Epilepsy Syndromes & Sleep

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Differential Diagnosis of Nocturnal Events

	NREM Parasomnia	REM Behavior Disorder	Nocturnal Seizures	Psychogenic Events
Time of Occurrence	First 1/3 of night	During REM; latter 2/3 of night	Any time (most common during first 2 hours and last 2 hours of sleep)	Anytime
Memory of Event	Usually none	Dream recall	Usually none but frontal lobe may have some recall	None
Stereotypical Movements	No	No	Yes	No
PSG Findings	Arousal from delta sleep	XS EMG tone during REM sleep	Potentially epileptic activity	Occur from awake state

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Frontal Lobe Seizures vs NREM Parasomnias

Differential Diagnosis

	Frontal Lobe Seizures	NREM Parasomnias
Age of onset	11.8 +/- 6.3	Usually < 10 yo
Attacks per month	20 to 40 (multiple events per night)	1-4
Clinical course	Increasing frequency or stable	Decreasing/disappearing
Movement semiology	Stereotypic	Polymorphic
Attack onset	Any time during night	First third of night
Attack distribution	2- NREM (65%)	3-4 NREM
Motor Pattern	2-3 repetitive types of attacks	Absence of motor pattern
Duration of attacks	< 1 minute (usually 15 to 30 sec)	Several minutes

Diagnostic Evaluation

1) **Daylab video EEG (awake only): essentially all normal**
2) **Daylab videoEEG (after sleep deprivation): 52.2% abnormal**
3) **24 hour videoEEG (daytime and nocturnal): 87% abnormal**

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Importance of Sleep in Epilepsy Patients

- Sleep disorders are frequently overlooked
- Diagnosis and treatment can improve daily functioning
- Diagnosis and treatment can (in some cases) improve seizure control

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Influence of Sleep on Epilepsy

- Nocturnal seizures occur in 60% of children with epilepsy, many of whom have seizures limited to sleep
- Most nocturnal seizures arise during nonREM sleep (primarily stage 2)
- Localization of seizure focus– frontal onset associated with sleep
- REM-onset seizures rare

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Effects of Sleep Deprivation on Epilepsy

- Sleep deprivation occurs in the real world from inadequate sleep and associated primary sleep disorders, even in children with epilepsy
- Direct effects of epilepsy and medication on sleep duration and sleep architecture
- Correction of sleep-deprivation from any source can improve seizure control

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Epilepsy and Sleep Apnea

- Importance of sleep apnea
  - Apnea associated with higher seizure rate
  - Almost 1/3 of patients with intractable epilepsy have evidence of sleep apnea
  - Treatment of apnea decreases seizure frequency
- Weight gain from AEDs (i.e. VPA, GBP, Lyrica) may induce or worsen apnea
- Sedating AEDs (i.e. PB, BZDs) produce upper airway relaxation and reduce arousability

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Impact of Epilepsy on Sleep

- Seizures can disrupt the regulation of the sleep-wake cycle
  - Frequent seizures (and even frequent interictal discharges):
    - produce sleep fragmentation
    - suppression of REM
    - increased spontaneous arousals
- Untreated epilepsy associated with feelings of non-restorative sleep

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Using Sleep Knowledge to Improve Understanding of Epilepsy

- Direct effects of sleep loss, fragmentation and oxygen desaturation predispose to seizures
- Daytime sleepiness from disturbed sleep may exacerbate epilepsy
- Treating associated primary sleep disorder improves seizure control and daytime alertness

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Effects of Sleep Deprivation on EEG

- Activation of interictal discharges, especially in presence of sleep-related seizures
- Age-dependent sleep deprivation may yield epileptic abnormalities in 35% of patients with initially normal waking EEG
- Sleep-deprived EEG not recommended as standard for initial study

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Certain types of epilepsy are closely associated with sleep

