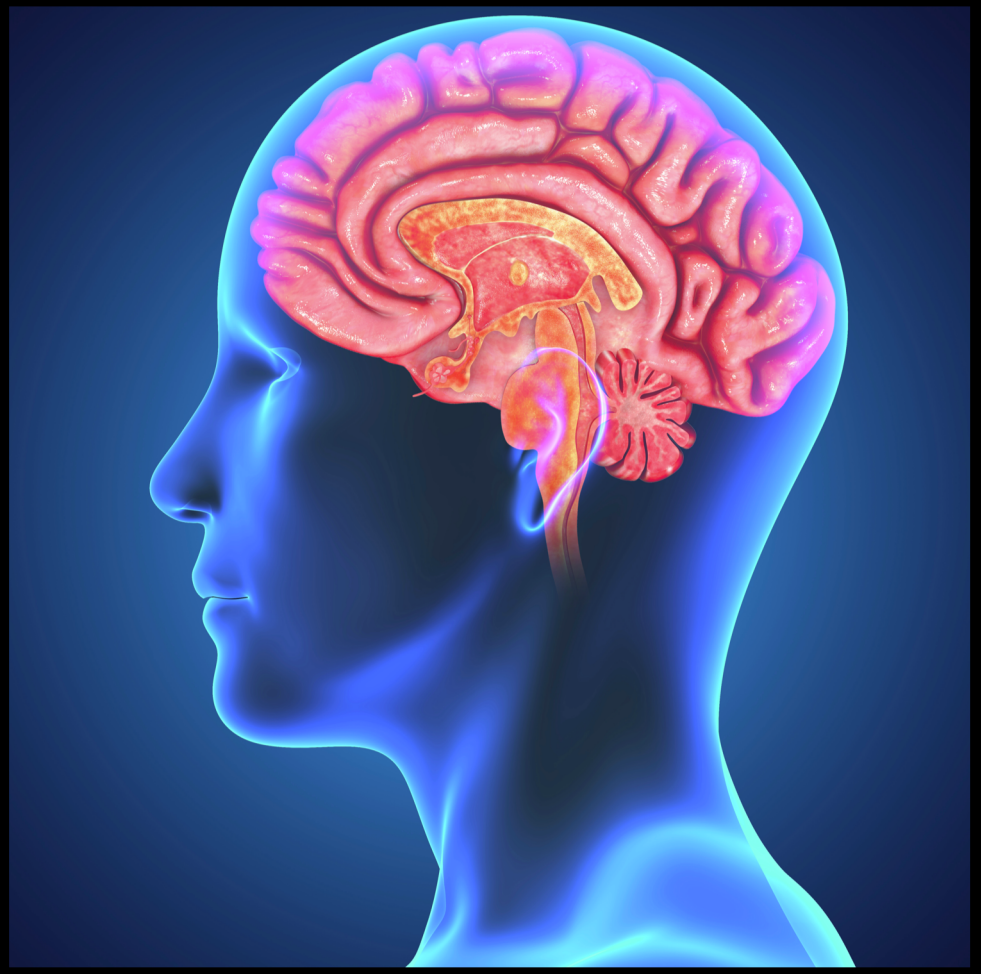
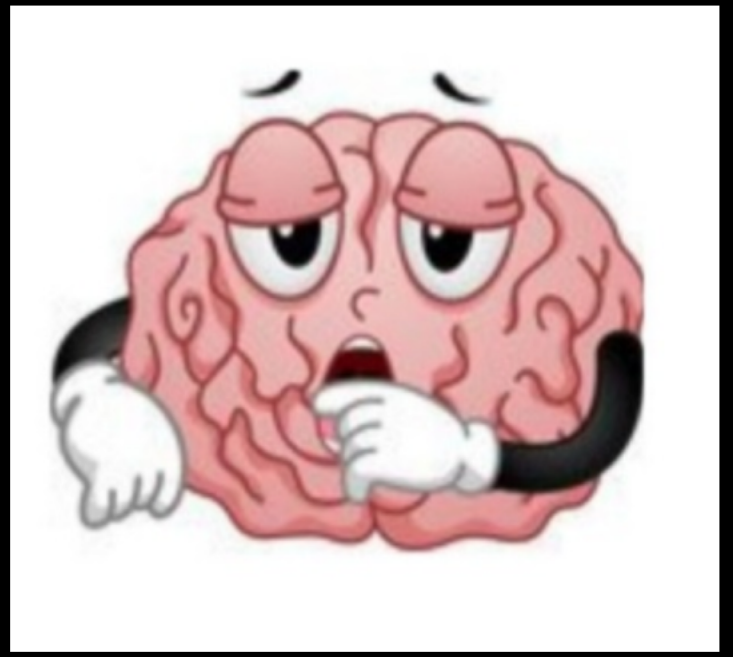
Cerebral Metabolism



By Sarah A. Stone, MD
Neuroanesthesia Fellow
2018-2019

Why do I need to understand cerebral physiology…

It’s SOOOOOOO boring

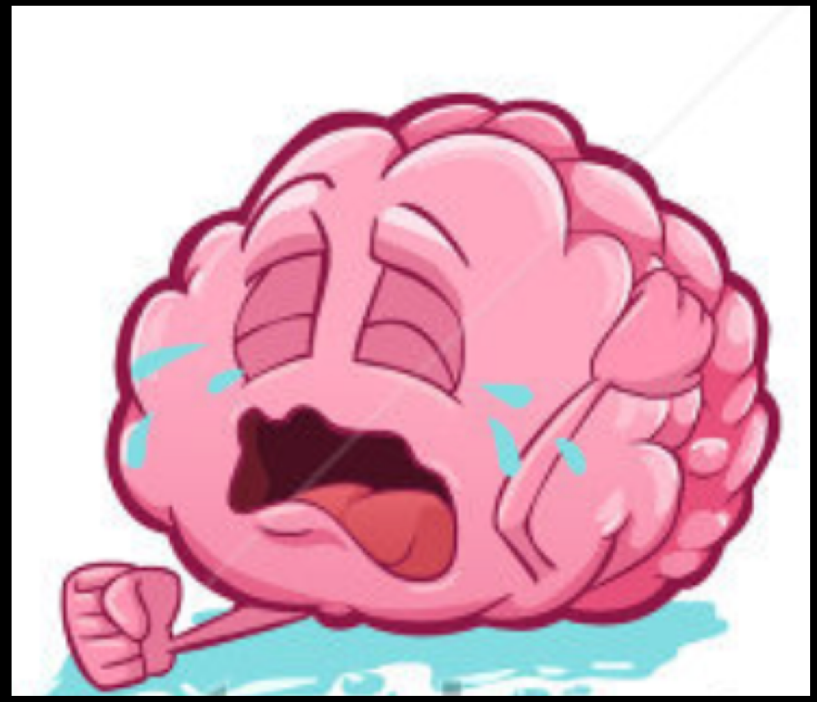


Because it’s on the BOARDS…..

