Regulation of Cerebral Blood Flow

Myogenic- pressure autoregulation
Chemical: PaCO2, PaO2
Metabolic
Flow through rigid tube

Pressure [mm Hg] vs. Flow [ml/min]

Resistance $= 0.98 \text{ mm Hg}/(\text{ml/min})$
Cerebral Blood Flow and Oxygen Consumption in Man

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Fig. 1. Cerebral blood flow and blood pressure. Mean values of 11 groups of subjects reported in 7 studies have been plotted. Various acute and chronic conditions have been selected, characterized by a change in blood pressure. In all, this figure is based on 376 individual determinations.

Experimental data: Falling CPP. Lassen was right!
Cerebral autoregulation following head injury

Lassen’s curve by averaging large number of measurements in TBI (nearly 200 patients, monitored with TCD day-by-day)
Autoregulation of cerebral blood flow

CBF = CPP/R

Thanks to Dr. A Lavinio
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‘Historical’ block diagram illustrating general control loops for CBF

Figure 3-7 Systemic influence of physiologic elements. mABP: mean arterial blood pressure, ICP: intracranial pressure, CPP: cerebral perfusion pressure, CBF: cerebral blood flow, CVR: cerebral vascular resistance, ICP_{csf}: cerebrospinal fluid pressure, ICP_{ven}: cerebro venous blood pressure. ‘→’ excitatory, ‘—’ inhibitory and ‘-----’ variable influence

Figure 3-8 Three different CPP zones related to clinical status

Thanks to Dr.DJ Kim
General scheme of various factors controlling simultaneously CBF.

Endothelial and non-endothelial factors acting upon vascular smooth muscle in arterioles. **Abbreviations:** Cap, capillary; SN, sympathetic nerve; NE, norepinephrine; VSM, vascular smooth muscle; NO, nitric oxide; ET-1, endothelin-1; PGI₂, prostacyclin; EC, endothelial cell; Epi, epinephrine; AII, angiotensin II, ADH, antidiuretic hormone; 5HT, serotonin; + and -, contraction and dilation, respectively.
Responses of cerebral arteries and arterioles to acute hypotension and hypertension

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**FIG. 1.** Comparison of pial arteriolar responses to hypotension induced by either inferior vena cava constriction or by intravenous ATP infusion. Mean ± SE of control diameter is given in square in upper part of figure. Number of animals is shown in parentheses after control diameter. Similar notation is used in subsequent figures.

**FIG. 2.** Comparison of pial arterial responses to hypotension induced by either arterial bleeding or intravenous ATP infusion.

1978 the American Physiological Society
FIG. 4. Steady-state responses of pial arteries and arterioles to induced hypotension. Means ± SE for each group of vessels at mean arterial blood pressures (MABP) from 130 to 40 mmHg are shown.

FIG. 5. Steady-state responses of pial arteries and arterioles to induced hypertension. Means ± SE for each of four groups of vessels are shown at mean arterial blood pressures from 120 to 200 mmHg.
Delay of autoregulation - around 10 seconds. Is it always constant?

**Fig. 8.** Diameter of a pial artery during transient hypotension induced by stimulation of right vagus nerve. Note initial passive reduction in vessel caliber followed by marked dilation.

**Fig. 10.** Pial arteriolar diameter in response to variations in blood pressure induced by changes in rate of infusion of ATP. Note that threshold for dilation of this vessel is about 80 mmHg. Subsequently, vessel diameter follows blood pressure with a lag of about 10 s.
Fig. 2.8. Reactivity of cerebral blood flow (CBF) to (A) changes in arterial oxygen content (\(Ca_{O2}\)) and (B) carbon dioxide tension (\(P_{CO2}\)). Similarly to plot B) the response on CBF to arterial oxygen flattens for unphysiologically high values. Adapted from Jones et al, 1981, and Reivich et al. 1963, respectively.
Distribution of vascular reactivity to CO$_2$

\[ R_{\text{arterial}}(D) = \exp((3.57)-(1.1)\log(D))+(.68) \quad [\%/{\text{mmHgCO}}_2] \]

\[ R_{\text{venous}}(D) = 0.20 R_{\text{arterial}}(D) \quad [\%/{\text{mmHgCO}}_2] \]

Ref: Tuor '84
Ref: Levasseur '89
Ref: Wei '80 (norm)
Ref: Wei '80
Ref: Bouma '91
Ref: Raper '71
Ref: Lee '01
Ref: Auer '80

Arterial Model

Venous Model

Thanks to Dr. S. Piechnik
CO₂ Cerebrovascular Reactivity as a Function of Perfusion Pressure – a Modelling Study

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Fig. 2. A simulated relationship between (A) cerebrovascular resistance (CVR) and cerebral perfusion pressure (CPP), (B) cerebral blood flow (CBF) and CPP for two exemplary levels of PaCO₂, 35 and 50 mmHg, and (C) change in mean CBF recorded during the rise in PaCO₂ from 35 to 50 mmHg plotted as a function of CPP.
Interaction between cerebral autoregulation and cerebrospinal pressure-volume compensation—potential for unstable behaviour
Clinical AUTOREGULATION assessment.

