Vasomotor reactivity and functional TCD

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What is Vasomotor - reactivity

• Capability of the brain vasculature to maintain constant supply of blood
  – Changes of homœostasis
    • pH
    • CO2
    • NO (?)
    • Electrolytes
  – Changes of perfusion pressure
    • Blood pressure / ICP
    • Heart rate

• Both mechanisms combine for „autoregulation“
• Both mechanisms can be tested independently
Changes of homöostasis

Shift in hydrogen-ion content mediates CBFV changes

Linear segment of curve
from Ringelstein et al Stroke 1988
Testing CO2-reactivity

- Breath holding Index (BHI)
- Apnea-hyperventilation test
- Re-breathing of CO₂ (reservoir bag)
- Inhalation of Carbogen gas (5-10% CO₂ + 90-95% O₂)
- „Diamox“ – test (Acetazolamide infusion)

Common effect:
- Change (increase) of CO₂ concentration in blood –
  dilation of arterioles – increased blood volume –
  increase of blood flow velocity
CO$_2$ – reactivity

\[ NCR = \frac{\Delta v}{v_{\text{normo}}} \]

\[ VMR = \frac{\Delta v}{v_{\text{min}}} \]

Hyper-/Hypokapnie: Änderung > 10%

Widder, Görtler
<table>
<thead>
<tr>
<th>Test</th>
<th>Instruction</th>
<th>calculation</th>
<th>Which means?</th>
<th>literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathholding Index (BHI)</td>
<td>Hold your breath as long as possible. Determine duration and BFV.</td>
<td>( \frac{(v_{\text{apnea}} - v_{\text{baseline}}) \times 100}{v_{\text{baseline}} \times t_{\text{apnea}} \text{[s]}} )</td>
<td>Normal &gt; 1,2 (±0,6)</td>
<td>Markus 1992</td>
</tr>
<tr>
<td>Apnea / Hyperventilation</td>
<td>Hyperventilation for 30-40s. Hold your breath as long as possible. Determine BFV baseline, max., min.</td>
<td>( \frac{v_{\text{challenge}} - v_{\text{baseline}}}{v_{\text{baseline}}} )</td>
<td>&gt; 15% change from baseline = normal</td>
<td>Widder 1992</td>
</tr>
<tr>
<td>CO₂ – re-breathing</td>
<td>Breathing in plastic bag. Measure end tidal CO₂ (etCO₂)</td>
<td>Normalized CO₂ reactivity (NCR): ( \frac{\Delta v[%CO₂]}{v_{\text{baseline}}} )</td>
<td>NCR: &gt;25% / %[CO₂]</td>
<td>Widder 1986</td>
</tr>
<tr>
<td>Carbogen Gas</td>
<td>By tight face mask (5% CO₂ / 95% O₂). Measure end tidal CO₂ (etCO₂)</td>
<td>Vasomotor reserve capacity (VMR): ( \frac{\Delta v}{v_{\min}} )</td>
<td>VMR &gt; 50%</td>
<td>Ringelstein 1988</td>
</tr>
<tr>
<td>Diamox test</td>
<td>Infusion of Acetacolamide (Diamox). 1g or 15mg/kgKG. Determine BFV baseline, max., min.</td>
<td>( \frac{v_{\text{challenge}} - v_{\text{baseline}}}{v_{\text{baseline}}} )</td>
<td>&gt; 40% normal. Invers: highly pathological</td>
<td>Piepgras 1990</td>
</tr>
</tbody>
</table>
Why testing?

Kleiser and Widder 1992

Stroke and TIA rate

- exhausted (n = 11)
- diminished (n = 26)
- sufficient (n = 48)

Stroke rate

- exhausted (n = 11)
- diminished (n = 26)
- sufficient (n = 48)
10-15% stroke rate in pts. with ICA occlusions and highly impaired VMR
Patterns of cerebral infarction and CO2 reactivity in 140 ICA occlusions

Kleiser and Widder 1991
Hypoperfusion & Embolism

“Impaired Washout”

1) Hypoperfusion promotes the formation of thromboemboli

2) Border zones are favoured destination for microemboli

3) The two conditions are complementary. Low perfusion pressure affects the destination and clearance of embolic particles
What else?

Ischemic Ophthalmopathy in ICA occlusion and insufficient collaterals (Rubeosis iridis)

Indication for EC-IC Bypass?
Cerebral autoregulation (AR)

• „The intrinsic capacity of cerebral vasculature to maintain constant cerebral blood flow“.

• Static AR
  – overall efficiency of the autoregulation system
  – assessed by monitoring the CBF during different levels of BP
  – In-vivo testing very invasive, demands active BP manipulation

• Dynamic AR
  – the ability to restore CBF despite sudden changes in perfusion pressure
  – reflects the latency of the system
  – In-vivo testing non invasive, calculation complicated
Cerebral autoregulation (pressure-dependent)

- Normal autoreg
- Abnormal autoreg in hytens

CBF
100%

mean art BP [mm Hg]
120-150
80
155-170

60
Static autoregulation tests from individual subjects with intact (top) and impaired (bottom) autoregulation
Cerebral autoregulation (pressure-dependent)

- Normal autoreg
- Abnormal autoreg in hytens

![Graph showing cerebral blood flow (CBF) and mean arterial blood pressure (BP)]
Autoregulatory tests

- Respiratory manoeuvres
  - Valsalva test, deep breathing

- Autoregulatory index (ARI) by cuff deflation (Aaslid 1989; Tiecks 1995; White and Markus 1997)

- Spontaneous fluctuations of arterial blood pressure
  - Correlation coefficient approach (Czosnyka 1996, Reinhard 2003)

