Vasomotor reactivity and functional TCD

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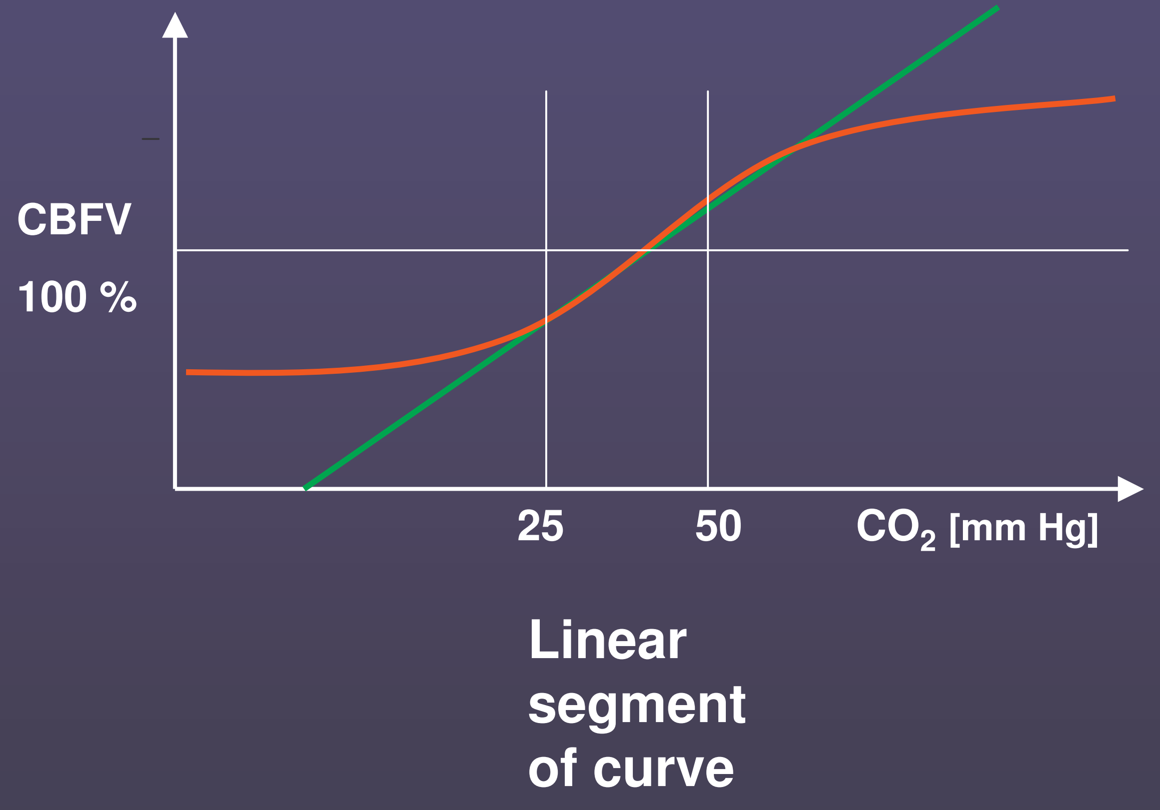
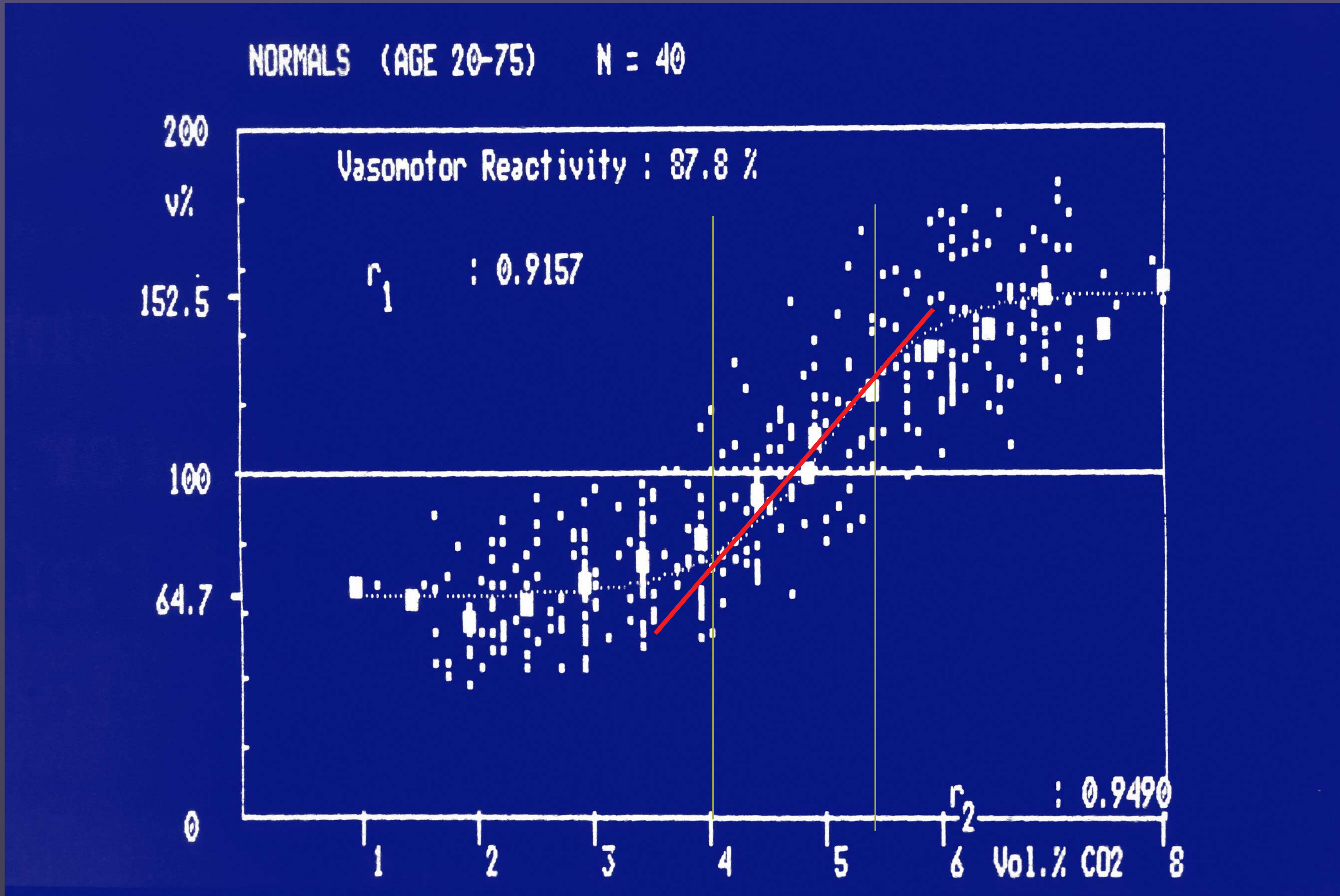
What is Vasomotor - reactivity

- Capabilty of the brain vasculature to maintain constant supply of blood
  - Changes of homöostasis
    - pH
    - CO_2
    - NO (?)
    - Electrolytes
  - Changes of perfusion pressure
    - Blood pressure / ICP
    - Heart rate
- Both mechnisms combine for „autoregulation“
- Both mechanisms can be tested independenty

