The Effects of Long Covid and ME/CFS on Sleep

SleepScore Labs™

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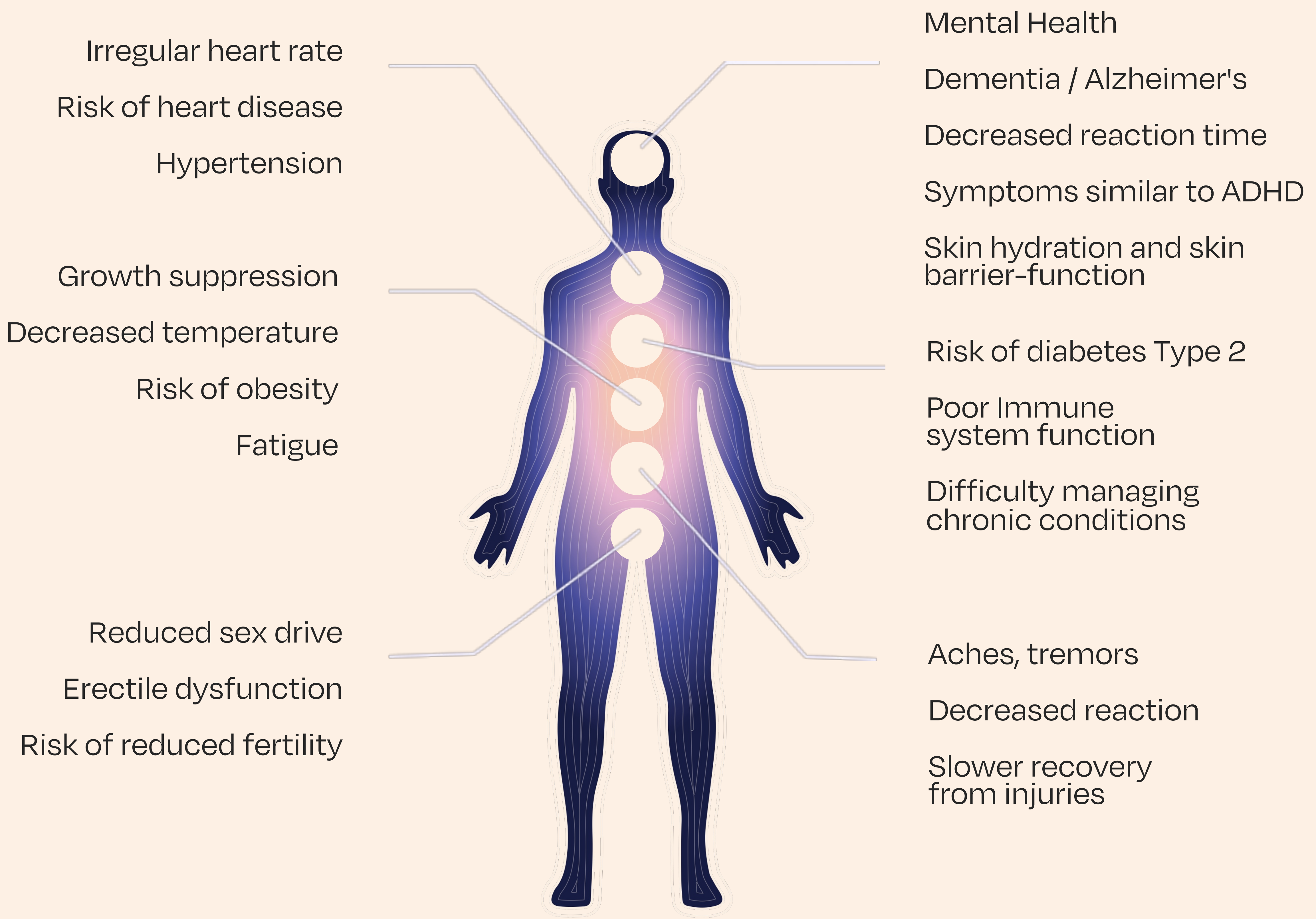
April 27, 2022

Sleep: the Swiss army knife of human health

- **Sleep deprivation impacts every physiological function in the body**, while sleep extension can improve health & wellness
- Individuals with ME/CSF and Long-COVID are differentially affected by poor and unrefreshing sleep



Sleep is remarkably dynamic – not binary

NON RAPID EYE MOVEMENT (NREM) SLEEP

- NREM 1
- NREM 2
- NREM 3

RAPID EYE MOVEMENT (REM) SLEEP

- REM

Prevalence of sleep problems in those with long COVID or ME/CFS

Long-COVID

Prevalence ranges from 7% to over 70% depending on the timing post-COVID and sleep problem

- **After 16+ weeks[1]:**
  - **Insomnia = 32% of 500 patients**
  - **Obstructive sleep apnea = 62% of 60 patients**
  - **Non-restorative sleep = unknown**

