Impact of induced hypertension on cerebral oxygen delivery in subarachnoid hemorrhage

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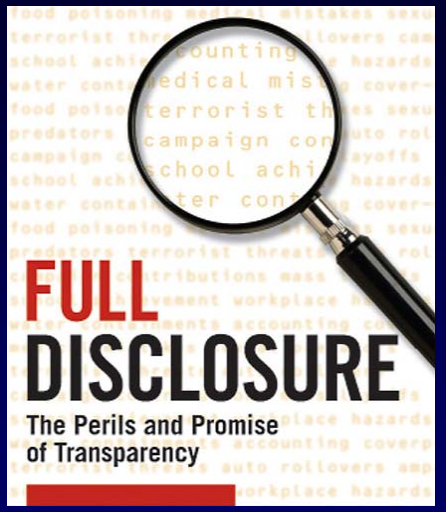
Disclosure

- Research
  - National Institutes of Health (NINDS)
- Consulting
  - Actelion Pharmaceuticals
- Financial interest
  - None



Delayed cerebral ischemia

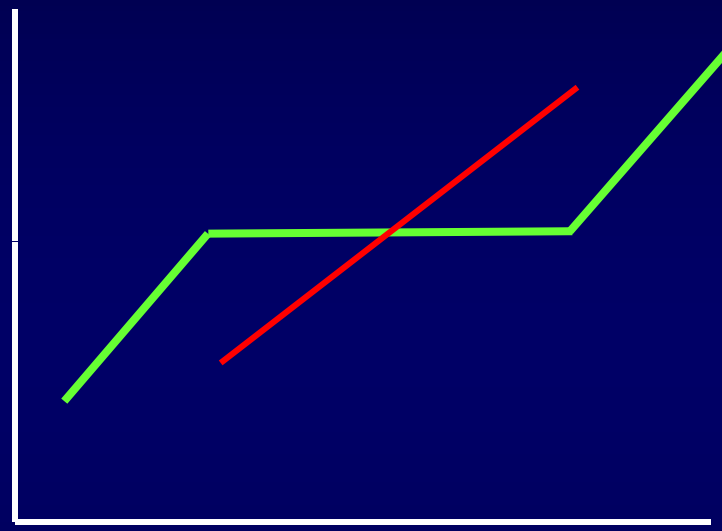
- Delayed cerebral ischemia (DCI) is a major cause of secondary neurological injury following SAH
- DCI results from reduced CBF and oxygen delivery (DO_2) attributed to:
  - Arterial vasospasm
  - Intravascular volume depletion
  - Impairment of autoregulatory function

Treating DCI

- Interventions targeted at restoring CBF and oxygen delivery in symptomatic patients include:
- Endovascular intra-arterial
  - Angioplasty
  - Vasodilators
- Hemodynamic augmentation
  - Augmenting cardiac output
  - Induced hypertension

Autoregulation

- Impaired in ischemic brain
- Frequently impaired in SAH patients
- Impaired autoregulation is associated with poor outcome



Autoregulation

- But –

  Impaired autoregulation may be necessary for induced hypertension to be effective in improving oxygen delivery (DO_2)

Hypothesis

- Induced hypertension improves oxygen delivery only if autoregulation is impaired

Methods

- Patients part of a blinded of simvistatin 80 mg/d or placebo
- Early aneurysm repair, nimodipine and aggressive hydration
- On post-hemorrhage day 7-9
  - Routine conventional angiography
  - Static autoregulation assessed with PET

Methods

- CBF, CBV, OEF and $CMRO_2$ measured with ^{15}O PET
- Measurements made before and >10 minutes after change in blood pressure
- MAP raised by 20 ± 5% with phenylephrine

Definitions

- Oxygen delivery (DO_2)
  - Arterial oxygen content (CaO_2) x CBF
- Autoregulatory index (AI)

$$AI = \frac{\%\Delta \text{ CBF}}{\%\ \Delta \text{ MAP}}$$

- Oligema
  - DO2 < 4.5 ml/100g/min and
  - OEF > 0.5

Patients	N=8
Age	60 ± 10.3
Gender	4 each
WFNS 1	0
WFNS 2	2
WFNS 3	4
WFNS 4	1
WFNS 5	1
Modified Fisher 1	0
Modified Fisher 2	1
Modified Fisher 3	5
Modified Fisher 4	2
Hypertension	5
Elevated troponin	5
Ventriculostomy	7

