

Central Obesity and Hypertension

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Framingham Offspring Study.
1987

75 and 65% of hypertension in men and women are attributable to obesity.

Adiposity stands out as a major controllable contributor to hypertension.

Waist circumference is more closely linked to cardiovascular disease risk factors than is BMI.

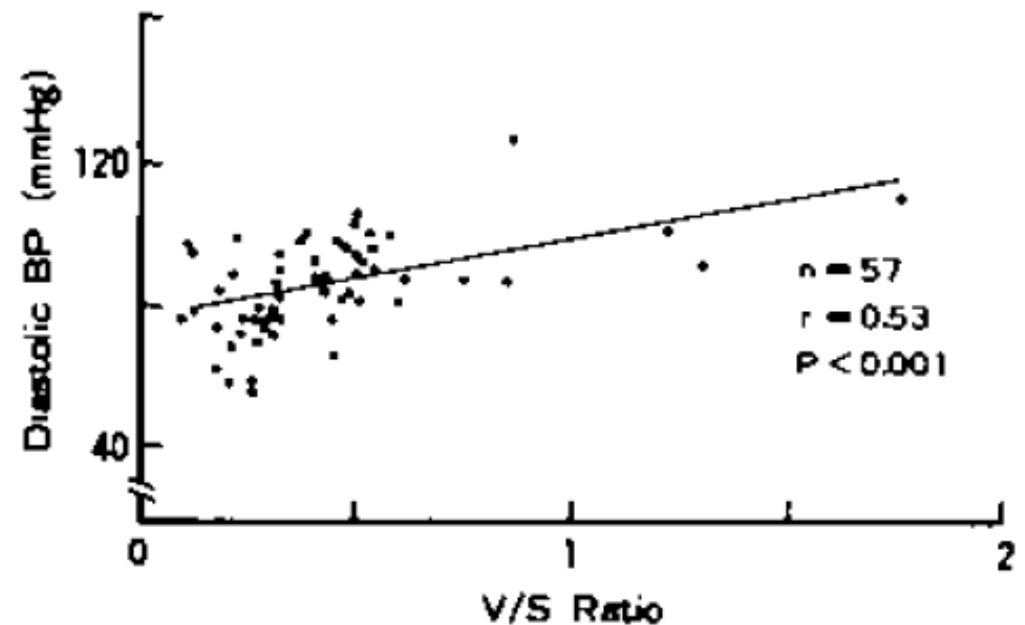
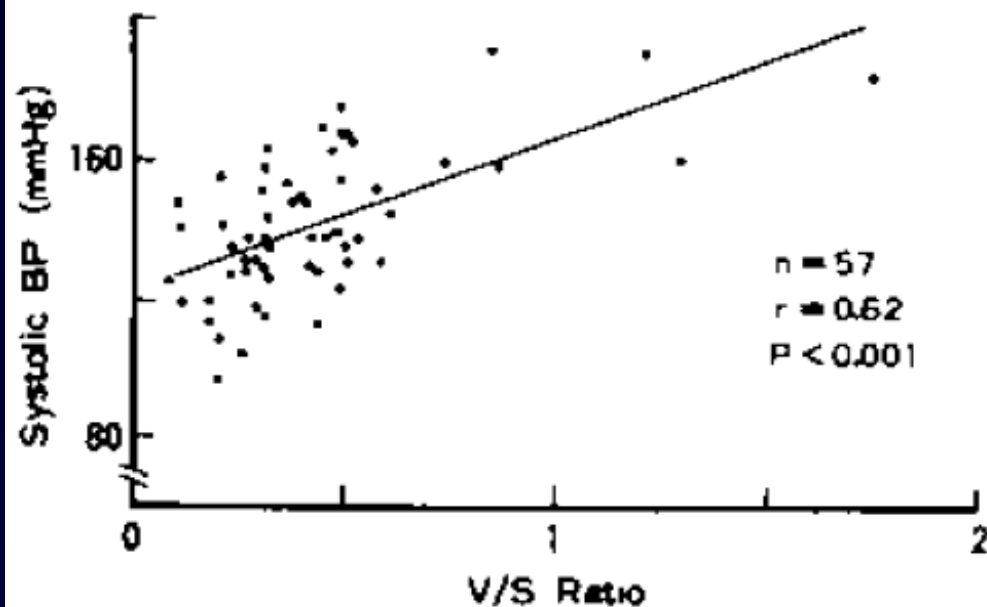
Zhu et al. Am J Clin Nutr 2002

A central distribution of body fat is associated with increased BP, independently of body mass index.

Siani et al. Am J Hypertens 2002

Close Correlation of Intra-abdominal Fat Accumulation to Hypertension in Obese Women

Hideyuki Kanai, Yuji Matsuzawa, Kazuaki Kotani, Yoshiaki Keno, Takashi Kobatake, Yoshiyuki Nagai, Shigenori Fujioka, Katsuto Tokunaga, and Seiichiro Tarui

