



Bidirectional Relationships of Sleep and Epilepsy in Adults with Epilepsy

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Prevalence of sleep disorder in epilepsy patient

Table 3

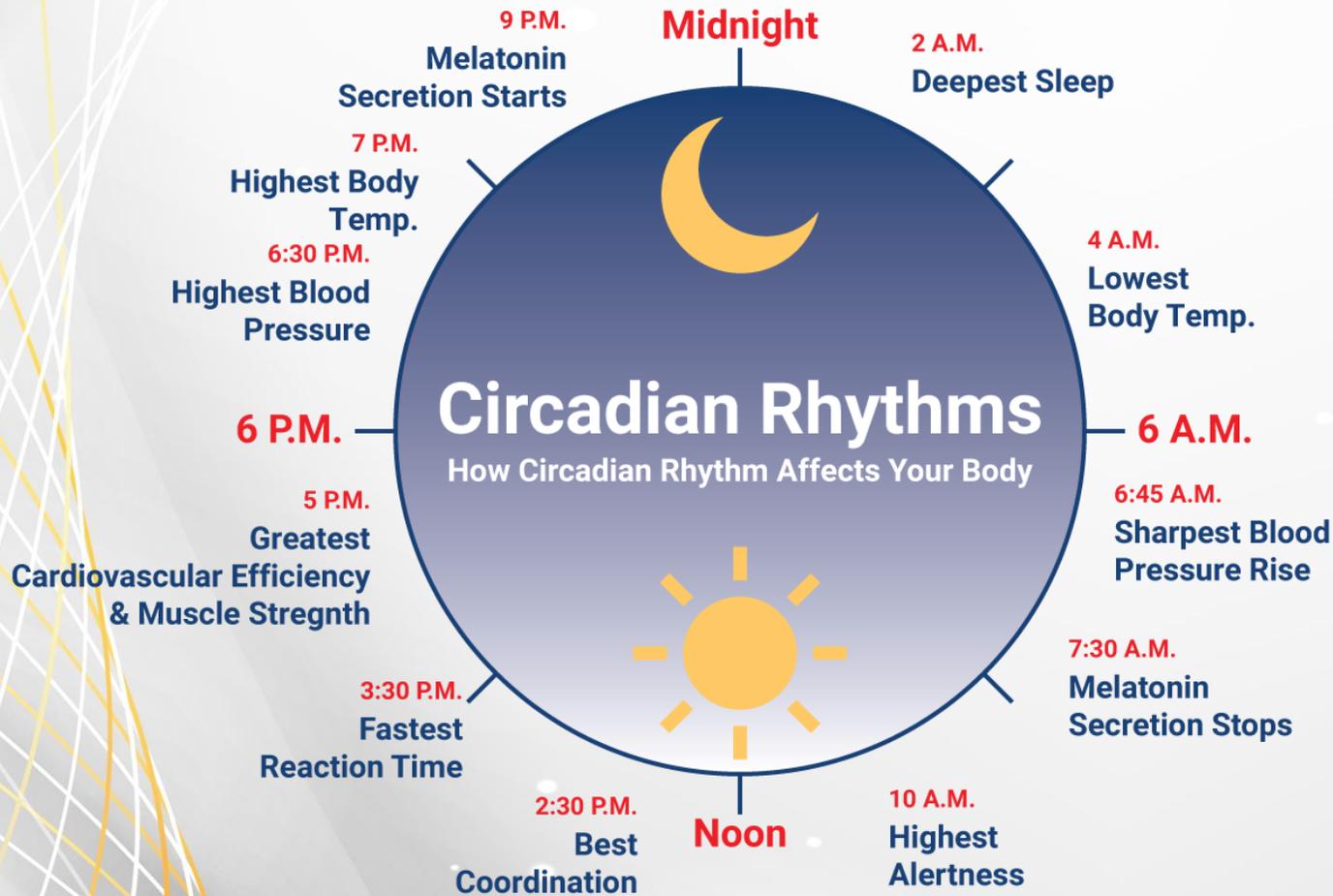
The differences in sleep complaints/disorders between the epilepsy and the control groups.

	Patients with Epilepsy %(n = 208)	Healthy Control Group %(n = 212)	p
Sleep Onset Insomnia	24	20	<0.01
Sleep Maintenance Insomnia	12	6	0.02
Insomnia	36	15	<0.01
Excessive daytime sleepiness	18	7	0.01
Epworth Sleepiness Score (>10)	23	21	0.7
Epworth Sleepiness Score (>14)	7	5	0.3
Parasomnia		8	0.32
Somnambulism	11	15	0.07
Night terror	22	40	0.10
Sleep Paralyzes	32	6	0.05
Probable RBD	12	33	0.21
Sleep talking	39		
Restless Legs Syndrome	5	3	0.2
Berlin Questionnaire (Sleep Related Breathing Disorder)	14	8	0.04
Bad Quality of Sleep – PSQI	30	16	<0.01
Depression (BDS-PC)	40	23	<0.01

PSQI, Pittsburgh Sleep Quality Index; RBD, REM Behavioral Disorder; BDS-PC, Beck Depression Scale for Primary Care.



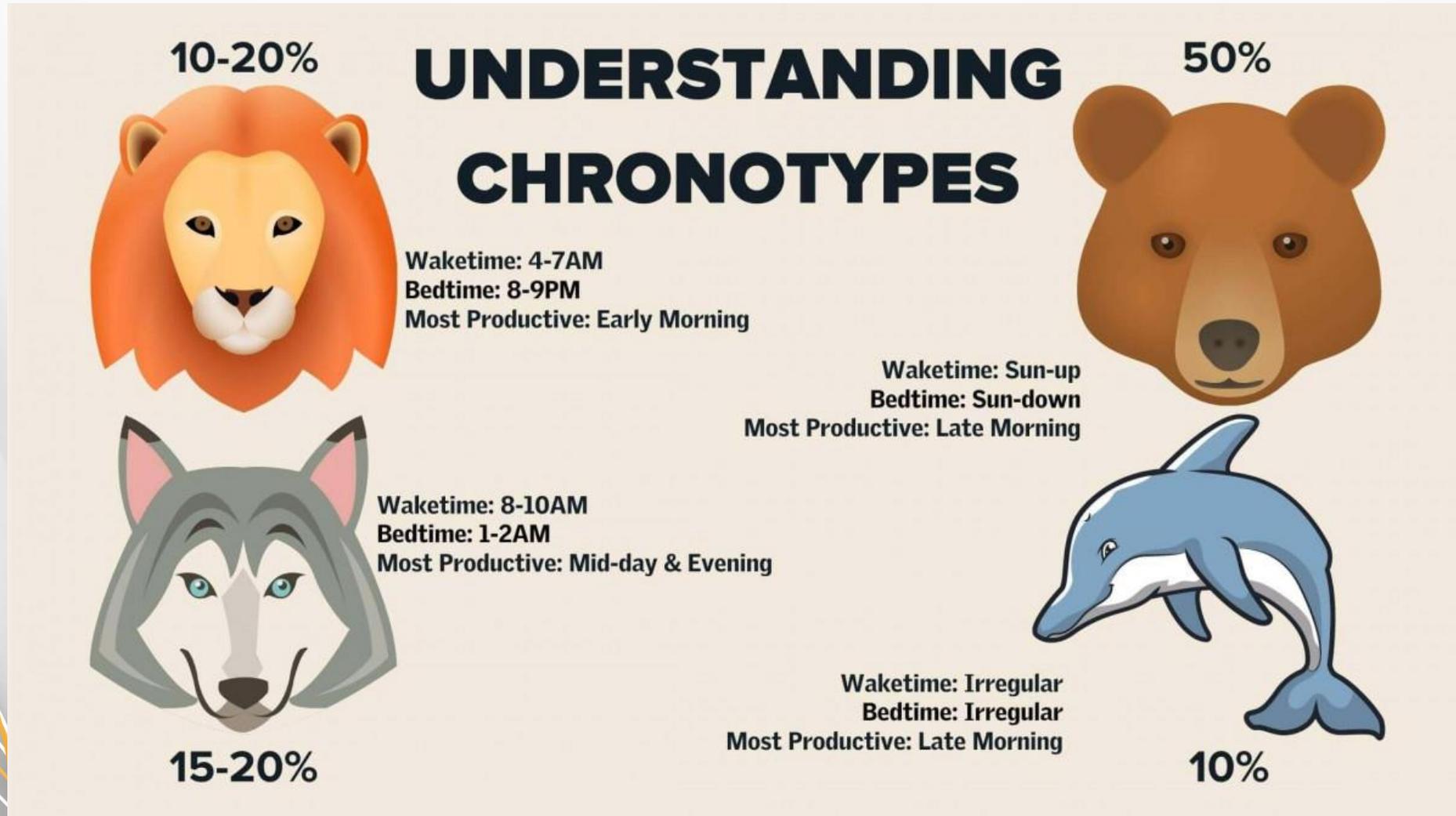
Definition of terms



- Circadian rhythm
 - “about daily”
 - An endogenous free-running (approximately) 24 h period even in the absence of day-night cycle.
 - Should be entrainable

