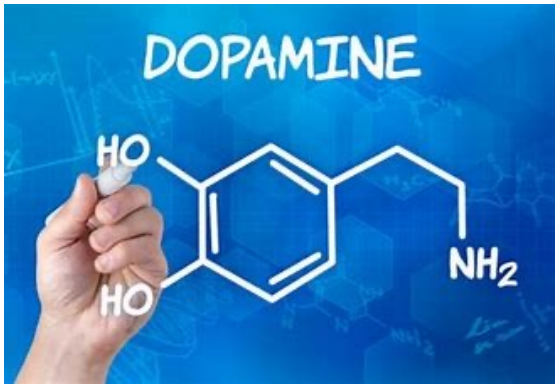
dopamine agonists > amantadine > levodopa

Adjusting medications will often reduce or eliminate hallucinations.

Reduce or eliminate dopamine agonists and amantadine

Downward titration of carbidopa/levodopa dosing

Is dopaminergic therapy usually the cause of hallucinations in PD ?



Not necessarily:

- Hallucinations can occur in untreated patients
- Non-dopaminergic drugs can also trigger hallucinations in PD
- Patients receiving dopaminergic therapy for other reasons seldom develop hallucinations
- Many other causes of hallucinations / delirium

Avoid over-medication !

Avoid under-medication !

Hallucinations / acute confusion can be triggered by factors unrelated to PD

- **Medications**
  (e.g. narcotics, anticholinergics)
- **Infections** with or without fever:
  (e.g. pneumonia, urinary tract, wounds, sepsis, flu, covid-19)
- **Sleep deprivation**
- **Metabolic abnormalities**
  (e.g. dehydration, liver, renal, thyroid, electrolytes, blood sugar)
- **Other:** stroke, head trauma, tumors, etc.

What can you do if severe hallucinations and psychosis persist ?

“antipsychotic medications”

(quetiapine, clozapine, pimavanserin)

can be very helpful but must be used with caution

Case #3: Mr. Charles worries about his memory

"My memory isn't like it used to be".

"Sometimes I have trouble recalling names or finding words".

"It is difficult for me to participate in conversations with friends".

"I am an excellent driver, but my wife complains that I don't always stay in my lane, and she doesn't like to let me drive any more".

Common symptoms in older persons who are healthy and competent:

- Occasional difficulty recalling a name or finding a word
- Working at a slower pace
- Difficulty multi-tasking or making plans

"cognitive efficiency declines with age"

Definitions: mild cognitive impairment

MILD COGNITIVE IMPAIRMENT refers to acquired cognitive problems that are mild and do not substantially interfere with daily routines.

(the person with MCI is competent)

Definitions: dementia

Dementia is not a specific disease.

"Dementia" is the term used to describe an acquired loss of cognitive function that impairs the person's ability to function independently (usually accompanied by impairment of judgement and insight).

Mild cognitive impairment is common in persons with Parkinson disease

Neurol 2017, 88: 767-774

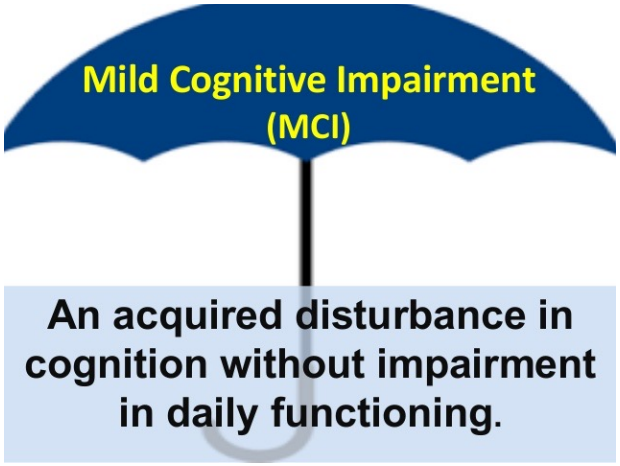
A prospective 5 year study of 178 newly diagnosed persons with PD revealed:

- **142 (80%) had normal cognitive function**
- **36 (20%) had MCI at baseline**

Among the 142 with normal cognition at baseline

- **10% had PD-MCI at 1 year**
- **29% had PD-MCI after 5 years follow-up**

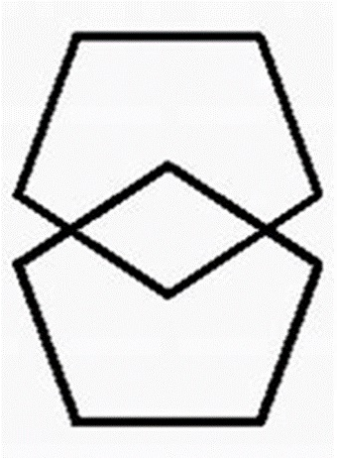
Subtypes of "**mild cognitive impairment**" in PD



Categories of cognitive symptoms typical of MCI in persons with PD:

- **Impaired executive function** ("fronto-striatal")
- **Impaired attention** ("fronto-striatal")
- **Visuo-spatial** ("posterior cortical")
- **Amnestic**

What's wrong with Mr. Charles ?



