The Role of Cerebrospinal Fluid Circulation in Sleep Apnea

TIGRAN KHACHATRYAN MD
JAMES HERNANDEZ
MONDA MAHMOUD MD
JOE SAM ROBINSON MD

Outline

- Introduction – breaking the code
- Definition
- History
- Epidemiology
- Etiology and classification
- Vicious cycle of Sleep Apnea
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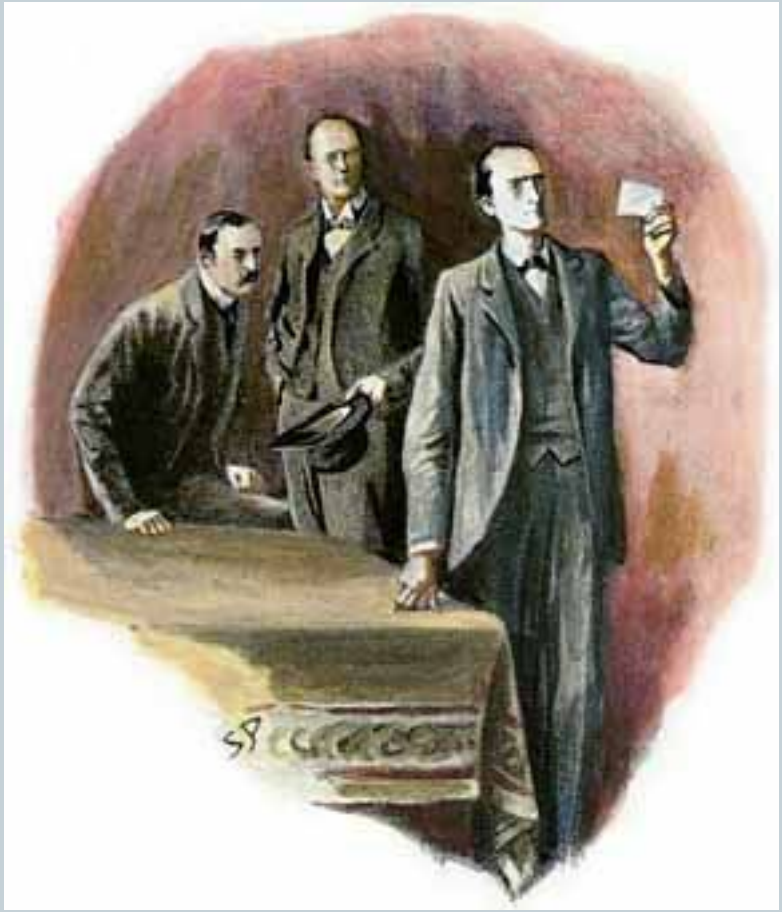
  - CSF flow arrangements
    - Normal CSF circulation
    - Compensation and Feedback
    - Altered CSF circulation
  - Increased intracranial pressure
  - Sleep arrangements
  - Global impact
  - Neurological impact
- Therapy
- Suggestions
- Conclusion

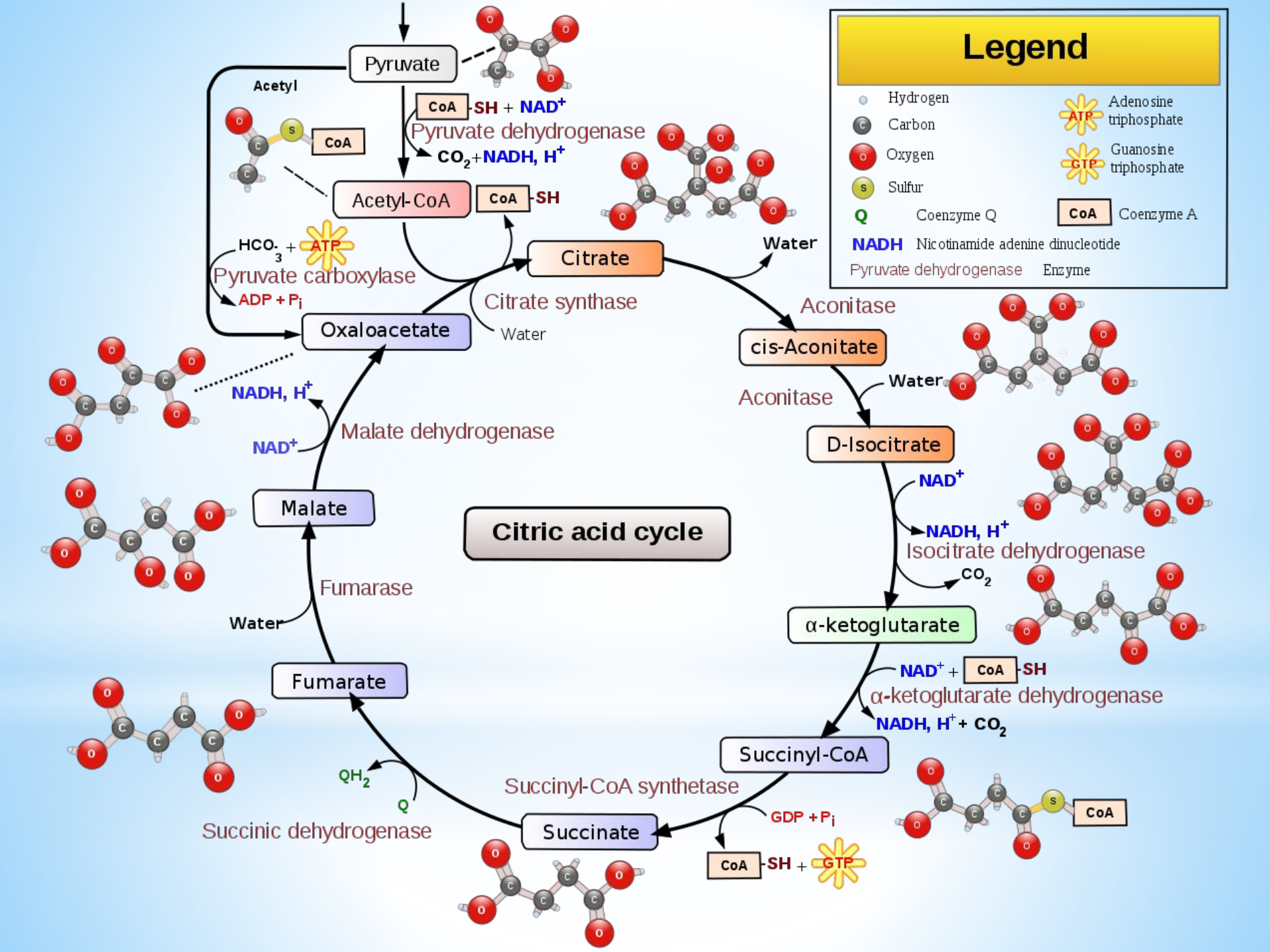
Introduction – breaking the code

"The Adventure of the Dancing Men”

Sherlock Holmes

Sir Arthur Conan Doyle, 1903




Legend
Hydrogen
Carbon
Oxygen
Sulfur
Q Coenzyme Q
NADH Nicotinamide adenine dinucleotide
Pyruvate dehydrogenase Enzyme
Adenosine triphosphate
Guanosine triphosphate
CoA Coenzyme A
Citric acid cycle
Pyruvate
Acetyl
CoA -SH + NAD+
Pyruvate dehydrogenase
CO2+NADH, H+
Acetyl-CoA
CoA -SH
HCO3- + ATP
Pyruvate carboxylase
ADP + Pi
Oxaloacetate
Citrate
Citrate synthase
Water
Water
Aconitase
cis-Aconitate
Water
Aconitase
D-Isocitrate
NAD+
NADH, H+
Isocitrate dehydrogenase
CO2
α-ketoglutarate
NAD+ + CoA -SH
α-ketoglutarate dehydrogenase
NADH, H+ + CO2
Succinyl-CoA
Succinyl-CoA synthetase
GDP + Pi
CoA -SH + GTP
Succinate
QH2
Q
Succinic dehydrogenase
Fumarate
Water
Fumarase
Malate
NADH, H+
NAD+
Malate dehydrogenase

Definition

Sleep apnea is a serious sleep disorder which is characterized by periodic (sometimes hundreds of times) interruptions of breathing during sleep. This results in insufficient oxygen supply to the brain and the rest of the body.

Arterial Blood Gases in Sleep Apnea

- Borderline ↓PH - 7.380 ± 0.23
- ↑P_{CO2}, especially in the morning - 41.70 ± 4.28 mmHg
- ↓P_{O2} - 88.14 ± 17.83 mmHg
- ↑Lactic Acid - 2.23 ± 0.59 mmol/L

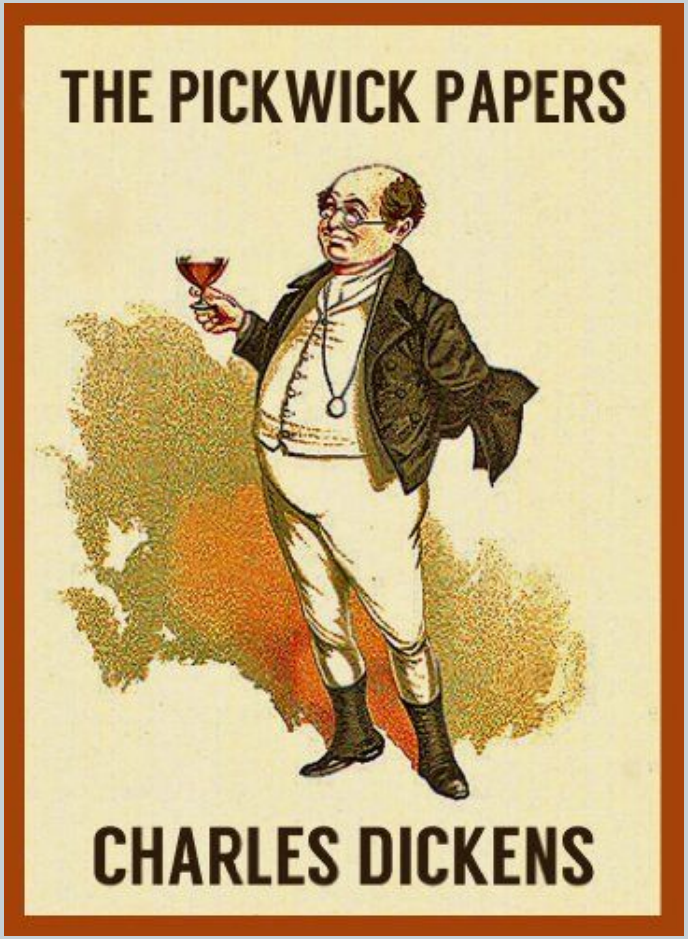
Sleep Breath. 2017 May;21(2):303-309. doi: 10.1007/s11325-016-1409-x. Epub 2016 Sep 29.

The effect of CPAP treatment on venous lactate and arterial blood gas among obstructive sleep apnea syndrome patients.

Lin T[1], Huang JF[1], Lin QC[2], Chen GP[1], Wang BY[1], Zhao JM[1], Qi JC[1].

First description

First Description of Some Sleep Apnea Symptoms



On the box sat a fat and red-faced boy, in a state of somnolency . . .

'Damn that boy,' said the old gentleman, 'he's gone to sleep again.'

'Very extraordinary boy, that,' said Mr Pickwick, 'does he always sleep in this way?'

'Sleep!' said the old gentleman, 'he's always asleep. Goes on errands fast asleep, and snores as he waits at table.'

'How very odd!' said Mr Pickwick.

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First scientific publications

Acta Med Scand. 1949 Jan 20;132(4):378-83.

On changes in the organism resulting from insufficient gas exchange; on the cause of the lowered tissue respiration in insufficient gas exchange and on the effect of high carbon dioxide concentrations in tissue respiration.

COLLDAHL H.

PMID: 18120823

[Indexed for MEDLINE]

J Appl Physiol. 1953 Apr;5(10):614-8.

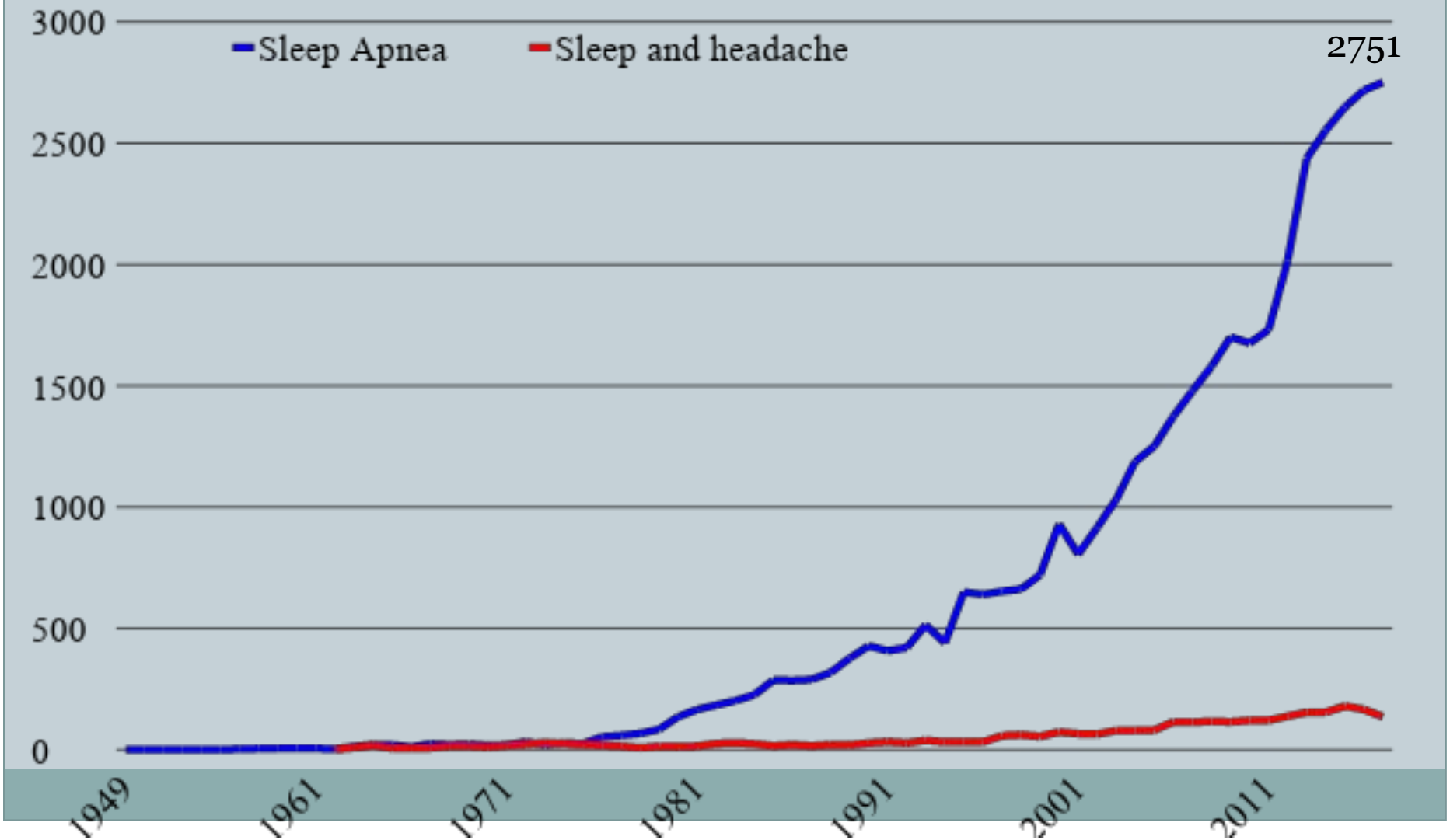
Obstructive apnea in artificially hyperventilated subjects during sleep.

PELTIER LF.

PMID: 13044741 DOI: 10.1152/jappl.1953.5.10.614

[Indexed for MEDLINE]

Published articles related to Sleep Apnea – 40,634



Epidemiology

Prevalence of Sleep Apnea

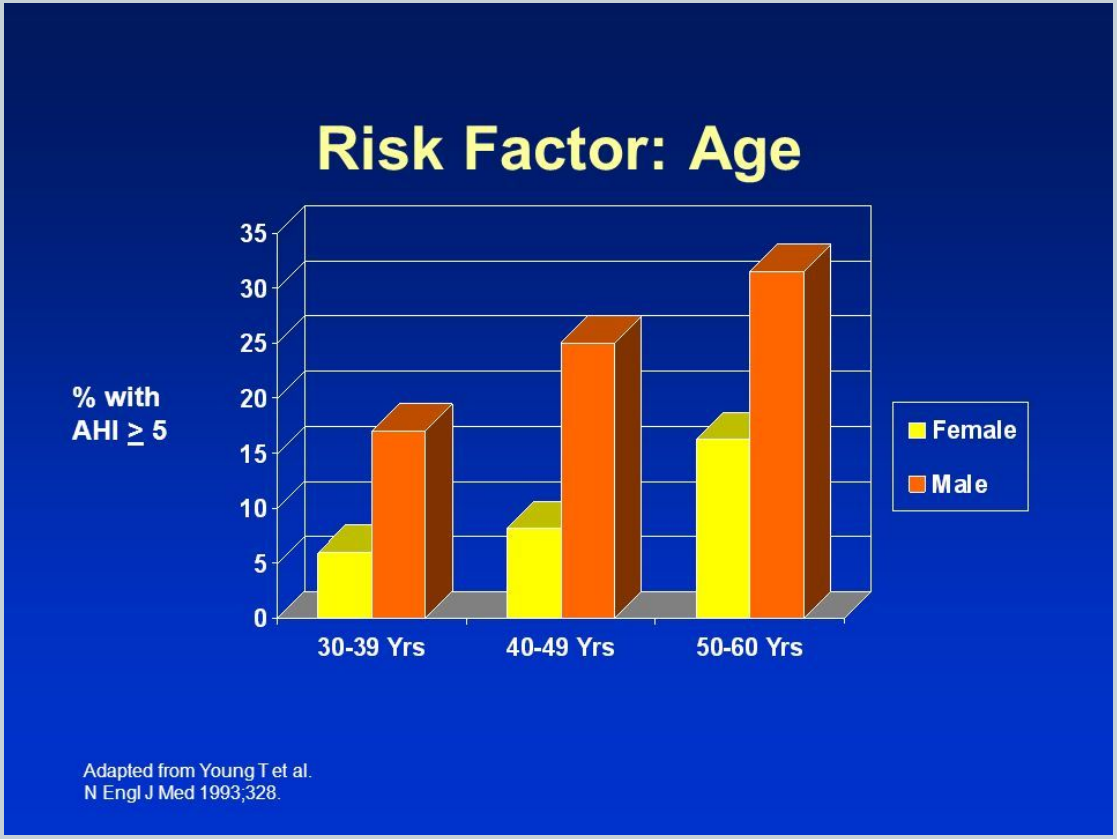
- 22 million Americans suffer from Sleep Apnea

➢ Mild, moderate or severe Sleep Apnea
  - 24% of middle aged men
  - 9% of middle aged women
  - These patients stop breathing >40 times per night

➢ Moderate or severe sleep apnea
  - 15% of middle aged men
  - 5% of middle aged women
  - These patients stop breathing >120 times per night

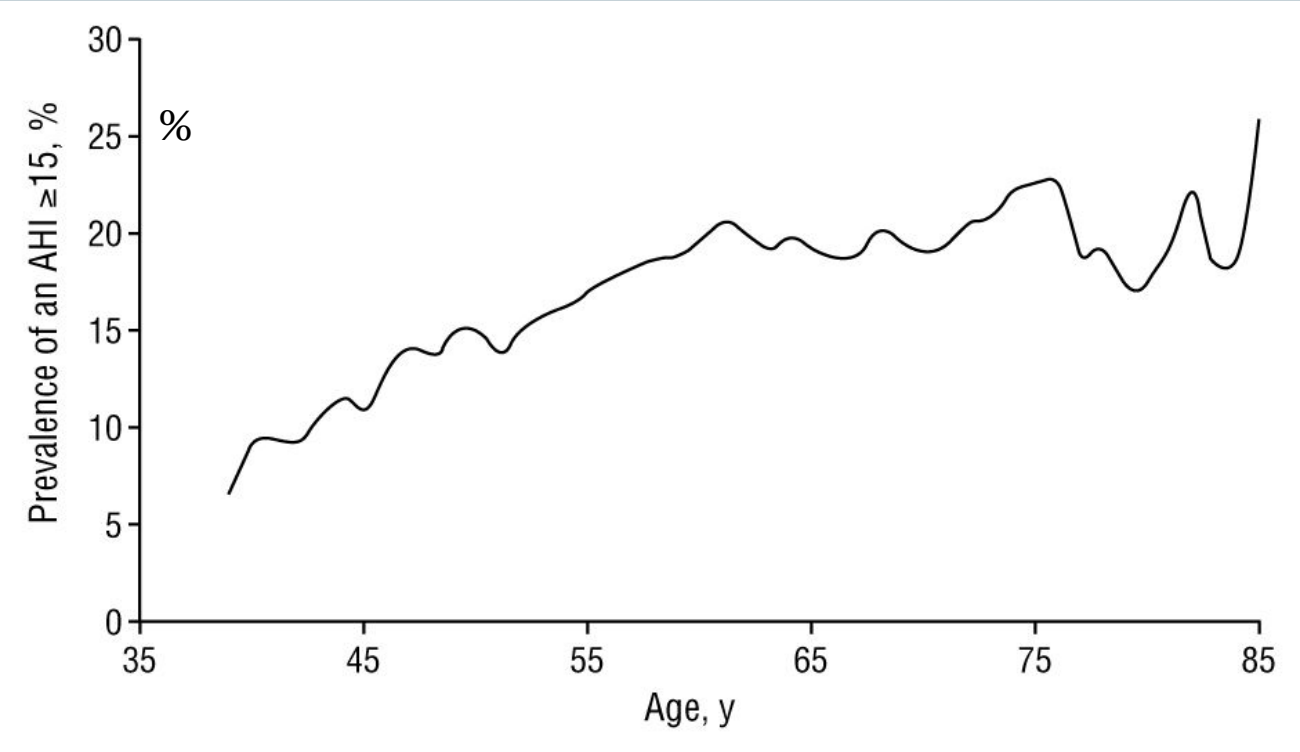
Source: The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults; Terry Young, Mari Palta, Jerome Dempsey, James Skatrud, Steven Weber, and Safwan Badr; N Engl J Med 1993; 328:1230-1235

Sleep Apnea and age



Source: The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults; Terry Young, Mari Palta, Jerome Dempsey, James Skatrud, Steven Weber, and Safwan Badr; N Engl J Med 1993; 328:1230-1235

Sleep Apnea and age



Arch Intern Med. 2002 Apr 22;162(8):893-900.

Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study.

Young T[1], Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, Walsleben JA, Finn L, Enright P, Samet JM; Sleep Heart Health Study Research Group.

Contemporary Etiology and Classification

Classification

Obstructive Sleep Apnea (OSA):

- Apnea with ventilatory efforts due to pharyngeal collapse
- Patient tries to breathe but can't due to upper airway obstruction
- ~90% of sleep apnea cases[1]

Central Sleep Apnea (CSA):

- Apnea without ventilatory effort due to withdrawal of central drive
- Cheyne-Stokes respiration a subset of CSA
- ~10% of sleep apnea cases[1]

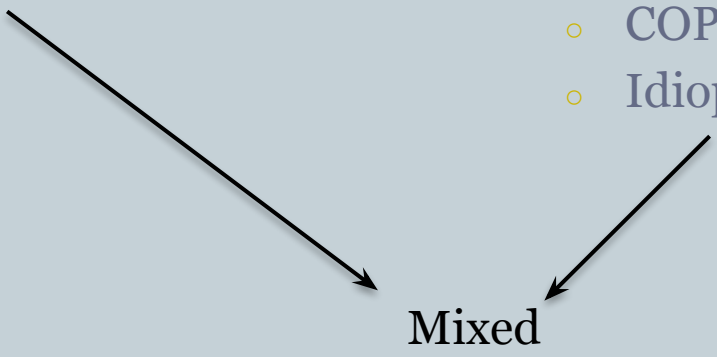
Mixed Sleep Apnea:

- Apnea with central component followed by obstructive compone
- Often classified as obstructive sleep apnea

Source: The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults; Terry Young, Mari Palta, Jerome Dempsey, James Skatrud, Steven Weber, and Safwan Badr; N Engl J Med 1993; 328:1230-1235

Causes of Sleep Apnea – Contemporary view

- Obstructive
  - Enlarged tonsils
  - Adenoids
  - Dental conditions
  - Birth defects
  - Down syndrome (enlarged tongue)
  - Pierre-Robin Syndrome (mandibular hypoplasia)
  - Obesity
- Central – brainstem conditions
  - Infection
  - Stroke
  - Degenerative cervical spine disease
  - Certain medications, such as narcotics
  - High-altitude periodic breathing
  - Chiari Malformation
  - COPD
  - Idiopathic



A new code?

Sleep Apnea has more than a solitary cause - Ockham's razor

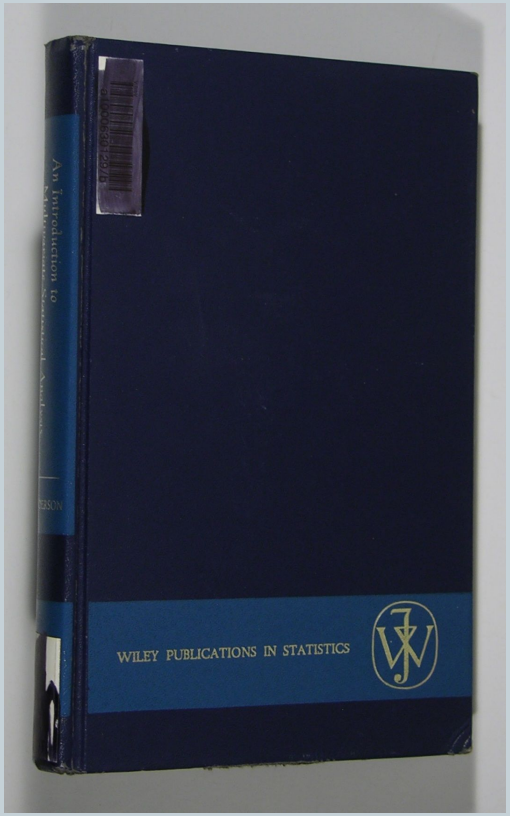
"With all things being equal, the simplest explanation tends to be the right one."

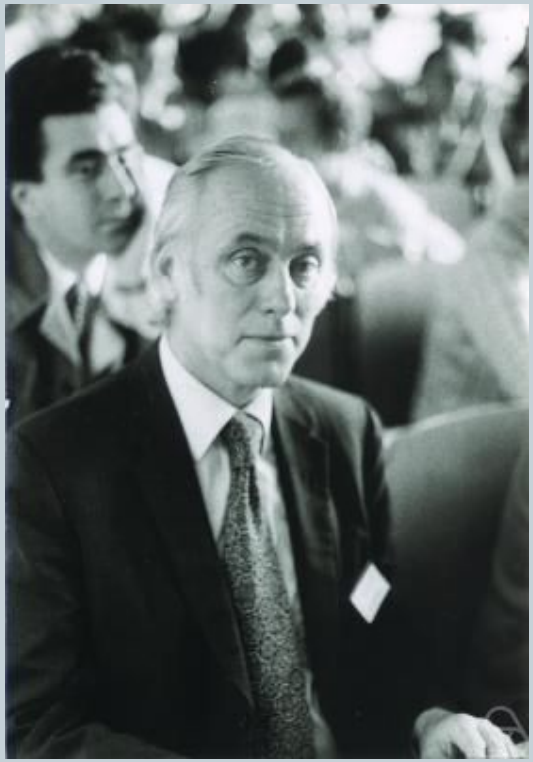
(a 14th century philosophical argument for the existence of God as the origin of all causality)

By extension the traditional unitary thought process employed by physicians to explain medical maladies.

William of Ockham (ca. 1287–1347)

A more contemporary viewpoint…
Multiple interconnected causation – biostatistics in the 21st century





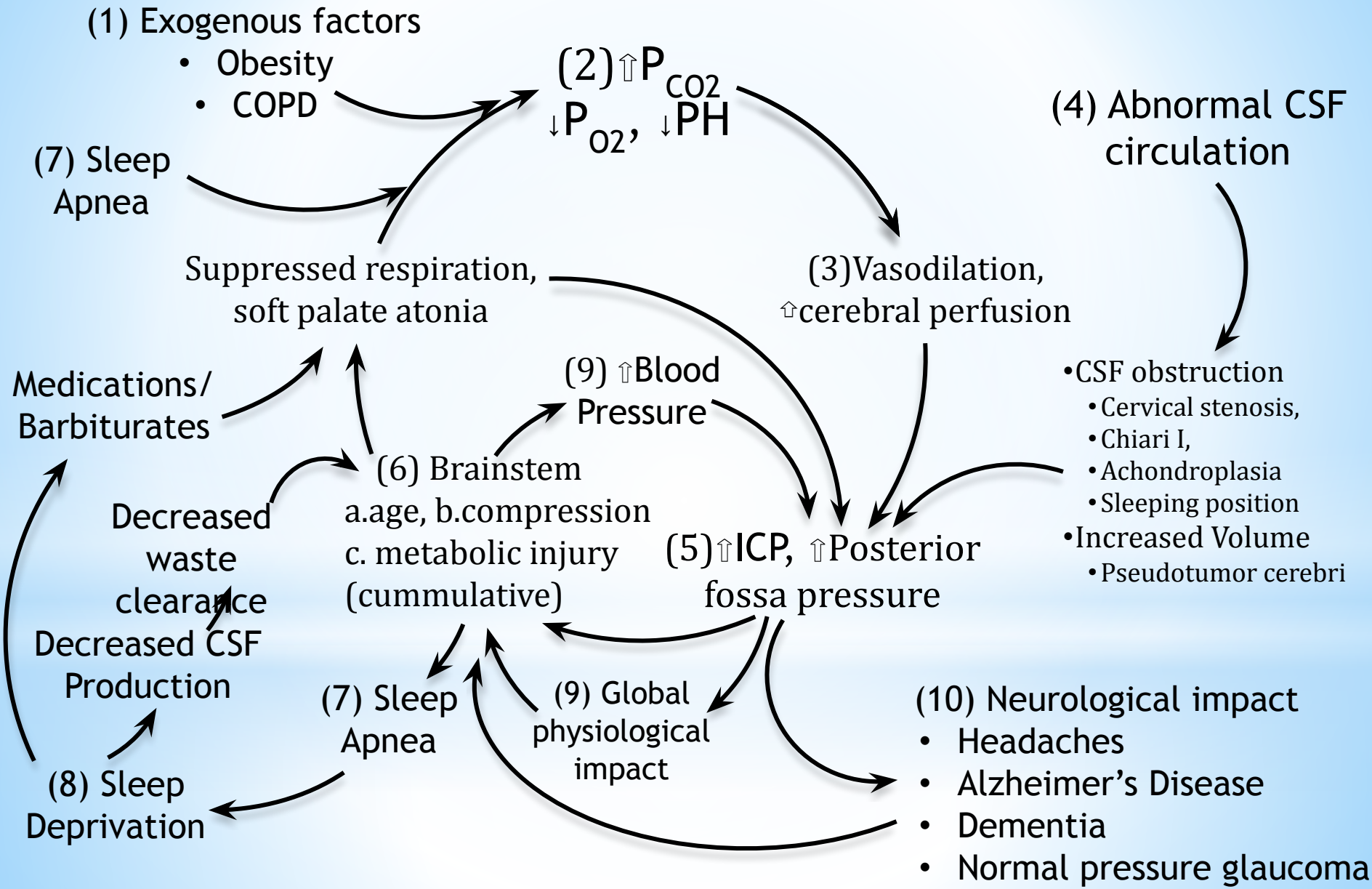
An Introduction to Multivariate Statistical Analysis by T. W. Anderson, 1958

Another causal agent

- Obstructive
  - Enlarged tonsils
  - Adenoids
  - Dental conditions
  - Birth defects
  - Down syndrome (enlarged tongue)
  - Pierre-Robin Syndrome (mandibular hypoplasia)
  - Obesity
- Central – brainstem conditions
  - Infection
  - Stroke
  - Degenerative cervical spine disease
  - Certain medications, such as narcotics
  - High-altitude periodic breathing
  - Chiari Malformation
  - COPD
  - Idiopathic
  - Altered CSF circulation?
    - Pseudotumor cerebri
    - Normal Pressure Hydrocephalus

Increased ICP

Sleep Apnea – a Vicious Cycle



Cumulative Risk Factors of Sleep Apnea (some examples)

1. Congestive heart failure

Clin Chest Med. 1998 Mar;19(1):99-113.

Sleep apnea in congestive heart failure.

Naughton MT[1], Bradley TD.

2. COPD

Int J Chron Obstruct Pulmon Dis. 2014 Apr 8;9:349-62. doi: 10.2147/COPD.S42394. eCollection 2014.

Update on obstructive sleep apnea and its relation to COPD.

Mieczkowski B[1], Ezzie ME[1].

1.Exogenous factors

Obesity Hypoventilation Syndrome

- Presence of hypoventilation during wakefulness (Pa_{CO_2} greater than 45 mm Hg) as measured by arterial P_{CO_2}, end-tidal P_{CO_2}, or transcutaneous $_{PCO_2}$
- Presence of obesity (body mass index or BMI greater than 30 kg/m2; greater than the 95th percentile for age and sex for children)

Ventilation, Obesity-Hypoventilation Syndrome.

Katyal N[1], Bollu PC[2].

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018-.
2018 Feb 15.

PLoS One. 2015 Feb 11;10(2):e0117808. doi: 10.1371/journal.pone.0117808. eCollection 2015.

Obesity-hypoventilation syndrome: increased risk of death over sleep apnea syndrome.

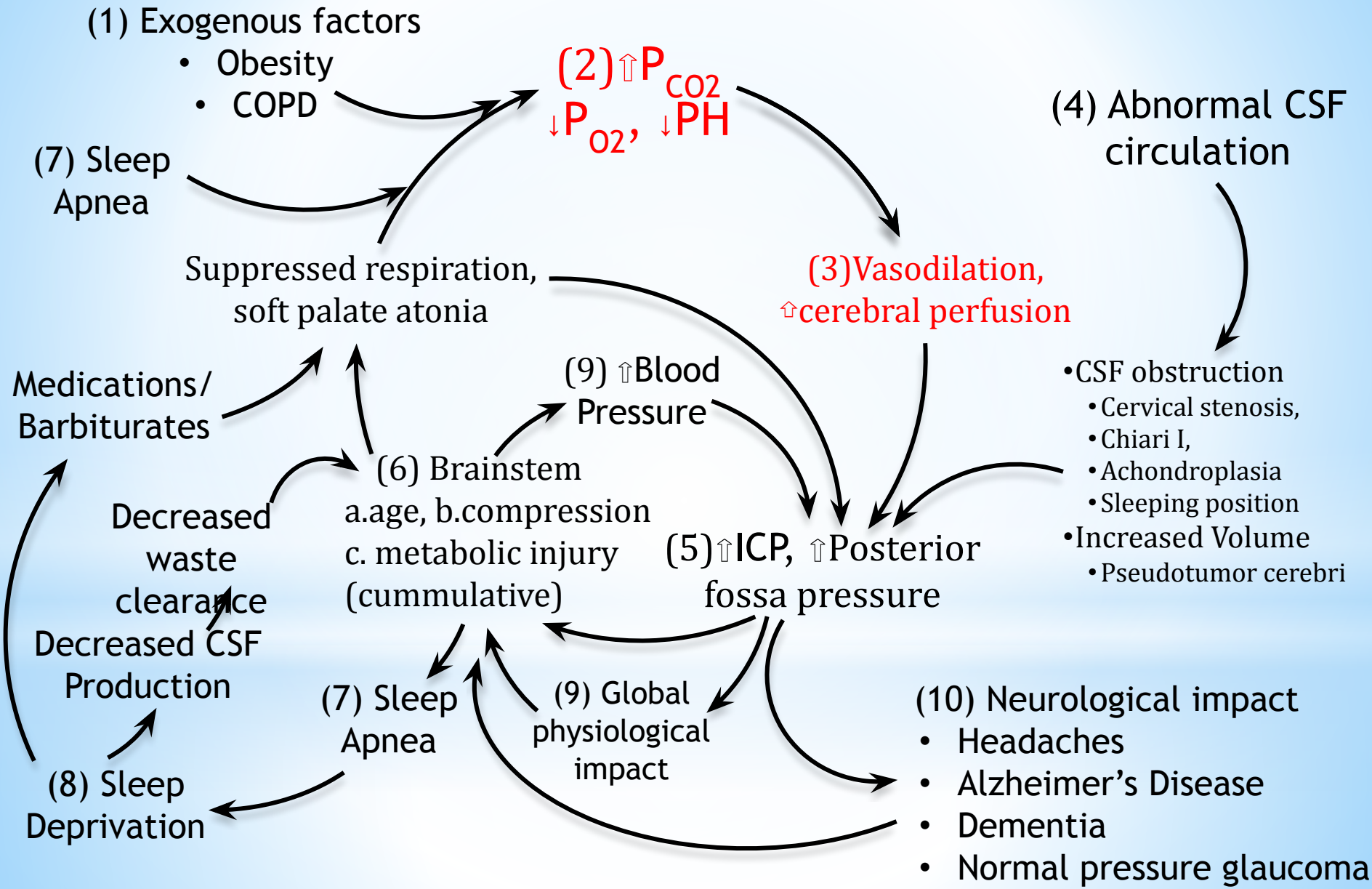
Castro-Añón O[1], Pérez de Llano LA[1], De la Fuente Sánchez S[2], Golpe R[1], Méndez Marote L[1], Castro-Castro J[3], González Quintela A[4].

Curr Pulmonol Rep. 2015 Mar 1;4(1):42-55.

Obesity Hypoventilation Syndrome.

Shetty S[1], Parthasarathy S[2].

Sleep Apnea – a Vicious Cycle

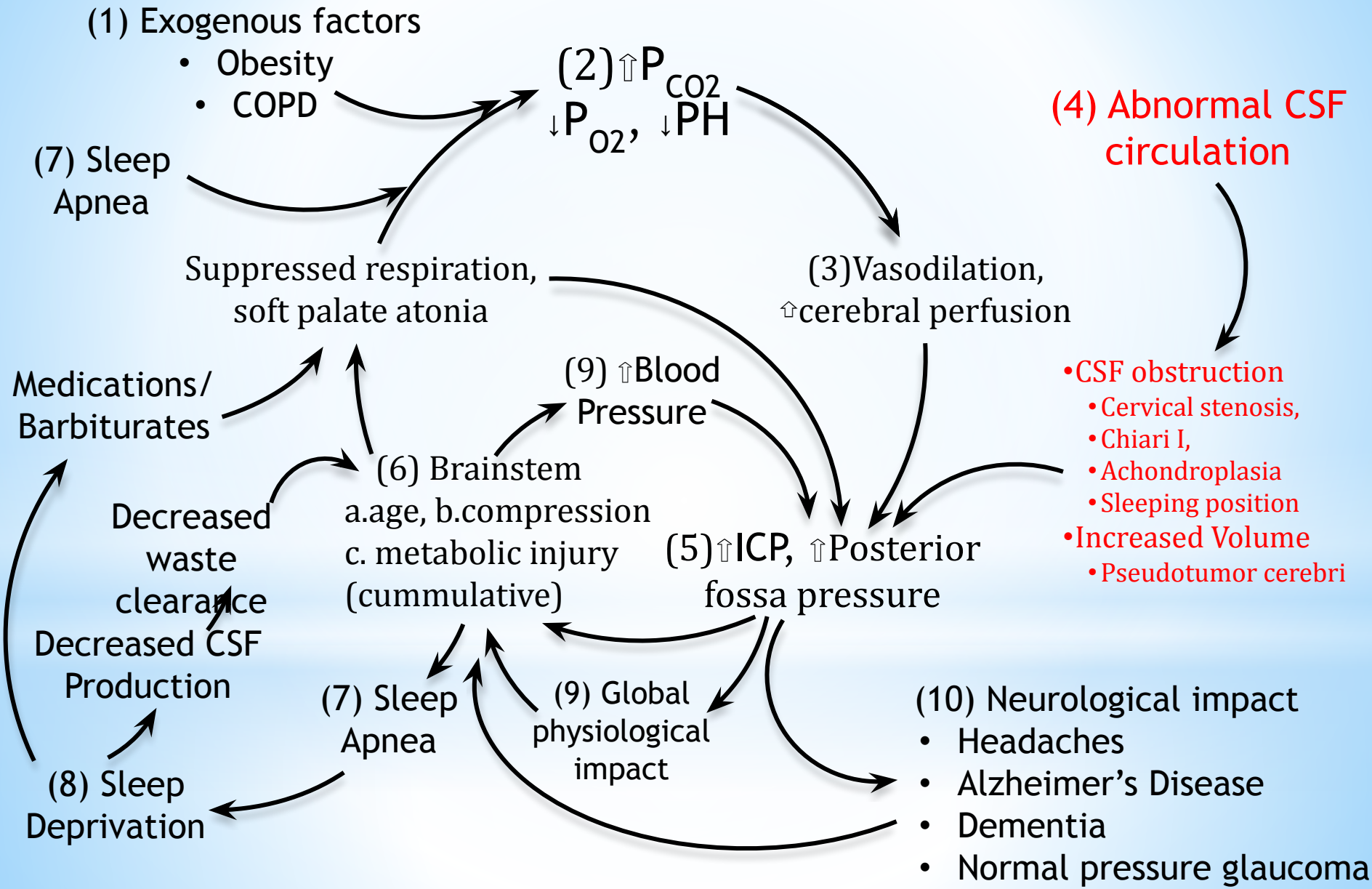


Mechanisms of increased ICP in Sleep Apnea

- Hypercapnia has been shown to increase ICP by augmentation of cerebral blood volume.
- Hypoxia also increases ICP, the mechanisms by which this pressure increase occurs being at least twofold:
  - vasodilatation
  - cerebral edema
- Hypertension may also be contributing to the increase in ICP.
- Increase in central venous pressure due to increased intrathoracic pressure at the termination of the apnea may also be involved

Source: Intracranial hypertension associated with obstructive sleep apnea: A discussion of potential etiologic factors; D.E. Wardly; Medical Hypotheses 83 (2014) 792–797

Sleep Apnea – a Vicious Cycle



Normal CSF circulation arrangements – a quick journey

absence of substantial range of normal data makes the journey a bit difficult

CSF circulation - not an existentialist variable

CSF circulation should be considered physiologically similar to blood pressure in that it may be chronically injurious if not maintained in ideal configuration.

Normal CSF circulation

CSF Functions

Buoyancy:

- The brain suspended in the CSF is equivalent to a mass of 25-50 grams (instead of 1400–1500 grams). Without CSF it would be impaired by its own weight, which would cut off blood supply in the lower sections.

Protection:

- CSF protects the brain tissue from injury when jolted or hit, by providing a fluid buffer that acts as a shock absorber from some forms of mechanical injury.

Prevention of brain ischemia:

- Decreasing amount of CSF decreases total intracranial pressure and facilitates blood perfusion.

Homeostasis:

- CSF allows for regulation of the distribution of substances between cells of the brain, and neuroendocrine factors, to which slight changes can cause problems or damage to the nervous system.

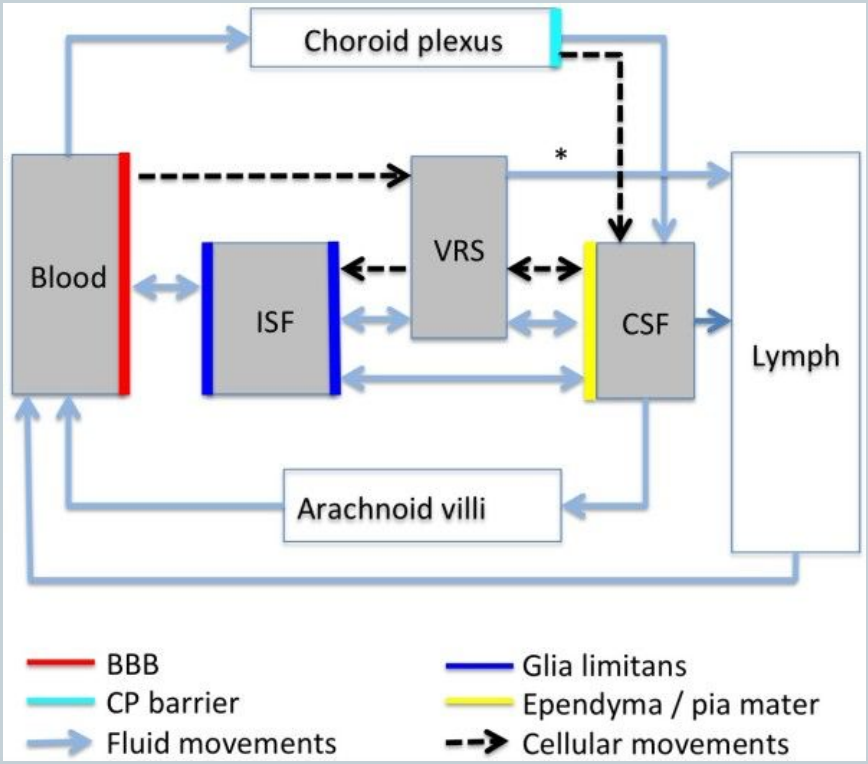
Clearing waste:

- CSF allows for the removal of waste products from the brain, and is critical in the brain's lymphatic system. Metabolic waste products diffuse rapidly into the CSF and are removed into the bloodstream as CSF is absorbed.

