



The role of sleep in migraine

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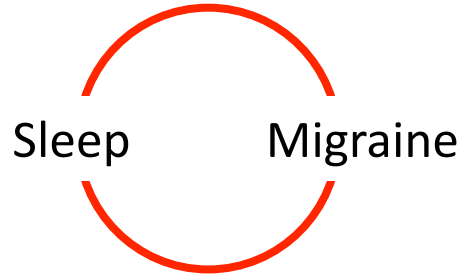
IRCCS San Raffaele



Disclosures

	ADVISORY BOARD	SPEAKER BUREAU	INVESTIGATION STUDIES
ABBVIE	●		●
ALDER			●
ANGELINI	●		
ASSOSALUTE		●	
BAYER		●	
BIOHEAVEN			●
ELI-LILLY	●	●	●
FONDAZIONE RICERCA E SALUTE	●		
GSK			●
LUNDBECK	●	●	●
MSD		●	
NEW PENTA			●
NOEMA PHARMA			●
NOVARTIS	●	●	●
PFIZER	●	●	●
TEVA	●	●	●
VISUFARMA		●	
ZAMBON	●		

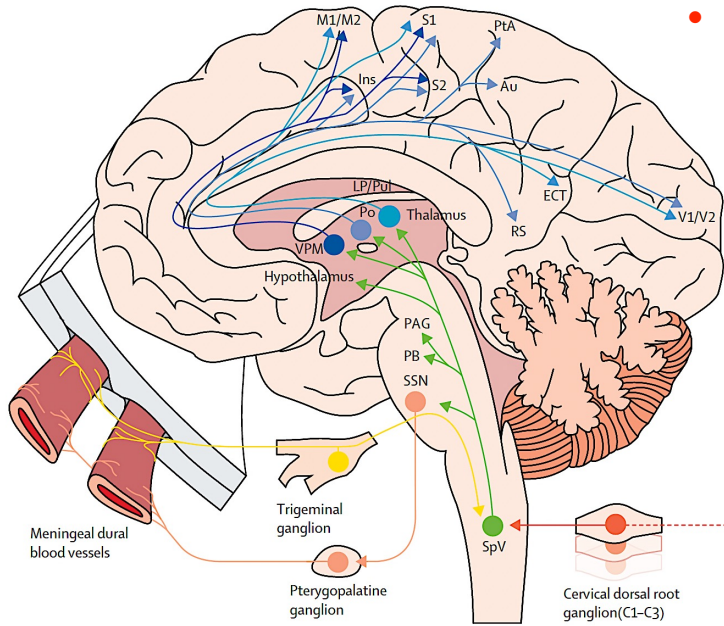
What clinicians know



1. Sleepiness may precede, follow or accompany the migraine attack
2. Migraine chronobiology is closely tied to the sleep-wake cycle
3. Sleep disorder are more frequent in migraine patients
4. Sleep affects migraine, migraine affects sleep

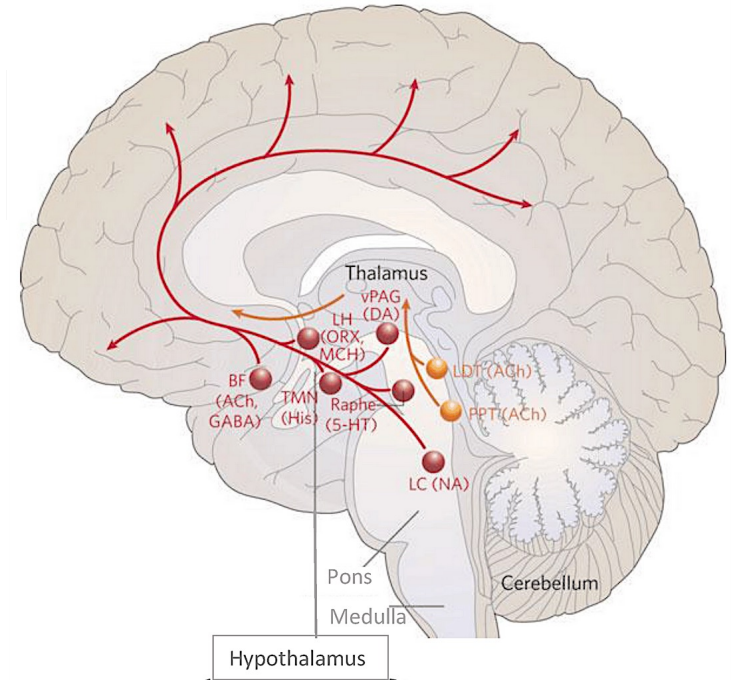
Migraine

- suprachiasmatic n.
- tuberomammillary n.
- locus coeruleus
- raphe n.



