



UNIVERSITY HOSPITALS  
LEUVEN



## *Urgent CPPopt Questions that need to be solved*



B Depreitere, MD, PhD  
Neurosurgeon, Leuven, Belgium

CPPopt meeting, Boston, June 28 2016

Disclosure

Johnson & Johnson research chair

It's the physiology, stupid!

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# PHYSIOLOGICAL REVIEWS

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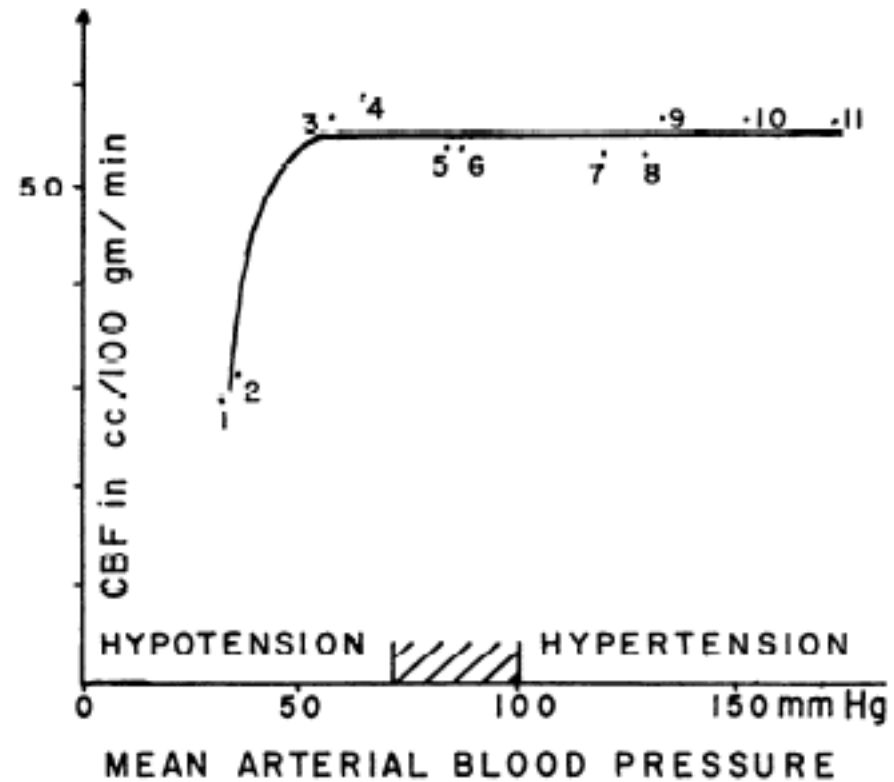
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## Cerebral Blood Flow and Oxygen Consumption in Man

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of Health, Bethesda, Maryland*



## Cerebrovascular autoregulation

- Intrinsic vasomotor mechanisms
  - pressure
  - flow
- Neurogenic mechanisms
  - peripheral autonomic vasomotor regulation
    - orthosympathic: ggl.cervicale sup.
    - parasympathic: ggl.sphenopalatinum
      - attenuation of CPP peaks, ULA
    - Sensory: trigeminovascular system
      - ↑ CBF in response to harmful stimuli
  - central:
    - intrinsic central neural pathways (nc.Meynert, locus coeruleus, nuclei raphe)
    - neurovascular coupling
- Metabolic regulation
  - CO<sub>2</sub>: vasodilation
  - O<sub>2</sub>: vasoconstriction