Source: Bhattacharjee IR. Self Gravity: The Major Investigation Gap in Life Science (Part I). WebmedCentral BIOPHYSICS 2013;4(6):WMC004279 doi: 10.9754/journal.wmc.2013.004279

Normal CSF circulation

CSF circulation arrangements



Fluids Barriers CNS. 2014 May 1;11:10. doi: 10.1186/2045-8118-11-10. eCollection 2014.

A new look at cerebrospinal fluid circulation.

Brinker T[1], Stopa E[1], Morrison J[1], Klinge P[1].

Author information

1 Department of Neurosurgery, The Warren Alpert Medical School of Brown University, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903, USA.

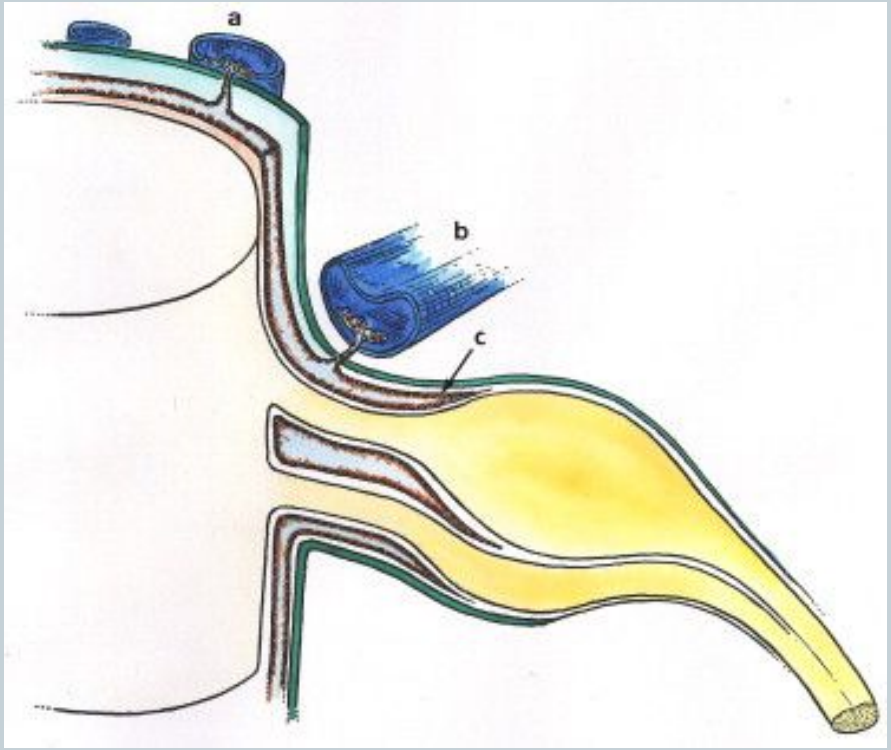
Normal CSF circulation

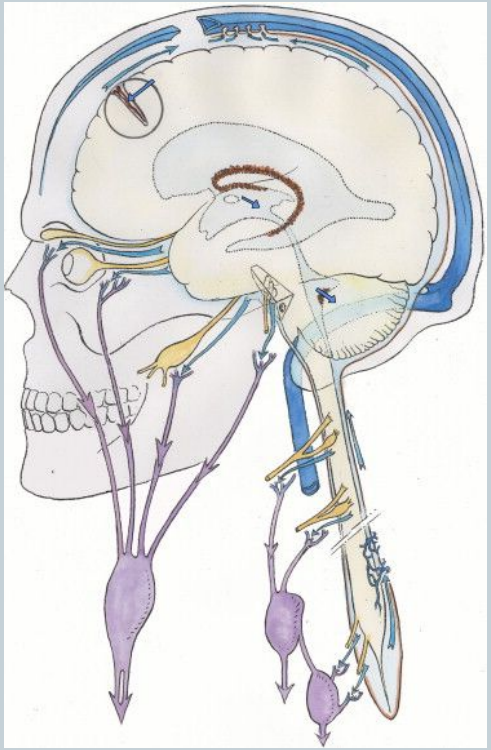
- Basic principles of fluid movements in the brain
  1. Diffusion
  2. Bulk flow or convection
  3. Active transport
  4. Filtration and secretion

Source: Mechanisms of fluid movement into, through and out of the brain: evaluation of the evidence; Stephen B Hladky and Margery A Barrand; Fluids Barriers CNS. 2014; 11: 26.

Normal CSF circulation

CSF absorption in spinal arachnoid villae and lymphatic system of cranial nerves





Eur Ann Otorhinolaryngol Head Neck Dis. 2011 Dec;128(6):309-16. doi: 10.1016/j.anorl.2011.03.002. Epub 2011 Nov 18.

Anatomy and physiology of cerebrospinal fluid.

Sakka L[1], Coll G, Chazal J.

Author information

1 Laboratoire d'anatomie, faculté de médecine, université d'Auvergne, 28, place Henri-Dunant, 63001 Clermont-Ferrand cedex 1, France. lsakka@chu-clermontferrand.fr

Normal CSF circulation

CSF flow – not a constant steady stream

- CSF is not produced exclusively by choroid plexus
- CSF production changes by age
- CSF production changes throughout the day
- CSF flow alterations maybe transient and positional
- Intracranial pressure is variable

Fluids Barriers CNS. 2014 May 1;11:10. doi: 10.1186/2045-8118-11-10. eCollection 2014.

A new look at cerebrospinal fluid circulation.

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1 Department of Neurosurgery, The Warren Alpert Medical School of Brown University, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903, USA.

CSF abnormalities may be transient and may depend on secondary factors

24-hour erratic flow dynamics of CSF

Fluids Barriers CNS. 2014 May 1;11:10. doi: 10.1186/2045-8118-11-10. eCollection 2014.

A new look at cerebrospinal fluid circulation.

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1 Department of Neurosurgery, The Warren Alpert Medical School of Brown University, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903, USA.

Abstract

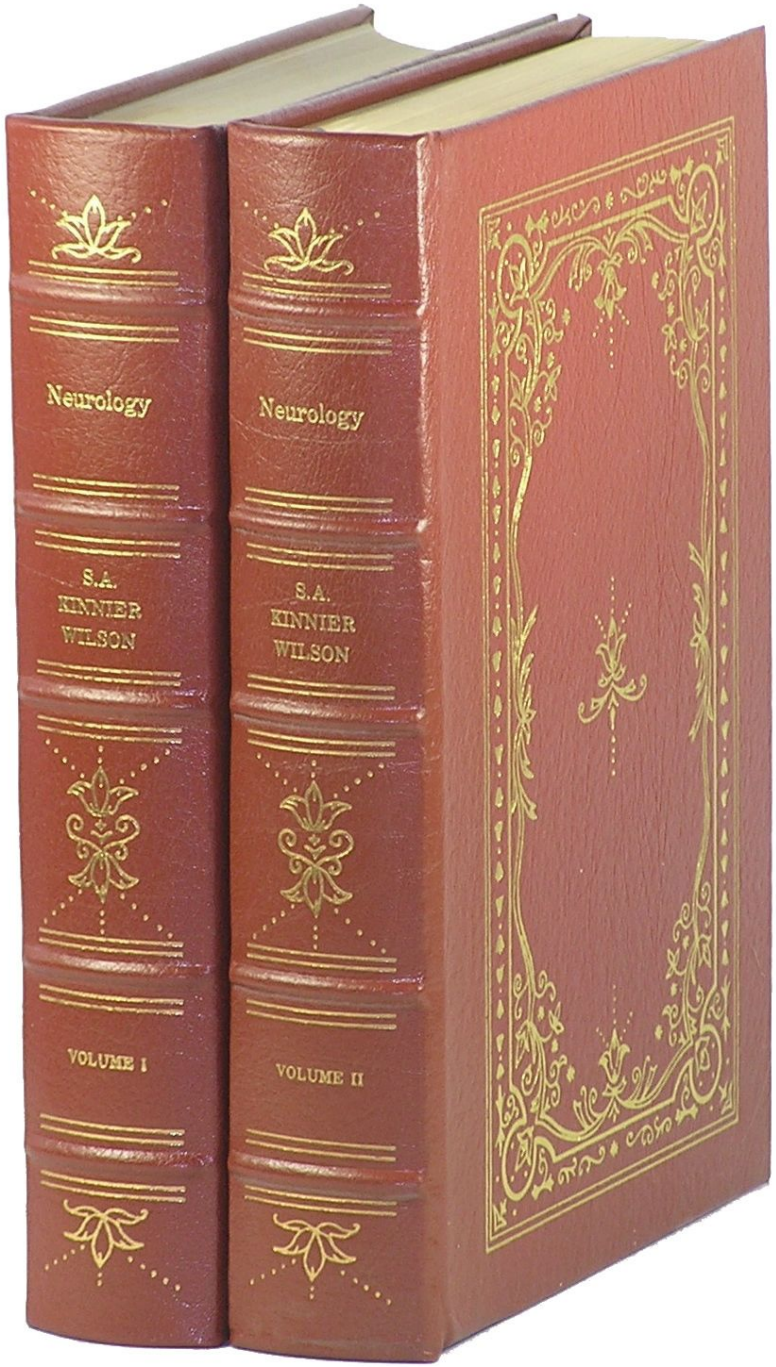
According to the traditional understanding of cerebrospinal fluid (CSF) physiology, the majority of CSF is produced by the choroid plexus, circulates through the ventricles, the cisterns, and the subarachnoid space to be absorbed into the blood by the arachnoid villi. This review surveys key developments leading to the traditional concept. Challenging this concept are novel insights utilizing molecular and cellular biology as well as neuroimaging, which indicate that CSF physiology may be much more complex than previously believed. The CSF circulation comprises not only a directed flow of CSF, but in addition a pulsatile to and fro movement throughout the entire brain with local fluid exchange between blood, interstitial fluid, and CSF. Astrocytes, aquaporins, and other membrane transporters are key elements in brain water and CSF homeostasis. A continuous bidirectional fluid exchange at the blood brain barrier produces flow rates, which exceed the choroidal CSF production rate by far. The CSF circulation around blood vessels penetrating from the subarachnoid space into the Virchow Robin spaces provides both a drainage pathway for the clearance of waste molecules from the brain and a site for the interaction of the systemic immune system with that of the brain. Important physiological functions, for example the regeneration of the brain during sleep, may depend on CSF circulation.

KEYWORDS: Aquaporin; Astrocyte; Blood brain barrier; Cerebrospinal fluid circulation; Virchow Robin space

PMID: 24817998 PMCID: PMC4016637 DOI: 10.1186/2045-8118-11-10

Compromised CSF circulation – a tree in the forest

Altered CSF circulation



Causes of CSF Circulation Alterations - (a non-inclusive list)

- Production problems
  - Decreased CSF production due to diminished neuronal activity
  - Tumors of choroid plexus
  - Hypertrophy of choroid plexus
  - Genetic disorders
  - Hypertension
  - Medications
  - Intraoperative ablation
- Flow Obstructions
  - Aqueductal stenosis
  - Meningitis
  - Chiari Malformation
  - Tumors and cysts
  - Cervical Stenosis
  - Congenital abnormalities
  - Arachnoid cysts
  - Medications, drugs, alcohol
- Absorbtion problems
  - Head Trauma
  - Meningitis
  - Subarachnoid Hemorrhage
  - Intraventricular hemorrhage
  - Venous outflow obstruction
  - Venous hypertension
  - Pulmonary pathology

CSF circulation balance

- Venous outflow difficulties
  - Cervical stenosis
  - Chiari malformation
- Increased CSF viscosity

- Increased CSF flow through non-blocked pathway
  - Cerebral atrophy
- Decreased CSF production

Is there an intrinsic feedback mechanism that maintains Cerebrospinal Fluid production and absorption at an optimal level?

An example - Diminished CSF production with age

- CSF is renewed four to 5 times per 24 hours in young adults.
- Ageing is characterised by a reduction of CSF turnover to 3 times a day at the age of 77 years.
- Catabolites of neurotransmitters and beta-amyloid (Aβ) accumulate in the interstitial compartment, Virchow-Robin perivascular spaces, choroidal epithelium and ependyma during ageing and also in patients with adult chronic hydrocephalus (ACH) and Alzheimer's disease (AD).
- Forty percent of patients with ACH present histological lesions of AD
- Decreased CSF Aβ levels have been reported after an VP shunting.

Eur Ann Otorhinolaryngol Head Neck Dis. 2011 Dec;128(6):309-16. doi: 10.1016/j.anorl.2011.03.002. Epub 2011 Nov 18.

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Altered CSF circulation – Absorption issue

An Example - Venous outflow difficulties

- Increased venous pressure gradient through jugular foramen

J Neurosurg. 1989 Jul;71(1):42-8.

Hydrocephalus in achondroplasia: the possible role of intracranial venous hypertension.

Steinbok P[1], Hall J, Flodmark O.

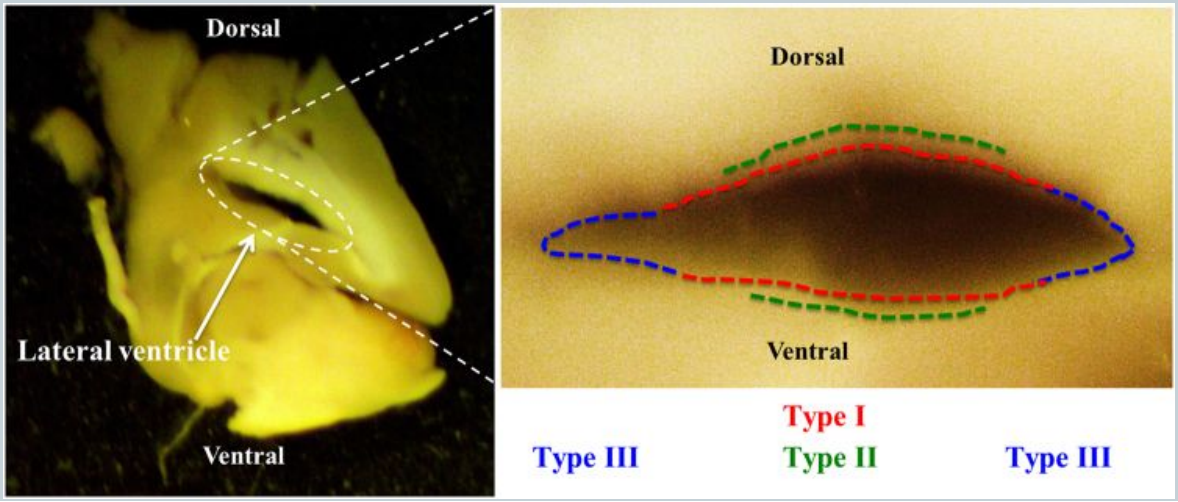
Author information

Abstract

The significance and cause of ventriculomegaly in achondroplasia was investigated in five achondroplastic children. The intraventricular pressure (IVP) was monitored over 24 hours, followed by intraventricular injection of radionuclide alone or in combination with water-soluble contrast material. The IVP was elevated and the reabsorption of cerebrospinal fluid (CSF) into the sagittal sinus was slow in all cases, but there was no obstruction to CSF flow. The spinal subarachnoid space was well seen in all patients. Jugular venograms with pressure monitoring were obtained in four patients (bilaterally in one). These studies confirmed a narrow jugular foramen in all patients with a significant venous pressure gradient (3 to 10 mm Hg) obtained while the catheter was being pulled back from the sigmoid sinus through the foramen. A second gradient was found in the jugular vein in two patients at the level of the upper thoracic aperture. This gradient was 6 and 14 mm Hg, respectively. Identical venograms and monitoring of the venous pressure in a control group showed no pressure gradients across the jugular foramen and smaller gradients (2 to 5 mm Hg) across the thoracic inlet. It is concluded from these studies that ventriculomegaly in achondroplastic children represents hydrocephalus, which is likely secondary to raised intracranial venous pressure due to hemodynamically significant stenosis of the jugular foramen and, in some cases, the jugular vein in the thoracic aperture.

An Example - Effect of Alcohol on CSF flow

- In vivo study of ependymal ciliary motility before and after alcohol consumption.
- Oral gavage of ethanol decreased the beating frequency of all three types of ependymal cilia in both the third and the lateral rat brain ventricles in vivo.
- Thus, ethanol is a risk factor for the impairment of ependymal cilia motility in the brain and hydrocephalus.



Sci Rep. 2017 Oct 20;7(1):13652. doi: 10.1038/s41598-017-13947-3.

Alcohol consumption impairs the ependymal cilia motility in the brain ventricles.

Omran AJA[1], Saternos HC[1], Althobaiti YS[2], Wisner A[1], Sari Y[1], Nauli SM[3], AbouAlaiwi WA[4].

Altered CSF circulation – Volume issue

An Example - Effect of Increased Cerebral Volume

1. Pseudotumor Cerebri and increased intracranial pressure are significant risk factors for Sleep Apnea

J Neurol. 2013 Jul;260(7):1748-51. doi: 10.1007/s00415-013-6858-6. Epub 2013 Feb 15.

Obstructive sleep apnea in idiopathic intracranial hypertension: comparison with matched population data.

Thurtell MJ[1], Trotti LM, Bixler EO, Rye DB, Bliwise DL, Newman NJ, Biousse V, Bruce BB.

Occasional Intermittent CSF Obstruction

- 15 patients were included in this prospective study
- CINE MRI was performed before the surgery, after positioning and after the surgery.
- 14 out of 15 patients (93%) demonstrated significant improvement of CSF flow through the foramen magnum dorsal to the tonsils with positioning only.
- This improvement was so notable that changes in CSF flow as a result of the bone decompression were difficult to discern.
- These results put into question intraoperative flow assessments that suggest adequate decompression by PFD, whether by iMRI or intraoperative ultrasound.

Reference: Changes in cerebrospinal fluid flow assessed using intraoperative MRI during posterior fossa decompression for Chiari malformation. Bond AE, Jane JA Sr, Liu KC, Oldfield EH. J Neurosurg. 2015 May;122(5):1068-75.

Markers - Cine MRI in Cervical stenosis

STUDY

- 45 subjects
- three groups: no stenosis and cervical stenosis with and without intramedullary T2 hyperintensity.
- CSF waveform scaling (0 absent; 1 serrated; 2 bi-directional with small amplitude; and 3 normal bi-directional waveform)
- CSF motion pattern (0 absent; 1 interrupted; and 2 intact).

RESULTS

- Maximal CSF velocity was significantly lower in cervical myelopathy (2.72 cm/s) than in stenosis without myelopathy (3.27 cm/s, $p = 0.027$) and no stenosis (3.80 cm/s, $p < 0.001$).
- Bi-phasic CSF motion was lost in cervical stenosis.

Eur Spine J. 2017 Jan;26(1):40-48. doi: 10.1007/s00586-016-4874-9. Epub 2016 Nov 17.

Cervical compressive myelopathy: flow analysis of cerebrospinal fluid using phase-contrast magnetic resonance imaging.

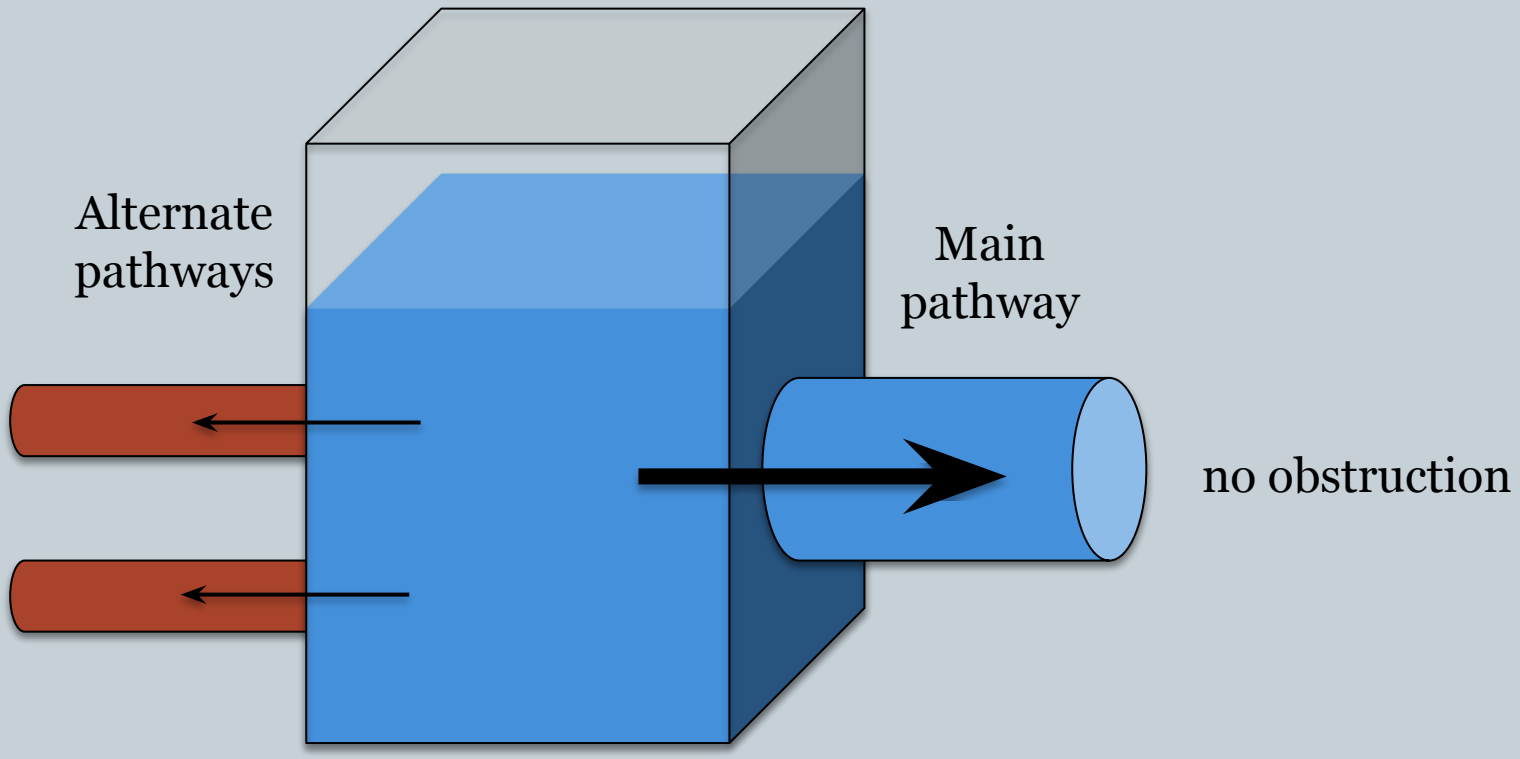
Bae YJ[1], Lee JW[2], Lee E[1], Yeom JS[3], Kim KJ[4], Kang HS[1].