Definition of terms

- Chronotypes

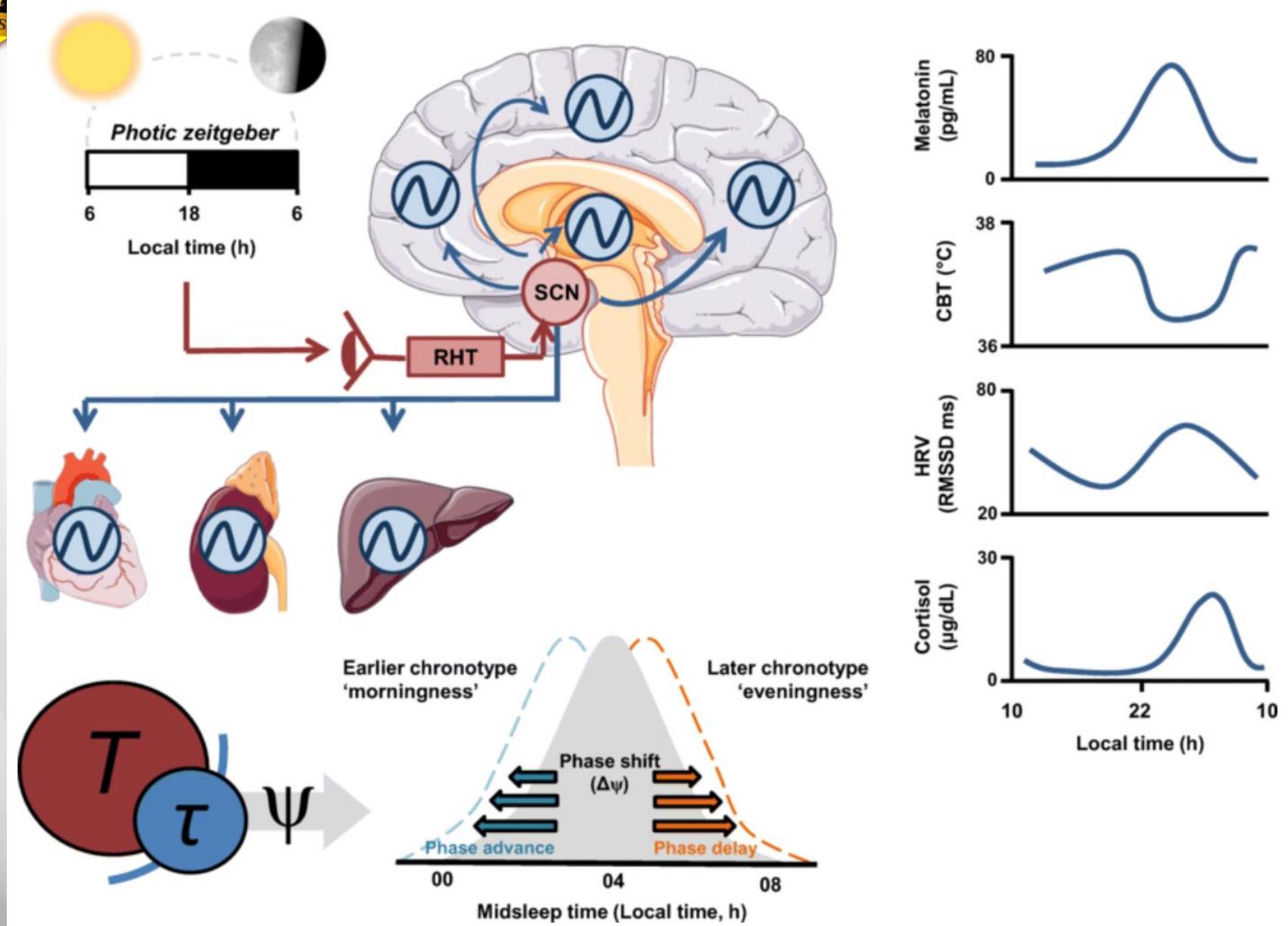




Definition of terms

- Diurnal rhythm
 - Diurnal rhythm is a biological rhythm that is synchronized with the day-night cycle.
 - A diurnal rhythm may or may not be a circadian rhythm
- Multidien rhythm (infradian)
 - Refers to rhythm with a time period covering several days
- Untradian rhythm
 - Refer to rhythms with periods of less than 24 hr
- Zeitgeber
 - Time giver , is an external or environmental temporal cue that can entrain or synchronize a biological rhythm

Circadian time keeping system



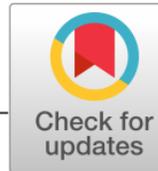


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SUPPLEMENT ARTICLE

Epilepsia®

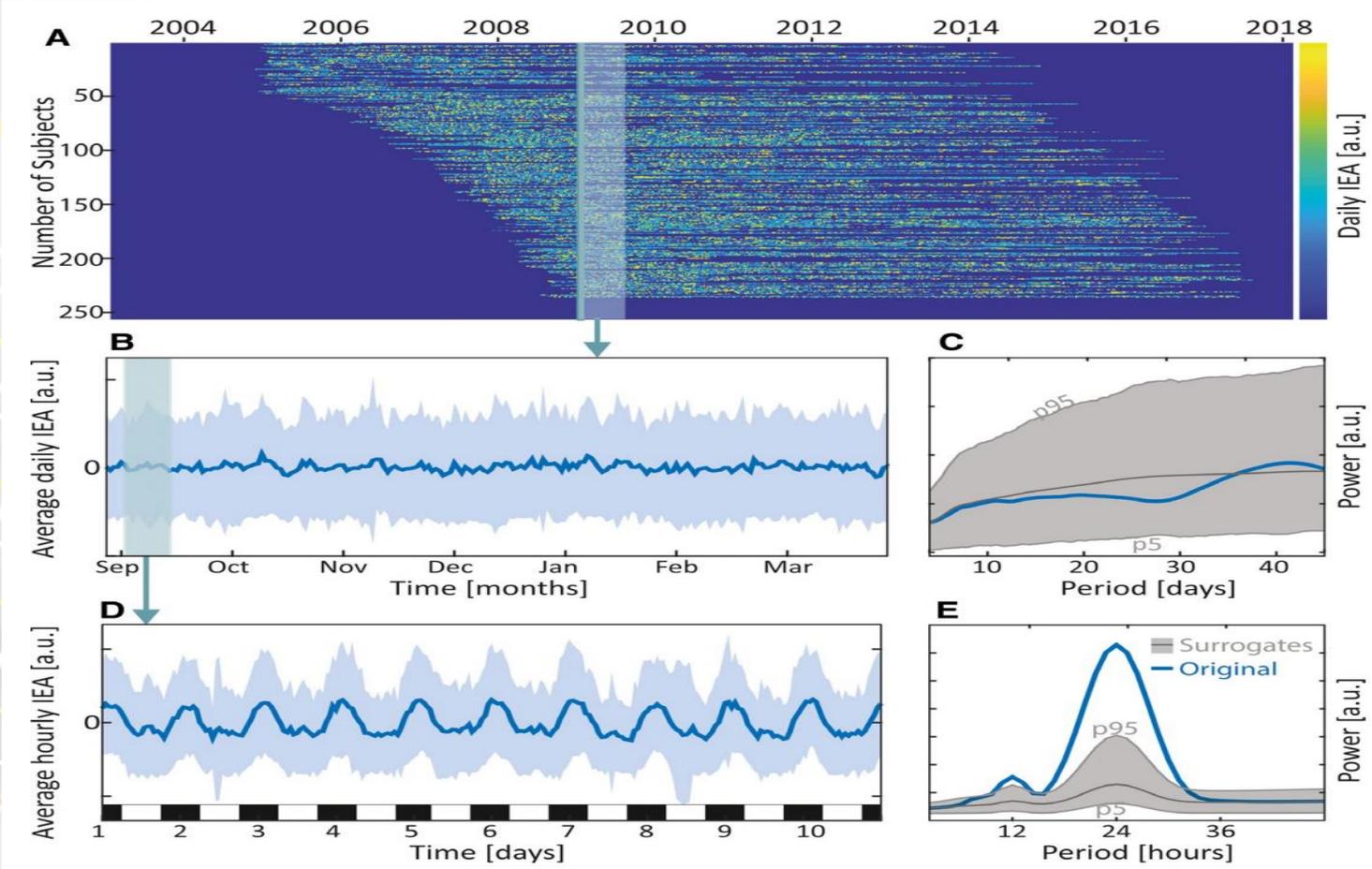
Cues for seizure timing

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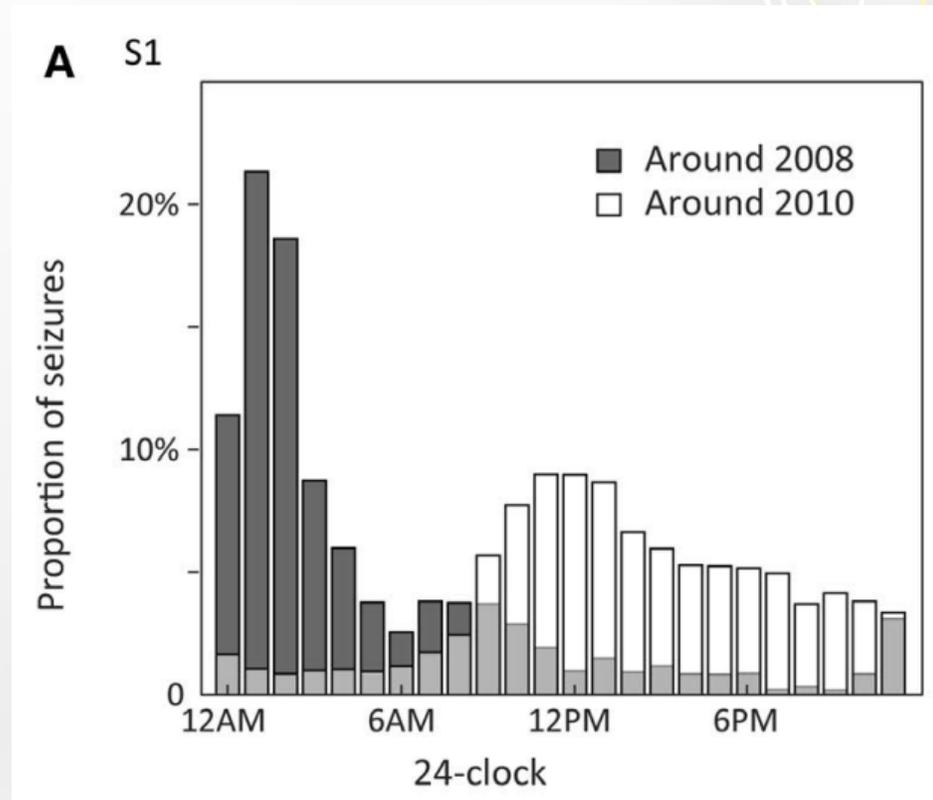
- Day night cycle, reflecting the rotation of the Earth in 24 hours, is considered the first order zeitgeber in mammals
- Rhythms of activity, social interactions, food intake, and body temperature are considered second-order zeitgebers.