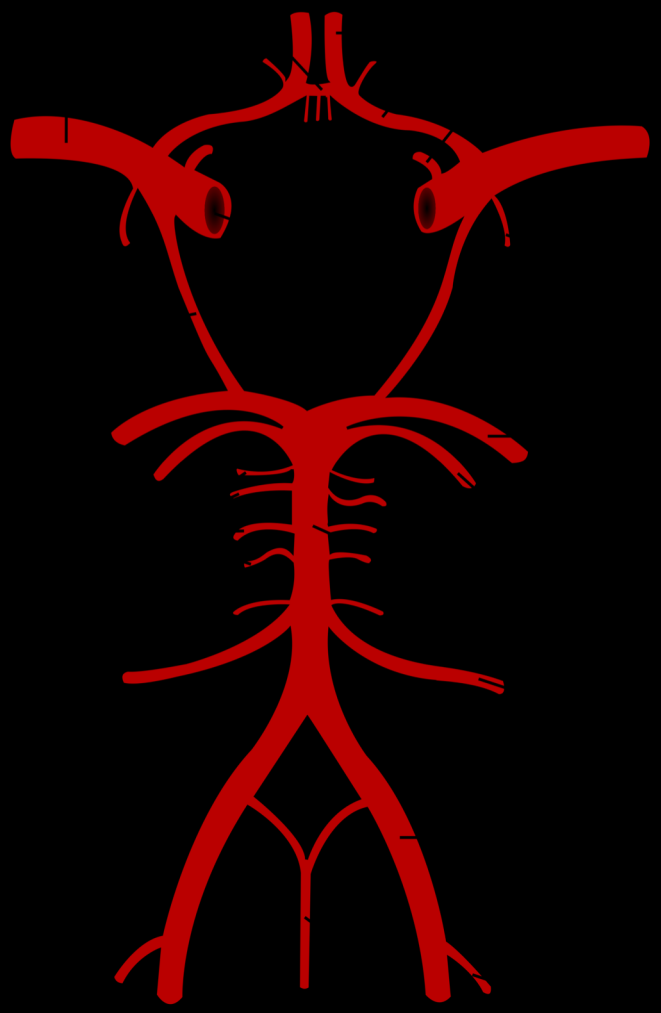
And it’s kind of important

The balance between supply and demand is poor…

- Constant oxygen & nutrients
- Black out within seconds of ischemia
- With total lack of perfusion → permanent brain damage within 3-8 minutes!!!
- *Who came up with this system for the most important organ in the body?!?*



Supply



- Arrives: internal carotid a. and vertebral aa.
- Leaves: cerebral veins, dural venous sinuses and into the internal jugular veins
- Brain is only 2% of body mass (1400 gm) but receives 12-15% of cardiac output
  - ***4-5%*** *(225 ml/min) goes to the heart*
- Cerebral Perfusion Pressure

CPP = MAP – ICP*

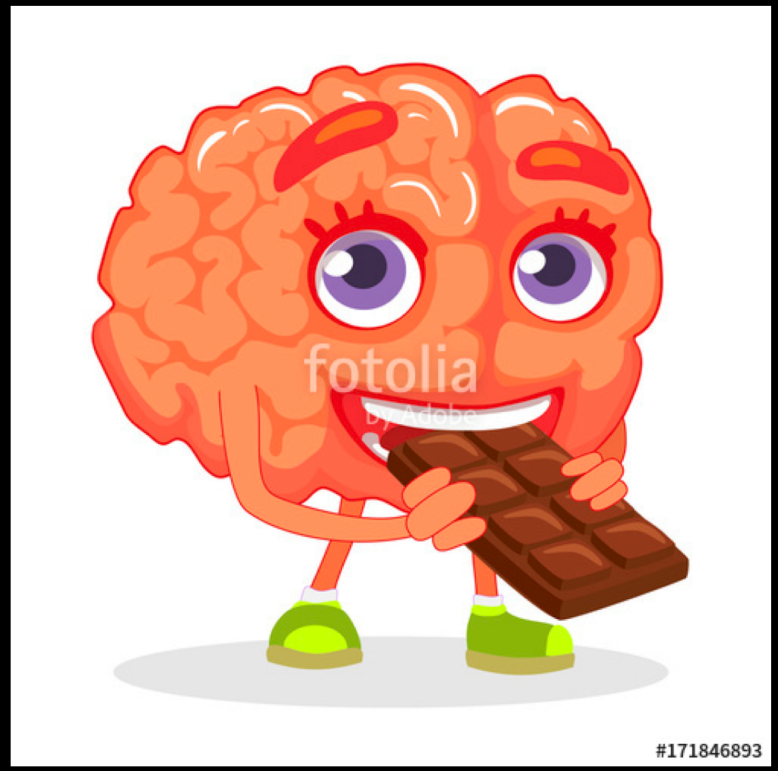
**or CVP, whichever is higher*

- Normal = 70-90 mm Hg

Demand

- Brain has highest metabolic requirement of any organ in the body
- Glucose = main energy substrate
  - Also used as a precursor for neurotransmitters

Dr. Jaffe's Brain:



Distribution of blood flow and oxygen consumption in a normal, resting subject.

Circulation	Blood flow (mL/min)	O_2 consumption (mL/min)	Total O_2 consumption (%)
Splanchnic	1400	58	25
Renal	1100	16	7
Cerebral	750	46	20
Coronary	250	27	11
Skeletal Muscle	1200	70	30
Skin	500	5	2
Other organs	600	12	5
Total	**5800**	**234**	**100**

But these tissues have different mass…

	Mass kg	Blood flow ml. min^{-1}	ml. min^{-1} $100g^{-1}$	Max blood flow $ml.min^{-1}$	O_2 consump ml. min^{-1}	ml. min^{-1} $100g^{-1}$	a-v diff ml O_2. $100ml^{-1}$	Resistance $kPa.l^{-1}.min.kg^{-1}$
Brain	1.4	750	(54)	1500	46	(3.3)	6.2	24.4
Heart	0.3	250	(83)	1200	29	(9.7)	11.4	15.7

The brain consumes more oxygen than the heart but when comparing equal amounts of tissue, the heart consumes more oxygen