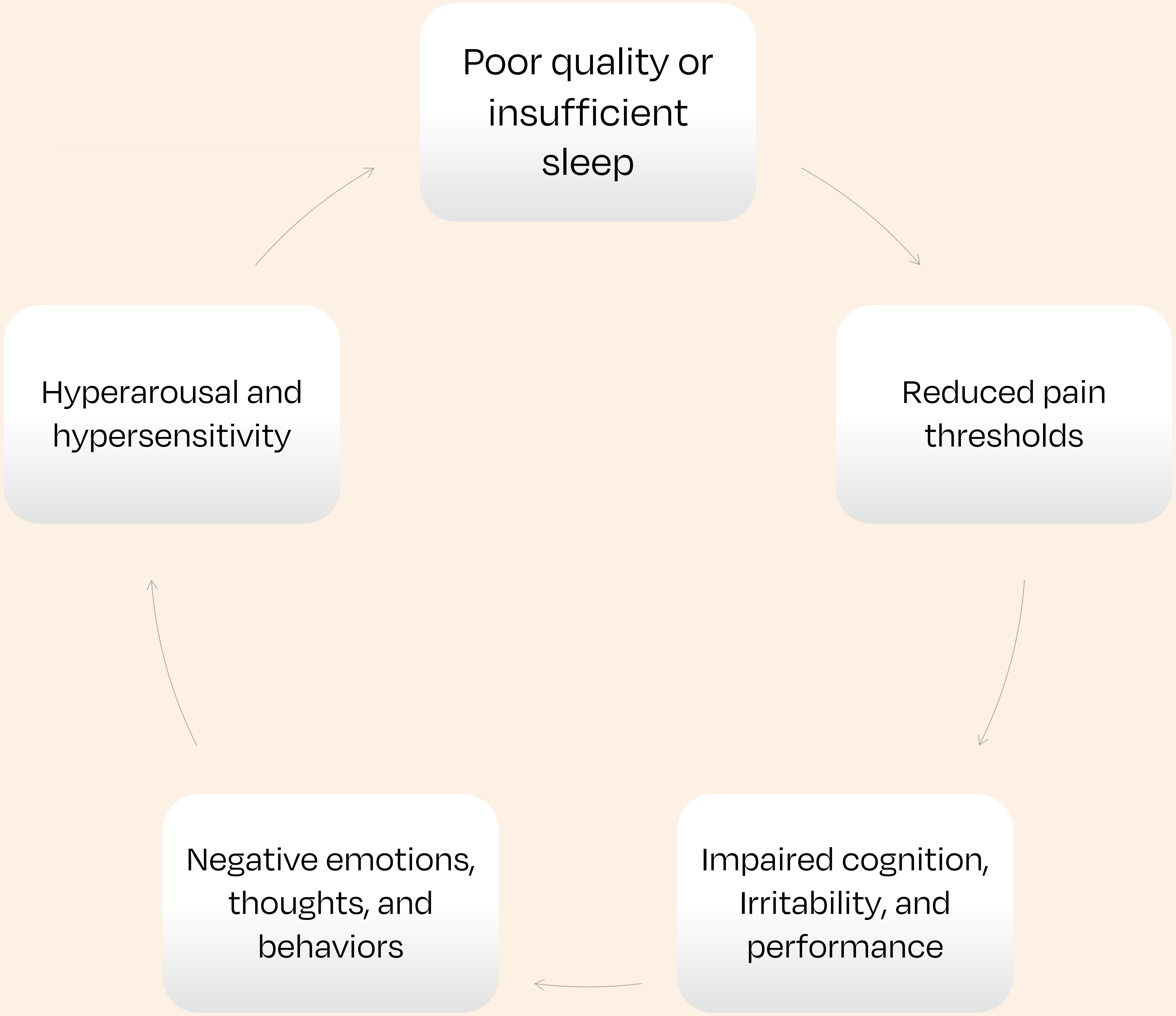
ME/CFS

Symptoms of ME/CFS are clearly distinct from those of primary sleep disorders, and the illness is more than simply a somatic expression of an underlying sleep disorder or sleepiness (from Jackson & Bruck, 2012)[2]

- **Obstructive sleep apnea = 46% of 46 patients**
- **Narcolepsy or OSA = 23% of 65 patients**
- **Non-restorative sleep = 87-95% of 1,655 patients**

[1]Tedjasukmana et al., (2023). Sleep disturbance in post COVID-19 conditions: Prevalence and quality of life.
[2]Jackson & Bruck (2012). Sleep Abnormalities in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: A Review.

Cyclical effects of poor sleep on long COVID and ME/CF symptoms



The neurological connections between long COVID, ME/CFS, and sleep disturbances

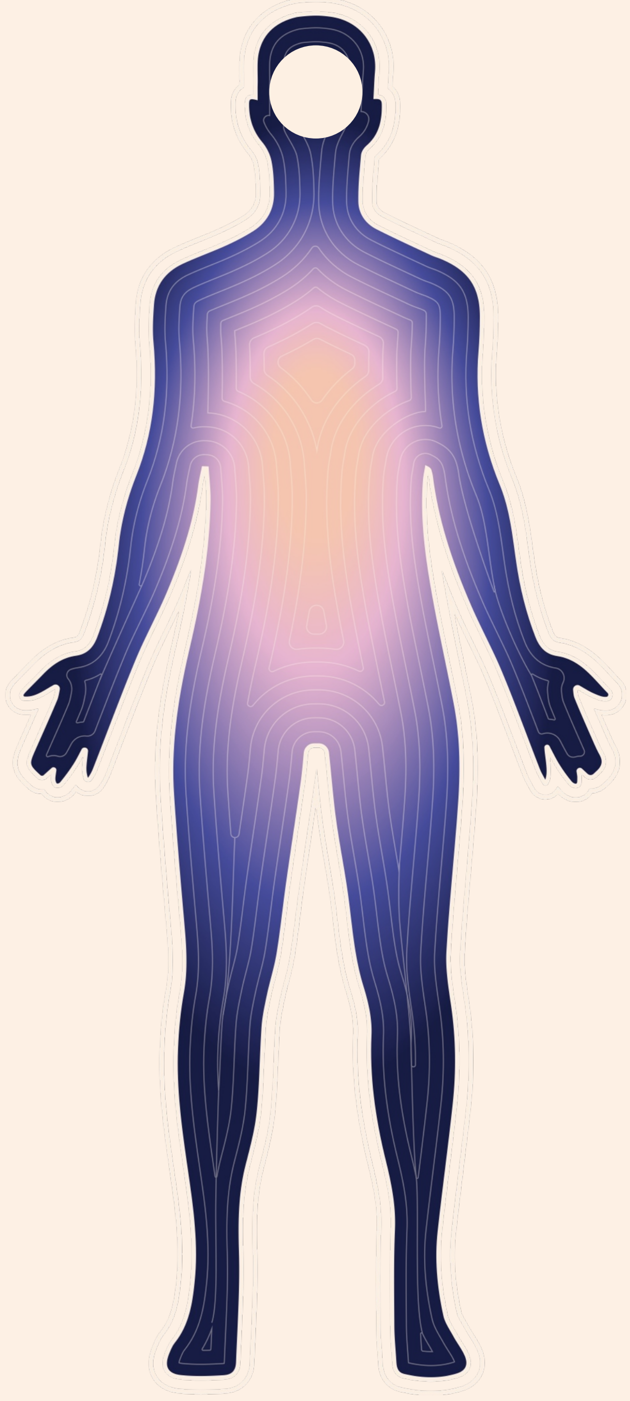
- **A bidirectional relationship likely exists between long COVID, ME/CFS and sleep-wake functioning**:
  - Poor sleep exacerbates disease severity and symptoms which in turn can worsen sleep problems
- Several neurological differences have been described in those with ME/CFS compared with healthy controls[1]

↓ cerebral blood flow

↑ neuroinflammation in the brain regions involved in sleep

↑ brain metabolites

↓ functional connectivity, gray matter volume, and white matter volume



↓ EEG sleep quality

↓ subjective sleep quality (+correlated with brain regions) but no objective sleep differences in twins