- Idiopathic generalized epilepsy
  - awakening grand mal
  - juvenile myoclonic epilepsy
- Idiopathic partial epilepsies
  - benign rolandic
  - childhood epilepsy with occipital paroxysms
  - autosomal dominant frontal lobe epilepsy
  - Landau-Kleffner syndrome

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Sleep and Epilepsy: Seizure Type

- Frontal lobe seizures more commonly begin during sleep, while temporal lobe seizures begin more commonly awake
- Temporal and occipital lobe seizures in particular generalize more during sleep whereas frontal lobe seizures less commonly generalize
- All types of partial seizures are rare in REM sleep

Herman et al, Neurology 2001;56:1453-9.[1,2]

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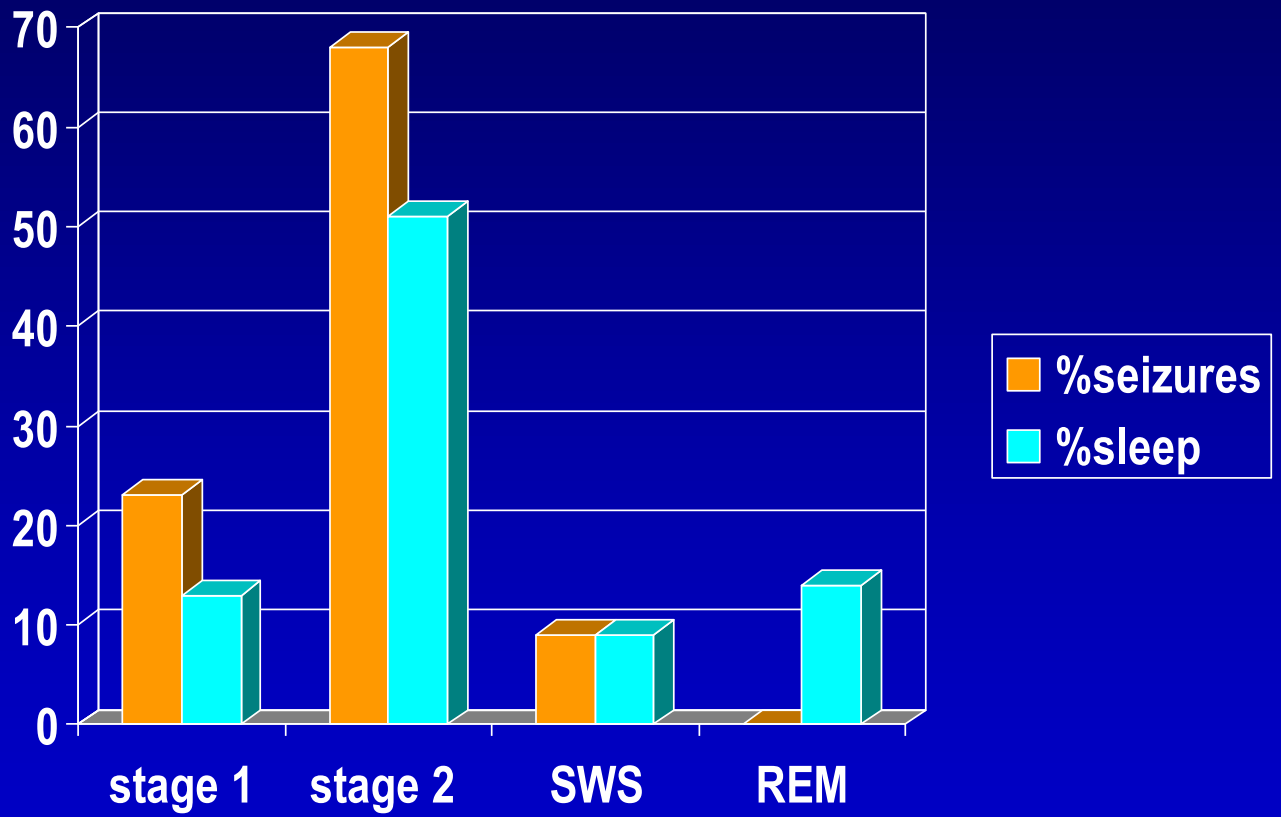
In what stage of sleep do seizures happen?