Changes of homöostasis

Shift in hydrogen-ion content mediates CBFV changes



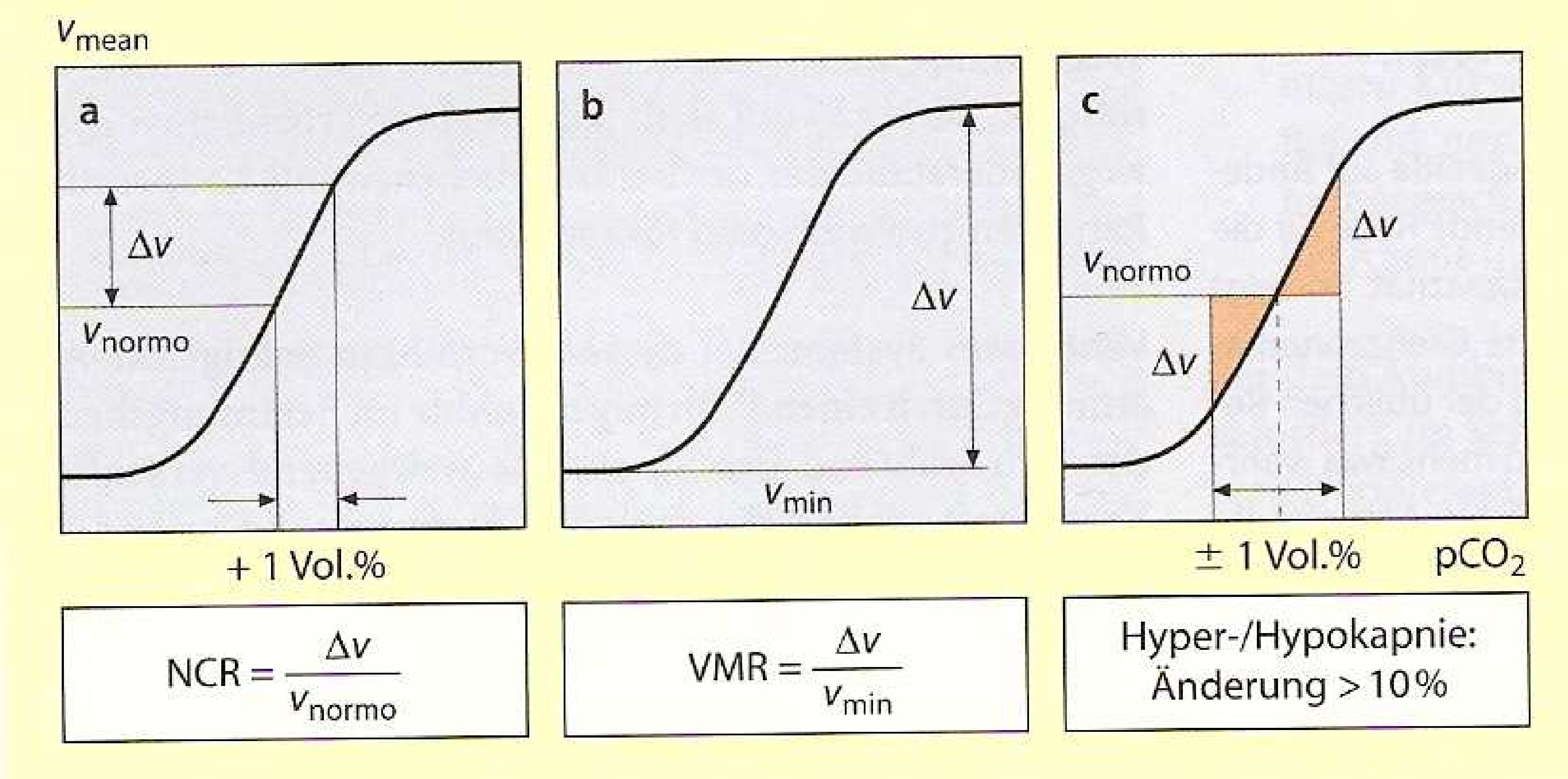


from Ringelstein et al Stroke 1988

Testing CO2-reactivity

- **Breath holding Index (BHI)**
- Apnea-hyperventilation test
- Re-breathing of CO_2 (reservoir bag)
- Inhalation of Carbogen gas (5-10% CO_2 + 90-95% O_2)
- „Diamox“ – test (Acetacolamide infusion)
- Common effect:
  - Change (increase) of CO_2 concentration in blood – dilation of arterioles – increased blood volume – increase of blood flow velocity