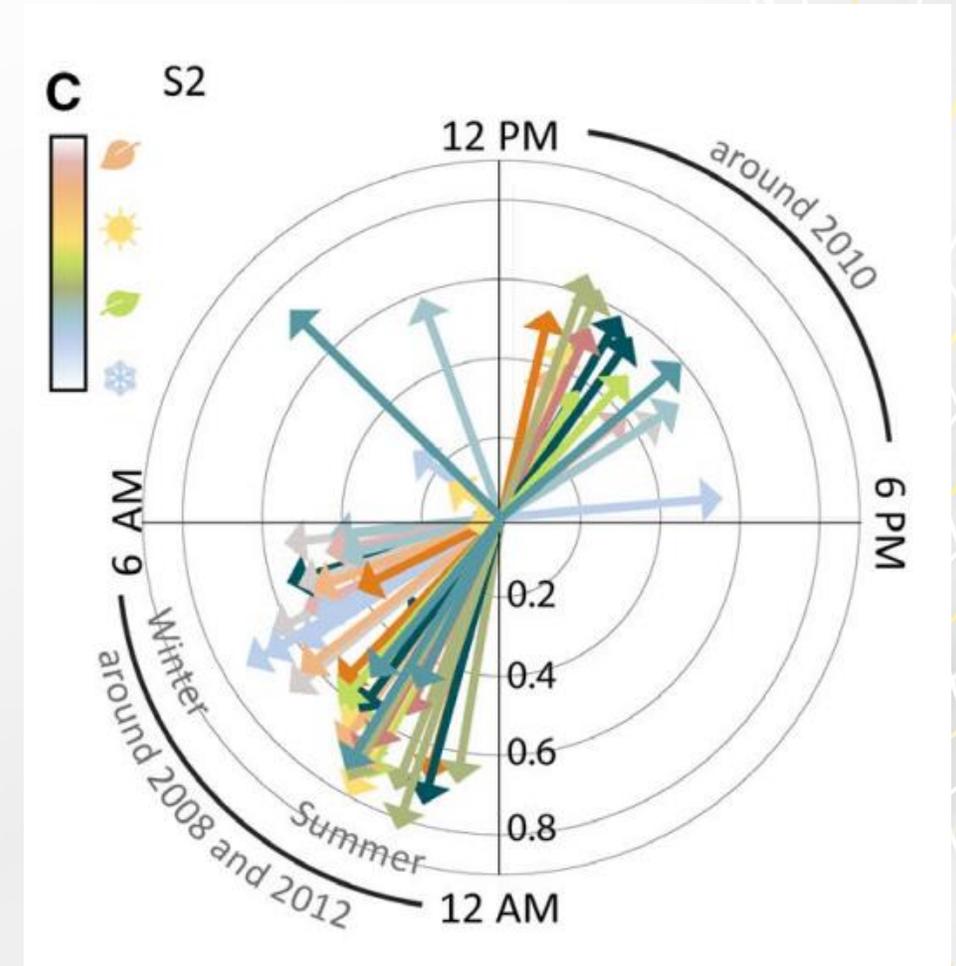
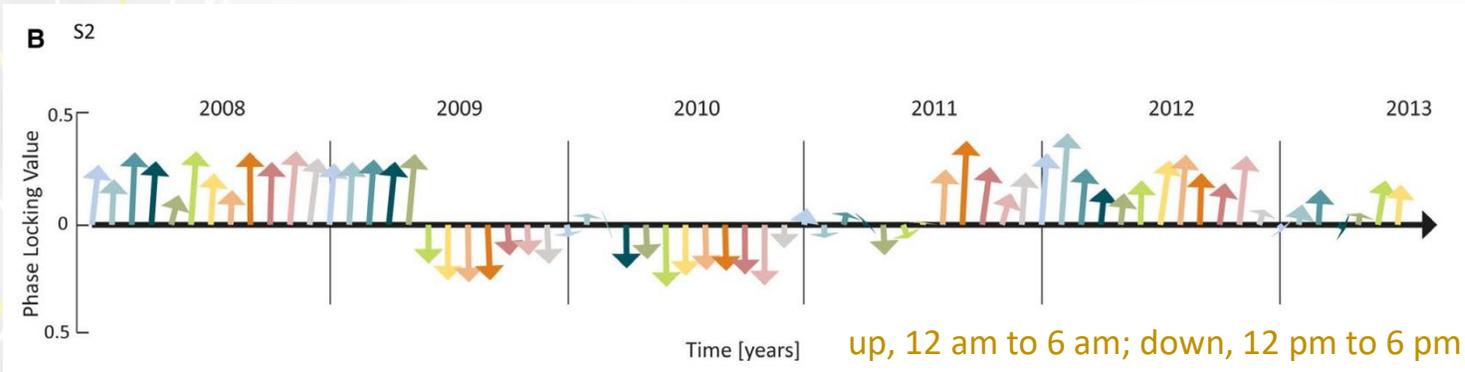
Putative zeitgebers: circadian timescale



The rare phenomenon of complete day-night flip



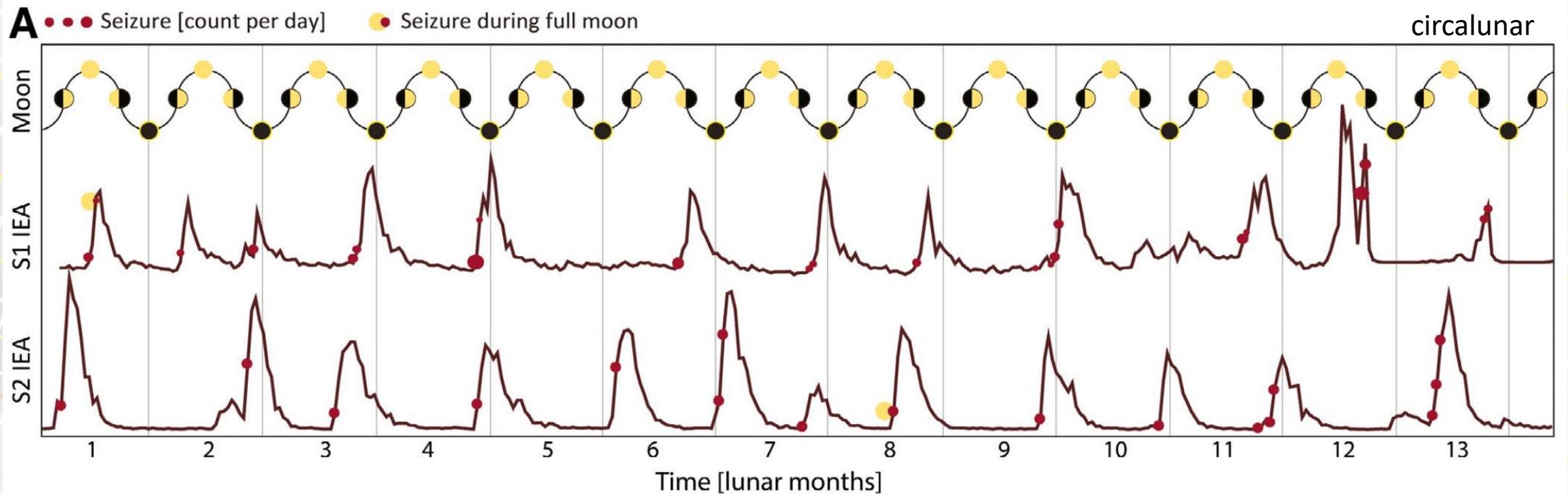
Putative zeitgebers: circadian timescale



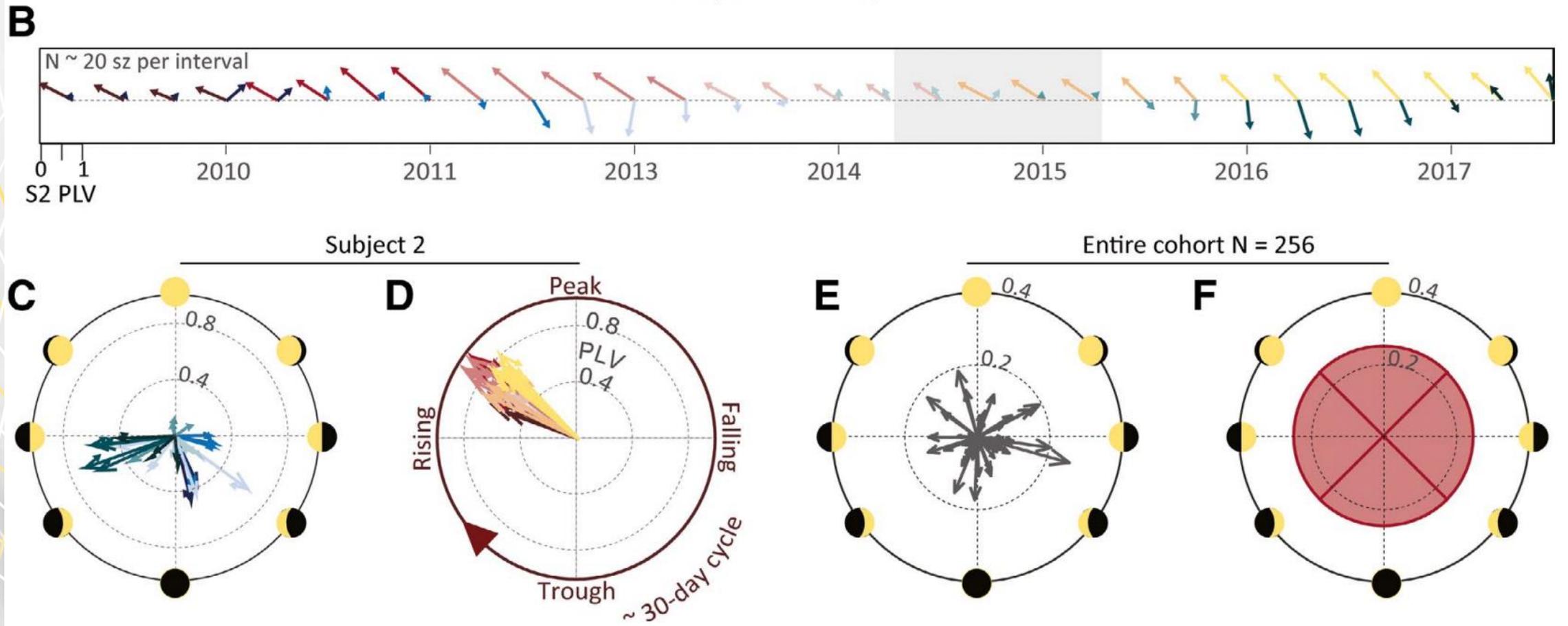
- Seasons modulated the peak circadian time for seizures
- One subject had seizures at night for years, but seizures occurred closer to the morning during winter months and closer to the evening during summer months

Putative zeitgebers: multidien timescale

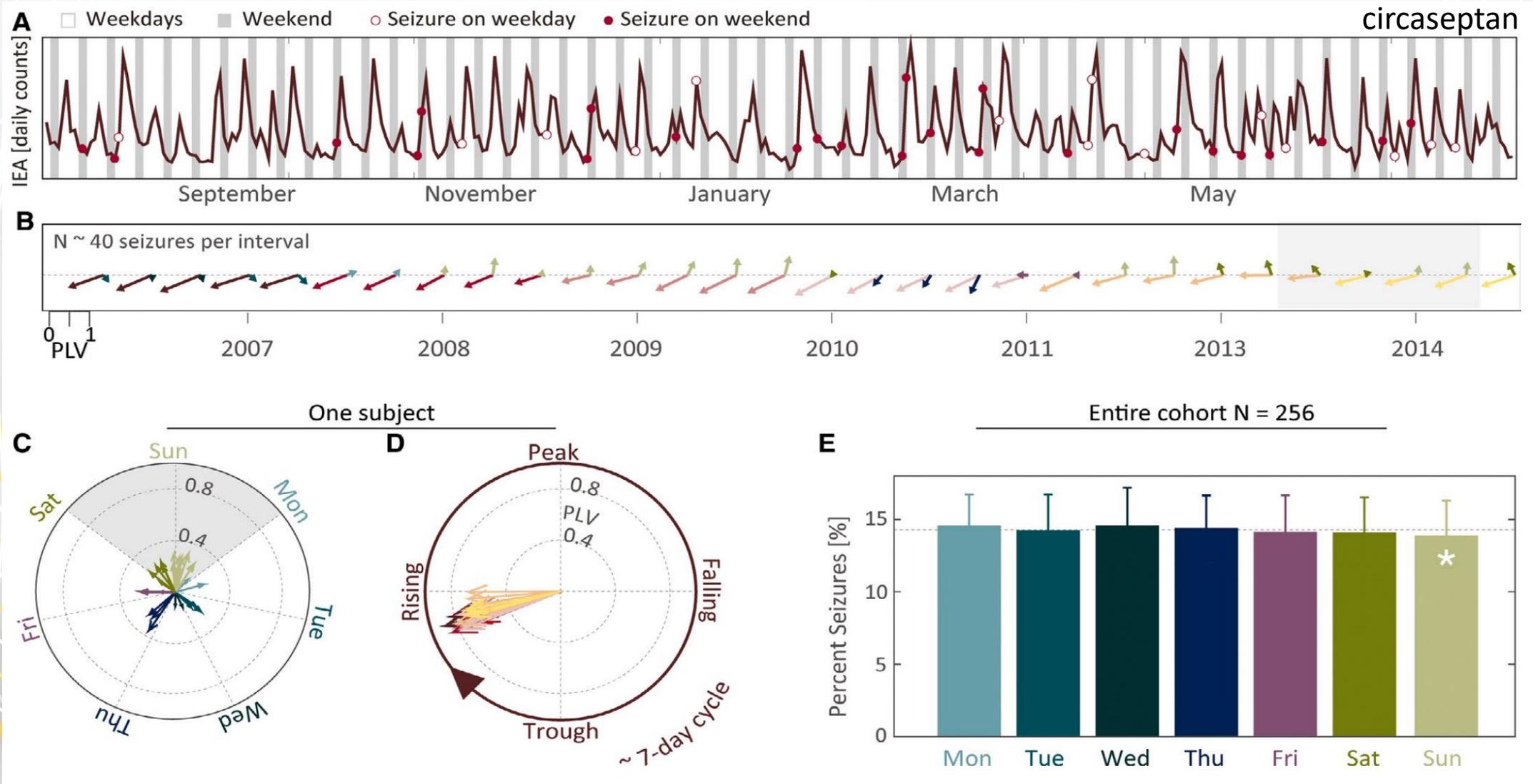
- Multidien cycle of IEA often have a period of 25-35 days, so approximate synchrony with lunar cycles will occur occasionally by chance



