



Solve ME/CFS Initiative

Leveraging patient-centered
research to cure ME/CFS

Webinar Series | Friday, Nov. 14, 2014 | 2:00 PM Eastern

Can ME/CFS and Fibromyalgia Research Help You Sleep?

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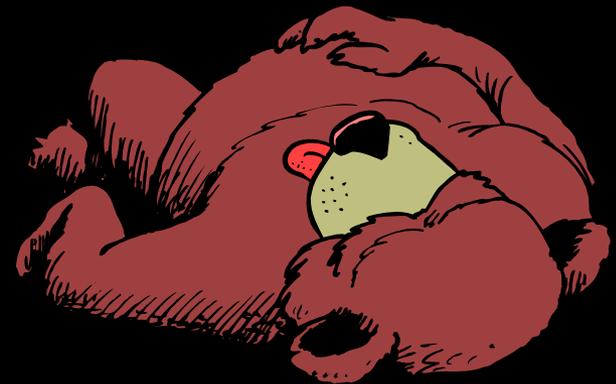


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Can ME/CFS and FM Research Help You Sleep?

Lucinda Bateman MD

Nov 14, 2014



What can be done
to treat sleep ?

Treat the source of sleep disruptions

Some medications may disrupt sleep architecture or contribute to primary sleep disorders

- Caffeine, stimulants
- Decongestants (pseudoephedrine)
- Antidepressants (fluoxetine, sertraline...)
- Opioids
- Benzodiazepines
- Drugs that increase dopamine (inhibit melatonin release)
- polypharmacy (taking too many drugs!)

Treatable comorbid conditions may contribute to fatigue and sleep disturbances

- Pain conditions
- Mental health conditions
- Urinary frequency disorders
- Snoring spouse, active pets, etc...
- Primary sleep disorders
 - Obstructive sleep apnea, airway resistance
 - Central sleep apnea
 - Movement disorders (RLS, myoclonus)
 - Narcolepsy (MSLT on no medications)

ME/CFS/FM sleep research

- **Sleep disturbances are common**
 - Included in all CFS ME/CFS, ME and FM case definitions or symptom criteria
 - Present in >90% of all diagnosed (Jason)
- Sleep abnormal in
 - **Quality** (light, restless, interrupted, heavy)
 - **Duration/timing** (delayed, prolonged, irregular)

MECFS/FM research

1. Polysomnography (sleep studies)
2. Central sensitivity, sensory amplification and hyperalgesia (increased pain and sensation)
3. Autonomic nervous system
Sympathetic : Parasympathetic
4. HPA-axis (hypothalamus-Pituitary-Adrenal ...)

1. Polysomnography (PSG)

- PSG reveals Primary Sleep Disorders
 - Common in ME/CFS and FM patients*
- **PSG is non-diagnostic in ME/CFS/FM****
but does show:
 - Delayed sleep onset
 - Fragmentation of sleep
 - Increased alpha sleep (dozing, light sleep)
 - Decreased delta (slow wave, deep sleep)