DLB: pentagon copy

What is the prognosis in persons who have PD and MCI ?

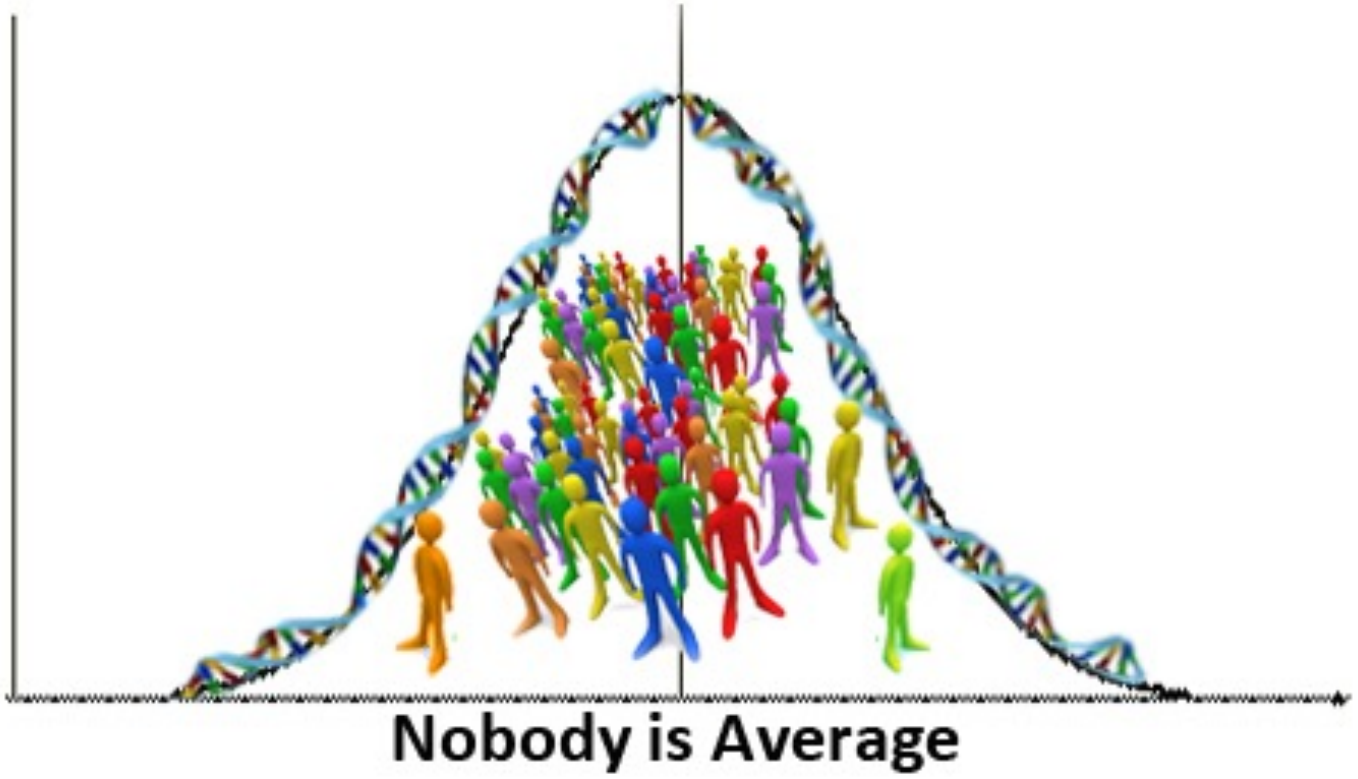
Only the television doctors know the prognosis

because they have a script.

