Integrative Human Cardiovascular Control

The Panum Institute/ Rigshospitalet, University of Copenhagen 2017

Cerebral blood flow and oxygenation, static and dynamic autoregulation, and relation to orthostatic stress
The following trick is sometimes played in a mess or at a party: a victim is persuaded to hyperventilate for about a minute and then his chest is suddenly compressed by someone standing behind him. He usually loses consciousness in a few seconds.
Fig. 1  Finger arterial pressure at heart level; ETCO₂: end-tidal carbon dioxide concentration. Recording obtained by JJ van L with volunteer WW.
Fig. 1  Finger arterial pressure at heart level; $ETCO_2$: end-tidal carbon dioxide concentration. Recording obtained by JJ van L with volunteer WW.
Fig. 1  Finger arterial pressure at heart level; ETCO$_2$: end-tidal carbon dioxide concentration. Recording obtained by JJ van L with volunteer WW.
E. P. Sharpey-Schafer, F.R.C.P.
Professor of Medicine, London University

The schoolboys have combined three different methods of affecting the blood supply to the brain and devised a procedure for making any normal man unconscious in 60 seconds without outside interference. They are to be congratulated on their ingenuity.
PULMONARY OEDEMA WITH NEUROLOGICAL SYMPTOMS AFTER THE FAINTING LARK AND MESS TRICK

BY

Air Vice-Marshall Sir AUBREY RUMBALL, K.B.E., Q.H.P., F.R.C.P.
Consultant in Medicine, the Central Medical Establishment, Royal Air Force
The ‘fainting lark’

Combining the effects of

a) acute arterial hypotension by gravity and

b) raised intrathoracic pressure with

c) cerebral vasoconstriction in response to hypocapnia
Outline of Presentation - Measurement and Regulation of Cerebral Blood Flow

• Techniques and Methodological Issues
• What determines Brain Blood Flow?
• Static and Dynamic Cerebral Autoregulation
Cerebral Blood Flow (CBF) and Imaging Techniques

- Global CBF (arterial-venous diff N$_2$O, $^{133}$Xe, O$_2$)
- Magnetic Resonance Imaging (MRI)
- MRA (Magnetic Resonance Angiography & Venography)
- Regional CBF (Ultrasound - Transcranial Doppler)
- Single-Photon Emission Computed Tomography (SPECT)
- Positron Emission Tomography (PET)
- SPECT/CT and PET/CT, Near-Infrared Spectroscopy
THE BLOOD FLOW IN THE BRAIN AND THE LEG OF MAN, 
AND THE CHANGES INDUCED BY ALTERATION OF 
BLOOD GASES ¹ 

By WILLIAM G. LENNOX AND ERNA LEONHARDT GIBBS 
(From the Department of Neuropathology, Harvard Medical School, and the Thorndike 
Laboratory of the Boston City Hospital, Boston) 

(Received for publication July 5, 1932) 

It is therefore believed that observed changes in arteriovenous difference were due to alterations in the speed of blood flow.
Measurement of Global Cerebral Circulation - Inert Gas Nitrous Oxide

Fig. 1. Typical Arterial (A) and Internal Jugular (V) Curves of N₂O Concentration during a Ten-Minute Period of Inhalation of 15 Per Cent N₂O

Kety and Schmidt, J Clin Invest 1948
• Systemic circulation: \( \text{VO}_2 = \text{CO} \times (C_a - C_v) \)
• Cerebral circulation: \( \text{CMRO}_2 = \text{CBF} \times (C_a - C_{v\text{jug}}) \)
Ohm’s Law

\[ \text{voltage (V)} = \text{amperage (I)} \times \text{resistance (R)} \]

\[
\text{CPP} = \text{CBF} \times \text{CVR}
\]

Cerebral Perfusion Pressure \hspace{1cm} Cerebral Blood Flow \hspace{1cm} Cerebral Vascular Resistance

Applied to TransCranial Doppler Ultrasonography

\[
\text{MAP} = \text{CBFV} \times \text{CVR}
\]

Mean Arterial Pressure \hspace{1cm} Cerebral Blood Flow Velocity \hspace{1cm} Cerebral Vascular Resistance

at brain level
Transcranial Doppler Cerebral Blood Flow Velocity
TCD middle cerebral artery blood velocity