? Potential sleep state misperception

↓ circadian functioning

[1]Maksoud et al., (2020). A systematic review of neurological impairments in myalgic encephalomyelitis/ chronic fatigue syndrome using neuroimaging techniques

Unrefreshing sleep vs. quality sleep: changes in the power of sleep stages in ME/CFS patients

- **55-100% of ME/CFS patients report unrefreshing sleep**, but the cause is unclear, and several studies have not identified objective sleep differences [1,2]

- Using more advanced EEG analytic methods, a recent study found that, compared with controls, ME/CFS patients had:

    - Reduced power of cortical delta activity during slow-wave sleep[3]
    - Reduced power of cortical alpha activity, with the greatest reduction occurring during REM sleep[3]

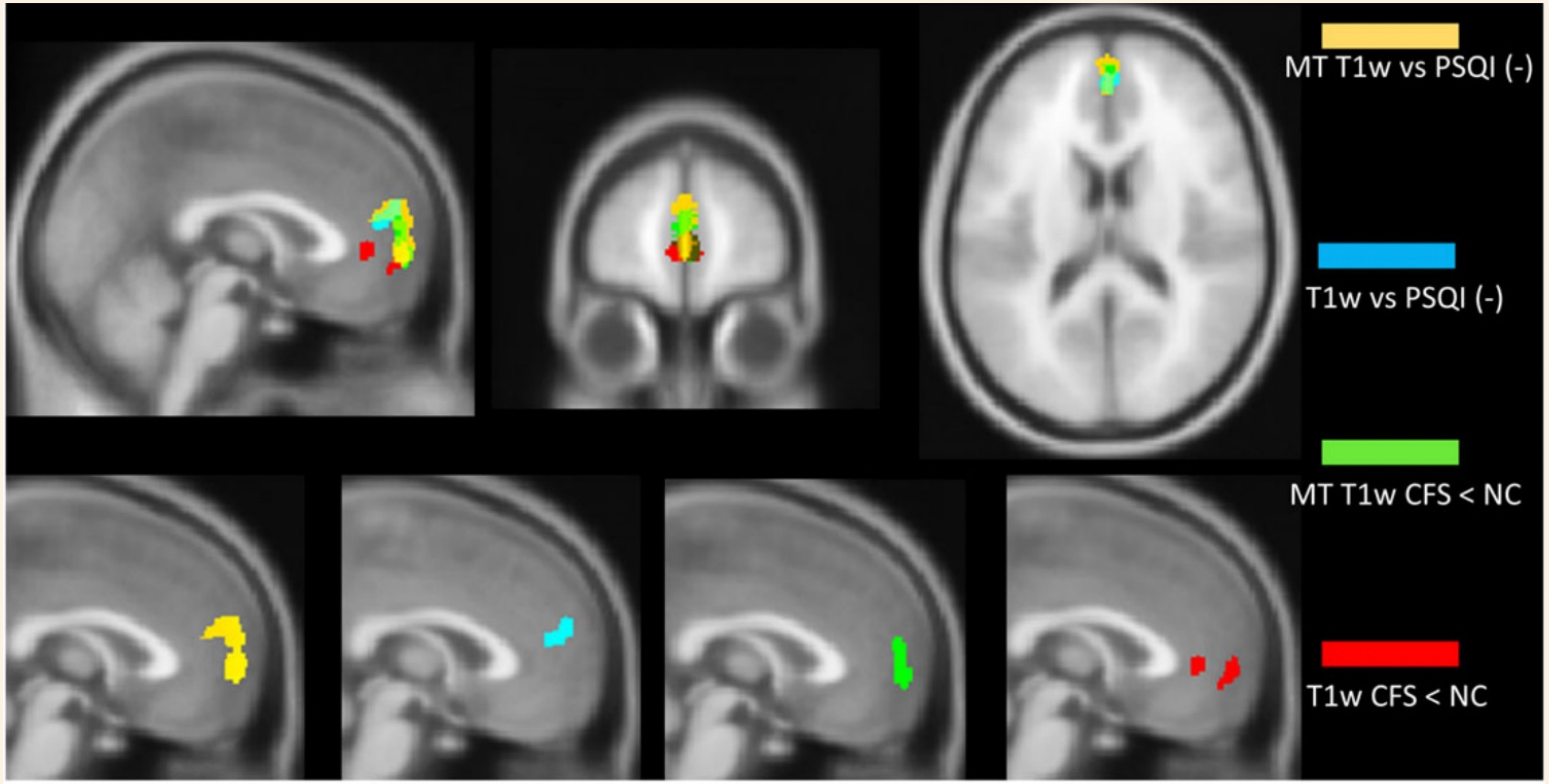
	Stage 1	Stage 2	Slow Wave Sleep	REM
CFS (n = 35)	4.87E-9 ± 7.16E-11	1.17E-08 ± 5.26E-11	3.48E-08 ± 2.29E-10	3.76E-09 ± 2.73E-11
Control NF (n = 40)	4.22E-9 ± 5.86E-11	1.16E-08 ± 8.02E-11	3.83E-08 ± 2.36E-10	3.54E-09 ± 5.35E-11
Two Tailed Significance	P < 0.0001	P = 0.323	P < 0.0001	P < 0.0001

Figure taken from Decker et al. (2009) denotes that spectral power of cortical delta activity was significantly reduced in slow wave sleep but increased in both Stage 1 sleep and REM

[1] Jain et al., (2017). Prevalence of and risk factors for severe cognitive and sleep symptoms in ME/CFS and MS
[2] Knook et al., (2000). High nocturnal melatonin in adolescents with chronic fatigue syndrome.
[3] Decker et al., (2009). Electroencephalographic correlates of Chronic Fatigue Syndrome.

