Perugia
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The Impact of Cerebral Hemodynamics on Cognitive Functioning in Patients with Carotid Artery Stenosis

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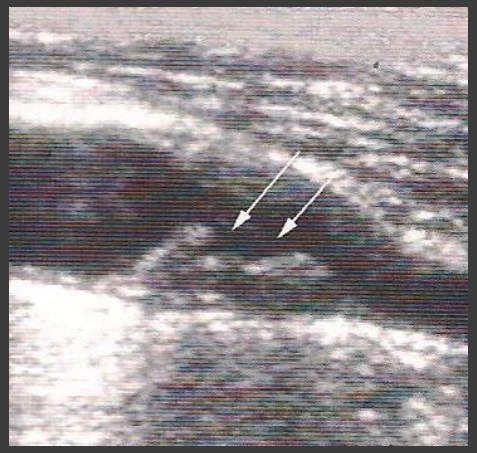
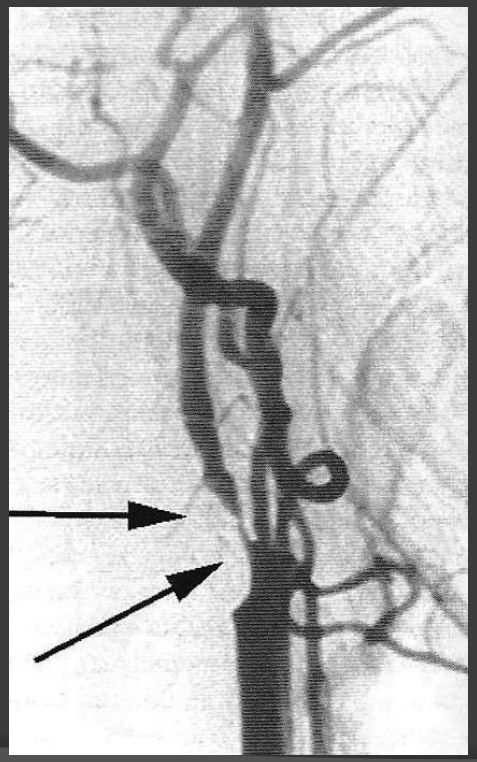




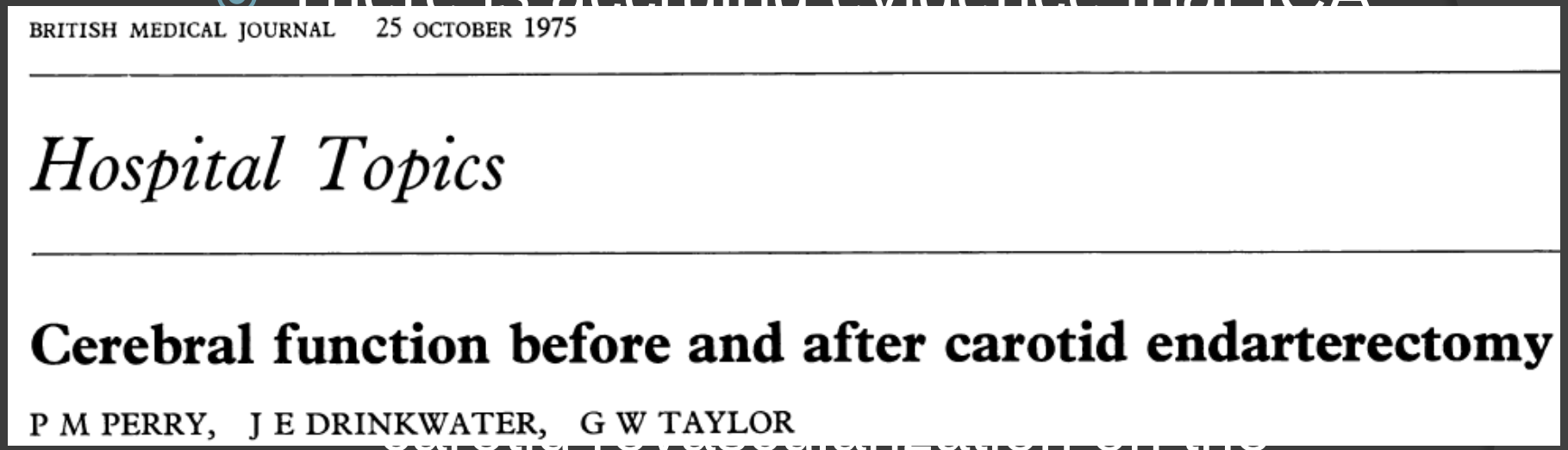
- Moderate to severe internal carotid artery (ICA) is common (10% by the 8th decade)