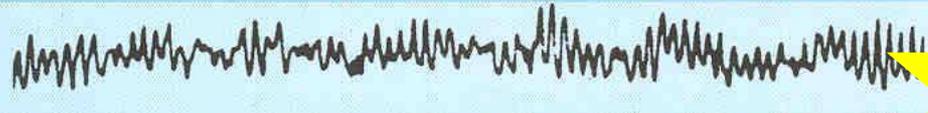
*LeBon 2000

**Cunnington 2011, Togo 2008, Neu 2009, Manu 1994, Jackson 2012

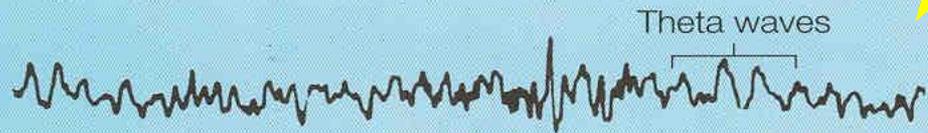
EEG Patterns in Sleep and Wakefulness



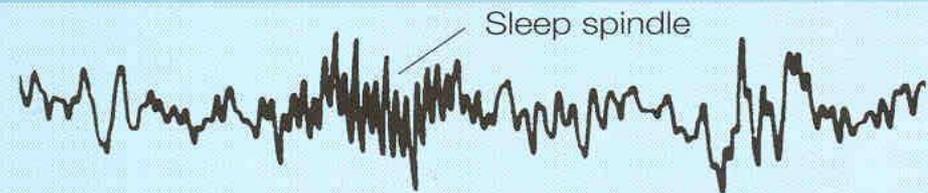
Awake
Low-voltage, high-frequency beta waves



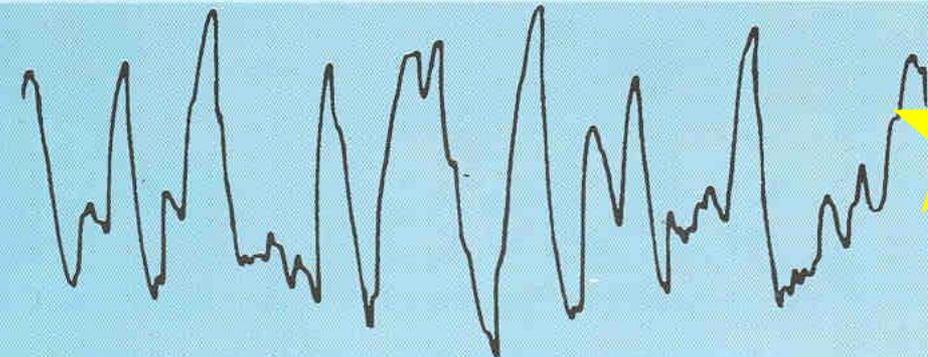
Drowsy
Alpha waves prominent



Stage 1 sleep
Theta waves prominent



Stage 2 sleep
Sleep spindles and mixed EEG activity



Slow wave sleep (stage 3 and stage 4 sleep)
Progressively more delta waves (stage 4 shown)



REM sleep
Low-voltage, high-frequency waves

Polysomnography (PSG)

Can tell us about
"primary sleep disorders"
but, so far, not much about what
primarily disturbs ME/CFS sleep

2. Central Sensitivity

- Pain amplification/hyperalgesia (FM)
 - Pain causes alpha waves that disrupt sleep*
- Sensory amplification in ME/CFS/FM
 - Noise. Bright light. Temperature.
- Central “overload” PEM in ME/CFS/FM
 - Tired but wired
 - Too exhausted to sleep
 - “over-signalling”

Calm Central Sensitivity

- Prevent over-signaling. Pace.
- Sleep wind down: Quiet. Dark. Good temp.
- Reduce activation (no bright screens)
- Medications
 - gabapentin or Lyrica/pregabalin
 - low dose naltrexone (LDN)*
 - low dose clonazepam
 - habituating and long acting
 - amitriptyline, doxepin, cyclobenzaprine

3. Autonomic Nervous System

- **Sympathetic** >> *parasympathetic**
 - Adrenalin/epinephrine and NA/NE
 - Adrenal gland, alpha and beta receptors throughout the body.
 - **Increased HR (heart rate) and decreased HRV (heart rate variability) during sleep.**
 - increased sympathetic tone
 - decreased vagal tone (parasympathetic)