Putative zeitgebers: multidien timescale

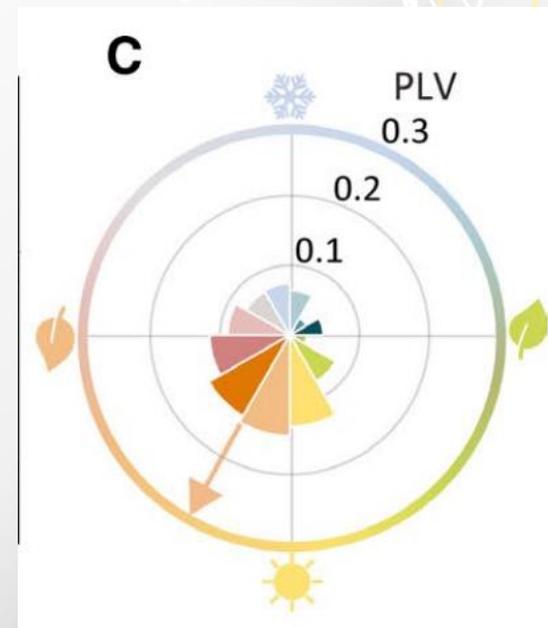
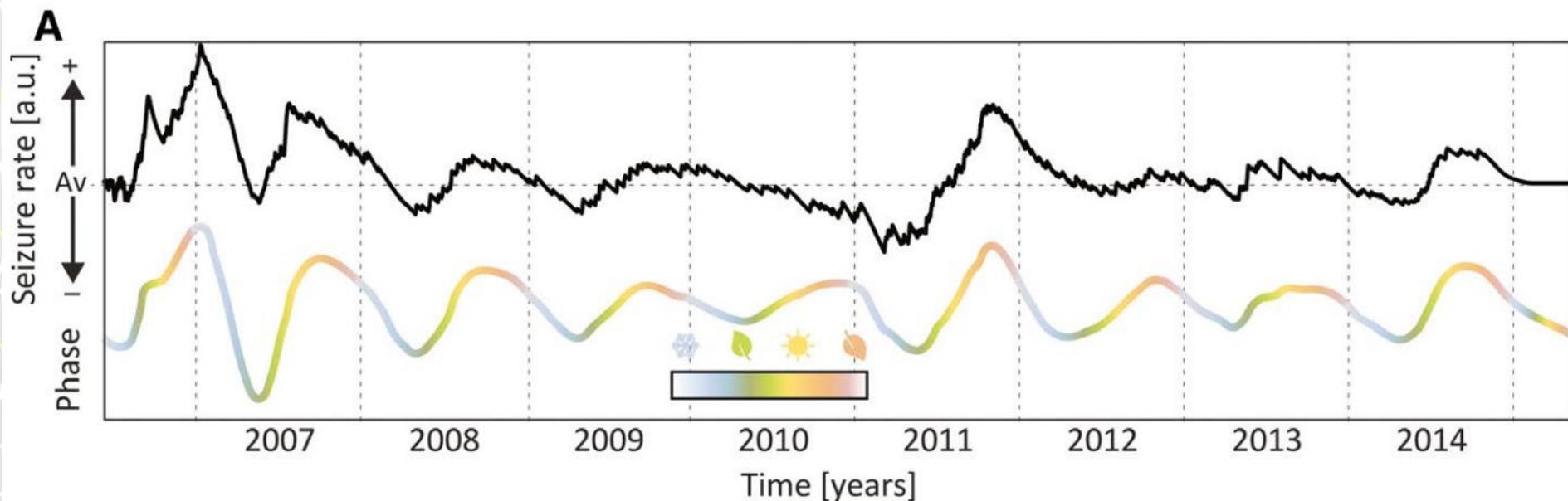


Putative zeitgebers: multidien timescale



Putative zeitgebers: circannual timescale

“seizure rate systematically increases in summer-autumn”





Biological rhythms relevant to epilepsy and their zeitgebers

Cycle	Period	Examples of endogenous cycle	Possible zeitgebers (period)	Planetary cycle
Ultradian	<24 h	NREM-REM sleep cycle	Tidal cycles (12.5 h) ^a	Earth rotation
Circadian	~24 h	Brain states Activity cycle Hormonal/metabolic cycles	Day-night cycle (24 h) ^b Atmospheric temperature cycle (24 h) ^a	Earth rotation
Multidien	~5 to ~60 d	Menstrual cycle Other hormonal/metabolic cycles	Weekdays cycle (7 d) ^c Gregorian calendar (28-31 d) ^c Moon cycle (27.3 and 29.5 d) ^c Modulation of tidal cycle (13.7, 14.8, 206 d) ^a Weather ^a	Moon revolution
Circannual	~365 d	Seasonal influences on physiology Hormonal/metabolic cycles (?)	Photoperiod cycle (365 d) ^a Atmospheric temperature ^a Seasonal Weather ^a	Earth revolution

Note.: Endogenous cycles modulating seizure rates and their possible zeitgebers are listed in four categories from shortest to longest period.

^aNot thoroughly investigated.

^bConfirmed as important.

^cLikely unimportant.



External-endogenous borderland

TABLE 3 Precipitating factors for seizures

Precipitants

Medication noncompliance

Alcohol or drugs

Stress

Physical exercise

Sleep deprivation^a

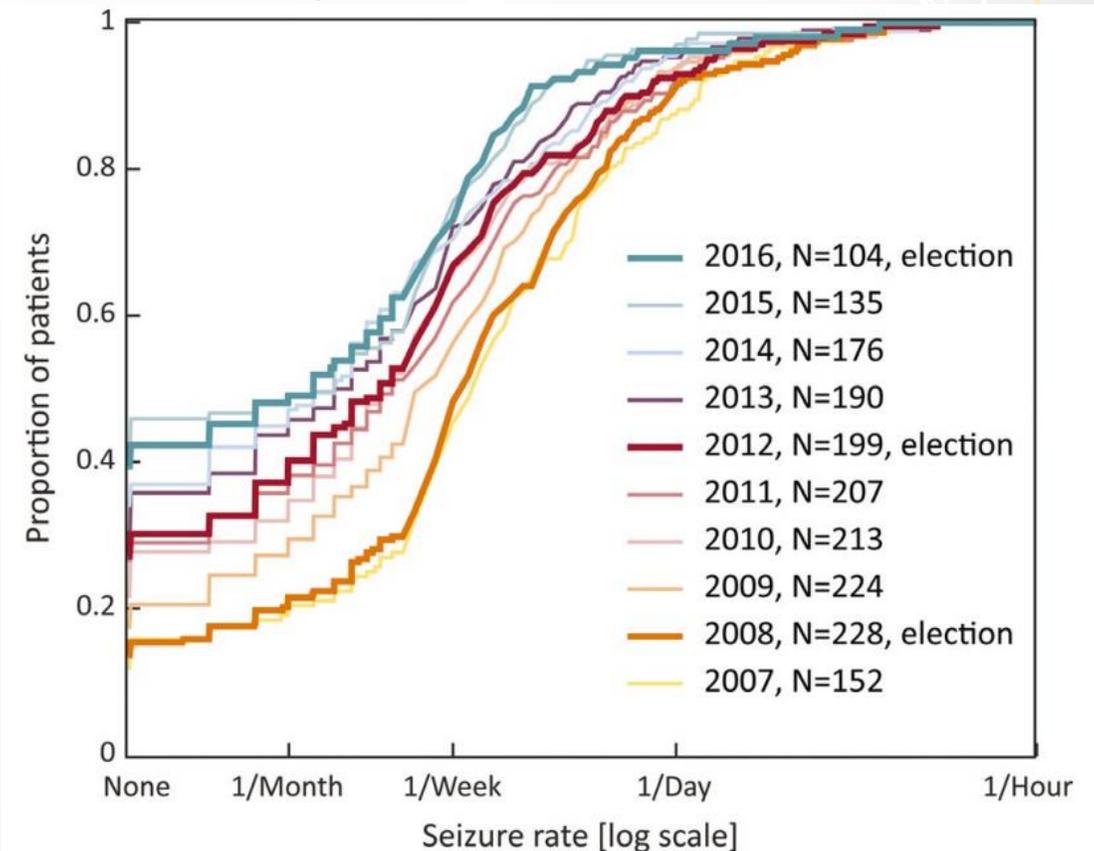
Fatigue^a

Flashing lights (rarely)

Reflex seizures (rarely)

^aCommonly accepted precipitants for which evidence is lacking.