Unrefreshing sleep is associated with structural brain differences

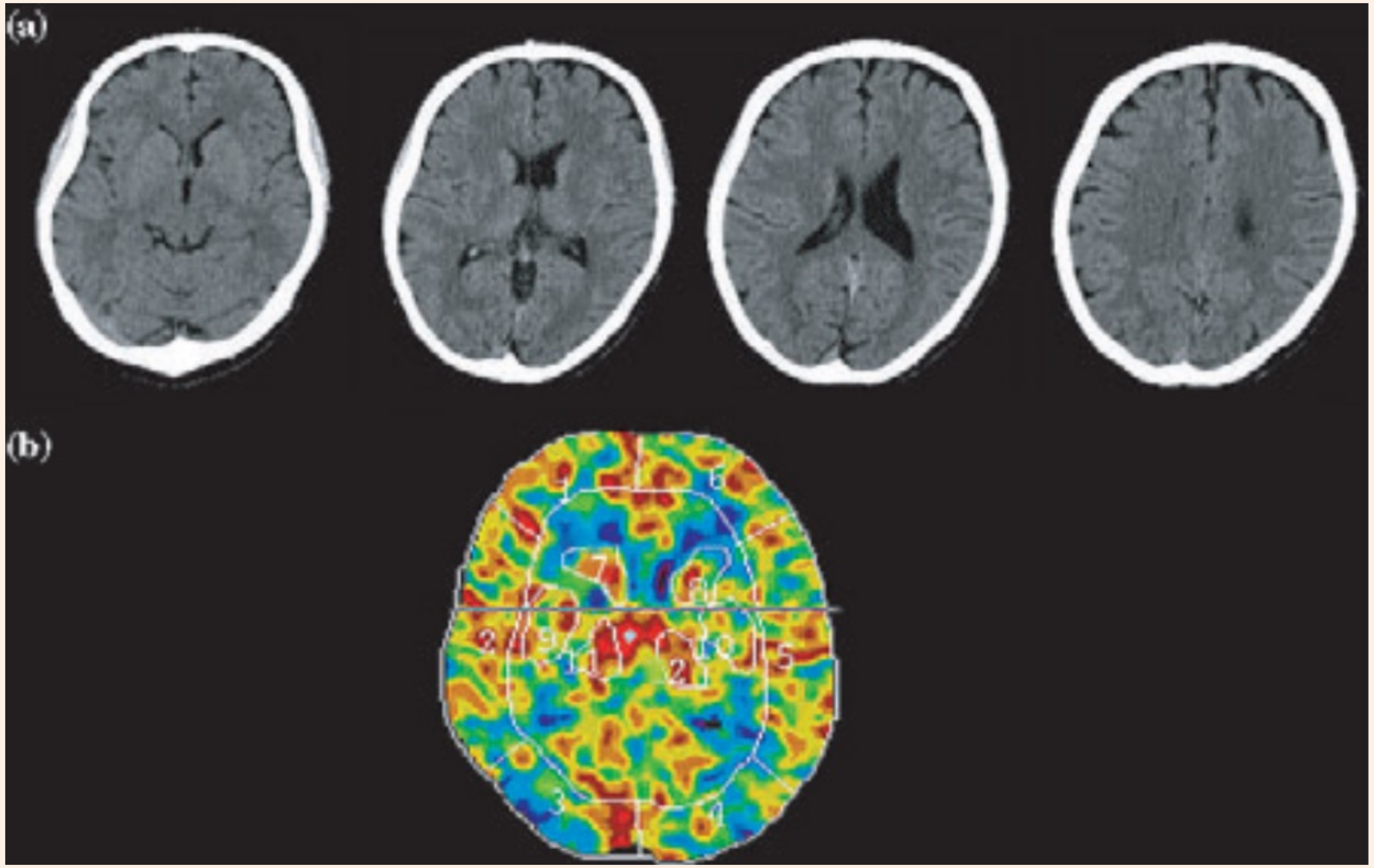
- **Figure from Shan et al (2017) showing that ME/CFS patients with unrefreshing sleep may have damage to the medial prefrontal cortex[1]**
- Persistent sleep problems in long-COVID may be associated with prolonged dysfunction of brainstem[2]
- Damage to the medial prefrontal cortex & brainstem are associated with diminished slow wave (deep) sleep
- These findings potentially refute the suggestion that unrefreshing sleep is a misperception in ME/CFS patients



[1]Shan et al., (2017). Medial prefrontal cortex deficits correlate with unrefreshing sleep in patients with chronic fatigue syndrome
[2]Yong et al., (2021). Persistent brainstem dysfunction in long-COVID: a hypothesis

Changes in brain blood flow in those with ME/CFS

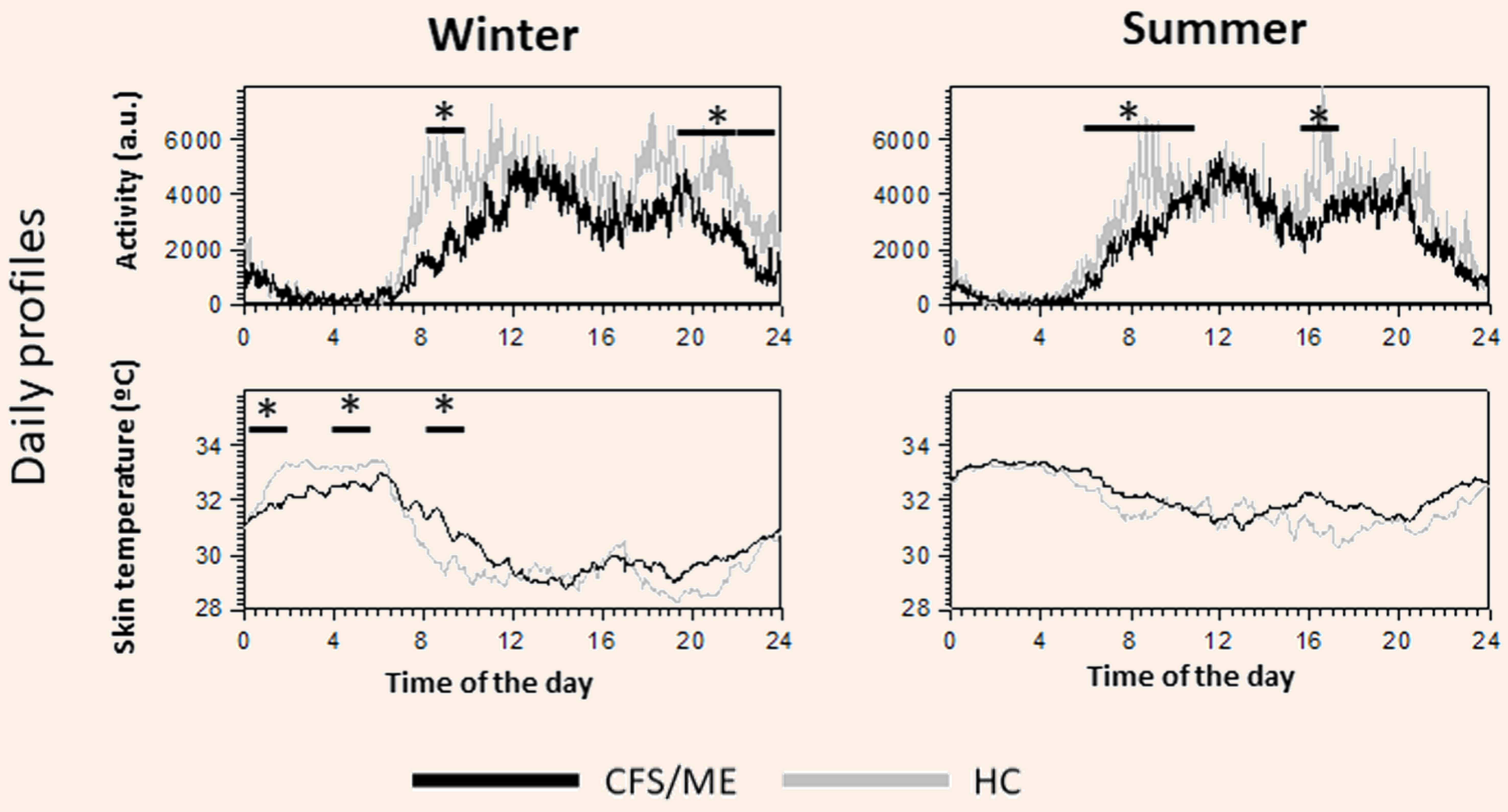
- **Several studies have shown that patients with ME/CSF have significantly lower cerebral blood flow compared to controls**[1,2,] although this has been refuted in some studies[3]
- Figure from Yoshiuchi et al (2006) showing that significantly lower cortical and cerebellar regional cerebral blood flow in ME/CFS
- Reduced activity to these regions may be risk factors for severe cognitive and sleep problems[4]