- NA
- 5-HT
- DA
- His
- PACAP
- OR
- Adenosine
- Melatonin

Sleep



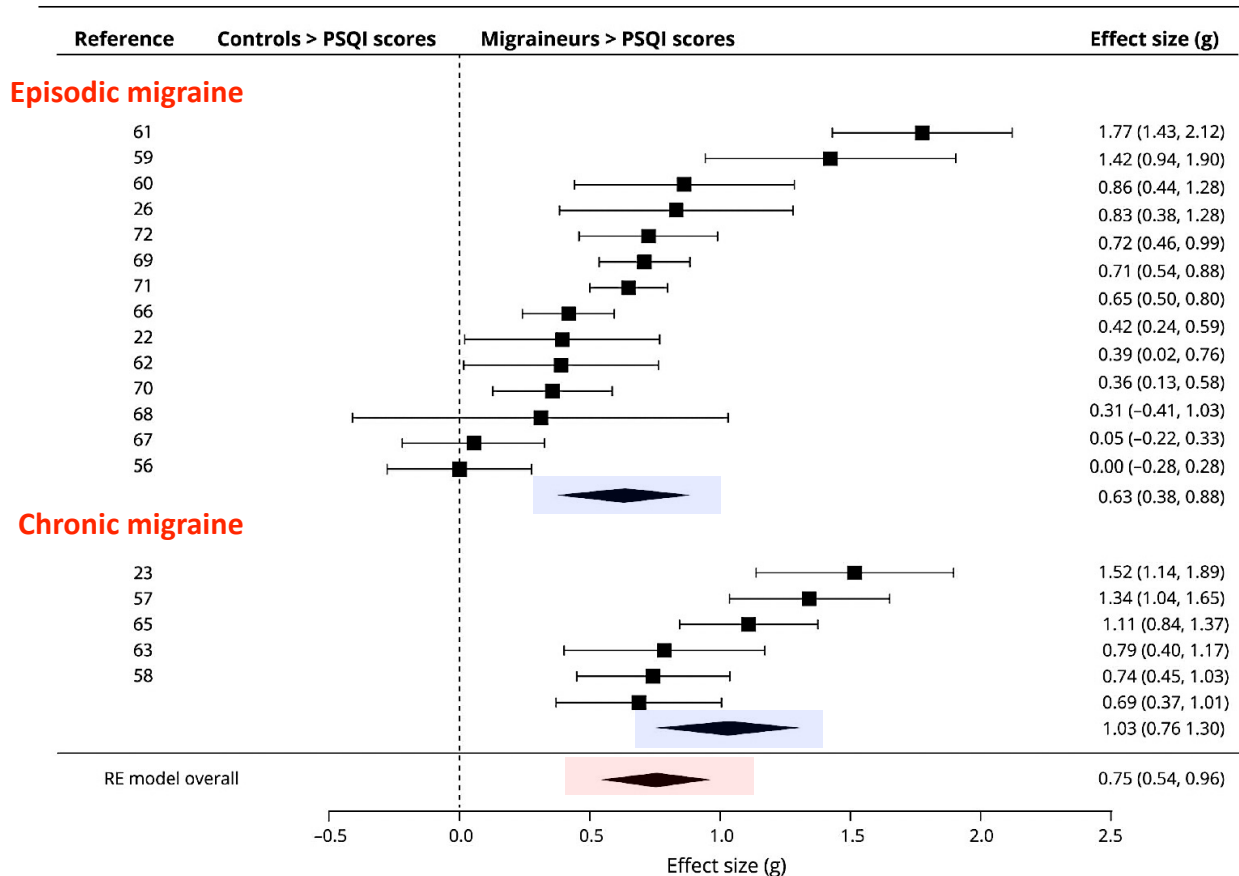
Sleep **complaints** reported by migraine patients

	Very Frequent	Frequent	Occasional	Never
Sleep Complaint				
Trouble Falling Asleep	13%	18%	22%	53%
Trouble Staying Asleep	15%	24%	22%	61%

Sleep disorders reported by migraine patients

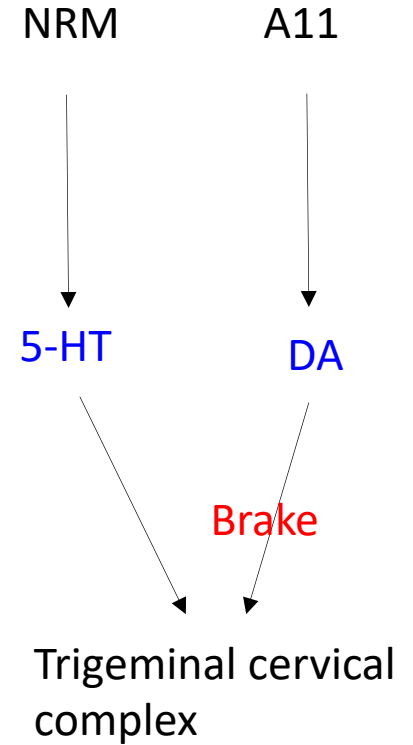
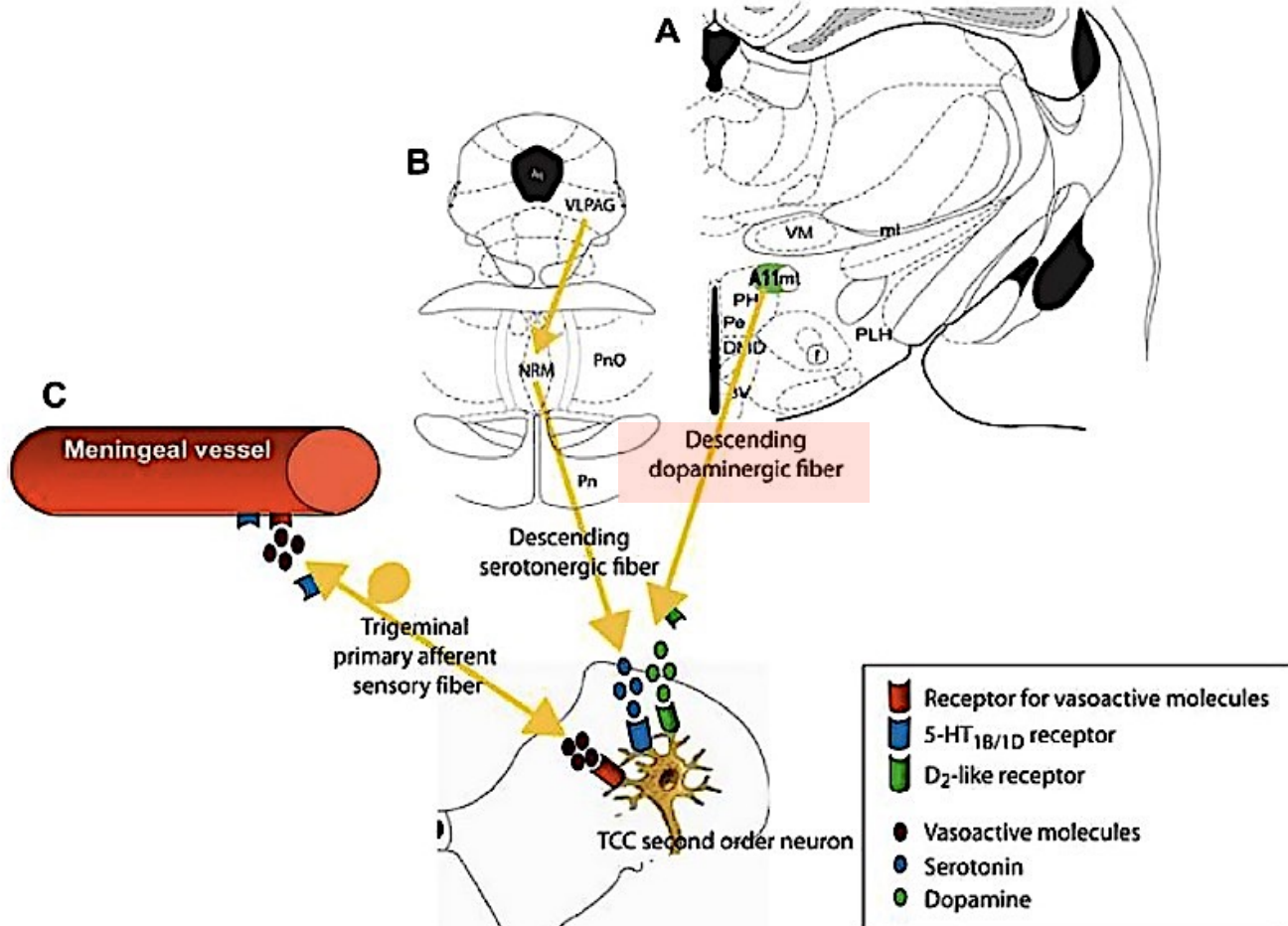
	Prevalence	OR/RR
Insomnia	25.9%	OR 2 (<i>MMD</i> >7: 2.1 vs 1)