- Transfer function analysis (Diehl 1995, Hu 1998)
  - Phase shift analysis (CBF versus ABP in degrees; Immink 2005)
  - Coherency (ABP versus CBFV in degrees)
Responses of cerebral autoregulation model to a step change in blood pressure

Tiecks, F. P. et al. Stroke 1995;26:1014-1019
Dynamic autoregulation tests from individual subjects with intact (left) and impaired (right) autoregulation

Tiecks, F. P. et al. Stroke 1995;26:1014-1019
Autoregulatory tests

- Respiratory manoeuvres
  - Valsalva test, deep breathing, cross spectral analysis

- Autoregulatory index (ARI) by cuff deflation (Aaslid 1989; Tiecks 1995; White and Markus 1997)

- Spontaneous fluctuations of aterial blood pressure
  - Correlation coefficient approach (Czosnyka 1996, Reinhard 2003)

- Transfer function analysis (Diehl 1995, Hu 1998)
  - Phase shift analysis (CBF versus ABP in degrees; Immink 2005)
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Some parameters of interest

a) Arterial blood pressure

b) MCA BFV

„Period“ describes the spontaneous fluctuations over time, frequently 10 s (0.1 Hz)

„Phase shift“ in degrees or fractions of π describes the latency between ABP and BFV changes.
Large shift (π/4) = good, no phase shift = bad
Disturbed cerebral autoregulation

- Lack of protection from hypotension
  - Impaired wash-out of emboli
  - Less protection against ischemic damage
  - Risk of chronic hypoperfusion

- Lack of protection from hypertension
  - Brain edema (break-through mechanism)
  - Brain hemorrhage
Functional TCD

• Region specific tasks increase demand of nutrition
• Dilation mediated by „neurovascular coupling“
• Increase in CBF is proportional to increase in CBFV, because mainstems maintain constant diameter
The cerebral blood flow (CBF) changes that are induced by neural activity have long been used to probe brain function. In the 1800s, Angelo Mosso studied patients with skull defects to monitor the changes in brain volume or temperature that are produced by brain activity\textsuperscript{10,151,152}. The figure shows the volume changes of the brain (top trace) and feet (middle trace) evoked by an emotional stimulus (arrow) in one of his study subjects, L. Cane (pictured). Mosso writes: “Mr Cane was resting peacefully when ... I said just a few words expressing the impression that his wife had made upon me when I first saw her. Cane did not speak. The blood to the brain increased immediately and the volume of the feet markedly diminished”\textsuperscript{152}. These findings reflect the cerebro-
The neurovascular unit

Iadecola 2004
Functional TCD – areas of application

• Visual stimuli – increase in PCA, preferably P2-segment
  – Identification of PCA in clinical routine
  – „Neurovascular coupling“ e.g. Rosengarten

• Mental tasks – increase in MCA
  – Hemispheric dominance
  – Preceded functional MRI
  – Visuo-construction tasks (faces, complex figures)
Visually evoked flow

- **Object should be**
  - Bright
  - Rich in contrast
  - Colorful
  - E.g. checkboard

- **Present and investigate bilaterally for 20 s**
  - Preferably P2-segment
  - Increase in CBFV begins immediately
  - Peaks within 10s
  - Decreases to a plateau thereafter

- **Determine**
  - Rel. CBFV increase (normal ~40%)
  - Latency to max. CBFV
  - Repeat a couple of times and average results
Visually evoked flow
Visually evoked flow
fTCD and mental tasks

- Speech lateralisation (left hemispheric)
- Face recognition (right hemispheric)
- Comparison of similar images (right hemispheric)
- Investigation of the MCA (M1)
- Comparison of left and right hemisphere
fTCD and mental tasks

- Increases less dramatic than in visual evoked flow

- 15-20% of M1-territory BFV + ~10%
- 100% of P2-territory BFV+ ~40%
fTCD and mental tasks – more problems

- Some studies report increase of right hemispheric BFV in language tasks
  - Attention increase while awaiting verbal stimulus (right hemispheric!)
  - Can be higher than intended stimulus!
fTCD and mental tasks – solving the problems

- Attention dependent increase short lived
  - “announce” verbal task seconds before the tasks will bring BFV to baseline when task start
  - Do left and right hemispheric tasks to subtract attention increase
  - Average multiple test results

(Knecht 1996)
(Rihs 1999)
fTCD and mental tasks – solving the problems

Fig. 1. Example setup of a fTCD study for the assessment of attention and language dominance (Knecht et al., 1996). Two ultrasound probes are mounted on both temples of a volunteer and are adjusted for assessment of the blood flow velocity of the left and right middle cerebral arteries (MCAs). The cerebral blood flow velocity (CBFV), displayed in the middle column as typical raw signal with signal modulations due to heart beat, is recorded simultaneously with trigger signals by a TCD device. One trigger channel represents the occurrence of a letter on the computer screen and the other a preceding cueing tone. The simultaneous recording guarantees the synchronization between stimulation and CBFV response. Details of the study are described in Knecht et al., 1996. Data analysis is performed off-line by the analysis software AVERAGE 1.30 described in the present work.
fTCD: applications

- Determination of speech dominant hemisphere
  - tumor
  - epilepsy surgery
- Neurovascular coupling can best be tested in the posterior circulation
  - Testing in various clinical conditions
  - Probably reflects functionality of „neurovascular unit“
Take home messages

• Tests of vasomotor reactivity test flow changes to CO$_2$ changes

• Autoregulation tests invastigate flow changes to pressure changes

• In clinical practise Vasomotor reactivity tests are much easier to perform

• A classical indication is to test for exhausted reactivity in high grade carotid stenosis or occlusion
  – Stroke risk
  – EC-IC bypass indication?
Take home messages

• Autoregulation testing is far more complicated

• Functional TCD is an illustrative tool to highlight the „neurovascular unit“

• Some clinical applications for both exist
Thank you!