[1] Maksoud et al., (2020). A systematic review of neurological impairments in myalgic encephalomyelitis/chronic fatigue syndrome using neuroimaging techniques
[2] Yoshiuchi et al., (2006). Patients with chronic fatigue syndrome have reduced absolute cortical blood flow.
[3] Staud (2018). Task Related Cerebral Blood Flow Changes of Patients with Chronic Fatigue Syndrome: An Arterial Spin Labeling Study
[4] Jain et al., (2017). Prevalence of and risk factors for severe cognitive and sleep symptoms in ME/CFS and MS

Circadian rhythm disruption in ME/CFS

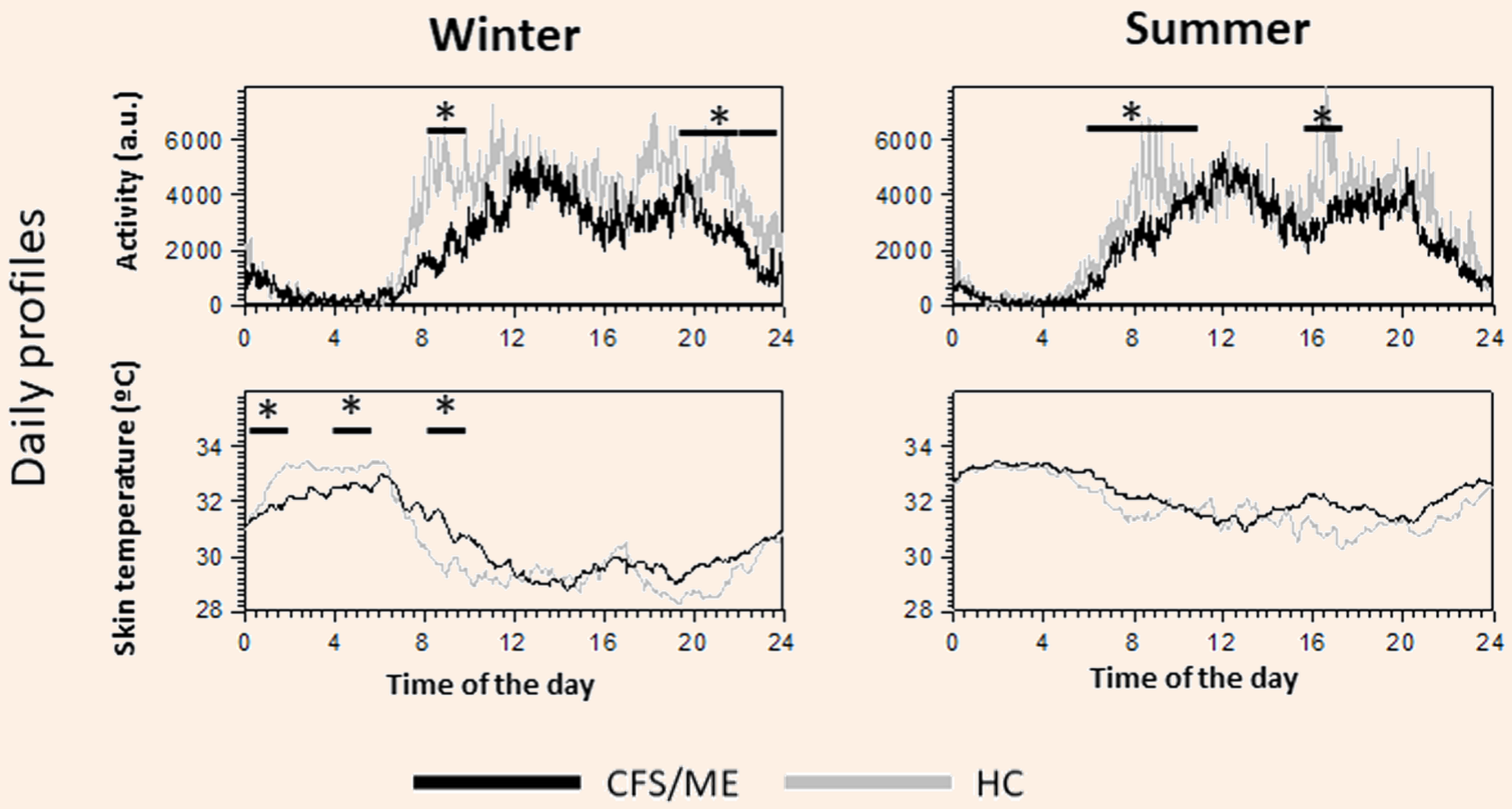
- Energy level, activity, alertness, and mood all follow daily circadian rhythms in healthy people
- Individuals with ME/CFS show irregular activity patterns with **decreased total activity, lower activity rhythm amplitude, and less stable rhythms (Figure from Cambras et al., 2018)**[1]
- Fatigue and inactivity in the context of ME/CFS may be both a cause and effect of circadian disruption



[1]Cambras et al.. (2018). Circadian rhythm abnormalities and autonomic dysfunction in patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.

