Fatigue and Parkinson’s Disease

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www.parkinsons.va.gov/Northwest

Outline

- What is fatigue?
- How differs from sleepiness, depression
- How do doctors measure it?
- Why is fatigue such a problem in PD?
- How if fatigue in PD different?
- How will exercise and nutrition help?
- Will medications work?

What is Fatigue?

- One of most common symptoms in medicine.
- Fatigue is the desire to rest. No energy.
- Chronic fatigue: "overwhelming and sustained exhaustion and decreased capacity to physical or mental work, not relieved by rest
- Acute (days) or chronic (months, years)
- May be incapacitating
- Cannot be checked with doctor's exam
  - Not like tremor, stiffness

Fatigue: What Is It?

- Not sleepiness (cannot stay awake)
- Not depression (blue, hopeless, cranky)
- Rather is sustained exhaustion and decreased capacity for physical and mental work that is *not relieved by rest*
  - Get up tired after a night's sleep, always tired.
- Also, a subjective lack of physical and/or mental energy that interferes with *usual and desired activities*

Fatigue: A Big Problem

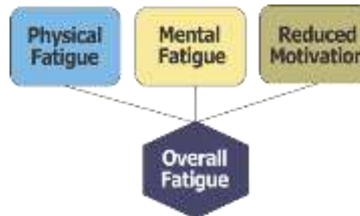
- 10 million physician office visits/year in USA.
- Usual cause for this fatigue in general doctor's office = depression.
- Different in Parkinson's disease, various other medical illnesses.

Many Illnesses and Drugs Cause Fatigue

- Medical diseases
  - Diabetes
  - Thyroid disease (too low or too high)
  - Emphysema, heart failure
  - Rheumatologic diseases
  - Cancer or radiation therapy
  - Anemia
- Drugs
  - Beta blockers, antihistamines, pain killers, alcohol
- Other neurological diseases
  - Strokes
  - Post polio syndrome
  - Narcolepsy, obstructive sleep apnea
  - Old closed head injuries
  - Multiple sclerosis

5 Dimensions of Fatigue

- General fatigue
- Physical fatigue
- Mental fatigue
- Reduced motivation
- Reduced activity

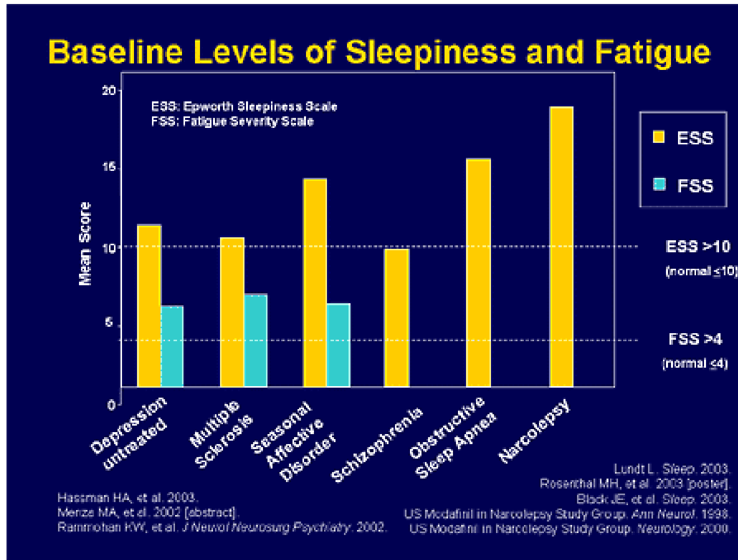


Depression correlates with all 5 dimensions.