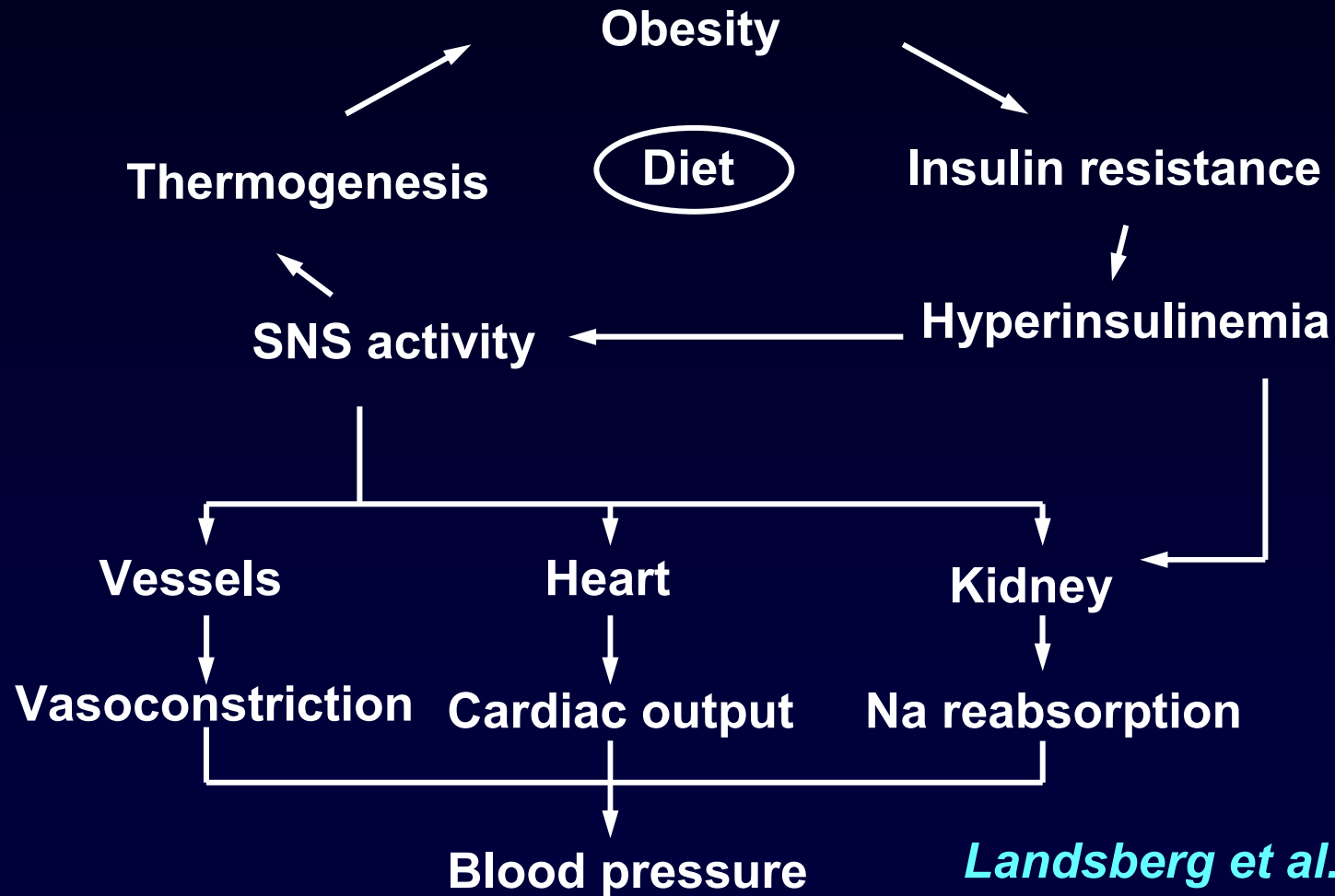


Kanai et al. Hypertension 1990

Factors Linking Obesity to Hypertension

- **Insulin resistance and endothelial dysfunction**
- **Sympathetic nerve system (SNS) activation**
- **Adipocytokines**
- **Hemodynamic alterations**

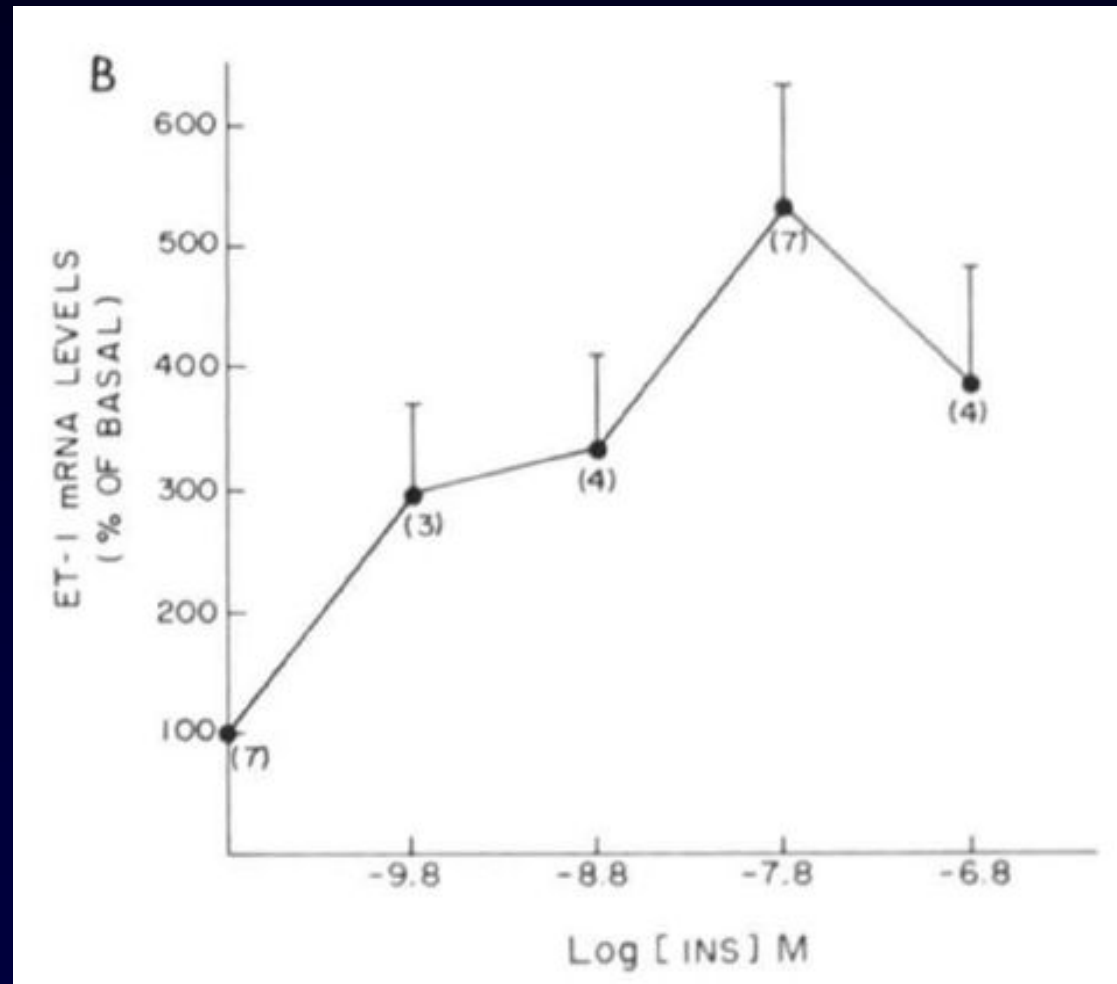
Insulin and blood pressure: by Landsberg et al