CO_2 – reactivity

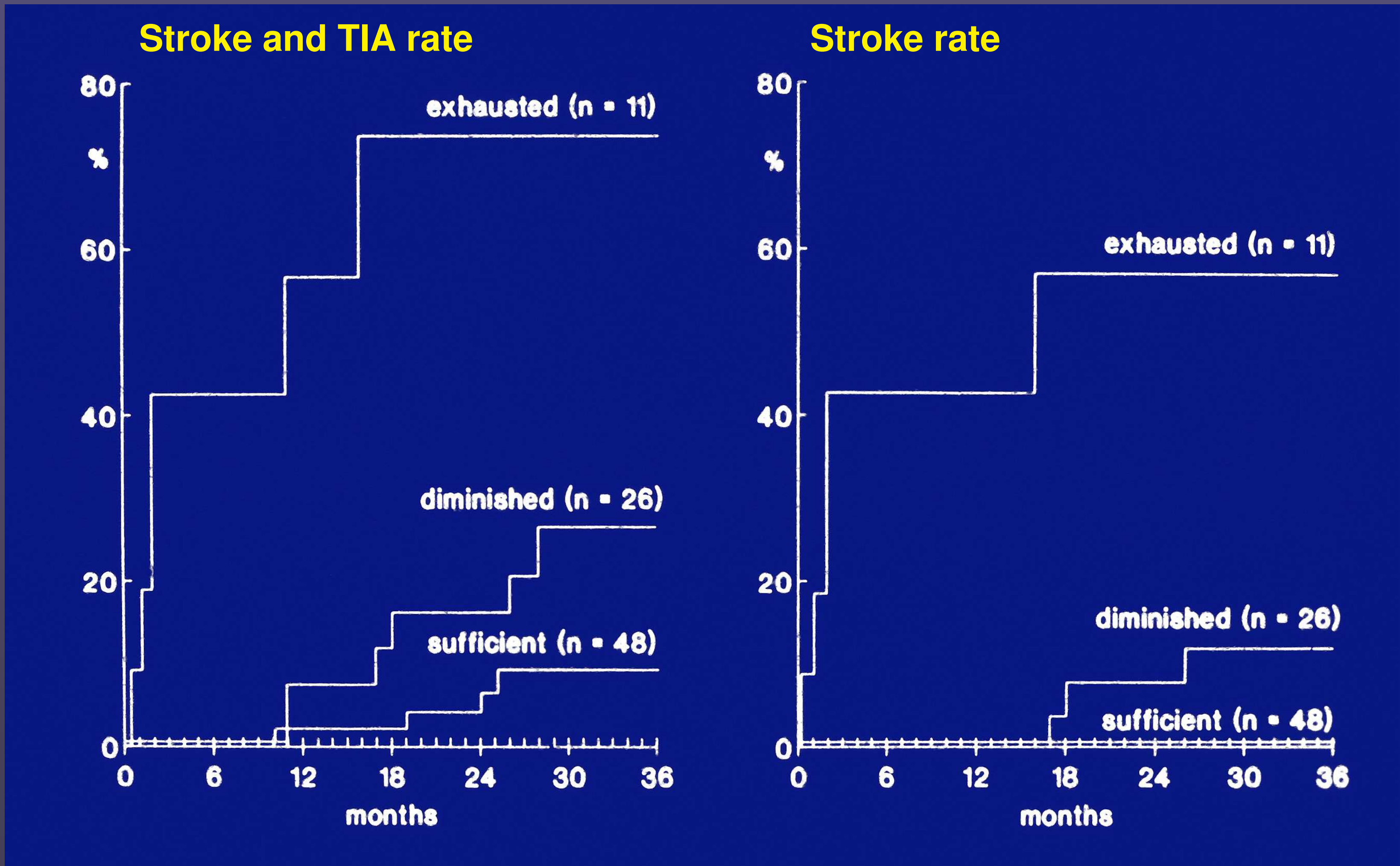


Widder, Görtler

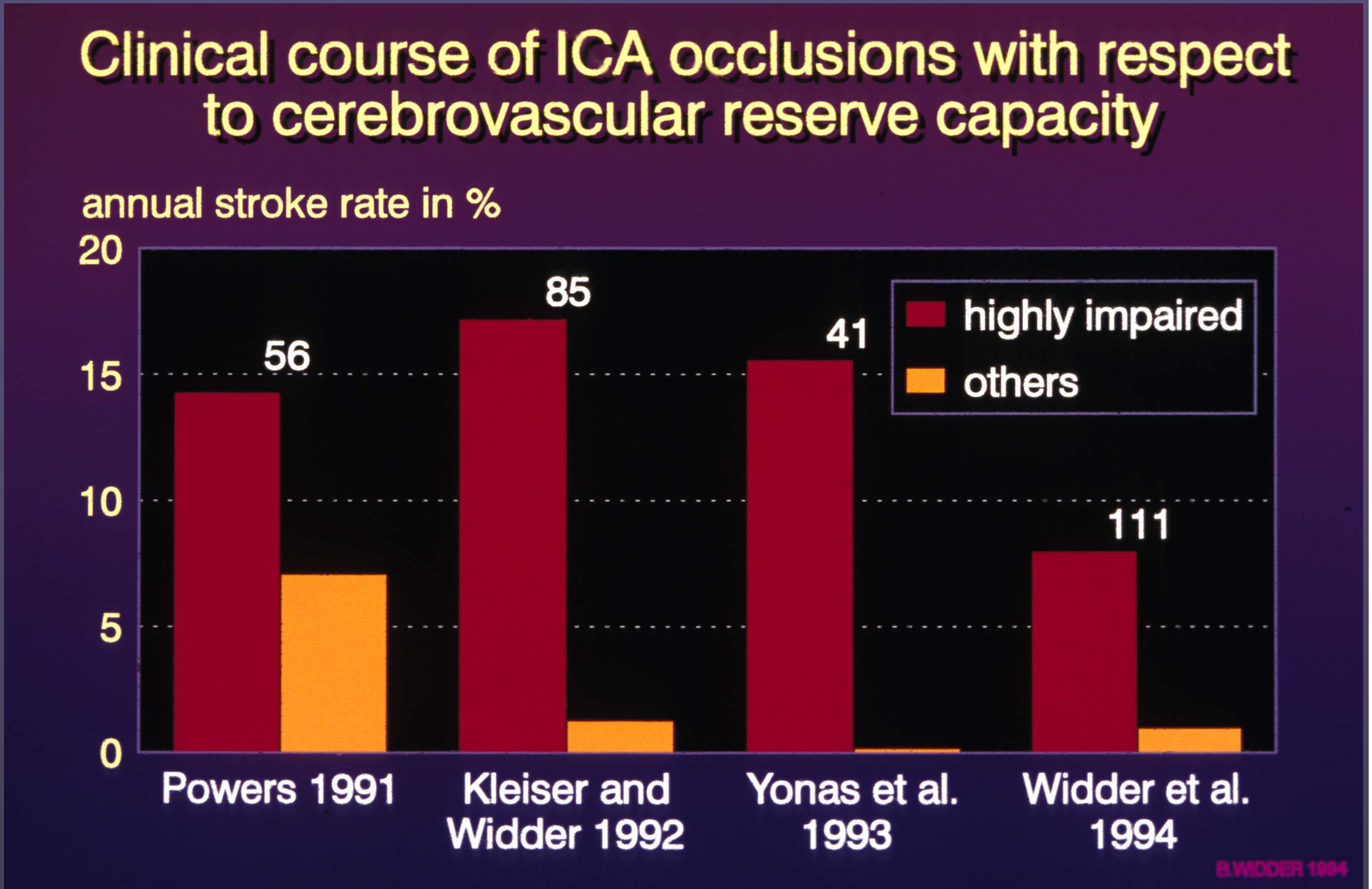
How to do them ?

Test	Instruction	calculation	Which means?	literature
Breathholding Index (BHI)	Hold your breath as long as possible Determine duration and BFV	$\frac{(v_{apnea} - v_{baseline}) \times 100}{v_{baseline} \times t_{apnea}\,[s]}$	Normal > 1,2 (±0,6)	Markus 1992
Apnea / Hyperventilation	Hyperventilation for 30-40s Hold your breath as long as possible Determine BFV baseline, max., min.	$\frac{v_{challange} - v_{baseline}}{v_{baseline}}$ Challange = apnea or hyperventilation	> 15% change from baseline = normal	Widder 1992
CO_2 – re-breathing	Breathing in plastic bag measure end tidal CO_2 ($etCO_2$)	Normalized CO_2 reactivity (NCR): $\Delta v[\%CO_2] / v_{baseline}$	NCR: >25% / %[CO_2]	Widder 1986
Carbogen Gas	By tight face mask (5% CO_2 / 95% O_2) measure end tidal CO_2 ($etCO_2$)	Vasomotor reserve capacity (VMR): $\Delta v/v_{min}$	VMR > 50% < 10% pathological Invers: highly pathological	Ringelstein 1988
Diamox test	Infusion of Acetacolamide (DIamox) 1g or 15mg/kgKG Determine BFV baseline, max., min.	$\frac{v_{challange} - v_{baseline}}{v_{baseline}}$	> 40% normal < 10% pathological Invers: highly pathological	Piepgras 1990 Ringelstein 1992

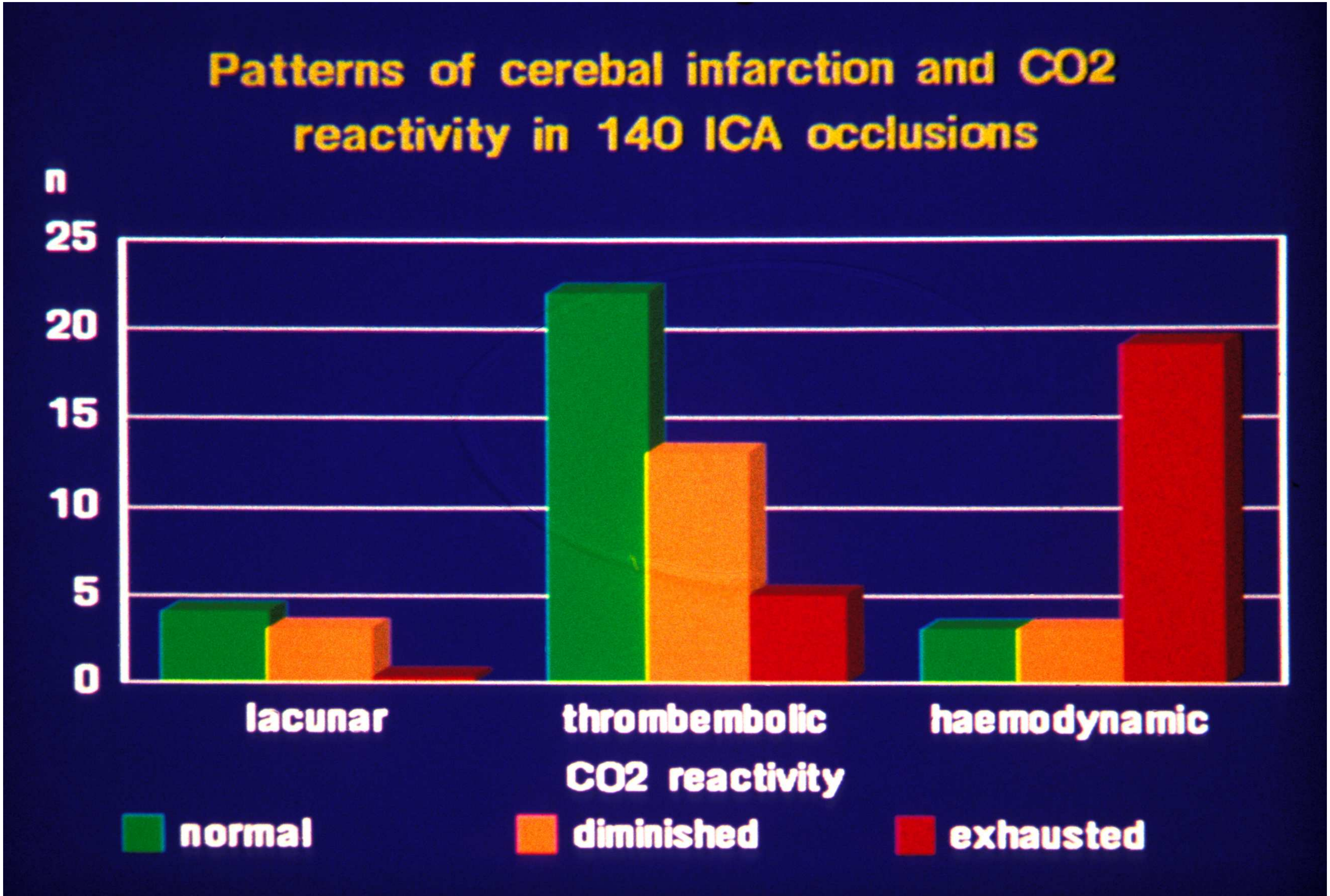
Why testing?



Kleiser and Widder 1992



10-15 % stroke rate in pts. with ICA occlusions and highly impaired VMR



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 ?