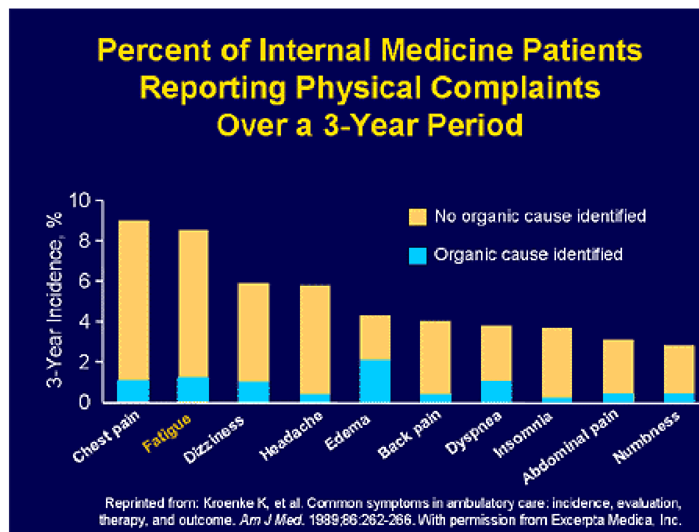
Disease severity, as measured by walking and balance measures, does not.

Source:Multidimensional Fatigue Inventory. Mov Disord. 2001 Mar;16(2):190-6.

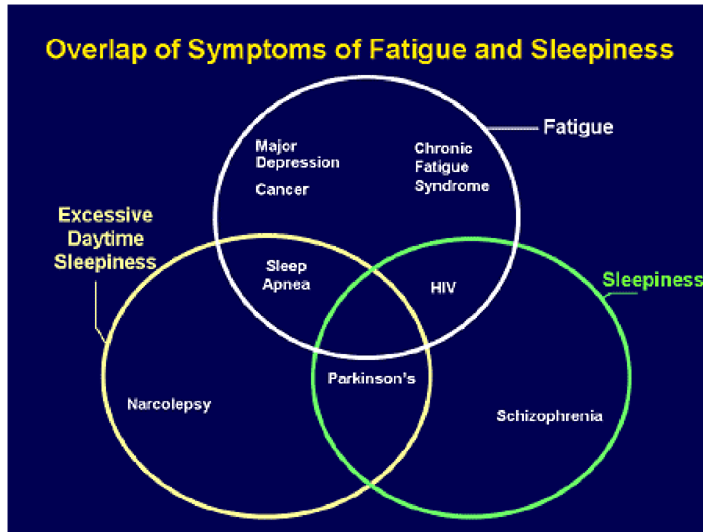
Sleepiness and Fatigue



Fatigue in General Medical Practice



Different Kinds of Fatigue



Excessive Daytime Sleepiness

- EDS = inability to stay awake, even when doing critical tasks like driving.
- Different from fatigue.
  - Overwhelming exhaustion, cannot work, even after resting
- EDS usually from medical problem, often treatable.
  - Restless legs syndrome, sleep apnea, narcolepsy

Depression

- Can cause fatigue, or make it worse
- Feel bad
  - Blue, sad, tearful
  - Hopeless
  - Worthless
- Don't enjoy your hobbies, activities
- Irritable, short-tempered
- Poor concentration
- Change in appetite, sleep, sex drive

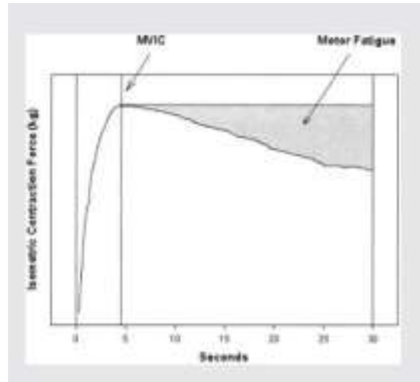
"Portrait Du Dr Gachet"
[illegible]

History of Fatigue in Medicine

- 1850 "Neurasthenia" – George Beard, American neurologist
- 1900 Most common neuropathologic diagnosis
- 1917 Soldier's Heart Syndrome
- 1927 "Industrial fatigue". Harvard Fatigue Laboratory. Psychological disorder
- 1950 "Neuromyasthenia" -- outbreaks and epidemics, public health problem
- 1960 Psychiatry abandons syndrome now sub-feature of depression.
- 1980 Fatigue remerges in immunology and infectious disease -- chronic Epstein Barr syndrome, chronic fatigue syndrome.
- 1990 Fatigue critical in cancer, lupus, hepatitis C – research active again
- 1995 Neurology, others operationalize symptoms, explore objective measures
  - EMG, EEG electrophysiologic measures for peripheral,and central components
  - SPECT, PET, tMRS tease out cortical components.