Landsberg et al. NEJM 1978

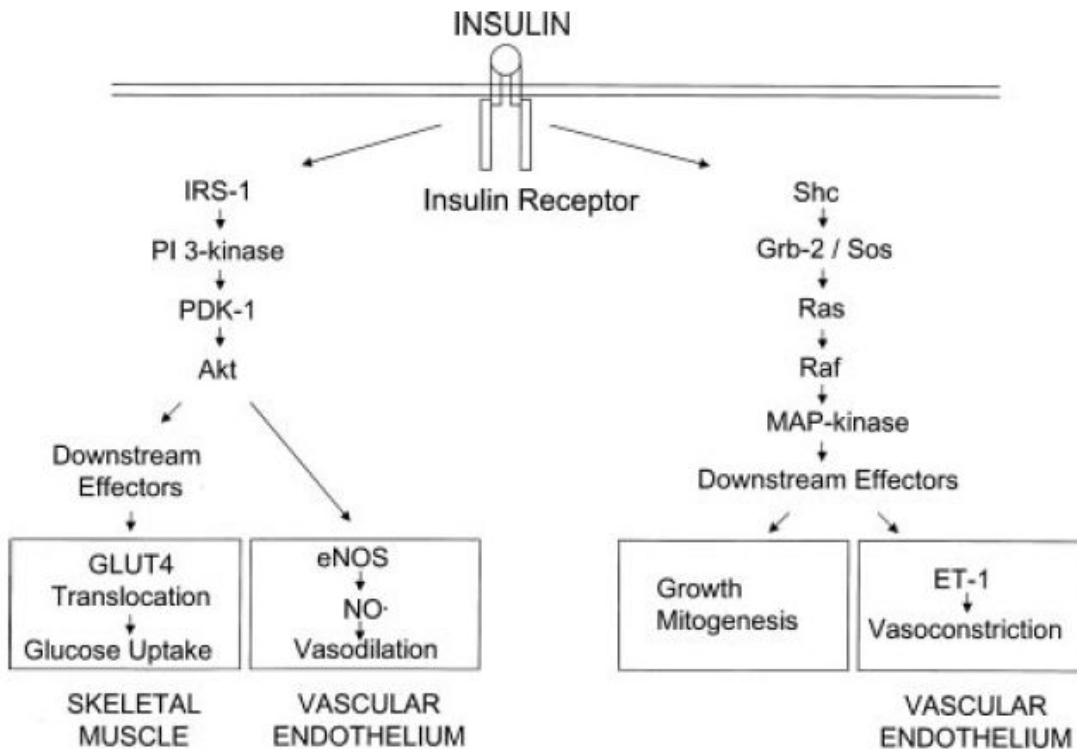
Landsberg. J Hypertens 2001

Stimulation of Endothelin-1 Gene Expression by Insulin in Endothelial Cells*

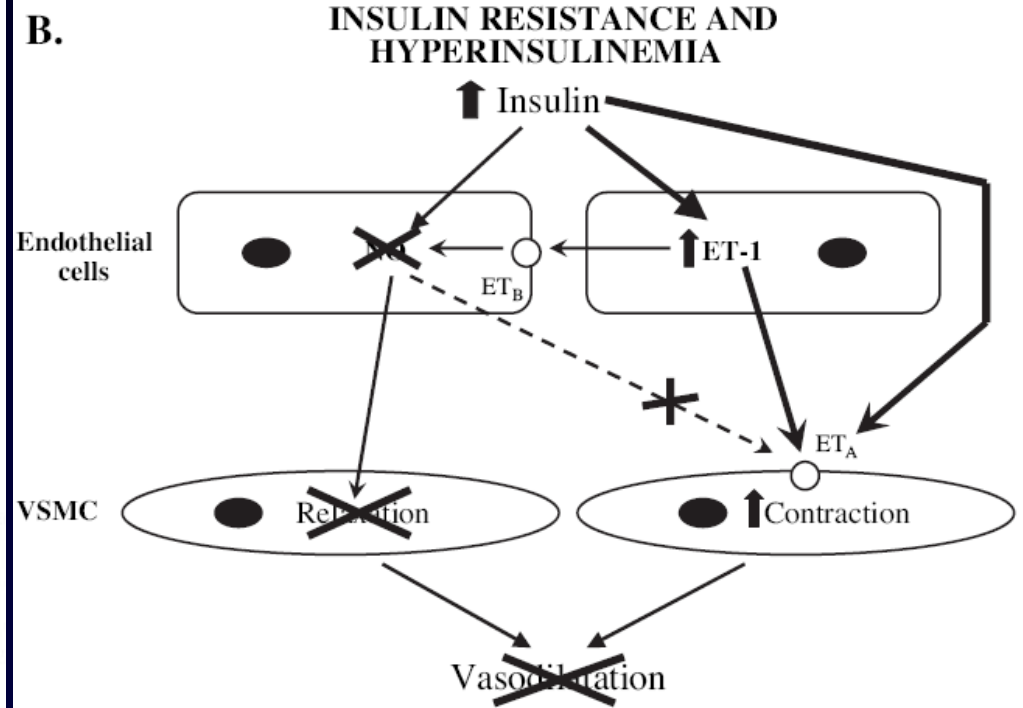


Oliver et al. J Biol Chem 1991

Effects of insulin on ET-1 and NO production

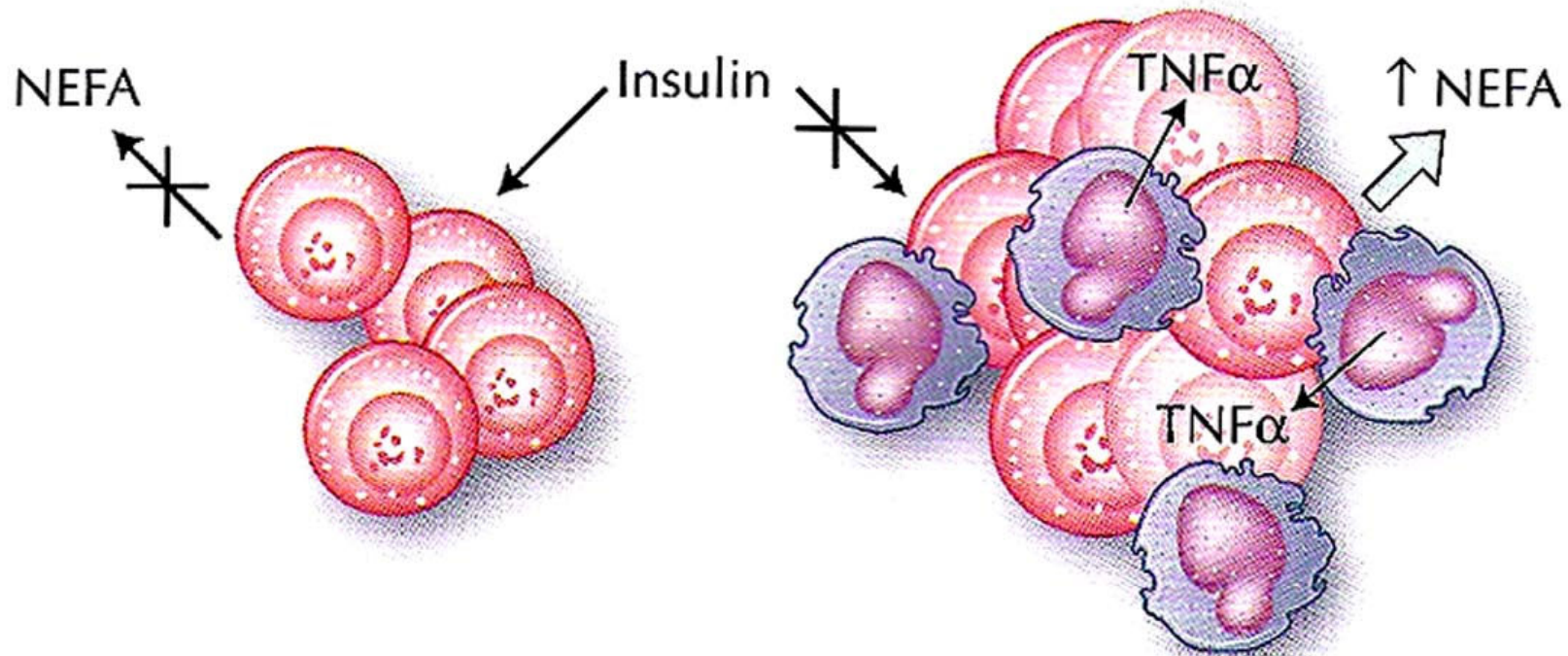


Kim et al. Circulation 2006



Sarafidis et al. J Clin Endocrinol Metab 2007

Obesity and insulin resistance

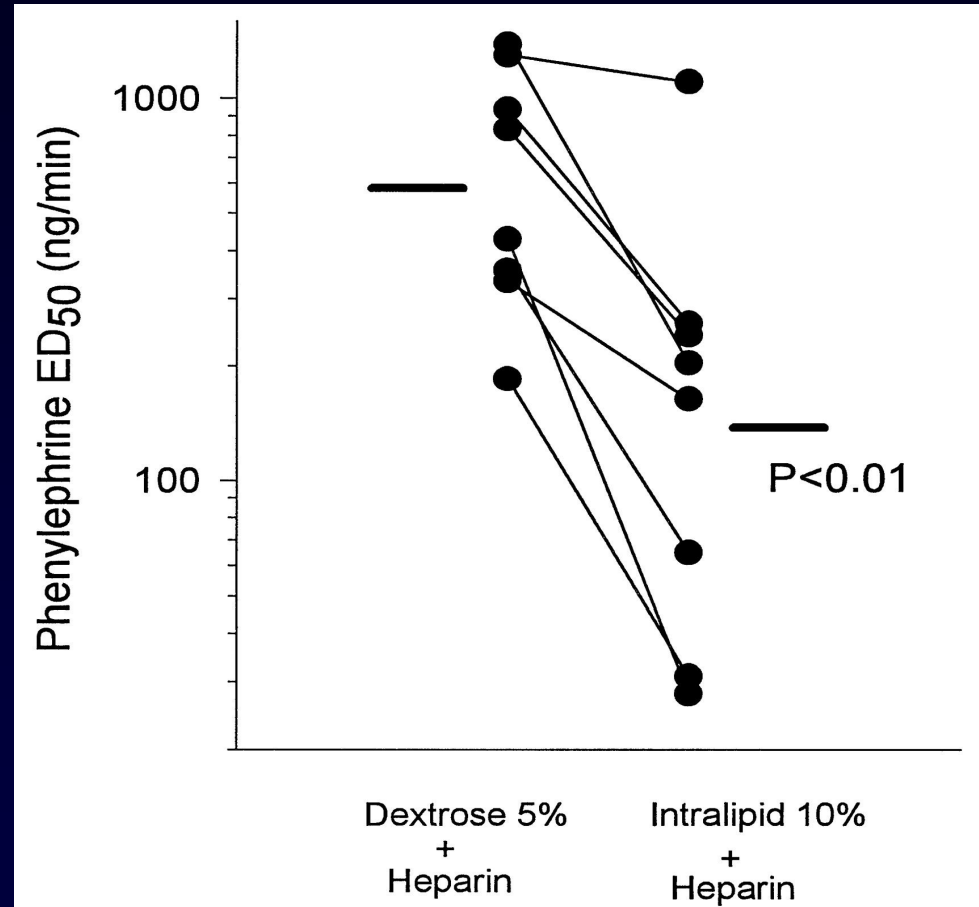


Normal adipocytes
