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San Francisco

Postoperative Delirium and Sleep Apnea

Sakura Kinjo, MD
Clinical Professor
Anesthesia Medical Director, Orthopaedic Institute
Department of Anesthesia and Perioperative Care
University of California, San Francisco

Objectives

- Discuss possible risk factors and pathophysiology of postoperative delirium (POD) and postoperative cognitive dysfunction/decline (POCD).
- Discuss how co-morbidities of sleep apnea affect cognition.
- Discuss the effects of continuous positive airway pressure (CPAP) on cognition.

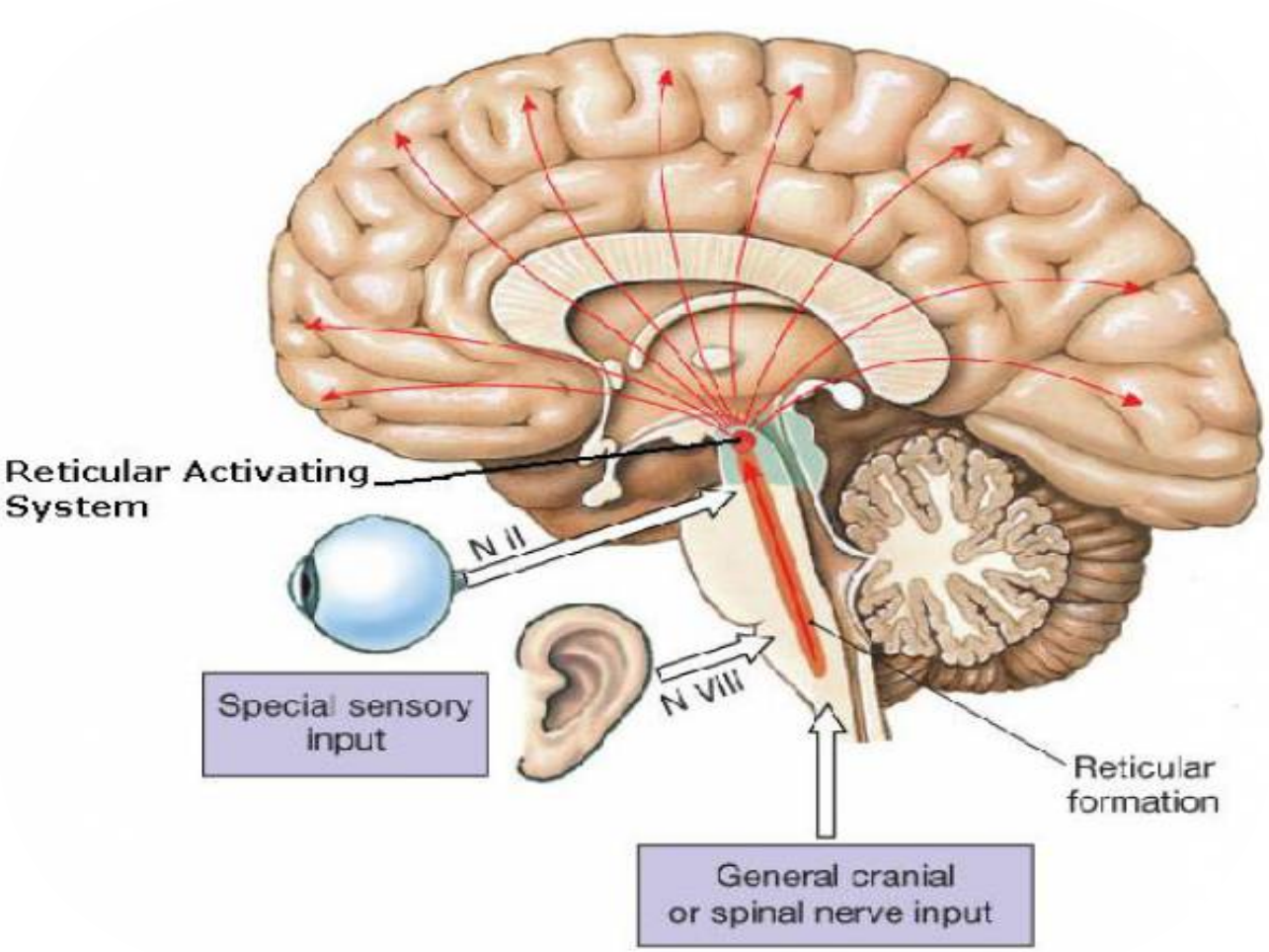
Postoperative Delirium (POD)

- **Definition of Delirium:** Acute confusional state, presence of acute onset and fluctuating course, and attention deficits, and either disorganized thinking or an altered level of consciousness.
- Common complication, especially in elderly.
- Usually transient, but may last longer, especially in ICU survivors (> 1 year).
- Associated with prolonged hospitalization, increased morbidity and mortality, and increased costs.

