

UNIVERSITY OF FERRARA - ITALY



Vascular Diseases Center

UNIVERSITY OF FERRARA, ITALY

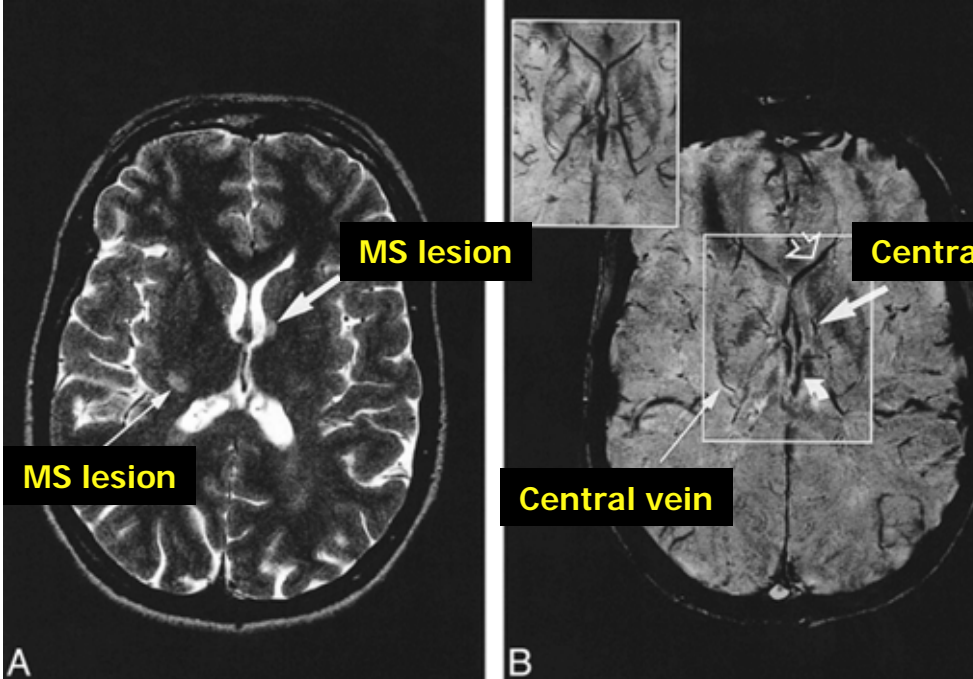
Vascular Diseases Center

Director: Prof. Paolo Zamboni

**Cerebro spinal venous outflow
impairment and multiple sclerosis:
a new challenge?**

London, Charing Cross Symposium 14-17 April 2007

BACKGROUND



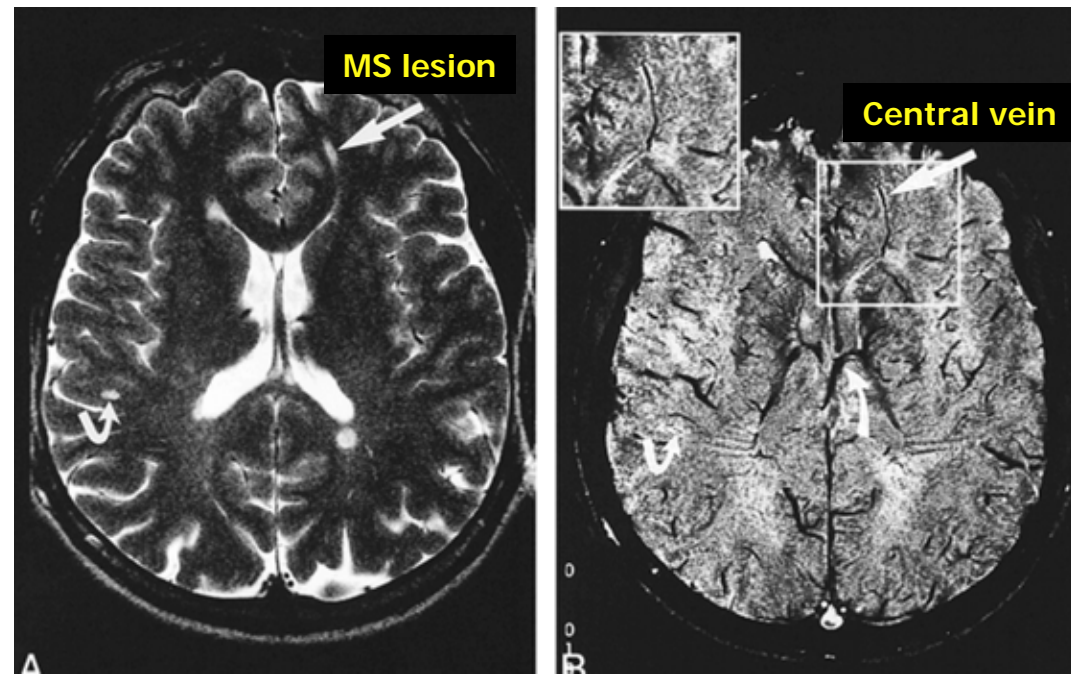
MR venography of multiple sclerosis.

Tan IL, van Schijndel RA, Pouwels PJ, van Walderveen MA, Reichenbach JR, Manoliu RA, Barkhof F.