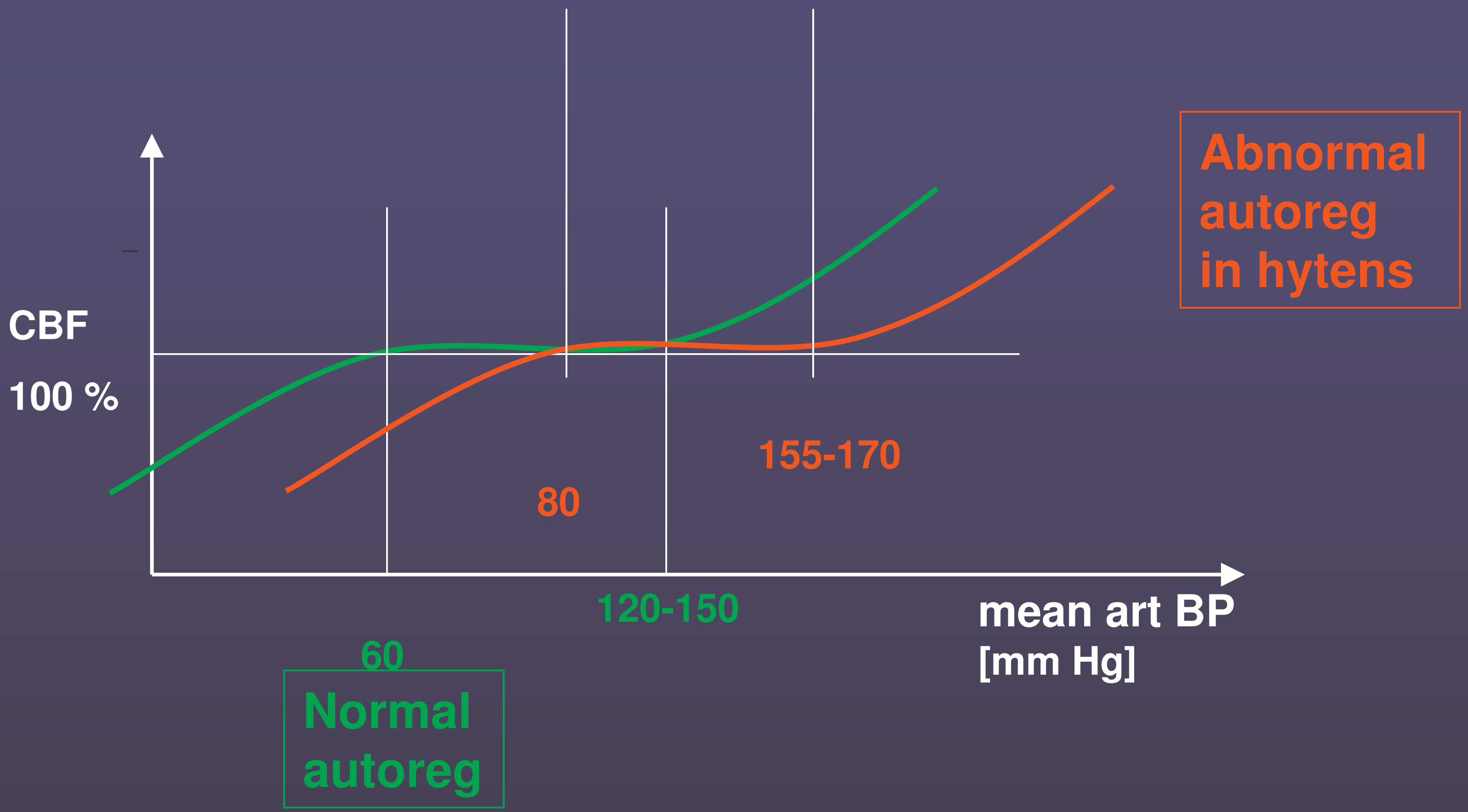
Cerebral autoregulation (AR)

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

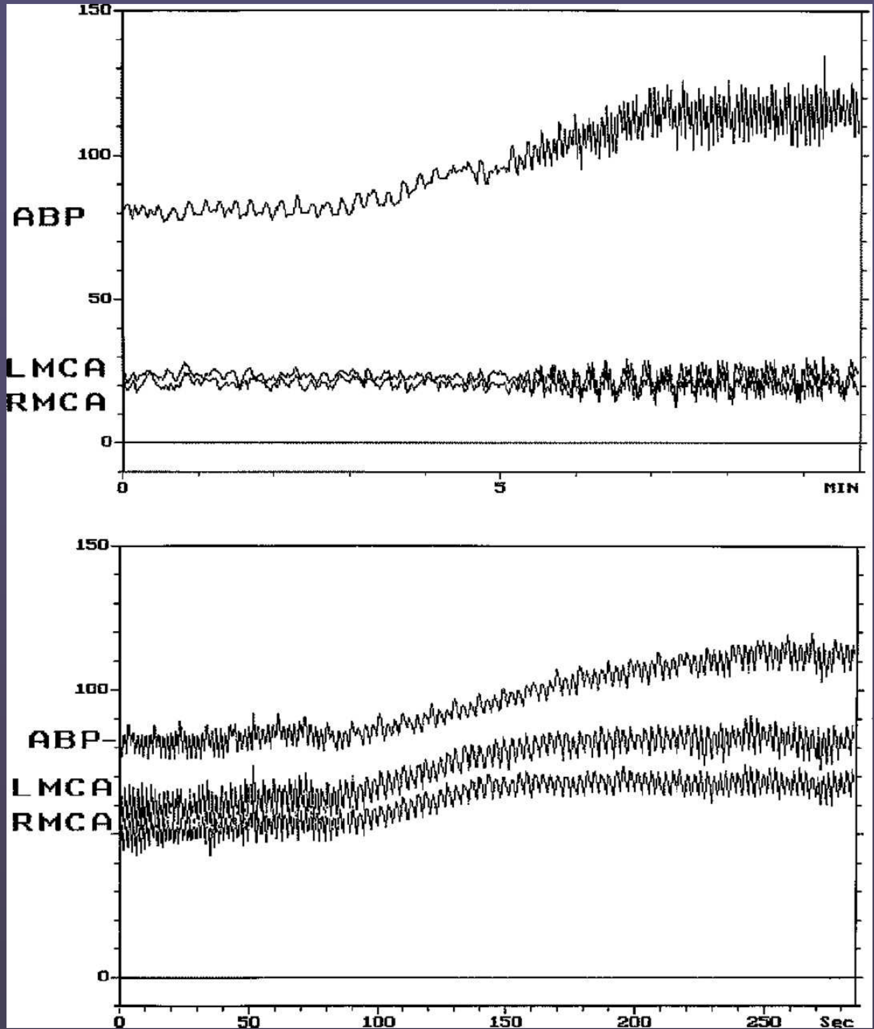
- Static AR
  - overall efficiency of the autoregulation system
  - assesssed by monitoring the CBF during different levels of BP
  - In-vivo testing very invasive, demands active BP manipulation

- 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)

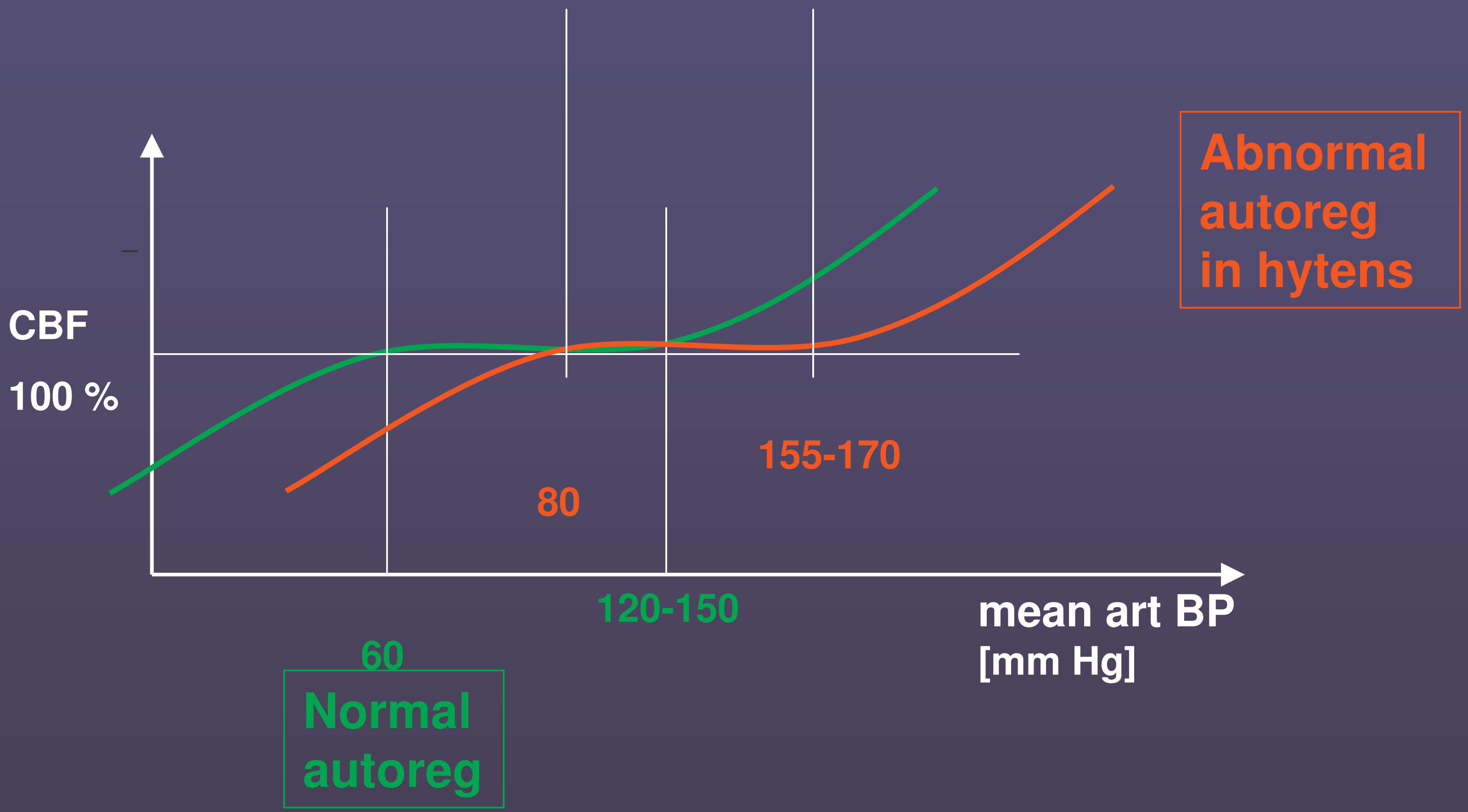


Static autoregulation tests from individual subjects with intact (top) and impaired (bottom) autoregulation