POD-Pathophysiology

- Unknown, multiple factors have been reported in the literature.
- **Pre-existing patient related factors:** increased age, cognitive impairment, depression, poor functional status, abnormal electrolytes or glucose, and alcohol abuse.
- **Intraoperative factors:** blood loss/blood transfusion and type of surgery (e.g., cardiac, orthopedic), **neuro-Inflammation**.
- **Postoperative factors:** pain, anemia, electrolyte and metabolic derangements, infection and hypoxia.

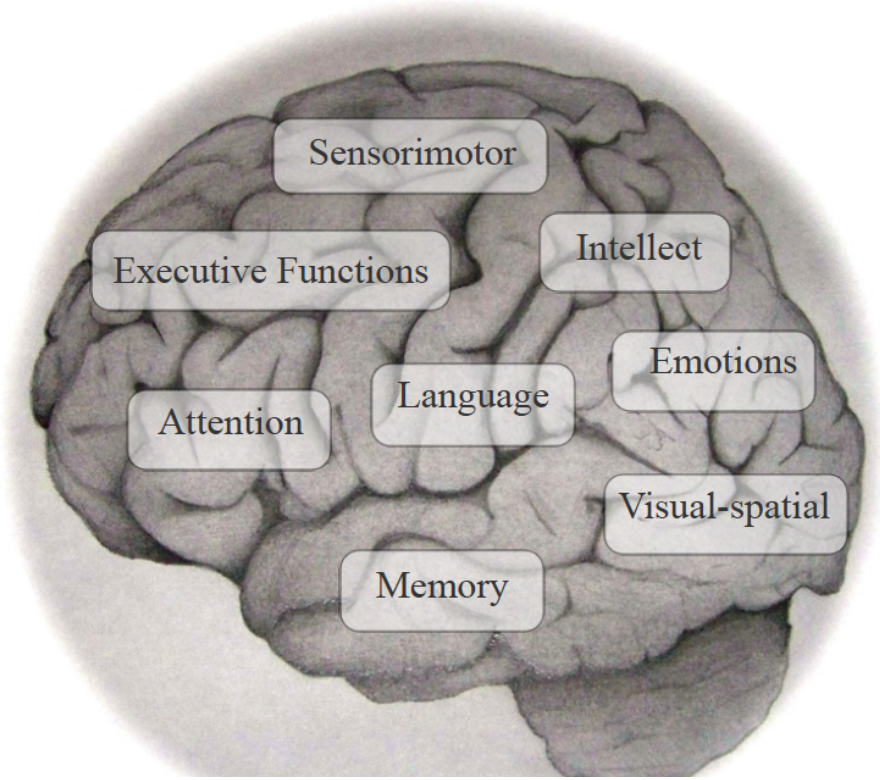
Pathophysiology of Delirium- Reticular Activating System