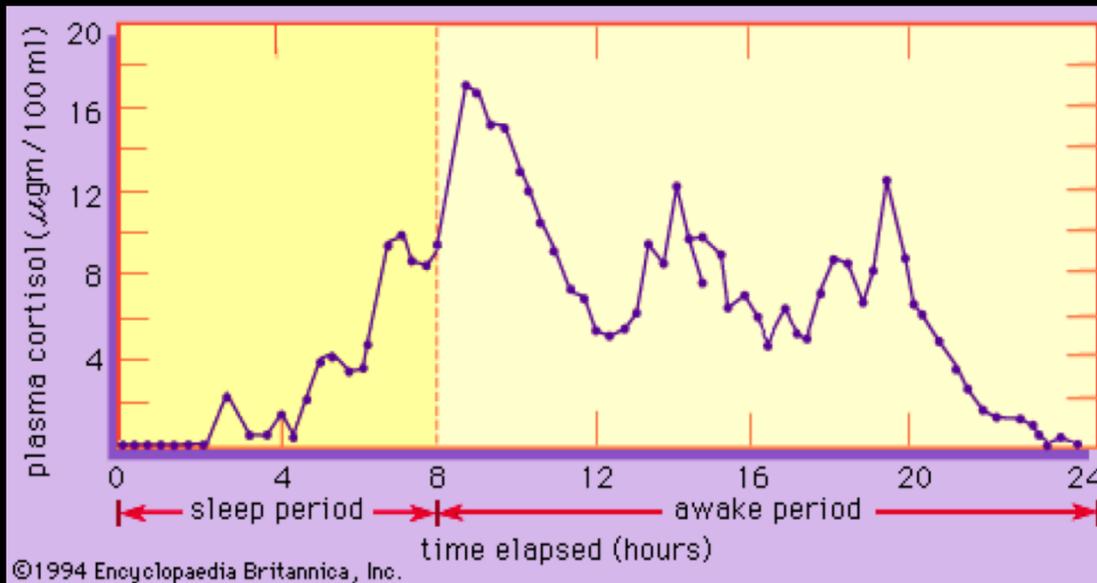
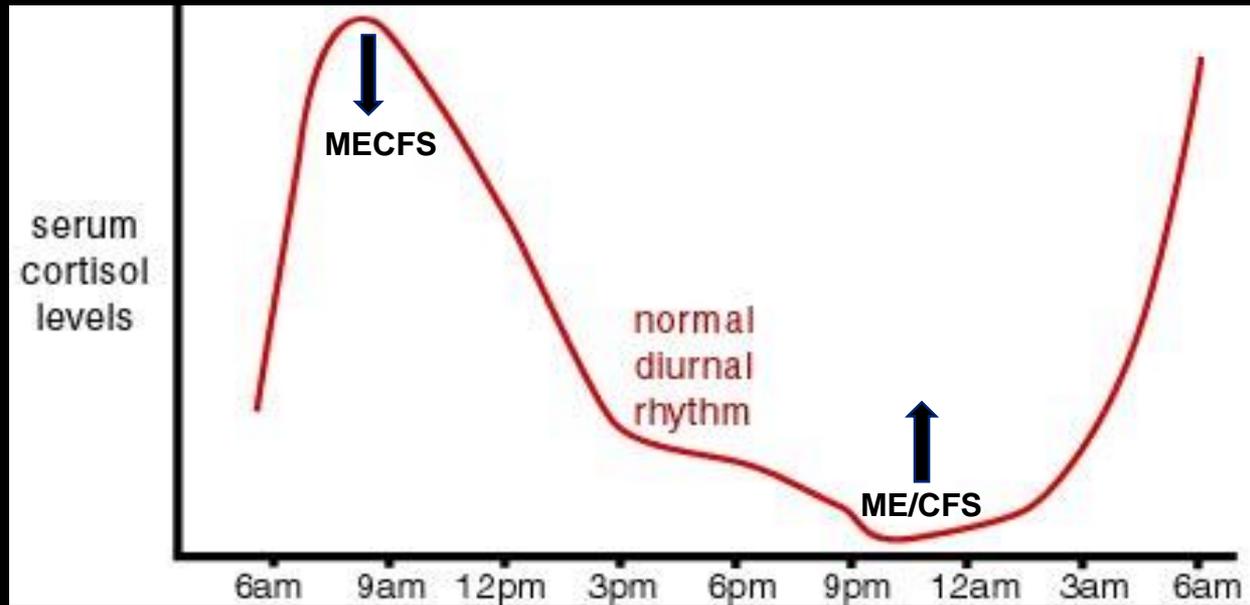
Autonomic Nervous System

- If... **Sympathetic** > *parasympathetic* ...then
- Change to: **Parasympathetic** > *Sympathetic*
 - Deep breathing and relaxation exercises.
 - Push back thoughts of worries and stress
 - Read a boring book before bed.
 - Calming, not activating, activities
- **Beta receptor blockade/inhibition:**
 - 10-20 mg propranolol 2-3 hours before bed?