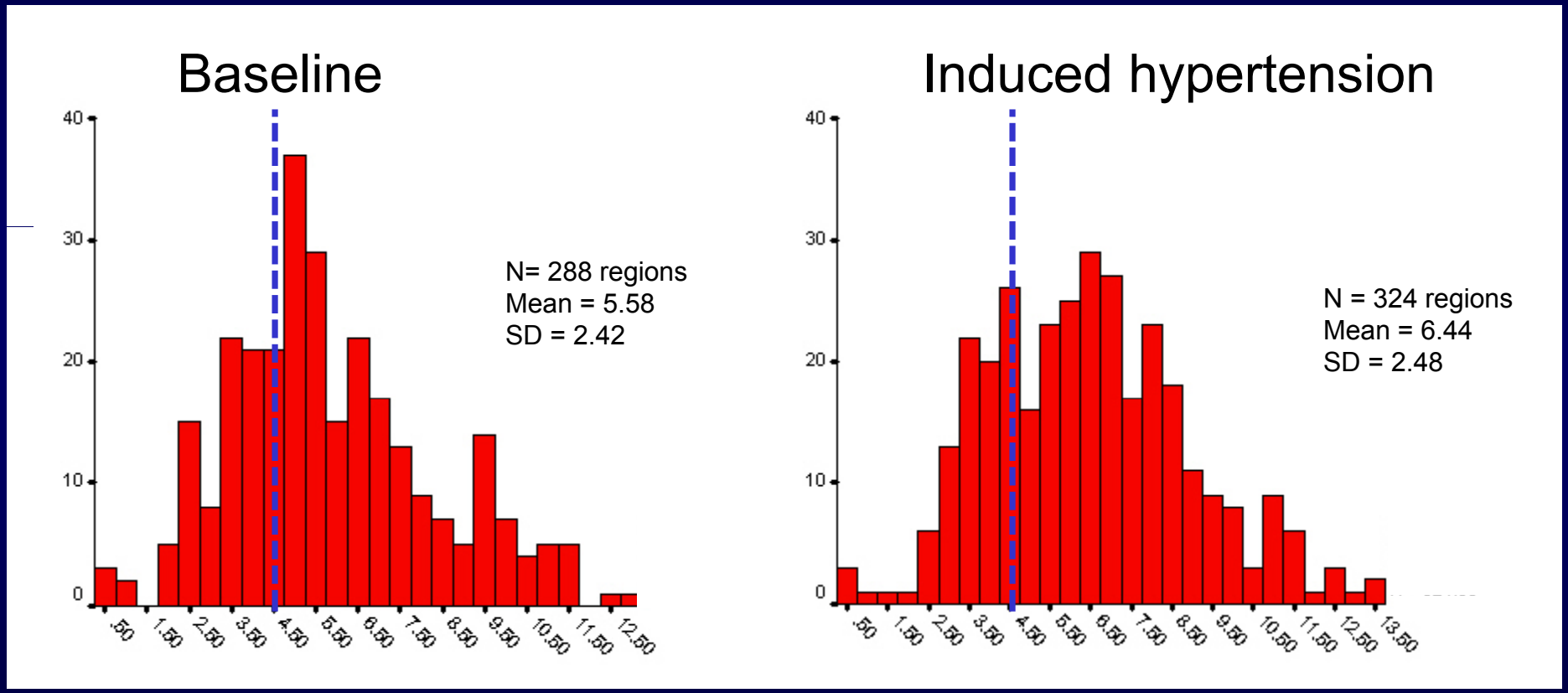
Course and outcome

Angiographic vasospasm	1	
Clinical vasospasm	0	
Hospital disposition	Home	2
	Rehabilitation	4
	SNF	1
	Died	1