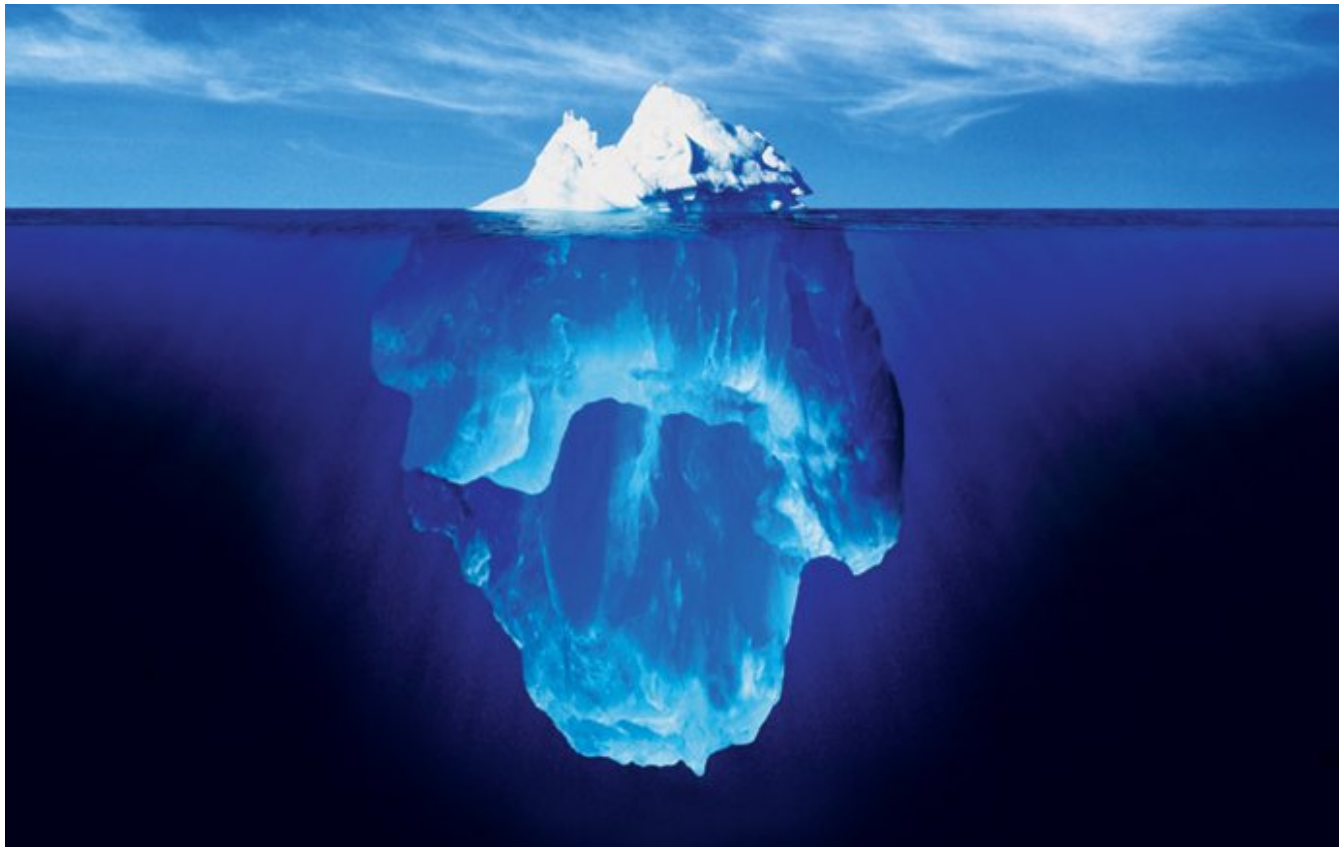


Postoperative Cognitive Dysfunction/Decline (POCD)

- POCD refers to a decline in cognitive function. However, no consensus exists regarding a specific diagnostic criteria.
- Cognitive decline lasts from a few days to a few weeks, sometimes longer.
- The incidence of POCD is 30-50% within the first week of surgery, and 10-15% for 3 months after major surgery (Monk et al, 2008, Moller et al, 1998).

Cognitive Domains





Is OSA a key risk factor of POD? Clinical Studies

1. **Flink et al, 2012.** Preoperative OSA predisposes to postoperative delirium (OR 4.3, p=0.012).

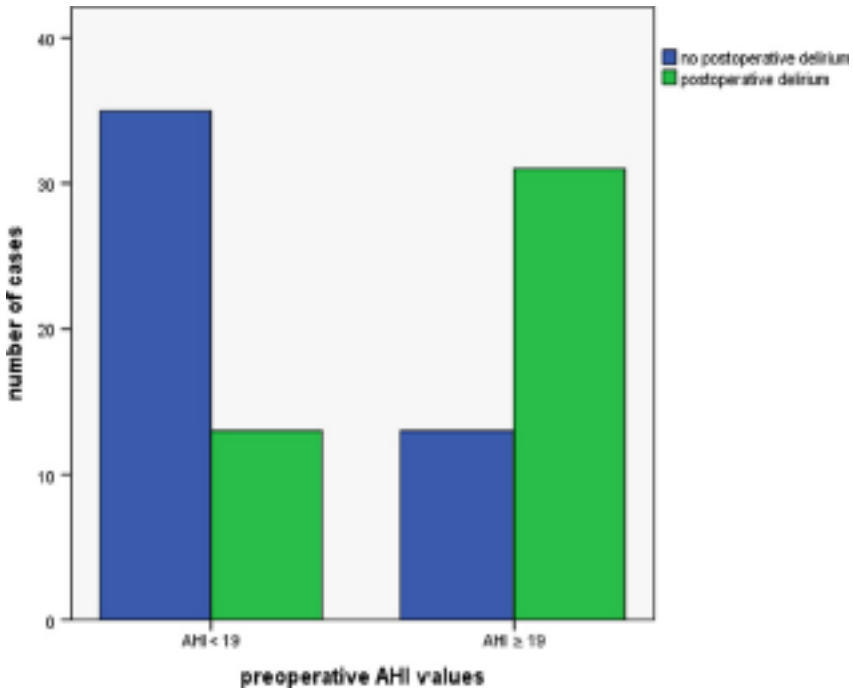
2. **Roggenback et al, 2014.** Preoperative AHI 19 or higher was associated with six-fold increase risk of POD (OR 6.4, p<0.001).

Obstructive Sleep Apnea and Incidence of Postoperative Delirium after Elective Knee Replacement in the Nondemented Elderly (Flink et al, 2012)

- 65 years or older, elective knee arthroplasty.
- Out of 106 patients, 27 patients (25%) developed POD.
- Higher incidence of POD in OSA patients than patients without OSA: 53% vs. 20%.

