



Are Your Medications Causing MS-Related Fatigue?

Pharmacologic effects and treatments for MS-related fatigue

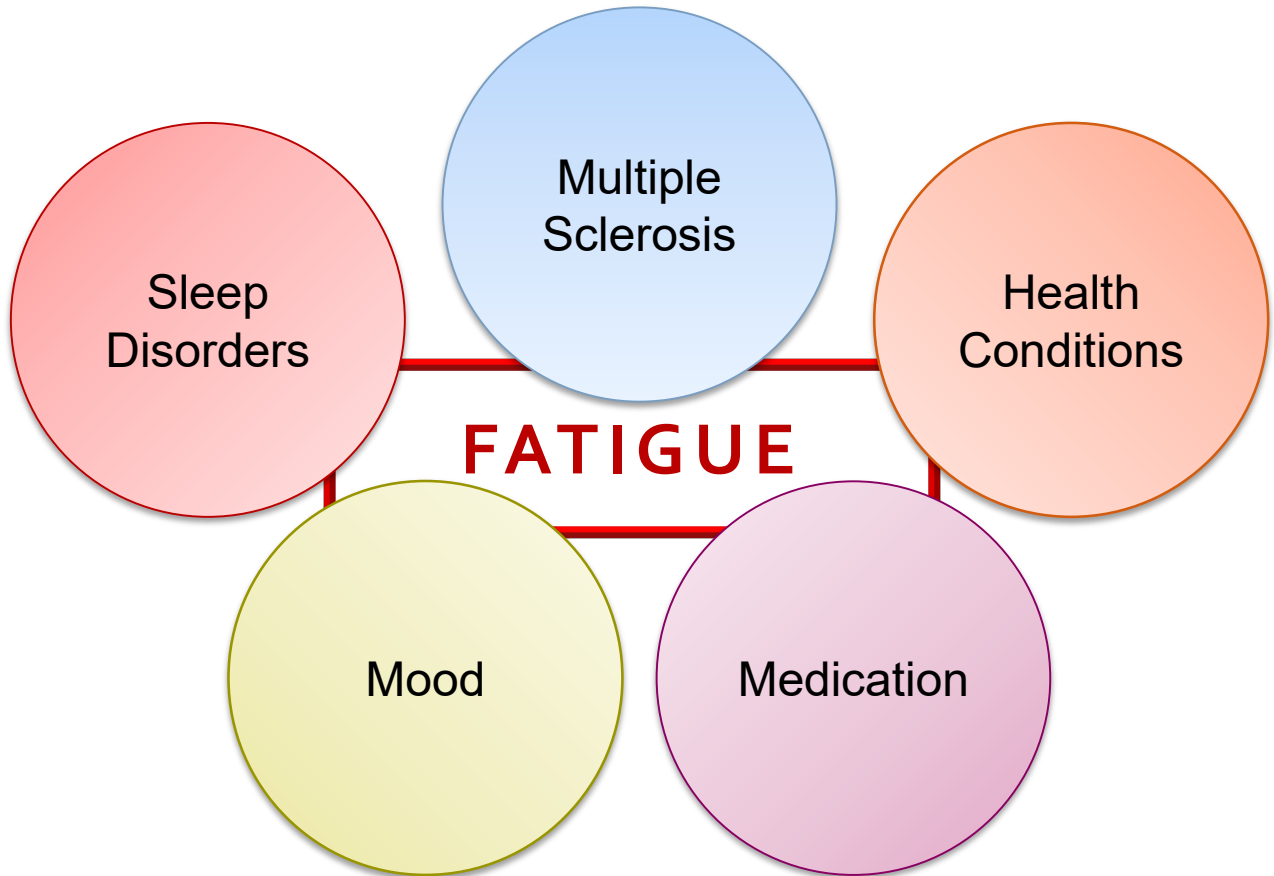
Margaret Hansen, PharmD
December 9, 2021

Multiple Sclerosis Related Fatigue

- Reported by 70-90% people with MS
- Impacts Quality of Life
- Decreased work hours
- Early Retirement
- Social Isolation



Factors Affecting Fatigue



Medications That Can Worsen Fatigue

Pain Medications	Muscle Relaxers	Benzodiazepines
Opioids	Baclofen	Alprazolam (Xanax)
Gabapentin	Tizanidine (Zanaflex)	Diazepam (Valium)
Pregabalin (Lyrica)	Cyclobenzaprine (Flexeril)	Clonazepam (Klonopin)
Amitriptyline (Elavil)	Carisoprodol (Soma)	Lorazepam (Ativan)
Nortriptyline (Pamelor)	Methocarbamol (Robaxin)	
Doxepin		

Medications That Can Worsen Fatigue

Sleep Medications	Anti-seizure Medications	Other
Zolpidem (Ambien) Eszopiclone (Lunesta) Zaleplon (Sonata) Suvorexant (Belsomra) Lemborexant (DayVigo) Mirtazapine	Carbamazepine (Tegretol) Oxcarbazepine (Trileptal) Topiramate (Topamax) Primidone / Phenobarbital Levetiracetam (Keppra)	Interferon beta (Rebif, Avonex) Oxybutynin Hydroxyzine Diphenhydramine (Benadryl) Beta blockers Quetiapine (Seroquel) Diuretics Caffeine Alcohol Marijuana

What to do if you think your medications may be making your fatigue worse?