Objective Measures of Fatigue

- Measure max force generation before and after exhausting task.
- Measure ability during sub-maximal repetitive, sustained task
- Can also study cortical input during tasks.



Motor Fatigue in the Lab

- Finger tapping, hand moving tasks
- SPECT brain scans
  - Frontal lobe problems
  - Expensive, research only
- Electromyography
  - Looks OK in PD

Fatigue is Subjective

Fatigue Severity Scale (FSS)

During the past week, I have found that	Disagree ⟷ Agree						
1. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2. Exercise brings on my fatigue.	1	2	3	4	5	6	7
3. I am easily fatigued.	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is among my 3 most disabling symptoms.	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7
Total Score							
FSS mean score = total score for 9 items divided by 9. Mean Score							

FSS mean score >4 indicates severe fatigue.

Krupp LB, et al. *Arch Neurol.* 1989;46:1121-1123.
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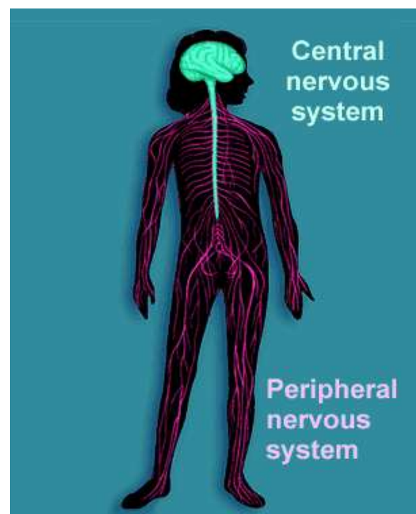
Fatigue + Nervous System

- Fatigue occurs in both
- Central fatigue
  - Multiple sclerosis
  - Parkinson's Disease
- Peripheral fatigue
  - Myasthenia gravis
  - Post polio syndrome



Non-Motor Symptoms in PD

- Cognitive problems
- Psychosis and hallucinations
- Mood disorders
- Sleep disturbances
- **Fatigue**
- Autonomic dysfunction – bladder, bowel changes, low blood pressure standing up
- Olfactory dysfunction
- Pain and sensory disturbances
- Oily scaly skin patches (seborrhea)
- Rhinorrhea

Why So Much Fatigue in PD?

- Peripheral nerves ok
  - Muscle exhaustion from constant tremor, rigidity?
  - Peripheral nerves normal with lab testing.
- Central nerves not keeping up
  - Deconditioning, disuse syndrome, contractures
  - Sensory processing deficits
    - Brain does not integrate somatosensory inputs
  - Your "forget" motor program for routine movements
    - Walking, turning around
    - Back up memory programs less efficient – like using your wrong hand to write
  - Motor processing deficits
    - Central dopamine deficiency, so less cortical drive for motor, cognitive tasks

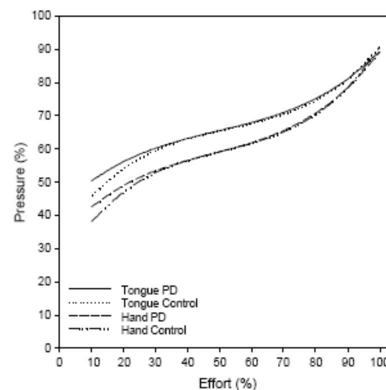
Sensory Losses Drive PD Fatigue

- Kinesthesia – sensory processing
  - Proprioception more than sense of joint position and motion
  - Also perception of force, weight, effort
- Deep brain circuit deficit → limb "heaviness"
  - Basal ganglia do not process incoming sensory data
  - Do not guide motor and premotor cortex, which in turn do not estimate force + effort of muscle work
- So you move less but feel are working harder
  - Knowledge of motor commands decays
  - Smaller corrective movements when balance lost
  - Rigidity arises in part from this central sensory processing deficit.

