

Cerebrovascular *PHYSIOLOGY*

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- CNS has 400 miles of vasculature associated with BBB (overall exchange surface area $\geq 12 \text{ m}^2$).

CNS METABOLIC DEMANDS

Nors smegenys sudaro tik 2% kūno svorio ($\approx 1400\text{-}1500 \text{ g}$) 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 $\mu\text{mol}/100 \text{ g}/\text{min}$; $\approx 72 \text{ L}/\text{d}$);
 - a-vO₂ difference** – 62 ml/L (myocardium – 114 ml/L).
- smegenys išekstrahuoja iš pratekančio kraujo: $\approx 50\%$ **O₂** ir tik $\approx 10\%$ **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 $\approx 30\%$ while **O₂ consumption** increases only 5% (luxurious oxygen supply) – foundation of fMRI
- brain uses **glucose** as exclusive fuel (badaujant prisitaiko naudoti ir **ketone bodies**) $\approx 5.5 \text{ mg}$ or 30-33 μmol glucose/100 g/min (150 g glucose/d) – patenkina $\approx 90\%$ 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 $\approx 69\text{-}75$, white matter $\approx 25\text{-}30$)

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

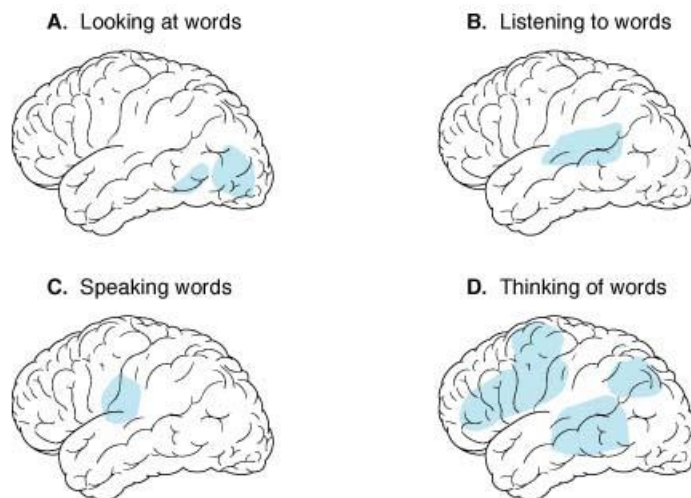
- normal blood volume is 3-4 ml/100 g of brain tissue.
- smegenys praktiškai neturi „degalų“ atsargų - turi pastoviai gauti O₂ ir gliukozę (brain relies on sizable and well-regulated blood flow to satisfy its immediate needs for energy).
- nutrūkus kraujotakai, **šamonės netenkama po 8-10 sekundžių, 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 $\frac{1}{2}$ patiekiamo O₂ ir tik $\frac{1}{10}$ 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.



- 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:

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 S50 p.
- 2) cerebral vessels also respond to **PaO₂, H⁺ ions**: PaO₂↓ or [H⁺]↑ → 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 \approx mean ICP \geq 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 from rupture

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):

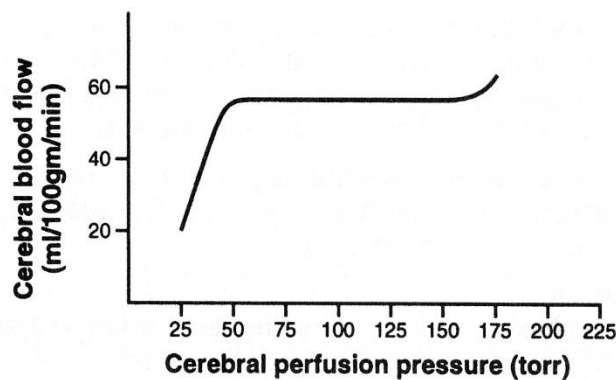


FIGURE 27-2. Cerebral blood flow versus cerebral perfusion pressure. Note that normal autoregulation that occurs for cerebral perfusion pressure is 50–150 mm Hg.

- **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:

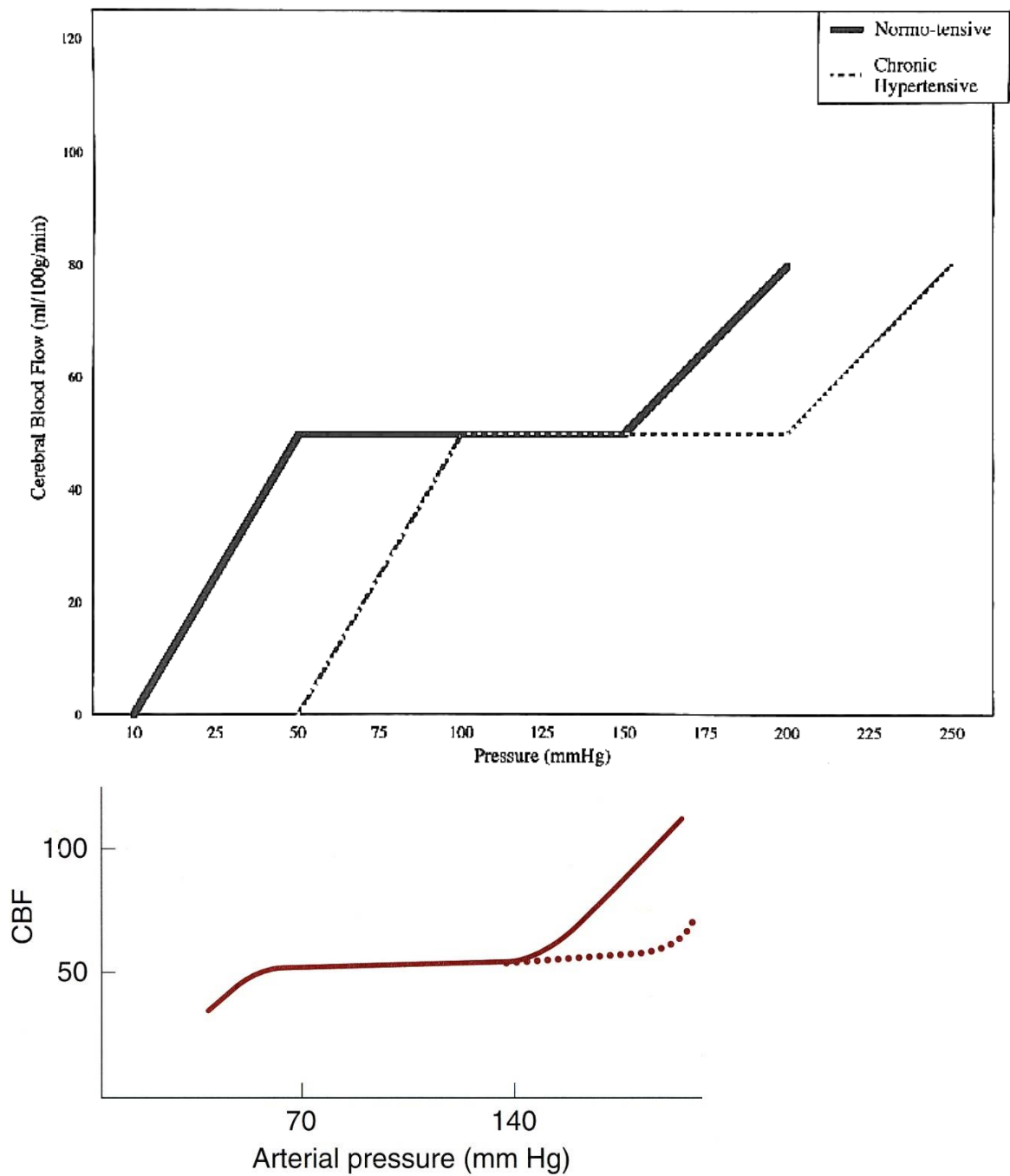
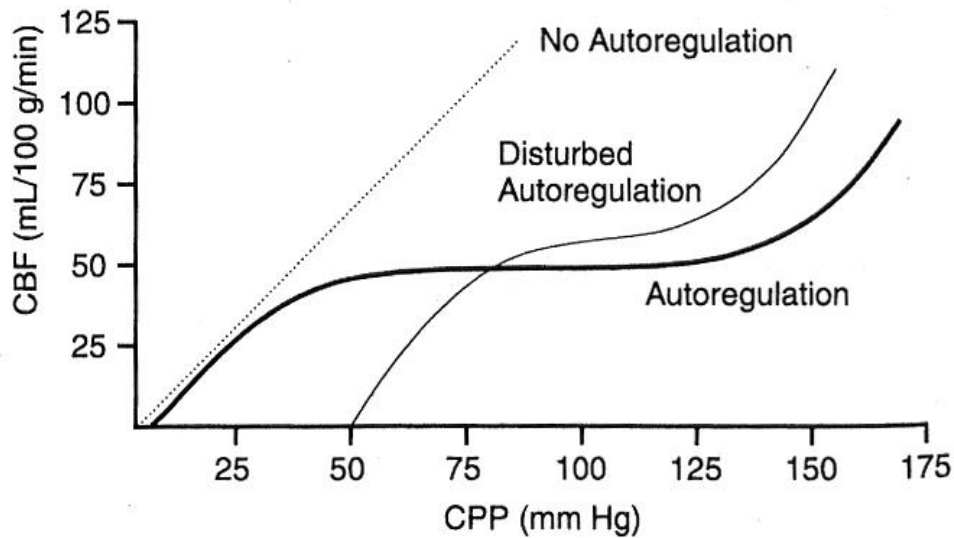


Figure 32-10. Autoregulation of cerebral blood flow (CBF) during steady-state conditions. The dotted line shows the alteration produced by sympathetic stimulation during autoregulation.

Cerebral Blood Flow in Response to Changes in Cerebral Perfusion Pressure



- 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 >>](#)