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

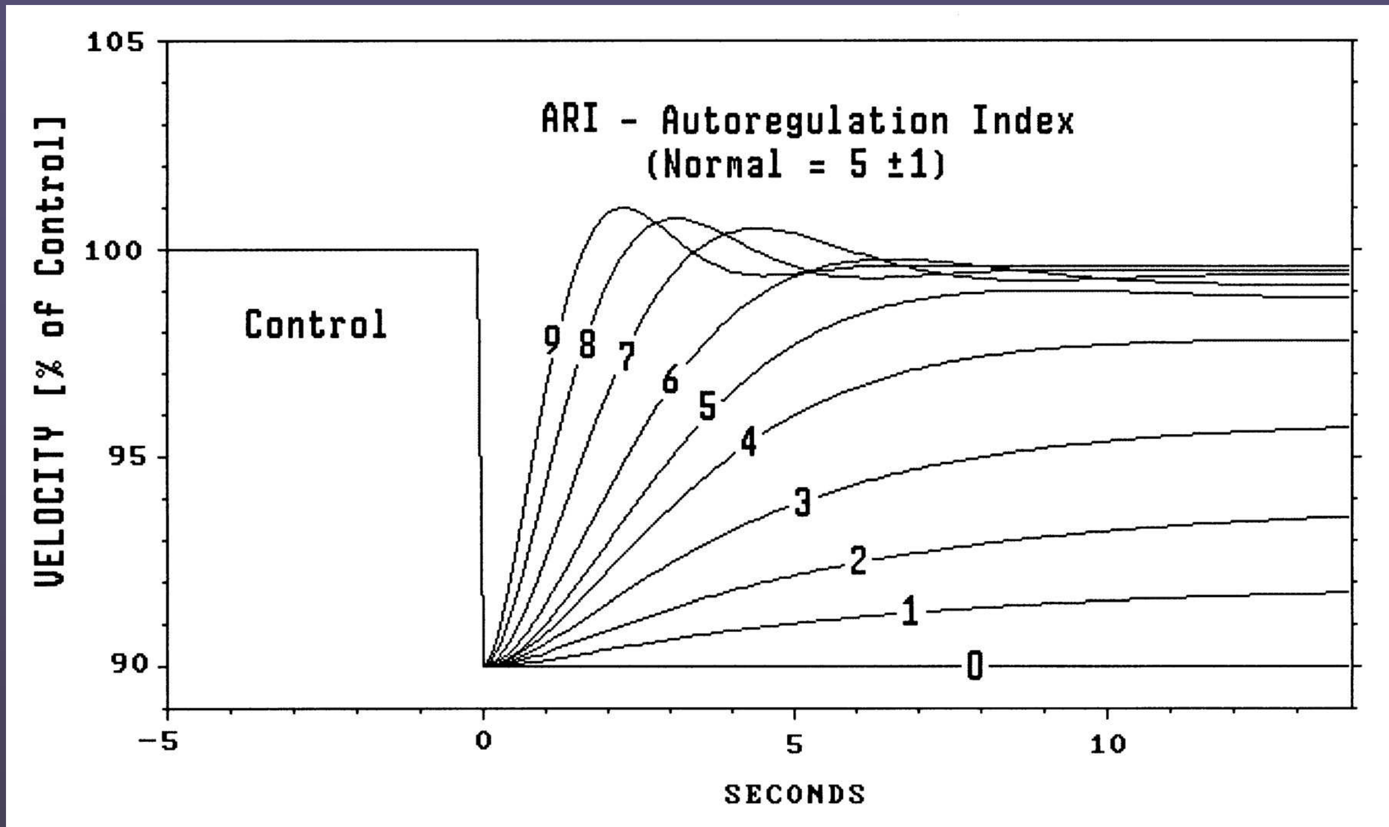
Cerebral autoregulation (pressure-dependent)



Autoregulatory tests

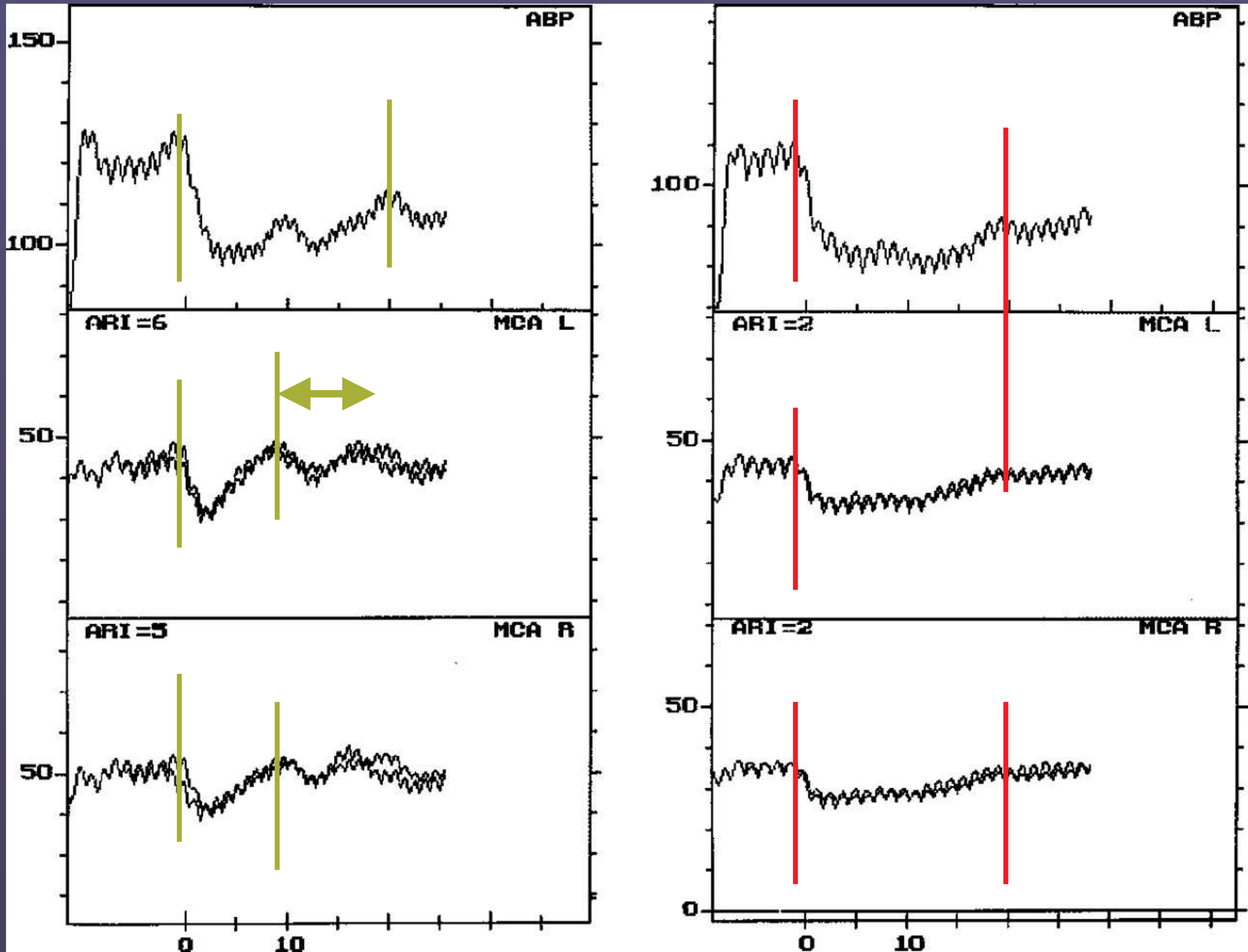
- Respiratory manoeuvres
  - Valsalva test, deep breathing
- Autoregulatory index (ARI) by cuff deflation (**Aaslid 1989; Tiecks 1995; White and Markus 1997**)
- Spontaneous fluctuations of aterial blood pressure
  - Correlation coefficient approach (**Czosnyka 1996, Reinhard 2003**)
- Transfer function analysis (**Diehl 1995, Hu 1998**)
  - Phase shift analysis (CBF versus ABP in degrees; **Immink 2005**)
  - 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**)
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  - Phase shift analysis (CBF versus ABP in degrees; **Immink 2005**)
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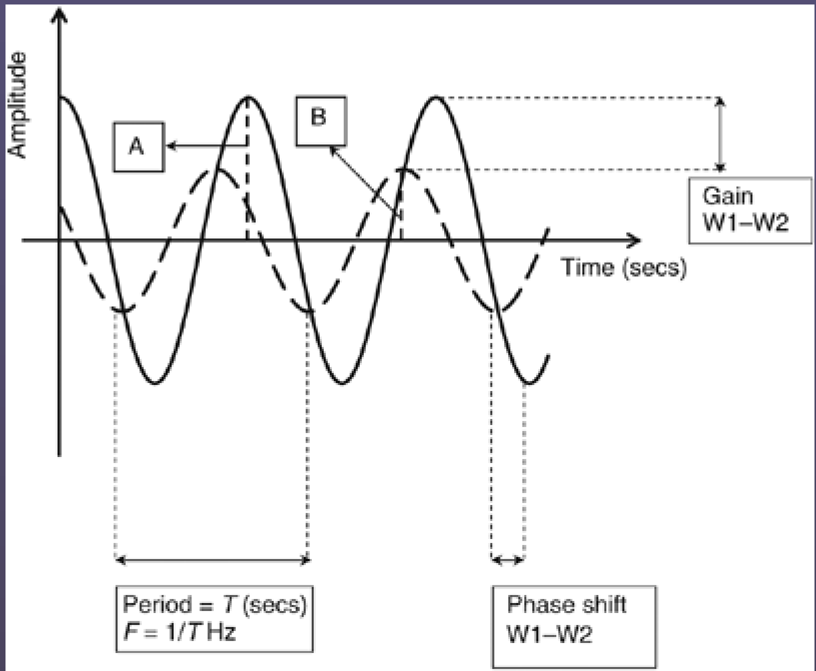
Some parameters of interest