one model fits all

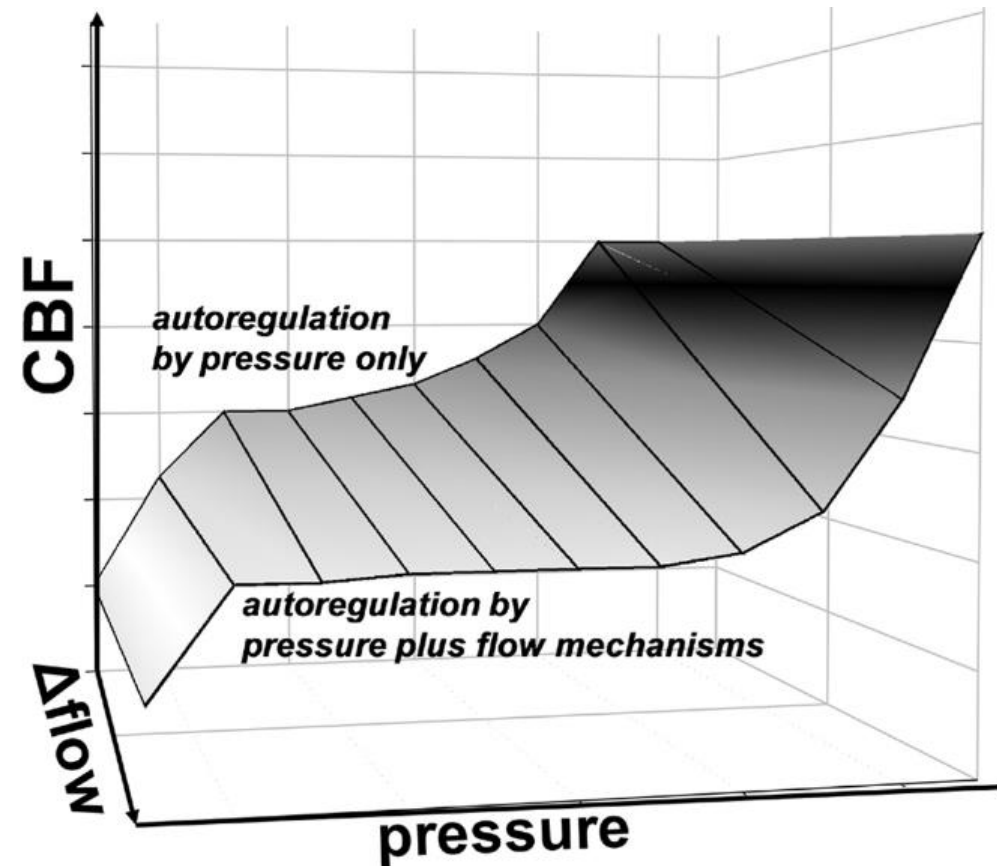
VS

overlap of several dynamic models

*“Combined effect of changes of intraluminal pressure and intraluminal flow ( $\Delta$  flow) achieves a more effective autoregulation of cerebral blood flow (CBF), whereas only pressure-induced diameter responses still allow substantial increases in CBF, thus inefficient autoregulation. It is likely that in vivo the “plateau” of autoregulation is not perfectly flat, i.e. the gain is less than 1, thus there is a slight increase in CBF as systemic pressure increases. Nevertheless, it is effective enough to prevent an exponential increase of CBF. Also, the range and shape of autoregulatory curve is likely to be more “rounded” at low and high pressure values.”*

*“Entire cerebrovascular tree is involved, including larger arteries.”*

*“Changes in PaCO<sub>2</sub> ranging from 15 – 65 mmHg lead to a change in diameter of the internal carotid artery of approximately 20%, however a significantly lower reactivity of the vertebrobasilar circulation was demonstrated.”*