Herman et al, Neurology 2001;56:1453-9.

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Effects of Seizures on Sleep

- Seizures during sleep result in brief awakening
- Many patients, however, report decreased functioning after even a brief nocturnal seizure
- Investigation of seizure effects in patients with temporal lobe epilepsy, using all-night polysomnography in patients hospitalized for video-EEG monitoring

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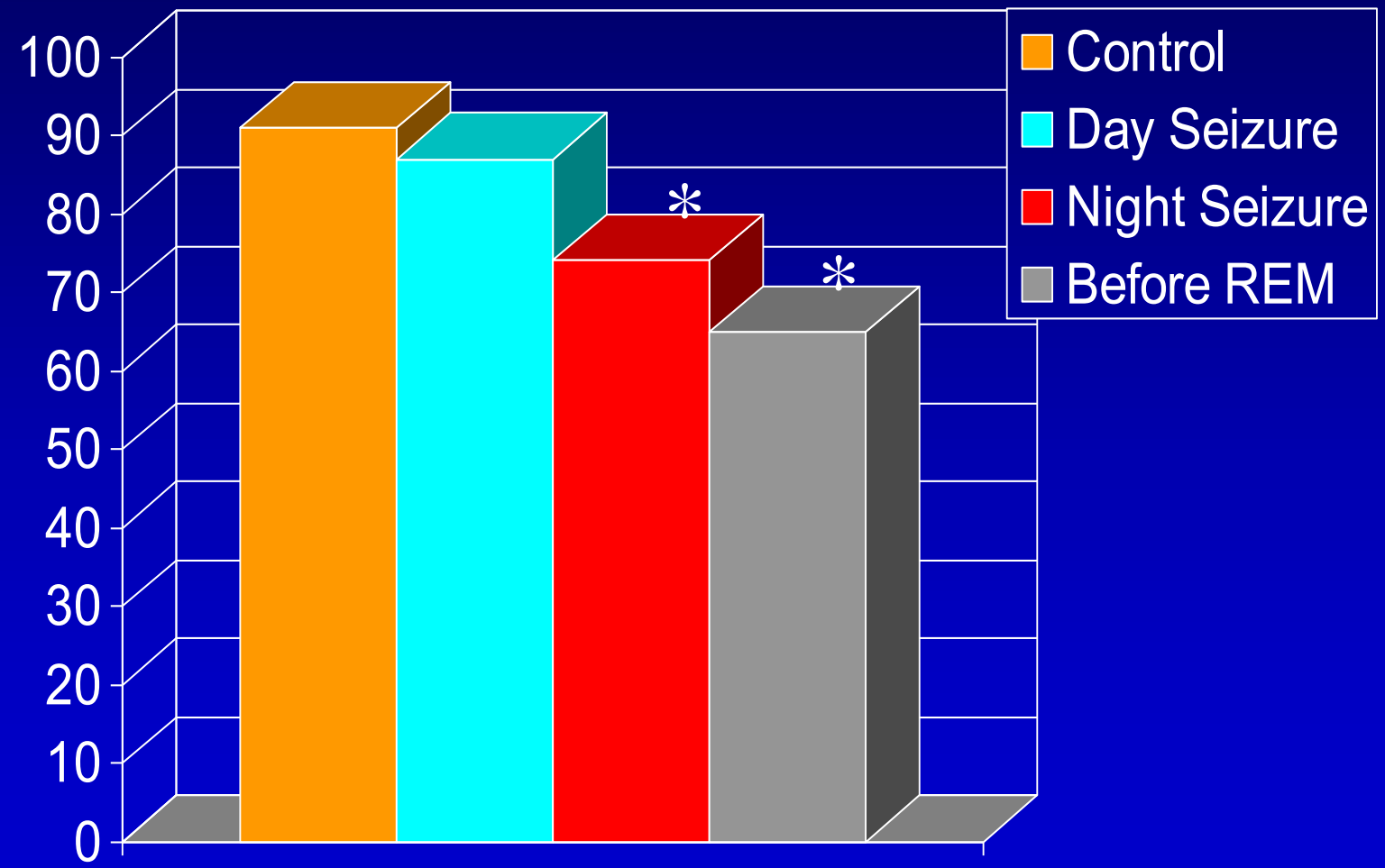
Seizure Effects on Sleep Efficiency