**pro:** Beat-to-beat evaluation of (regional) CBF

**con:** larger changes in arterial distending pressure may affect MCA diameter with under/overestimation of CBF heterogeneity in cerebral vascular responsiveness
Limitations

- arterial pressure may not fully reflect CPP (the pressure driving CBF in the large cerebral arteries)
- transcranial Doppler cerebral artery velocity is taken as 'a surrogate' for CBF
- cerebral blood flow/velocity is the outcome measure, and a relationship to vascular control is only inferred
Reviewer’s comment:

Constant diameter under the conditions of the study?
Fig. 1. Representative example of high-resolution MRI scans planned perpendicular to the middle cerebral artery (MCA). From left to right: the white square depicts the location of the zoomed images, and zoomed image at hypocapnia (-1 kPa), baseline normocapnia (0 kPa), and hypercapnia (+1 and +2 kPa end-tidal CO₂), respectively.
Sympathetic activation by handgrip exercise reduces MCA cross-sectional area
Brain vascular control during exercise

- Effects of exercise on cerebral metabolism are highly heterogeneous
- Increases in CBF are not global but localized to specific areas of the brain

Limitations to be considered

• arterial pressure may not fully reflect the pressure driving CBF in the large cerebral arteries

• transcranial Doppler cerebral artery velocity is taken as 'a surrogate' for CBF

• cerebral blood flow/velocity is the outcome measure, and a relationship to vascular control is only inferred
Outline of Presentation – Measurement and Regulation of Cerebral Blood Flow

- Techniques and Methodological Issues
- What determines Brain Blood Flow?
• Which influences for brain blood flow?

- brain activation (visual stimulation, exercise)
- metabolic (from rest to exercise)
- chemical - $\text{PaCO}_2$, $\text{O}_2$
- autoregulation
- neurogenic - sympathetic system influence
- endothelial cell ↔ smooth muscle cell
- ATP, adenosine, brain-derived neurotrophic factor (BDNF)
- cardiac output
- ageing
Control of Cerebral Circulation in Health and Disease

FIGURE 1

Schematic representation of the control of cerebral blood flow (CBF). ECF = extracerebral fluid.
- **CHEMICAL (PaCO₂, PaO₂)**

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>0</th>
<th>30</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP (mm Hg)</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MCAV (cm·s⁻¹)</td>
<td>150</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>PETCO₂ (mm Hg)</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

**HYPERVENTILATION**

Graph showing changes in BP, MCAV, and PETCO₂ over time.
Cerebral Responsiveness to Carbon Dioxide (CO₂ reactivity of the brain)
• Activation

Ingvar DH. Functional landscapes of the dominant hemisphere. Brain Res 1976
Activation of the brain by exercise enhances CBF
Changes in MCA $V_{\text{mean}}$ during exercise are similar to those recorded with the initial slope index of the $^{133}\text{Xe}$ clearance method

During heavy dynamic exercise, MCA $V_{\text{mean}}$ increases 24 (10-47)\%
Effects of exercise intensity and duration on indices of cerebral blood flow and oxygenation during exercise.
Reductions in Q accomplished by lower body negative pressure (LBNP), increases in Q by infusions of 25% human serum albumin
• With one-legged exercise CBFV is maintained but declines with two-legged exercise
• AGEING

~15% reduction in gray matter flow between the 3rd and 5th decade


Meyer JS, Terayama Y, Takashima S. Cerebral circulation in the elderly. Cerebrovasc Brain Metab Rev 1993
CO and CBF

In heart failure:

*CBF substantially, but reversibly, reduced*

*redistribution of cardiac output inadequately secures brain perfusion*

**Figure 1.** a. CBF in patients with CHF (right; n=12) and an age-matched control group (left; n=12). *P<0.05 compared with control. b. CBF in 5 patients with CHF before (left) and 1 month after (right) heart transplantation (n=5). *P<0.05 compared with pretransplantation.
• BODY POSITION

Pott F, et al. JAP 2000
Assumption of the upright position carries the head above heart level

⇒ BP at brain level ~ 20 mmHg ↓
⇒ Cardiac output 20-30% ↓
⇒ PCO₂ ↓
⇒ Cerebral Blood Velocity 15% ↓

Brain consumes ~20% of cardiac output
Middle cerebral artery blood velocity declines when standing