AJNR Am J Neuroradiol. 2000;21:1039-42

MS and the venous system

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system characterized by focal venocentric lesions. In MS, MRI venography and dissection demonstrate a central vein oriented on the long axis of the inflammatory lesion, almost constantly a DMCVs



BACKGROUND: HISTOLOGY

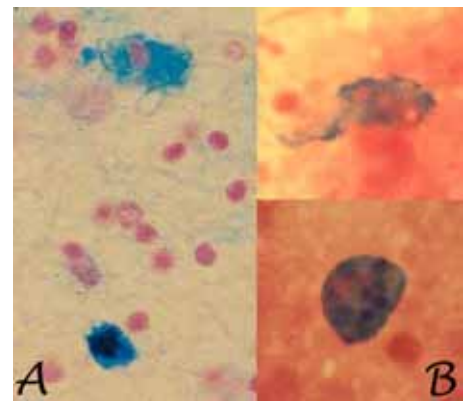
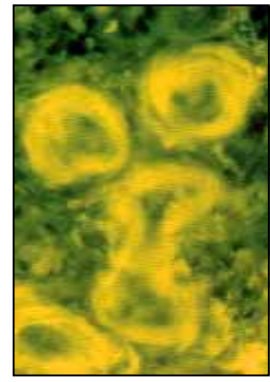
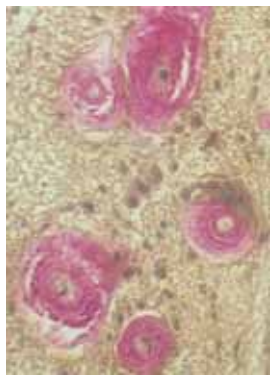
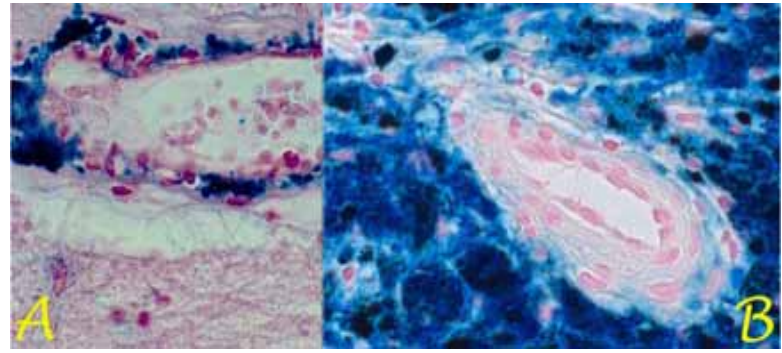
- perivenous iron stores

- Fibrin Cuffs

- Iron-laden macrophage

Multiple sclerosis

CVD



INFLAMMATION IN VENOUS DISEASE

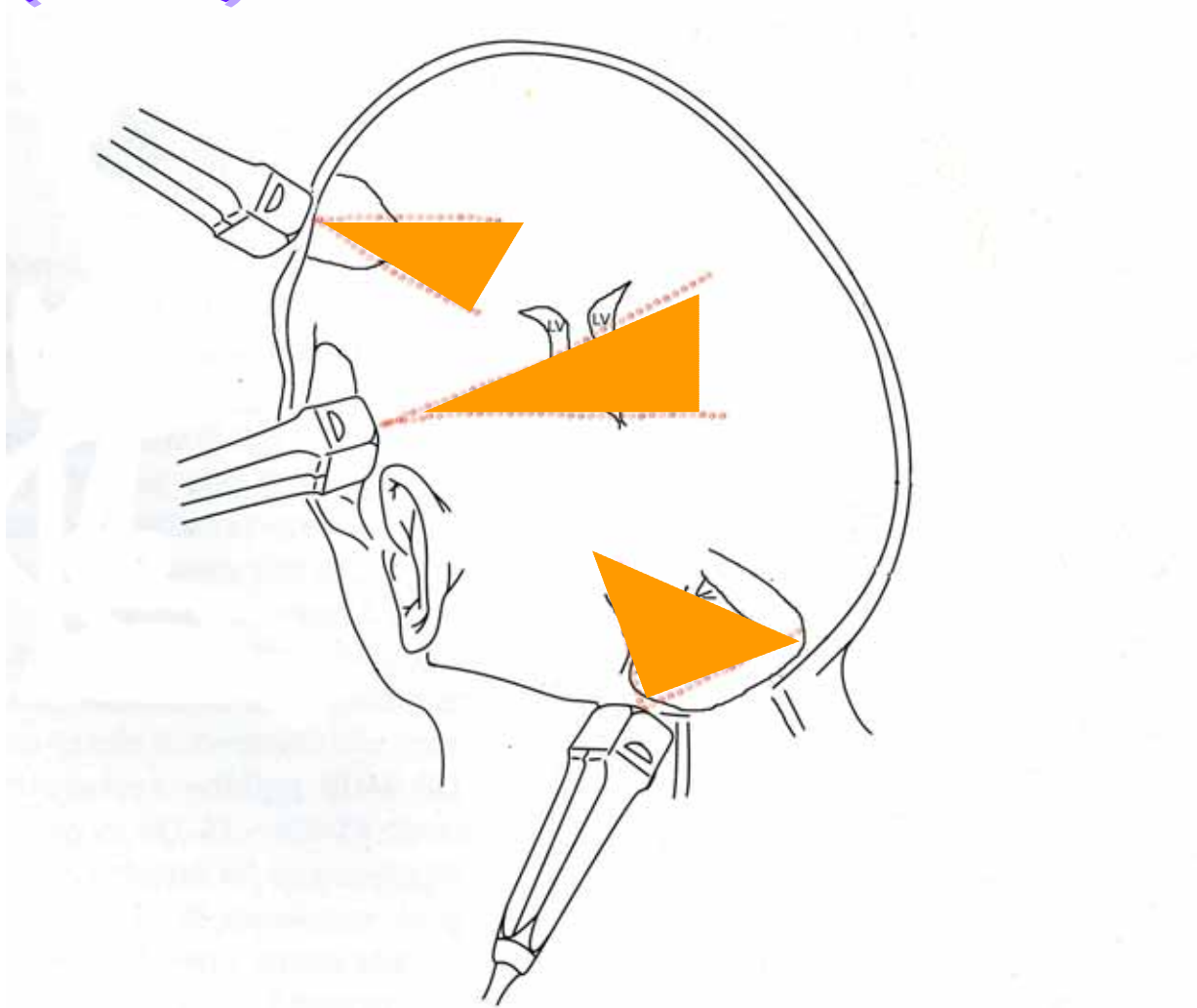
Key elements	CVD	MS
♣ altered venous haemodynamics	+	?
♣ microcirculation overload	+	+
♣ red blood cells and macromolecules extravasation	+	+
♣ increased iron deposits	+	+
♣ macrophages recruitment and infiltration	+	+
♣ iron-laden macrophages	+	+
♣ up-regulation of MMPs and down regulation of TIMPs	+	+
♣ association with HFE mutation	+	+
♣ Fibrin cuffs	+	+
♣ Perivenous iron deposits		