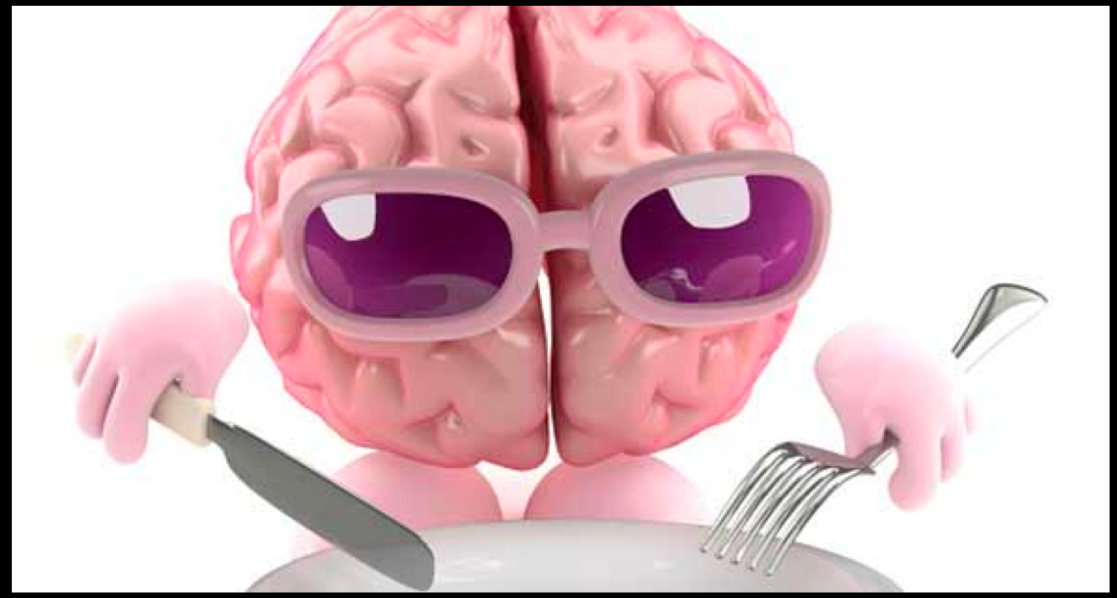
Table I Average values in normal healthy individuals

	Grey matter	White matter	Average (whole brain)
CBV (ml per100 g tissue)	4–6	1.5–2.5	3.5–4.5
CBF (ml per 100 g tissue per min)	100–110	20–25	45–55
$CMRO_2$ (ml per 100 g tissue per min)	4–4.5	0.7–1.0	3–3.5
CMR_{glu} (mg per 100 g tissue per min)	6.5–8.5	1.2–2.2	4–5

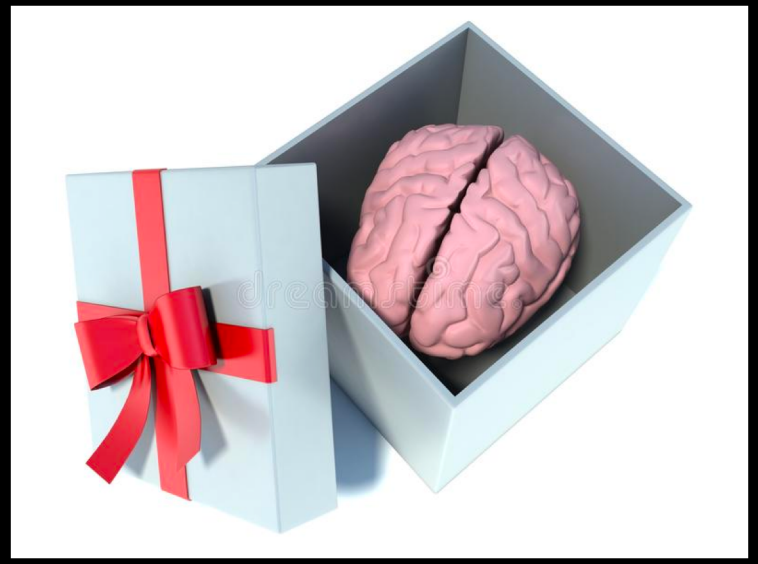
***CBF ~ 50 ml/100g tissue/min**

***CMRO2 ~ 3 ml/100g tissue/min**

So how do we manipulate supply to meet our demands…



Intracranial Pressure



Alexander Monro *secundus*, coloured engraving (1800) by James Heath after Henry Raeburn

- Monro-Kellie Hypothesis = Brain in a Box
  - Brain = 80%
  - CSF = 10% (150 mL)
  - Blood = 10% (150 mL)
- ***Normal ICP 5-15 mm Hg***
- ***CPP = MAP – ICP***
- So how do we manage increased ICP….

- Volume Buffering (Pressure-Volume Relationship)
  - Blood
    - Decrease flow into the brain
    - Increase flow out of the brain
  - CSF
    - ***Displacement into spinal canal***