**Effects of Body Position on the (a-ET)PCO₂ gradient**

Fig. 4. PaCO₂ vs. PETCO₂ from supine to upright. Postural decrease is shown in PaCO₂ (○) vs. PETCO₂ (solid line) in 6 subjects (means ± SE) in the early steady state of the head-up position. In the first 2 min following head-up tilt, PaCO₂ did not change, whereas PETCO₂ decreased to 37 ± 1 Torr after 2 min. Vertical dotted line indicates the onset of tilt.
Fig. 3. PETCO₂ clamping. Representative example is shown of PETCO₂ response in one subject to hyperventilation (solid bar) during spontaneous breathing (A) and with isocapnic clamp (B).
Contribution of CO\(_2\) on the postural restraint in cerebral perfusion

- spontaneous breathing
- isocapnic tilt
**Contribution of CO$_2$ on the postural restraint in cerebral perfusion is TRANSIENT**

- **PET, CO$_2$ (mmHg)**
- **MCA $V_{\text{mean}}$ (cm$^2$s$^{-1}$)**
- **MAP (mmHg)**

- **Spontaneous breathing**
- **Isocapnic tilt**
Outline of Presentation - Measurement and Regulation of Cerebral Blood Flow

• Techniques and Methodological Issues
• What determines Brain Blood Flow?
• Static and Dynamic Cerebral Autoregulation
Dynamic Cerebral Autoregulation

Graph showing the relationship between time (s) and changes in blood pressure and MCAV (%). The graph includes error bars indicating variability.
Effect of Dynamic Exercise on Blood Pressure

What will brain blood flow do?
... and on Cerebral Blood Velocity

autoregulation malfunction?
Static CA
reflects the overall efficiency of the system

Dynamic CA
ability to restore cerebral blood flow within seconds in response to BP changes
reflects latency of regulatory system
In biological systems reflex gain is not infinite

Courtesy of Eubank and Raven
• Inducing a fall in mean arterial pressure (cuff release; Aaslid manoeuvre)

• Rest and steady-state orthostatic stress
  *Spontaneous* and *induced* oscillations
Cerebrovascular autoregulation

Cerebrovascular adaptation following release of muscle ischemia

![Graph showing cerebrovascular adaptation](image)

The graph illustrates the changes in MCAV and MAP over time following the release of muscle ischemia. The slopes and ROR values are indicated as follows:

- Slope: 0.047
- ROR: 0.199

Key points:
- Minimum MCAV
- Minimum MAP

Reference:
ABP to CBFV transfer described in terms of phase and gain.
Dynamic Cerebral Autoregulation - Phase Difference
Dynamic Cerebral Autoregulation - Gain

![Graph showing CBFV and BP over time](image-url)
Normal Dynamic Cerebral Autoregulation

- MCA $V_{\text{mean}}$ = MAP brain

### Frequency Analysis

- **0.067 Hz**
  - Phase: 50°
  - Gain: 0.33

- **0.100 Hz**
  - Phase: 119°
  - Gain: 0.53

- **0.167 Hz**
  - Phase: 77°
  - Gain: 0.33
Between-centre variability in transfer function analysis, a widely used method for linear quantification of the dynamic pressure–flow relation: The CARNet study

Aisha S.S. Meel-van den Abeelen a, David M. Simpson b, Lotte J.Y. Wang a, Cornelis H. Slump c, Rong Zhang d, Takashi Tarumi d, Caroline A. Rickards e, Stephen Payne f, Georgios D. Mitsis g, Kyriaki Kostoglou g, Vasilis Marmarelis h, Dae Shin i, Yu-Chieh Tzeng j, Philip N. Ainslie k, Erik Gommer l, Martin Müller m, Alexander C. Dorado n, Peter Smielewski o, Bernardo Yelicich p, Corina Puppo p, Xiuyun Liu o, Marek Czosnyka o, Cheng-Yen Wang q, Vera Novak r, Ronney B. Panerai s, Jurgen A.H.R. Claassen a,*

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n KU Leuven, Department of Electrical Engineering-ESAT, SCD-SISTA and iMinds Future Health Department, Leuven, Belgium
o Academic Neurosurgical Unit, Cambridge University Hospital Trust, UK
p Emergency Department, Clinics Hospital, Universidad de la Republica, School of Medicine, Montevideo, Uruguay
q Research Center for Adaptive Data Analysis, National Central University, Taiwan
r Division of Gerontology, Beth Israel Deaconess Medical Center, Boston, MA, United States
s Leicester NIHR Biomedical Research Unit in Cardiovascular Sciences, Glenfield Hospital, Leicester, UK