a) Arterial blood pressure
b) MCA BFV

„Period“ describes the spontanous 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

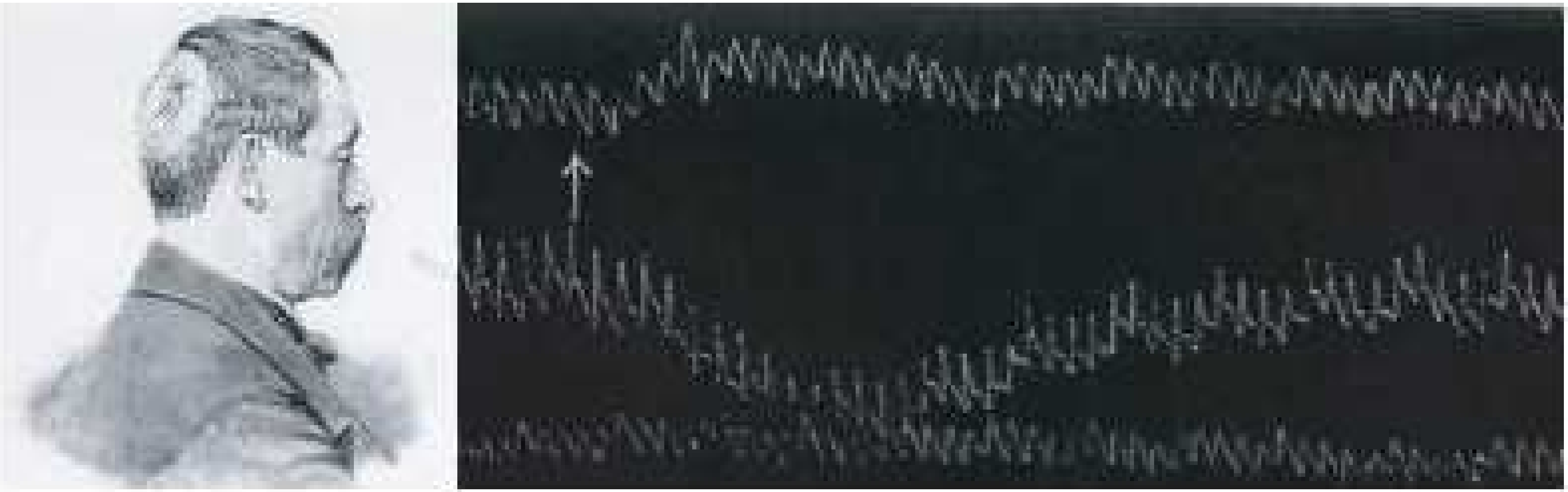
Disturbed cerebral autoregulation

- 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

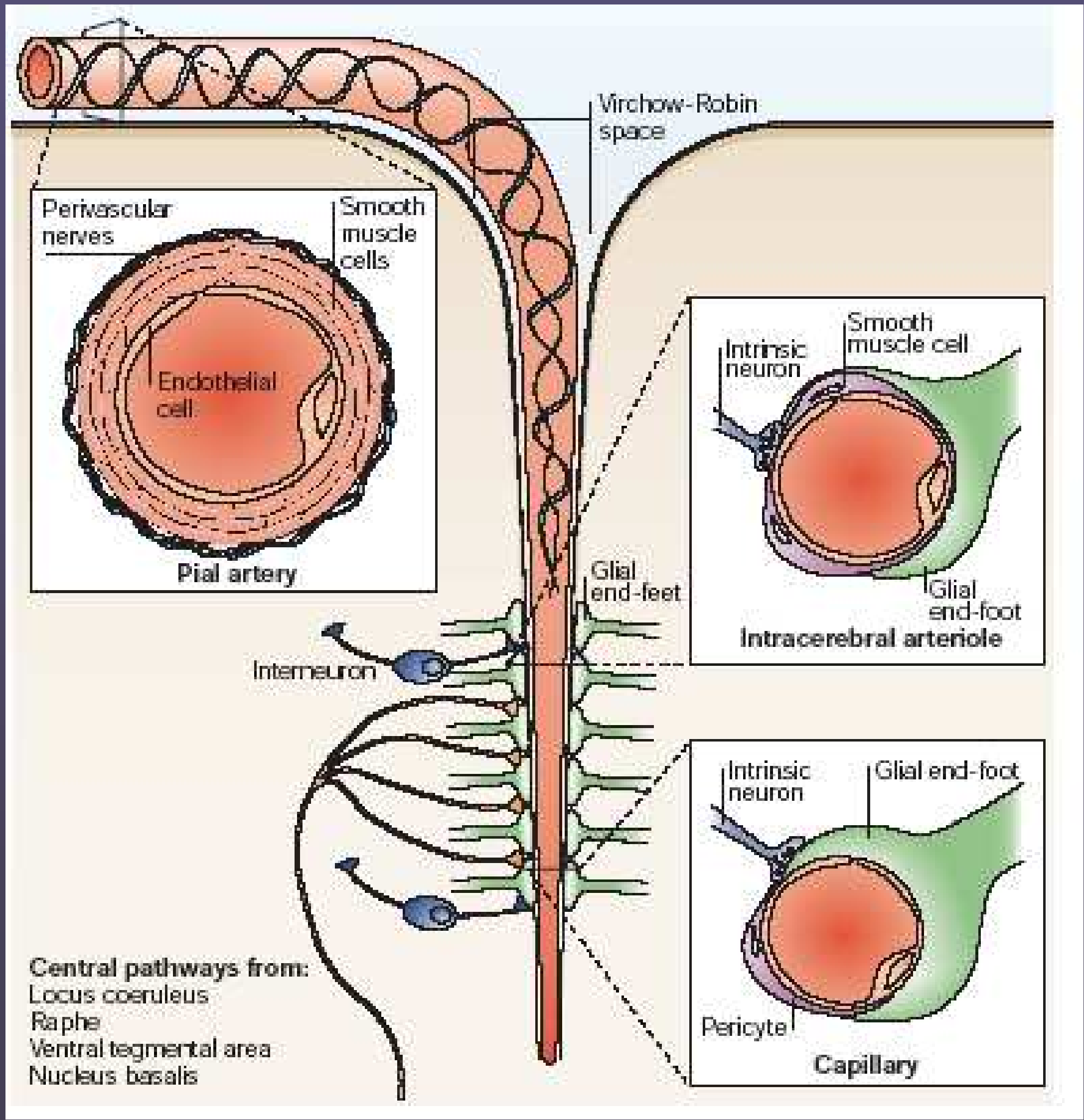
Box 1 | **Neurovascular coupling: a window on brain function**