*J Vasc Res. 2012 ; 49(5): 375–389.*

**CONTRIBUTION OF FLOW-DEPENDENT VASOMOTOR MECHANISM TO THE AUTOREGULATION OF CEREBRAL BLOOD FLOW**

Akos Koller<sup>1,2</sup> and Peter Toth<sup>1,2</sup>

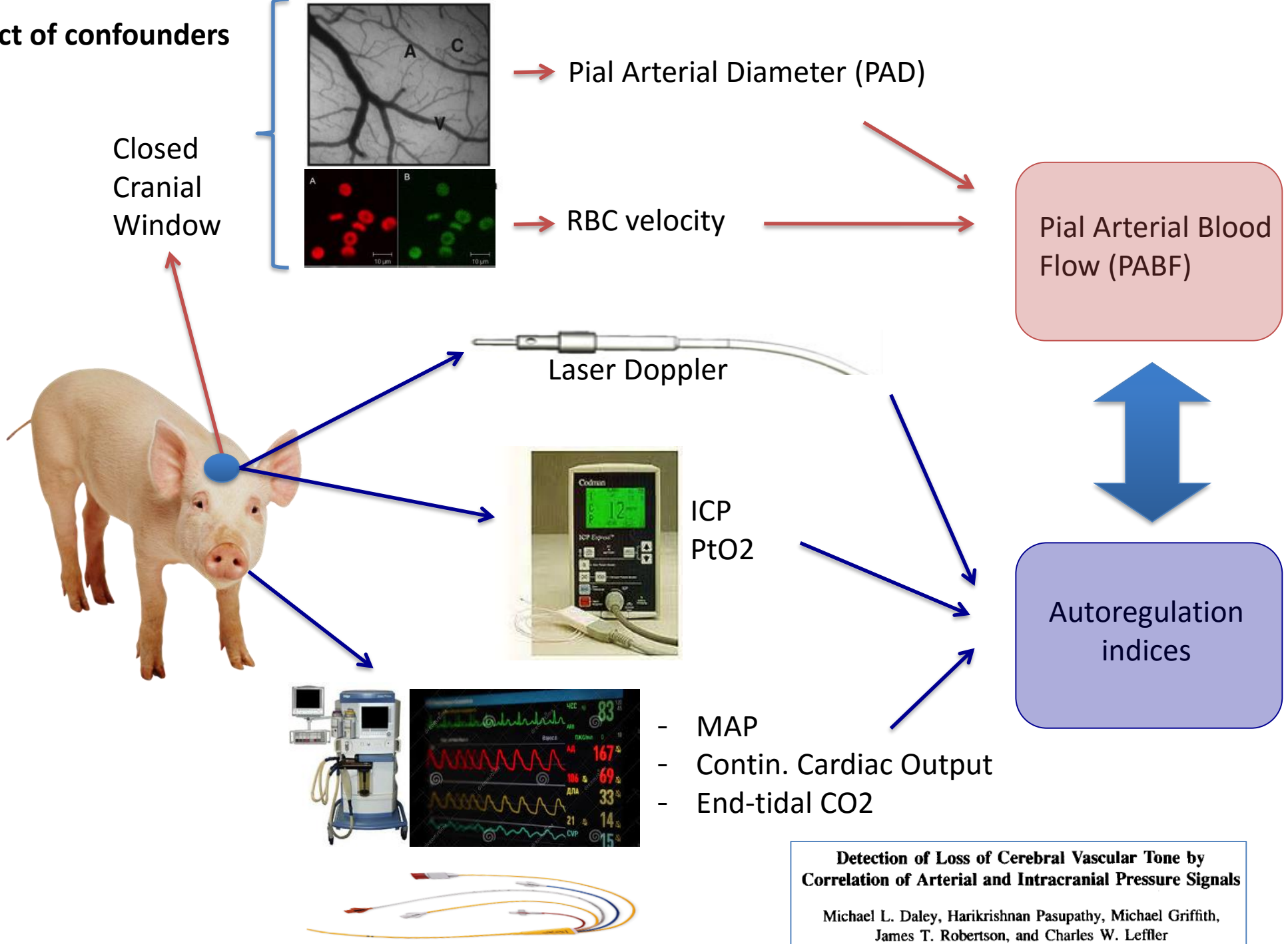
<sup>1</sup>Department of Pathophysiology and Gerontology, Medical School, University of Pecs, Pecs, Hungary

<sup>2</sup>Department of Physiology, New York Medical College, Valhalla, New York, USA