Pittsburgh Sleep Quality (PSQI) score



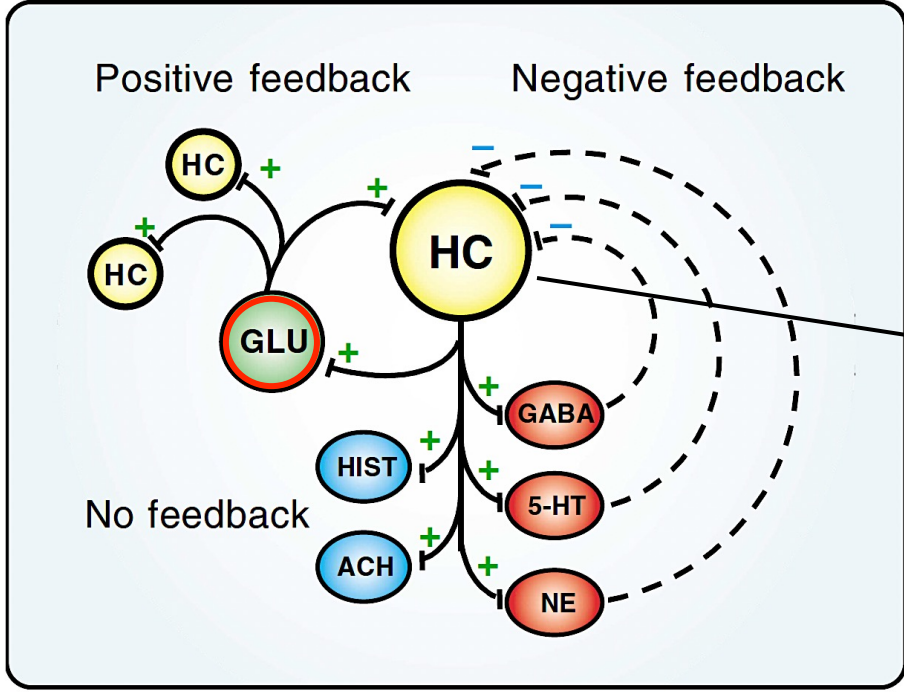
Sleep disorders reported by migraine patients

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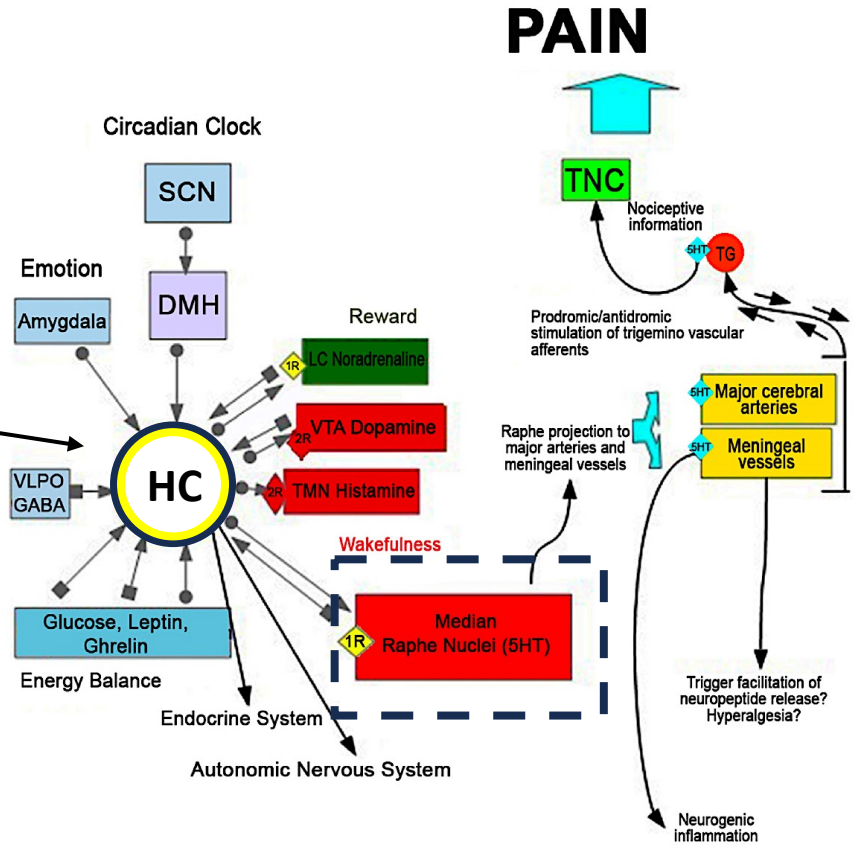


Sleep disorders reported by migraine patients

	Prevalence	OR/RR
Insomnia	25.9%	OR 2 (<i>MMD</i> >7: 2.1 vs 1)
RLS	13.7-25%	OR 2.65 (<i>MA</i> > <i>MwA</i>)
Shift work disorder	11.3%	OR 1.60