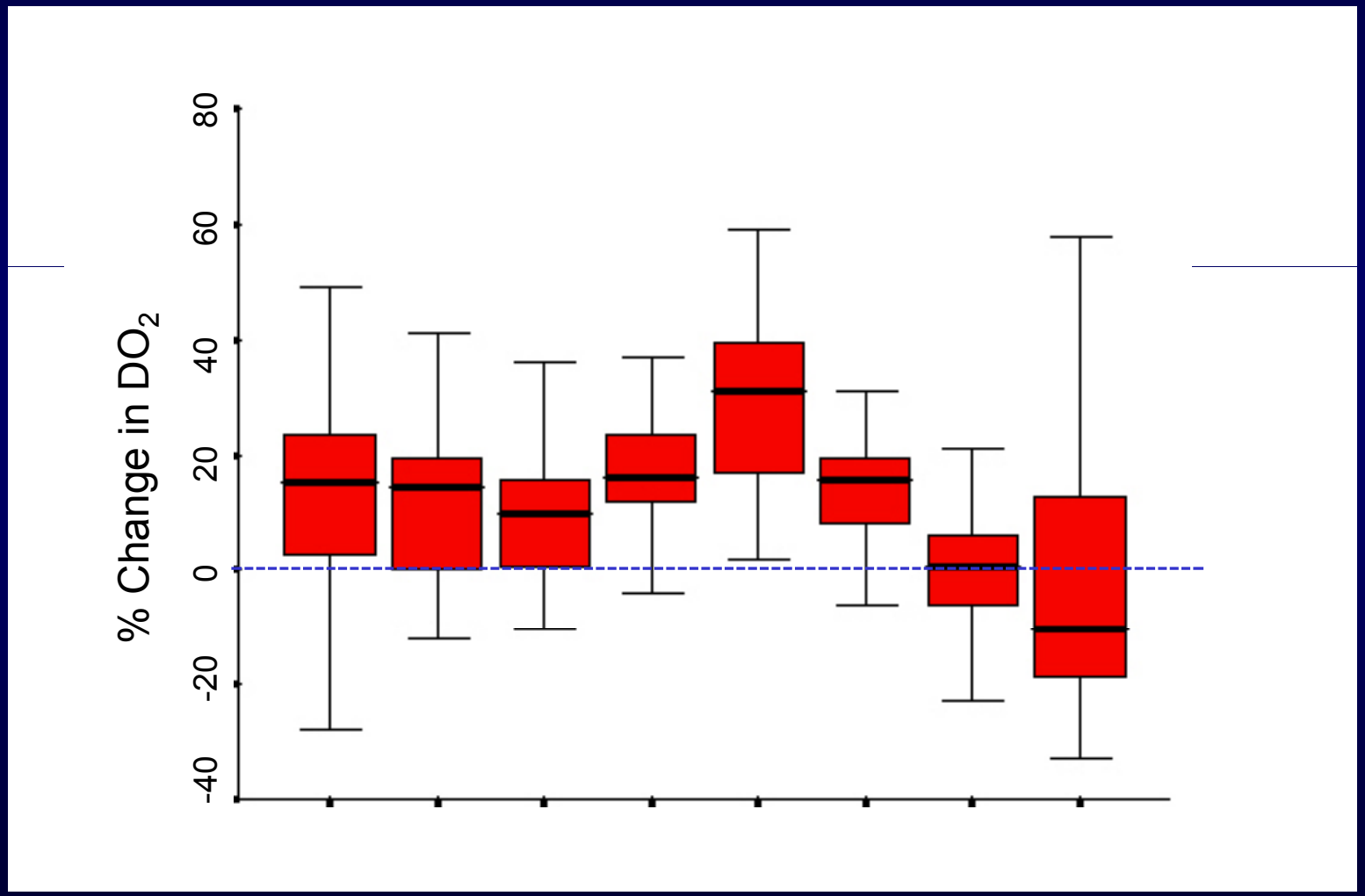
Response to induced hypertension

Global response			
	Baseline	Elevated MAP	p
MAP (mm Hg)	107.70 ± 7.6	136.2 ± 5.25	< 0.000
CBF (ml/100g/min)	40.8 ± 16.2	44.5 ± 17.0	0.001
DO_2 (ml/100g/min)	3.93 ± 1.37	4.30 ± 1.50	0.03