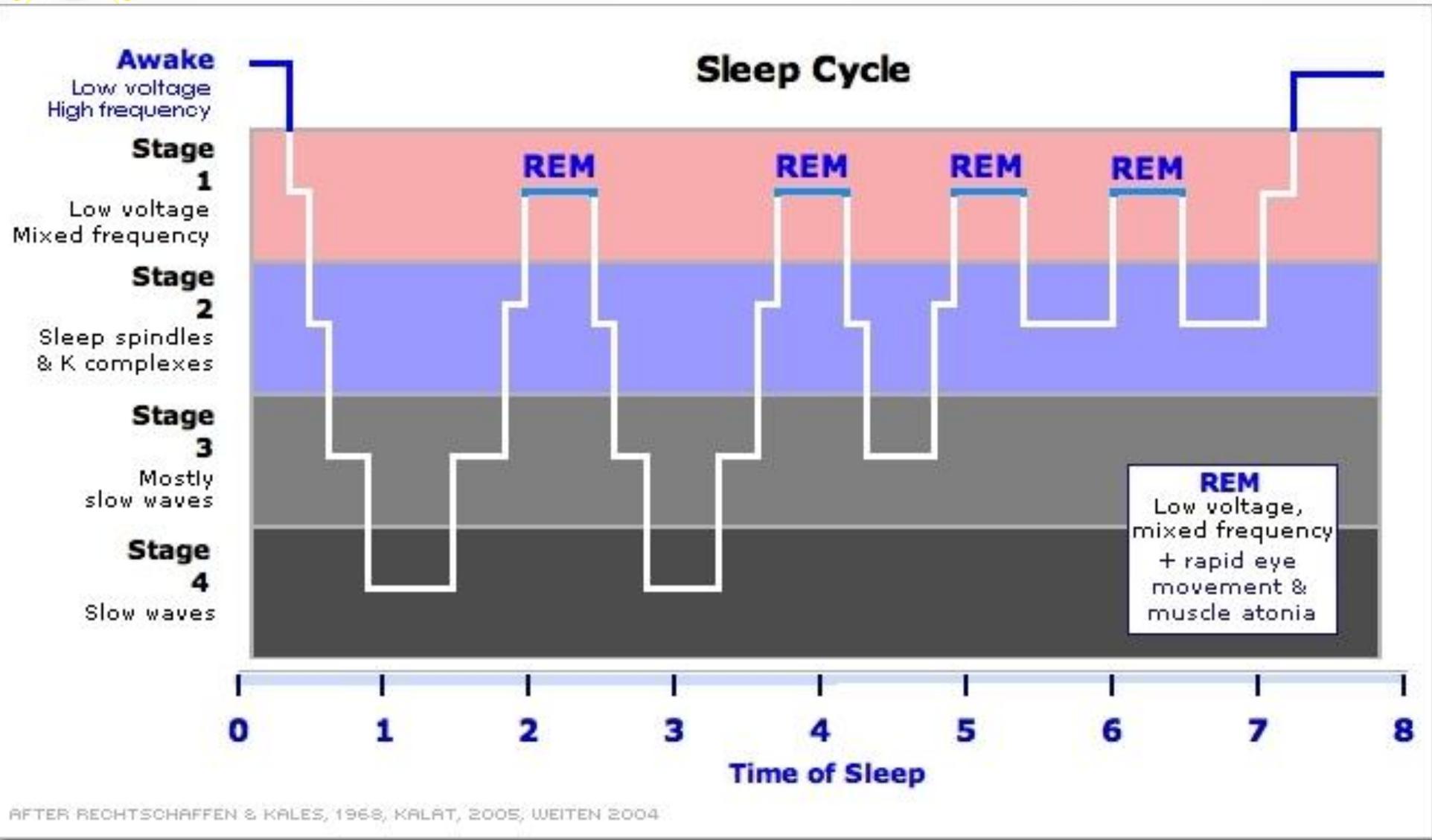
Election years and seizure rates





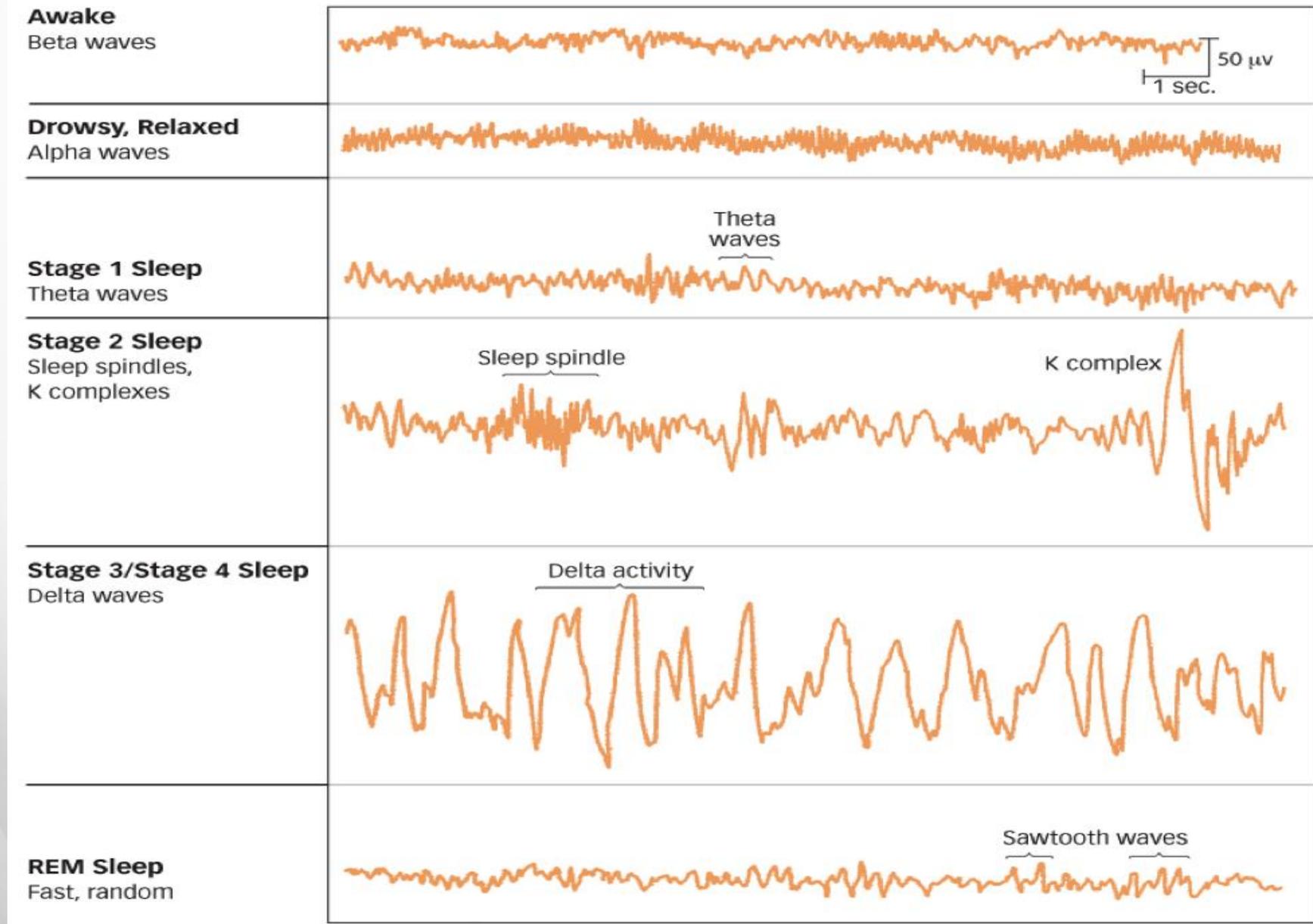
Endogenous cycles

- Sleep-wake cycle : brain arousal states
- Hormonal cycle
- Other cycle
- Chronotypes