+ lots of *potential* confounding factors

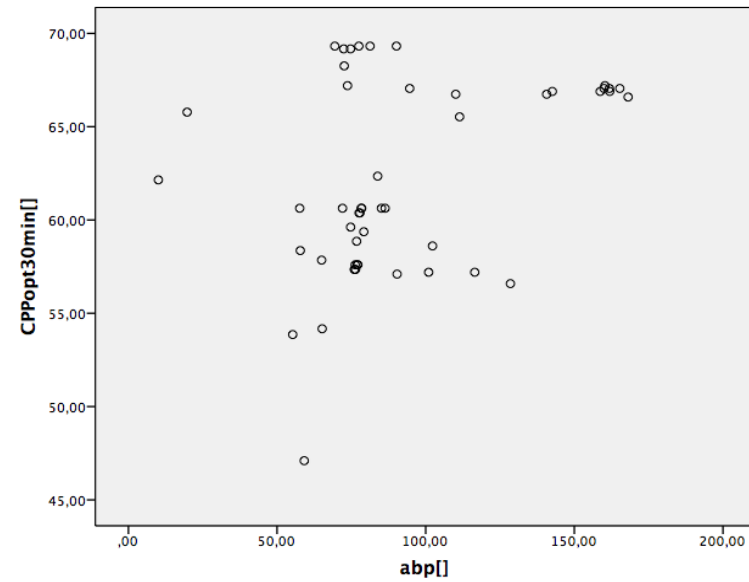
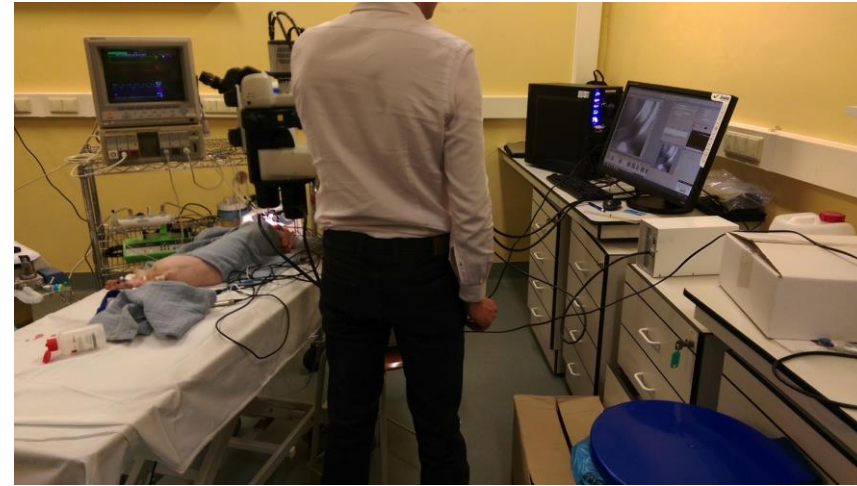
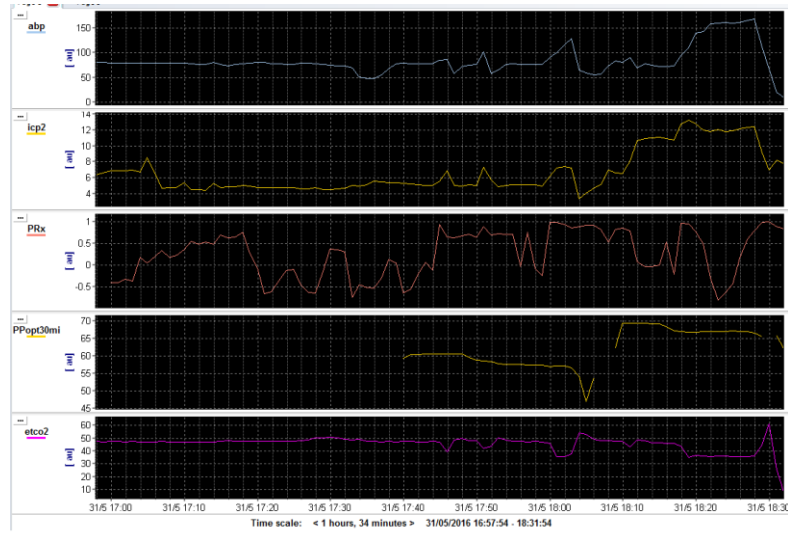
- Age
- Gender
- Genetic constitution
- Drugs: statines (eNOS upregulation), ACE-I (bradykinine), ...
- Sedatives: desflurane>sevoflurane, propofol, ...
- Ventilator settings
- Type and location of brain injury
- Epilepsy
- Blood viscosity
- Cardiovascular comorbidity
- Renal and liver failure
- Intracranial pressure: ↑ ICP
- ....

**Goal: test effect of confounders**





# Preliminary pig model data:



Spearman  $r = 0.081$



# Conclusions

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Still many questions open

Need for conjoined animal and clinical research