Cerebrovascular PHYSIOLOGY

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* CNS has 400 miles of vasculature associated with BBB (overall exchange surface area ≥ 12 m2).

CNS metabolic demands

Nors smegenys sudaro tik 2% kūno svorio (≈ 1400-1500 g) ir neatlieka jokio mechaninio darbo, bet *elektrofiziologiniam aktyvumui* palaikyti tenka didelės sąnaudos:

* gauna 14-20% **cardiac output** (i.e. 700-1000 ml/min);
	1. **kidney** – 420 ml /100 g /min
	2. **myocardium** – 84 ml /100 g /min
	3. **liver** – 58 ml /100 g /min
	4. **brain** – 53 (50-60) ml /100 g /min.
* sunaudoja 18-20% viso **deguonies** (in resting state):

**O2 consumption** – 46-49 ml/min (3.0-3.8 ml or 156-160 μmol/100 g/min; ≈ 72 L/d);

**a-vO2 difference** – 62 ml/L (myocardium – 114 ml/L).

* smegenys išekstrahuoja iš pratekančio kraujo: ≈ 50% **O2** ir tik ≈ 10% **gliukozės** (i.e. ratio 5 : 1).

N.B. brain is highly aerobic tissue, with oxygen rather than metabolic substrate serving as limiting substance!

N.B. *with focal cortical activity*, local **CBF** increases ≈ 30% while **O2 consumption** increases only 5% (luxurious oxygen supply) – venous blood has more oxygen = foundation of fMRI.

* brain uses glucose as exclusive fuel (badaujant prisitaiko naudoti ir ketone bodies) ≈ 5.5 mg or 30-33 μmol glucose/100 g/min (150 g glucose/d) – patenkina ≈ 90% smegenų energijos poreikio.

*Aerobic glucose metabolism* – main source of energy.

N.B. insulin is not required for CNS!

N.B. smegenys tik 70-80% gliukozės oksiduoja energijos gavybai; 10-15% gliukozės metabolizuojama į laktatą (ir grįžta atgal į kraują); likę 5-20% panaudojama įvairių medžiagų (pvz. neurotransmiterių) sintezei – todėl iš 1 molio gliukozės gaunama 30 mol (o ne 38) ATP.

* + glucose uptake from blood mechanizmo pajėgumas normoje viršija smegenų gliukozės poreikį 2-3 kartus; tačiau glucose uptake mechanizmo pajėgumas labai priklauso nuo blood [glucose] (e.g. hypoglycemic coma).
* *ammonia* (very toxic to neurons – e.g. hepatic coma) removal from brain:

**glutamate** uptake from blood → coupling with ammonia → **glutamine** secretion into blood.

Cerebral blood flow (CBF)

In normal, conscious\* human CBF ≈ 53 (50-60) ml /100 g /min

(grey matter ≈ 69-75, white matter ≈ 25-30)

\*i.e. it is relative (e.g. it is lower during anesthesia, higher in epileptic cortex)

* normal blood volume is 3-4 ml/100 g of brain tissue.
* smegenys praktiškai neturi „degalų“ atsargų - turi pastoviai gauti O2 ir gliukozę (brain relies on sizable and well-regulated blood flow to satisfy its immediate needs for energy).
* nutrūkus kraujotakai, sąmonės netenkama po 8-10 sekundžių, neuronai žūti pradeda jau po 5 minučių! *glikogeno atsargos (≈ 1.6 mg/g) sunaudojamos per 2 minutes*

N.B. *vegetative centers in brainstem are more resistant to hypoxia* / *hypoglycemia than cerebral cortex* – patients may recover from prolonged hypoxia / hypoglycemia with normal vegetative functions but severe intellectual deficiencies!

CBF in ischemia with clinical correlates → see [p. Vas3 >>](http://www.neurosurgeryresident.net/Vas.%20Vascular%5CVas3.%20Ischemic%20Stroke%2C%20TIA.pdf#PATHOPHYSIOLOGY)

Factor that regulates regional CBF

- **synaptic activity**:

* nors smegenys pasiima tik 1/2 patiekiamo O2 ir tik 1/10 patiekiamos gliukozės, tačiau tai pačių smegenų uptake mechanizmo galimybių riba – norint paimti daugiau, reikia didinti patiekiamus kiekius (i.e. blood vascular reserves for both O2 and glucose are small) – bet koks sinaptinio (metabolinio) aktyvumo pokytis keičia to regiono blood flow (coupling of CBF to regional synaptic / metabolic activity), bet nekeičia oxygen extraction;
	+ *all changes of synaptic activity* (thinking, talking, directing muscular activity, etc) *are tightly coupled,* both temporally and anatomically, to almost instantaneous, proportional *change in regional CBF* → ever-changing mosaic of regional metabolic/blood flow values that reflect moment-to-moment changes in electrophysiologic activity – this allows exploration of functional networks working in synchrony even in resting state (resting state fMRI).



