Cerebrovascular PHYSIOLOGY

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CNS METABOLIC DEMANDS

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

CEREBRAL BLOOD FLOW (CBF)

- Factors that regulate regional CBF
- Factors that regulate total CBF

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.
- sunauja 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) – 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) – patenka į ≈ 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 laktațą (ir grįžta atgal į kraują); likę 5-20% panaudojama įvairių medžiagų (pvz. neurotransmiteriių) sintezei – todėl iš 1 molio gliukozės gaunama 30 mol (o ne 38) ATP.
- glucose uptake from blood mechanism pajuogumas normoje viršija smegenų gliukozės poreikių 2-3 kartus; tačiau glucose uptake mechanismo pajuogumas 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 prada jau po 5 minučių!

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 >>

**FACTOR THAT REGULATES REGIONAL CBF**

- **synaptic activity:**
  - nors smegenys pasiima tik ½ patiekiamo O₂ ir tik 1/10 patiekiamos gliukozės, tačiau tai pačių smegenų uptake mechanizmo galimybų 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 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.

  - 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 brain function!

1. **Metabolic regulation**
   1) **PaCO₂** – most potent regulator!
      - **linear relationship** with PaCO₂ values 20-80 mmHg:
        \[ \text{PaCO}_2 \downarrow 1 \text{ mmHg} \rightarrow \text{diameter of cerebral vessels} \downarrow 2-3\% \rightarrow \text{CBF} \downarrow = 1.1 \text{ ml/100 g/min}. \]
- used clinically (via controlled hyperventilation) to *treat intracranial hypertension*. see S50 p.

2) cerebral vessels also respond to \( \text{PaO}_2, \text{H}^+ \) ions: \( \text{PaO}_2 \downarrow \) or \( [\text{H}^+] \uparrow \rightarrow \text{vasodilatation} \).

2. **Cerebral perfusion pressure (CPP)** - pressure gradient across brain:

\[
\text{CPP} = \text{mean arterial pressure} - \text{mean venous pressure} = \text{mean arterial pressure} - \text{mean ICP}^* \\
\]

*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 AUTOREGULATION** - 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):

![Cerebral blood flow versus cerebral perfusion pressure](image)

**FIGURE 27-2.** Cerebral blood flow versus cerebral perfusion pressure. Note that normal autoregulation that occurs for cerebral perfusion pressure is 50–150 mm Hg.

- 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:
**Figure 32-10.** Autoregulation of cerebral blood flow (CBF) during steady-state conditions. The dotted line shows the alteration produced by sympathetic stimulation during autoregulation.
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).

3. **Cushing reflex** – systemic hypertension (in response to medullary hypoxia due to ICP↑) – maintains CPP.

**BIBLIOGRAPHY** for ch. “Vascular” → follow this [LINK >>](#)