- It may be responsible of:
  - distal **embolization** (plaque vulnerability)
  - impairment of cerebral **hemodynamics** (dilation of cerebral arterioles to counteract the drop in cerebral perfusion pressure)

- It causes about 10% of all strokes
- Carotid endarterectomy (CEA) is effective to prevent cerebral ischemia in patients with symptomatic ICA stenosis

Beyond stroke ...

- There is accruing evidence that ICA



BRITISH MEDICAL JOURNAL 25 OCTOBER 1975

Hospital Topics

Cerebral function before and after carotid endarterectomy

P M PERRY, J E DRINKWATER, G W TAYLOR

neurocognitive functioning remains unclear

Research Project

To evaluate the **changes** in **cognitive performance** and **cerebrovascular reactivity** and identify their **predictors** in patients with symptomatic high-grade ICA stenosis undergoing CEA

Study Design I

- Patients who underwent CEA, had suffered TIA within the past 6 months, and had an ipsilateral severe ICA stenosis
- Age- and sex- matched controls (1:1)

- Evaluations (T0 - T6 months) of:

  - cerebral hemodynamics [CVR to hypercapnia through the breath-holding index (BHI)];

  - neuropsychological functions

  [right: CPM, CFCT; left: (ph) and (ca) VF]

Study Design II

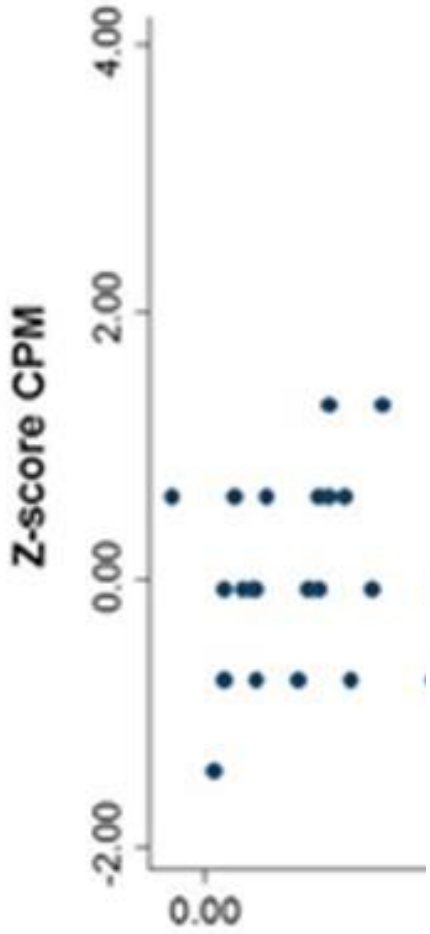
- Change in CVR and cognitive performance (delta between follow-up and baseline values)