4. HPA-axis*

- Attenuated (reduced) AM cortisol production.
- Loss of normal circadian rhythm changes in cortisol levels. (less pm dip and am peak)
- Overall cortisol levels are lower than average (low normal)
- Adrenals and pituitary seem to work OK
- Hypothalamus?

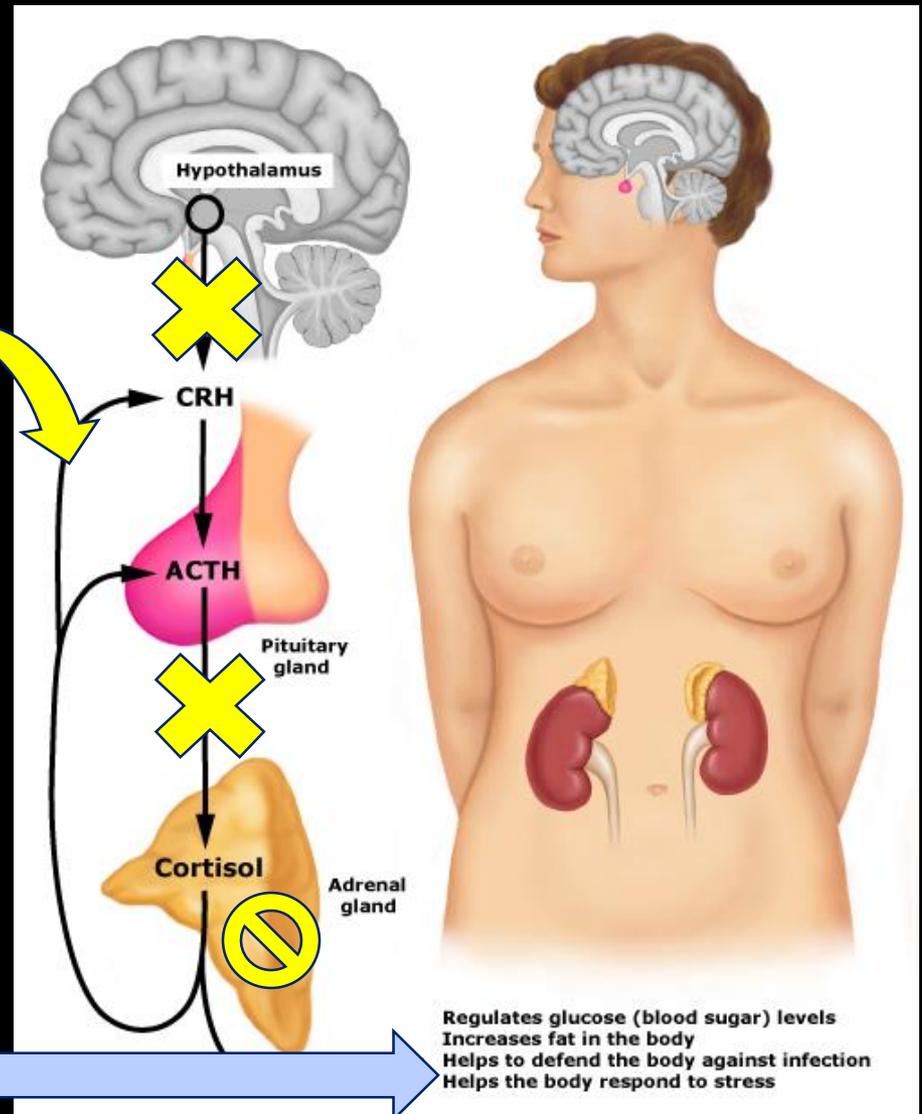
Cortisol secretion



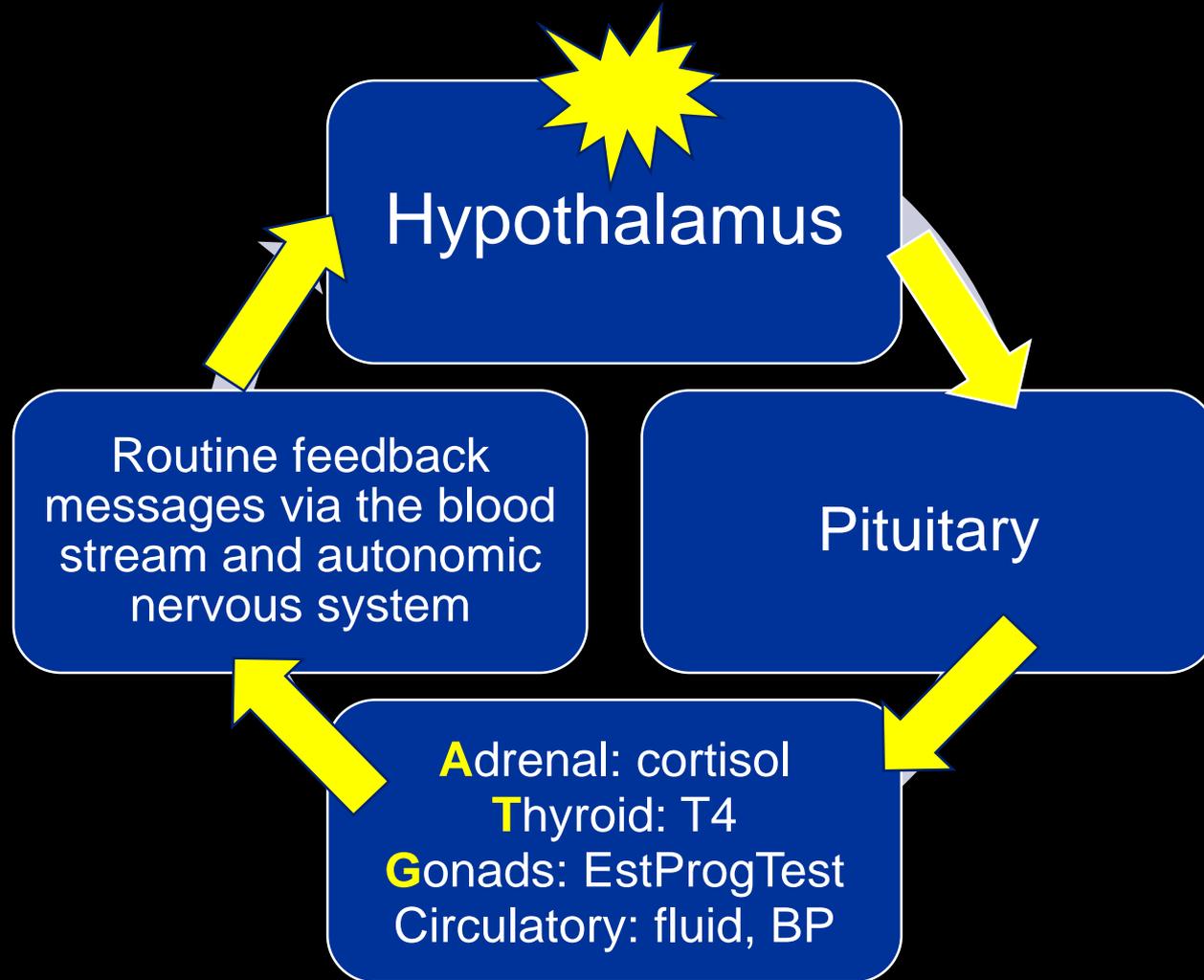
Cortisol is secreted during the day in response to stress, including sleep deprivation. Elevated PM cortisol can then impair sleep!