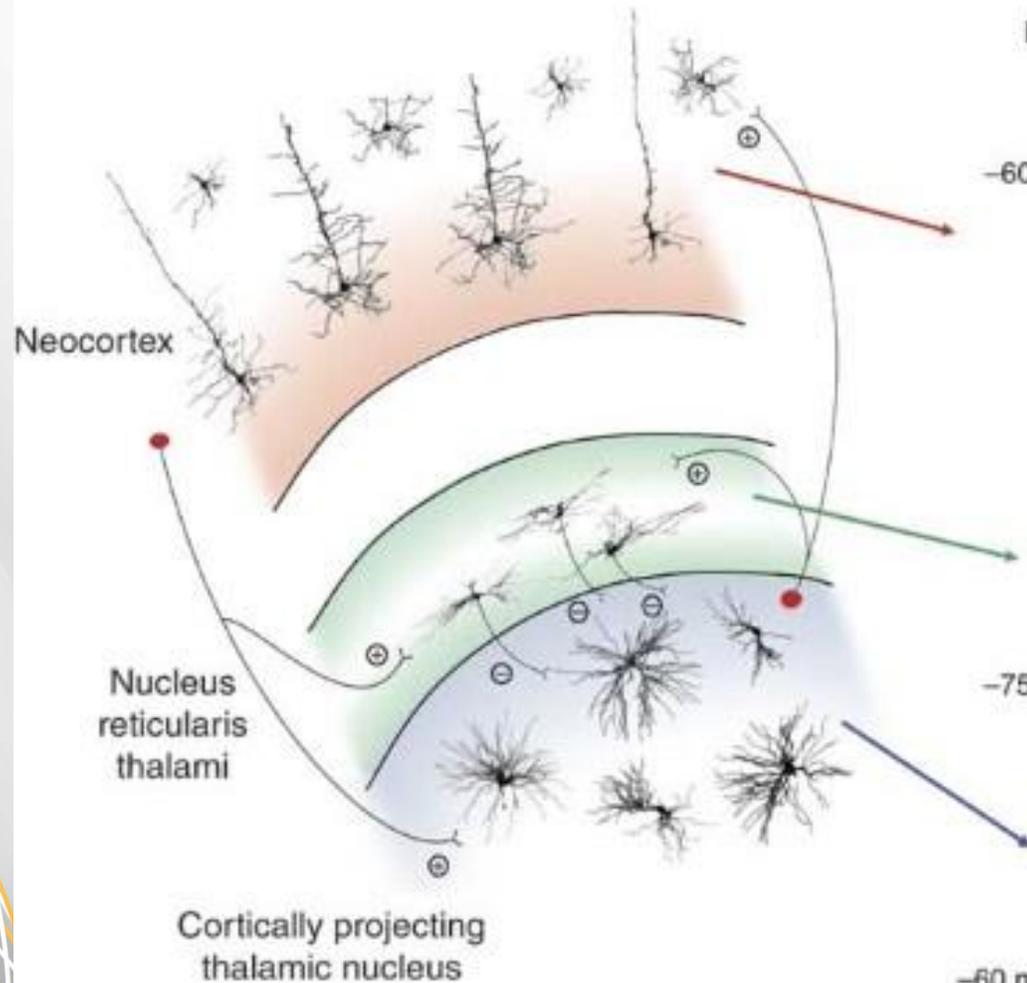




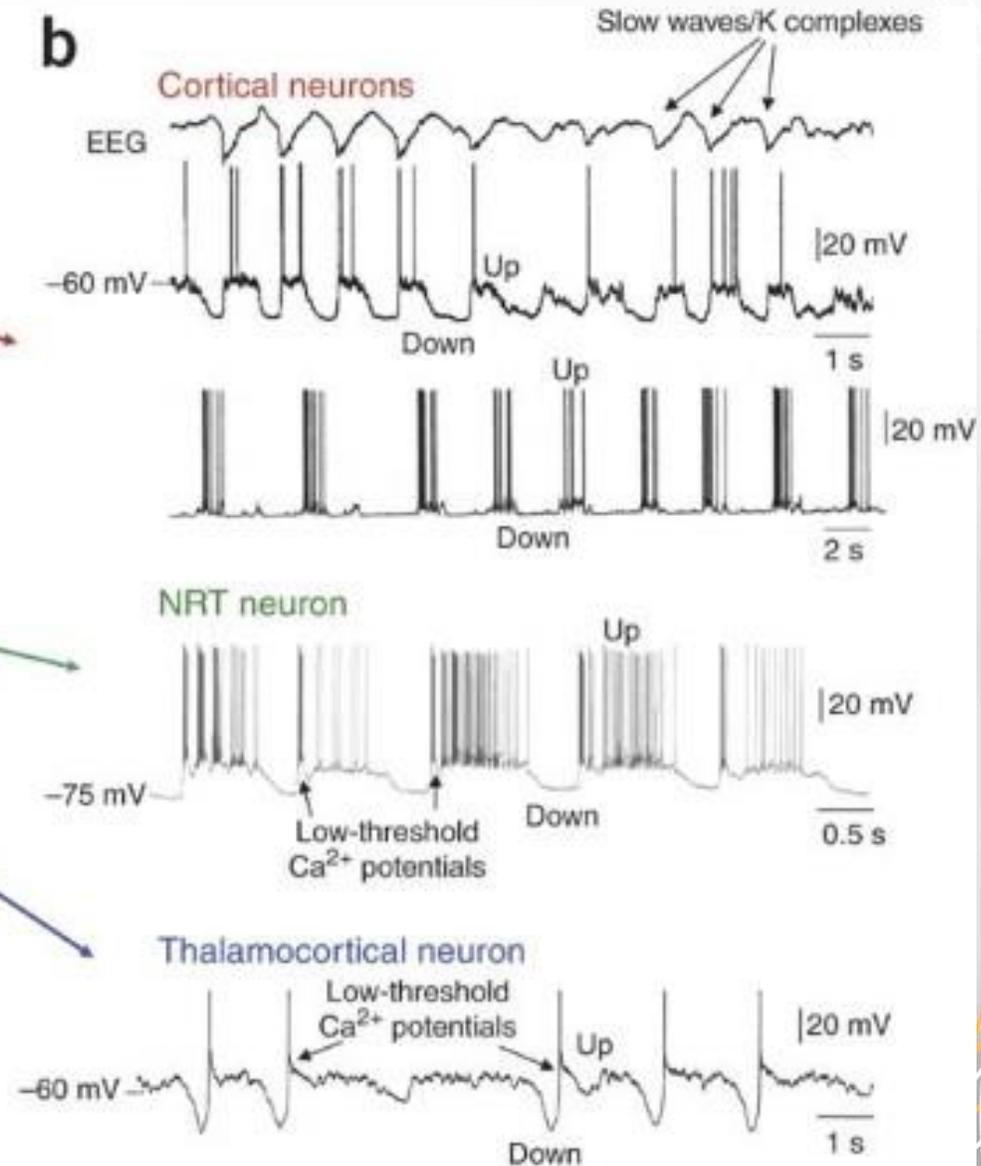
EEG recording during sleep



a

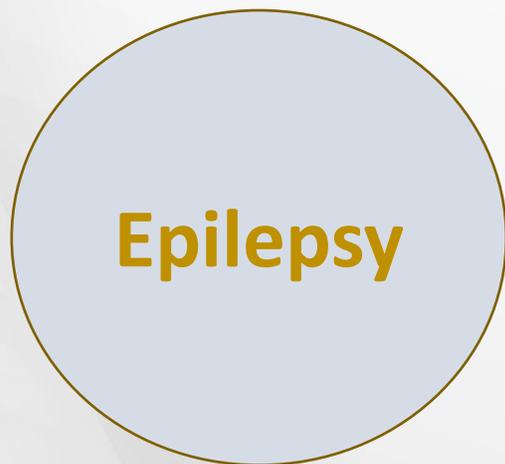


b





Complex interaction between sleep disorder and epilepsy



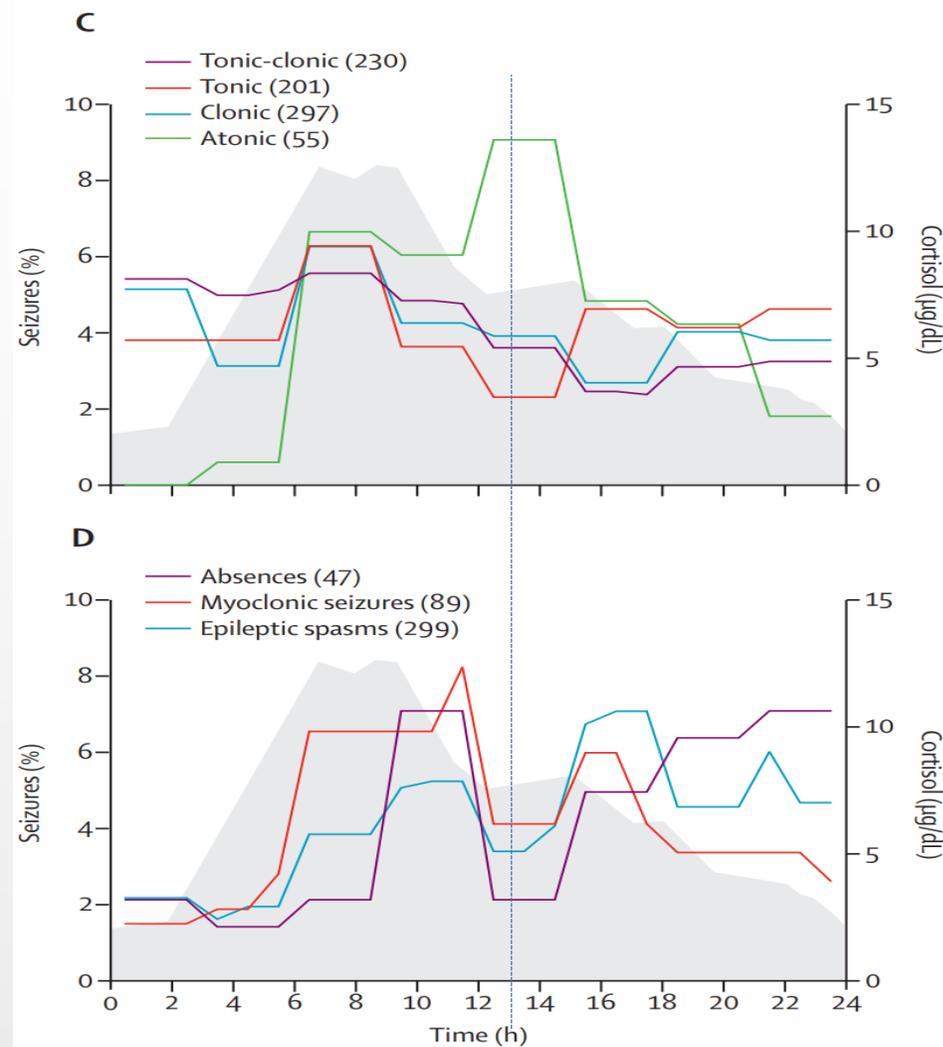
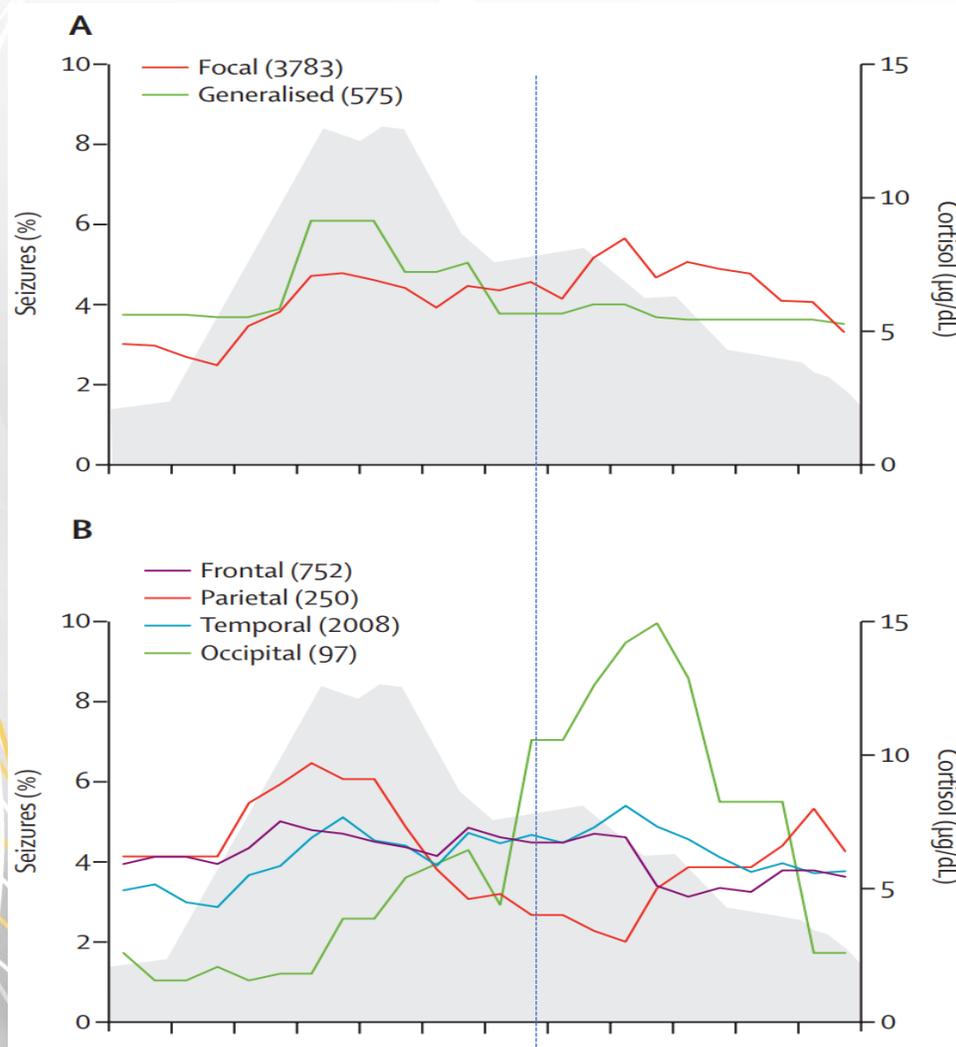
- ❖ Increase IEDs in NREM (N1-N2>N3) awake and REM