AIMS: to investigate cerebral venous return in MS

PATIENTS POPULATION

	Group A: MS patients (n=60)	Group B: Controls (n=60)
Age (\pmSD)	40.5 \pm 1.3	37.8 \pm 1.9
Sex, M/F	21M/39F	24M/36F
Clinical class RR/SP	39RR/21SP	-
EDSS	2.9 \pm 0.4	-
Disease Duration (years)	7.7 \pm 1	-

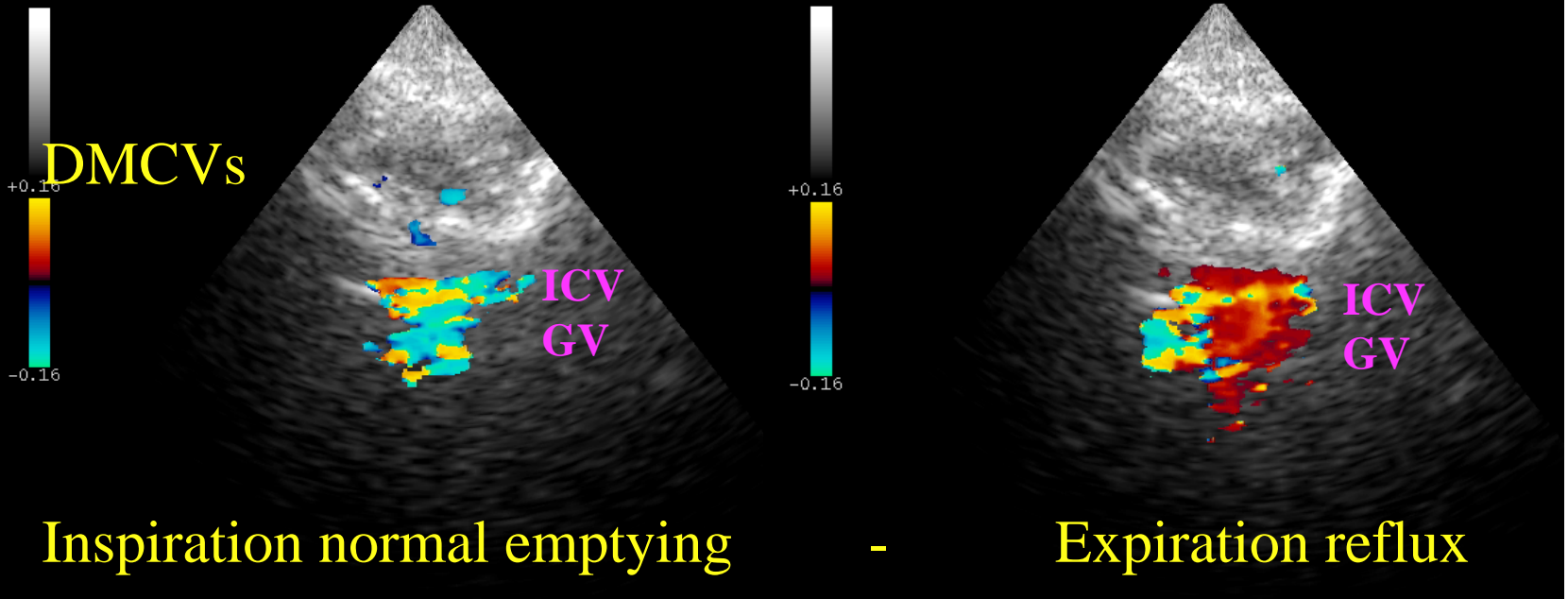
Transcranial coded color Doppler of the venous system (TCSS)





QuickTime™ and a
YUV420 codec decompressor
are needed to see this picture.

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YUV420 codec decompressor
are needed to see this picture.



FLOW →	MONODIRECTIONAL		BIDIRECTIONAL		REFLUX	
	Controls	MS	Controls	MS	Controls	MS
Veins↓						
TSs	48/60 80%	12/60 20%	8/60 13%	11/60 18%	4/60 7%	37/60 62%
dMCVs	58/58 100%	26/60 43%	0/58 0%	7/60 12%	0/58 0%	27/60 45%