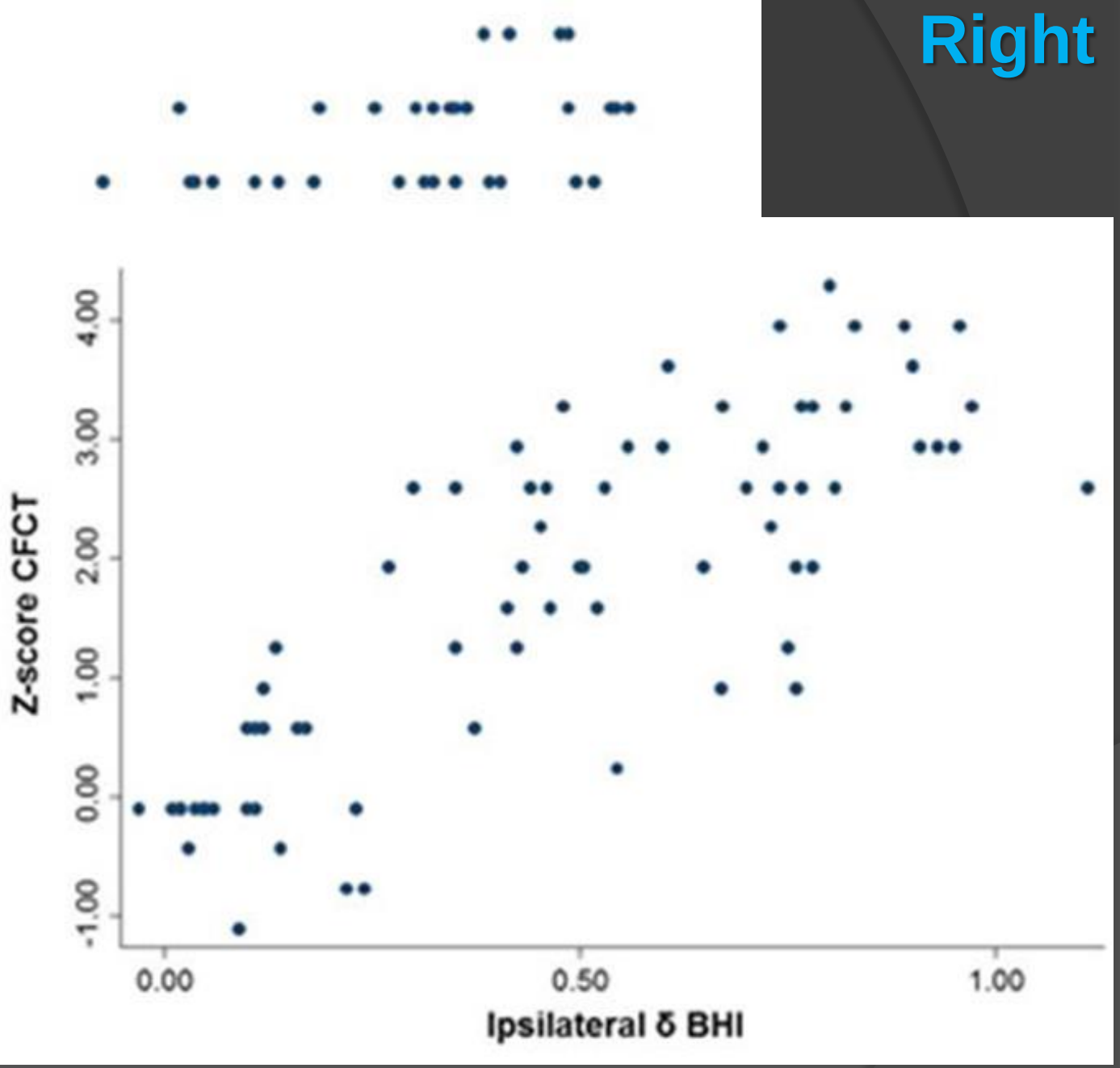
- In order to account for practice effect, Z-scores for CEA patients were derived from the reference control group's performance
  Z-score= [(change score $_{CEA}$ - mean change score $_{control}$)/SD of change score $_{control}$]

	Right ICA stenosis	Left ICA stenosis	Control Group
Demographics			
Age (years)	73.5 (7.2)	72.9 (6.4)	73.3 (6.7)
Male sex	53 (70.7)	42 (67.7)	95 (69.3)
Education (years)	8.5 (3.9)	9.1 (4.0)	9.1 (3.9)
Neurocognitive functioning			
Phonemic Verbal Fluency	19.9 (3.04)	12.0 (4.80)*	20.1 (1.99)
Category Verbal Fluency	22.0 (3.16)	13.8 (4.34)*	22.3 (1.96)
Coloured Progressive Matrices	26.6 (3.53)*	33.0 (2.77)	33.2 (1.53)
Complex Figure Copy Test	27.2 (3.54)*	33.4 (3.42)	33.9 (1.56)
Cerebral hemodynamics			
Ipsilateral BHI	0.54 (0.30)†	0.52 (0.31)†	1.08 (0.13)
Contralateral BHI	1.04 (0.22)	1.05 (0.20)	1.08 (0.13)