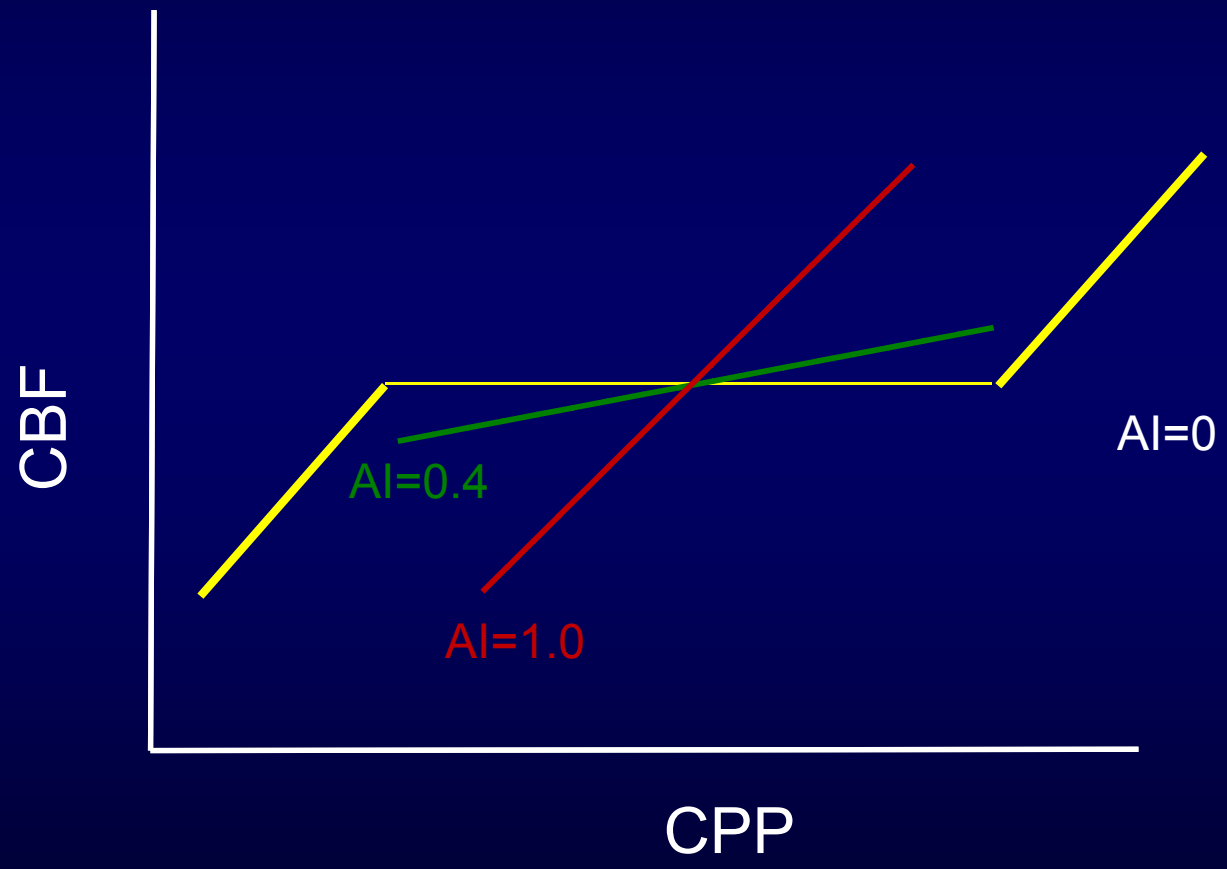
Change in regional distribution of DO_2



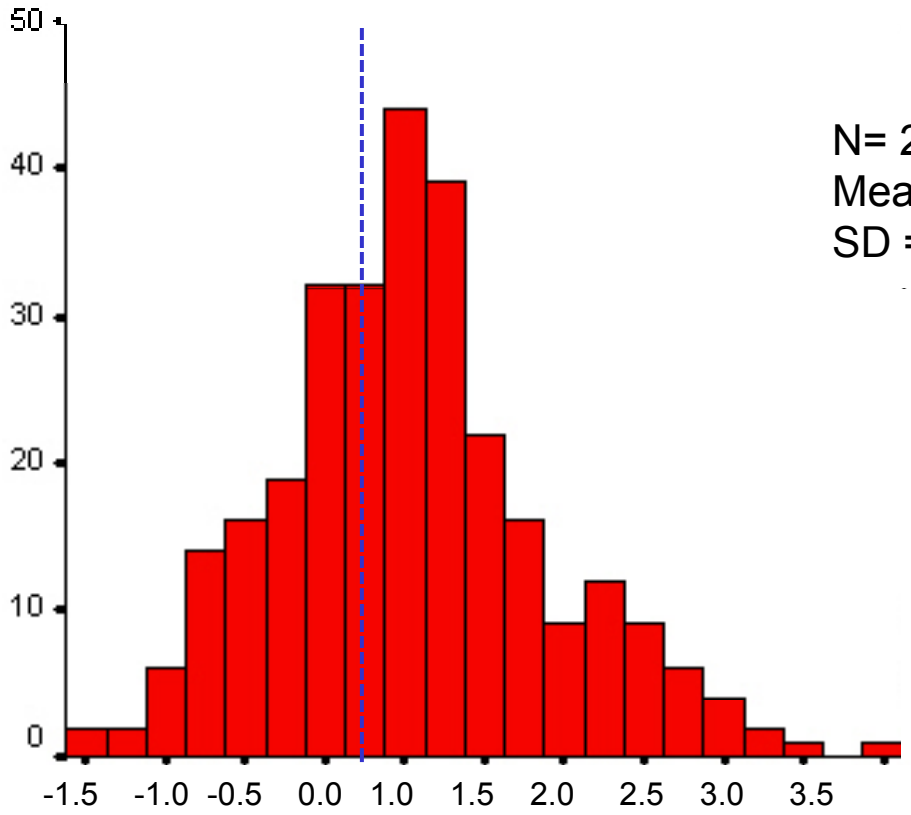
Regional change in DO_2 for individual patients