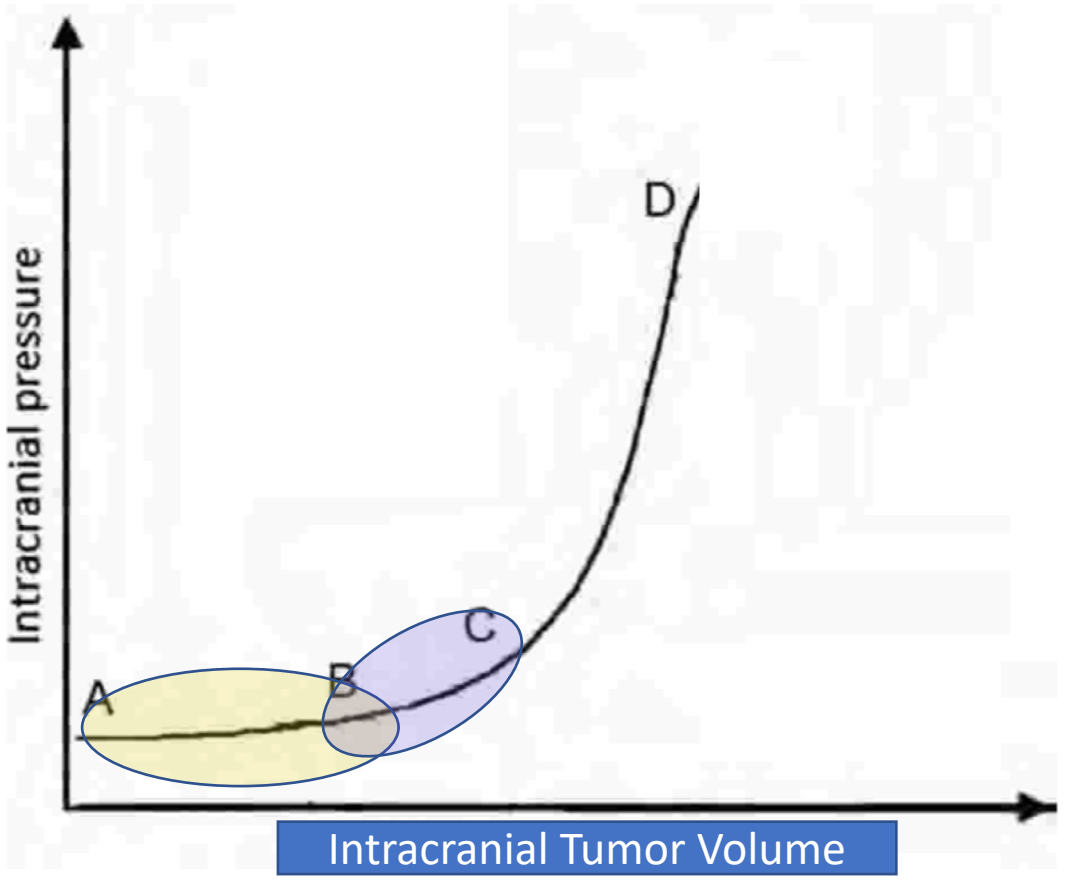
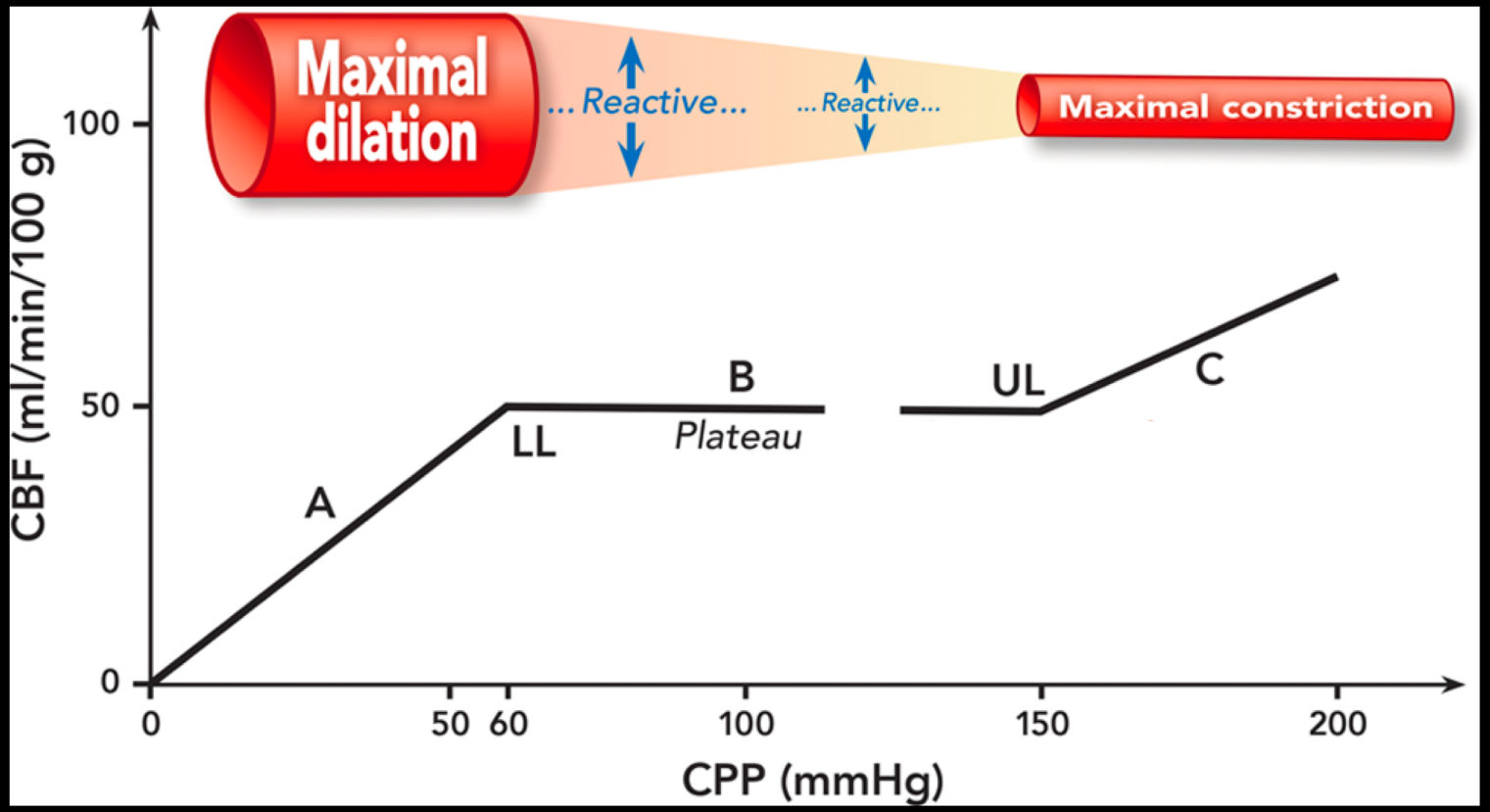


Fig 2 ICP–volume compliance curve. (A and B) Compensation phase—ICP nearly constant with increase in intracranial volume initially. (C and D) Decompensation phase—ICP increases rapidly with increasing intracranial volume as the buffers are exhausted.

- **Autoregulation:** intrinsic ability of an organ to maintain a constant blood flow despite changes in perfusion pressure