Excess cortisol supplementation reduces native cortisol production from the adrenal gland

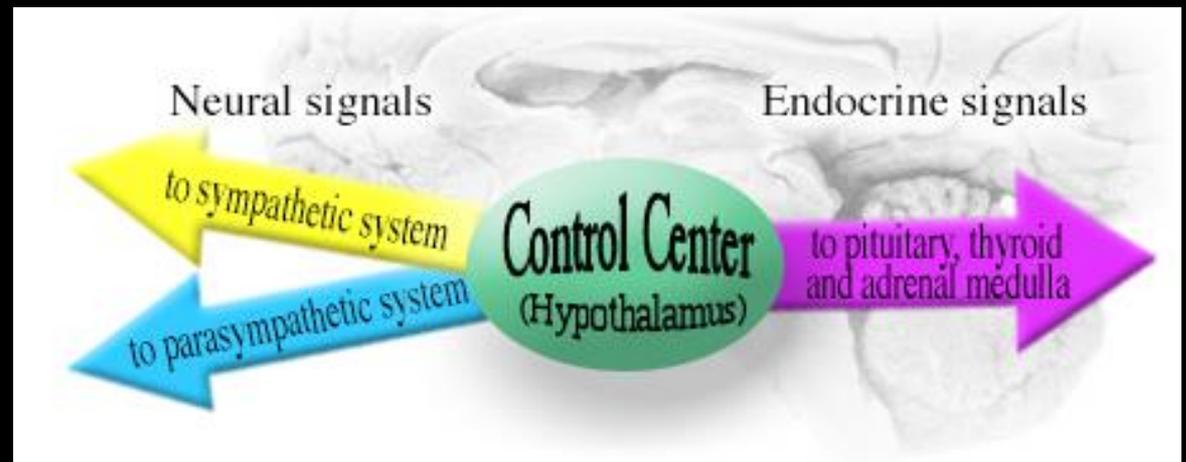
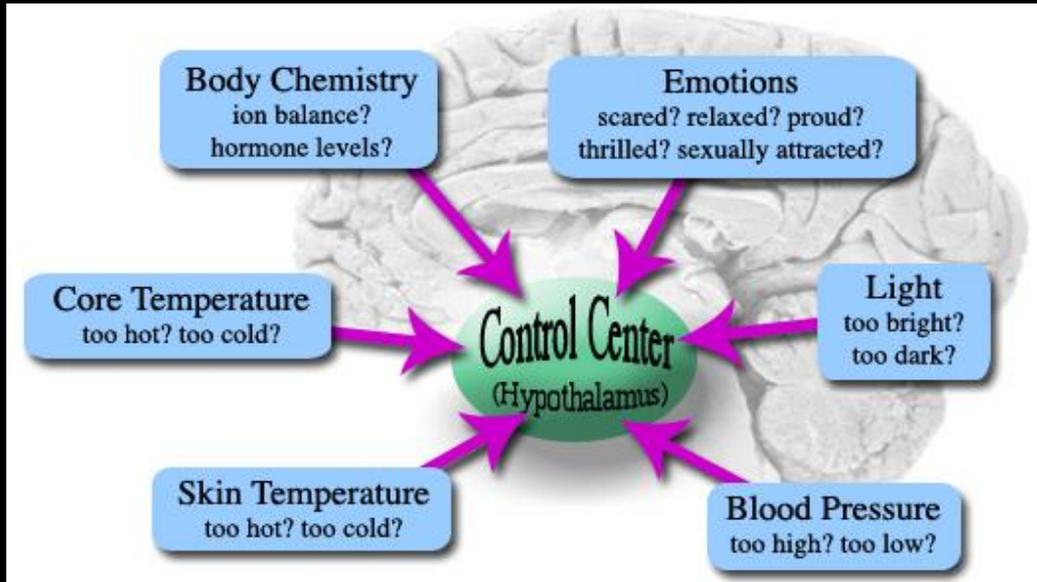
Hydrocortisone
(cortisol)