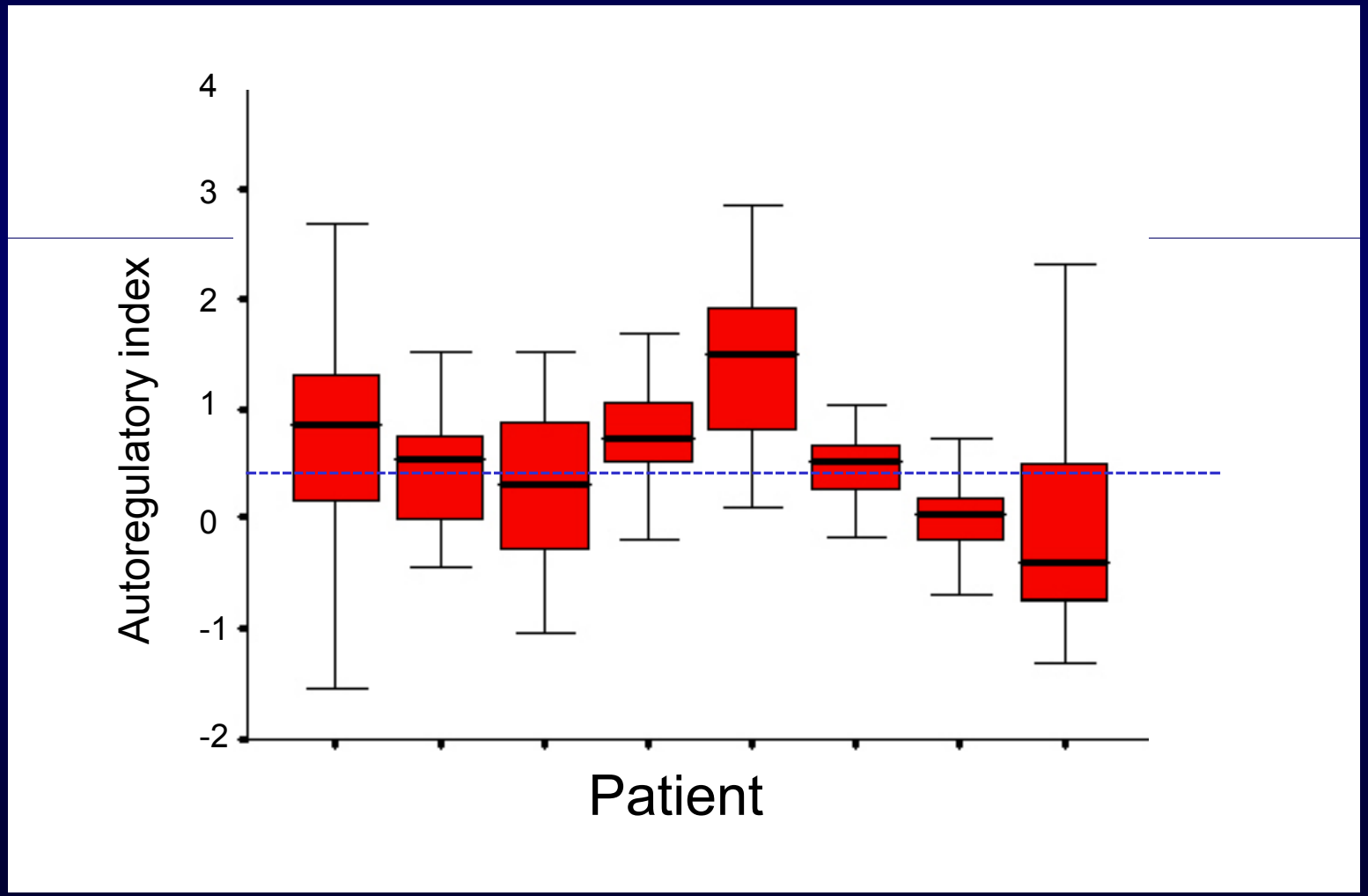
Autoregulatory index = $\frac{\%\Delta \text{ CBF}}{\%\ \Delta \text{ MAP}}$