Autoregulation

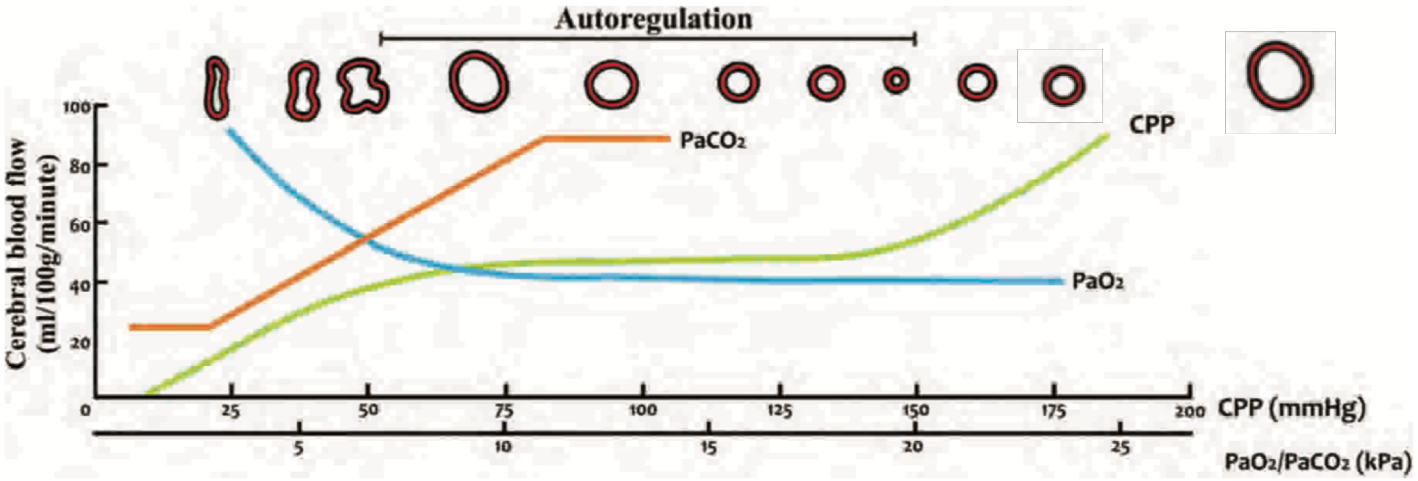
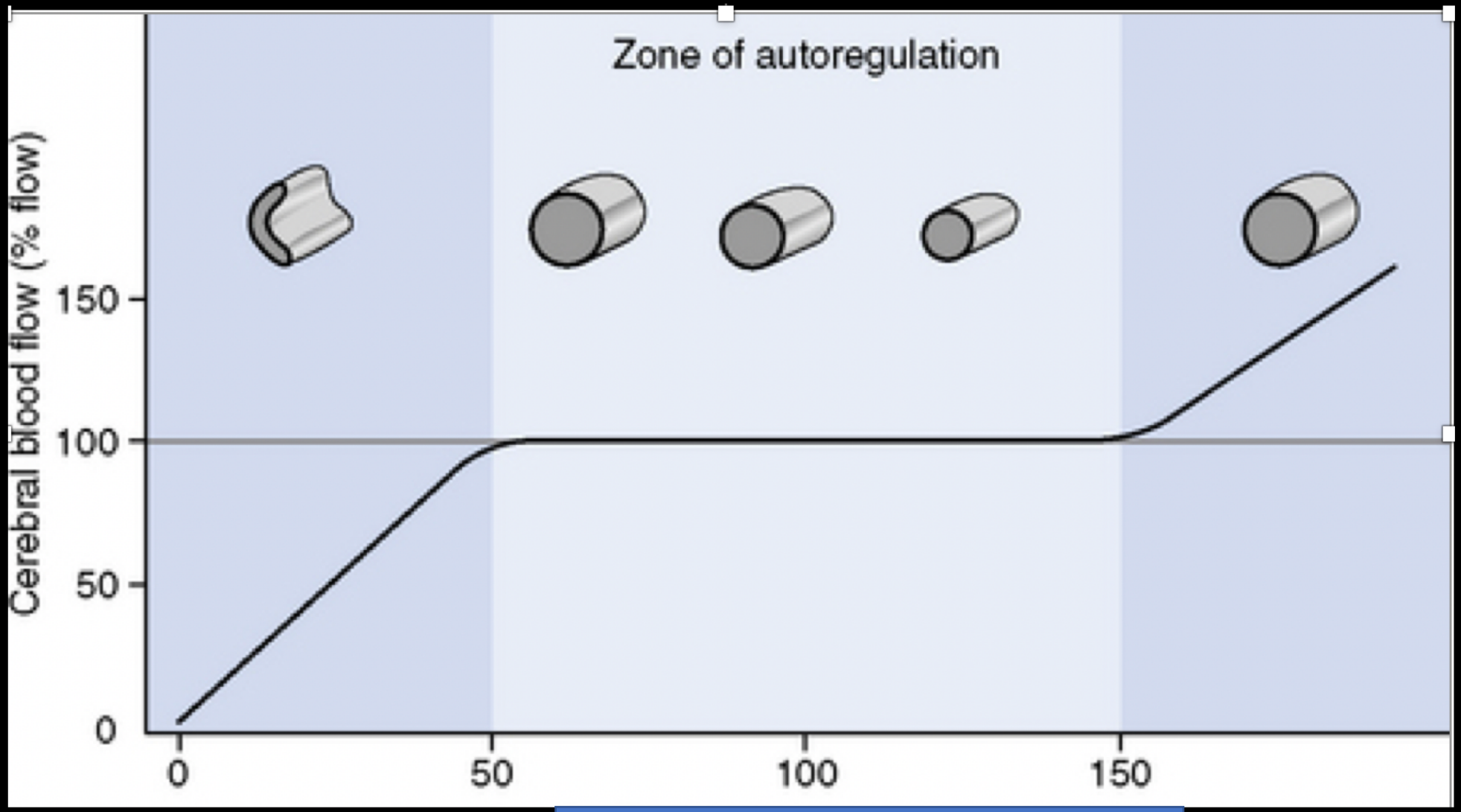


Fig 3 Effect of changes in MAP, arterial oxygen and carbon dioxide tensions, and cerebral vascular resistance on cerebral blood flow. Reproduced with permission from Shardlow and Jackson.[10] Elsevier Limited.

- Increased MAP = increased transmural vessel tension → depolarization of vascular smooth muscle → vasoconstriction
  - ***Occurs between MAP 60-160 mm Hg/ CPP 50-150 mmHg***
- Above the plateau CBF becomes pressure dependent
- Chronic HTN shifts the curve ***RIGHT***



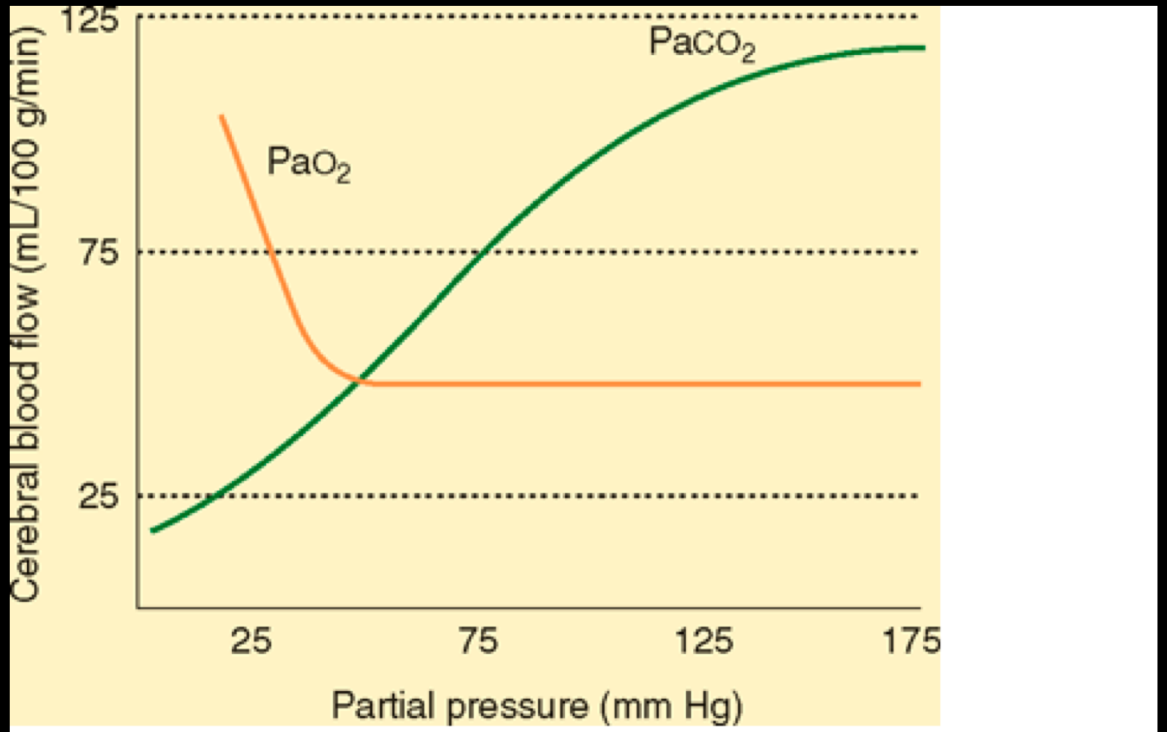
MAP (mm Hg)

