



UPDATE

NARCOLEPSY NEWS

Narcolepsy is a life-long central nervous system disorder characterized by excessive daytime sleepiness and one or more symptoms thought to reflect intrusion of REM sleep into wakefulness (i.e. **cataplexy**, sleep paralysis, hypnagogic hallucinations). There have been two important developments recently in understanding and treating narcolepsy.

1. In the year 2000, human narcolepsy with cataplexy was found to be associated with absent or very low CSF levels of a newly identified neuropeptide, hypocretin, and also called orexin. Hypocretin is suspected of playing a critical role in regulating REM sleep. Researchers are currently investigating whether the hypocretin deficiency in CSF of narcoleptics reflects an auto-immune or selective neurodegenerative process of hypocretin-rich neurons in the hypothalamus. Indeed, post-mortem analysis of narcoleptic brains has shown fewer hypocretin-containing neurons in the usually hypocretin-rich areas. The discovery of a key role of hypocretin neurotransmission in the etiology of narcolepsy raises real hopes for an eventual cure. Until then, narcolepsy continues to be managed by symptom control.

2. The excessive sleepiness of narcolepsy is typically treated with stimulant medication. Tricyclic antidepressants and SSRI's are used generally to control cataplexy and other REM-related narcolepsy symptoms, although these are all off-label applications. **The FDA has just approved Xyrem (Sodium Oxybate) for the treatment of cataplexy.** This is the first drug with FDA approval specifically for cataplexy. Because of its extremely short half-life (30-60 min) dosing is required at bedtime and again 2.5-4 hrs later. The recommended starting dose is 4.5 g/day divided into two doses of 2.2 grams. Most common side effects are nausea, vomiting, dizziness and enuresis.

The mechanism whereby nighttime dosing with Xyrem controls daytime cataplexy is not known. Studies have suggested that Xyrem is also helpful in treating excessive daytime sleepiness and other symptoms of narcolepsy, although FDA approval is currently only for cataplexy. Xyrem is a Schedule III drug with CNS depressant effects and known potential for abuse (formerly named GHB, the so-called "date rape drug")

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