Bazil et al. *Arch Neurol*. 2000; 57:36

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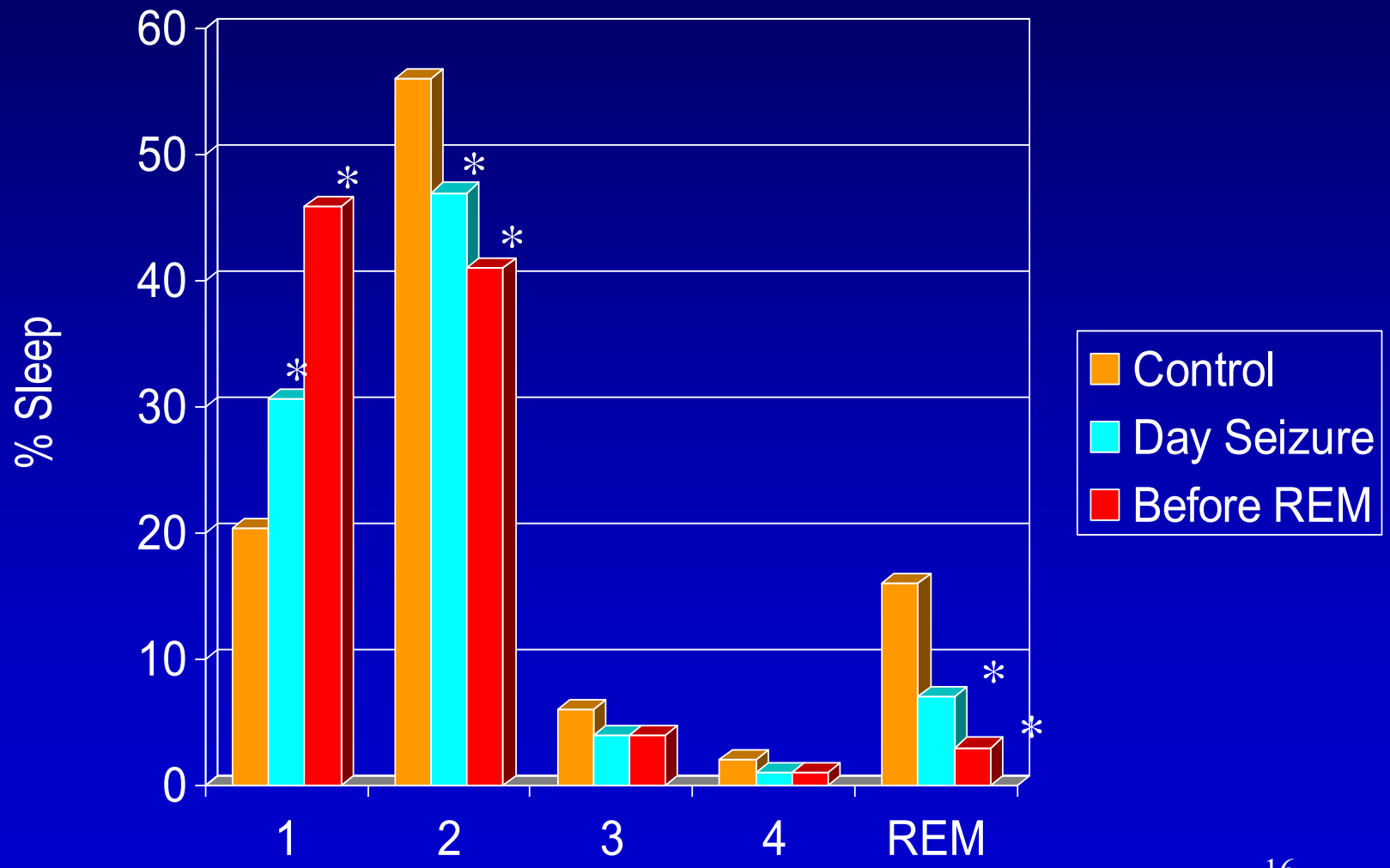
Effects of Nocturnal Seizure