- ✓ **Do** talk to your doctor or pharmacist about which medications could be making fatigue worse
- ✓ **Do** consider decreasing doses or trial stopping medications that may not be helping you
- ✓ **Do** use benzodiazepines and sleep medications minimally and for the shortest durations
- ✓ **Do** continue to take your MS disease modifying medications
- ✗ **Do not** stop taking your medications without talking to your doctor first
- ✗ **Do not** be afraid to take the medications on this list

Medications to Treat MS-Related Fatigue

- No FDA-approved medications for MS-related fatigue
- Central Nervous System Stimulants
 - Amantadine
 - Modafinil (Provigil)
 - Methylphenidate (Concerta, Ritalin)
 - Dextroamphetamine / Amphetamine (Adderall)



Amantadine

- Dose: 100mg twice a day
- Side effects: dizziness, low blood pressure, insomnia, dry mouth, constipation, swelling in legs, hands, or feet
- Monitoring:
 - Kidney function
- Avoid in:
 - Pregnancy or breast feeding (limited data)
- Tips:
 - Morning and midday dosing
 - Effects seen in 2-4 weeks

Modafinil (Provigil)

- Dose: starting 100mg once a day; increase to 200mg daily
- Side effects: headache, insomnia
- Warnings: rare severe skin reactions
- Avoid in:
 - Pregnancy or breast feeding (limited data)
 - Some heart conditions
- Drug Interactions:
 - Hormonal birth control (pills, shot, implant, ring)
- Tips:
 - Once or twice a day dosing (morning and midday)
 - Effects seen in 2-4 weeks
 - Class IV controlled substance

Methylphenidate (Concerta, Ritalin) & Dextroamphetamine / Amphetamine (Adderall)

- Dose:
 - Methylphenidate IR 5mg once or twice daily; maximum 40mg/day
 - Amphetamine salts IR 5-10mg per day; maximum 40mg/day
- Side effects: headache, decreased appetite, insomnia, dry mouth
- Avoid with:
 - Some heart conditions, severe high blood pressure
 - Some psychiatric disorders
- Tips:
 - Once or twice a day dosing (morning and midday)
 - May use as needed
 - Class II controlled substance

Effectiveness of MS-Fatigue Medications

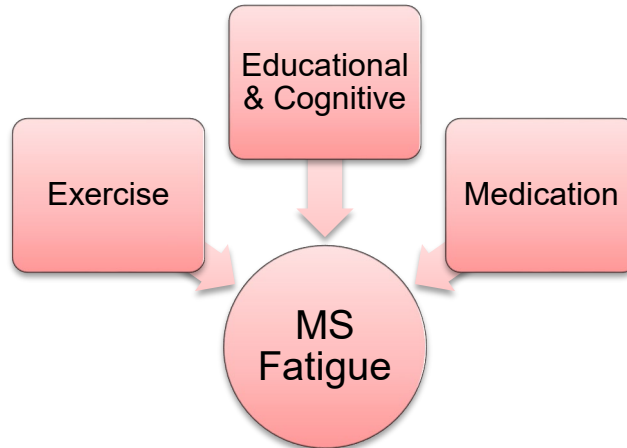
TRIUMPHANT-MS: 2021 randomized, placebo-controlled, double-blinded study

- Average baseline fatigue score for group: **51.3**
 - Amantadine 5-week fatigue score: **41.3**
 - Modafinil 5-week fatigue score: **39.0**
 - Methylphenidate 5-week fatigue score: **38.6**
 - Placebo 5-week fatigue score: **40.6**
- Conclusions
 - Amantadine, modafinil, methylphenidate were not better than placebo at improving MS-related fatigue
 - Modafinil and methylphenidate may improve wakefulness in people with excessive daytime sleepiness

Safety and efficacy of amantadine, modafinil, and methylphenidate for fatigue in multiple sclerosis. *Lancet Neurol.* 2021; 20:38-48.

MS-Related Fatigue Treatment

- Identifying and treating other causes of fatigue
- Optimizing sleep
- Optimizing overall health and nutrition





Thank You

www.wexnermedical.osu.edu



**THE OHIO STATE
UNIVERSITY**
WEXNER MEDICAL CENTER