Sleep-disordered breathing is a risk factor for delirium after cardiac surgery: a prospective cohort study (Roggenbach et al, 2014)

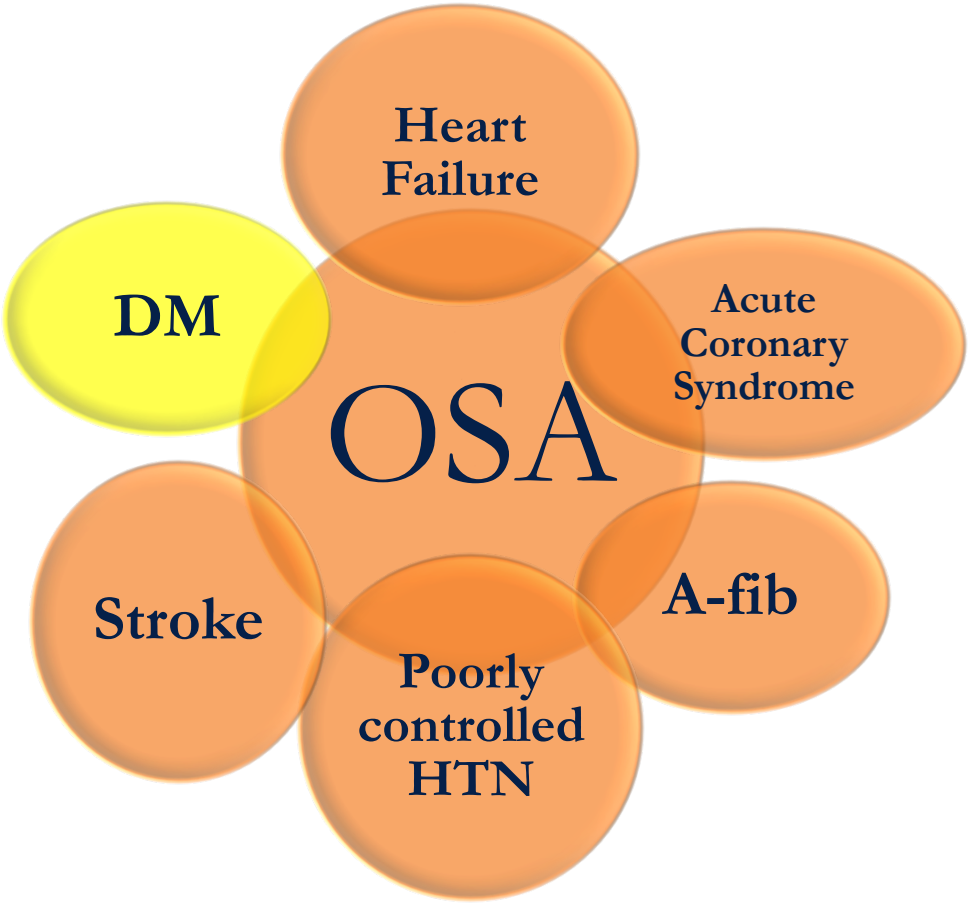
- Elective cardiac surgery.
- The incidence of POD was 48% (44/92).
- Preoperative AHI 19 or higher was associated with six-fold increased risk of POD (odds ratio 6.4, p< 0.001).



Microglia mediate postoperative hippocampal inflammation and cognitive decline in mice (Feng et al, 2017)

- Surgery increases pro-inflammatory cytokines, IL-1, MCP-1.
- Inflammatory activation of hippocampal microgria activation.
- Microglial depletion reduces surgically induced neuro-inflammation in hippocampus.
- Obese mice develop exaggerated and persistent postoperative neuro-inflammation and memory loss.

Sleep Apnea and Co-Morbidities



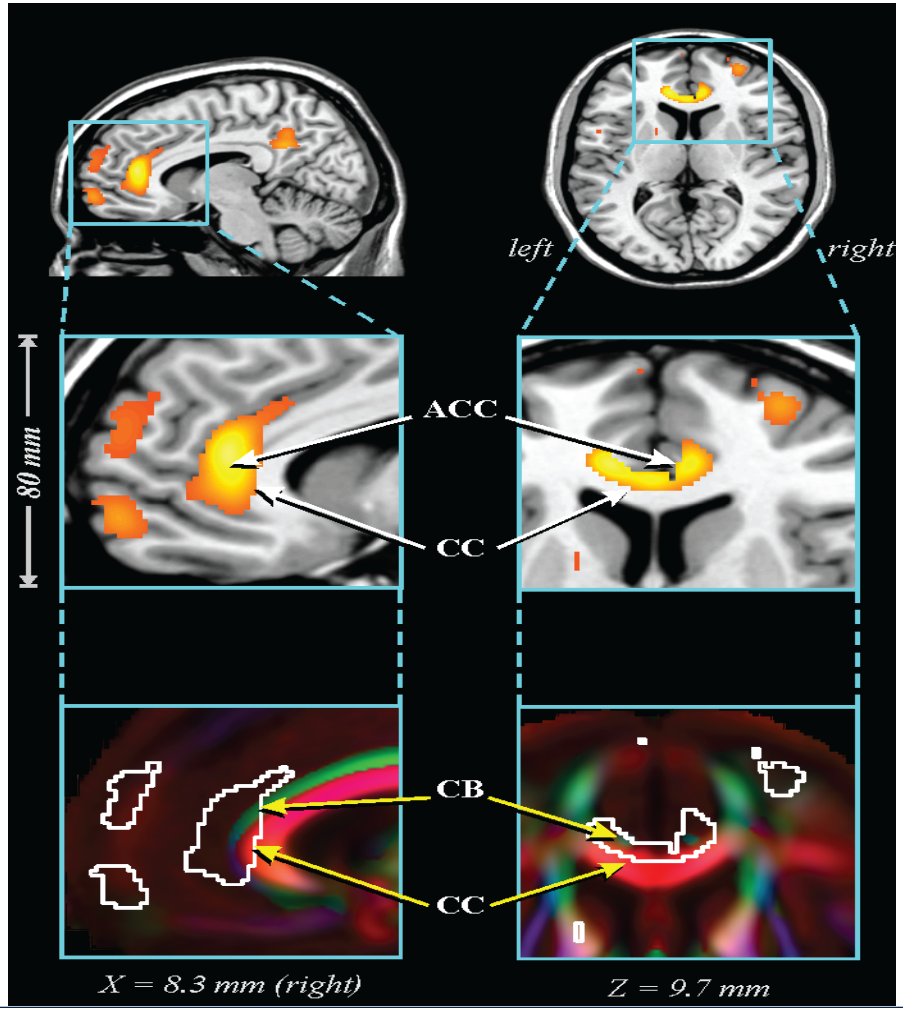
Possible Mechanisms of POD/POCD in Sleep Apnea Patients