Bazil et al. *Arch Neurol*. 2000; 57:363-8.

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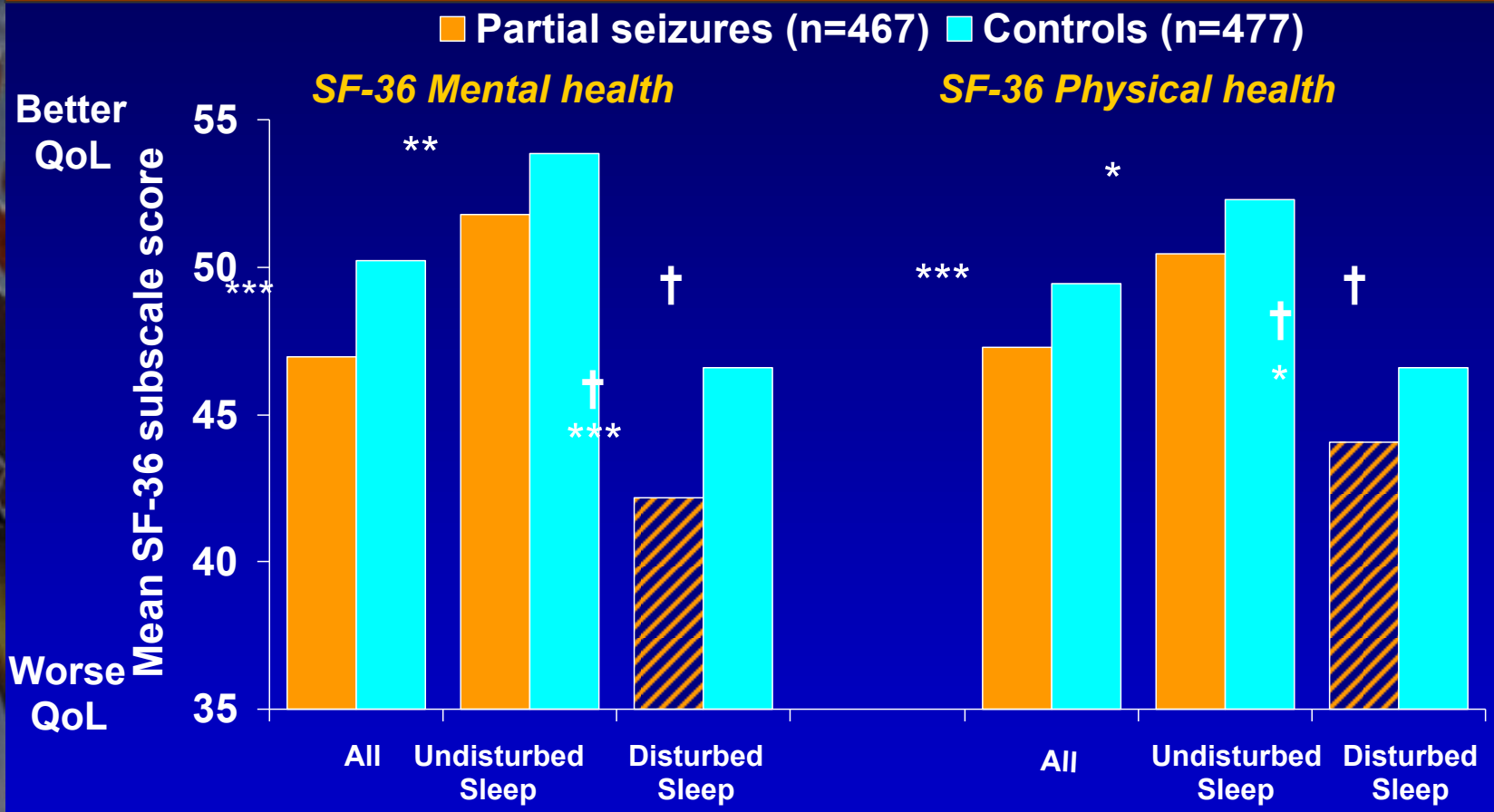
Patients with Partial Seizures AND Sleep Disturbance Have Worse Quality of Life