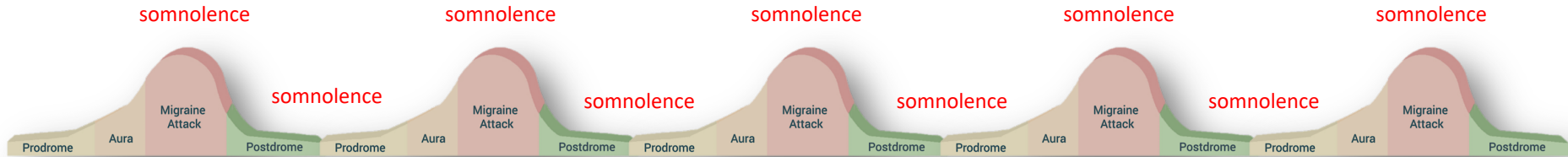
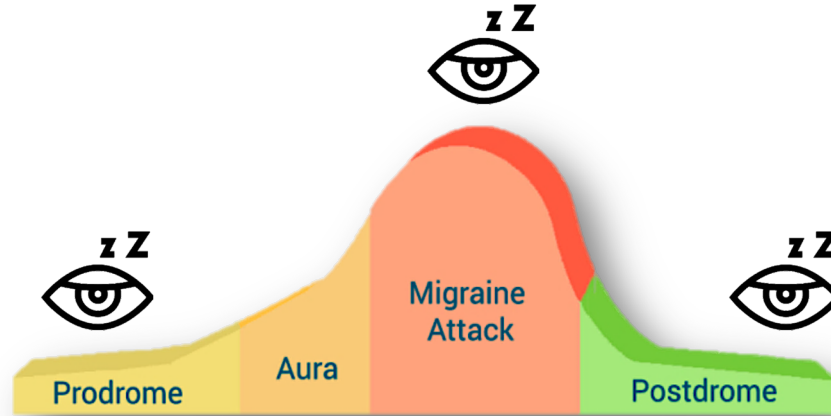


Hajak G, Geisler P. Nat Med 2003; 9(2): 170-171



Messina A, et al. Front Neurol. 2018 Feb 28;9:95.