Medical Engineering & Physics 36 (2014) 620–627
• NEUROGENIC - SYMPATHETIC INFLUENCE
Sympathetic effects on CBF during exercise

- role of sympathetic activation for CBF controversial
- dense sympathetic innervation middle size brain arteries
- sympathetic innervation of larger cerebral arteries
- NE “spillover” from brain vasculature in healthy humans but not in patients with autonomic failure
- sympathetic activation reduces MCA cross-sectional area
Control of Cerebral Circulation in Health and Disease

**FIGURE 1**

_Schematic representation of the control of cerebral blood flow (CBF). ECF = extracerebral fluid._
Coupling of synaptic activity with substrate utilization (neurovascular coupling)

Pellerin L and Magistretti PJ. J Cereb Blood Flow Metab. 2003
Quistorff B, Secher NH, Van Lieshout JJ. FASEB J 2008
Summing up …

- Postural decline in cerebral perfusion/oxygenation not explained by CO₂ - no infinite gain in CA capacity
- Influence of cardiac output on cerebral perfusion independent from arterial pressure
- CBF measurement techniques have limitations
- Heterogeneity in cerebral vascular responsiveness and probably in dynamic autoregulatory capacity
Dynamic Cerebral Autoregulation

- Time (s) from 0 to 10
- Blood Pressure (%)
- MCAV (%)

Graph showing changes in Blood Pressure and MCAV over time.
Cerebral Autoregulation in Acute Ischemic Stroke (MCA Territory)

Immink RV, Van Montfrans GA, Stam J, Karemaker JM, Diamant M, Van Lieshout JJ. Stroke 36: 2595-2600, 2005
Dynamic Cerebral Autoregulation in “Uncomplicated” Type 2 Diabetes Mellitus

Static Cerebral Autoregulation in Type 2 Diabetes during intensive blood pressure control

Benefit for patients?
Static and Dynamic CA
Outline of Presentation – Measurement and Regulation of Cerebral Blood Flow

• Techniques and Methodological Issues
Cerebral blood flow velocity underestimates cerebral blood flow during modest hypercapnia and hypocapnia

Nicole S. Coverdale,1 Joseph S. Gati,2 Oksana Opalevych,2 Amanda Perrotta,1 and J. Kevin Shoemaker1,3

Assessment of middle cerebral artery diameter during hypocapnia and hypercapnia in humans using ultra-high-field MRI

Jasper Verbree,1,2 Anne-Sophie G. T. Bronzwaer,3,6 Eidrees Ghariq,1,2 Maarten J. Versluis,1,2 Mat J. A. P. Daemen,4 Mark A. van Buchem,1 Albert Dahan,5 Johannes J. van Liers et al.7 and Matthias J. P. van Osch1,2
Competition brain vs. working muscles
The brain activates the muscles, but the muscles represent a potent competitor for continuous provision of oxygen and substrate upon which the brain relies.
Brain vs. Skeletal Muscle

- The brain is active under all living conditions
- Postural change affects brain blood flow
- Brain vascular bed is small, strongly regulated by cerebral autoregulation and the partial pressure of arterial carbon dioxide (PaCO2)
- Brain ~ 2% of total body mass but ~20% whole-body oxygen consumption at rest
- Brain function deteriorates if oxygenation $\downarrow > 10\%$
Cerebral Tissue Oxygenation - Near Infra-Red Spectroscopy (NIRS)
• Near-InfraRed Spectroscopy cerebral oxygenation

**pro:** NIRS follows changes in cerebral oxygenation in parallel with CBF as determined by $^{133}$Xe

NIRS tracks brain capillary oxygen saturation (halfway arterial and jugular venous $O_2$) for $SvO_2$ 40 – 80 % and CBFV 29 – 65 cm/s

**con:** hemoglobin is contained in arterioles, capillaries, and venules, but the relative position of pigments determined by NIRS is unknown