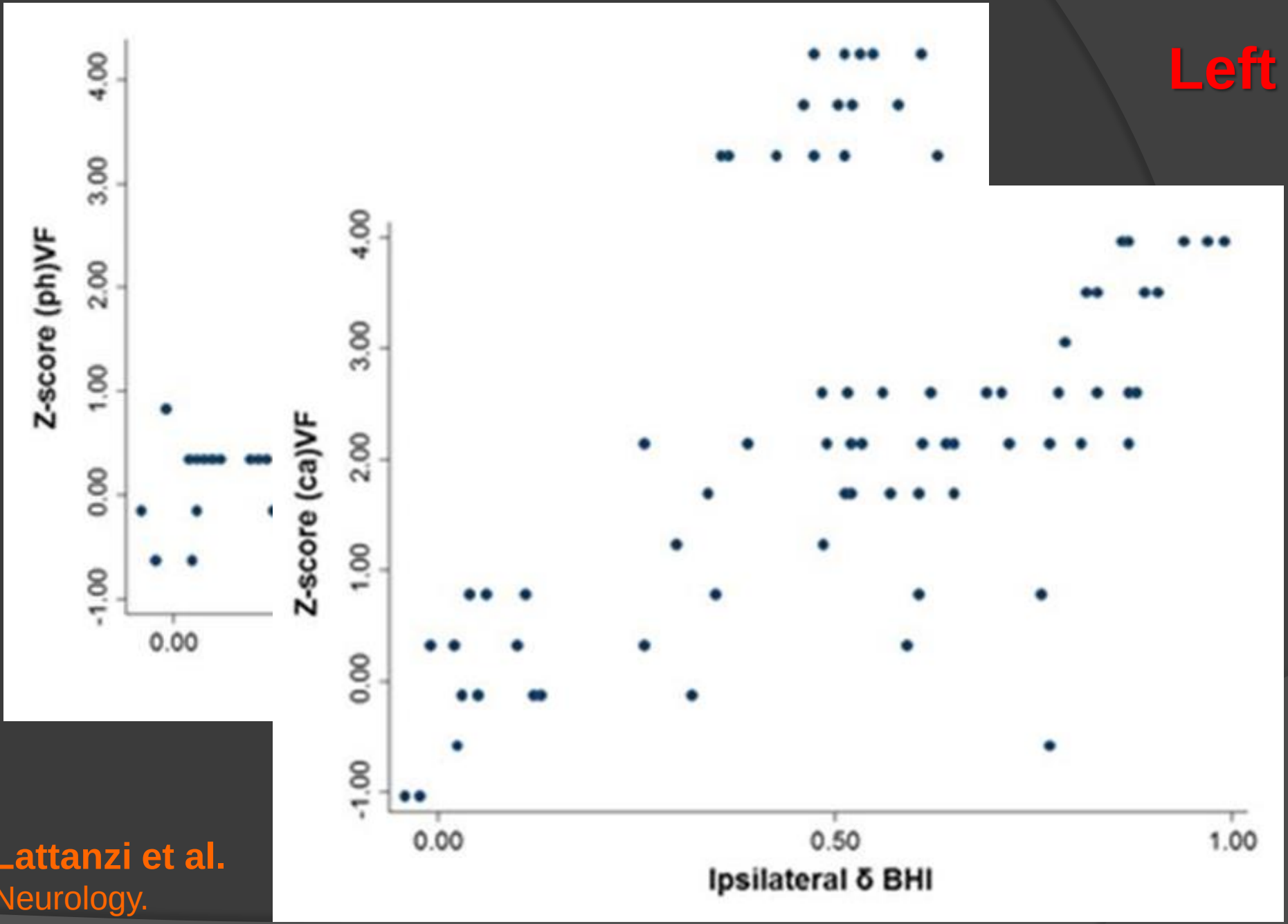
	Before CEA	After CEA	p value*
Right ICA stenosis			
Phonemic Verbal Fluency	19.9 (3.04)	20.4 (2.92)	0.106
Category Verbal Fluency	22.0 (3.16)	22.4 (2.69)	0.109
Coloured Progressive Matrices	26.6 (3.53)	29.2 (2.82)	<0.001
Complex Figure Copy Test	27.2 (3.54)	29.9 (2.62)	<0.001
Ipsilateral BHI	0.54 (0.30)	1.00 (0.19)	<0.001
Contralateral BHI	1.04 (0.22)	1.07 (0.13)	0.074
Left ICA stenosis			
Phonemic Verbal Fluency	12.0 (4.80)	16.1 (3.70)	<0.001
Category Verbal Fluency	13.8 (4.34)	17.7 (3.51)	<0.001
Coloured Progressive Matrices	33.0 (2.77)	33.3 (1.97)	0.262
Complex Figure Copy Test	33.4 (3.42)	33.6 (2.24)	0.152
Ipsilateral BHI	0.52 (0.31)	1.03 (0.17)	<0.001
Contralateral BHI	1.05 (0.20)	1.08 (0.11)	0.124