CPP (mm Hg)

Autoregulation is affected by:

- $PaCO_2$
- PaO_2
- Flow-Metabolism Coupling
- Neurogenic Control
- Temperature
- Rheology
- Chronic HTN

Arterial CO_2 Tension

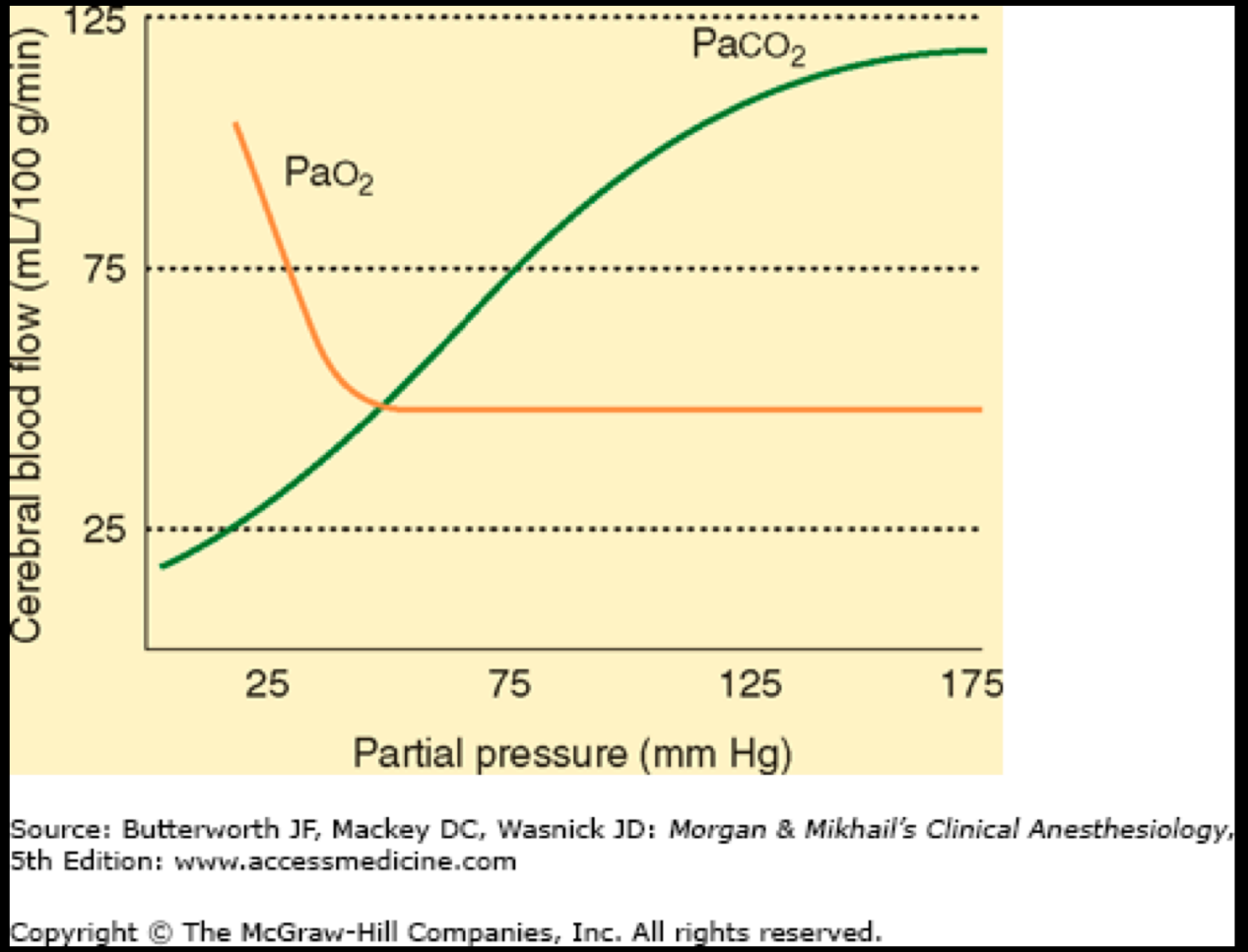


Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com

- Decreased $PaCO_2$ = vasoconstriction,
  - Decreased CBF
- Increased $PaCO_2$ = vasodilation
  - Increased CBF
- CBF increases (or decreases) ~2% for every mm Hg increase (or decrease) in $PaCO_2$
  - That is… ***1 mL / 100 g / min****

Arterial O_2 Tension

- Hypoxia increases CBF by cerebral vasodilation
- Ion channels in vascular smooth muscle are activated ***when PaO_2 falls below 50 mm Hg***