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[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"[152]. These findings reflect the cerebro-

Iadecola 2004

The neurovascular unit



Iadecola 2004

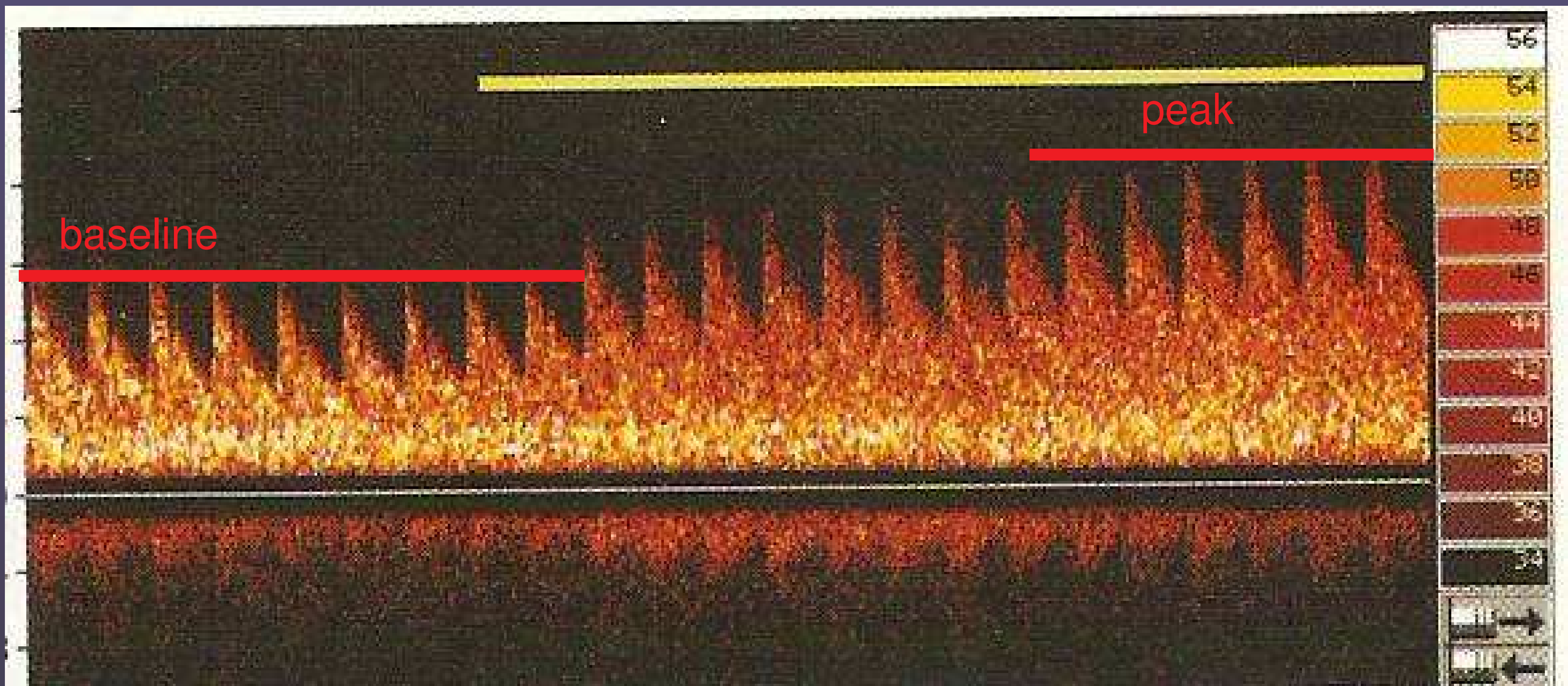
Functional TCD – areas of application

- 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)

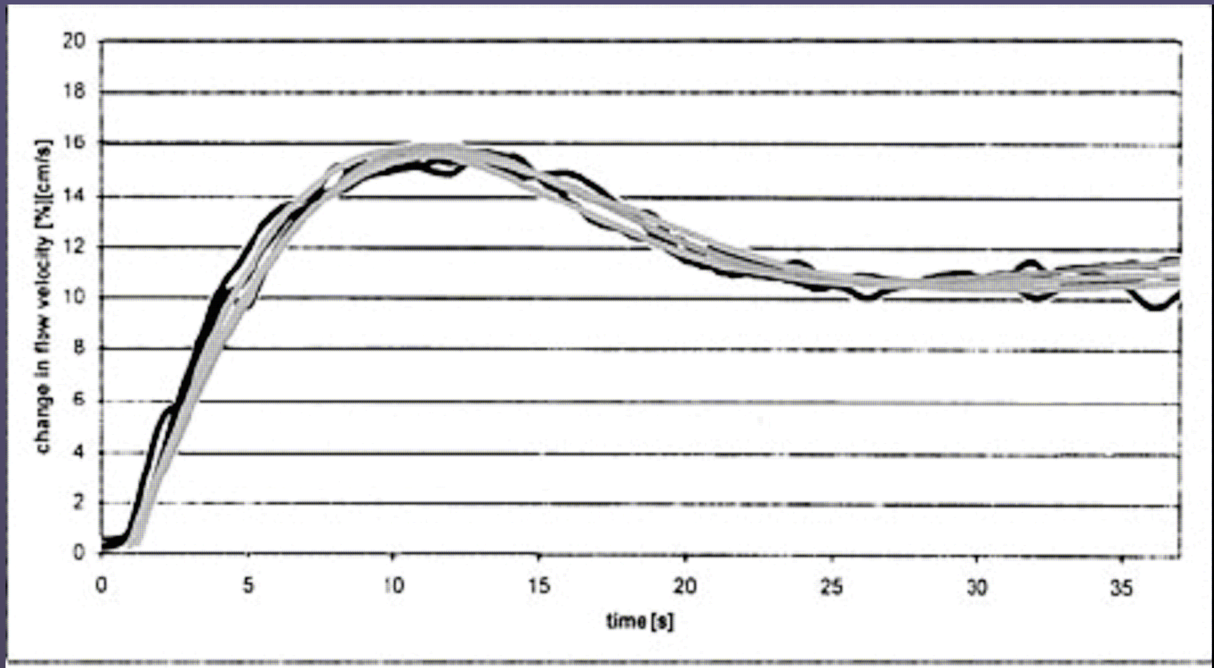
Visually evoked flow

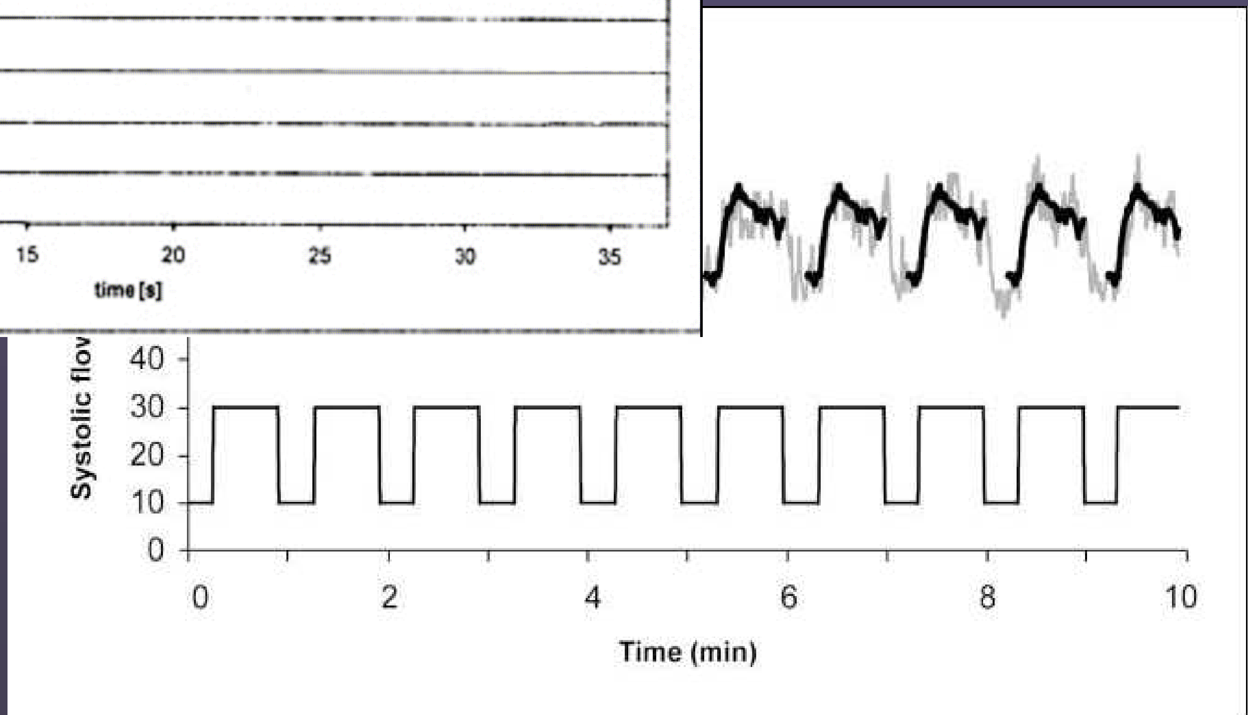
- Object should be
  - Bright
  - Rich in contarst
  - Colorful
  - E.g. checkboard
- Present and investigate bilaterally for 20 s
  - Preferably P2-segment
  - Increase in CBFV begins immediately
  - Peaks within 10s
  - Decreases to a plateau thereafter
- Determine
  - Rel. CBFV increase (normal ~40%)
  - Latency to max. CBFV
  - Repeat a couple of times and average results