Perceptions of effort during handgrip and tongue elevation in Parkinson's disease

Nancy Pearl Solomon[a,*], Donald A. Robin[b]

- Normal speech produced at 10-25% of maximum
- In PD, cannot gauge these submaximal efforts
- So in PD, people thinking gripping hard or speaking loudly or raising their tongues strongly even when they are not.



How Fatigue Starts, Impacts

- May precede stiffness, tremor
- Half of fatigued PD patients say fatigue came first
- Presenting symptom in 2%
- Prevalence 40 – 50%
  - Missed often by neurologists, who identify only 14%
- Degrades quality of life in PD
  - Worst symptom in 15% - 33%
  - As bad as stiffness, slowness, tremor in 54%

PD Fatigue is different

- Does increase with disease severity but not disease duration.
- Course varies
  - Constant in 1/3, intermittent in 1/3, absent in 1/3
  - Troublesome for 3/4 of all PD at some time.
- Not associated with age or sex.
- Physical and mental components distinct, may not occur together. Mental component common even in non-depressed.
  - Distinct from depression, though may accompany it
- Impairs balance, walking safety.
- Lowers quality of life.
- May not correlate with "on" state.

Fatigue Features in PD

- Not the usual "ups and downs"
- Can come on suddenly and sometimes never stop
- Feel too tired to do normal activities
- Feel easily exhausted with no apparent reason
- Feel no better after a good night sleep
- May come on after a cold, or high stress

Parkinson Fatigue Scale (Brown 2005)

- I have to rest during the day.
- My life is restricted by fatigue.
- I get tired more quickly than other people I know.
- Fatigue is one of my three worst symptoms.
- I feel completely exhausted.
- Fatigue makes me reluctant to socialize.
- Because of fatigue it takes longer to get things done.
- I have a feeling of heaviness.
- If I wasn't so tired I could do more things.
- Everything I do is an effort.
- I lack energy for much of the time.
- I feel totally drained.
- Fatigue makes it difficult to cope with everyday activities.
- I feel tired even when I haven't done anything.
- Because of fatigue I do less in my day than I would like.
- I get so tired I want to lie down wherever I am.

Mental Fatigue in PD

- Prevalence: 35% - 55%
- More common if also depressed, but 1/3 have when not depressed
- For half, fatigue will come and go
- For other half, will persist
- Increases as motor problems increase

What Predicts PD Physical Fatigue?

- The less you do, the less you can do
  - Get Up and Go Test
  - Six-Minute Walk
  - Maximal oxygen uptake exercise test
- Will be more fatigued if do
  - Less leisure physical activity
  - Less vigorous physical activity
  - Less daily tasks

Fatigue Prescription

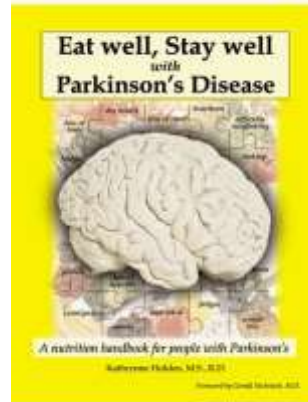
- Determine if you have fatigue, drowsiness, or depression (or some combination)
- Discuss concerns with neurologist and primary provider.
- Follow sensible lifestyle ideas
  - Exercise
  - Nutrition
  - Sleep
- Keep active mentally to avoid boredom

Does Exercise Help PD Fatigue?

- Anecodotal evidence: persons w PD who exercise fare better
  - Patients improve functional overall w/o any change in PD meds
- Biology of improvements unclear
  - Brain cells handle stress better, less cell death?
  - Better production of proteins that nurture cells brain – CNS trophic factors?
- What kind of exercise is best?
  - Flexibility (Tai chi, pilates, yoga)
  - Strength, balance
  - Aerobic exercises (water aerobics, stationary bike, walking)
    - Normals report fatigue 15 – 20 min, PD report 5 – 10 min
- Exercise: hard to find motivation if tired all the time
  - Start exercise early in disease course
  - Join support group that will exercise together