Compensation Mechanisms with Obstruction

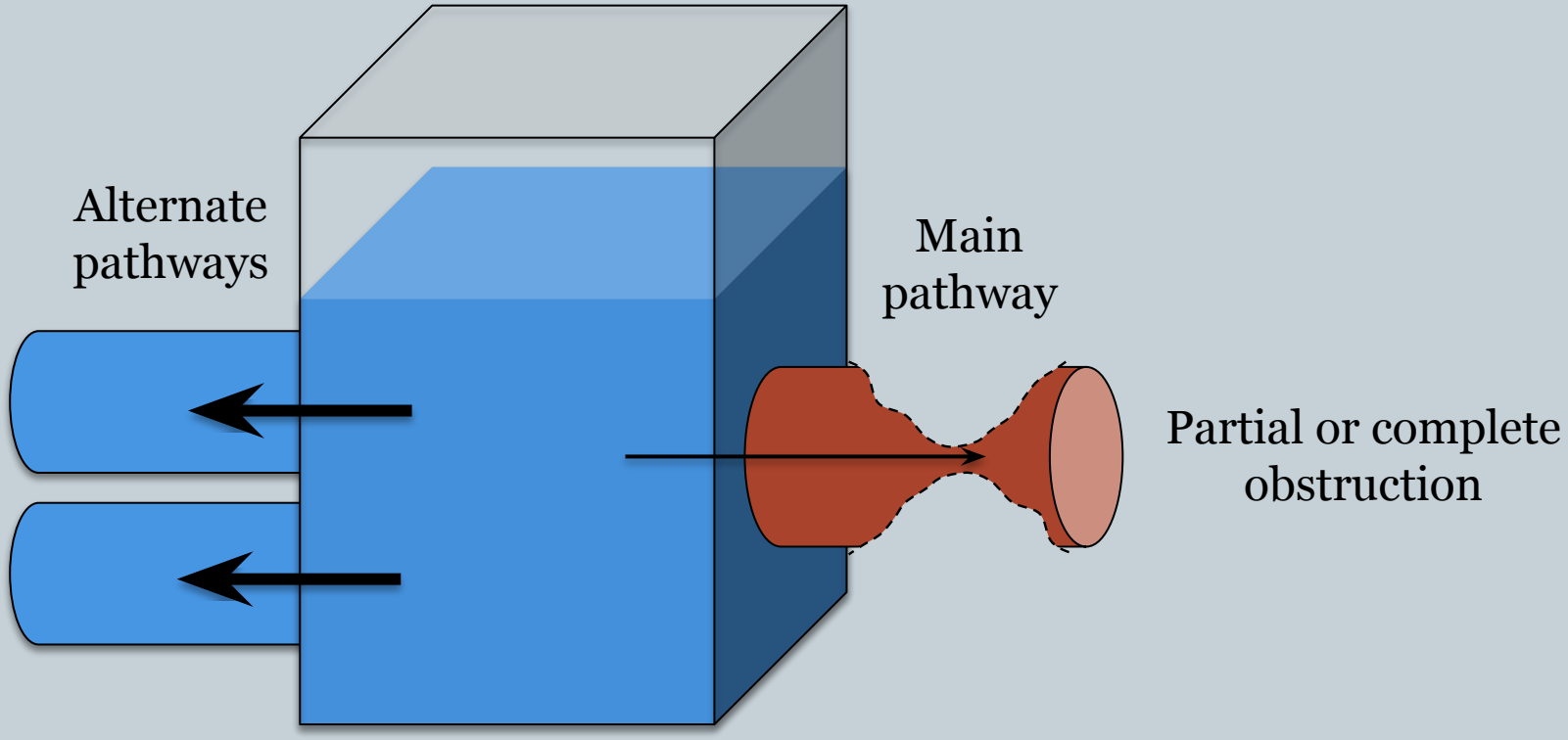
Compensation

- Compensation can reduce the impact of flow obstruction by neuronal damage, which opens up additional CSF flow channels and reduces CSF production as Cerebral blood flow and metabolic requirements diminish.
- Additionally, other CSF circulation channels may become more engaged to minimize obstruction problems, thereby diminishing CSF pressure concerns and dural pressure.
- Thus, often obstruction issues are self-correcting with the unfortunate sequel of neuronal damage.

Compensation

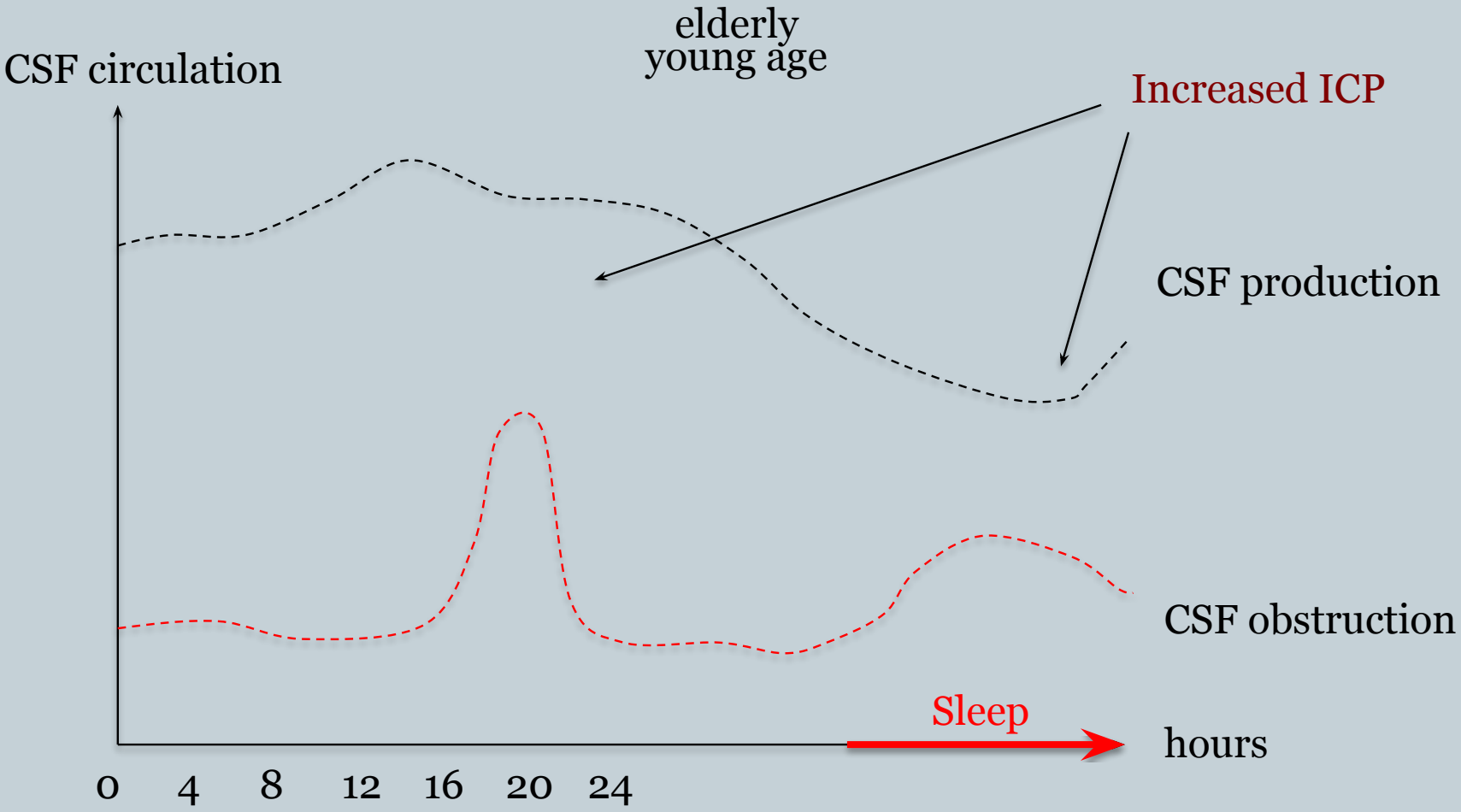


Compensation



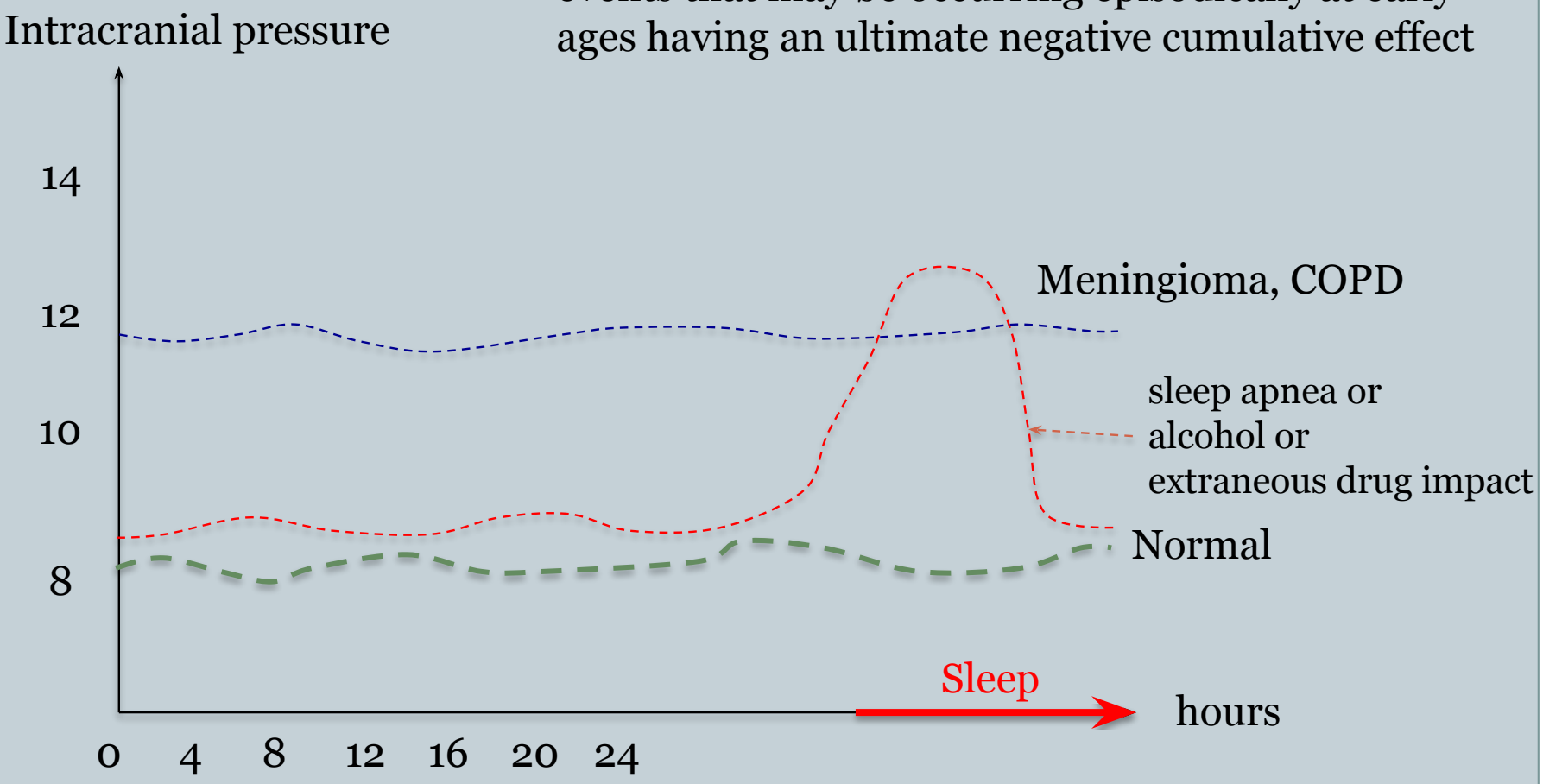
- In some circumstances the intermittent flow problems are more likely during sleep.

Time factor (Cerebrospinal Fluid Balance)



Time factor (Cerebrospinal Fluid Balance)

events that may be occurring episodically at early ages having an ultimate negative cumulative effect



Cumulative Risk Factors of Sleep Apnea

- Degenerative cervical spine disease is a significant risk factor for Sleep Apnea

- Is there a correlation between sleep disordered breathing and foramen magnum stenosis in children with achondroplasia? White KK, Parnell SE, Kifle Y, Blackledge M, Bompadre V. Am J Med Genet A. 2016 Jan;170A(1):32-41.
- Obstructive sleep apnoea associated with syringomyelia. Shao C, Li SQ. Br J Hosp Med (Lond). 2015 Apr;76(4):200-3.
- Sleep apnea and cervical spine pathology. Khan A, Than KD, Chen KS, Wang AC, La Marca F, Park P. Eur Spine J. 2014 Mar;23(3):641-7.
- Reversible and delayed isolated central sleep apnea after cervical laminectomy: report of the first case. Massimiliano V, Della Pepa GM, Giuseppe B, Aldo S. Acta Neurochir (Wien). 2014 Feb;156(2):267-8.
- Cervical vertebral column morphology in patients with obstructive sleep apnoea assessed using lateral cephalograms and cone beam CT. A comparative study. Sonnesen L, Jensen KE, Petersson AR, Petri N, Berg S, Svanholt P. Dentomaxillofac Radiol. 2013;42(6):20130060.

Obstruction

Chiari Malformation and Sleep Apnea

- Chiari patients with Sleep Apnea
  - present more with MRI pattern of brainstem compression and crowding of posterior fossa
  - have longer history of symptoms
  - show significant improvement on polysomnography studies after Chiari decompression

Pediatr Neurol. 2013 Apr;48(4):299-307. doi: 10.1016/j.pediatrneurol.2012.12.009.

MRI findings and sleep apnea in children with Chiari I malformation.

Khatwa U[1], Ramgopal S, Mylavarapu A, Prabhu SP, Smith E, Proctor M, Scott M, Pai V, Zarowski M, Kothare SV.

High prevalence of sleep apnea in Chiari I patients

- 11 patients with Chiari I malformation
  - 90% complained of sleep problems (snoring, choking, and witnessed apneas)
  - 72% presented hypersomnolence.
  - Polysomnographic findings
    - sleep fragmentation in 81% of the patients
    - reduction of REM sleep in 63%.
    - The apnea/hypopnea index was above 5 in 72%, with a predominance of central apnea.

Neurosurg Rev. 2000 Sep;23(3):151-5.

Polysomnographic respiratory findings in patients with Arnold-Chiari type I malformation and basilar invagination, with or without syringomyelia: preliminary report of a series of cases.

Botelho RV[1], Bittencourt LR, Rotta JM, Tufik S.

Obstruction

Sleep hygiene

1. Supine sleeping position increases intracranial pressure in Sleep Apnea

Graefes Arch Clin Exp Ophthalmol. 2018 Apr;256(4):783-790. doi: 10.1007/s00417-018-3919-7. Epub 2018 Feb 28.

Effect of prolonged supine position on the intraocular pressure in patients with obstructive sleep apnea syndrome.

Fang SY[1], Wan Abdul Halim WH[1], Mat Baki M[2], Din NM[3,4].

2. Prone sleeping position improves symptoms and consequences of Sleep Apnea

Sleep Breath. 2015 Sep;19(3):1027-34. doi: 10.1007/s11325-014-0985-x. Epub 2015 Jan 26.

Effect of prone positioning in mild to moderate obstructive sleep apnea syndrome.

Afrashi A[1], Ucar ZZ.

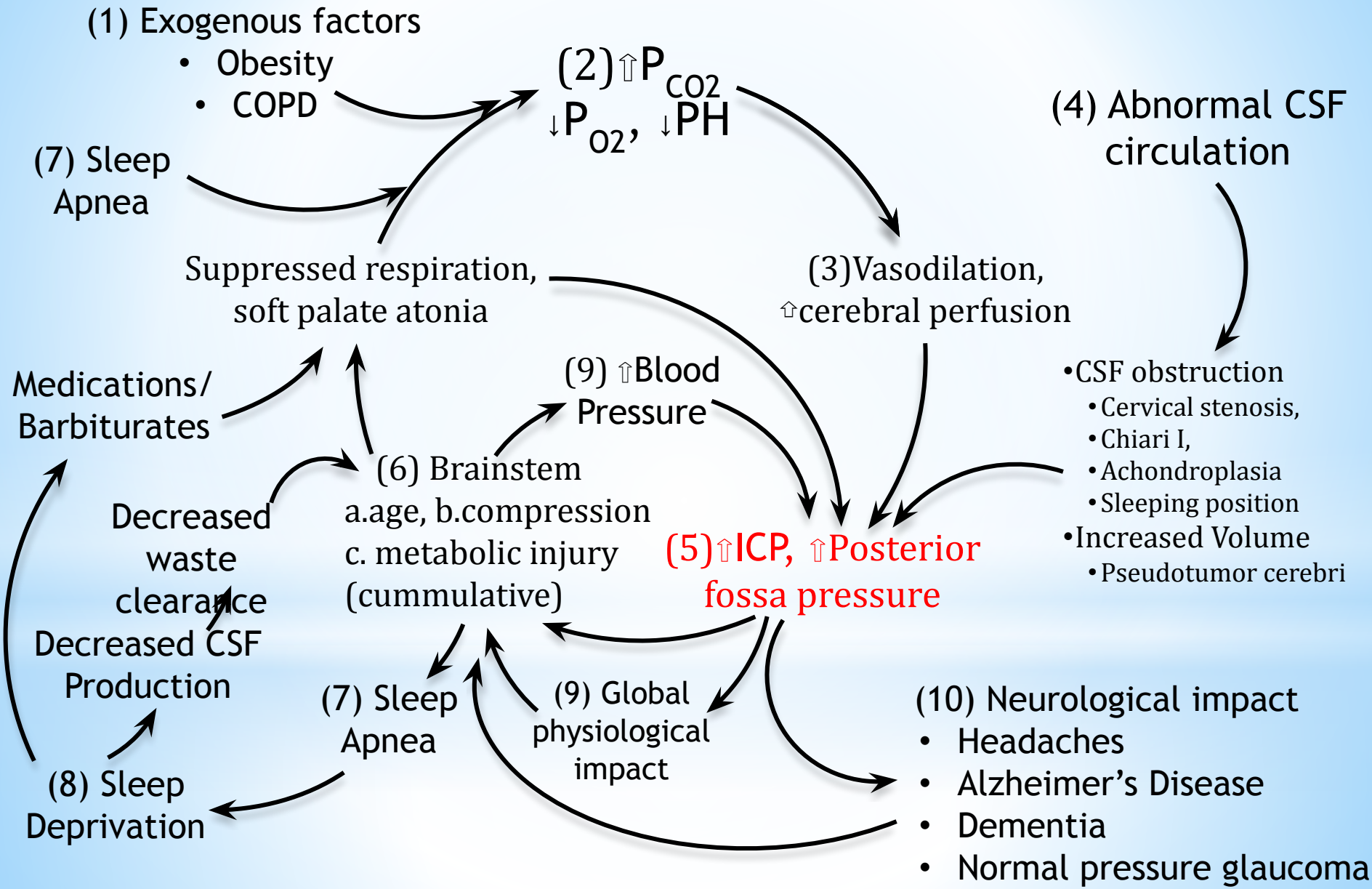
3. Head extension can exacerbate the presence of cervical stenosis and potentially worsen Sleep Apnea

Spine J. 2015 Apr 1;15(4):668-74. doi: 10.1016/j.spinee.2014.12.001. Epub 2014 Dec 5.

Evaluation of spinal cord compression and hyperintense intramedullary lesions on T2-weighted sequences in patients with cervical spondylotic myelopathy using flexion-extension MRI protocol.

Zeitoun D[1], El Hajj F[2], Sariali E[3], Catonné Y[3], Pascal-Moussellard H[3].

Sleep Apnea – a Vicious Cycle



Sleep Apnea and Increased ICP

Med Hypotheses. 2014 Dec;83(6):792-7. doi: 10.1016/j.mehy.2014.10.011. Epub 2014 Oct 19.

Intracranial hypertension associated with obstructive sleep apnea: a discussion of potential etiologic factors.

Wardly DE[1].

Author information

Abstract

Obstructive sleep apnea has been shown to increase intracranial pressure, and to be a secondary cause of intracranial hypertension. There are a few theories that attempt to explain this relationship, however there is little data, and even less recognition among physicians that this actually occurs. This paper discusses multiple pieces of data, from anatomical correlates to biochemical information involving neuro-excitotoxicity, as well as hematologic factors and issues surrounding brain edema and blood-brain barrier dysfunction. A complex paradigm for how obstructive sleep apnea may lead to increased intracranial pressure is thus proposed. In addition, suggestions are made for how obstructive sleep apnea must as a result be managed differently in the setting of idiopathic intracranial hypertension.

Chest. 1989 Feb;95(2):279-83.

Intracranial pressure and obstructive sleep apnea.

Jennum P[1], Børgesen SE.