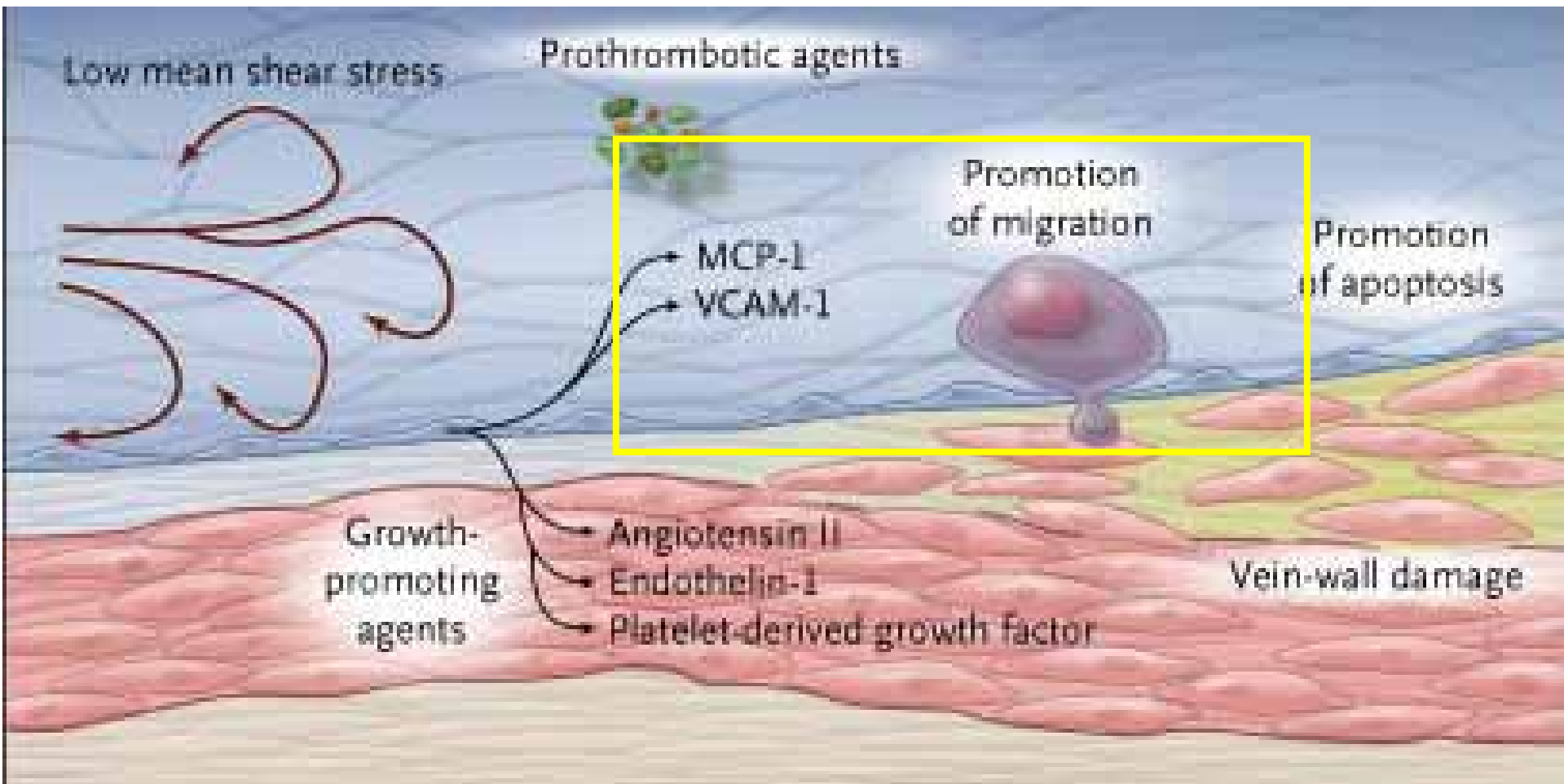
$P < 0.0001$

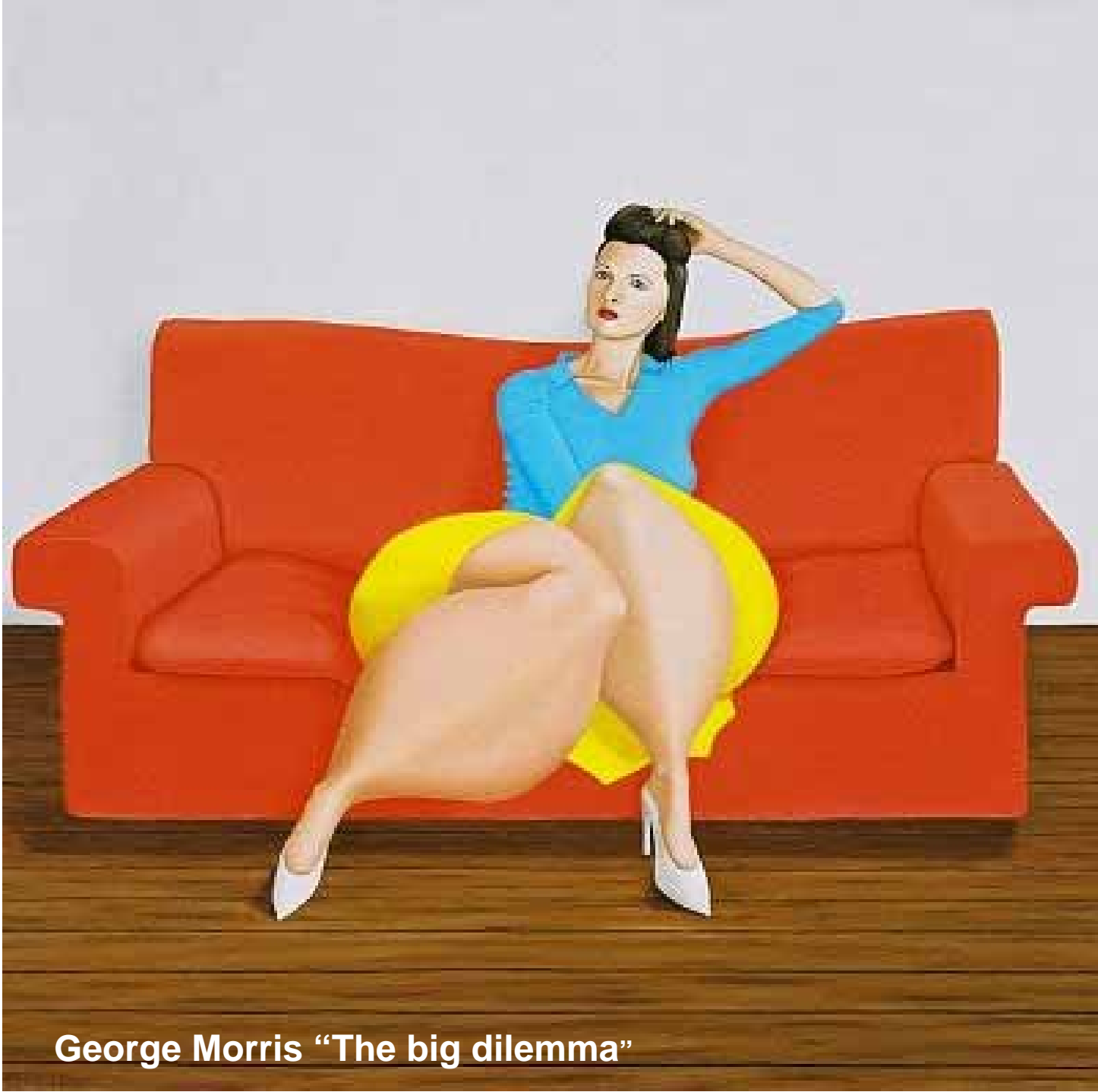
Venous reflux promotes expression of adhesion molecules on the venous wall, and white cells migration