HP-A, HP-T, HP-G, HP→



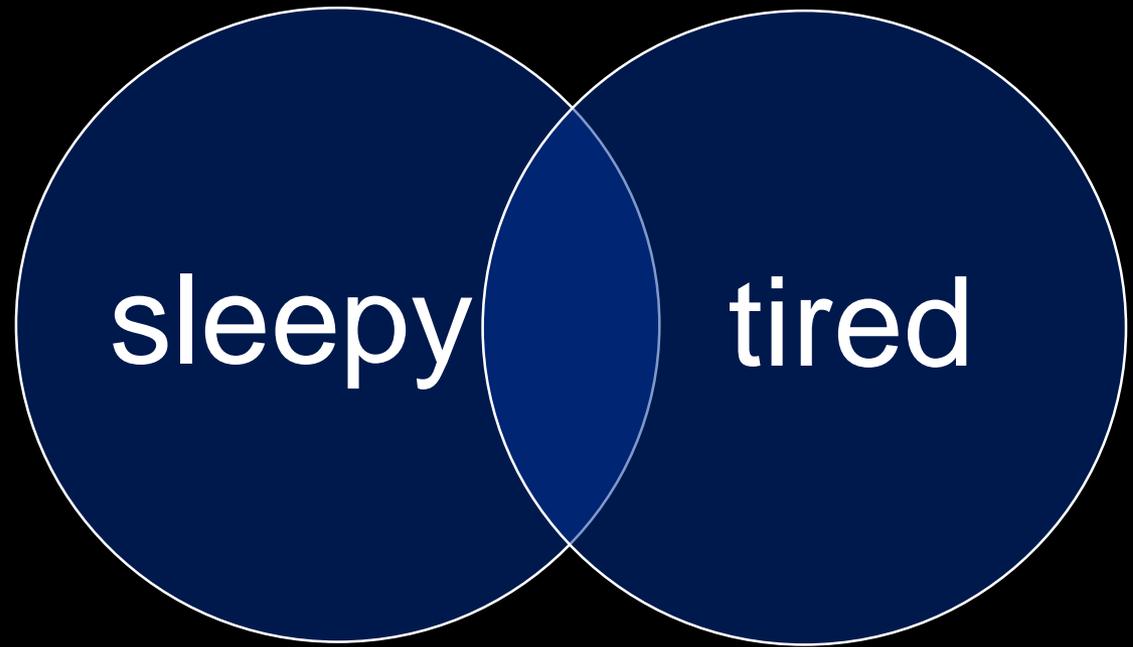
hypothalamus



Treating sleep with medications

- Unlikely to cure ME/CFS/FM
 - May reduce pain and daytime somnolence
- Sleep disturbances are one of the more "treatable" aspects of illness (fixing "*unrefreshing*" may be more challenging)

Proven benefits and risks of meds unknown



Somnolence may be more treatable

- Sleep deprivation (all causes)
- Medications that cause sleepiness
- Illness (neurologic, endocrine, inflammation)

ESS (Epworth Sleepiness Scale)

General Recommendations:

- Improve sleep hygiene (routine timing, environment).
- Identify stimulating medication impacts on sleep
- Daytime activity. Get physically tired---but not exhausted, “wound up” or relapsing (PEM).
- Be wary of long or late naps.
- Minimize sedating drugs during the day.
- Aim at all the CAUSES of sleep disruption.
- Simplify use of medications and use them skillfully
 - Sleep onset (wind down, establish cycles, short acting drugs, earlier dosing of longer acting sedating medications)
 - Light sleep and frequent awakening (reduce interruptions, low dose longer acting meds)
 - Early morning awakening (med rebound or withdrawal? Too much sleep? Establish cycles...)





Natural sleep (drug free) is best,
but chronically
disrupted or inadequate sleep
may be insidiously harmful as well.

There is no perfect medication for sleep.
Almost all have some adverse effects.

Work toward restorative sleep.



ME/CFS/FM research may lead to strategies for better sleep

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2. Central sensitivity, sensory amplification and hyperalgesia (increased pain and sensation)
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Sympathetic : Parasympathetic
4. HPA-axis (hypothalamus-Pituitary-Adrenal ...)

Sleep and MECFS/FM Bibliography

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Solve ME/CFS Initiative

Leveraging patient-centered
research to cure ME/CFS

Thank You!

Our Mission:

Make ME/CFS understood, diagnosable and treatable.

Our Strategy:

Stimulate participatory research aimed at the early detection, objective diagnosis and effective treatment of ME/CFS through expanded public, private and commercial investment