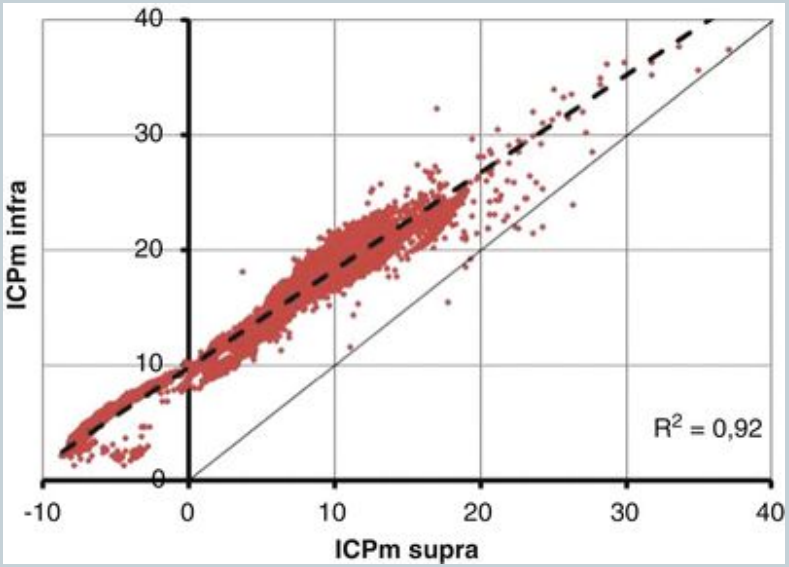
Author information

Abstract

In order to describe variation in AP and ICP during OSA, six patients with severe OSA were examined, with determination of ICP, AP, CVP, respiration, tcPO2, tcPCO2, and nocturnal sleep polygraphy. During apnea, elevations of AP and ICP were observed, related to the apneic episodes. The elevations in pressure were only observed in relation to apneic episodes. While awake, none of the patients showed pressure elevations. There were highly significant correlations between duration of apnea and variation in AP and ICP and between variations in AP and ICP. Values for ICP while awake were above normal (greater than 15 mm Hg; intracranial hypertension) in four of six patients. Morning ICP was higher than evening ICP. Systolic, mean, and diastolic ICP and AP increased during sleep above awake values. The ICP increased during NREM stages 1 to 4, and the highest values were observed during REM sleep. Vascular response was not changed during REM sleep, and the higher ICP during REM could solely be explained by the longer apneas during REM sleep. The CPP decreased during apnea.

Transtentorial pressure gradient

- Posterior fossa pressure is generally higher than supratentorial pressure



Acta Neurochir Suppl. 2016;122:37-40. doi: 10.1007/978-3-319-22533-3_7.

Characterisation of Supra- and Infratentorial ICP Profiles.

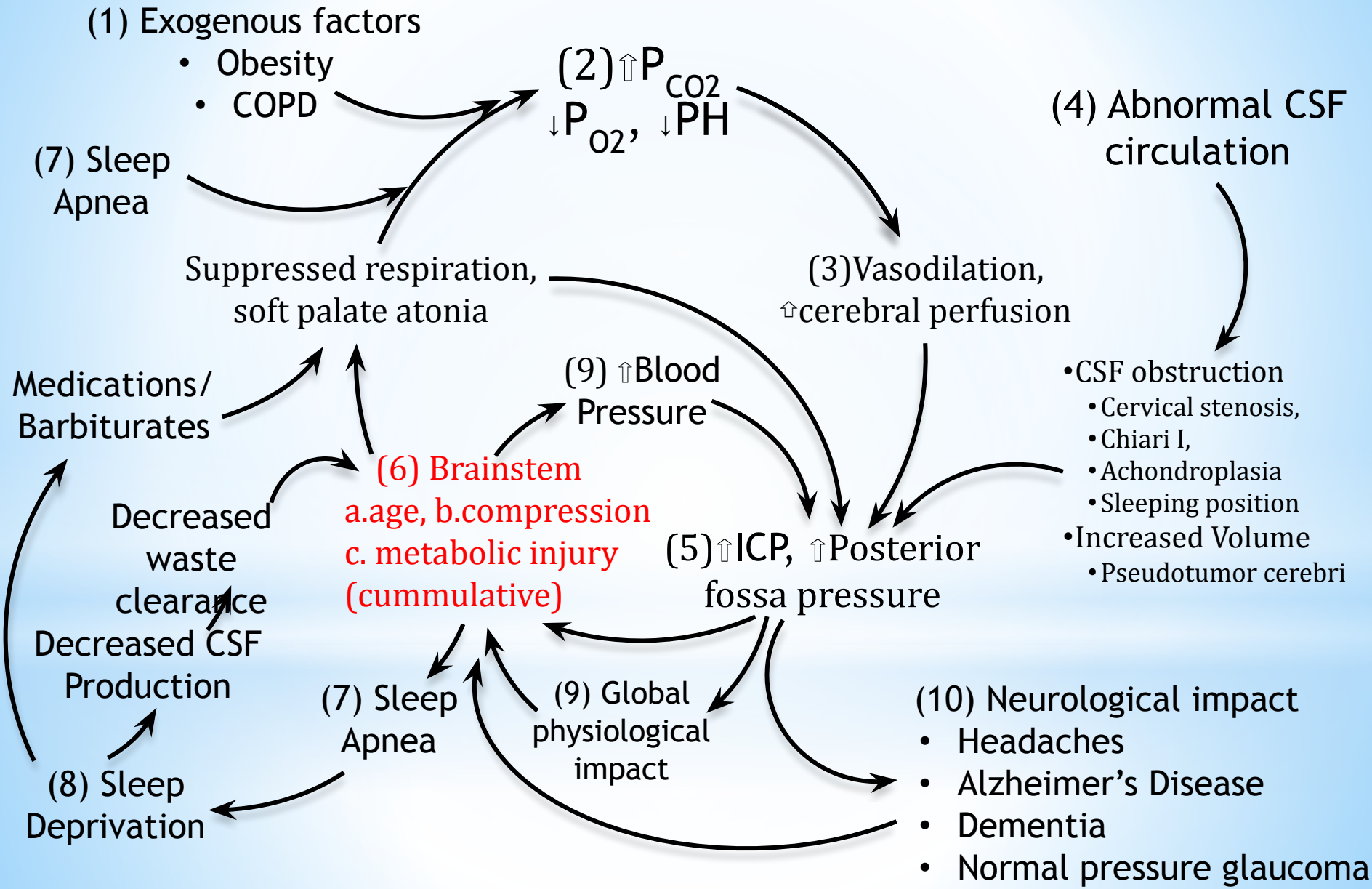
Moyse E[1], Ros M[2], Marhar F[3], Swider P[4], Schmidt EA[2].

J Neurosurg. 1989 Oct;71(4):503-5.

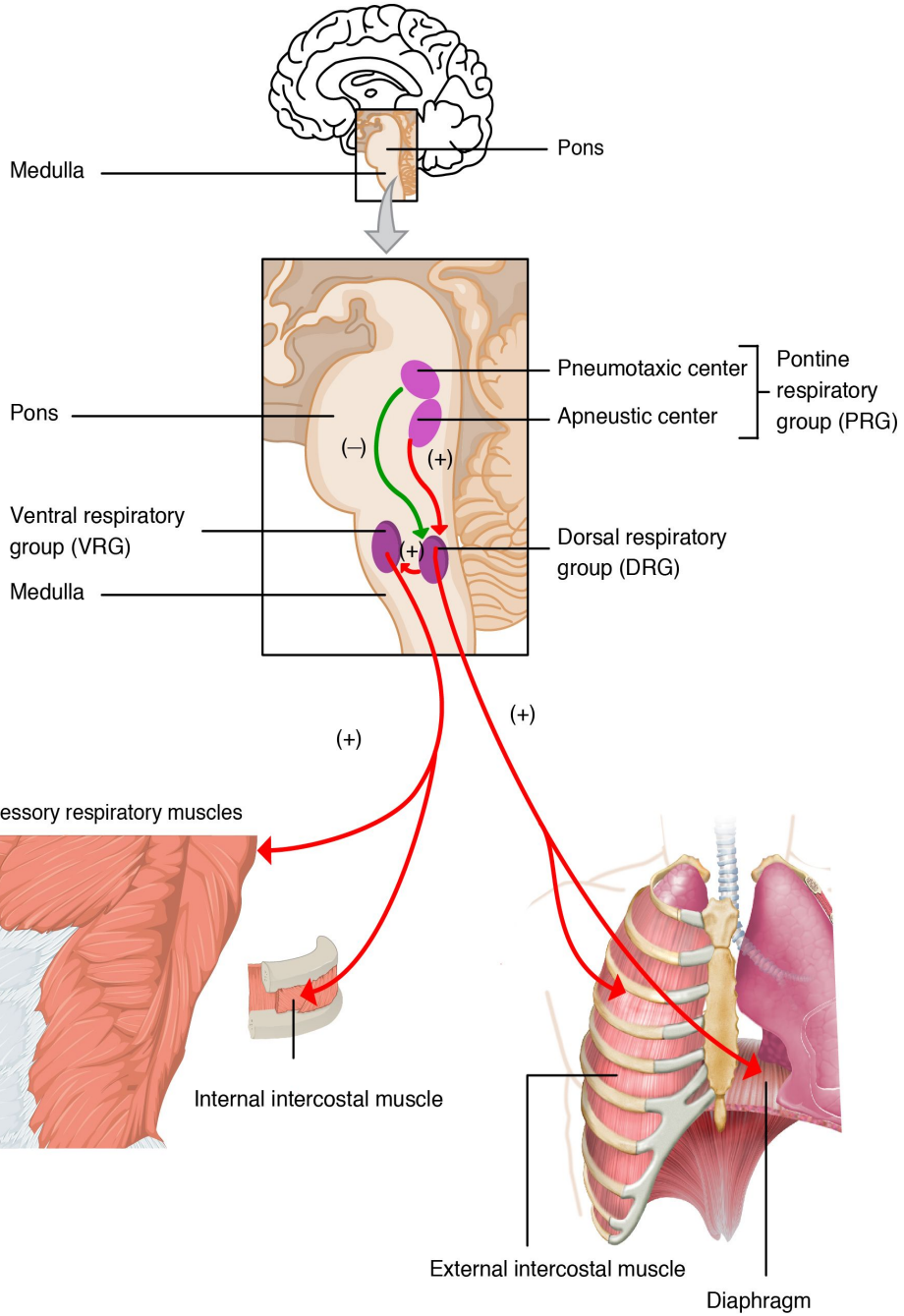
Intracranial pressure monitoring in the posterior fossa: a preliminary report.

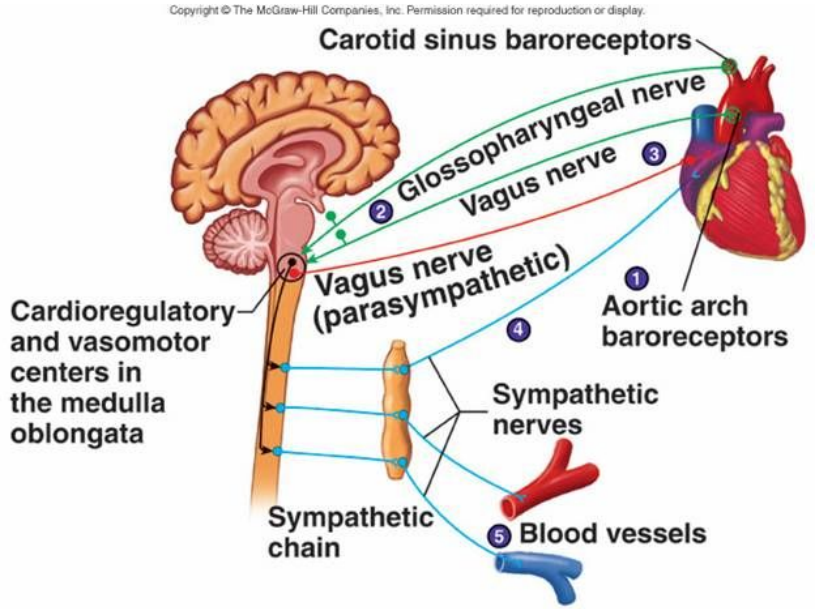
Rosenwasser RH[1], Kleiner LI, Krzeminski JP, Buchheit WA.

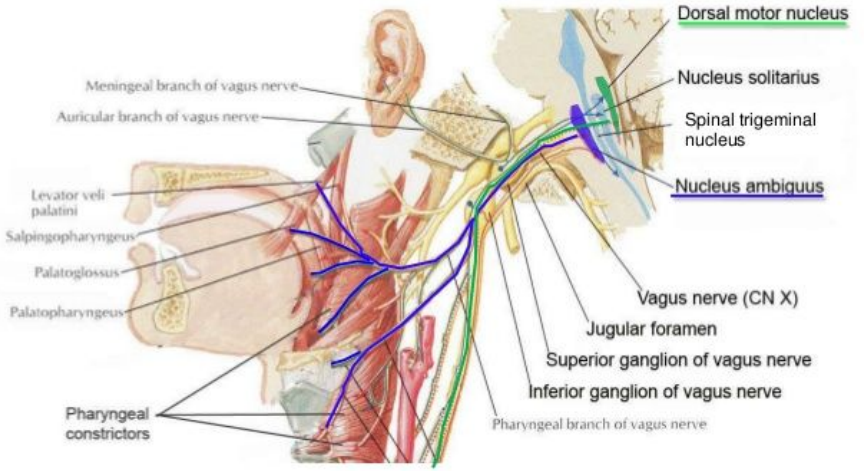
Sleep Apnea – a Vicious Cycle



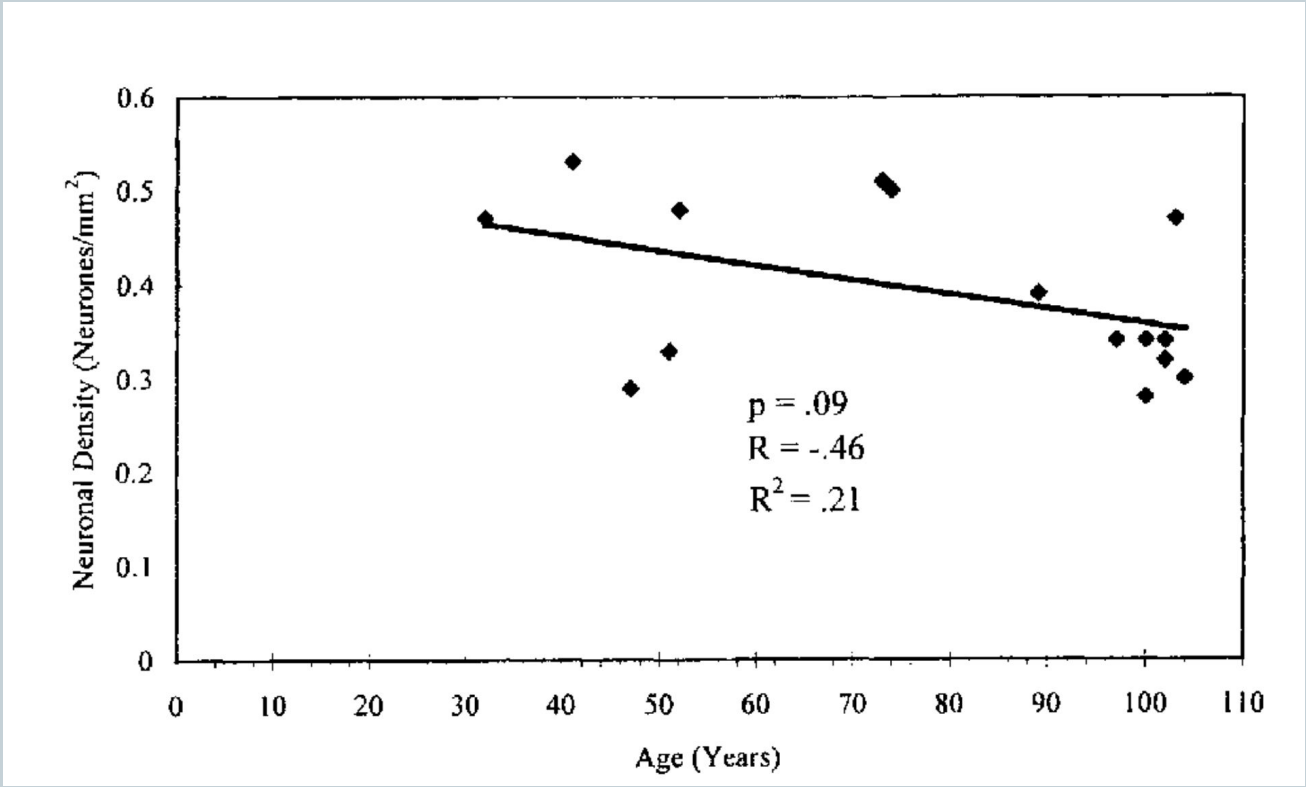
6. Brainstem age, compression and metabolic injury







Neuronal Density in the Brainstem With Age



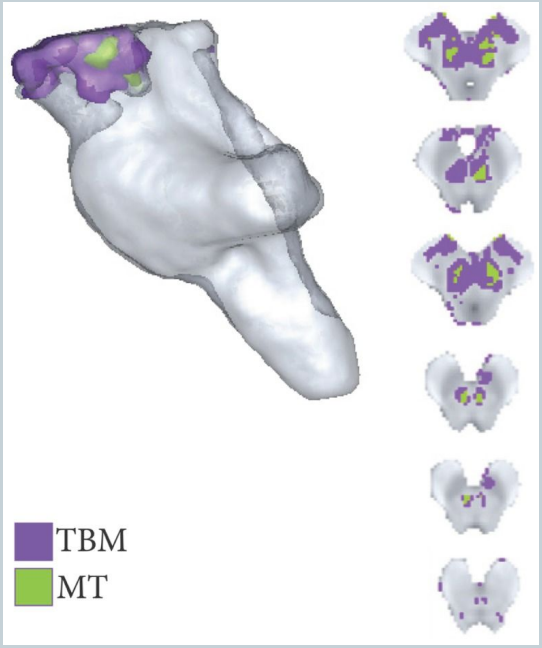
J Gerontol A Biol Sci Med Sci. 1999 Sep;54(9):B363-8.

Neuronal loss in the brainstem and cerebellum--part of the normal aging process? A morphometric study of the vermis cerebelli and inferior olivary nucleus.

Sjöbeck M[1], Dahlén S, Englund E.

MRI changes in Brainstem with age

- 3 Tesla MRI in 23 subjects
- Results
  - No total volume loss
  - However…
    - Significant atrophy of the midbrain probably due to loss of substantia nigra
    - Atrophy of superior cerebellar peduncles
    - Decreased myelin content throughout the brainstem due to axonal loss
    - Increased iron concentration in brainstem nuclei



Front Hum Neurosci. 2013 Aug 20;7:462. doi: 10.3389/fnhum.2013.00462. eCollection 2013.

Characterizing aging in the human brainstem using quantitative multimodal MRI analysis.

Lambert C[1], Chowdhury R, Fitzgerald TH, Fleming SM, Lutti A, Hutton C, Draganski B, Frackowiak R, Ashburner J.

Negative Effect of Hydrostatic Pressure on Neuronal Tissue

- **Human neuronal changes in brain edema and increased intracranial pressure;** Nóra Faragó, Ágnes Katalin Kocsis, Csilla Braskó, Sándor Lovas, Márton Rózsa, Judith Baka, Balázs Kovács, Katalin Mikite, Viktor Szemenyei, Gábor Molnár, Attila Ozsvár, Gáspár Oláh, Ildikó Piszár, Ágnes Zvara, Attila Patócs, Pál Barzó, László G. Puskás, and Gábor Tamás; Acta Neuropathol Commun. 2016; 4: 78.
- **The effects of high hydrostatic pressure on the electrical characteristics of Helix neurons;** K.T. Wann, A.G. Macdonald, A.AHarper; Comparative Biochemistry and Physiology Part A: Physiology Volume 64, Issue 1, 1979, Pages 149-159
- **The Effect of Hydrostatic Pressure on Neuronal Cell Morphology In Vitro**; Etten, Kallie, (2017). All Theses. 2798. https://tigerprints.clemson.edu/all_theses/2798
- **Pressure waves in neurons and their relationship to tangled neurons and plaques**; Helmut Barz, Ulrich Barzb; Medical Hypotheses Volume 82, Issue 5, May 2014, Pages 563-566
- **Effects of repetitive low-pressure explosive blast on primary neurons and mixed cultures;** Nicole E. Zander, Thuvan Piehler, Rohan Banton, Richard Benjamin; Journal of Neuroscience Research; Volume94, Issue9 September 2016

Waste clearance in the brainstem

- Large quantities of neurofibrillary tangles are present in the brain stem in senile dementia as opposed to Alzheimer's disease, where most of neurofibrillary tangles are found in basal ganglia.

Folia Psychiatr Neurol Jpn. 1975;29(3):279-87.

Frequency of Alzheimer's neurofibrillary tangles in the basal ganglia and brain-stem in Alzheimer's disease, senile dementia and the aged.

Ishino H, Otsuki S.