* + in *awake subject at rest*, blood flow is greatest in premotor and frontal regions.
	+ in *anticipation of cognitive task*, brain areas that will be activated during task are activated beforehand, as if brain produces internal model of expected task.

Factors that regulate total CBF

N.B. *total* blood flow does not depend on (*regional*) brain function!

1. **Metabolic regulation**
	1. **PaCO2**– most potent regulator!
* ***linear relationship*** with PaCO2 values 20-80 mmHg:

PaCO2↓ 1 mmHg → diameter of cerebral vessels↓ 2-3% → CBF↓ ≈ 1.1 ml/100 g/min.

* used clinically (via controlled hyperventilation) to *treat intracranial hypertension*. [see p. S50 >>](http://WWW.NEUROSURGERYRESIDENT.NET/S.%20Symptoms%2C%20Signs%2C%20Syndromes/S50-64.%20Intracranial%20pressure%2C%20Brain%20edema%2C%20Herniation%2C%20Hydrocephaly/S50.%20GENERAL%20-%20Intracranial%20Hypertension.pdf#Hyperventilation)
	1. cerebral vessels also respond to **PaO2**, **H+** **ions**: PaO2↓ or [H+]↑ → vasodilatation.
1. **Cerebral perfusion** **pressure (CPP)** - pressure gradient across brain:

**CPP** = mean arterial pressure - mean venous pressure = mean arterial pressure - mean ICP\*

\*ICP is transmitted to compliant cerebral veins;

CSF pressure ≈ mean ICP ≥ venous pressure (any change in venous pressure promptly causes similar change in ICP)

* during Valsalva or downward acceleration, increase of arterial pressure at head level is compensated by increase of venous pressure\* at head level and ICP↑\*\*.

\*maintains unchanged CPP

\*\*protects intracranial vessels form rupture

* to calculate actual CPP both MAP and ICP need to be zero-calibrated to the same level; it is common practice to calibrate blood pressure to the right atrium and ICP to the level of the foramen of Monro (ear tragus as external landmark) - this introduces substantial difference, dependent on the size of patient and the degree of head of bed elevation.

**Pressure autoregu****lation** - brain arterioles maintain relatively constant CBF over range of systemic blood pressures;

* CBF remains constant when CPP is 50-160 mmHg (outside this range, CBF varies linearly with MAP):



* MAP > 150 mmHg → autoregulation is lost (vasoparalysis with massive dilatation) → CBF↑, capillary pressure↑ (→ brain edema, hypertensive encephalopathy, intracerebral hemorrhage).
* CPP < 40 mmHg (MAP < 50 mmHg) (due to ICP↑\* or systemic hypotension) → autoregulation is lost → CBF declines → ischemia.

\*repeated ICP↑ per se may damage autoregulation – increasing MAP won’t help restore CPP

* in patients with ***chronic hypertension***, *graph is shifted to right* (illustrates risk of rapid hypertension correction to apparently normal levels!) – possibly by **sympathetic vasoconstrictive discharge on cerebral arteries**; chronic antihypertensive treatment (esp. with vasodilators – ACE inhibitors, hydralazine) readjusts autoregulatory curve:







* most likely **autoregulation mechanism** - intrinsic ***sensitivity of vascular smooth muscle cells*** to tension across vessel wall (but some authors believe that myogenic mechanism serves only in dampening of arterial pulsations).
* it is unlikely that *innervation* (cholinergic-, noradrenergic-, neuropeptide) to vasculature contributes significantly to autoregulation (although certainly contributes to CBF).
1. **Cushing reflex** – systemic hypertension (in response to medullary hypoxia due to ICP↑) – maintains CPP.

Bibliography for ch. “Vascular” → follow this [link >>](http://www.neurosurgeryresident.net/Vas.%20Vascular%5CVas.%20Bibliography.pdf)

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