Visually evoked flow



Visually evoked flow



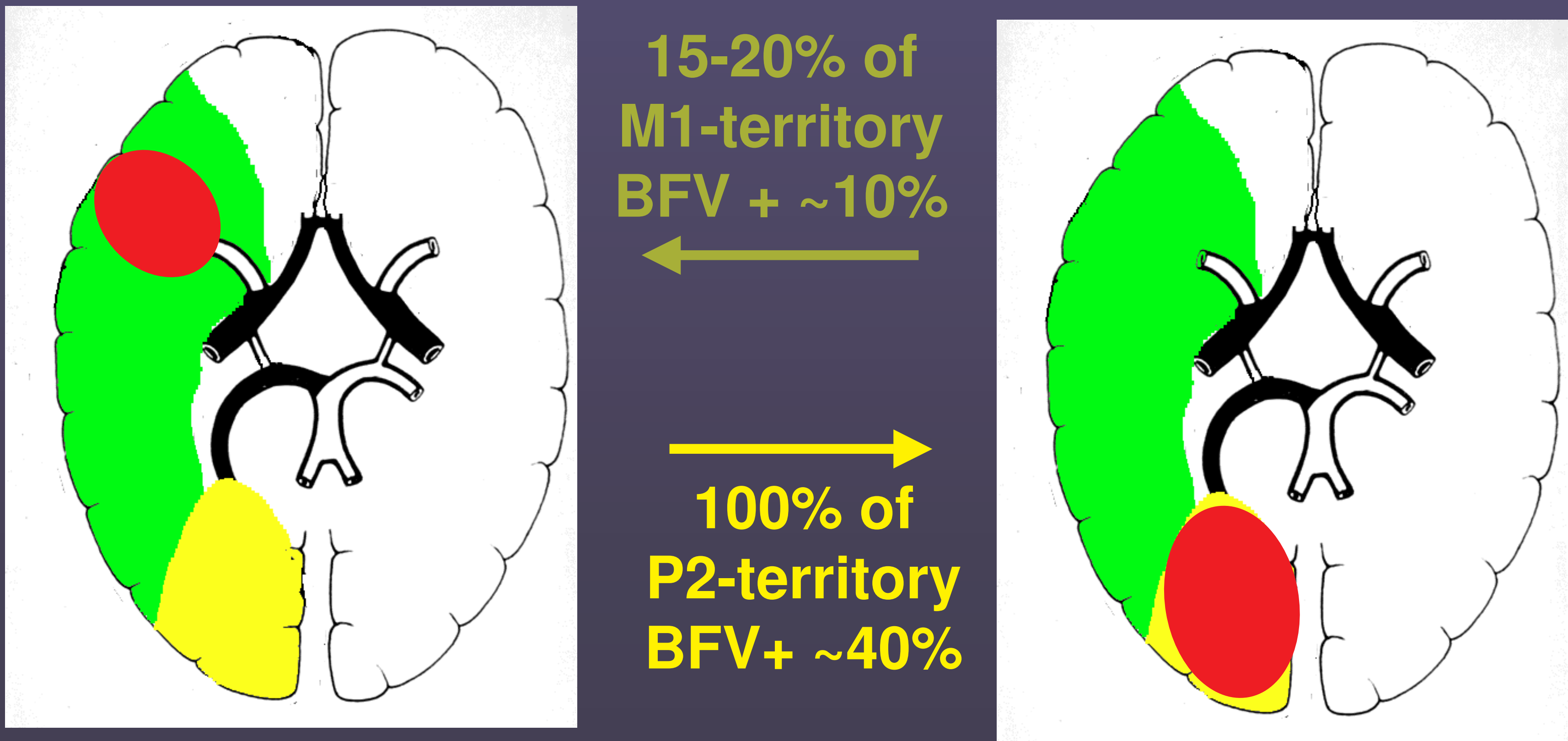


fTCD and mental tasks

- Speech lateralisation (left hemispheric)
- Face recognistion (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



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 **(Knecht 1996)**
  - Do left and right hemispheric tasks to subtract attention increase **(Rihs 1999)**
  - Average multiple test results

fTCD and mental tasks – solving the problems

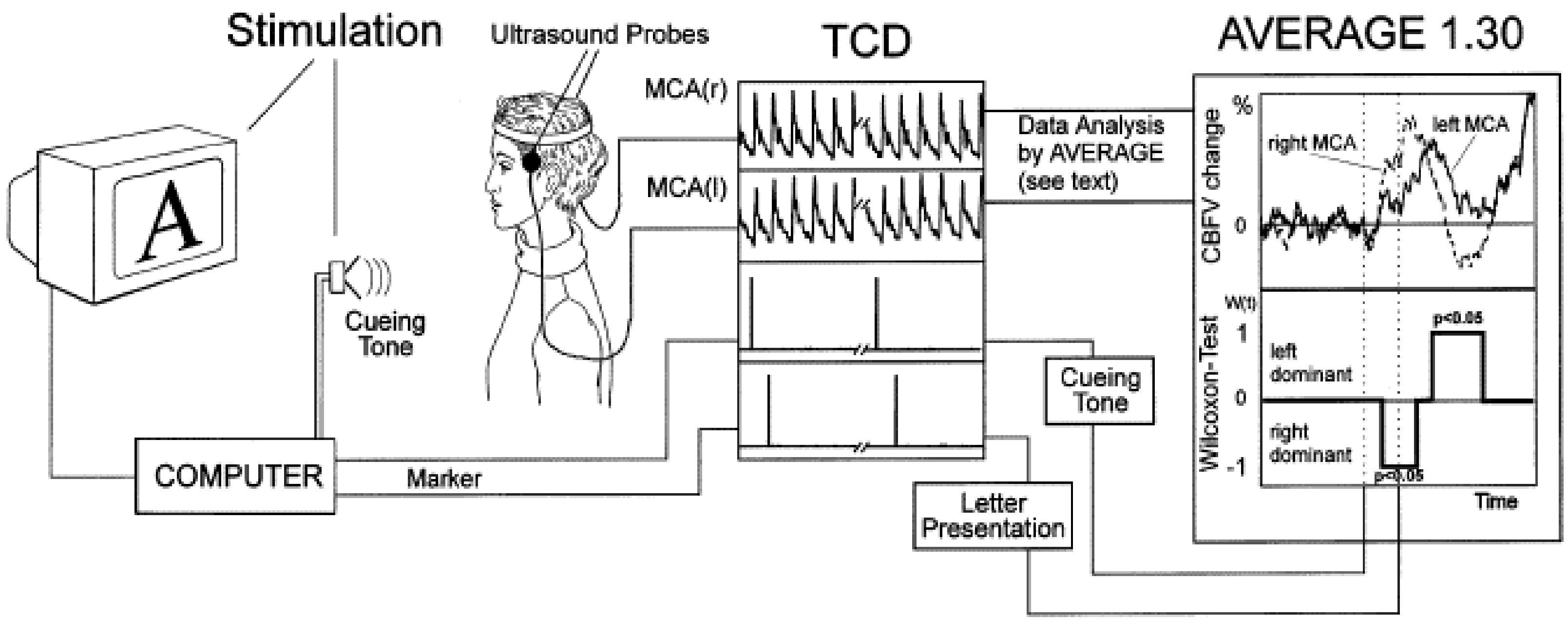


Fig. 1. Example setup of a fTCD study for the assessment of attention and language dominance (Knecht et al., 1996). Two ultrasound probes are mounted on both temples of a volunteer and are adjusted for assessment of the blood flow velocity of the left and right middle cerebral arteries (MCAs). The cerebral 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 !