Abstract

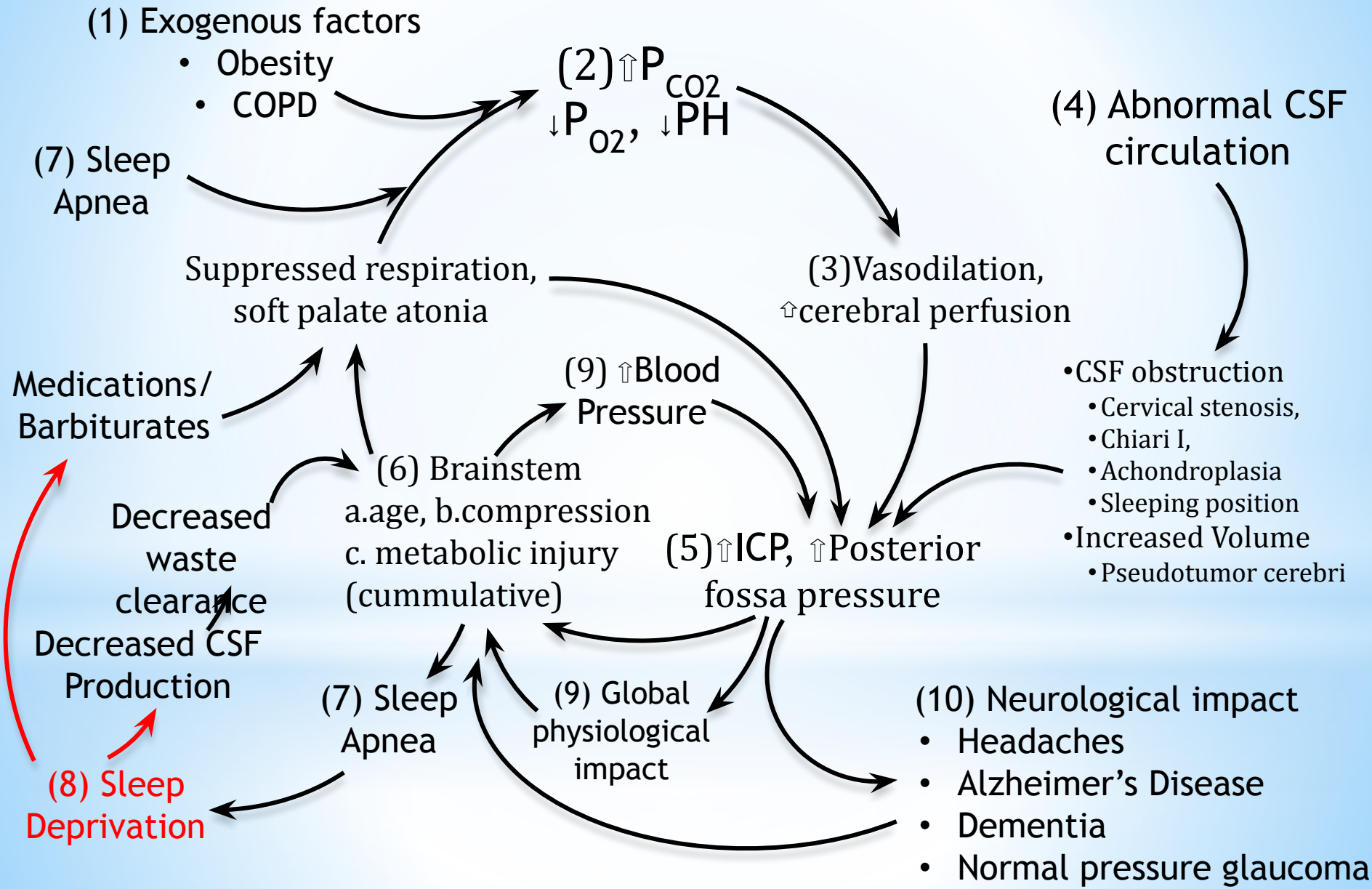
The authors studied the frequency of neurofibrillary tangles in the basal ganglia and brain-stem of two cases with Alzheimer's disease (average 55 years of age), six cases with senile dementia (average 82 years) and ten cases with cerebral softening and arteriosclerosis in old age (average 79 years). The distribution pattern of ANC was almost the same in Alzheimer's disease and senile dementia, i.e. plenty of ANC were found in the nucl. dorsalis raphe, nucl. centralis superior, nucl. mamilloinfundibularis and nucl. basilaris, but in senile dementia ANC were much fewer in the thalamus and lenticular nuclei. In the aged with cerebral softening and arteriosclerosis, a negligible number of ANC in the brain-stem made a marked contrast to a large quantity of ANC in the cases with senile dementia. Hence, as far as ANC in the brain-stem is concerned, no continuum seems to exist between normal senility and senile dementia.

Repetitive short-term hypoxia (hypoxic preconditioning)

- Brief repetitive episodes of hypoxia (hypoxic preconditioning) make neurons less vulnerable to global ischemia
- However…
  - hypoxia may cause a phenomenon of posthypoxic hyperexcitability during reoxygenation
  - global increase of the cytoplasmic Ca2+ concentration in a number on neurons followed by the apoptotic death of these cells

Source: Short-term hypoxia induces a selective death of GABAergic neurons; M. V. TurovskayaE. A. TurovskyA. V. KononovV. P. Zinchenko; Biochemistry (Moscow) Supplement Series A: Membrane and Cell Biology January 2014, Volume 8, Issue 1, pp 125–135

Sleep Apnea – a Vicious Cycle



Sleep Apnea causes Sleep Deprivation

- Sleep apnea causes sleep deprivation
- Sleep deprivation worsens mild obstructive sleep apnea
- Daytime sleepiness in the community is estimated to be as high as 18% and most of the cases are due to sleep apnea

Sleep Med Rev. 2018 Apr;38:39-49. doi: 10.1016/j.smrv.2017.03.005. Epub 2017 Mar 30.

Cognitive deficits in obstructive sleep apnea: Insights from a meta-review and comparison with deficits observed in COPD, insomnia, and sleep deprivation.

Olaithe M[1], Bucks RS[2], Hillman DR[3], Eastwood PR[3].

J Thorac Dis. 2012 Dec;4(6):608-16. doi: 10.3978/j.issn.2072-1439.2012.10.07.

Excessive daytime sleepiness in sleep disorders.

Slater G[1], Steier J.

Sleep Deprivation and CSF levels of Aβ

- Sleep disturbances are associated with risk of Alzheimer disease.
- Sleep deprivation increases overnight amyloid β38, amyloid β40, and amyloid β42 levels by 25 to 30% via increased overnight amyloid β production relative to sleeping controls.
- These findings suggest that disrupted sleep increases Alzheimer disease risk via increased amyloid β production.

Ann Neurol. 2018 Jan;83(1):197-204. doi: 10.1002/ana.25117.

Effect of sleep on overnight cerebrospinal fluid amyloid β kinetics.

Lucey BP[1,2], Hicks TJ[1], McLeland JS[1], Toedebusch CD[1], Boyd J[1], Elbert DL[3], Patterson BW[4], Baty J[5], Morris JC[1,2,6], Ovod V[1], Mawuenyega KG[1], Bateman RJ[1,2,6].

8. Sleep deprivation

Articles suggesting the role of sleep deprivation in Alzheimer's disease

- **Effect of sleep on overnight cerebrospinal fluid amyloid β kinetics;** Lucey BP, Hicks TJ, McLeland JS, Toedebusch CD, Boyd J, Elbert DL, Patterson BW, Baty J, Morris JC, Ovod V, Mawuenyega KG, Bateman RJ; Ann Neurol. 2018 Jan;83(1):197-204
- **Slow wave sleep disruption increases cerebrospinal fluid amyloid-β levels.** Ju YS1,2, Ooms SJ3,4,5, Sutphen C, Macauley SL, Zangrilli MA, Jerome G, Fagan AM, Mignot E, Zempel JM, Claassen JAHR, Holtzman DM; Brain. 2017 Aug 1;140(8):2104-2111
- **Poor sleep is associated with CSF biomarkers of amyloid pathology in cognitively normal adults.** Sprecher KE, Koscik RL, Carlsson CM, Zetterberg H, Blennow K, Okonkwo OC, Sager MA, Asthana S, Johnson SC, Benca RM, Bendlin BB. Neurology. 2017 Aug 1;89(5):445-453.
- **Effect of 1 night of total sleep deprivation on cerebrospinal fluid β-amyloid 42 in healthy middle-aged men: a randomized clinical trial.** Ooms S1, Overeem S, Besse K, Rikkert MO, Verbeek M, Claassen JA.JAMA Neurol. 2014 Aug;71(8):971-7.

8. Sleep deprivation

Articles suggesting that Glymphatic circulation is suppressed in sleep deprivation

- **Glymphatic distribution of CSF-derived apoE into brain is isoform specific and suppressed during sleep deprivation.** Achariyar TM1, Li B1,2, Peng W1, Verghese PB3, Shi Y3, McConnell E1, Benraiss A4, Kasper T1, Song W1, Takano T1, Holtzman DM3, Nedergaard M1, Deane R5. Mol Neurodegener. 2016 Dec 8;11(1):74.

- **Sleep facilitates clearance of metabolites from the brain: glymphatic function in aging and neurodegenerative diseases.** Mendelsohn AR1, Larrick JW. Rejuvenation Res. 2013 Dec;16(6):518-23

Additionally, Glymphatic system suppression during sleep

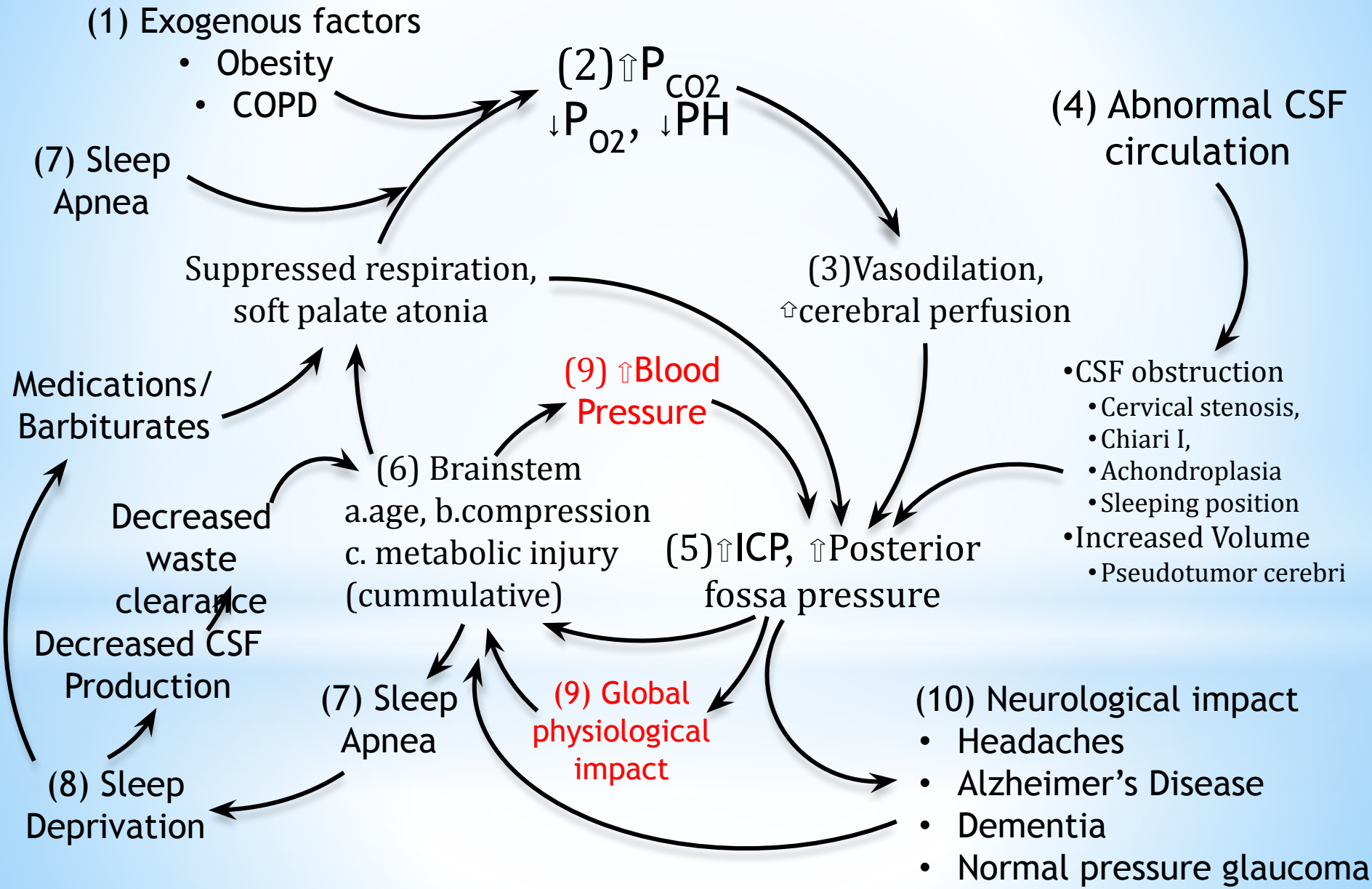
- In vivo MRI imaging after injection of a paramagnetic contrast agent or a fluorescent dye in the cisterna magna confirmed the existence of a brain-wide CSF circulation
- Contrary to what is traditionally thought, this study demonstrated that parenchymal CSF circulation is mainly active during wakefulness and significantly impaired during general anesthesia.
- This effect is especially significant when high doses of anesthetic agent are used (3% isoflurane).

Theranostics. 2018 Jan 1;8(3):710-722. doi: 10.7150/thno.19154. eCollection 2018.

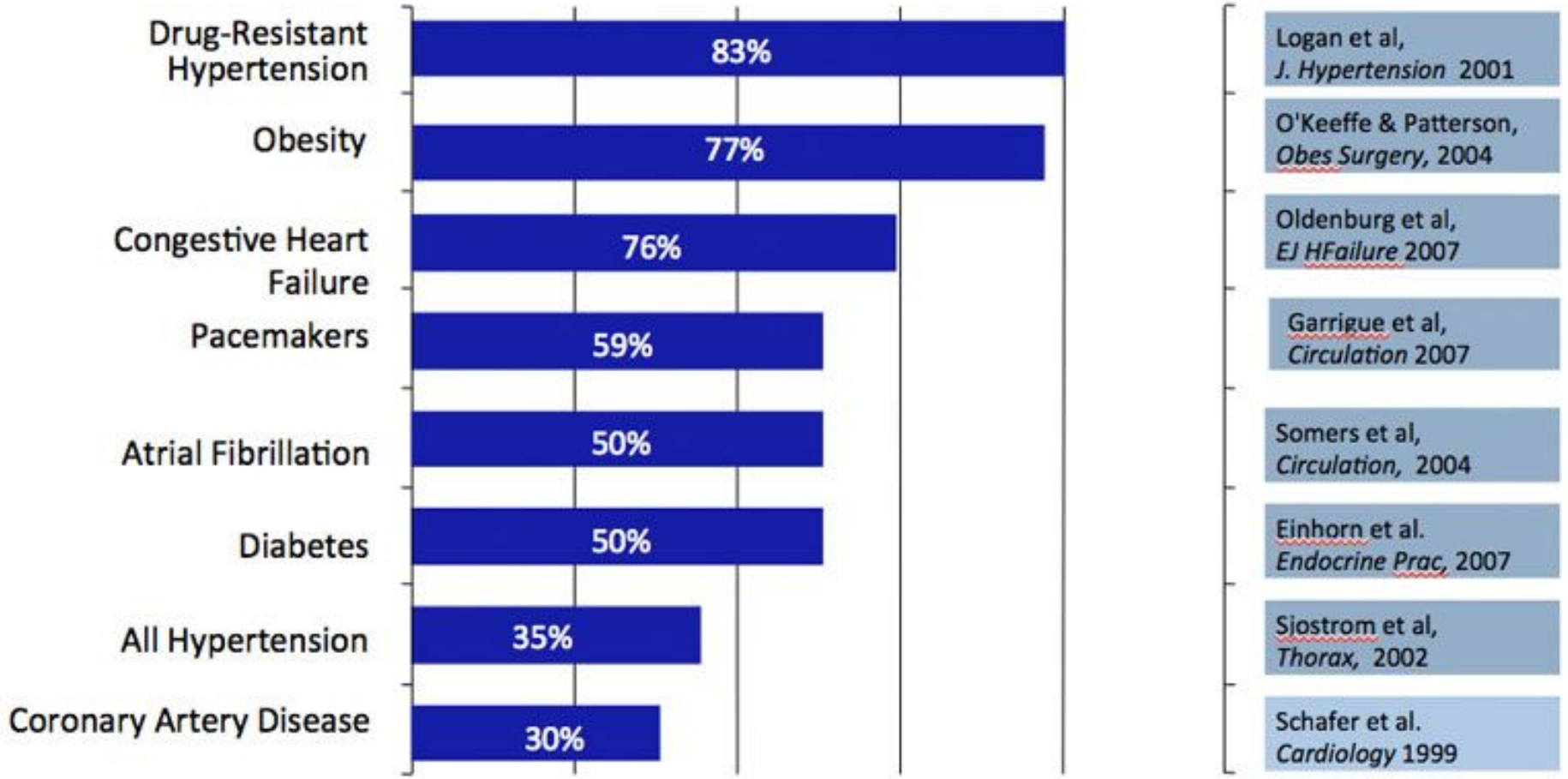
General Anesthesia Inhibits the Activity of the "Glymphatic System".

Gakuba C[1,2], Gaberel T[1,3], Goursaud S[1,2], Bourges J[1,2], Di Palma C[1,3], Quenault A[1], de Lizarrondo SM[1], Vivien D[1,4], Gauberti M[1,5].

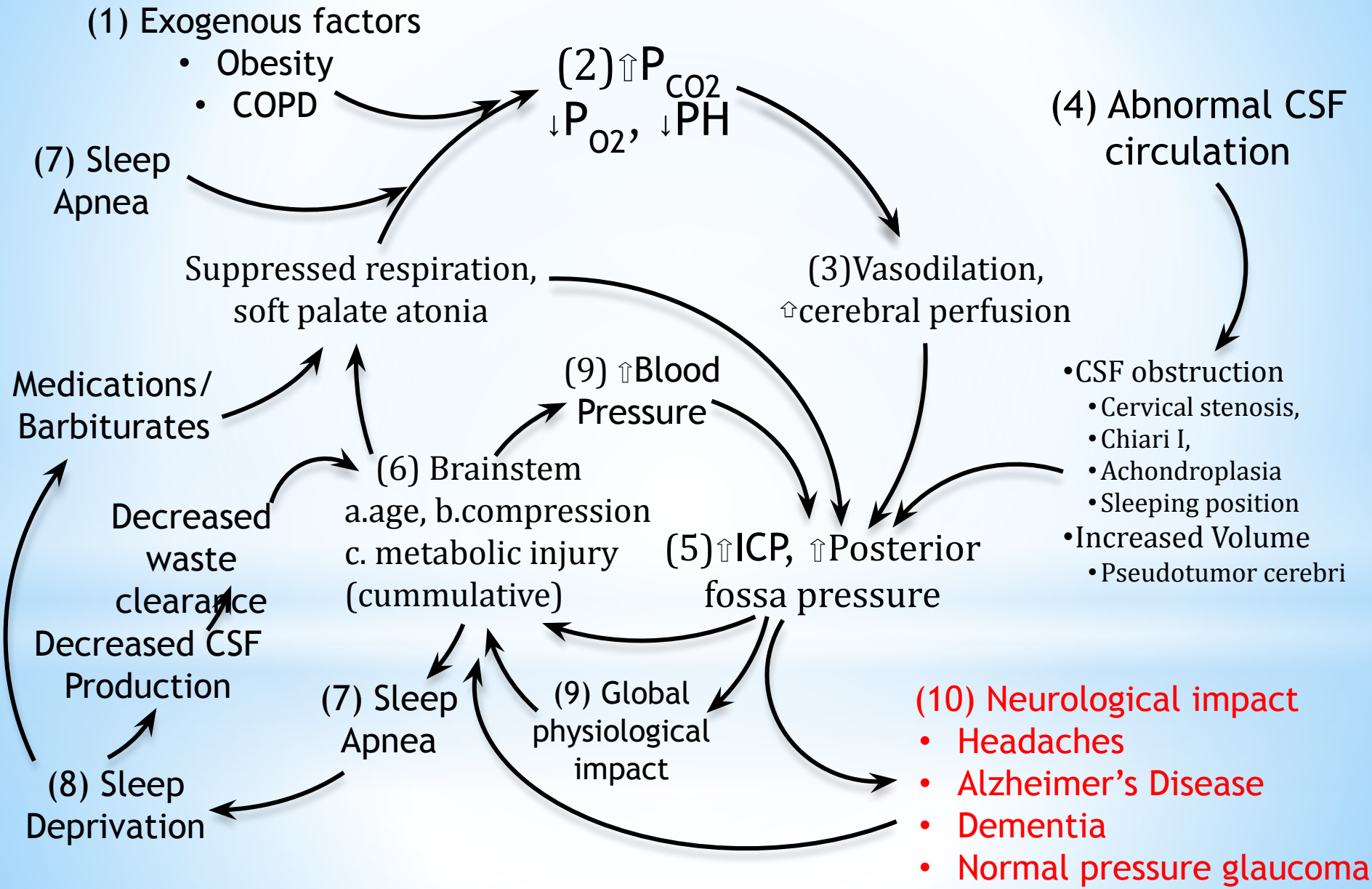
Sleep Apnea – a Vicious Cycle



Comorbidities of Sleep Apnea



Sleep Apnea – a Vicious Cycle



Common Neurological Disorders in Sleep Apnea

- Morning headaches – especially occipital
- Neurodegenerative diseases
- Stroke
- Epilepsy
- Cognitive impairment
- Alzheimer's disease
- Parkinson's disease
- Multisystem atrophy
- Daytime sleepiness
- Normal Tension Glaucoma

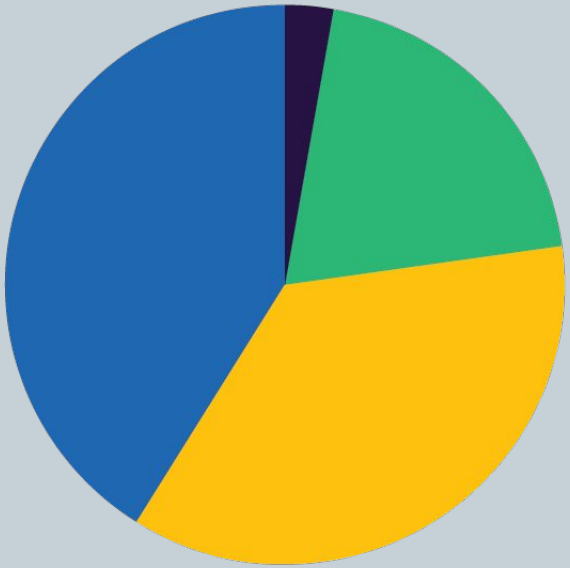
Curr Treat Options Neurol. 2017 Apr;19(4):16. doi: 10.1007/s11940-017-0451-8.

Neurological Deficits in Obstructive Sleep Apnea.

Ferini-Strambi L[1], Lombardi GE[2], Marelli S[2], Galbiati A[2].