- ❖ Disease itself
- ❖ Treatment consequence

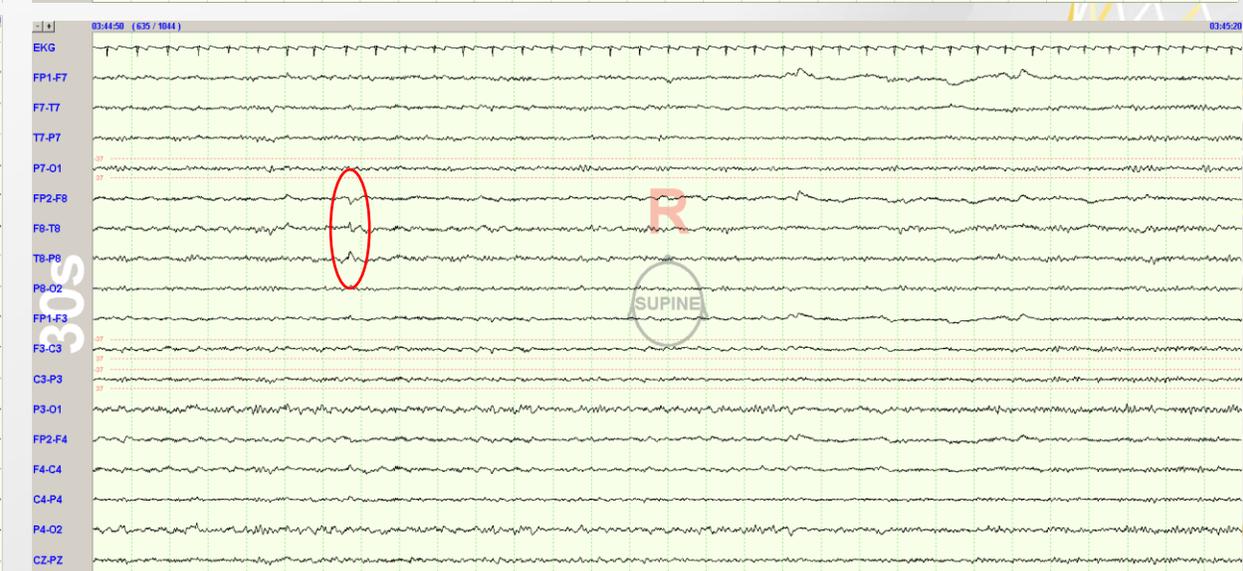
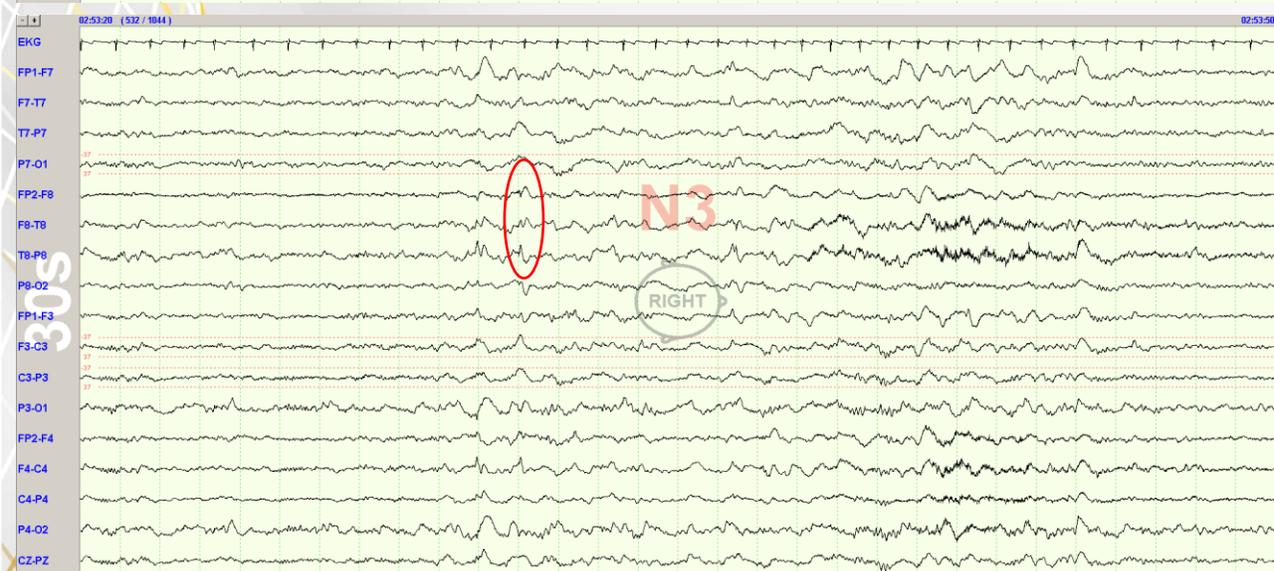
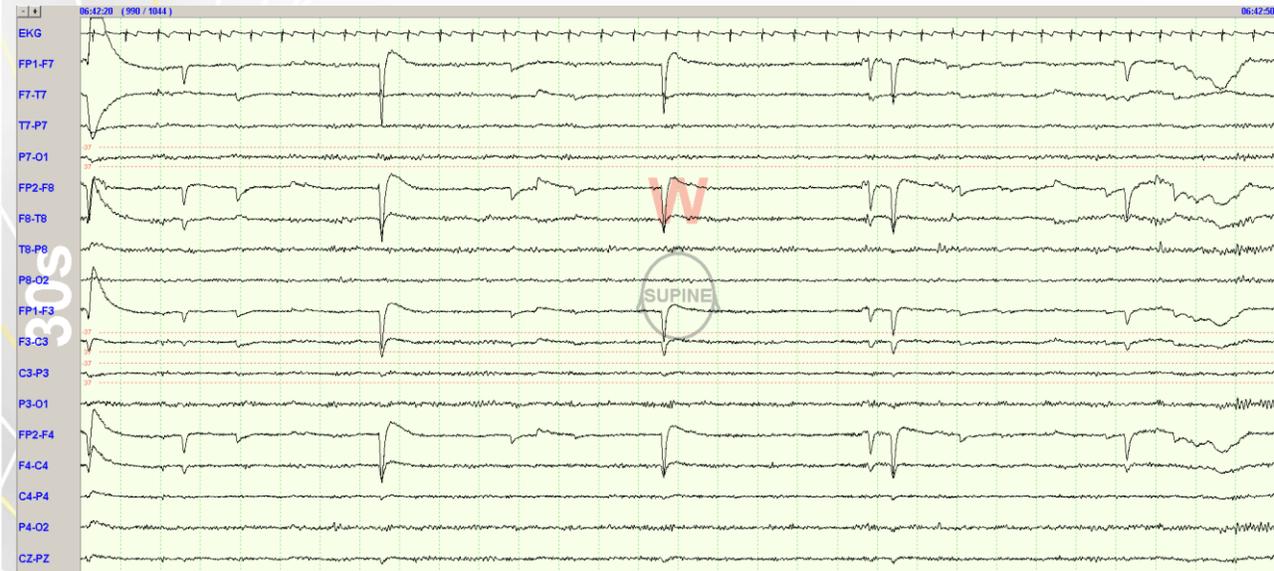


Distribution of seizure occurrence and cortisol concentrations over 24 h

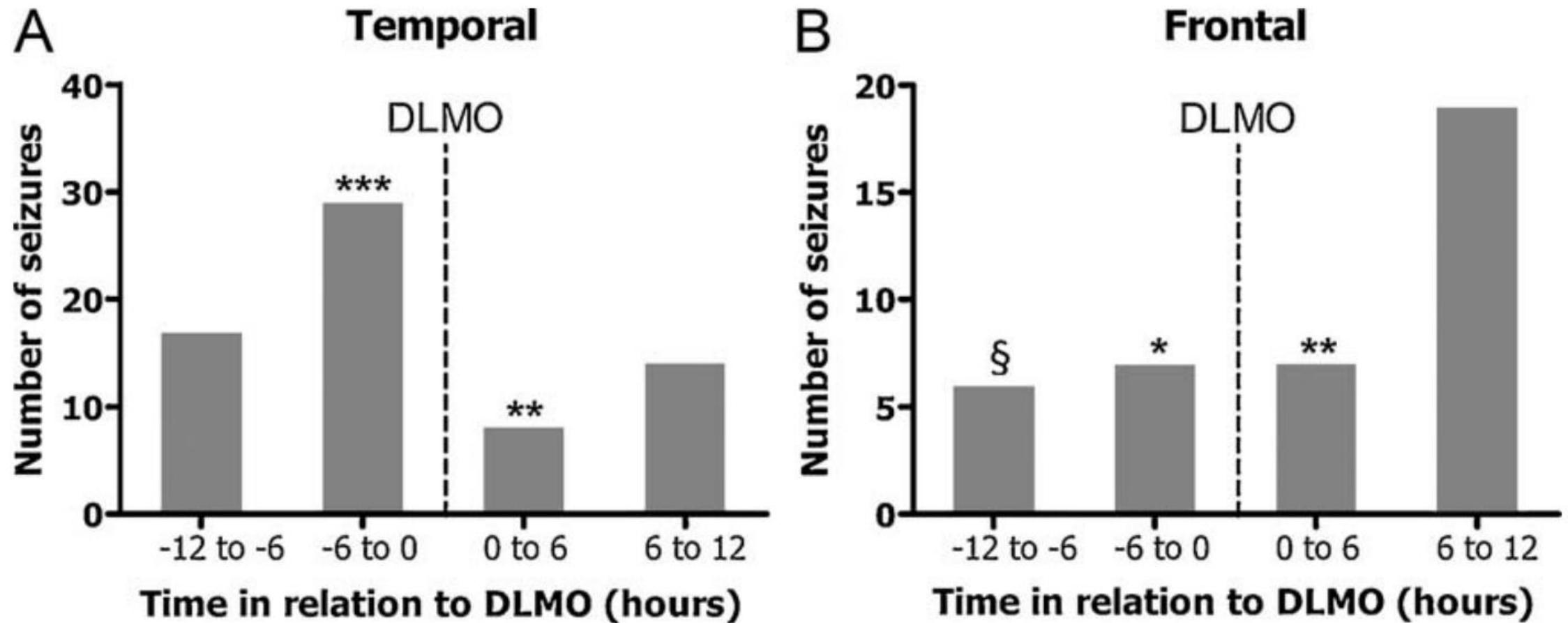




The demonstrate of interictal discharge (IED) compare with awake, NREM, SWS and REM sleep in Focal epilepsy



