
Fatigue

Last updated October 2023

Characteristics: Sleepiness as a result of medications, usually due to antidepressants. Typically, patients say they sleep more than enough at night, yet they feel like they could fall asleep at any point throughout the day.

Meds That Cause It: Antidepressants (especially paroxetine, mirtazapine, and tricyclics; bupropion is *least* likely to cause fatigue); antipsychotics (especially clozapine, quetiapine, olanzapine, but all can cause it); mood stabilizers; benzotropine; antihistamines (eg, diphenhydramine, hydroxyzine); opiates.

Mechanism: Various mechanisms, often due to antihistamine or anticholinergic effects.

General Management:

- Watchful waiting for spontaneous resolution (not usually effective).
- Change dosing to bedtime.
- Reduce dose.

Medications:

- If not clinically contraindicated, psychostimulants such as methylphenidate or dextroamphetamine. Depending on the response, you may switch to a long-acting stimulant eventually.
- Modafinil (Provigil) 100–300 mg daily in divided doses.
- Armodafinil (Nuvigil) 150–250 mg daily in divided doses.
- If a serotonergic antidepressant is causing fatigue, consider switching to bupropion.

Clinical Pearls:

- Rule out common non-medication causes of fatigue, such as obstructive sleep apnea, hypothyroidism, and anemia.
- Fatigue can be a residual symptom of partially treated depression.
- If patients are taking a benzodiazepine for anxiety or insomnia, this could be causing daytime fatigue. Consider decreasing the dose or switching to a different agent.

Fun Fact:

Some consider the US to be the most overworked developed country. The number of hours Americans work (86% of men and 67% of women work more than 40 hours weekly) and the absence of a national paid parental leave benefit contribute to this distinction, as does the lack of federal laws requiring maximum work week length, paid sick leave, or vacation days. No wonder so many experience fatigue.