Eat Right, Exercise Right

- Eat a balanced diet and get adequate rest
  - Kathyryn Holden MS RD book
  - www.nutritionucanlivewith.com/ eatwell.htm
- Exercise regularly but lightly
  - Light exercise, stretching
  - Yoga, Tai Chi, aqua aerobics
  - Don't overdo
- Pace yourself-physically, emotionally intellectually
  - too much stress can aggravate fatigue



Get Help from Your Providers

- Ask primary provider about general medical causes of fatigue
- Keep diary, see if your PD meds improve your fatigue
- Ask PD provide about PD meds, and special meds for fatigue
- See Physical therapist for exercise guides
- See Occupational Therapist for energy conservation ideas

Medications for Fatigue

- Pharmacologic approach
  - Stimulants
  - Wake promoting medicines
  - Anti-parkinson's medicines
  - Anti-depressants
  - Hormones

Medications for PD Fatigue

- **Sinemet**
  - Will relieve motor fatigue if "off" time problem.
- **Dopamine Agonists**
  - Pramipexole and Rotigotine associated with *increased* fatigue vs. placebo.
- **Fluoxetine** and **Bupropion** may help
  - Antidepressants with activating properties
  - No controlled data
- **Amantadine**
  - Limited controlled data in multiple sclerosis: modest benefit
  - No controlled data for fatigue in PD
- **Testosterone injections**
  - Small studies: no benefit for either motor or cognitive in PD
- **Modafinil**
  - Not effective for excessive daytime sleepiness in PD
  - No controlled data for fatigue

Ritalin in PD

- Caution: heart disease, hyperthyroidism
  - Dosed carefully, monitored
- Methylphenidate: a dopamine transporter blocker
  - First studied in PD in 1950's
  - Important determinant of extracellular dopamine concentrations.
- Improves finger tapping speed, walking speed.
  - When combined with levodopa
  - No impact of cognition
- Improves apathy (case report only)
- Improves cognition and gait speed
  - Attention significantly improved
  - Memory and visual-spatial did not.

Herbs for Chronic Fatigue Syndrome

Variable levels of the active compound

"Natural" does not mean safe

Irrelevant, potentially harmful fillers

Only primrose oil well studied in CFS

Some herbs -- comfrey and high-dose ginseng – are harmful

- Claims made for many products
  - Astralagus
  - Borage seed oil
  - Bromelain
  - Comfrey
  - Echinacea
  - Garlic
  - Ginkgo biloba
  - Ginseng
  - Primrose oil
  - Quercetin
  - St. John's wort
  - Shiitake mushroom extract

No Scientific Support for These

- Antioxidant “energy” drink

- adenosine monophosphate
- coenzyme Q-10
- Germanium
- Glutathion
- Iron
- Magnesium sulfate
- Melatonin
- NADH
- Selenium
- L-tryptophan,
- Vitamins B12
- Vitamin C
- Zinc

PD Caregiving Can Also Be Fatiguing

- English postal survey -- 123 caregivers of patients with PD , mostly women.
- Substantial burden
  - 40% health had suffered or were depressed
  - Most feel social life worse
- Younger and older caregivers cope equally well.
- Male and female caregivers cope equally well.
- Stressors: mental health problems
  - Depression (fatigue not mentioned)
  - Hallucinations or confusion
  - Falls
  - Caregiver dissatisfaction with their marital and sexual relationship.

Take Home Points

- Fatigue is common in PD, under recognized.
- Largely driven by cortical motor and sensory processing deficits.
- Independent of depression, persistent in many, with distinct mental and physical components.
- Common risk factors
  - Depression, poor sleep, advanced disease, sedentary lifestyle
- Bring up your concerns to neurologist
  - PD Fatigue scales help document severity
- Manage medical problems that can increase fatigue too
  - Arthritis, depression, sleep apnea, heart failure, anemia, hypothyroidism.
  - Review medication list to trim if possible

More Take Home Points

- Distinguish from simple "off" time. Sinemet responsive?
- Keep active!
  - Learn exercises for balance, strength, endurance, flexibility
  - Ask for referrals to physical therapy, occupational therapy.
  - Discuss exercise, cueing strategies, sleep hygiene.
- Consider Fatigue medications
  - Trial of ritalin?
  - Switch to "activating" antidepressant?

Thank You!