Regional distribution of AI



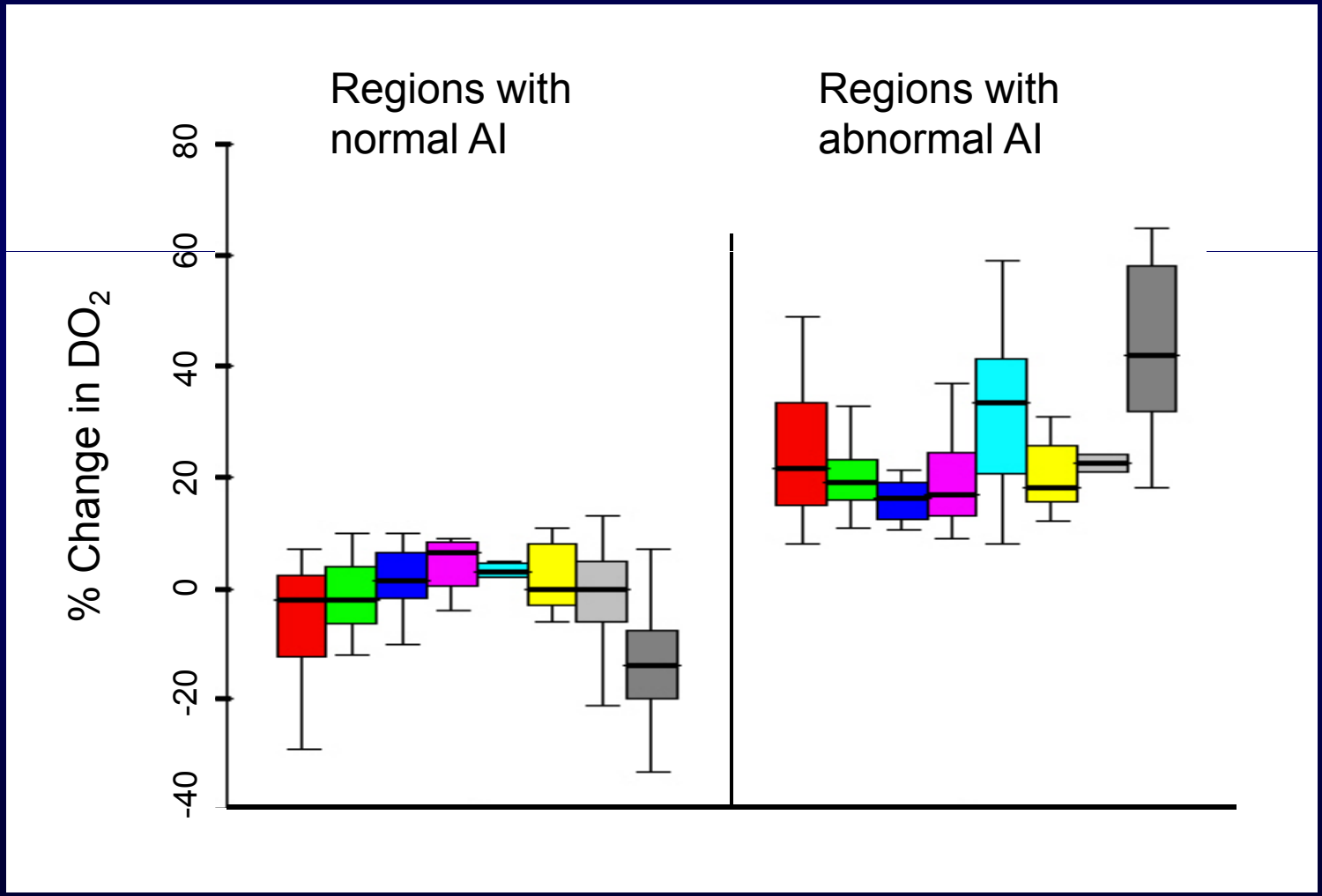
Autoregulatory index for individual patients