Normal cell number

Increased cell size
Increased cell number
Macrophage infiltration

*Grundy. Atlas of
atherosclerosis 2005*

Fatty acids enhance vascular α -adrenergic sensitivity



Stepniakowski et al.
Hypertension 1995

Glucotoxicity

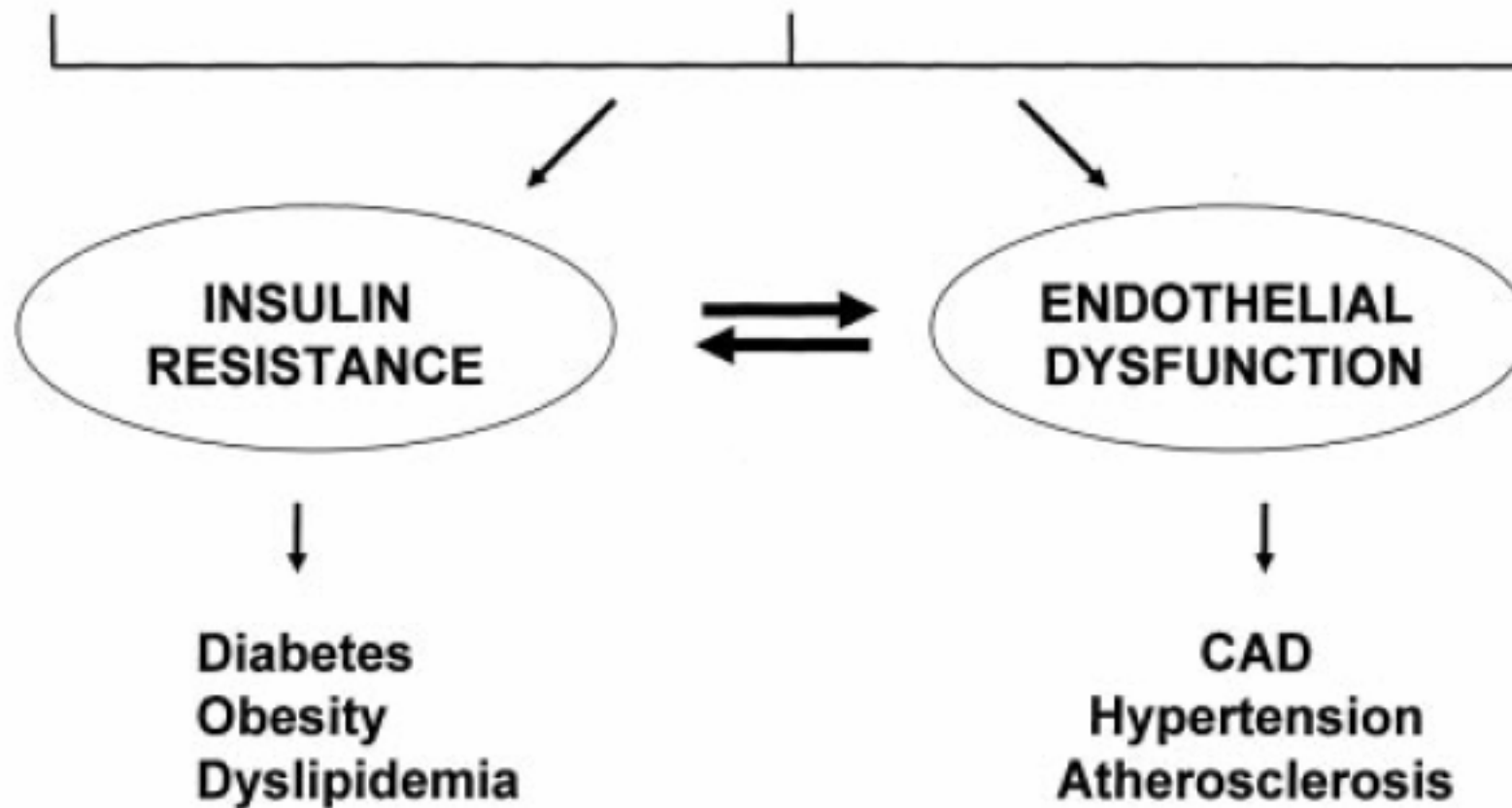
- Oxidative Stress
- AGE Formation
- Hexosamine Pathway
- Pro-inflammatory Signaling

Lipotoxicity

- Oxidative Stress
- Pro-inflammatory Signaling
- Ceramide

Inflammation

- Pro-inflammatory Factors (TNF- α , IL-1 β , IL-6, PAI-1, CRP)