New Engl J Medicine 2006

MS lesions are constantly venocentric and localized in the area of the DMCVs

Curr Opin Neurol 2006

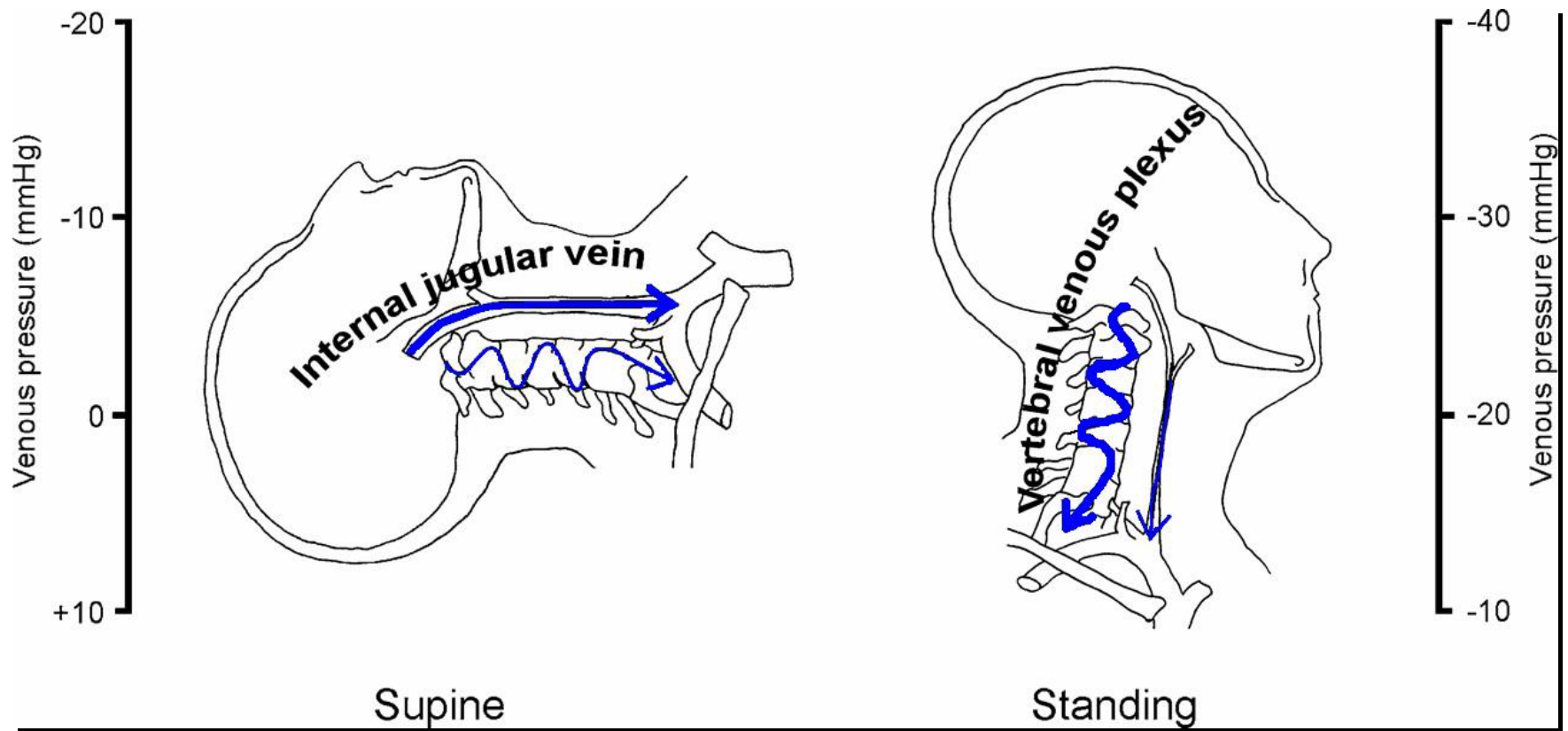




Is reflux a
consequence
of MS
inflammation
in turn
affecting the
cerebral
veins?