Timing of seizure in relation to the circadian phase

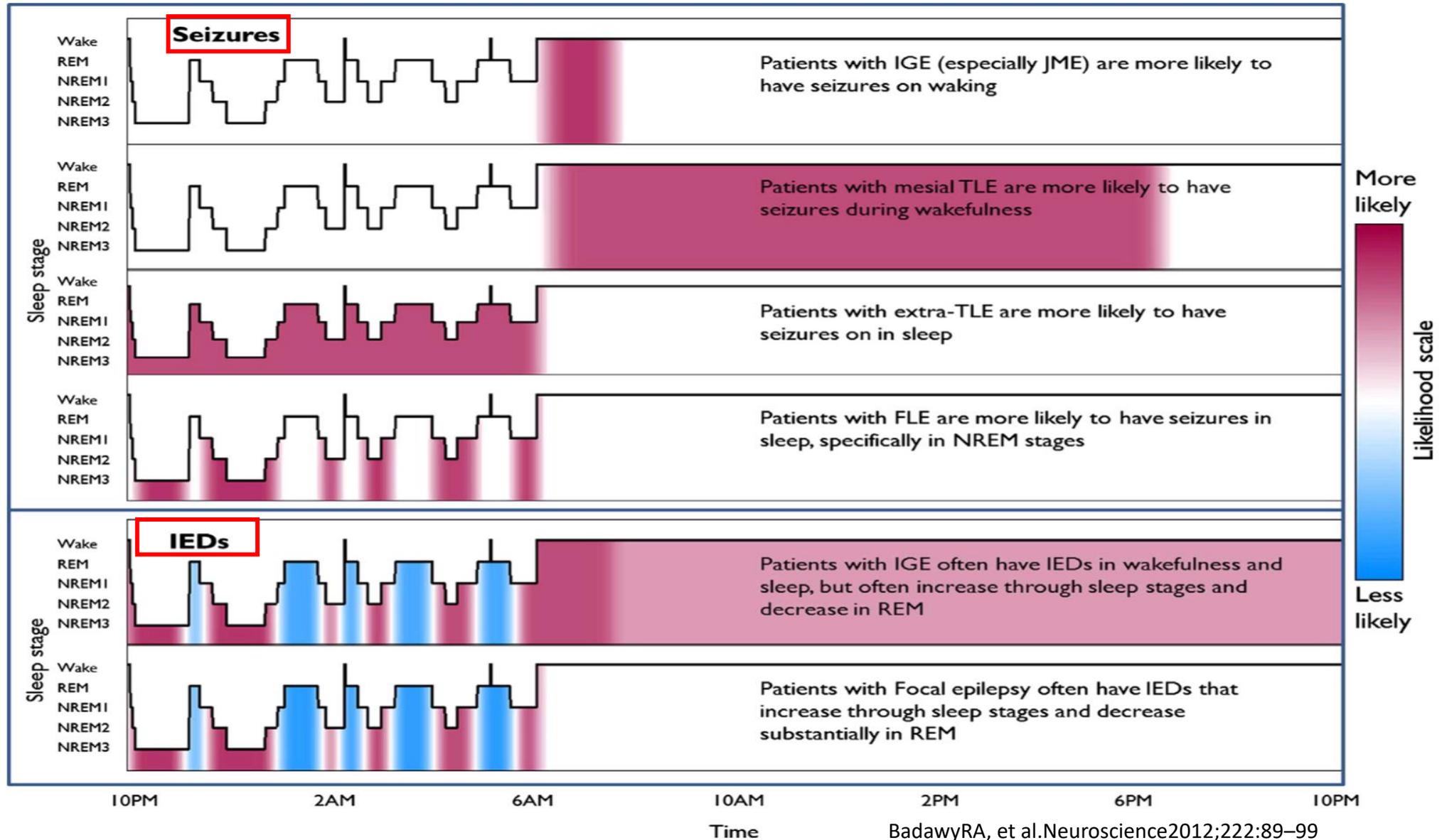




Result of some interesting studies that relate seizure location and most frequently time of day

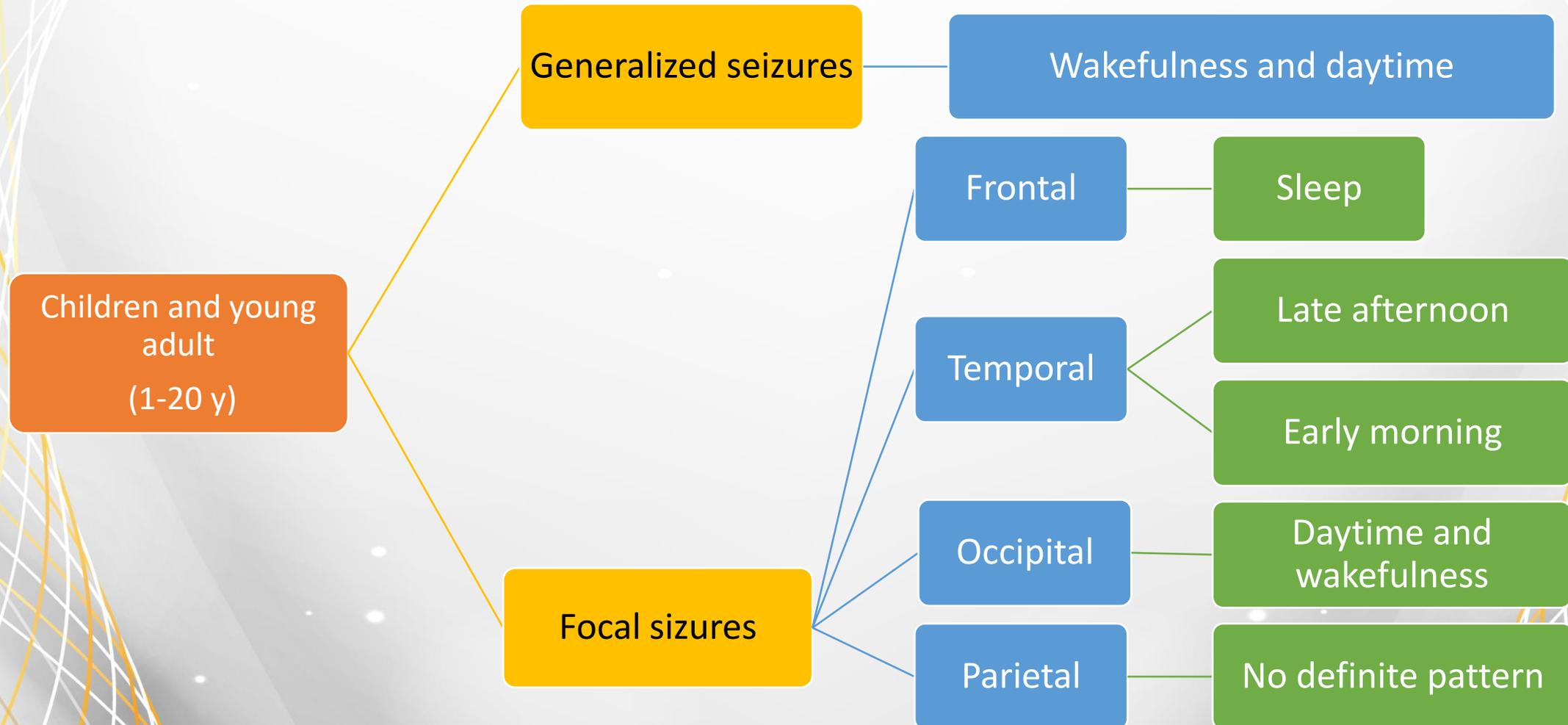
Author	Year	No. of Pt	No. of Sz	Focus	Peak hour
Parlova	2004	26	90	Temporal	15-19 hr
				Extratemporal	19-23 hr
Durazzo	2008	131	669	Occipital	16-19 hr
				Frontal and parietal	04-07 hr
				Temporal	16-19hr and 07-10 hr
Hofstra	2009	33	450	Temporal	11-17hr
				parietal	17-23 hr
				Frontal	23-05 hr

Schematic showing distribution of seizures and epileptiform discharges across a 'typical' 24-h sleep cycle for generalized and focal epilepsies.





Circadian rhythm and 24-h distributions of seizures and epilepsy activity





Antiepileptic drug effects on sleep

AEDs	Sleep disorder		Sleep architecture	
	Positive effects	Negative effects	Positive effects	Negative effects
PB	Insomnia	OSA	↓SL	↓ REM
BZD	Insomnia, RLS, RBD	OSA	↓SL, ↓arousal, ↓CAP	↓ REM, ↓ N3
CBZ	RLS	None	None	↓REM, ↑sleep stage shift
VPA	RLS	OSA	Sometime no effect	↑N1, ↓ REM
GBP	RLS, insomnia	OSA	↑N3, ↓ arousal, ↑SE	None
LTG	Consolidating sleep, reducing arousal stage shift	Insomnia, RBD	↓ Sleep stage shift, ↓arousals ↑ REM	↓N3 (possible)

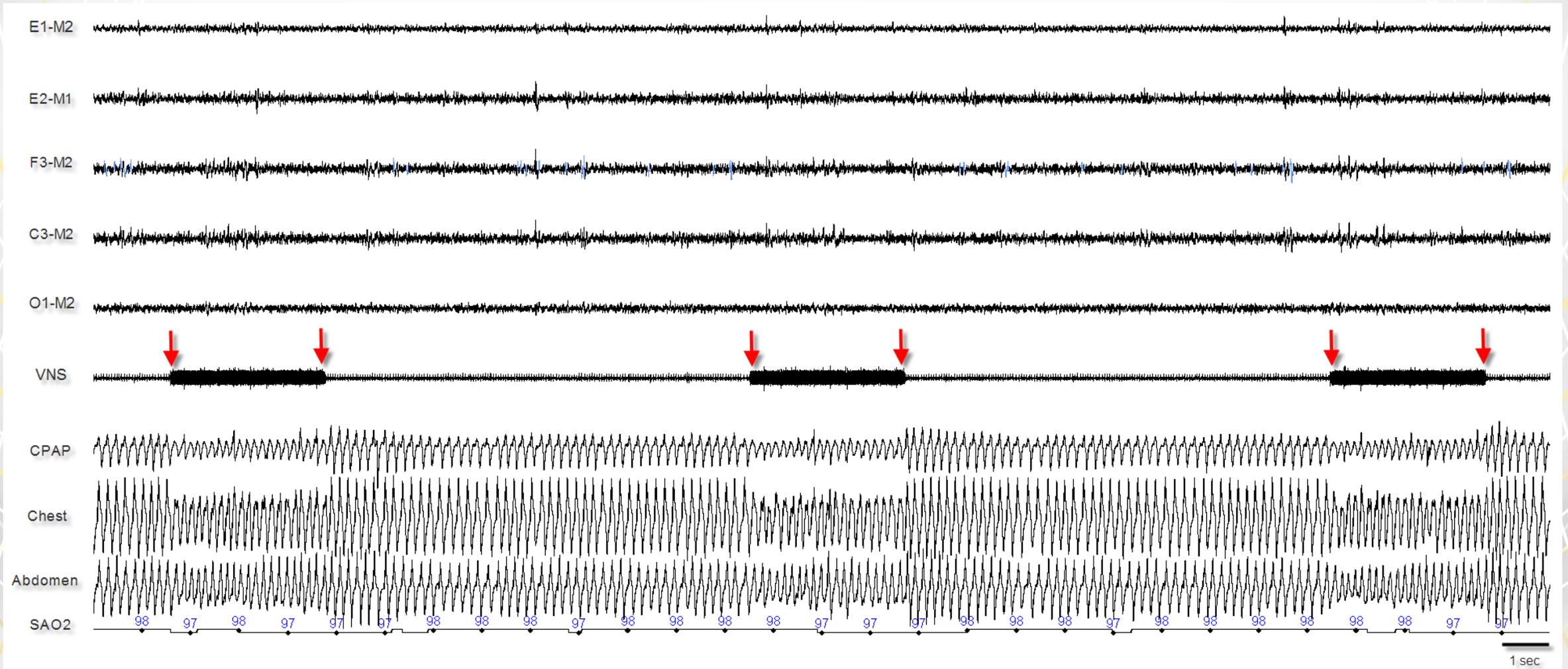


Antiepileptic drug effects on sleep

AEDs	Sleep disorder		Sleep architecture	
	Positive effects	Negative effects	Positive effects	Negative effects
LEV	RLS (case report)	Insomnia	↑N3, ↓WASO	None
PGB	Insomnia, RLS, daytime attention	OSA	↑N3, ↑REM, ↓arousal	None
TPM	Weight loss, OSA	RLS	No change	No change
ZNM	OSA	RLS	No change	No change
PER	Insomnia	?	↑N3, ↓WASO	None



VNS affects sleep and vigilance





t h a n k y o u