- Kinases and Transcription Factors (JNK, IKK β , IRAK, NF- κ B, AP-1)



Predictors of forearm blood during after Ach infusions

Variables	partial r^2	total r^2	p
Insulin	23.5	23.5	0.0001
WHR	16.6	40.0	0.0001
BMI	8.0	48.1	0.0003

Perticone et al. Diabetes 2001

Visceral adiposity and hypertension in Japanese Americans

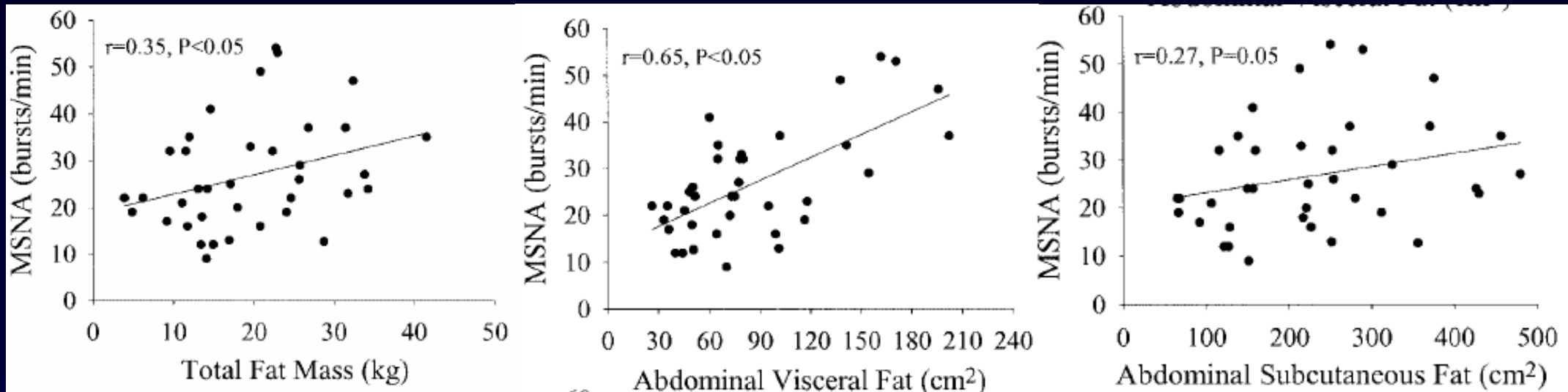
Variables	OR	p
Visceral fat area	1.68	0.003
Fasting insulin	1.49	0.001
Age	2.25	<0.001
2h plasma glucose	1.41	0.007

