Cerebrovascular PHYSIOLOGY

Last updated: October 6, 2023

- CNS has 400 miles of vasculature associated with BBB (overall exchange surface area ≥ 12 m^2).

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):
O_2 consumption – 46-49 ml/min (3.0-3.8 ml or 156-160 μmol/100 g/min; ≈ 72 L/d);
a-vO_2 difference – 62 ml/L (myocardium – 114 ml/L).

- smegenys išekstrahuoja iš pratekančio kraujo: ≈ 50% **O_2** 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 **O_2 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)

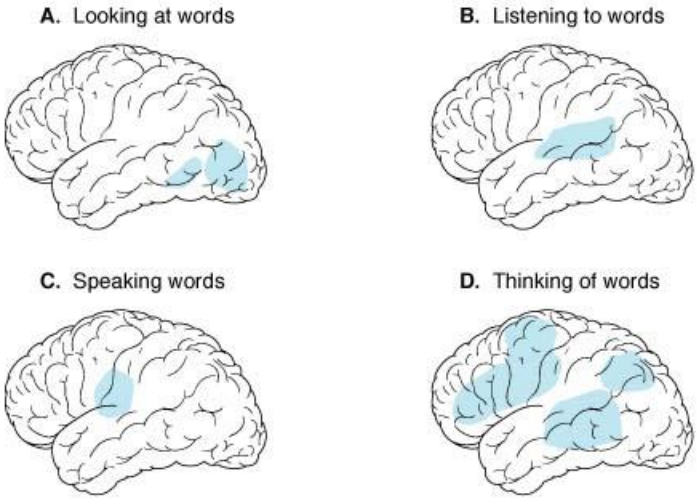
- normal blood volume is 3-4 ml/100 g of brain tissue.
- smegenys praktiškai neturi „degalų" atsargų - turi pastoviai gauti O_2 ir gliukozę (brain relies on sizable and well-regulated blood flow to satisfy its immediate needs for energy).
- nutrūkus kraujotakai, sąmonės netenkama po 8-10 sekundžių, neuronai 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 >>

FACTOR THAT REGULATES REGIONAL CBF

- **synaptic activity**:
  - nors smegenys pasiima tik $^1/_2$ patiekiamo O_2 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 O_2 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) **$PaCO_2$** – most potent regulator!
   - ***linear relationship*** with $PaCO_2$ values 20-80 mmHg:

$PaCO_2$↓ 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 >>

2) cerebral vessels also respond to **PaO_2**, **H^+ ions**: PaO_2↓ or $[H^+]$↑ → vasodilatation.

2. **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 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):

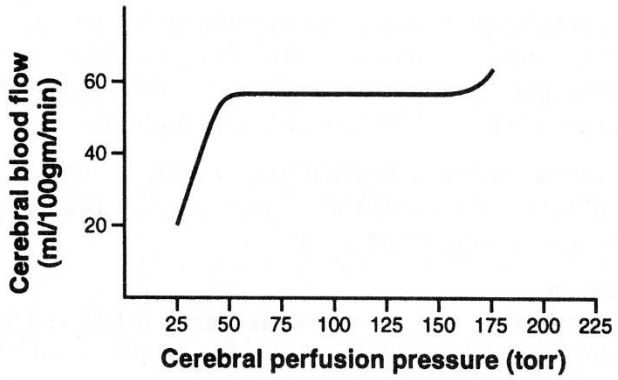


FIGURE 27-2. Cerebral blood flow versus cerebral perfusion pressure. Note that normal autoregulation that occurs for cerebral perfusion pressure is 50–150 mm Hg.

– 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:

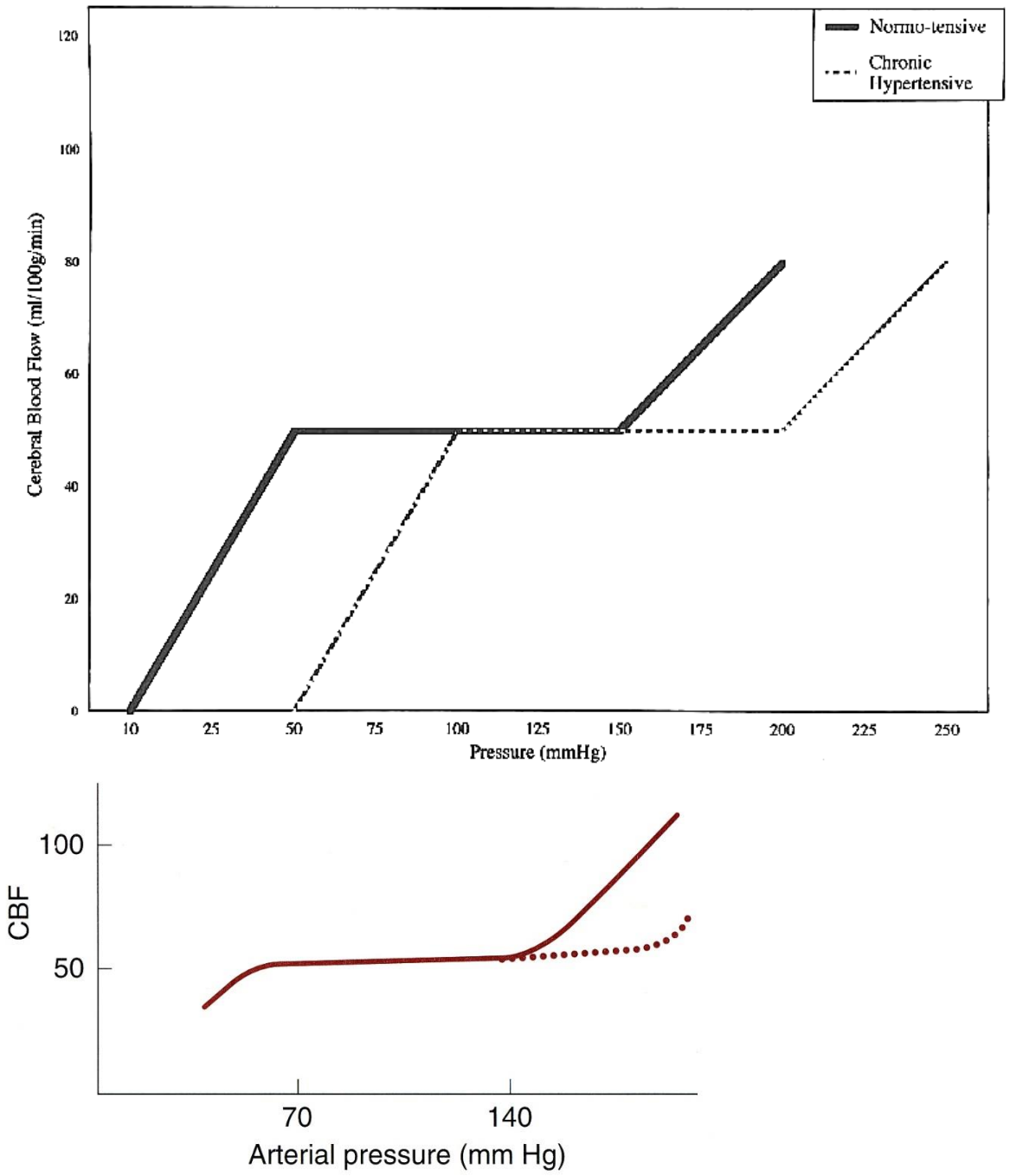
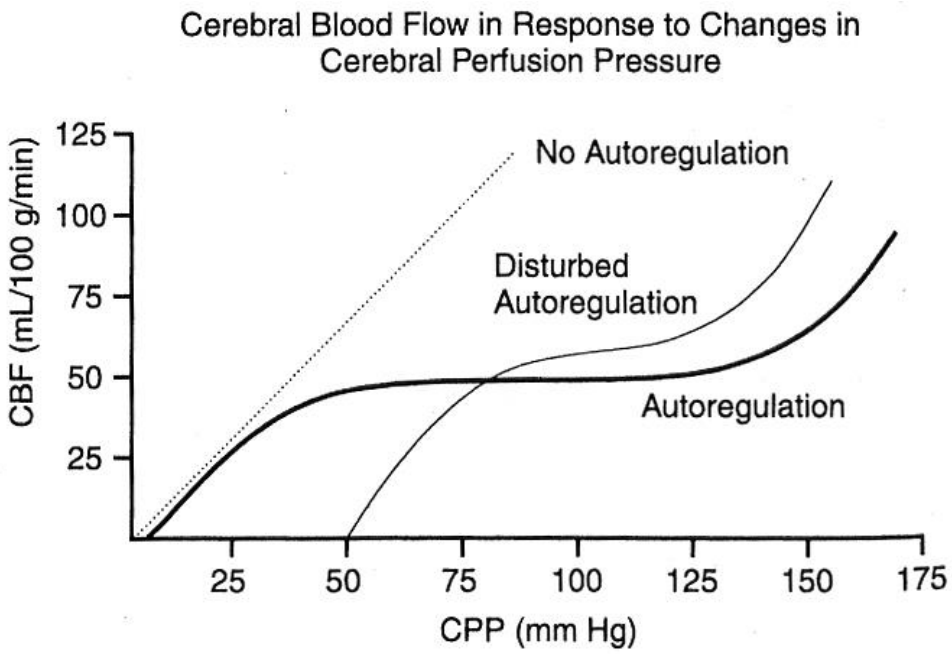


Figure 32–10. Autoregulation of cerebral blood flow (CBF) during steady-state conditions. The dotted line shows the alteration produced by sympathetic stimulation during autoregulation.



- 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 >>