The effects of OSA lead to a pathological cascade that is responsible for cerebrovascular and other cardiovascular diseases.

Effects of OSA
- Hypoxia/Reoxygenation
- Hypercapnia
- Arterial desaturation
- Sleep Deprivation
- Negative Intrathoracic Pressure

Pathological Cascade
- Oxidative Stress
- Inflammation
- Sympathetic Activation
- Hypoagglutination
- Endothelial Dysfunction
- Metabolic Dysregulation

Disease
- Cerebrovascular Disease
- Other Cardiovascular Diseases
- Stroke
- MI

SLEEP ↔ STROKE
- Sleep Apnea: an independent risk factor for MI, stroke
- RLS/PLMS, CRSD, primary insomnia: potential causes of vascular disease
- Arousal response, surge in sympathetic activity lead to BP elevations and acceleration of HR
OSA ↔ STROKE

- Increase in sympathetic activity - influences BP and HR
- Different mechanisms induce the surge in sympathetic activity: chemoreflex stimulation, baroreflexes, pulmonary afferents, the Müller maneuver, impairment of venous return to the heart, alterations in cardiac output, arousal response
- OSA influences HR variability (during sleep and wakefulness)
- Treatment of sleep apnea with CPAP leads to improvement of autonomic modulation and cardiovascular variability

OSA ↔ STROKE

- Proinflammatory vascular risk factors, oxidative stress, endothelial disease may be enhanced by OSA
- Repeated hypoxic may damage the endothelium and trigger release of proinflammatory factors (plasma cytokines, TNF-α, IL-6)
- Dipping vs. nondipping
- Refractory hypertension is a well known comorbidity of uncontrolled sleep apnea

OSA ↔ STROKE

- OSA increases the risk of HTN
- OSA linked to DM II by mechanisms of increased insulin resistance and cortisol levels
- OSA related to altered levels of leptin
OSA → AFIB → STROKE

- 3.03 Million persons in U.S. [2003]
- Epidemiological studies suggest that OSA is a risk factor for new onset AFIB
- OSA may confer a worse prognosis for recovery after AFIB interventions

OSA + PFO → STROKE

- PFO estimated to occur with a range of 10% to 30% in the general population
- Association between PFO and OSA described in one study where 27% of patients with OSA and 15% of control subjects had PFO
- Nocturnal apneic-related shunting could augment risk of paradoxical embolism and stroke, more so if pHTN develops
- OSA + PFO may be a risk factor for stroke on awakening

OSA → STROKE

- Cerebral hemodynamic changes lead to irreversible ischemic changes
- Conversely, healthy children with mild SDB exhibit cerebral hemodynamic and neurobehavioral changes that are potentially reversible after adenotonsillectomy, suggesting normalization of MCA blood flow as measured with TCDs
CPAP TREATMENT

- Shown to decrease the frequency of nocturnal arousals and suppress acute blood pressure fluctuations
- Lowers blood pressure levels in mod-sev OSA (stabilizing the sympathetic-vagal balance)
- Favorable effect on afib recurrence

POSTSTROKE SLEEP APNEA

- Prevalence of sleep apnea poststroke 50-75%
- CSAs predominate initially giving way to OSAs in chronic stages after an acute stroke
- Poor functional outcome, depressed mood, cognitive dysfunction, decline ability to perform ADL
- May be independently associated to length of hospital stay

RLS/PLMS → STROKE

- Emerging evidence suggests that RLS/PLMS represent risk factors for cardiovascular and cerebrovascular disease
- Repeated nocturnal HR and BP rises associated with PLMS and related microarousals may facilitate daytime HTN and open the way to heart disease and stroke
- Further studies are needed
INSOMNIA, SLEEP DURATION

- Self-reported insomnia associated with increased risk of CAD, MI, or death (ARCS)
- Insomnia with short sleep duration (<5 hrs) associated with HTN and DM
- U-shaped relationship between sleep duration and vascular outcomes

CIRCADIAN RHYTHM DISORDERS ↔ STROKE

- SWSD is the CRSD associated with most morbidity in adults
- 1.5 million Americans qualify as shift workers
- Shift work interferes with endogenous nocturnal BP decline
- SW increase risk of obesity, HTN, DM, CV disease and all-cause mortality, controversial whether it inc. stroke risk
- NHS ongoing study found a 4% increase in ischemic stroke risk for every five years of SW after controlling for vascular risk factors

SLEEP AND EPILEPSY

- Reciprocal interaction between sleep and epilepsy
- Accurate diagnosis of sleep-related epilepsy
- Relationship between OSA and epilepsy
- Role of sleep in SUDEP
**SLEEP ↔ EPILEPSY**