Visceral fat is a correlate of hypertension independent of fasting plasma insulin

Hayashi et al. Circulation 2003

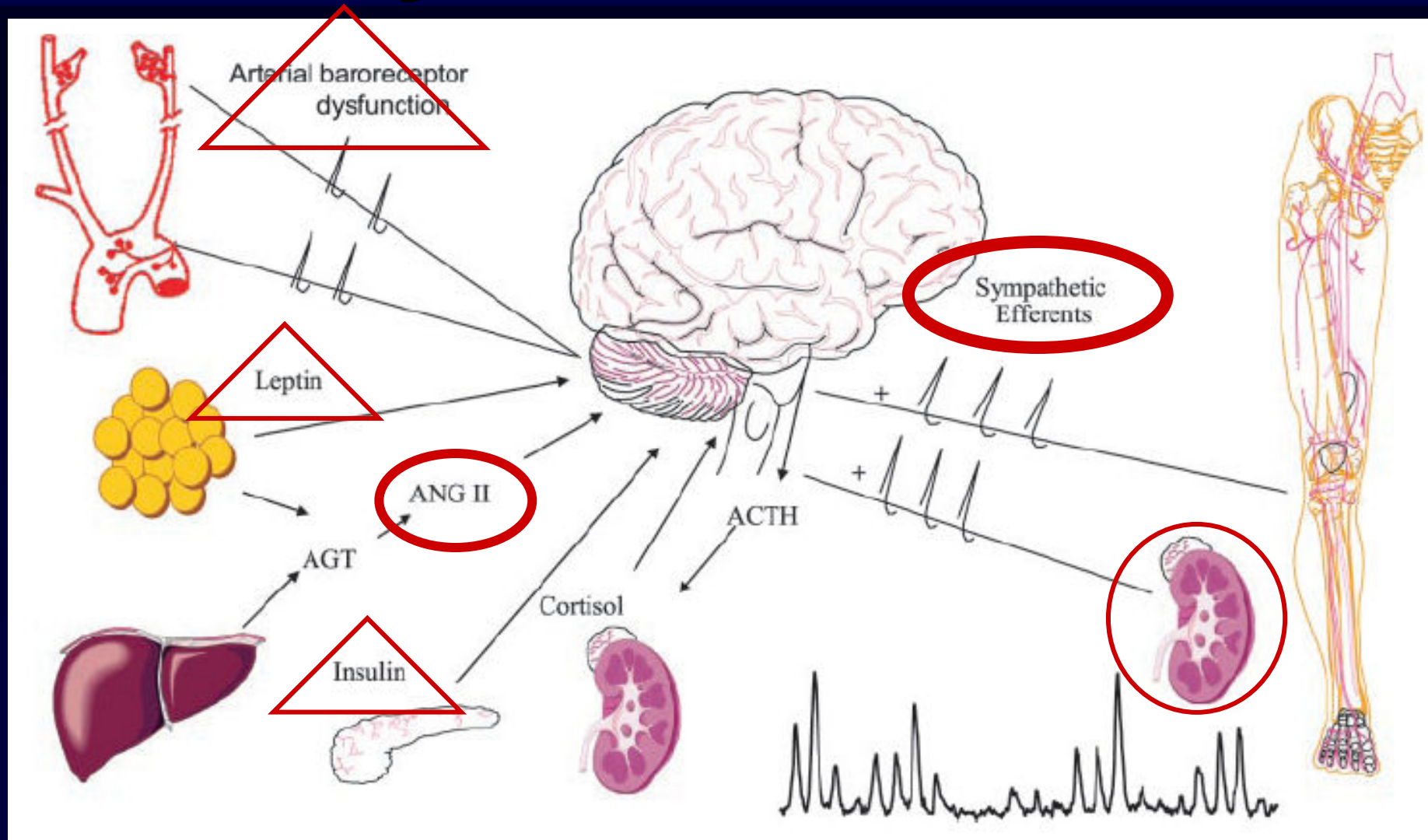
Poirier et al. Hypertension 2005

Obesity and SNS activation



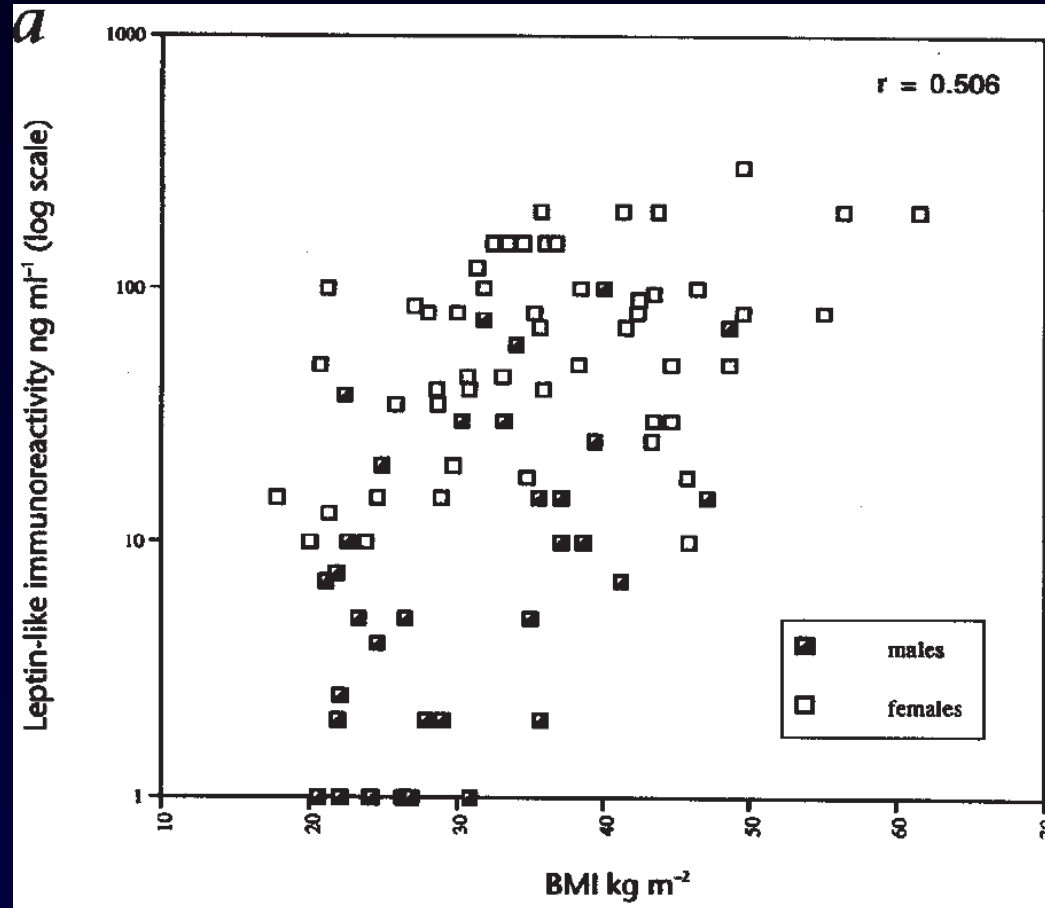