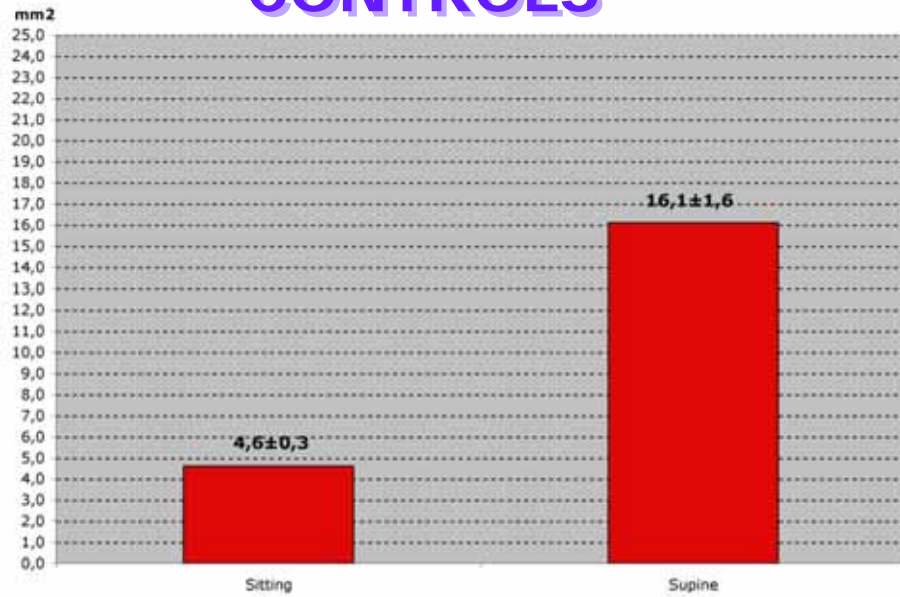
2ND PART OF
THE STUDY:
investigation
of extra-
cranial veins

George Morris "The big dilemma"

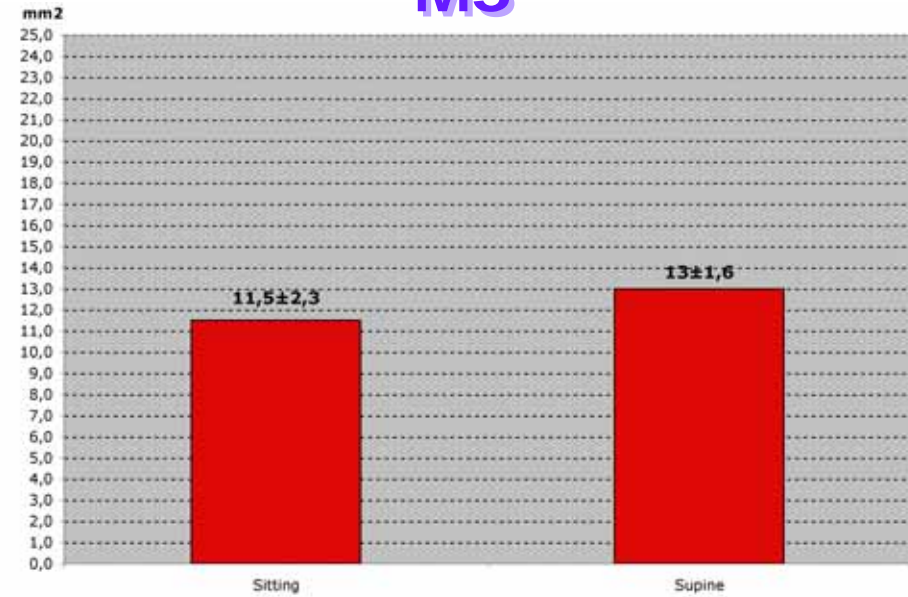


IN PHYSIOLOGY The IJV is the predominant venous outflow pathway in supine position, confirmed by an increased cross-sectional area (CSA), related to increased blood volume in that body position; redirection of venous flow to the vertebral veins (VVs) occurs in upright-position, with compliant reduction of the CSA of the IJV