Right





Lattanzi et al.
Neurology.
2018;90:e307-15



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Multivariate analysis

The improvement of cognitive performance was directly related to the entity of the increase in vasomotor response on the side of revascularization

Ipsilateral δ BHI

	Unadjusted			Adjusted*		
	β	95% CI	p	β	95% CI	p
Right ICA stenosis						
Colour Progressive Matrices	3.89	3.29-4.48	<0.001	3.62	3.01-4.24	<0.001
Complex Figure Copy Test	3.79	3.19-4.40	<0.001	3.55	2.91-4.18	<0.001
Left ICA stenosis						
Phonemic Verbal Fluency	3.77	3.11-4.43	<0.001	3.31	2.68-3.95	<0.001
Category Verbal Fluency	3.58	2.95-4.22	<0.001	3.26	2.61-3.92	<0.001

Does one size fit all?

- Looking at baseline patients characteristics to identify the potential **predictors** of cognitive outcome ...
- Identify **subgroups** of patients who might mostly **benefit** from stenosis correction …

Dependent Variable	Univariate Regression Analysis			Multivariable Regression Analysis		
	β coefficient	95% CI	p value	β coefficient	95% CI	p value
Age	-0.11	-0.17 to -0.05	<0.001	-0.17	-0.22 to -0.12	**<0.001**
Sex	-0.03	-0.91 to 0.86	0.951	-0.24	-0.93 to 0.45	0.488
Side of ICA sten						0.570
Education						0.699
Current smoking						0.805
Hypertension						0.455
Diabetes mellitus						0.546
Dyslipidaemia						0.391
Coronary artery						0.085
Antihypertensive						0.251
Antidiabetics	0.15	-0.89 to 1.18	0.777	-1.48	-4.46 to 1.51	0.329
Lipid lowering drugs	0.17	-0.76 to 1.10	0.720	-0.01	-0.82 to 0.79	0.976
Antiplatelets	0.74	-3.25 to 4.73	0.716	0.64	-2.34 to 3.63	0.670
Ipsilateral BHI	-5.41	-6.49 to -4.34	<0.001	-6.25	-7.40 to -5.10	**<0.001**
Contralateral BHI	-3.78	-5.85 to -1.72	<0.001	0.83	-0.93 to 2.60	0.353