Somnolence is common in migraine patients

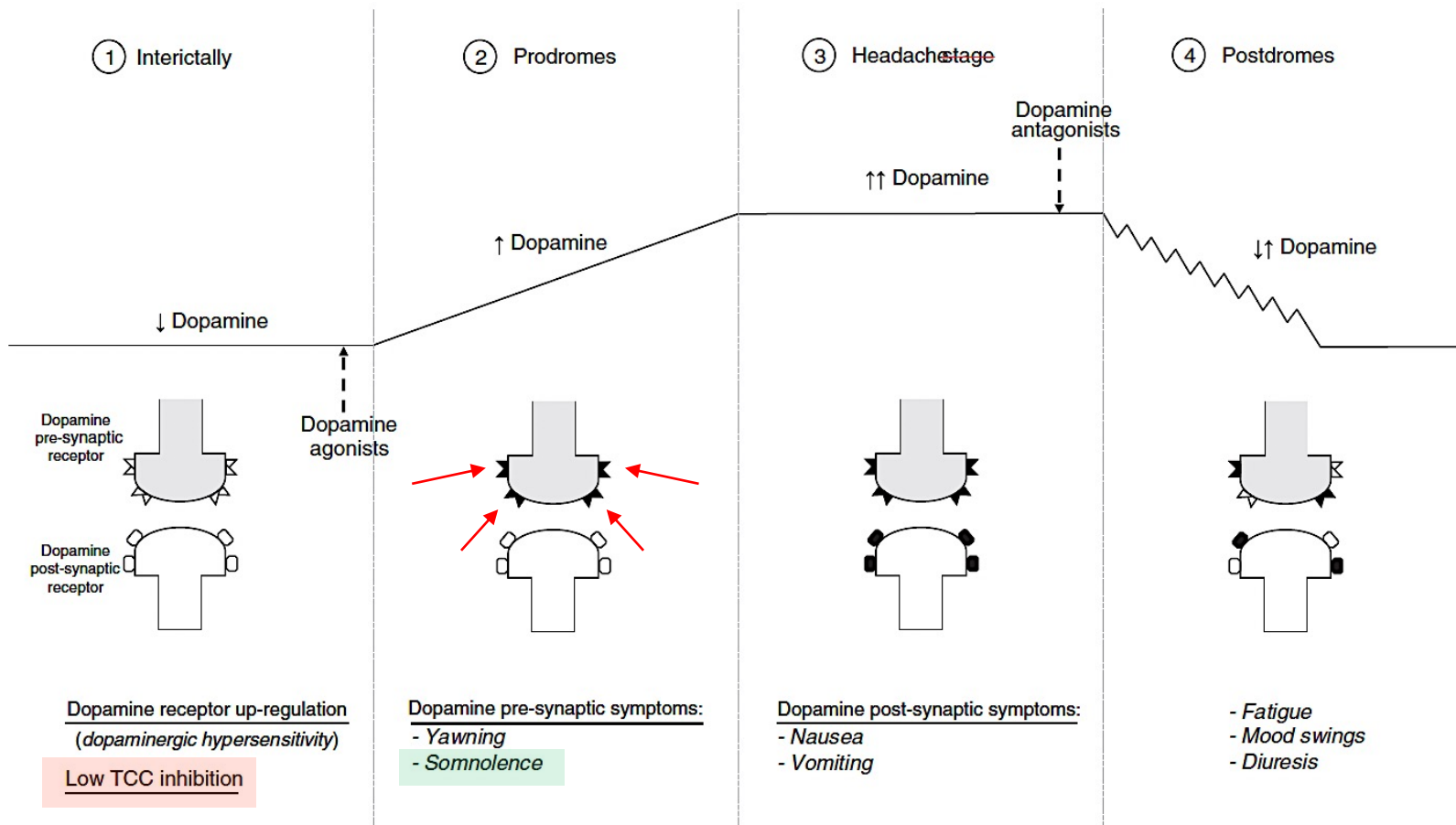


Somnolence in migraine: case-control studies

Episodic

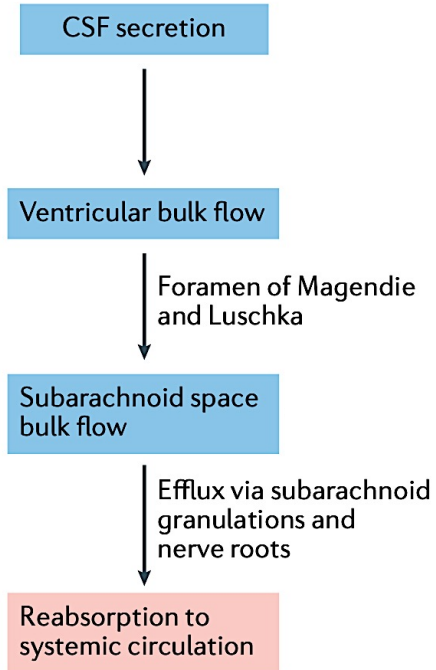
	Cases	Controls	<i>p</i> /OR (95%CI)
ESS	6.4 _± 3.3	5.8 _± 2.9	ns
ESS_≥10 (EDS)	14%	5%	3.1 (1.1–8.9)
PSQI	5.7 _± 3.2	4.1 _± 2.5	0.01
PSQI>5	56	32	2.7 (1.5–4.8)