Prevalence of Sleep Apnea in Patients with Headaches

- Of the 390 headache patients included in the study, 277 (71%) had a diagnosed sleep disorder



New Patients with Primary Headache Diagnosis with Diagnostic Polysomnogram

MIDAMERICA NEUROSCIENCE INSTITUTE
8550 Marshall Drive, Suite 100
Lenexa, KS 66214
913-894-1500 fax 913-894-1502
neurokc.com

STRIKING ASSOCIATION BETWEEN HEADACHE, SLEEP DISORDERS AND CERVICAL RADICULOPATHY

Vernon D. Rowe, MD[1]; John A. Hunter, PsyD[1]; Travis Mecum, RPSGT[1], Dana Winegarner, DO[1], Arkady Korotinsky, MD[2], Harnek Kahlon, MD[2]

CSF flow abnormalities and headache

- 4.1% of population suffers from cervicogenic headache (Male>Female) (Sjaastad O et al, 2008)
- It is usually attributed to the compression of C1/C2 nerve roots (Liselott CG et al, 2007)
- However, nerve root block results in symptom relief only in 50% of patients (Liselott CG et al, 2007)
- Occipital headaches are strongly associated with CSF flow abnormalities on CINE MRI, whereas frontal and generalized headaches are not. (McGirt MJ et al, 2005)

Sleep Apnea and cognitive decline

1. Sleep Apnea may increase risk of developing Alzheimer's disease

Am J Respir Crit Care Med. 2018 Apr 1;197(7):933-943. doi: 10.1164/rccm.201704-0704OC.

Obstructive Sleep Apnea Severity Affects Amyloid Burden in Cognitively Normal Elderly. A Longitudinal Study.

Sharma RA[1], Varga AW[2], Bubu OM[3], Pirraglia E[1], Kam K[2], Parekh A[4], Wohlleber M[1], Miller MD[1], Andrade A[1], Lewis C[1], Tweardy S[1], Buj M[1], Yau PL[1], Sadda R[5], Mosconi L[1], Li Y[1], Butler T[1], Glodzik L[1], Fieremans E[6], Babb JS[6], Blennow K[7,8], Zetterberg H[7,8,9], Lu SE[10], Badia SG[11,12,13], Romero S[14,15], Rosenzweig I[16,17], Gosselin N[18,19], Jean-Louis G[20], Rapoport DM[2], de Leon MJ[1], Ayappa I[2], Osorio RS[1].

2. Sleep Apnea is significantly associated with cognitive impairment.

Chest. 2012 Jun;141(6):1601-1610. doi: 10.1378/chest.11-2214.

Neurocognitive impairment in obstructive sleep apnea.

Lal C[1], Strange C[2], Bachman D[3].

3. Sleep Apnea is a significant risk factor for arterial hypertension which itself can cause increased intracranial pressure and neuronal damage

Curr Hypertens Rep. 2007 Dec;9(6):529-34.

Obstructive sleep apnea and hypertension: mechanisms, evaluation, and management.

Dopp JM[1], Reichmuth KJ, Morgan BJ.

The role if elevated intracranial pressure in pathophysiology of Alzheimer's Disease

- Articles suggesting that chronic increase of Intracranial Pressure may contribute to development of Alzheimer's disease

Med Hypotheses. 2004;62(6):925-30.

Can chronic increased intracranial pressure or exposure to repetitive intermittent intracranial pressure elevations raise your risk for Alzheimer's disease?

Wostyn P[1].

Med Hypotheses. 1994 Oct;43(4):219-22.

Intracranial pressure and Alzheimer's disease: a hypothesis.

Wostyn P[1].

Normal Tension Glaucoma and Sleep Apnea

- Incidence of Normal Tension Glaucoma is higher in patients with Sleep Apnea (P<0.05)

BMC Ophthalmol. 2014 Mar 10;14:27. doi: 10.1186/1471-2415-14-27.

Normal-tension glaucoma and obstructive sleep apnea syndrome: a prospective study.

Bilgin G[1].

J Glaucoma. 2007 Jan;16(1):42-6.

Prevalence of normal tension glaucoma in obstructive sleep apnea syndrome patients.

Sergi M[1], Salerno DE, Rizzi M, Blini M, Andreoli A, Messenio D, Pecis M, Bertoni G.

J Glaucoma. 2011 Dec;20(9):553-8. doi: 10.1097/IJG.0b013e3181f3eb81.

Normal tension glaucoma in patients with obstructive sleep apnea/hypopnea syndrome.

Lin PW[1], Friedman M, Lin HC, Chang HW, Wilson M, Lin MC.

Klin Monbl Augenheilkd. 2001 Apr;218(4):263-8.

[Normal tension glaucoma, sleep apnea syndrome and nasal continuous positive airway pressure therapy--case report with a review of literature].

[Article in German]
Kremmer S[1], Selbach JM, Ayertey HD, Steuhl KP.

Summary of the vicious cycle

1. A major problem may be episodic diminished brain PO2 secondary to disturbance of respiratory drive, which could occur when a patient goes to sleep and has an increase in PCO2 to which respiratory center is slow in responding

2. As the PCO2 increases in the brain we get cerebral swelling and altered blood flow and the presence of diminished PCO2 puts some marginal neurons at risk for neuronal injury

3. As the brain swells in response to the altered PCO2 the need for increased CSF circulation is increased. If there is any kind of obstruction the CSF pressure in the posterior fossa will increase causing a vicious cycle causing more respiratory depression.

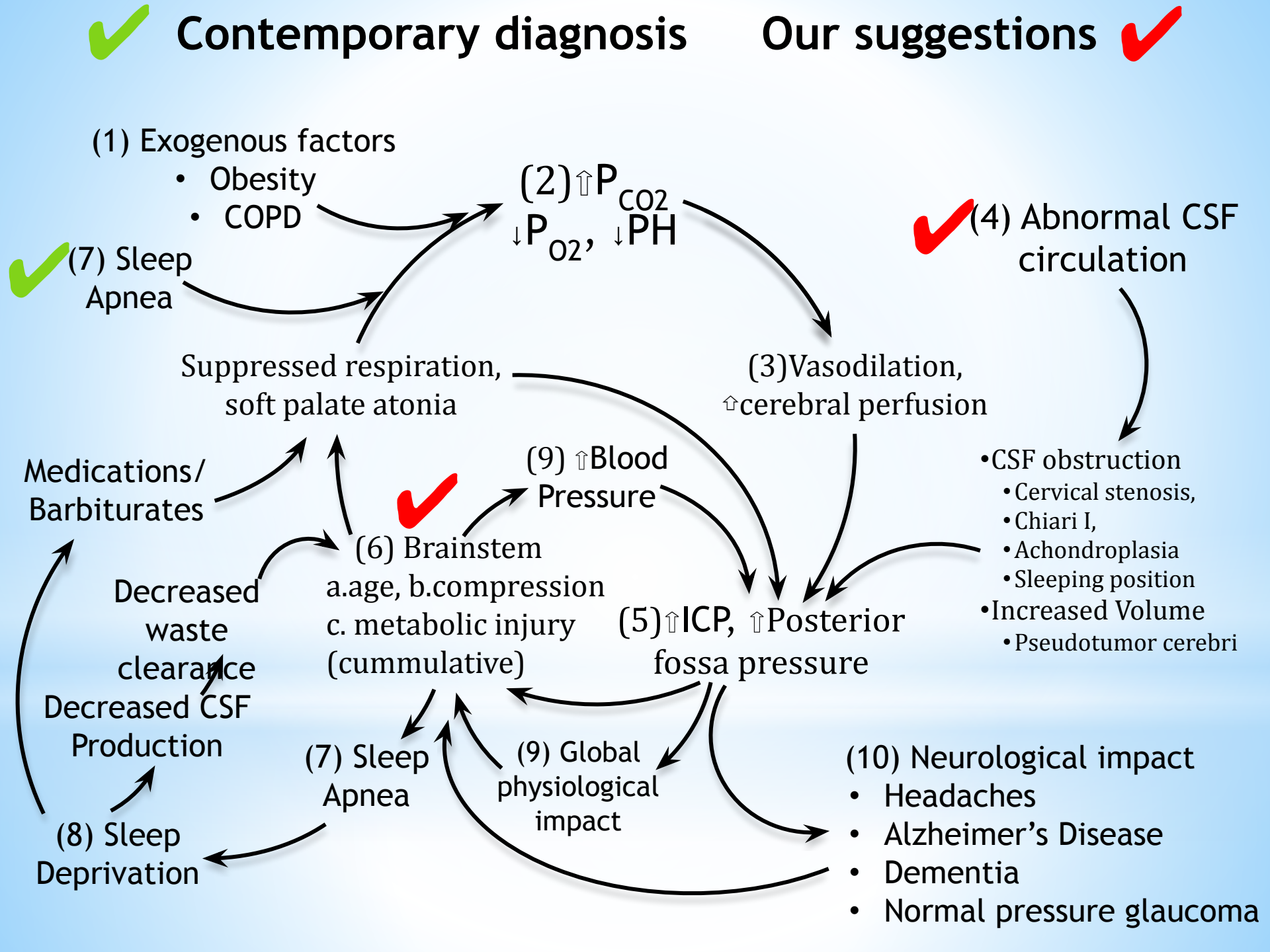
4. Moreover, at sleep the suboptimal geographical arrangement exist in the posterior fossa in which the patient maybe in a position that further retard the CSF circulation.

5. Additionally, these difficulties may encourage cardiac abnormalities which might diminish cerebral blood flow situation further exacerbating the problem.

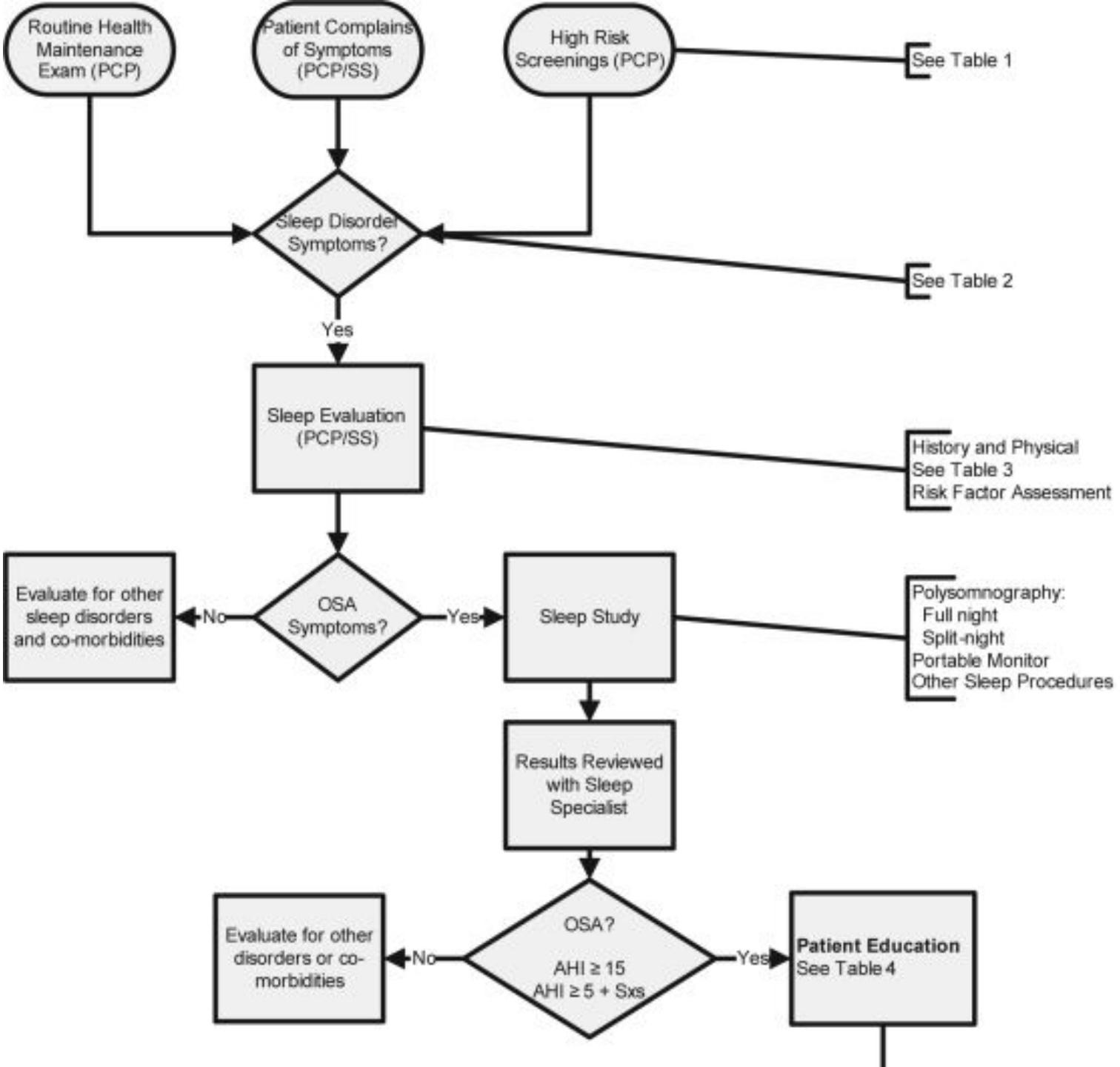
6. Is the cure to place such a person in a collar which maximizes the opening for CSF circulation or in extreme cases the posterior fossa decompression?

A little light on the subject and ideas about improvement…

Diagnosis


Contemporary diagnosis
Our suggestions
(1) Exogenous factors
• Obesity
• COPD
(2)⇧P_{CO2} ↓P_{O2}, ↓PH
(4) Abnormal CSF circulation
(7) Sleep Apnea
Suppressed respiration, soft palate atonia
(3)Vasodilation, ⇧cerebral perfusion
Medications/ Barbiturates
(9) ⇧Blood Pressure
•CSF obstruction
• Cervical stenosis,
• Chiari I,
• Achondroplasia
• Sleeping position
•Increased Volume
• Pseudotumor cerebri
Decreased waste clearance
(6) Brainstem
a.age, b.compression
c. metabolic injury
(cummulative)
(5)⇧ICP, ⇧Posterior fossa pressure
Decreased CSF Production
(7) Sleep Apnea
(9) Global physiological impact
(10) Neurological impact
• Headaches
• Alzheimer's Disease
• Dementia
• Normal pressure glaucoma
(8) Sleep Deprivation

Contemporary diagnosis

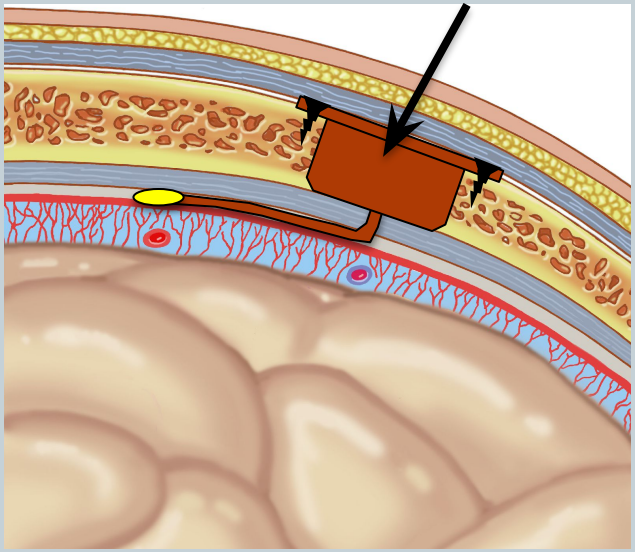

Routine Health Maintenance Exam (PCP)
Patient Complains of Symptoms (PCP/SS)
High Risk Screenings (PCP)
See Table 1
Sleep Disorder Symptoms?
See Table 2
Yes
Sleep Evaluation (PCP/SS)
History and Physical
See Table 3
Risk Factor Assessment
Evaluate for other sleep disorders and co-morbidities
No
OSA Symptoms?
Yes
Sleep Study
Polysomnography:
Full night
Split-night
Portable Monitor
Other Sleep Procedures
Results Reviewed with Sleep Specialist
Evaluate for other disorders or co-morbidities
No
OSA?
AHI ≥ 15
AHI ≥ 5 + Sxs
Yes
Patient Education
See Table 4

Our Suggestions

- Diagnosis
  - To better understand this we need
    - longer-follow up
    - better clinical studies
    - better litmus paper to detect the fourth abnormalities
  - Because there is no clear understanding about the transitory nature of CSF alterations, we need to find a manometer for ICP.
  - ICP implant
  - Eye tracking with CO_2 inhalation or directly after a sleep apnea episode

Better diagnosis

Fully implantable long-term rechargeable ICP monitor



Eye Tracking

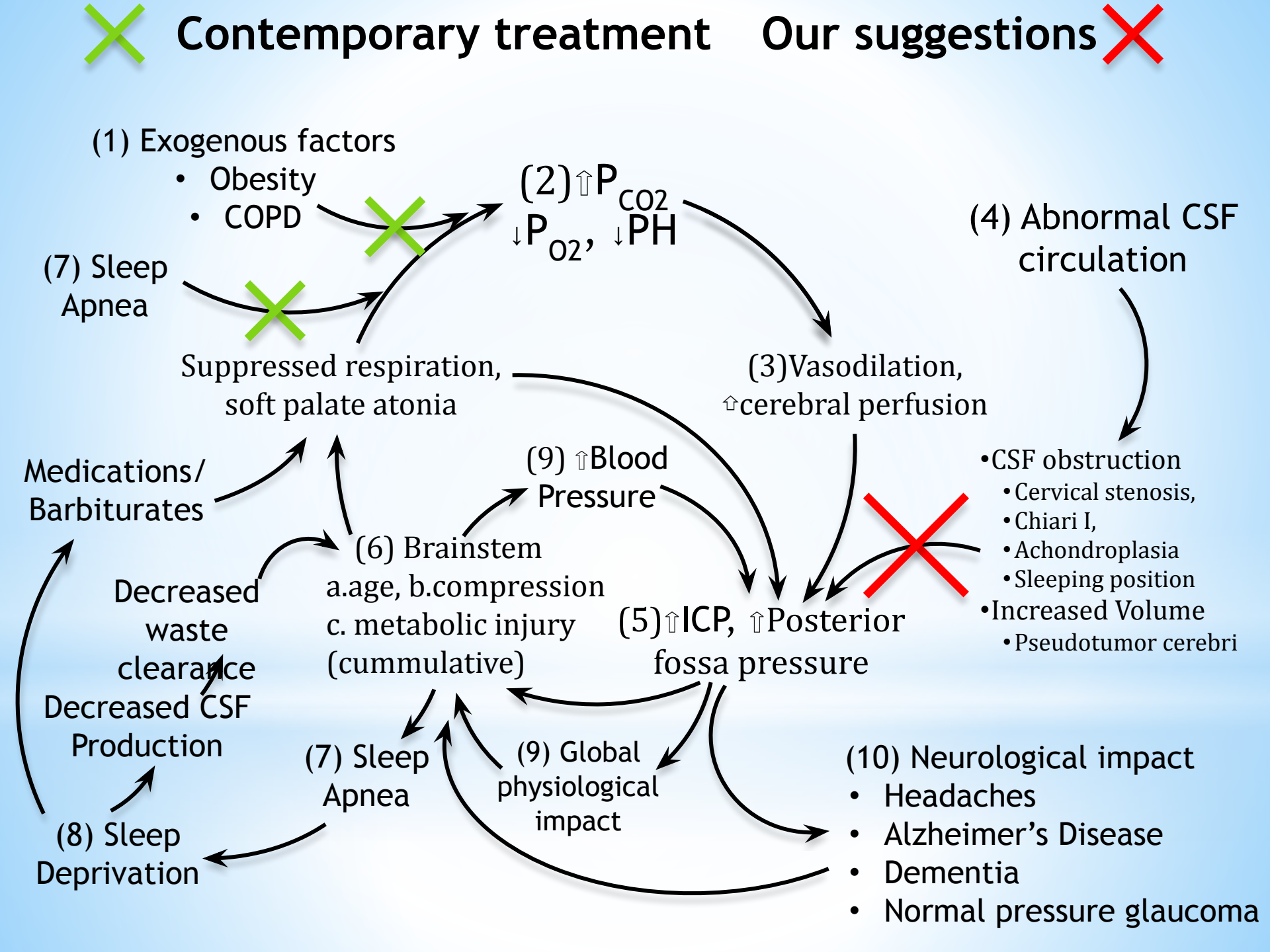
- Eye tracking is a useful tool for detection of subtle brainstem dysfunction and potentially can be used for evaluation of Sleep Apnea.

J Neurotrauma. 2015 Apr 15;32(8):548-56. doi: 10.1089/neu.2014.3687. Epub 2015 Feb 6.

Eye tracking detects disconjugate eye movements associated with structural traumatic brain injury and concussion.

Samadani U[1], Ritlop R, Reyes M, Nehrbass E, Li M, Lamm E, Schneider J, Shimunov D, Sava M, Kolecki R, Burris P, Altomare L, Mehmood T, Smith T, Huang JH, McStay C, Todd SR, Qian M, Kondziolka D, Wall S, Huang P.