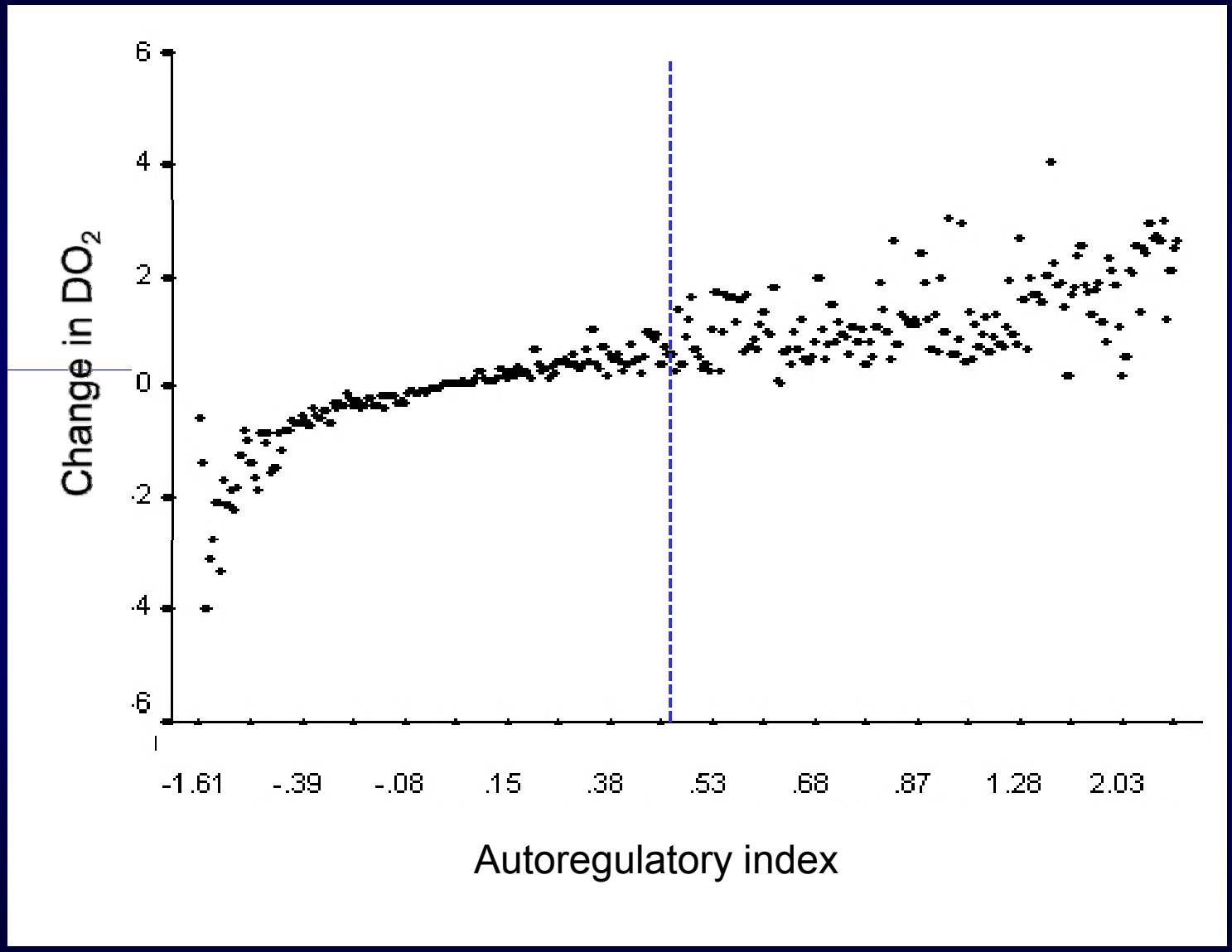


Regional O_2 delivery and autoregulation

DO_2 in regions by autoregulatory index			
	Baseline	Hypertension	p
Normal AI	4.05 ± 1.53	4.37 ± 1.77	0.1
Abnormal AI	4.07 ± 2.79	4.95 ± 2.77	0.03