- Preoperative cognitive impairment/low cognitive reserve.
- Hormonal changes; Hypothalamic-pituitary-adrenal axis (cortisol levels).
- Pro-inflammatory state (e.g.,diabetes, obesity)
- Perioperative hypoxia, fragmentation of sleep.

Neuropsychological Changes in Sleep Apnea

- Sleep Apnea causes brain structural changes in the frontal, parietal, temporal, hippocampal, and cerebellar regions (Macey et al, 2008, Canessa et al, 2011).
- It may be due to chronic continuous and/or intermittent hypoxia associated with sleep impairment.

Changes in Anterior Cingulate Cortex (ACC)



- Macey et al, 2008.
- Neural integrity was measured with Fractional Anisotropy (FA).
- White matter is extensively altered in sleep apnea patients.

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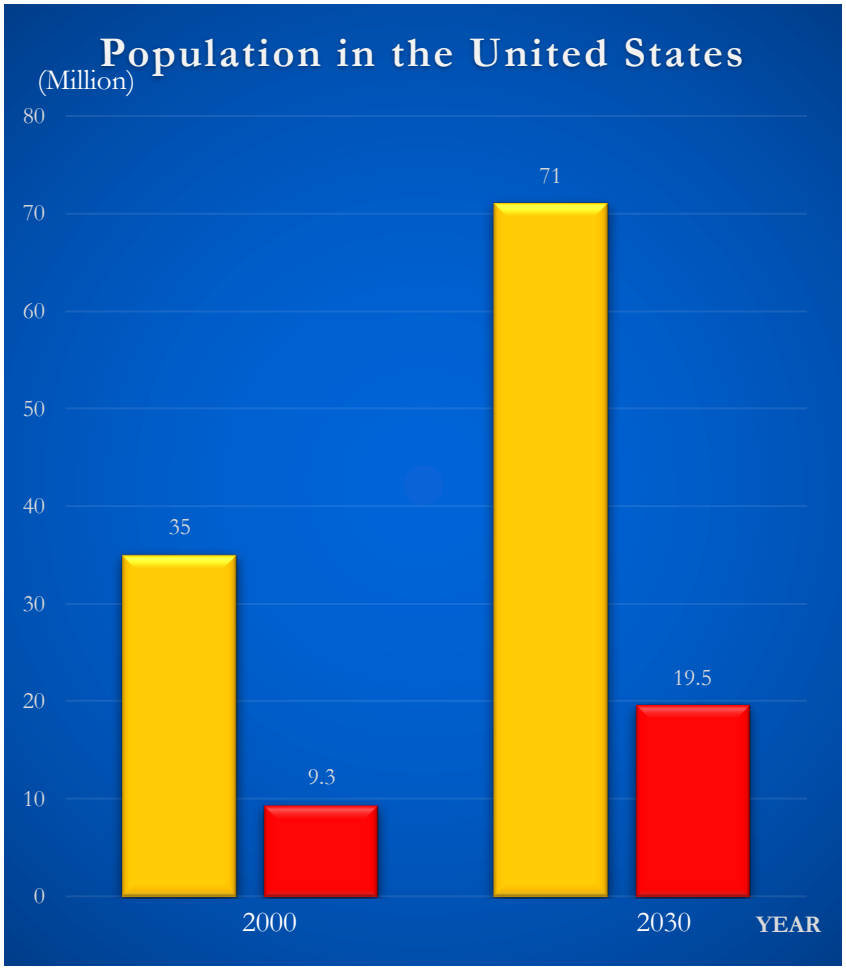
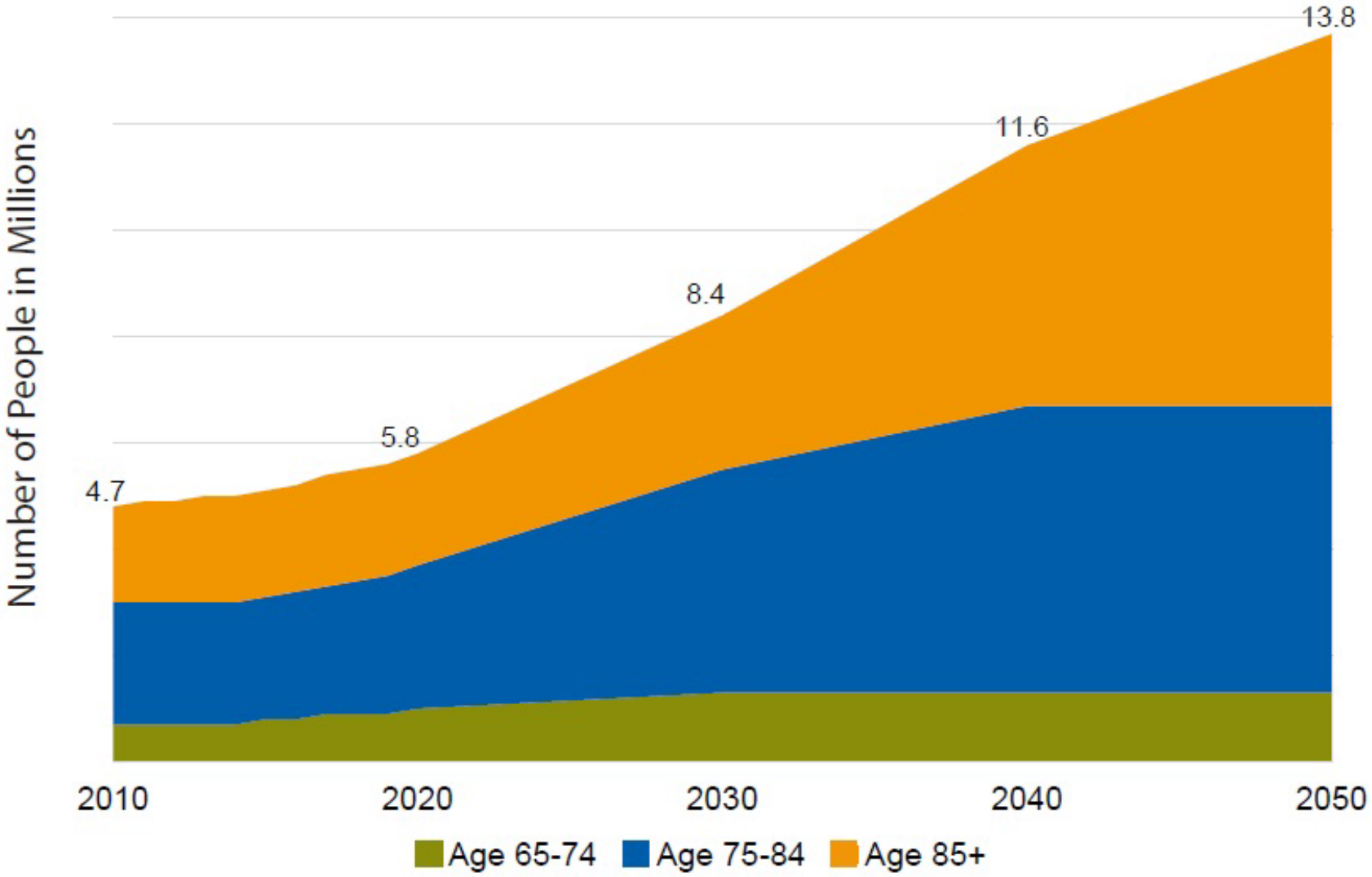
Increase in Geriatric Population



- 65 years old or older (Yellow bar): In 2000: 35 million and expected to increase to 71 million in 2030.
- 80 years old or older (Red Bar): 9.3 million in 2000 and expected to increase to 19.5 million in 2030.

Projected Number of People Aged 65 or Older With Alzheimer's Disease, by Age Group, United States, 2010-2050



Source: Created from data in Hebert LE, Weuve J, Scherr PA, Evans DA. Alzheimer disease in the United States (2010-2050) estimated using the 2010 Census. *Neurology* 2013;80(19):1778-83.

Sleep Apnea and Cognition

- Sleep Apnea-related sleep disruption reduces cognitive reserve (Alchanatis et al, 2005).
- Postoperative sleep disruption or restriction may precipitate delirium, particularly where cognitive reserves are low.
- SDB is associated with increased risk (26%) of cognitive impairment and small worsening in executive function (Leng et al, 2017).

Cognitive Decline in Elderly

- Cohen-Zion et al, 2001.