*P<0.05. **P<0.01, *** P<0.001 vs. controls
† P<0.001 vs. undisturbed sleep within group

De Weerd et al. Epilepsia. 2004;45:1397-1404

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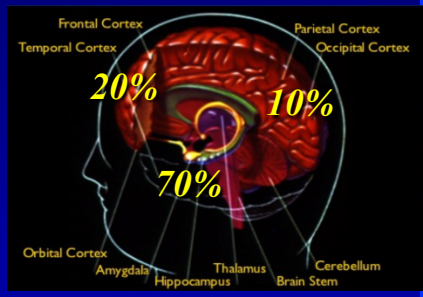
Sleep and Epilepsy

- I. Mechanisms
  - influence of sleep supported by specific seizure disorders have seizures only during sleep
    - Temporal lobe seizures are most common nocturnal seizures
    - Frontal lobe seizures have higher prevalence during sleep
      - possible thalamocortical activation
    - Frontal > temporal > parietal > occipital
  - interictal epileptiform discharges more prevalent in NREM
    - Light sleep (Stage 1 & 2) > Deep Sleep (Stage 3 & 4)
    - NREM sleep is a state of neuronal synchronization with thalamocortical networks allowing recruitment of a critical mass of neurons to initiate and sustain a seizure



NREM Sleep

Seizure Promoter

Synchronized sleep

xs diffuse cortical synchronization

enhanced interhemispheric impulses

REM Sleep

Seizure Protector

Desynchronized sleep

inhibition of thalamocortical synchronization

tonic reduction of interhemispheric impulses

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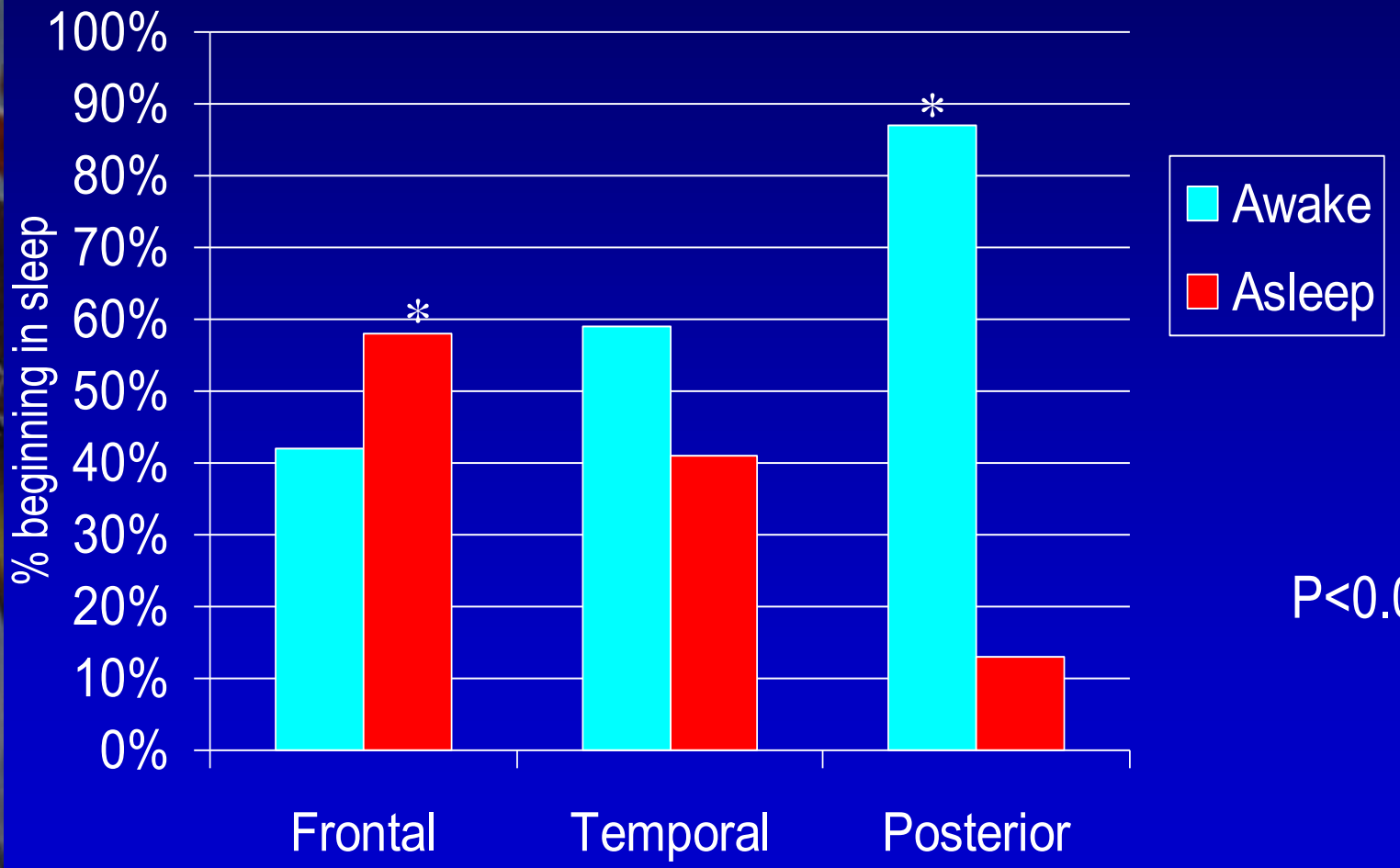
Do different seizures have a tendency to start during sleep?



P<0.0001

Herman et al, Neurology 2001; 56:1453-9.