Dopaminergic activity during migraine attacks

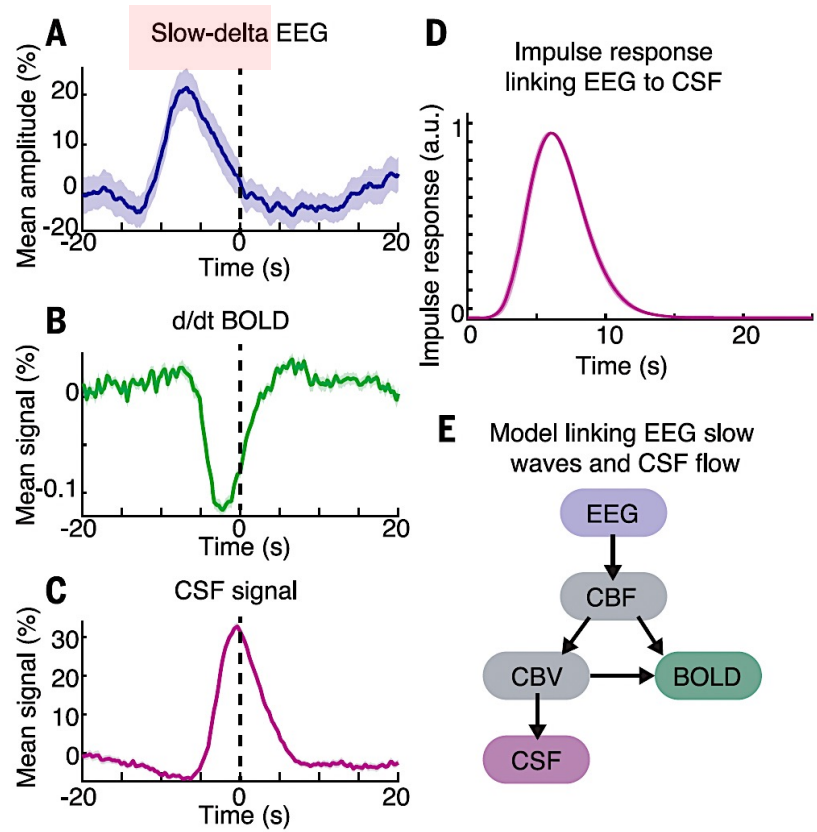


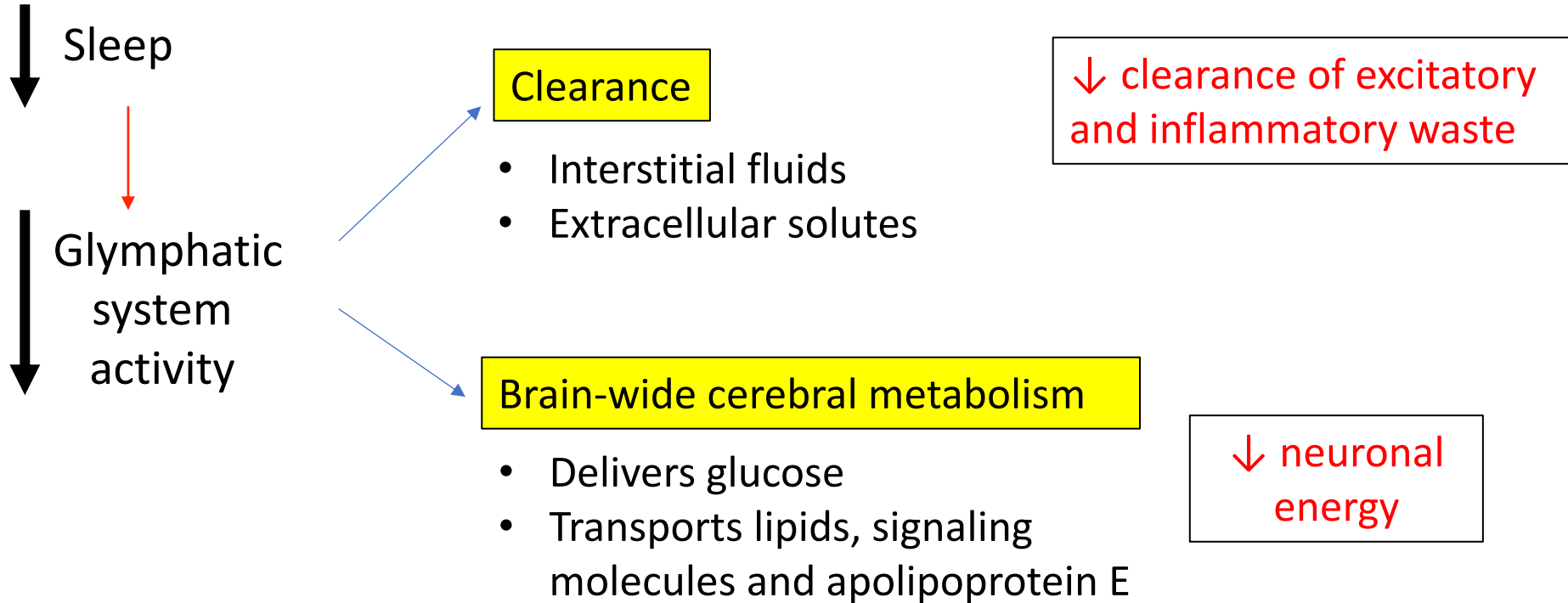
The glymphatic system

Conventional model

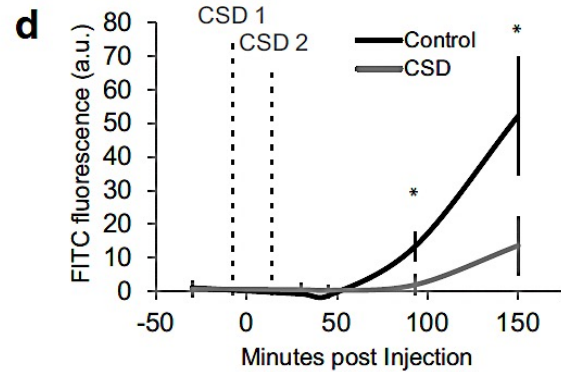
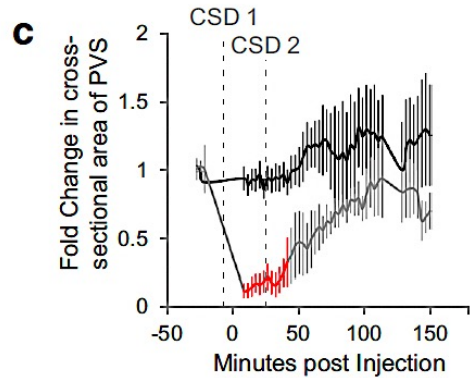


NREM sleep: oscillating electrophysiological, hemodynamic, and CSF dynamics

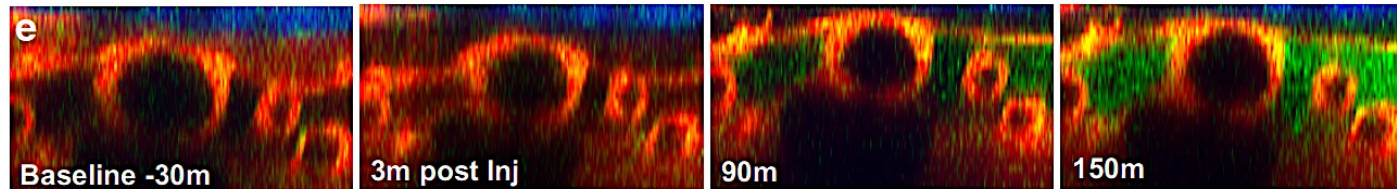




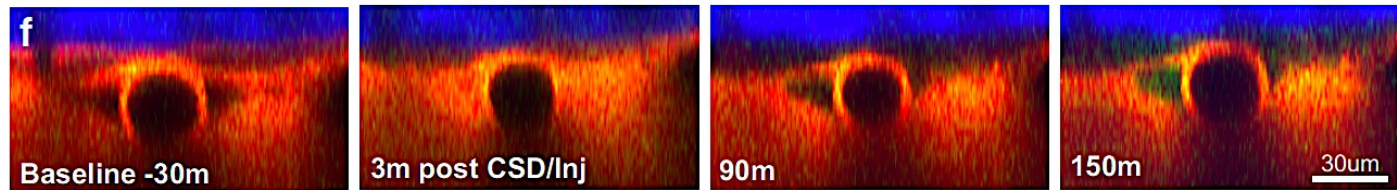
CSD closes paravascular space and impairs glymphatic flow