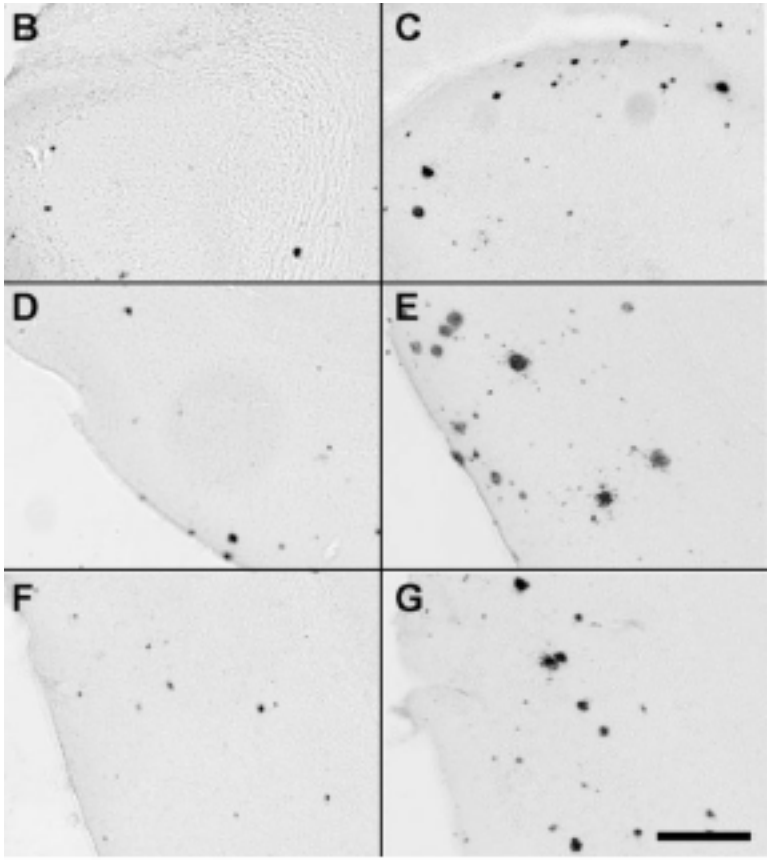
1. Declining cognitive function is associated primarily with increases in daytime sleepiness.
2. Older patients suffering from mild-moderate SDB may benefit from the treatment of SDB, even if they are not markedly hypoxic.

SDB Increases Risk of Mild Cognitive Impairment/Dementia

- Yaffe et al, 2011. Prospective observational study. 298 women enrolled. 105 women (35.2%) had SDB.
- SDB was associated with an increased risk of developing cognitive impairment 5 years laer.
- No SDB group: SDB Group 31.1% [n=60] vs. 44.8% [n=47]; adjusted odds ratio [AOR], 1.85; 95% confidence interval [CI], 1.11-3.08.

Sleep-Wake Cycle May Affect β-Amyloid levels

- Kang et al, 2009. Brain Aβ levels higher in mice after acute sleep deprivation. Brain Aβ level correlates with wakefulness in mice.



Diabetes and Dementia

- Insulin receptors (IR) exist in the brain.
- IR mediate cognitive function (attention, executive functioning, learning, memory).
- Insulin degrading enzyme regulates β Amyloid level in CNS: insulin resistance could be a predisposition to dementia.
- Insulin resistance induces changes in inflammatory response.
- Increase in micro and macro vascular disease.