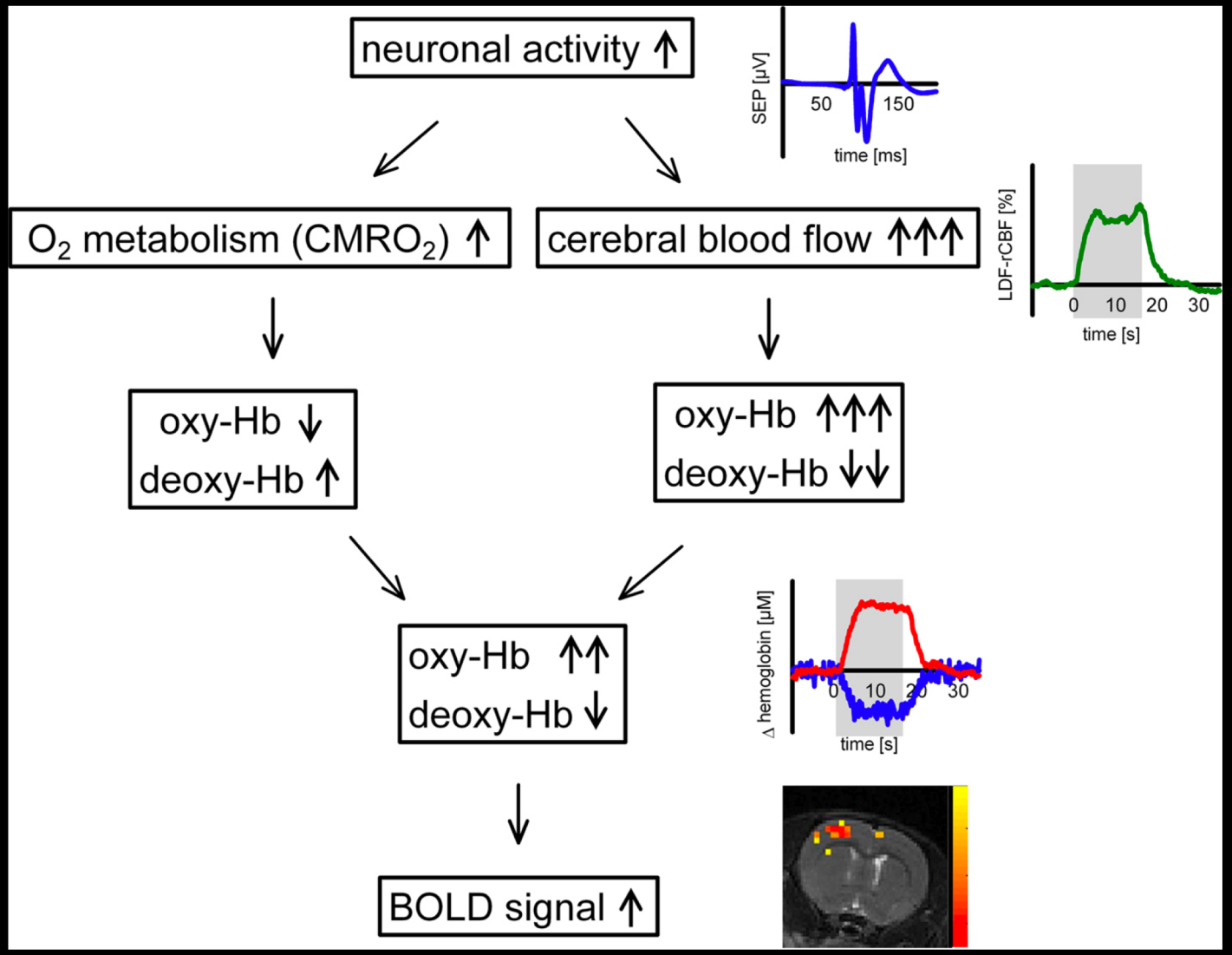


Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com

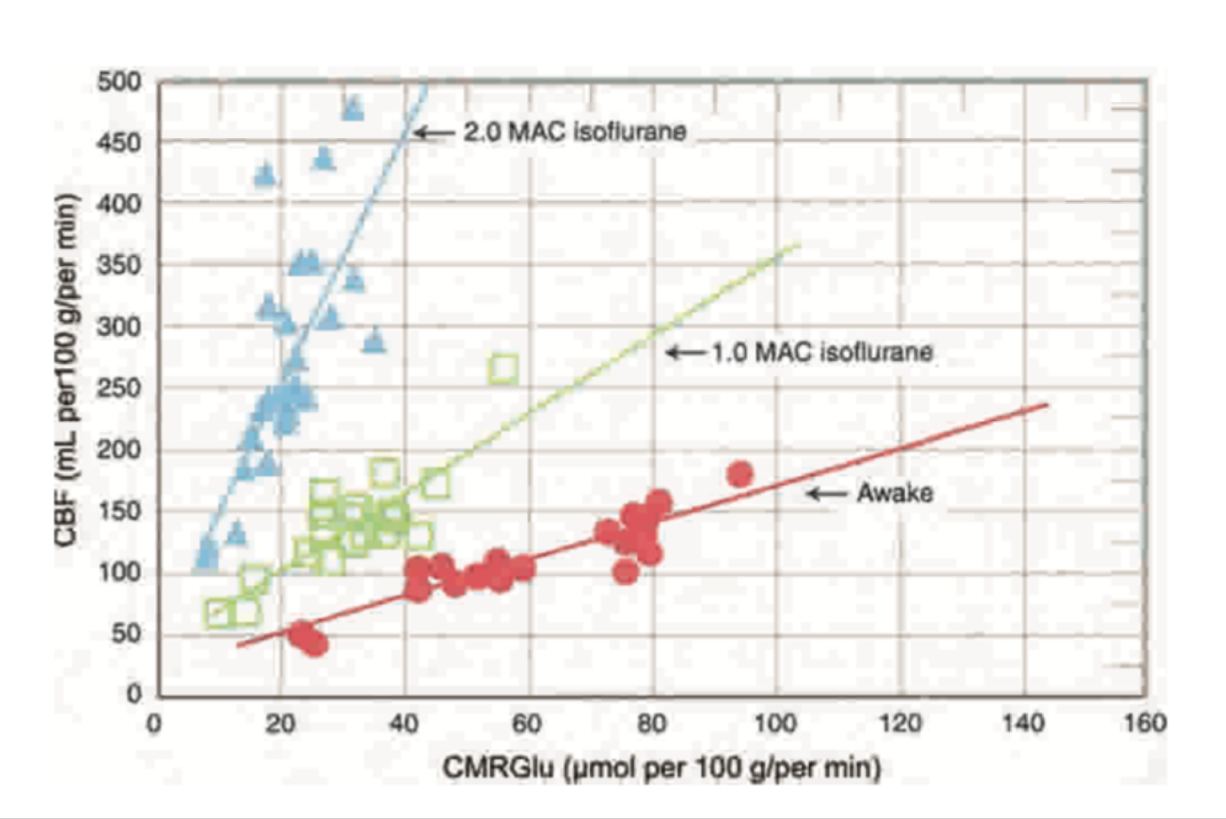
Flow-Metabolism Coupling (FMC)

- Matching oxygen or glucose delivery to metabolic requirements
- Increase in neuronal activity (CMR) → proportional increase in CBF

Blood Oxygen Level Dependent Imaging
-method using fMRI to observe different areas
Of the brain or other organs which are found to
Be active at any given time