Cerebral Circulation – Transcranial Doppler Blood Flow Velocity & NI RS Cortical oxygenation
Impaired cerebral autoregulation in patients with malignant hypertension
RV Immink, BJH van den Born, GA van Montfrans... - Circulation, 2004 - Am Heart Assoc
Background—In patients with a malignant hypertension, immediate parenteral treatment with blood pressure–lowering agents such as intravenous sodium nitroprusside (SNP) is indicated. In this study, we evaluated static and dynamic cerebral autoregulation (CA) during
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Reduced cerebral blood flow velocity and impaired cerebral autoregulation in patients with Fabry disease
MJ Hilz, EH Kolodny, M Brys, B Stemper, T Haendl... - Journal of ..., 2004 - Springer
In Fabry disease, there is glycosphingolipid storage in vascular endothelial and smooth muscle cells and neurons of the autonomic nervous system. Vascular or autonomic dysfunction is likely to compromise cerebral blood flow velocities and cerebral
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Monitoring of cerebral autoregulation in head-injured patients
M Czosnyka, P Smielewski, P Kirkpatrick, DK Menon... - Stroke, 1996 - Am Heart Assoc
Background and Purpose Disturbed cerebral autoregulation has been reported to correlate with an unfavorable outcome after head injury. Using transcranial Doppler ultrasonography, we investigated whether hemodynamic responses to spontaneous variations of cerebral
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Cerebral autoregulation in patients with obstructive sleep apnea syndrome during wakefulness
N Nasr, A Traon, M Czosnyka, M Tiberge... - European journal of ..., 2009 - Wiley Online Library
Background and purpose: Obstructive sleep apnea syndrome (OSAS) is an independent risk factor for stroke. Impairment of cerebral autoregulation may play a potential role in the pre-disposition to stroke of OSAS patients. In this study, we aimed to assess dynamic cerebral
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Cerebral autoregulation among patients with symptoms of hydrocephalus
ZH Czosnyka, M Czosnyka, PC Whitfield... - ..., 2002 - journals.lww.com
OBJECTIVE: To study the relationship between the resistance to cerebrospinal fluid (CSF) outflow and cerebral autoregulation. METHODS: We examined 35 patients who presented with ventricular dilation and clinical symptoms of communicating hydrocephalus. For all of
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Impaired cerebral autoregulation in patients with malignant hypertension
RV Immink, BJ van den Bom, GA van Montfrans... - Circulation, 2004 - Am Heart Assoc

Reduced cerebral blood flow velocity and impaired cerebral autoregulation in patients with Fabry disease
MJ Hilt, EH Kolodny, M Brys, B Stemper, T Haendel... - Journal of... - 2004 - Springer

Monitoring of cerebral autoregulation in head-injured patients
M Czosnyka, P Snielewski, P Kirkpatrick, DK Menon... - Stroke, 1996 - Am Heart Assoc

Cerebral autoregulation in patients with obstructive sleep apnea syndrome during wakefulness
N Nasa, A Tison, M Czosnyka, M Tilberg... - European journal of... - 2009 - Wiley Online Library

Cerebral autoregulation among patients with symptoms of hydrocephalus
ZJ Czosnyka, M Czosnyka, PW Whitting... - 2002 - journals.lww.com

Comparison of static and dynamic cerebral autoregulation measurements
FP Tiecks, AM Lam, R Aaslid, DW Newell - Stroke, 1995 - Am Heart Assoc

Functional loss of cerebral blood flow autoregulation in patients with fulminating hepatic failure
FS Larsen, E Eftersk, BA Hansen, GM Krudsen... - Journal of... - 1995 - Elsevier

Identification and clinical impact of impaired cerebrovascular autoregulation in patients with malignant middle cerebral artery infarction
C Dohmen, B Bosche, R Graf, T Reithmeier... - Stroke, 2007 - Am Heart Assoc

Hyperventilation restores cerebral blood flow autoregulation in patients with acute liver failure

Tip: alleen in het Nederlands zoeken. U kunt uw zoektocht bepalen in instellingen voor Scholair.
Saturation recording of the brain during cardiopulmonary bypass. (CPB)


NEUROSCIENCES AND NEUROANAESTHESIA

Risks for impaired cerebral autoregulation during cardiopulmonary bypass and postoperative stroke

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³Department of Pediatrics and Anesthesiology, Baylor College of Medicine, Texas Children’s Hospital, Huston, TX, USA
⁴Department of Anesthesiology, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China

* Corresponding author: The Johns Hopkins Hospital, 600 North Wolfe Street, Tower 711, Baltimore, MD 21287, USA. E-mail: chogue2@jhmi.edu

Conclusions. Impaired CBF autoregulation occurs in 20% of patients during CPB. Patients with impaired autoregulation are more likely than those with functional autoregulation to have perioperative stroke. Non-invasive monitoring autoregulation may provide an accurate means to predict impaired autoregulation.
Methods: Autoregulation was monitored during cardiopulmonary bypass in 450 patients undergoing coronary artery bypass grafting and/or valve surgery.