Obesity and Cognition

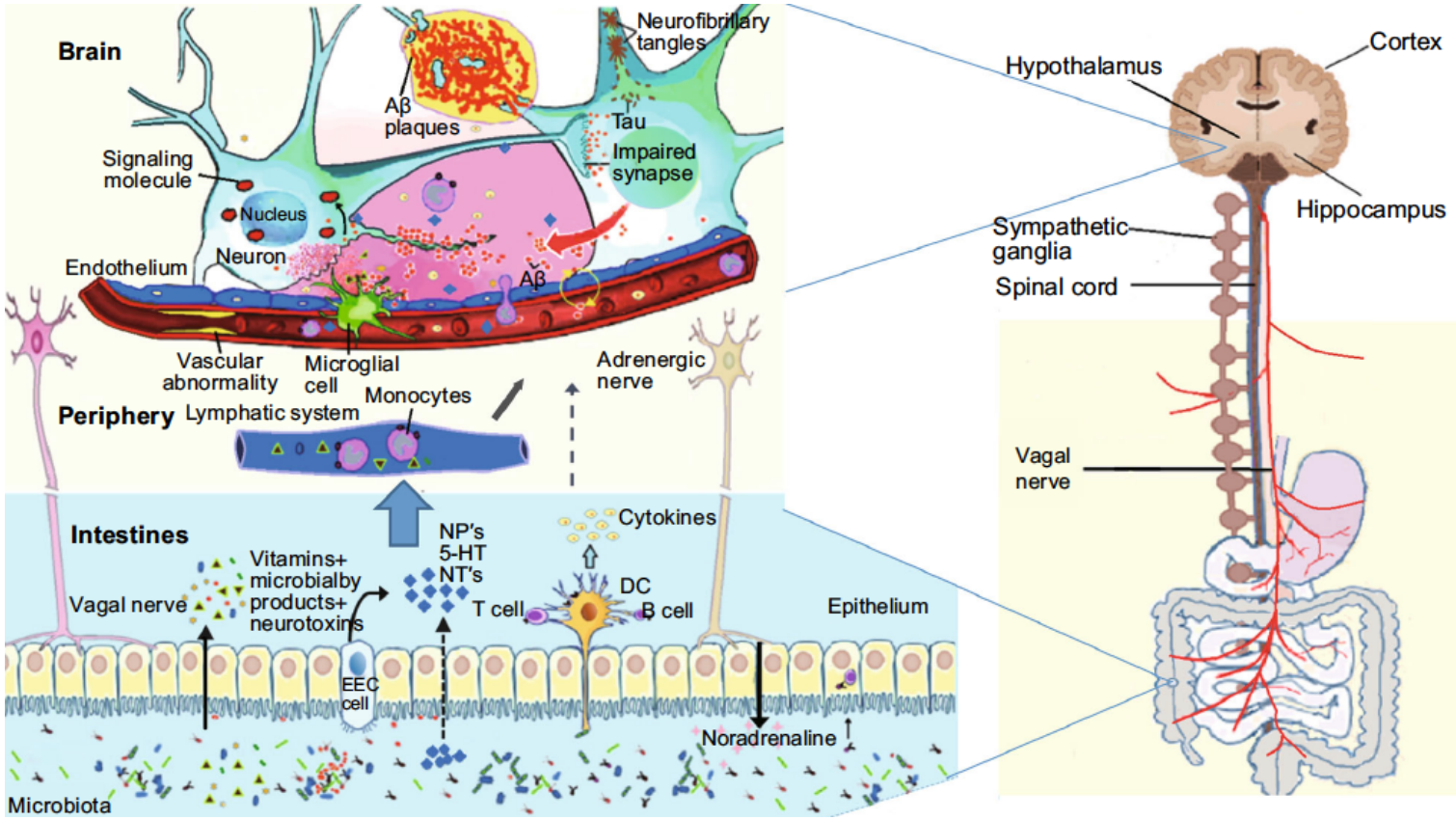
- Obesity Increases the risk of developing MCI/dementia.
- Negative effect on Cardiovascular and metabolic physiology.

1. Obesity is linked to systemic and central inflammation (e.g., increased TNFα, IL-6, IL-1).
2. May cause brain atrophy (e.g.,hippocampus).
3. May be associated with Blood brain barrier dysfunction.

Emerging Areas of Research

- The impact of gut microbiota on dementia is an emerging area of research.
- Gut Microbiota are linked to dementia pathogenesis through triggering metabolic diseases and low grade inflammation (Alkasir et al, 2017).

Gut Microbiota and Alzheimer Disease



Alkasir et al.2017

The Effect of CPAP on Cognition

- Lam et al, 2017 (Review article): 4/5 studies showed a long term use of CPAP helped to improve cognitive function.
    1. Martinez-Garcia et al, 2015. 3 months use of a CPAP improved QOL and performance on some cognitive tests.
    2. Dalmases et al, 2015. Improved cognition, increased brain tissue connectivity and increased cortical thinning.
    3. 3 months use of CPAP decreases evening cortisol level (Schmoller et al, 2009).

Does CPAP Mitigate POD/POCD?

- Nadler et al, 2017. 114 elderly patients scheduled for joint replacement were studied.
- Patients who were at risk for sleep apnea were randomized in a CPAP group vs. standard care.
- Perioperative use of CPAP did not change the incidence or severity of POD.
- There is no strong evidence that perioperative use of CPAP effectively reduced the incidence of POD.

Delirium Treatment
(Adapted from UCSF Delirium Pathway)

Evaluate the patient for underlying contributors to delirium:

- Physical exam: check surgical wound; check tubes/lines/drains;
- Brief neuro exam
- Vital signs, oxygen saturation, pain assessment
- Targeted Workup: Consider ABG, UA, CBC, BMP, TSH, LFTs, UTox, cultures, EKG, Chest X-ray

Evaluate for reversible precipitating or contributing factors:

- Drugs/Medications /polypharmacy
- Electrolytes (Na, Ca, acid-base disorders), Environment change
- Lack of drugs (withdrawal), Lack of sleep
- Infection, Immobility (catheters, feeding tubes), Iatrogenic
- Restraints, Reduced sensory input (vision, hearing), respiratory (hypoxemia/hypercarbia)
- Intracranial (stroke, bleed, seizure, meningitis)
- Urinary Retention, constipation, Uncontrolled pain
- Metabolic (hypoxia, hypercarbia, uremia, hepatic encephalopathy, thyroid)

Care pathway of delirium in patients with sleep apnea

- Identify patients who are at risk(e.g., pro-inflammatory state, low cognitive reserve).
- Initiate PAP therapy prior to surgery.
- In hospital: Enroll in care pathway including multicomponent intervention.

Conclusions

- Sleep Apnea increases the risk of POD/POCD.
- There is no strong evidence that perioperative use of CPAP mitigate POD/POCD.
- The research is needed to investigate to identify who are at risk for POD/POCD among sleep apnea patients.