Independent predictors

Ipsilateral BHI

Age

Submitted

Independent Predictors

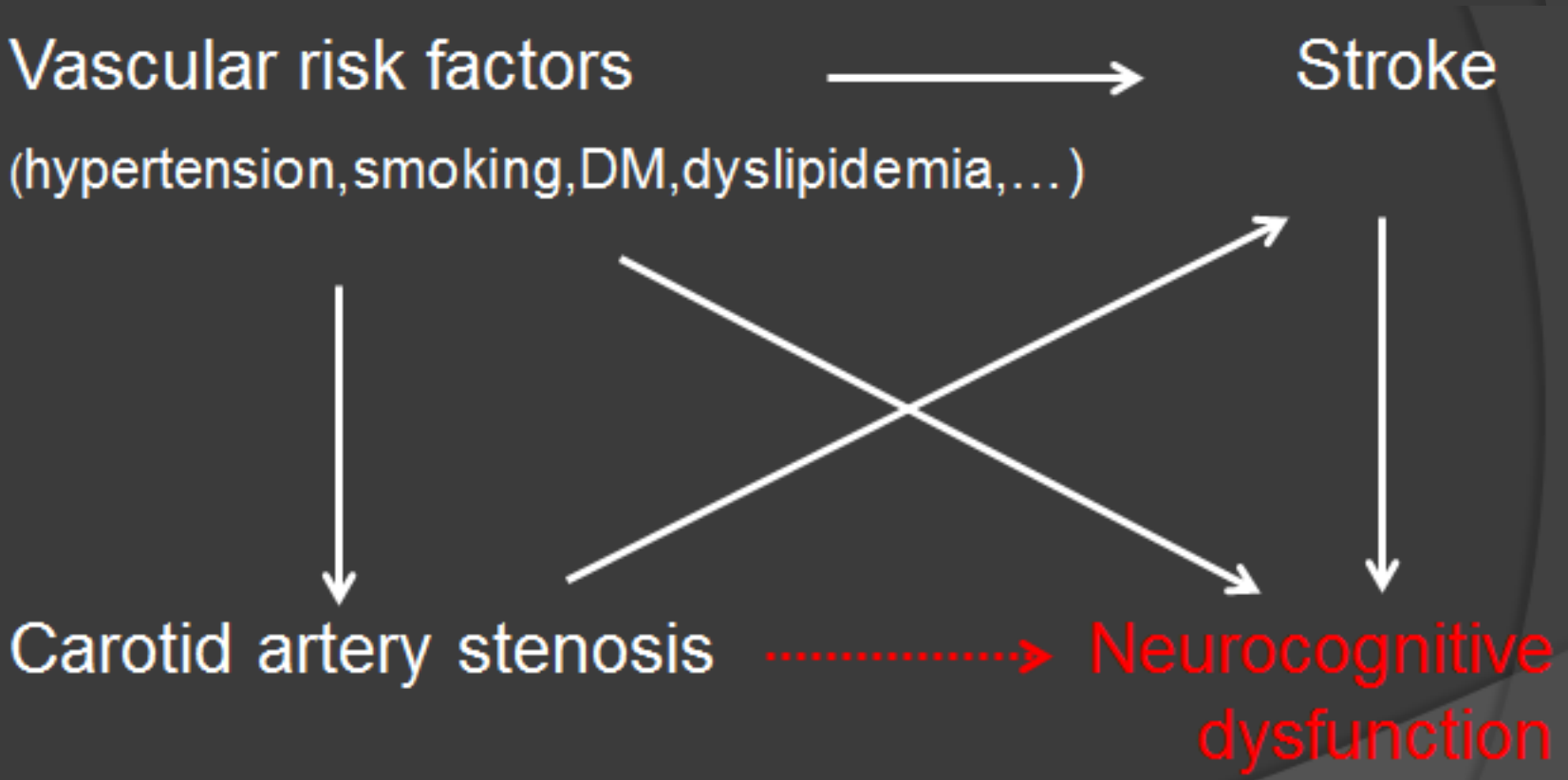
Ipsilateral BHI

greater pre-operative CVR impairment → greater neurocognitive benefit on the neuropsychological tests exploring the revascularized hemisphere following surgery → **hemodynamic contribution to cognitive impairment** could benefit from carotid revascularization

Age

- higher **burden of structural brain abnormalities** (e.g. silent infarcts, white matter lesions) not amenable to reverse
- structural, mechanical and functional changes of **vasculature** occuring with **aging** may hamper/reduce/delay the beneficial effects of blood flow restoration on CVR

Cerebrovascular hemodynamic insufficiency may represent one independent pathogenic mechanism underlying brain complications of carotid disease and a determinant of the cognitive dysfunction



Next Key Points & Clinical Implications

- Can threshold values in baseline hemodynamics/cognitive performance increase the accuracy of outcome prediction?

- Can **CEA** offer more than prophylaxis of cerebral ischemia and **contribute to improve the neurocognitive functioning** in “asymptomatic” carotid artery disease?

Refine the definition of symptomatic status and selection criteria for revascularization of ICA stenosis

Thanks

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