controls

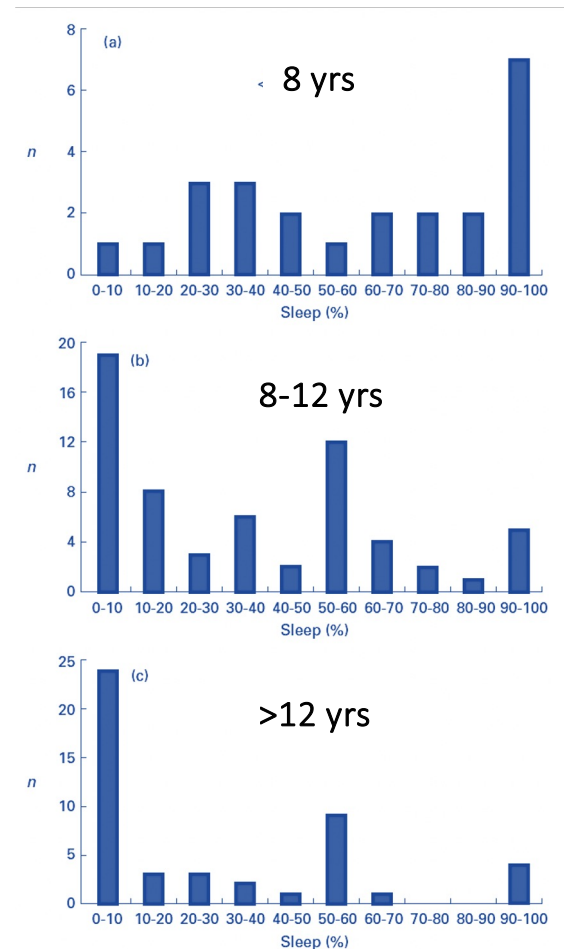


CSD mice

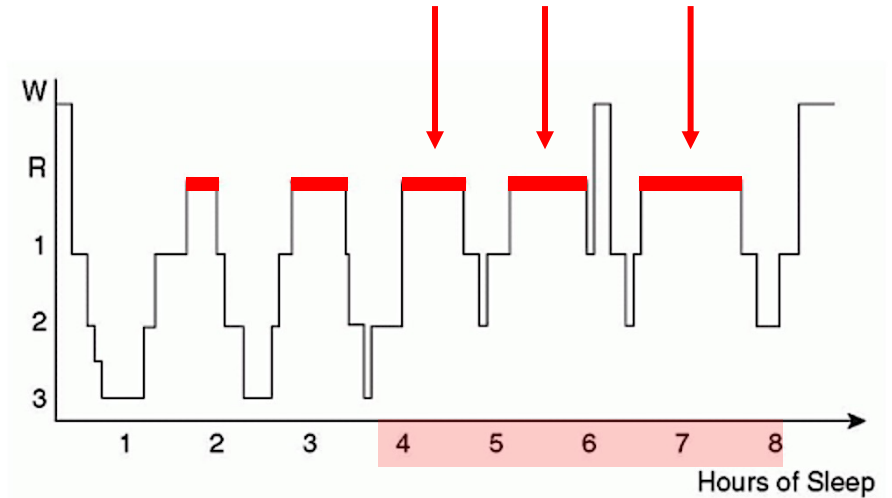
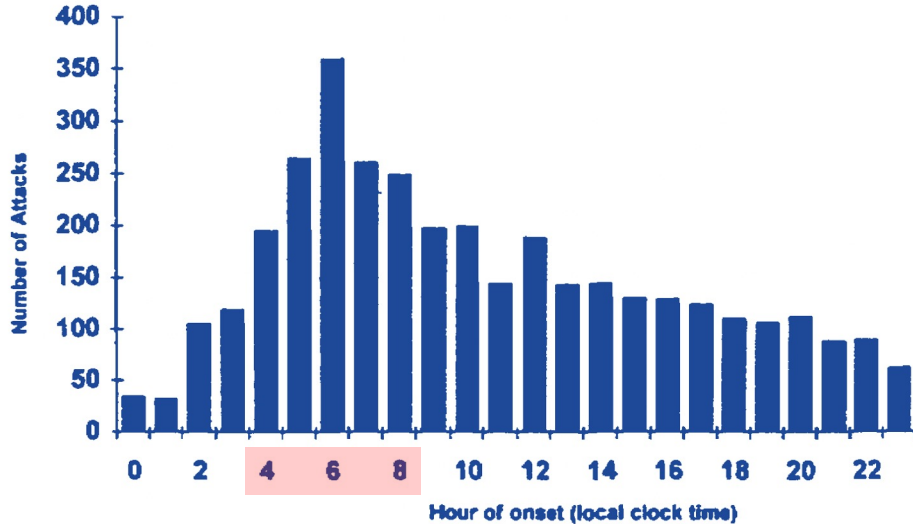


Sleep may stop the migraine attack in children

	<i>n</i>	Sleep frequency, mean (95% CI)	
<8 years	24	62% (49–75%)	M 53% F 70%
8–12 years	62	34% (26–41%)	M 39% F 26%
>12 years	47	24% (15–33%)	M 33% F 16%

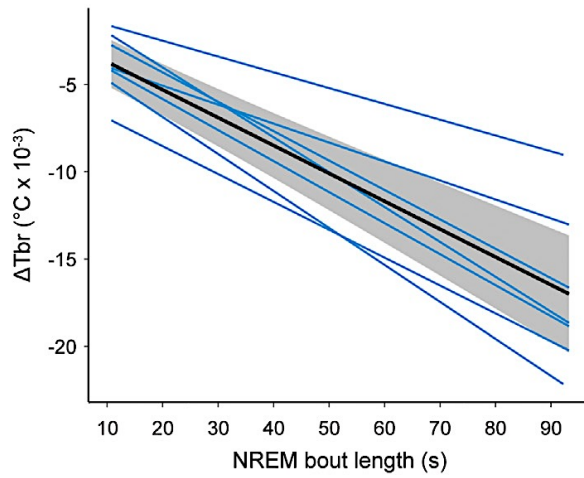


Migraine chronobiology parallels sleep phases

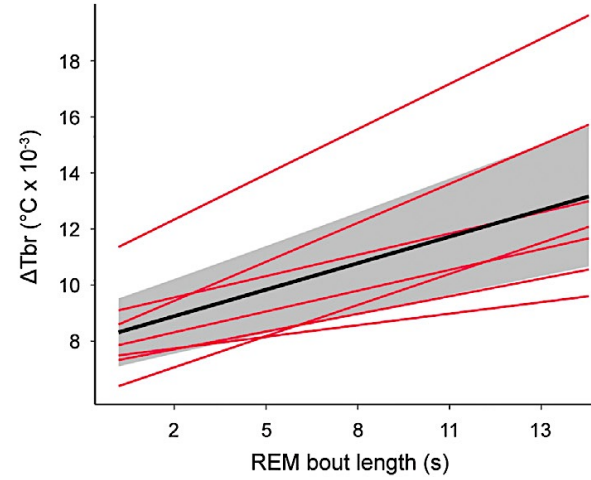


Circadian periodicity in the time of onset of 3582 migraine attacks experienced by 1696 patients

Brain cooling and warming during sleep



NREM

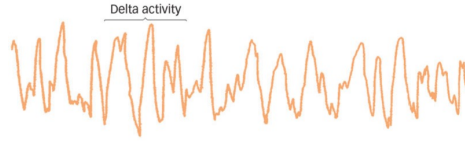


REM

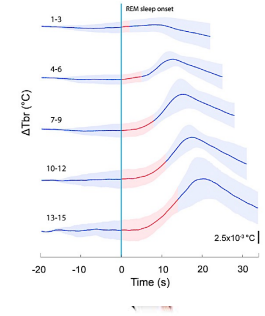
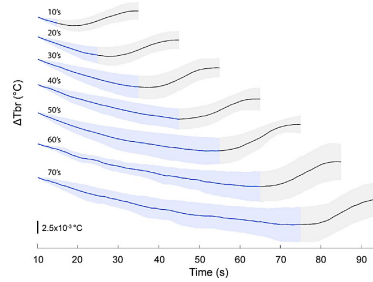
NREM

REM

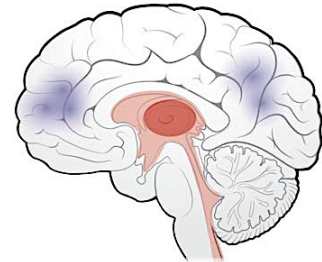
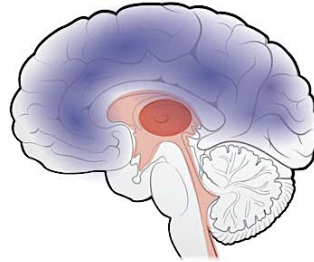
EEG