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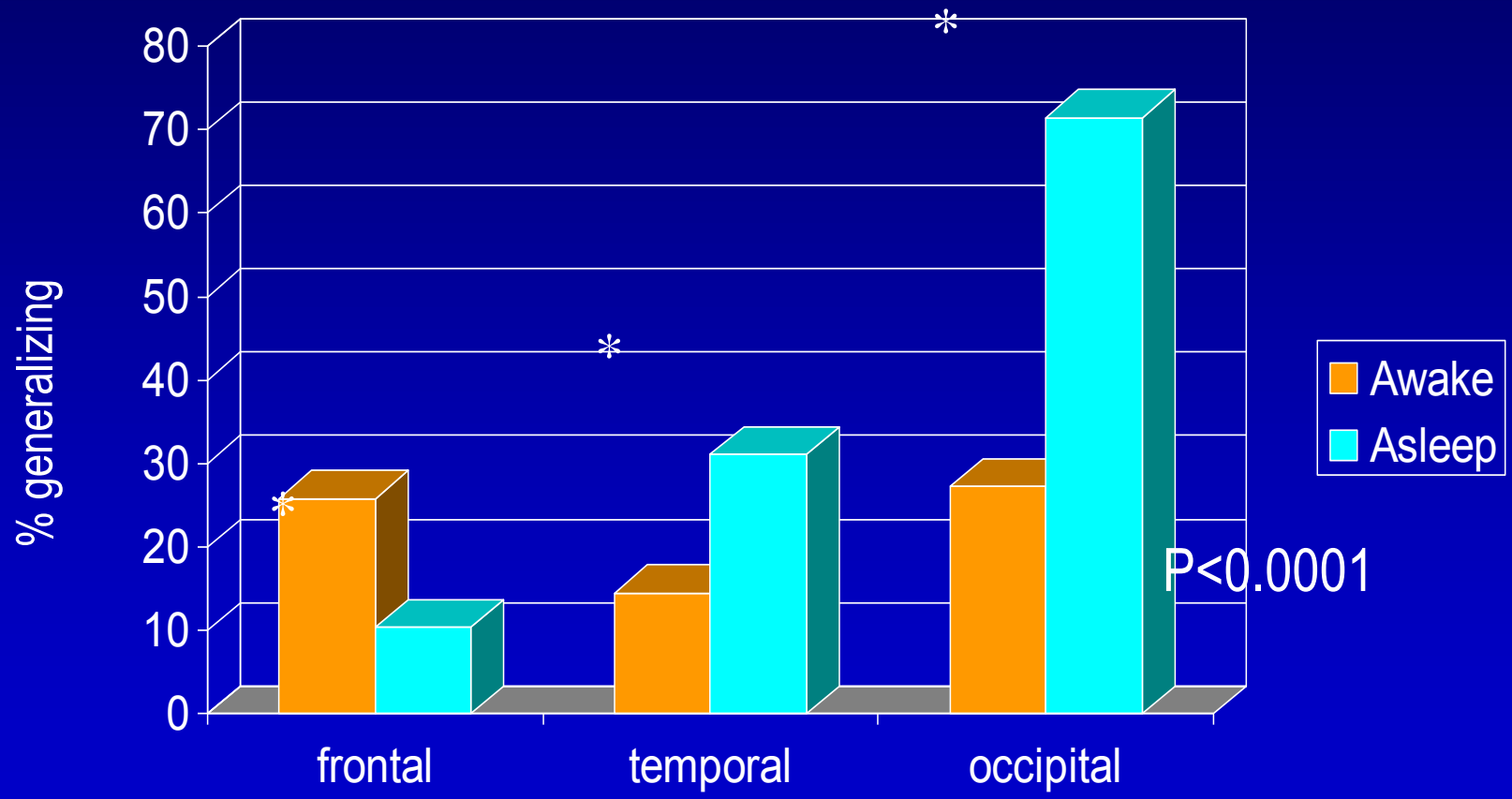
Do some seizures generalize more often during sleep?



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Effects of Treatment on Sleep

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Effects of AEDs on Sleep

- Complex interaction between direct effects of drugs on sleep architecture and stabilization of neuronal excitability
  - Sedating side effects with most older AEDs
  - Insomnia associated with some drugs (ACTH, felbamate)
  - Insomnia with AED withdrawal (PB, BZD)
- Incomplete data on newer AEDs

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AEDs Effect on Sleep Organization

- Barbiturates and benzodiazepines
  - Shorten sleep latency
  - Decrease arousals from sleep
- Phenobarbital
  - Decreases sleep latency, arousals
  - Increases Stage 2, decreases REM
  - Restlessness in latter part of night
  - REM rebound with drug withdrawal
- Benzodiazepines
  - Reduces sleep latency and awakenings
  - Increases Stage 2, decreases SWS
  - REM rebound with drug withdrawal

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Effects of AEDs on Sleep

- Carbamazepine
  - Decreases sleep latency, arousals; improves sleep efficiency
  - REM unchanged
  - Increase PLMS
- Valproate
  - Increases SWS
  - Decreases REM
- Phenytoin
  - Shorten sleep latency
- Lamotrigine
  - Decreased stage shifts and arousals
  - Increased REM sleep
- Topiramate
  - No sleep studies
- Zonisamide
  - Occasional reports of insomnia
- Levetiracetam
  - Increases stage 2, decreases SWS

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