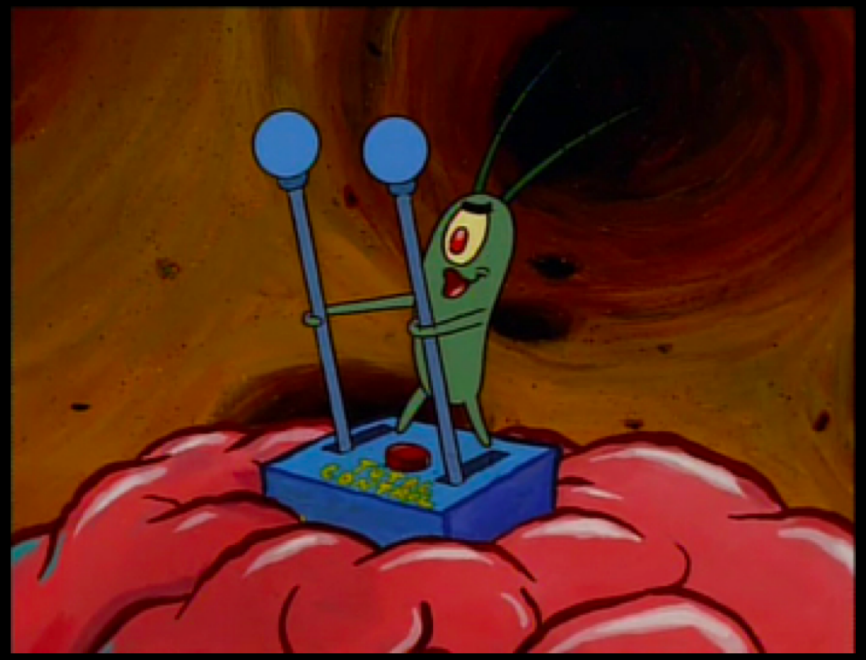
Volatile Anesthetics



- In an awake patient, decreased $CMRO_2$ = decreased CBF
- VA produce a dose dependent reduction in $CMRO_2$ → reduced CBF
  - VA's also increase CBF by vasodilation = little to no change in CBF
- Decrease CBF is greater with decrease of $CMRO_2$ when MAC is higher (~1.5-2 MAC)

Neurogenic Control

- Postganglionic sympathetic supply: Superior Cervical Ganglion
- Parasympathetic: Sphenopalatine and Otic ganglia
- Sensory fibers from Trigeminal Ganglion



- Postganglionic sympathetic supply: Superior Cervical Ganglion
  - NE, neuropeptide Y
  - Vasoconstriction, shifts the autoregulation curve to the right (e.g. chronic HTN)
  - Protective for acute increases in BP and disruption of BBB

- Parasympathetic: Sphenopalatine and Otic ganglia
  - ACh and VIP
  - Vasodilation in hypotensive states, postischemia reperfusion

- Sensory fibers from Trigeminal Ganglion
  - Substance P, Calcitonin gene related peptide
  - Vasodilation
  - Stimulation in HTN and seizures can cause vasodilation, increase in CBF

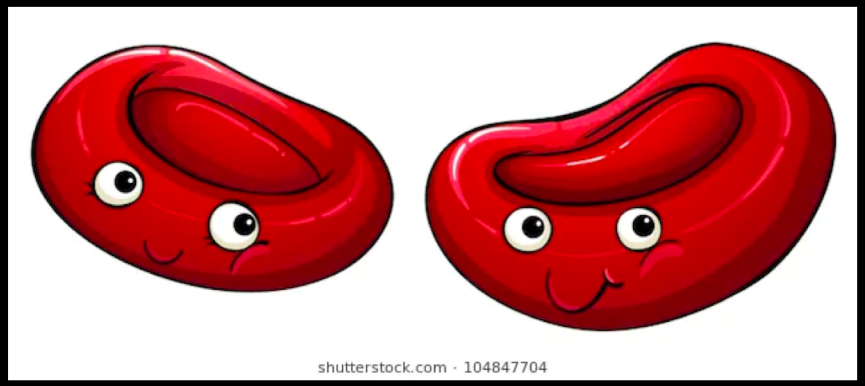
Temperature

- Decreasing temperature = decreased cerebral metabolism
- Increasing temperature = increased cerebral metabolism

For every 1 degree Celsius decrease in brain temperature:

CMR and CBF decrease ~6-7%

Rheology



- In ischemia, low CPP causes low flow state → compensatory VD
  - Decreased viscosity of blood may improve CBF
  - Decreased Hct lowers O_2 carry capacity
- No current guidelines for target Hct in neuroanesthesia

  - ***Best guess = 30-34***

$$CaO2=(1.34 \times Hgb \times SaO2) + (0.003 \times PaO2)$$

PRACTICE QUESTIONS!

727. Intracranial hypertension is defined as a sustained increase in intracranial pressure (ICP) above

A. 5 mm Hg

B. 15 mm Hg

C. 25 mm Hg

D. 40 mm Hg

E. None of the above

745. When intracranial hypertension exists, the main compensatory mechanism from the body is

A. Increased absorption of cerebrospinal fluid (CSF) at the intracranial arachnoid villi

B. Increased absorption of CSF in the spinal arachnoid villi

C. Shifting of CSF from intracranial to spinal subarachnoid space

D. Reduction of cerebral blood volume due to compression of intracranial arteries

E. Decreased production of CSF at the choroid plexus

742. For each 1° C decrease in body temperature, how much will $CMRO_2$ be diminished?

A. 3%

B. 5%

C. 6%

D. 10%

E. 20%

740. What is the normal cerebral metabolic rate for oxygen ($CMRO_2$) per minute?

A. 0.5 mL/100 g brain tissue

B. 2.0 mL/100 g brain tissue

C. 3.5 mL/100 g brain tissue

D. 7.5 mL/100 g brain tissue

E. 10 mL/100 g brain tissue

738. How much will CBF increase in a patient whose $Paco_2$ is increased from 35 to 45 mm Hg?

A. There is no relationship between $Paco_2$ and CBF

B. 10 mL/100 g/min

C. 25 mL/100 g/min

D. 40 mL/100 g/min

E. 50 mL/100 g/min

736. Normal global CBF is

A. 25 mL/100 g/min

B. 50 mL/100 g/min

C. 75 mL/100 g/min

D. 100 mL/100 g/min

E. 150 mL/100 g/min

730. By what percentage does cerebral blood flow (CBF) change for each mm Hg increase in $Paco_2$?

A. 1%

B. 2%

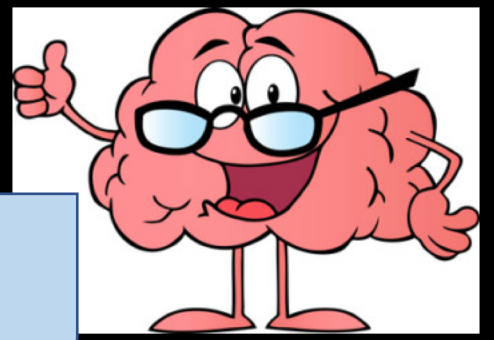
C. 7%

D. 10%

E. 25%

- When does ischemia become apparent on EEG?
  - A. 22 ml/100g/min
  - B. 15 ml/100g/min
  - C. 10 ml/100g/min
  - D. 5 ml/100g/min

Summary



- The brain requires a constant supply of energy and oxygen
- Our job: ensure balance between supply and demand
  - CPP = MAP – ICP, or CVP whichever is higher
- The brain lives in a box, affects ICP which is normally between 5-15 mm Hg
  - We can alter blood volume through various mechanisms e.g. $PaCO_2$
- Autoregulation occurs between MAP 60 – 160 mm Hg
  - Affected by CO_2, O_2, FMC, Neurogenic control, Temp, Rheology

References

- Cottrell and Young’s Neuroanesthesia – Fifth Edition
- Hall Questions
- Cerebral Physiology BJA