*Alvarez et al.
Circulation 2002*

Obesity and SNS activation



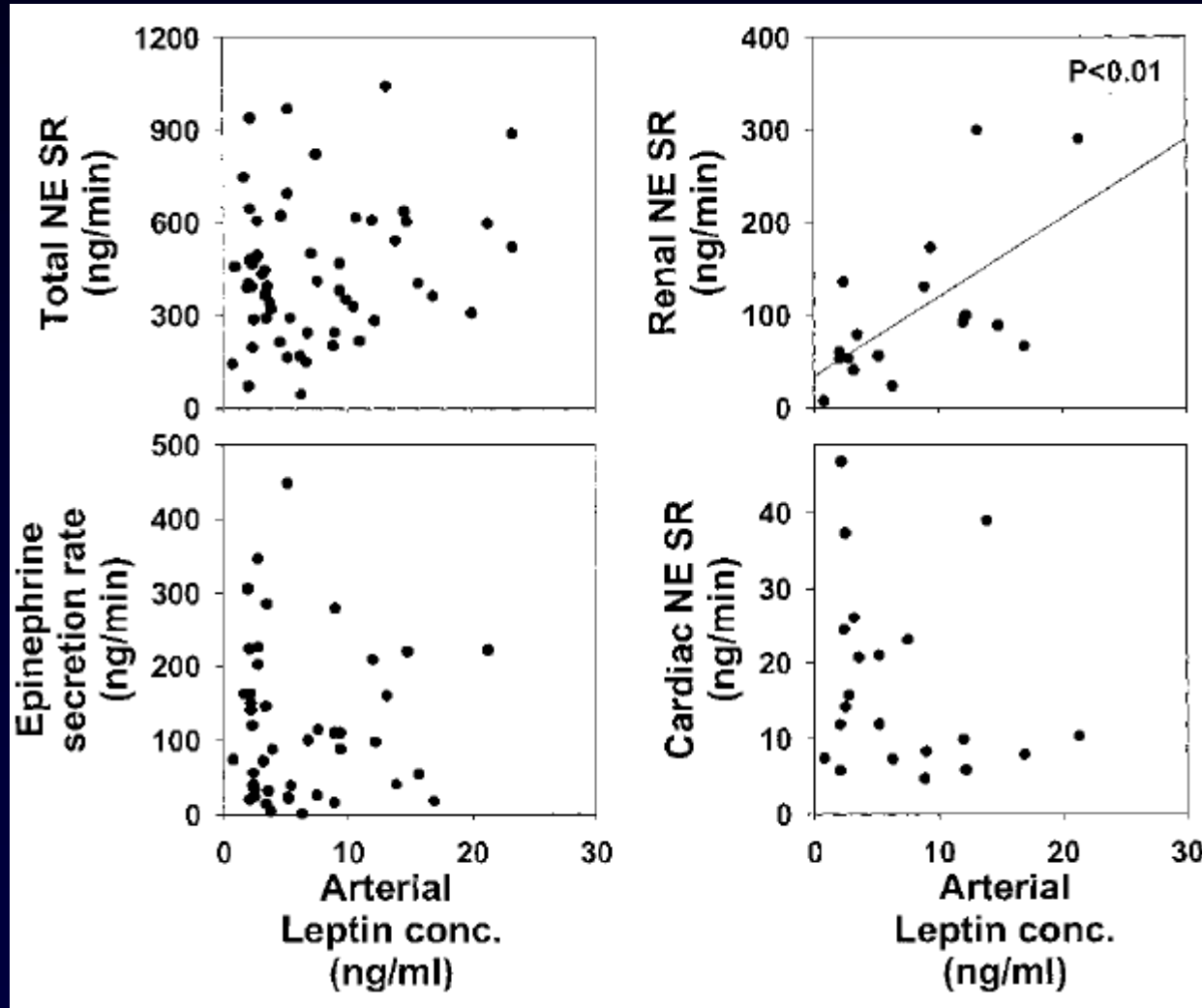
Davy et al. Am J Physiol 2004

Leptin levels in human and rodent: Measurement of plasma leptin and *ob* RNA in obese and weight-reduced subjects