CONTROLS

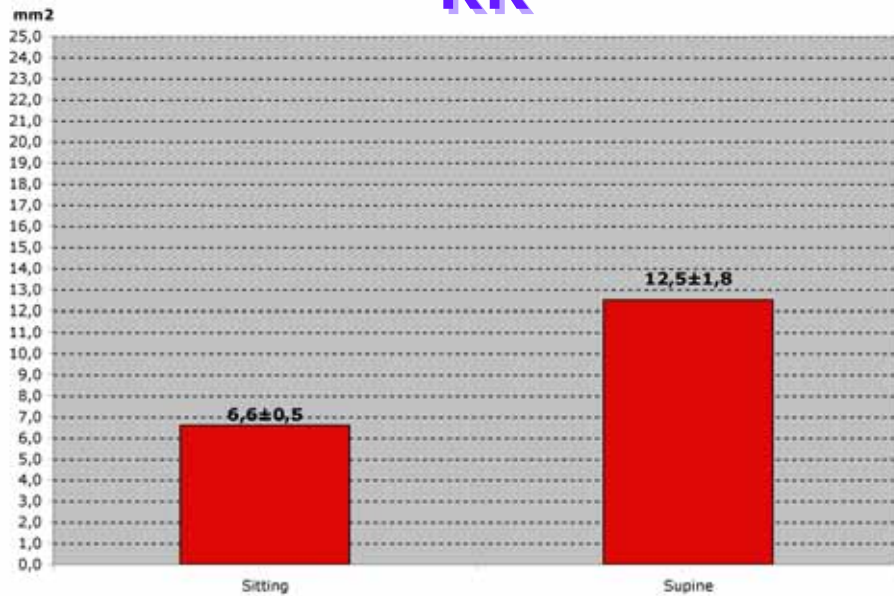


MS

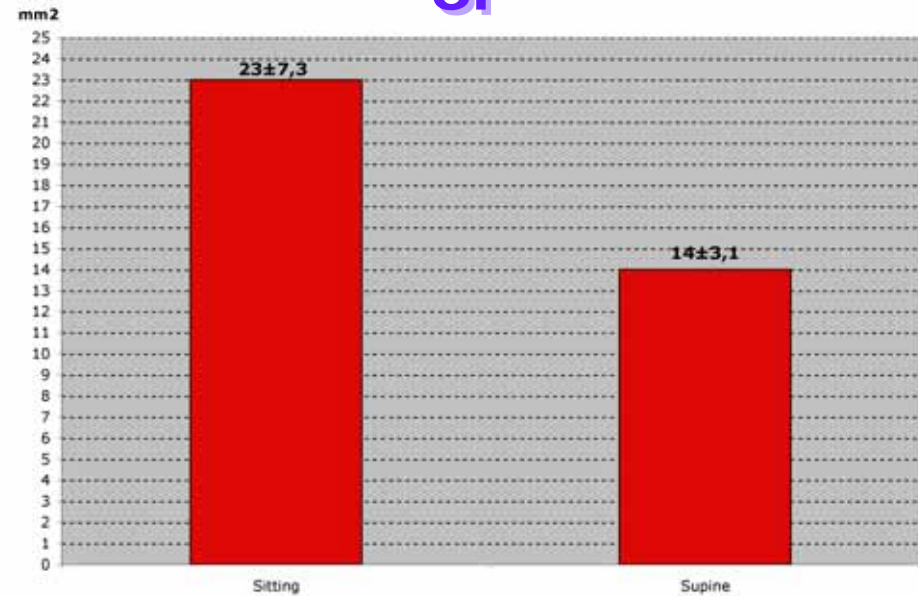


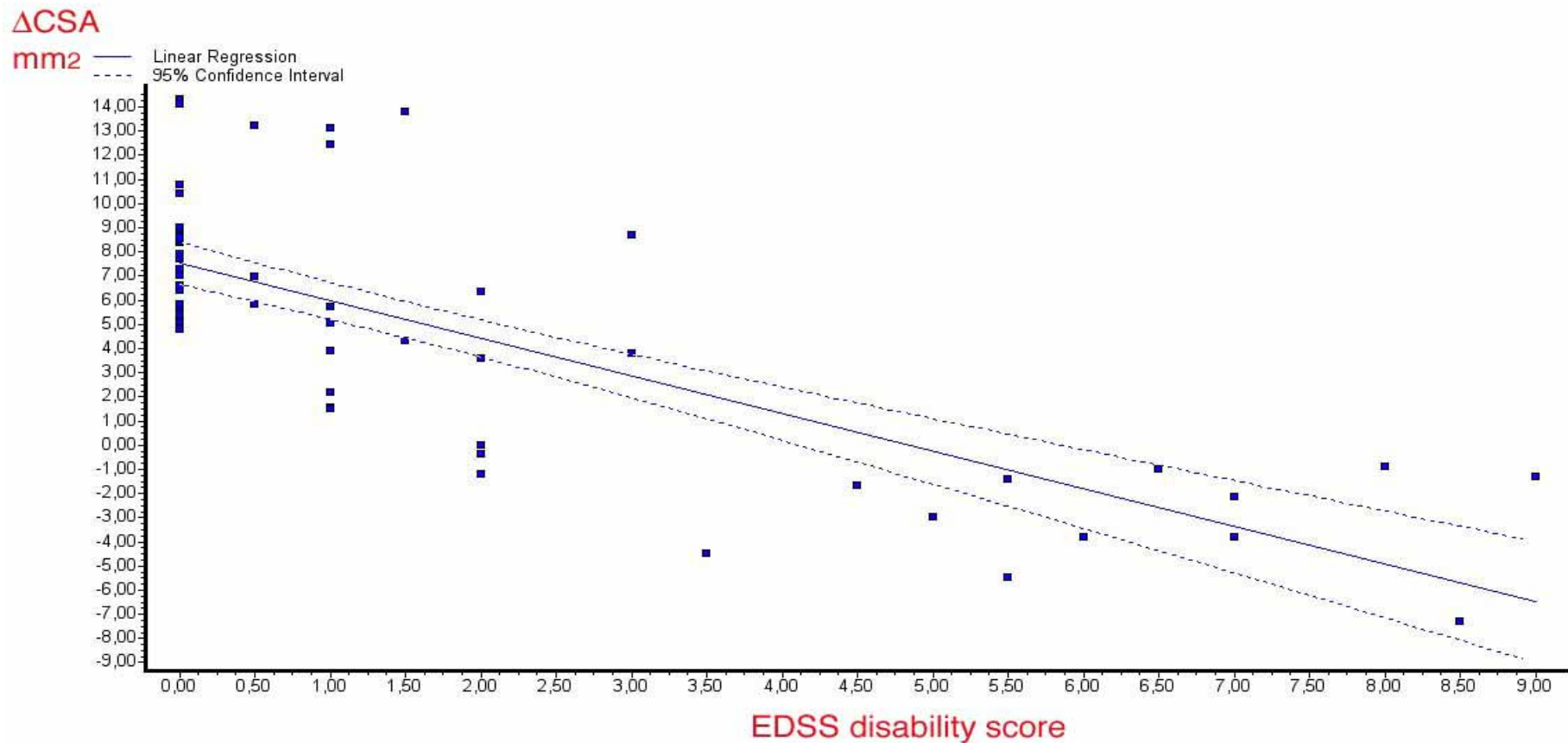
IJV CROSS SECTIONAL AREA IN SITTING AND SUPINE POSTURE

RR

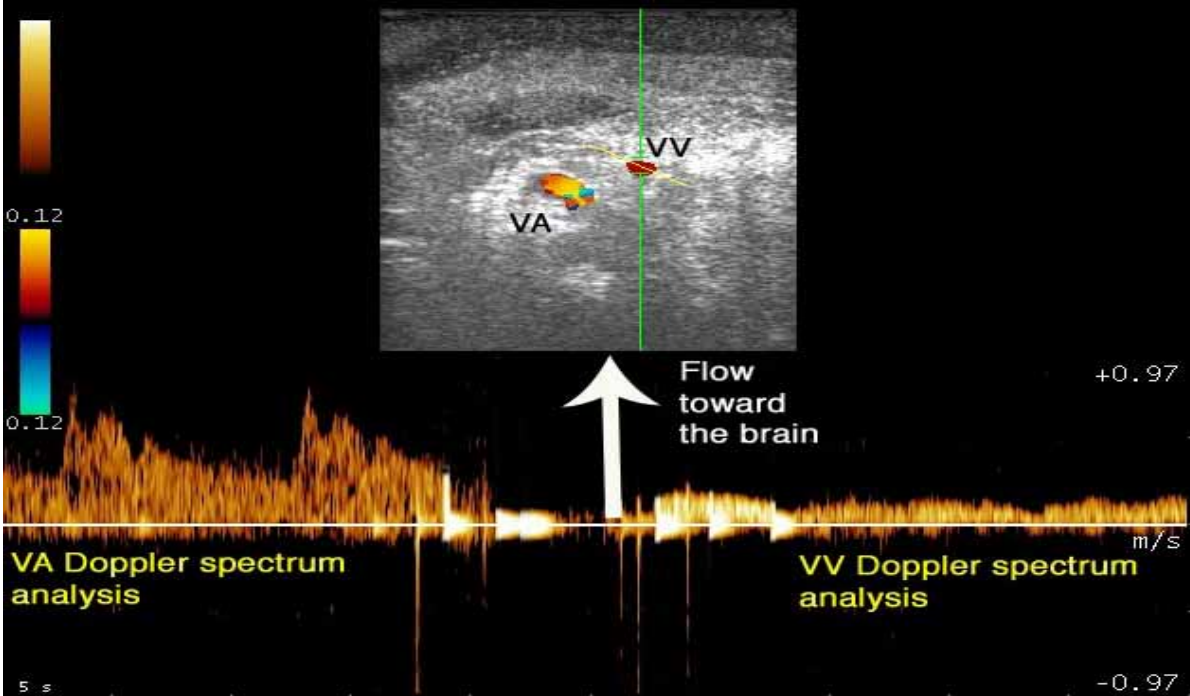


SP



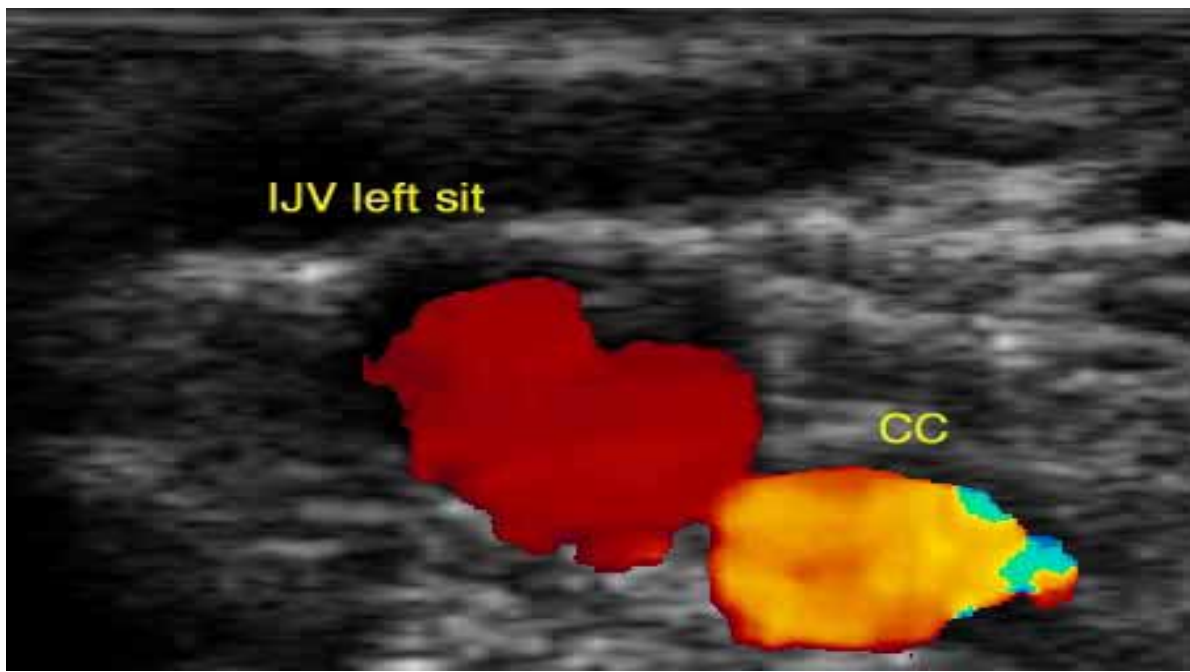


The difference between cross sectional area measured in supine and in sitting posture (Δ CSA) was inversely correlated to the EDSS disability score ($r^2 = - 0.6153$; $p < 0.0001$)



REFLUX RATE IN THE IJV, VV WAS SIGNIFICANTLY HIGHER IN MS ($P < 0.0001$).

IN MS PATIENTS REFLUX IN BOTH POSTURES WAS DETECTED IN 25% OF R-IJV, 43% L-IJV, AND IN 70% VV, VERSUS 0% IN CONTROLS



SUMMARY AND CONCLUSIONS

- ✓ **The postural mechanism regulating IJV out-flow is compromised in MS**
- ✓ **Δ CSA is correlated with the disability score**
- ✓ **Increased reflux rate in the extracranial veins**
- ✓ **Transmission of reflux in the DMCV, anatomically related to MS plaques**