What do we need? TCD, ABP and, possibly, ICP.
**CO2 reactivity** =  % change in FV / % change in CO2

Correction for changes in ABP?
Change in PaCO2 (at normal ICP and normal ABP), 0- hypocapnia, 1-normocapnia 2-hypercapnia. How ‘primary variables’ react to PaCO2?
Can Cerebrovascular Reactivity Be Assessed Without Measuring Blood Pressure in Patients With Carotid Artery Disease?

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\[ \text{CBF} = a \times \text{EtCO2} + b \times \text{ABP} \]
METHODS

Static rate of autoregulation: pharmacological increase in ABP

\[
\text{SRoR} = \frac{\% \text{ Change in CVR}}{\% \text{ change in CPP}}
\]
SRoR = \frac{\Delta \text{CVR}}{\text{CVR}} / \frac{\Delta \text{CPP}}{\text{CPP}}

- SRoR < 1: Insufficient AR
- SRoR = 1: Ideal AR
- SRoR > 1: 'Hyper' AR

- 'Critical closing'
- Maximal vasodilatation
- Maximal vasoconstriction

- CBF and CVR - 'geometrical' interpretation
‘INVERSE LASSEN CURVE’?

\[ RoR = \frac{dCVR}{dt} \cdot \frac{1}{CVR_{baseline}} \cdot \frac{ABP_{baseline}}{\Delta ABP} , \]

Tiecks FP, Lam AM, Aaslid R, Newell DW
Frank P. Tiecks, MD; Arthur M. Lam, MD, FRCPC; Rune Aaslid, PhD; David W. Newell, MD
Comparison of Static and Dynamic Cerebral Autoregulation Measurements (Stroke. 1995;26:1014-1019.)
The effect of the cerebral autoregulation on mean velocity (mV) was approximated by a second-order linear differential equation set with state variables x1 and x2, which were assumed to be equal to 0 during the control period. After the step in ABP, these equations were solved by the computer in steps of 100 milliseconds (sampling rate, f=10 Hz) by the algorithm where dP is the normalized change in mean arterial blood pressure (MABP) from its control value (cABP), including the effect of the critical closing pressure (CCP), which was assumed to be constant at 12 mm Hg in the present study. (This parameter can later be estimated individually.) MABP was obtained by filtering the pulsatile ABP at 0.5 Hz. cVmca is control velocity in the MCA. The control values were obtained as explained in "Methods." This mathematical model was characterized by three parameters: T, the time constant; D, the damping factor; and K, the autoregulatory dynamic gain.
The same ARI may be derived from slow waves of ABP and TCD

Transient hyperaemic response test

Cerebral autoregulation and gas exchange studied using a human cardiopulmonary model

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Fig. 7. Model-predicted cerebral hemodynamic response to 10-s carotid artery compression in the presence (A) and absence (B) of CBF autoregulation. Top to bottom: CBF, ICP, Rv, PaO2, and PaCO2. Dashed lines indicate the start and end of compression.
Consequence of disturbed autoregulation: ischaemic insult during plateau wave of ICP
Consequence of arterial hypotension
Arterial hypotension with baseline autoregulation probably deteriorated
Hypertension Can Drive Elevated Intracranial Pressure

- Passive Collapse
- Vasodilatory Cascade Zone
- Zone of Normal Autoregulation
- Autoregulation Breakthrough Zone

Cerebral Blood Flow (ml/100 g/min)

Cerebral Perfusion Pressure (mm Hg)

ICP (mm Hg)

GOAL

Stephan A. Mayer, MD
Carotid artery stenotic disease: left side impairment of reactivity, 85% of stenosis. Right side clear.
Association between dynamic cerebral autoregulation and mortality in severe head injury

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Table II. Distribution of ARI according to three grouped categories of GCS

<table>
<thead>
<tr>
<th>GCS</th>
<th>Survivors ( \text{mean} \pm \text{SD} \ (n) )</th>
<th>Non-survivors* ( \text{mean} \pm \text{SD} \ (n) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>3−4</td>
<td>5.89 ( \pm ) 2.76 (7)</td>
<td>3.51 ( \pm ) 2.73 (7)</td>
</tr>
<tr>
<td>5−6</td>
<td>6.62 ( \pm ) 1.97 (7)</td>
<td>2.31 ( \pm ) 3.28 (2)</td>
</tr>
<tr>
<td>7−8</td>
<td>6.34 ( \pm ) 0.65 (3)</td>
<td>3.92 ( \pm ) 3.40 (3)</td>
</tr>
</tbody>
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*p = 0.028 for combined p-values (see text).

Fig. 1. (Top) Representative recordings of CBFV, ABP and ICP from two different patients. (Bottom) Corresponding CBFV responses to a step change in ABP (continuous line) and Aulin’s model response fitted to the first 2 s of the step response (dashed line).
POINTS TO TAKE HOME:

- Several mechanisms of CBF regulation work simultaneously
- Pressure-autoregulation is a potent brain self-protecting mechanism
- Autoregulation fails if CPP is too low or too high
- Autoregulation fails if arterial CO2 is too high
- Autoregulation may be tested in clinical conditions

Consequences of disturbed autoregulation:
- Brain is exposed to ischemic insults when CPP decreases, this may reduce chance for good outcome after TBI
- With high CPP hyperaemia may aggravate brain oedema causing secondary rise of ICP