Therapy


Contemporary treatment
Our suggestions
(1) Exogenous factors
• Obesity
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(2)⇧P_{CO2} ↓P_{O2}, ↓PH
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(9) Global physiological impact
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• Headaches
• Alzheimer's Disease
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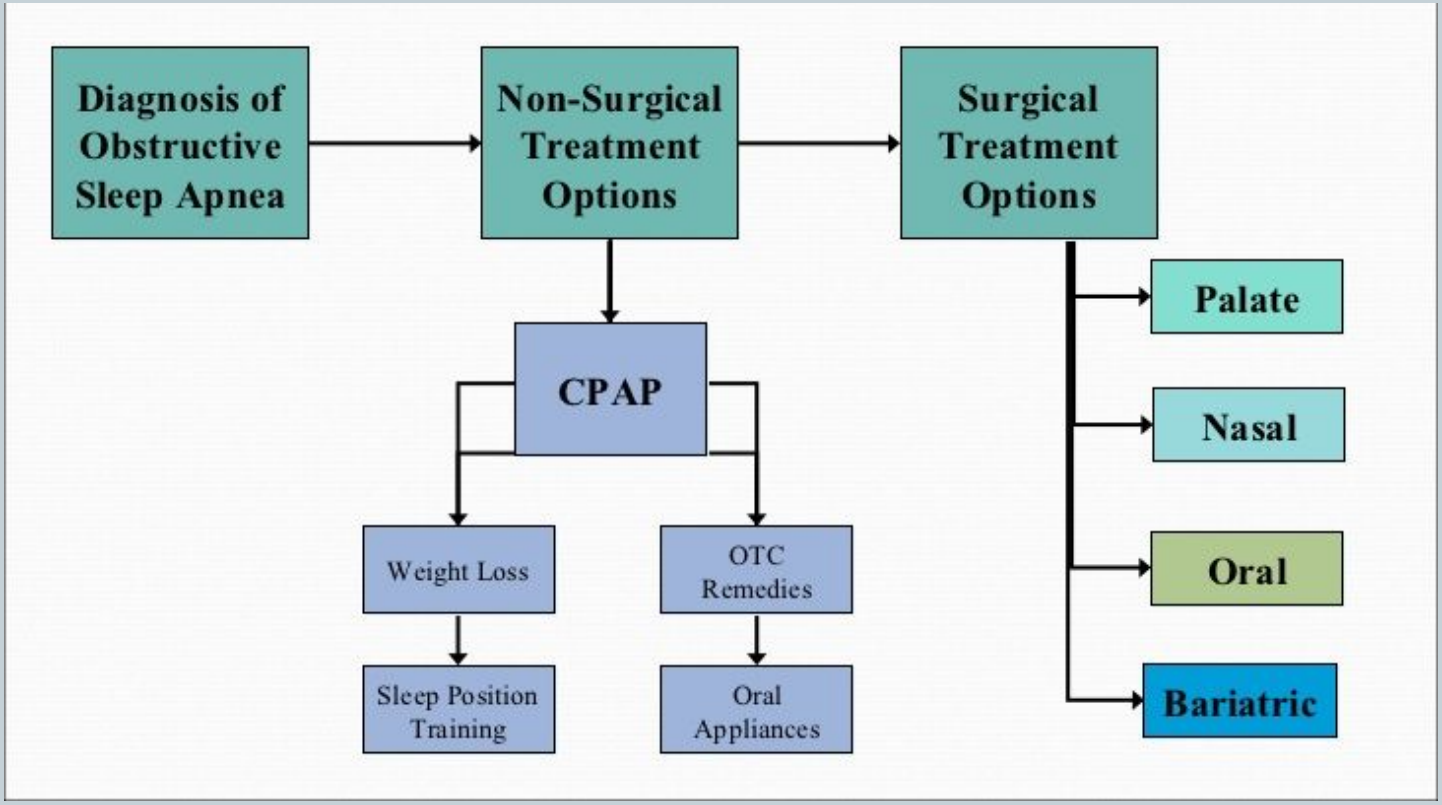
• Normal pressure glaucoma

Contemporary treatment

Contemporary Management of Sleep Apnea



J Clin Sleep Med. 2009 Jun 15;5(3):263-76.

Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults.

Epstein LJ[1], Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD; Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine.

Suggestions

- Therapy – if CSF abnormalities can be established
  1. Wear a soft cervical collar while sleeping (in the presence of substantial cervical osseous obstruction
  2. Consider upright sleeping posture
  3. Prophylactic shunting or decompressions may be suggested more aggressively.

Soft cervical collar

Therapy – cervical collar

Proper sleep position using a soft cervical collar

- Cervical collar is a relatively effective way of neutral head positioning in cervical stenosis

BMJ. 2009 Oct 7;339:b3883. doi: 10.1136/bmj.b3883.

Cervical collar or physiotherapy versus wait and see policy for recent onset cervical radiculopathy: randomised trial.

Kuijper B[1], Tans JT, Beelen A, Nollet F, de Visser M.

J Fam Pract. 2010 May;59(5):269-72.

PT or cervical collar for cervical radiculopathy?

Dmytriv M[1], Rowland K, Gavagan T, Holub D.

Upright sleep position

Therapy – sleep position

Sleeping position

1. The supine sleeping position is associated with significantly more apneas than the non-supine positions

Am J Otolaryngol. 1985 Sep-Oct;6(5):373-7.

Sleeping position and sleep apnea syndrome.

Kavey NB, Blitzer A, Gidro-Frank S, Korstanje K.

2. Lateral decubitus position often results in significantly fewer apneas

Sleep. 1988 Feb;11(1):90-9.

Sleep apnea and body position during sleep.

George CF[1], Millar TW, Kryger MH.

3. Left-sided sleeping position results in statistically higher AHI scores that right-sided sleeping position

Sleep Breath. 2012 Sep;16(3):617-20. doi: 10.1007/s11325-011-0547-4. Epub 2011 Jun 16.

Influence of the right- versus left-sided sleeping position on the apnea-hypopnea index in patients with sleep apnea.

Ozeke O[1], Erturk O, Gungor M, Hızel SB, Aydın D, Celenk MK, Dıncer H, Ilıcın G, Ozgen F, Ozer C.

Therapy – sleep position

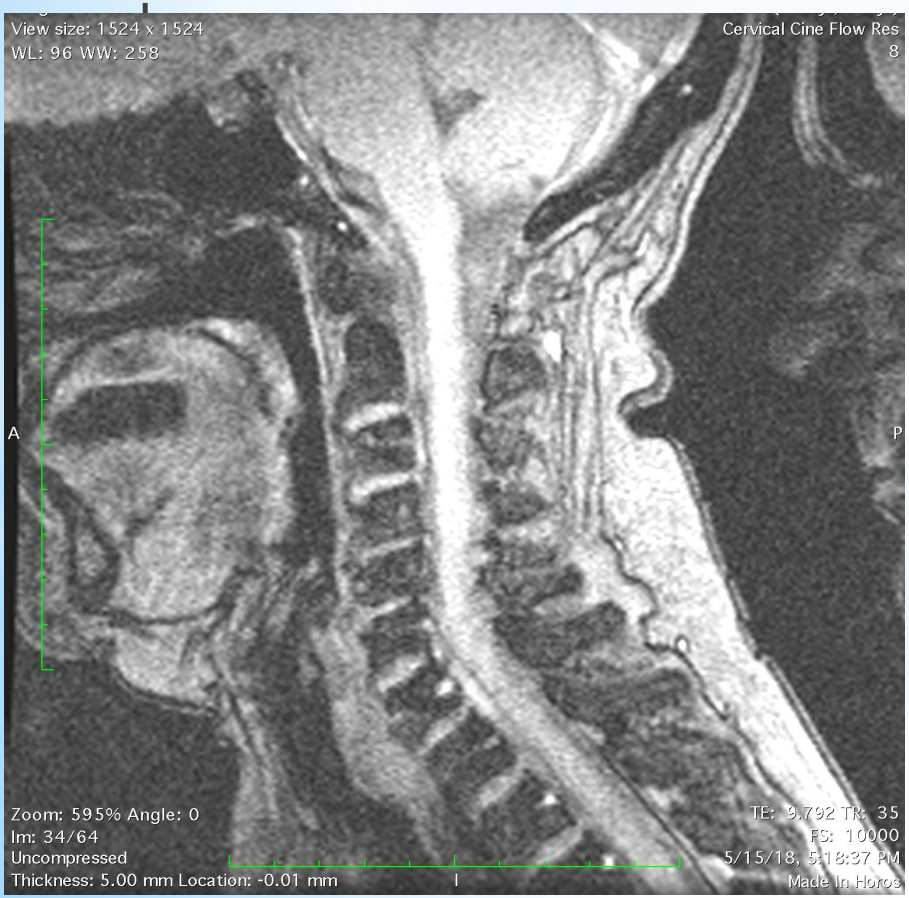
Prone Position Improves CSF Flow

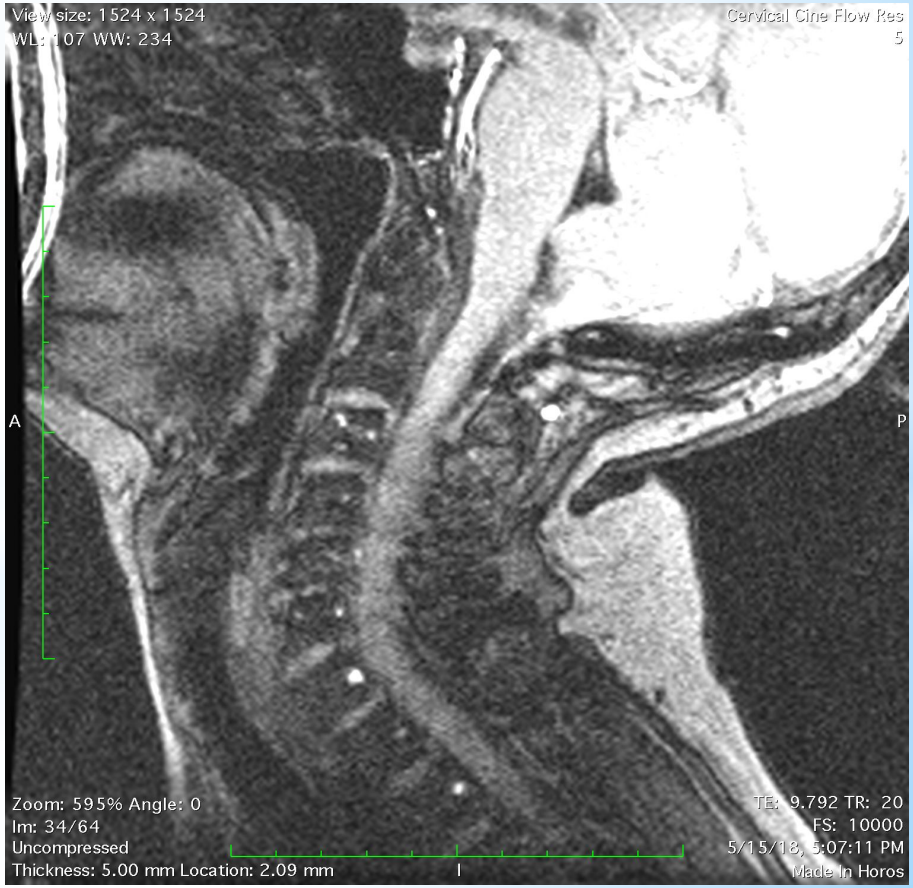
- 15 patients were included in this prospective study
- CINE MRI was performed before the surgery, after positioning and after the surgery.
- 14 out of 15 patients (93%) demonstrated significant improvement of CSF flow through the foramen magnum dorsal to the tonsils with positioning only.
- This improvement was so notable that changes in CSF flow as a result of the bone decompression were difficult to discern.
- These results put into question intraoperative flow assessments that suggest adequate decompression by PFD, whether by iMRI or intraoperative ultrasound.

Reference: Changes in cerebrospinal fluid flow assessed using intraoperative MRI during posterior fossa decompression for Chiari malformation. Bond AE, Jane JA Sr, Liu KC, Oldfield EH. J Neurosurg. 2015 May;122(5):1068-75.

However…

- our observation is that flexion and extension of the neck is more important than prone or supine position.
- flexion of the cervical spine improves CSF flow significantly as compared to extension
- improvement of CSF flow prone position could be due to flexion of the





Therapy – sleep position

Body posture and Glymphatic circulation

- The major finding of this study was that waste (including Aβ) removal from rodent brain was most efficient in the lateral position (compared with the prone position, which is the natural resting/sleeping position of rodents).

- This finding needs to be confirmed in humans.

J Neurosci. 2015 Aug 5;35(31):11034-44. doi: 10.1523/JNEUROSCI.1625-15.2015.

The Effect of Body Posture on Brain Glymphatic Transport.

Lee H[1], Xie L[2], Yu M[3], Kang H[2], Feng T[4], Deane R[2], Logan J[5], Nedergaard M[2], Benveniste H[6].

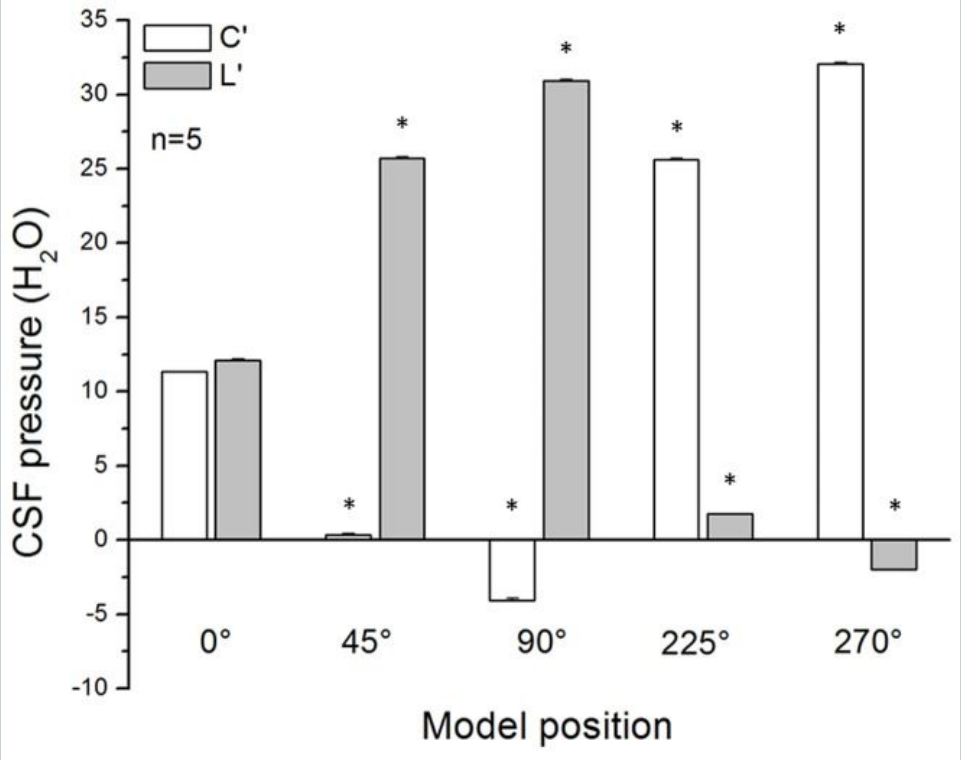
Therapy – sleep position

Body posture

- **The Effect of Body Posture on Brain Glymphatic Transport;** Hedok Lee, Lulu Xie, Mei Yu, Hongyi Kang, Tian Feng, Rashid Deane, Jean Logan, Maiken Nedergaard, and Helene Benveniste; J Neurosci. 2015 Aug 5; 35(31): 11034–11044.

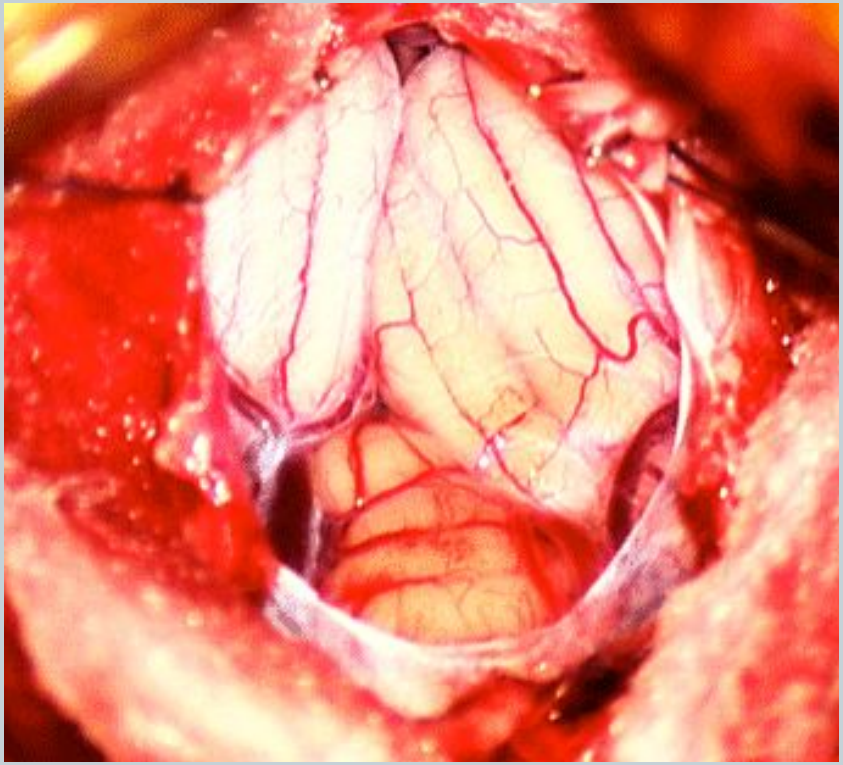
Therapy – sleep position

Upright position decreases Intracranial Pressure



Source: The Influence of Body Position on Cerebrospinal Fluid Pressure Gradient and Movement in Cats with Normal and Impaired Craniospinal Communication; Marijan Klarica,# 1 , * Milan Radoš, 1 Gorislav Erceg, 1 Antonio Petošić, 2 Ivana Jurjević, 1 and Darko Orešković# 3; PLoS One. 2014; 9(4): e95229. Published online 2014 Apr 18.

Surgery



Therapy – decompression of obstruction

Sleep Apnea improves after VP shunting

J Neuropsychiatry Clin Neurosci. 2015 Summer;27(3):e206-8. doi: 10.1176/appi.neuropsych.14120375.

Improvement of Central Sleep Apneas Following Ventricular Shunt for Normal Pressure Hydrocephalus.

Oliveira MF[1,2], Nacif SR[1,2], Castellano O[1,2], Sousa UO[1,2], Rotta JM[1,2], Pinto FC[1,2].

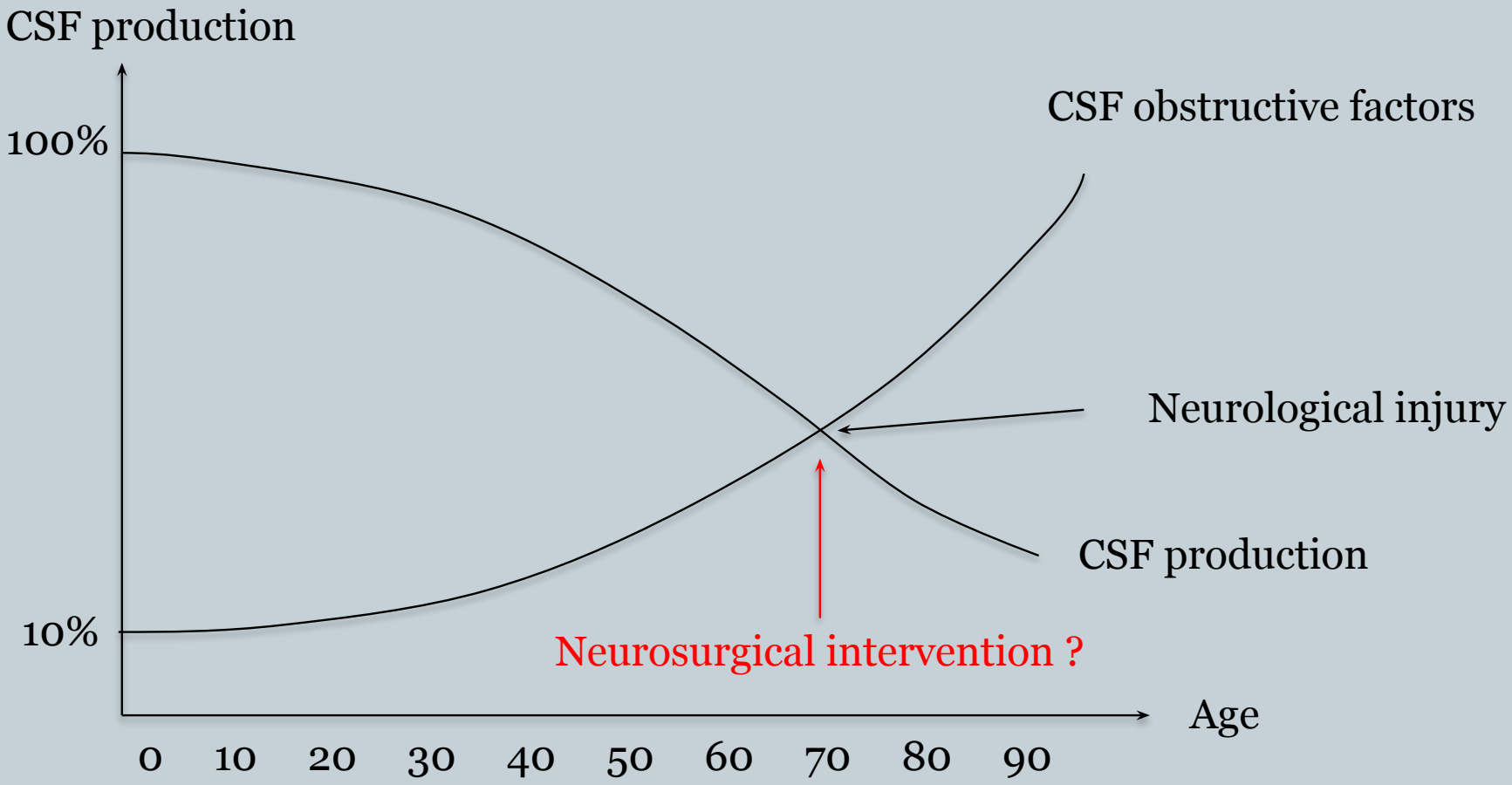
J Neurol Neurosurg Psychiatry. 1998 Oct;65(4):497-501.

Effects of transient and persistent cerebrospinal fluid drainage on sleep disordered breathing in patients with idiopathic adult hydrocephalus syndrome.

Kristensen B[1], Malm J, Rabben T.

Therapy – decompression of obstruction

End stage time factor (Cerebrospinal Fluid Balance)



Cine MRI after cervical decompression

- 47 patients with cervical myelopathy attributable to cervical stenosis
- 35 ACDF + 12 expansive laminoplasty.
- preoperative and postoperative 1.5-T cine phase contrast MRI

- Preoperatively, CSF flow reduction caudally compared to healthy controls.
- Both decompressive procedures essentially returned patient velocities to control values.
- Postoperative increase in flow velocity correlated with clinical recovery after posterior ($P < 0.0008$) but not anterior decompression.

Neurosurgery. 2002 Apr;50(4):791-5; discussion 796.

Quantitative assessment of surgical decompression of the cervical spine with cine phase contrast magnetic resonance imaging.

Tominaga T[1], Watabe N, Takahashi T, Shimizu H, Yoshimoto T.

Author information

1 Department of Neurosurgery, Kohnan Hospital, Tohoku University School of Medicine, Sendai, Japan. tomi@nsg.med.tohoku.ac.jp

Conclusion

- CSF circulation has an unappreciated role in Sleep Apnea and aggressive treatments offers the possibility of improvement of Sleep Apnea

- Understanding the vagaries of CSF circulation (which in some ways might be likened to the physiological impact of blood pressure variation) and instituting appropriate therapeutic interventions might effectuate neurological function improvement.