Circadian rhythm disruption in ME/CFS

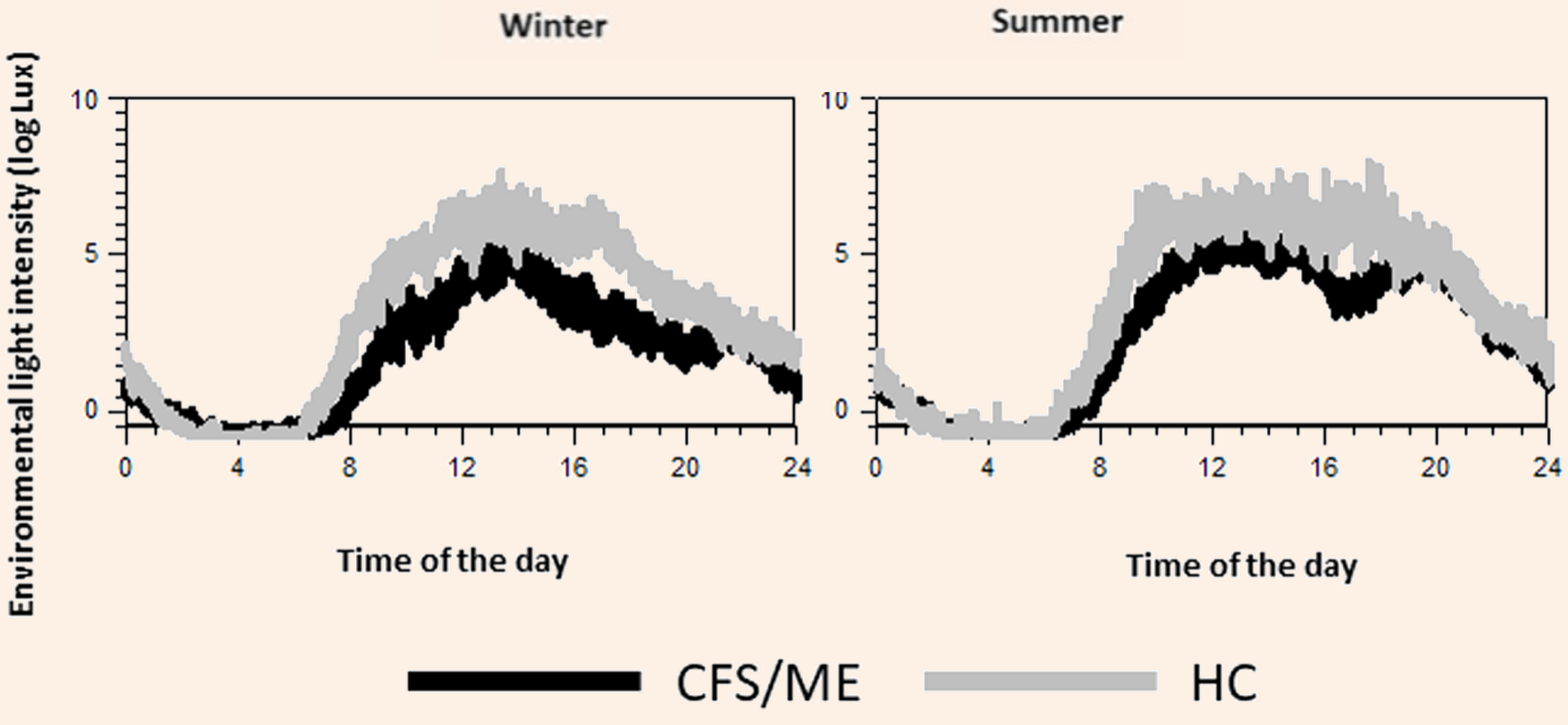
- These data suggest that **activity in individuals with ME/CFS peaks between 12-2PM (Figure from Cambras et al., 2018)** [1]
- Scheduling graded exercise therapy during this time may have a beneficial impact on fatigue, sleep and mood[2]
- **Exercise significantly improves sleep quality, increasing deep (slow wave) sleep[3]**
- However, graded exercise may worsen symptoms of post-exertional fatigue in some patients and its role in treating ME/CSF is controversial



[1]Cambras et al.. (2018). Circadian rhythm abnormalities and autonomic dysfunction in patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.
[2]Powell et al., (2006). Patient education to encourage graded exercise in chronic fatigue syndrome: 2-Year follow-up of randomised controlled trial.
[3]Park et al. (2021). Exercise improves the quality of slow-wave sleep by increasing slow-wave stability.

Harnessing the power of light for circadian functioning

- Light is an important factor for the synchronization of the circadian rhythms and can also impact mood and cognition
- **CFS/ME patients may be exposed to lower light intensity during the day than healthy controls (Figure from Cambras et al., 2018)[1]**
- Bright light therapy has been shown to improve pain sensitivity in fibromyalgia patients[2]



[1]Cambras et al.. (2018). Circadian rhythm abnormalities and autonomic dysfunction in patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis
[2]Burgess et al., 2017). Morning versus evening bright light treatment at home to improve function and pain sensitivity for women with fibromyalgia: A pilot study

Harnessing the power of light for circadian functioning

- While neither melatonin nor light therapy improved ME/CFS symptoms, **light therapy reduced self-reported sleep disturbances (Figure from Williams et al., 2002)**[1]
- Note: the light intensity used (2500 lux) was significantly lower than what's typically used clinically (10,000 lux)

Symptom	Effect of melatonin			Effect of phototherapy		
	Before Rx	End of Rx	*P* value*	*Before Rx*	*End of Rx*	*P* value*
Fatigue	7·1 (4·9–7·8)	6·1 (4·8–8·0)	0·57	6·6 (5·0–8·0)	7·2 (5·5–8·3)	0·34
Depression	5·8 (1·5–7·1)	4·4 (0·8–7·2)	0·69	3·4 (1·5–6·7)	5·8 (1·7–7·4)	0·18
Anxiety	5·7 (1·4–7·7)	4·3 (0·8–6·8)	0·08	5·0 (1·4–7·0)	4·9 (1·3–7·3)	0·76
Sleep disturbance	6·5 (3·4–8·5)	5·5 (2·8–7·3)	0·07	6·6 (5·1–8·1)	5·1 (2·5–7·8)	0·03
Waking refreshed	7·4 (5·8–9·2)	6·0 (4·4–8·3)	0·07	7·4 (5·6–8·8)	7·6 (6·3–9·3)	0·31
Low energy	7·2 (5·0–8·7)	6·6 (5·4–7·9)	0·42	7·2 (6·5–8·3)	7·1 (5·7–8·1)	0·70
Poor concentration	6·9 (4·9–8·1)	6·1 (4·2–8·3)	0·35	6·6 (4·0–8·5)	7·3 (5·5–8·2)	0·76
Muscle pain	5·6 (2·9–7·3)	5·2 (2·9–7·0)	0·68	6·0 (3·1–7·1)	4·4 (1·6–7·1)	0·18

[1]Williams et al., (2002). Therapy of circadian rhythm disorders in chronic fatigue syndrome: no symptomatic improvement with melatonin or phototherapy

5 evidenced-based tips for optimal sleep health

1. **Sleep hygiene.** For those not suffering from a sleep disorder (test test test!), basic sleep hygiene may be an effective first plan of attack.