Results: Of the 450 patients, 83 experienced major morbidity or operative mortality. The area under the curve of the product of the duration and magnitude of blood pressure below the limits of autoregulation was independently associated with major morbidity or operative mortality after cardiac surgery (odds ratio, 1.36; 95% confidence interval, 1.08-1.71; $P = .008$).

Conclusions: Blood pressure management during cardiopulmonary bypass using physiologic endpoints such as cerebral autoregulation monitoring might provide a method of optimizing organ perfusion and improving patient outcomes from cardiac surgery. (J Thorac Cardiovasc Surg 2014;147:483-9)
Predicting the Limits of Cerebral Autoregulation During Cardiopulmonary Bypass
Brijen Joshi, MD,* Masahiro Ono, MD,† Charles Brown, MD,* Kenneth Brady, MD,‡ R. Blaine Easley, MD,§ Gayane Yenokyan, PhD,‖ Rebecca F. Gottesman, MD, PhD,¶ and Charles W. Hogue, MD*

CONCLUSIONS: There is a wide range of MAP at the LLA in patients during CPB, making estimation of this target difficult. Real-time monitoring of autoregulation with cerebral oximetry index may provide a more rational means for individualizing MAP during CPB. (Anesth Analg 2012;114:503–10)
The Effect of Optimising Cerebral Tissue Oxygen Saturation on Markers of Neurological Injury during Coronary Artery Bypass Graft Surgery

Yakeen Harilall\textsuperscript{a}, Jamila Kathoon Adam\textsuperscript{d,}\textsuperscript{*}, Bruce Mclure Biccard\textsuperscript{b,c}, Anu Reddi\textsuperscript{a}

**Conclusion**

Monitoring brain oxygen saturation during on-pump CABG together with an effective treatment protocol to deal with cerebral desaturation must be advocated.
Dynamic cerebral autoregulatory capacity is affected early in Type 2 diabetes

Yu-Sok KIM†, Rogier Y. IMMINK†‡, Wim J. STOK†§, John M. KAREMAKER†§,
Niels H. SECHER||¶ and Johannes J. VAN LIESHOUT†‡

Reduced Dynamic Cerebral Autoregulatory Efficacy in Uncomplicated T2DM
Dynamic cerebral autoregulatory capacity is affected early in Type 2 diabetes

Yu-Sok KIM†, Rogier Y. IMMINK†, Wim J. STOK†§, John M. KAREMAKER†§, Niels H. SECHER||, and Johannes J. VAN LIESHOUT†‡

Reduced Dynamic Cerebral Autoregulatory Efficacy in Uncomplicated T2DM
Determination of delay between BP and CBFv
Time domain analysis

• Correlation between MAP and $MCAv_{\text{mean}}$
• Find maximal correlation
  – Phase (time domain, in seconds)
  – Gain
Correlation

r: 0.92

gain: 1.15

delay: 0.90 seconds
Cerebral Autoregulation during Anesthesia

\[ r: 0.96 \]
\[ \text{gain: } 2.66 \]
\[ \text{delay: } 0.20 \text{ seconds} \]
Back to degrees/radians

Previously,
now
and later
Future

• Pre-assessment prior to anesthesia
  – Measuring cerebral blood flow and at least
    • Blood pressure
    • CO₂
  – Extract models describing the relation between arterial blood pressure and cerebral blood flow

• Intra-operative application of cerebral blood flow model as developed during pre-assessment
Summarized

• Machine learning:
  – Requires **blood pressure** and **CO₂**

• ARX model
  – Requires **blood pressure** and **CO₂**

• xDCA
  – Requires **blood pressure** and **brain perfusion**
    monitoring with TCD or NIRS
  – Disregards CO₂ contribution
Concluding remarks

• Modeling of CBFv from BP and CO₂ feasible
• Machine Learning method has constant offset
• ARX model, faster but less consistent
• Ideally:
  – Build general model instead of pre -> intra anesthesia per subject