- "Pure sleep epilepsy": BCECTS, ADNFLE
- "Awakening epilepsy": JME, Epilepsy with GTC seizures on awakening
- EEG findings, seizure types, seizure frequencies may all be influenced by the sleep-wake state (epilepsy syndrome, sleep stage)

**SLEEP ↔ EPILEPSY**

- Generalized epileptiform discharges NREM > REM
- NREM sleep is a state of increased cerebral hypersynchrony
- Most sleep related seizures occur in NREM (stage II)
- K-complexes and sleep transient have been clearly associated with electroclinical epileptic phenomena (periodic arousal instability- CAP)
- Sleep deprivation (cortical excitability)

**EPILEPSY ↔ SLEEP**

- Epilepsy associated with marked increase in sleep-related complaints (EDS, insomnia, poor sleep quality), Fascical GE
- Although seizures during sleep might be expected to be the major factor in poor sleep quality and EDS in epilepsy, studies have generally failed to support this (coexisting sleep disorder/s poor sleep hygiene/s coexisting mood disorders?)
- Objective evidence that epilepsy affects sleep architecture (AEDs)
SEIZURE DISORDER VS. SLEEP DISORDER

• Kejjang fokal umum

NFLE VS. PARASOMNIA (FLEP SCALE)

• Age at onset (<55)
• Duration (>10 min)
• Clustering (>3 events/night)
• Timing (within 30 min of sleep onset)
• Stereology (aura, no wandering, no complex directed behaviors, posturing/dystonia/head turning)
• Stereotypy (high)
• Recall (lucid)
• Vocalization

NFLE VS. PARASOMNIA (FLEP SCALE)

Features strongly favoring parasomnias:
- Yawning, scratching and prominent nose rubbing, rolling over in bed, internal/external trigger (noise, cough, snore), physical or verbal interaction, sobbing emotional behavior, failure to fully arouse after event with complex behavior, prolonged duration
NFLE VS. PARASOMNIA

• Features which do not discriminate between NFLE and parasomnias:
  Brevity, sitting, standing or walking, preceding "normal" arousal, fearful emotional behavior

OSA + EPILEPSY

• Most publications describing this relationship are based on small numbers
• One study showed incidence of OSA to be 33% in a group of patients with medically refractory epilepsy, awaiting epilepsy surgery
• Does treating OSA with CPAP improve seizure control?
• Treatment of CPAP clearly improves EDS/QOL
• Is OSA a contributing factor in SUDEP?

MULTIPLE SCLEROSIS + SLEEP

• >50% of MS patients suffer from poor sleep
• Symptoms of narcolepsy, RLS, SDB, RBD have all been related to specific locations of MS lesions in the CNS
• Insomnia (>40%), CRSD, RLS (19-38%), PLMS (36%), SDB (12%), narcolepsy, parasomnias
• Drugs that cause sedation: baclofen, tizanidine, oxybutynin, RLS drugs
• Drugs that cause insomnia: amantadine, modafinil, beta-IFN, steroids
PARKINSON'S DISEASE + SLEEP

• Disease related causes: disease progression, wearing off leading to sleep disruption, SDB, depression, RBD
• Related to drug therapy: dopamine agonists, levodopa, hypnotics/sedatives, anxiolytics, anti-depressants

DEMENTIA + SLEEP

• Alzheimer's dementia (25-50%) have sleep problems
• DLBD (up to 85%) have sleep problems
• PDD (60-90%) have sleep problems

AD + SLEEP

• ISWR: Chronobiological changes caused by SCN degeneration and pineal/melatonin dysregulation
• Possibly higher incidence of OSA
• Increased stage I sleep
• NREM de-differentiation
• Reduced REM quantity in late stages
DLBD + SLEEP
- 50-80% with RBD
- Hypersomnia (changes in lateral hypothalamus)
- PLMS (est. at 7-4%)
- ISWR (not likely caused by same changes as AD)
- REM without atonia

PDD + SLEEP
- RBD (30-60%)
- Sleep maintenance insomnia
- Hypersomnia
- RLS/PLMS

MULTIPLE SYSTEMS ATROPHY
- RBD (70-80%)
- Nocturnal snoring (vocal cord abductor paralysis can lead to sudden death during sleep, RX: tracheostomy)
- Autonomic dysregulation (may contribute to sudden death during sleep)
PSP + SLEEP

- Insomnia
- Hypersomnia (pts can have low hypocretin)
- RBD uncommon

THANK YOU

REFERENCES