    - **Consistency is key.**
    - **Cut the caffeine after 2PM and alcohol before bed.**
    - **Think dark or dim before bed**
    - **View bright light (ideally sunlight) in the morning for 15-30 minutes**

5 evidenced-based tips for optimal sleep health

2. **Positive Psychology.** Charlotte Bronte once said, “A ruffled mind makes a restless pillow”. How can we unruffle the mind before drifting off?

    - **Mindfulness meditation**
    - **Practice gratitude before sleep**

5 evidenced-based tips for optimal sleep health

3. **Create A Sleep Oasis.** Your bedroom is where the magic happens: sleep.

    - **Try to only use your bed for sleep, sickness, and sex**
    - **Think like a bat in a cave — keep it cool, dark, and quiet**

5 tips for optimal sleep health

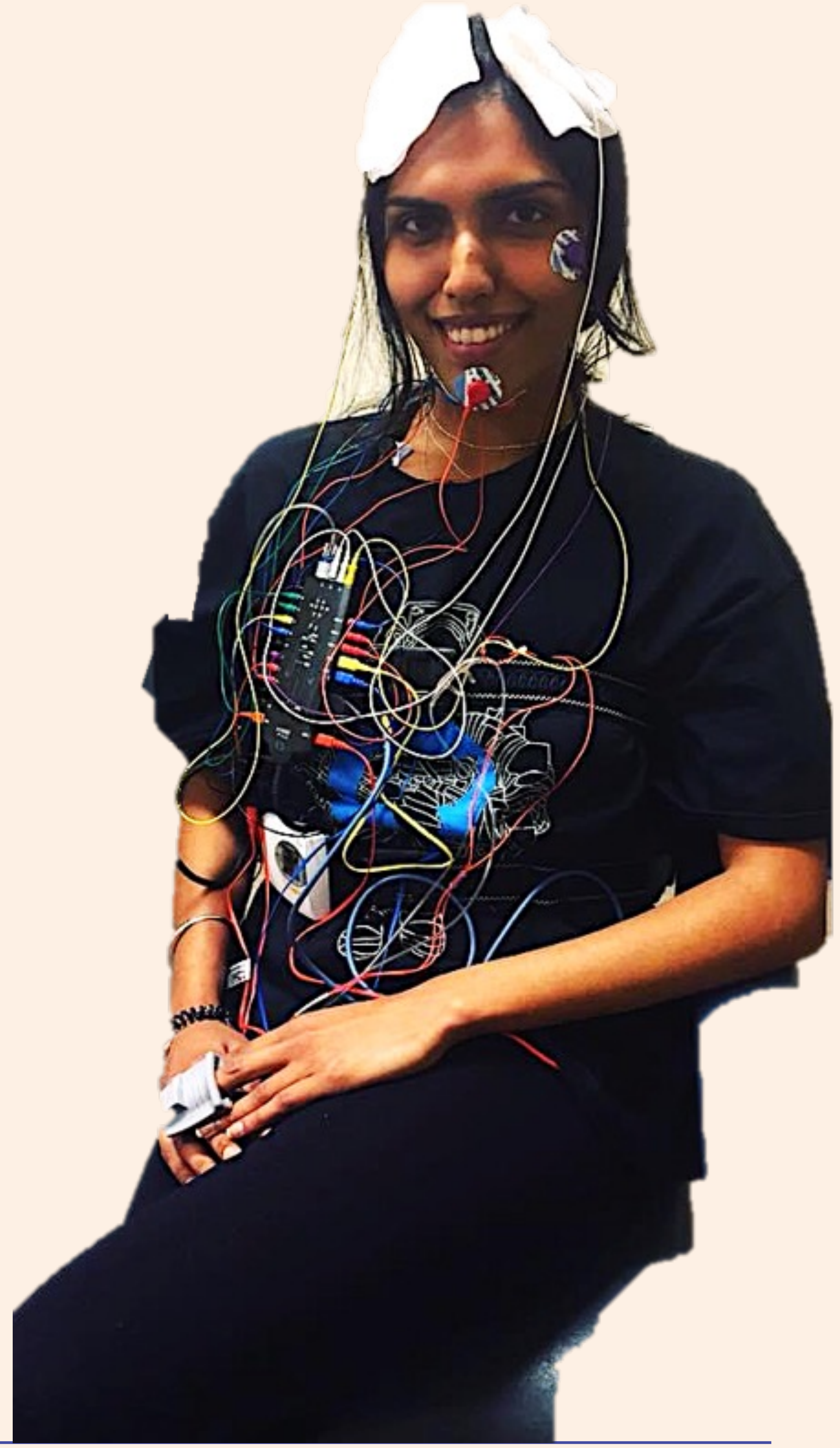
4. Take control of your circadian rhythm. Our brain synchronizes to morning sunlight viewing, exercise, & eating. Timing these consistently (daily) causes an anticipatory increase in alertness & attention.

- **Creating consistent daily habits entrained by our circadian rhythm can improve our energy & discipline for other activities.**
- **Go to bed and wake up at the same time (+/-30 min) every day.**

5 tips for optimal sleep health

5. Harness the power of technology. Knowledge is power, and the data provided by sleep trackers can give us an inside look at an otherwise difficult behavior to objectively measure.