DO_2 rises only in regions with abnormal autoregulatory index

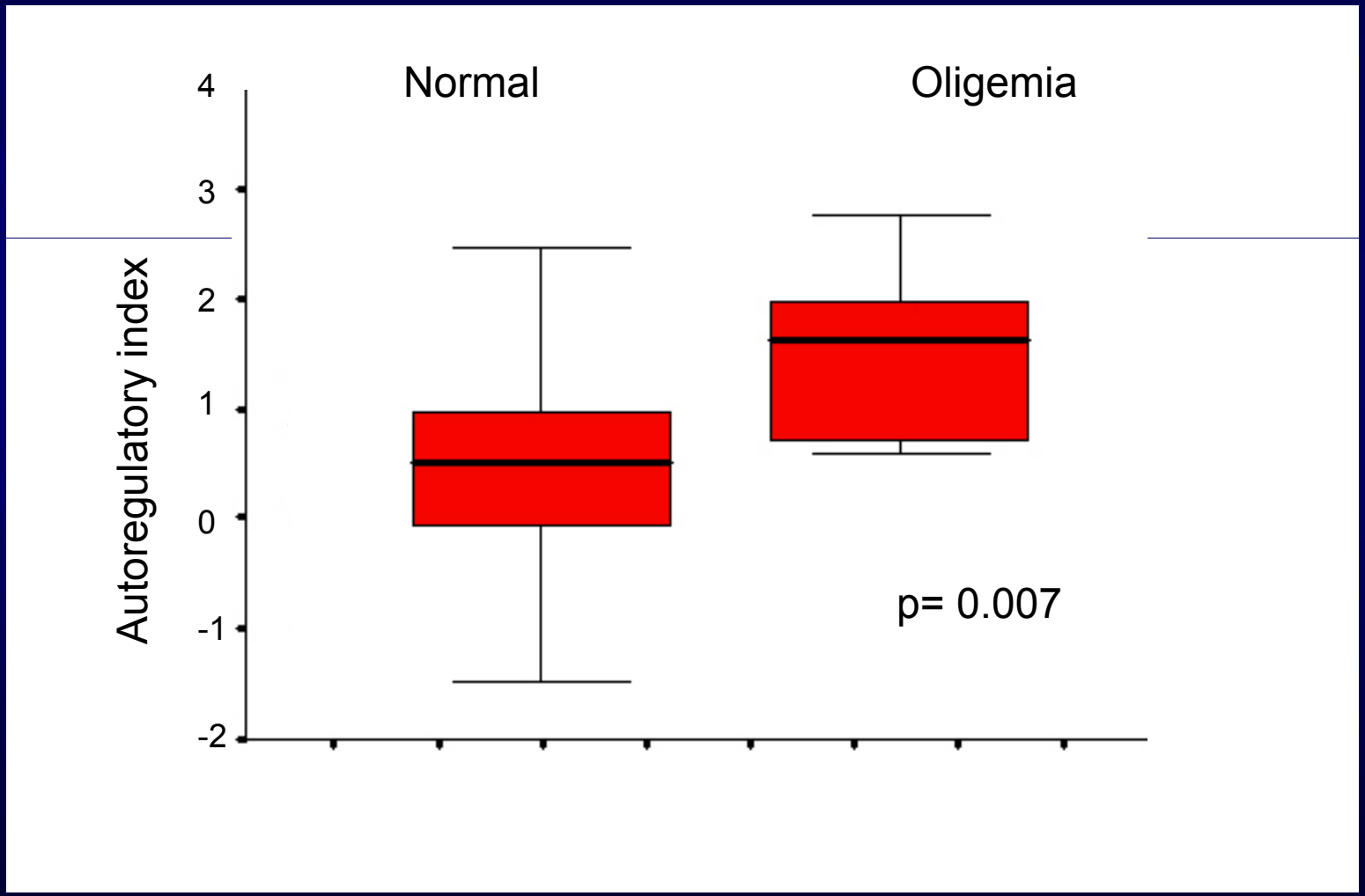



Change in DO_2
6
4
2
0
-2
-4
-6
-1.61
-.39
-.08
.15
.38
.53
.68
.87
1.28
2.03
Autoregulatory index

What regions have abnormal AI?

- Baseline low CBF
- Baseline low DO_2
- Angiographic vasospasm
- Baseline oligemia

AI is abnormal in oligemic regions



Conclusion

- Induced hypertension improves global oxygen delivery
  - More robust in patient with impaired AI
- Regional response limited to brain regions with impaired autoregulation
- Impaired autoregulation is associated with oligemia

Limitations

- Potential effect of simvastatin
- Few subjects
- No patients with clinical evidence of DCI