°C

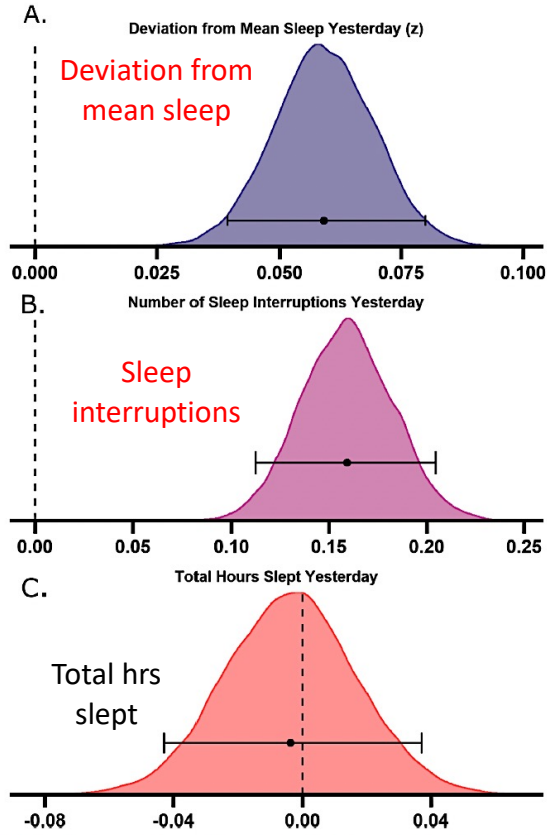


Brain metabolism



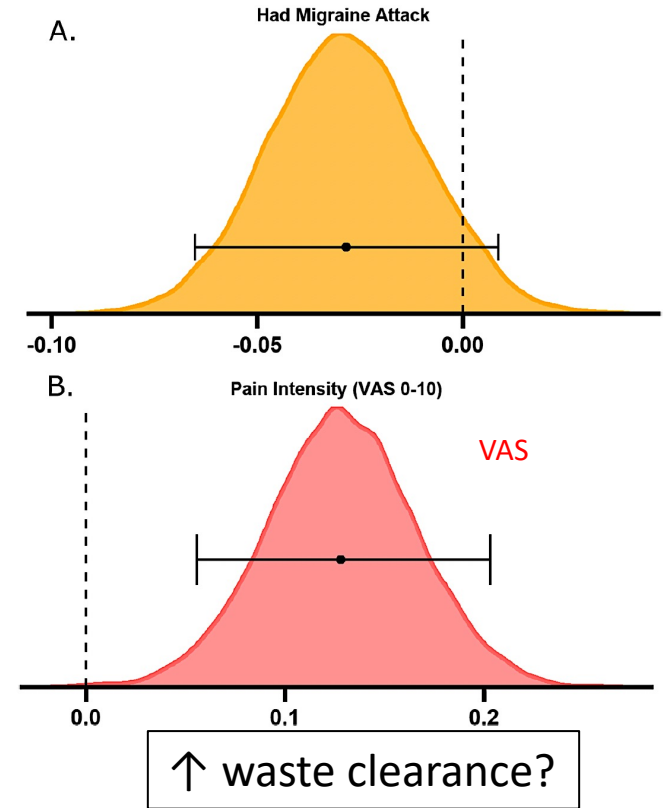
Sleep and migraine in a global sample: a Bayesian cross-sectional approach

Migraine the next day



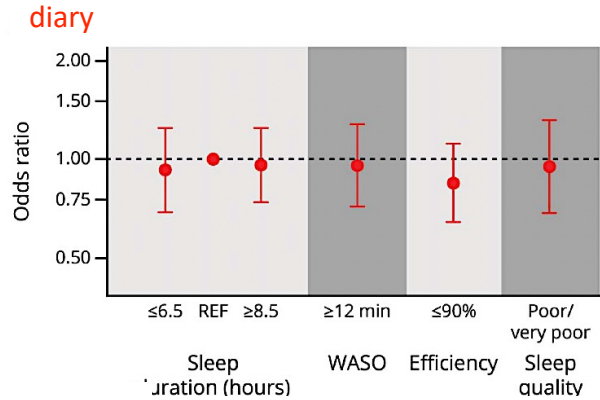
↑ sleep duration that same evening

- Retrospective
- Migraine Buddy app
- 11,166 global users
- 18–81 years



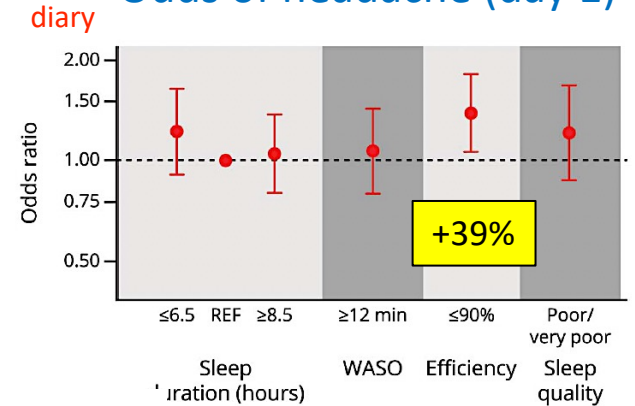
Sleep duration, fragmentation, and quality and daily risk of migraine

Odds of headache (day 0)



- Prospective
- 98 pts
- Episodic migraine
- E-diaries
- Wrist actigraphs
- 6 month

Odds of headache (day 1)



Migraine

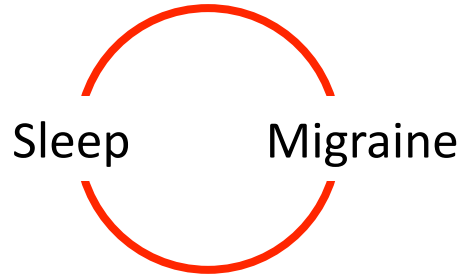
↑ risk of developing insomnia



Treat migraine



Check for insomnia evolution



- Involvement of diencephalic and brainstem regions, common neurotransmitters, neuropeptides and hormones
- Glymphatic system: potential *trait d'union*
- Shared lifestyle triggers and comorbidities

1. Investigate sleep
2. Consider sleep hygiene an inherent part of migraine management