- **Consumer Sleep Technology.** Data that was previously confined to a doctors office is now a lifestyle product giving us a lens into our own health



SleepScore's Non-Contact Sleep Measurement Technology & Improvement Program

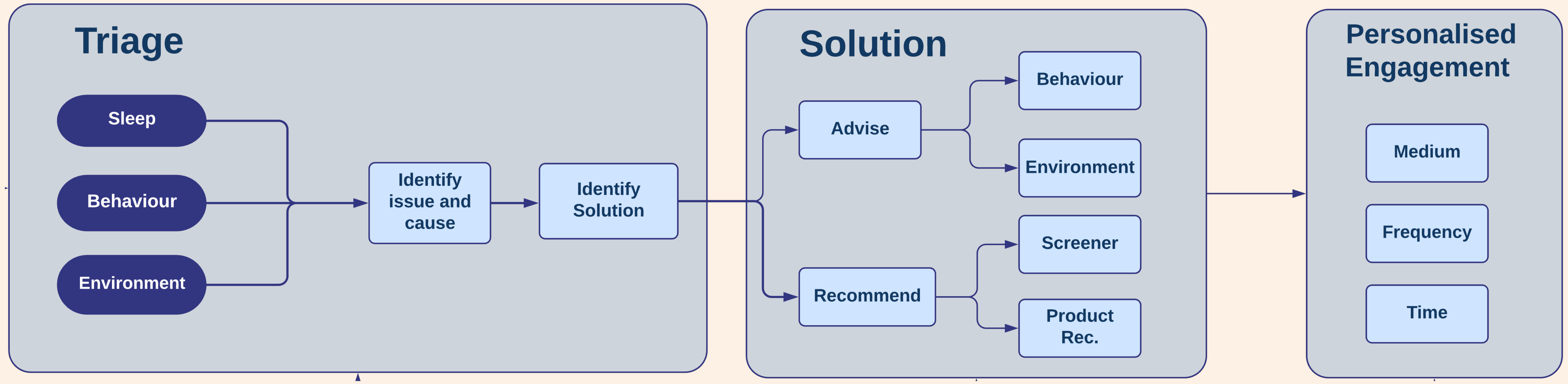
- Turns smartphone into active **sonar** device, measuring breathing and motion
- Free to download, allowing for reduced barrier to entry
- The only widely available mobile sleep app with publication of performance evaluated against the gold-standard (PSG) showing 85%+ overall accuracy.

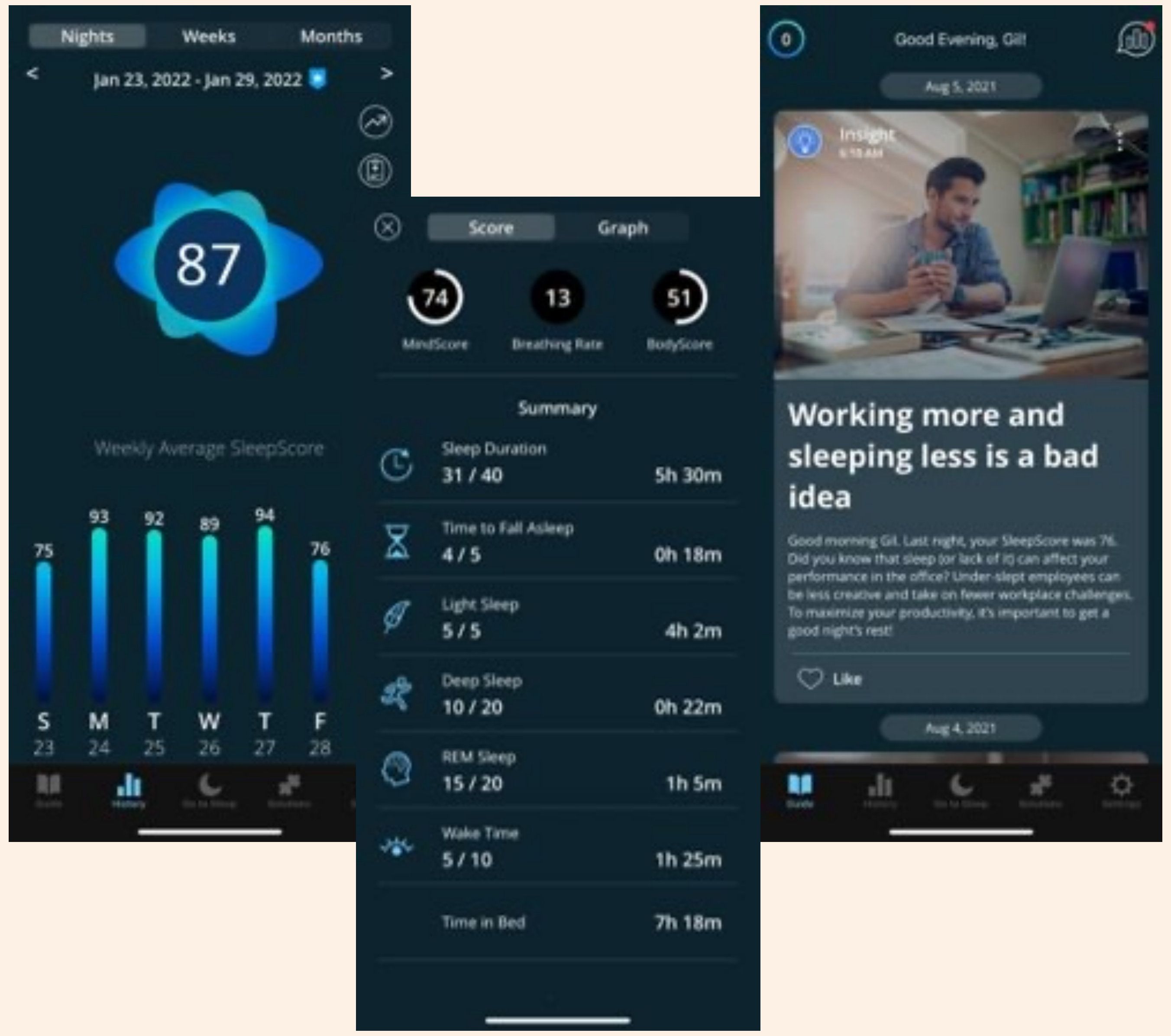
SleepScore App

Data & The Sleep Improvement Program

Beyond sleep tracking – proprietary advice engine leverage's objective sleep data, daily sleep log data, and contextual data to provide users with dynamic and personalized behavioral sleep advice

Personalized SleepScore, content, tips, and engagement activities





Variety of tools delivering personalized, actionable & impactful sleep improvement experience

Sleep Tracking | *Daily Reflection* | *Sleep History* | *Sleep Insights* | *Sleep Graph* | *Sleep Coaching* | *Sleep Content* | *Sleep Solutions*

✓*Articles* ✓*Videos* ✓*Gamification* ✓*Challenges* ✓*Follow Ups* ✓*Surveys* ✓*Smart Alarm* ✓*Screeners* ✓*Dr. Report*

Q&A

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