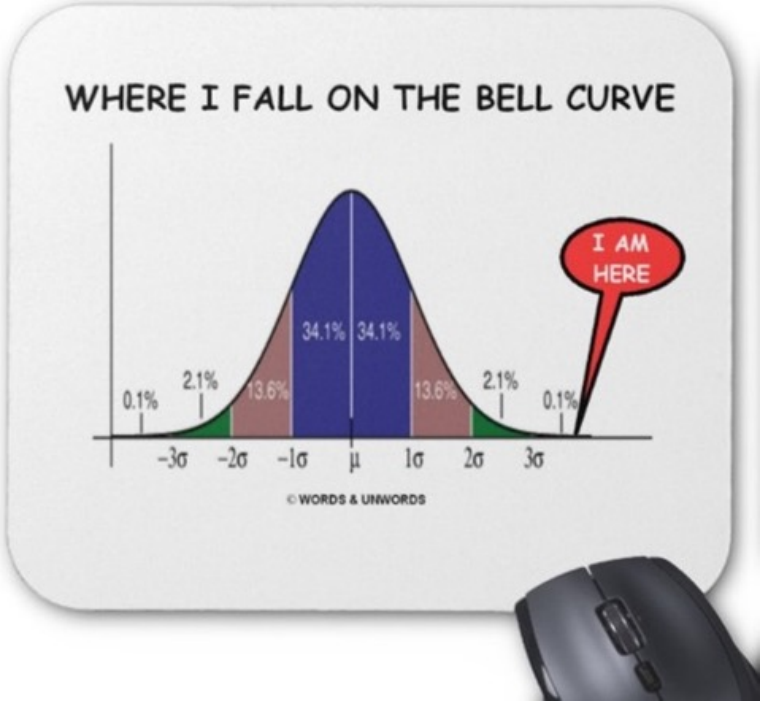
There is no definite script in life.

Every person is unique!

Information at the population level does not necessarily apply to the individual patient.



Every person's experience is different:



"Pessimists and optimists develop the same illnesses but lead very different lives!"

Natural course of mild cognitive impairment in Parkinson disease

Neurol 2017, 88: 767-774

- By 5 years, 39% of those with persistent PD-MCI at 1 year developed dementia, versus only 7% of those with normal cognition during the first year

However

- **27% of patients with baseline PD-MCI and 24% with incident PD-MCI had returned to normal cognition by the end of the 5 year study.**
- The likelihood of returning to normal fell to 9% in those with persistent PD-MCI at 2 consecutive visits

“bradyphrenia” in Parkinson disease

- PD often causes slowness of movement (this is known as “bradykinesia”)
- PD sometimes causes slowness of thought (this is known as “bradyphrenia”)

Bradyphrenia is considered to be the mental equivalent of bradykinesia.

Symptoms in persons with bradyphrenia:

- **Slowness of information processing**
- **Delays in answering or responding**
  (can be very prolonged in more severe cases)
- **Lack of spontaneity**

Bradyphrenia is very common in persons with PD dementia

However:

Many persons with bradyphrenia have normal cognitive function or only mild cognitive impairment and do **not** have dementia.

The slowness of thought makes these persons seem confused when they are not!

Impact of bradyphrenia

Persons with bradyphrenia are often

- **Excluded from conversations**
- **Reluctant to socialize or interact**
- **Ignored or disrespected**

Encourage spouses and friends:

- **Do not answer questions for the patient**
- **Allow the patient extra time to respond**

What is “Parkinson disease dementia” ?

Progressive decline in cognitive function years after developing Parkinson disease

- Psychosis and visual misperception are common
- Cognitive abilities can fluctuate considerably from day to day or week to week
- Apathy, depression, anxiety, bradyphrenia common
- Memory and language are less severely affected

What can be done to help persons with Parkinson disease dementia?

Behavioral recommendations:

- Consistent schedules
- Simple instructions
- Avoid distractions
- Continue familiar activities
- Avoid novelty
- Avoid over-stimulation
- One task at a time
- Encourage participation and socialization

What can be done to help persons with Parkinson disease dementia?

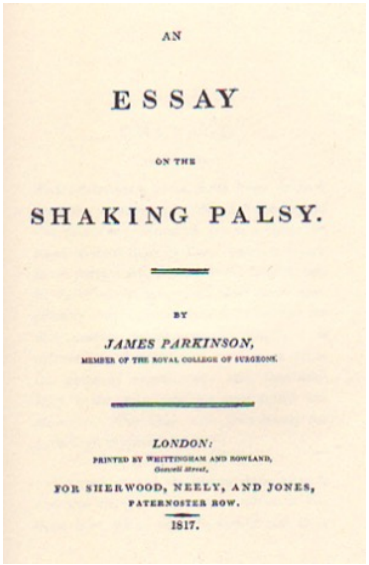
Other recommendations

- **Avoid over-medication and "polypharmacy"**
- **Rivastigmine** (oral or transdermal)
- **Anti-psychotic meds if hallucinations or delusions are troublesome**

Don't neglect the care-givers!

- **Support groups / counselling**
- **Palliative care**
- **Respite care for care-partners**

Much has been accomplished, but more work still needs to be done: In the near future we will "knock out" Parkinson Disease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ESSAY

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SHAKING PALSY.

BY

JAMES PARKINSON,

MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

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