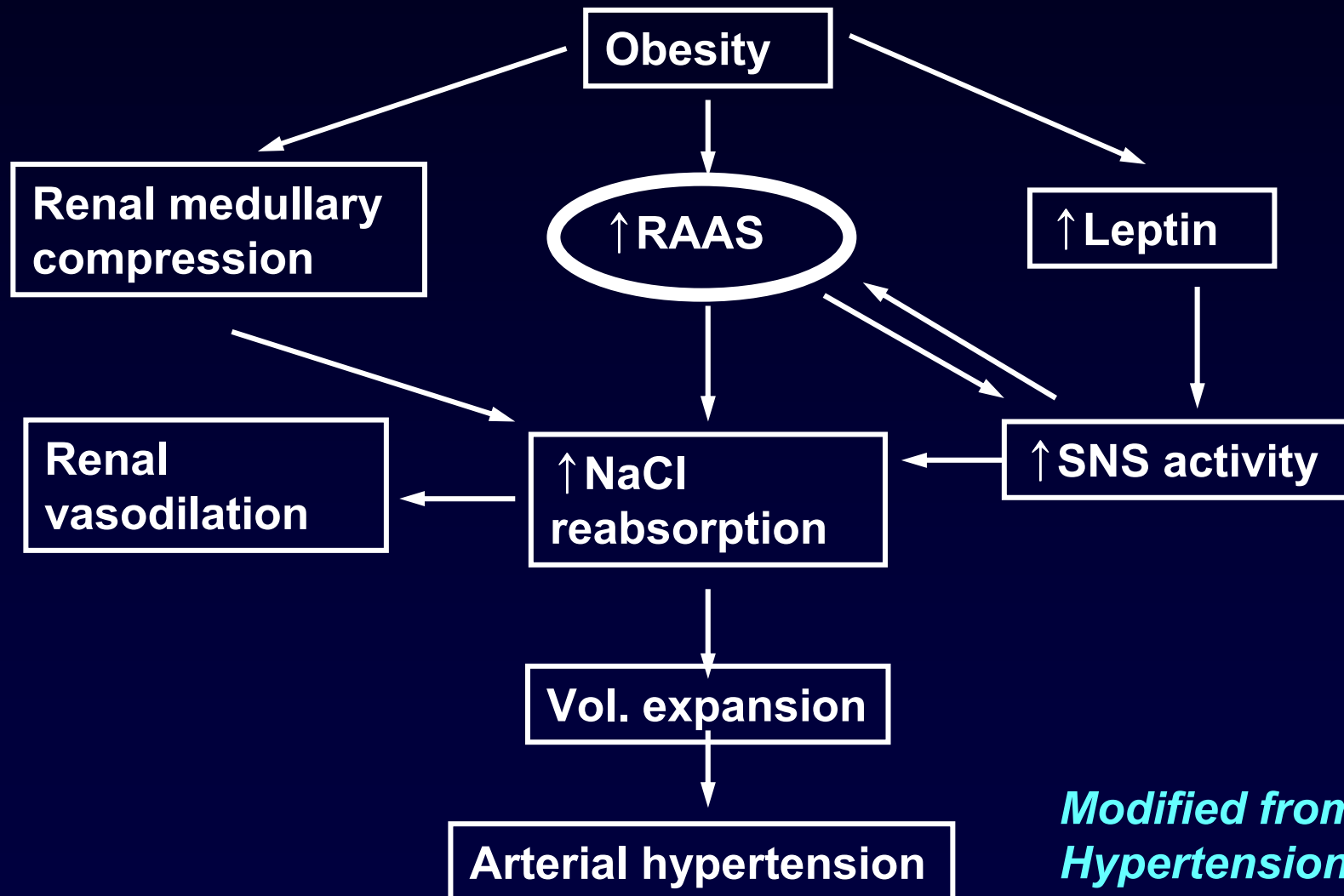
Maffei et al. Nat Med
1995

Sympathetic nerve system and leptin



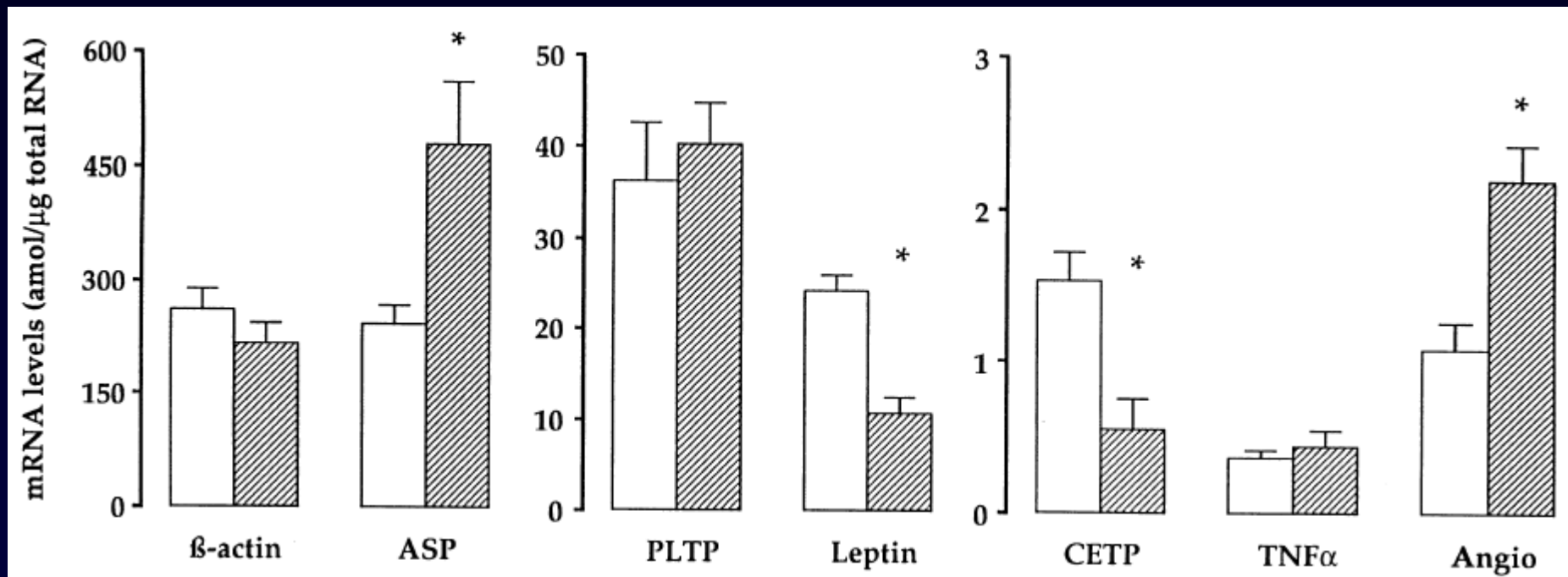
*Eikelis et al.
Hypertension 2003*

Obesity and renin angiotensin system



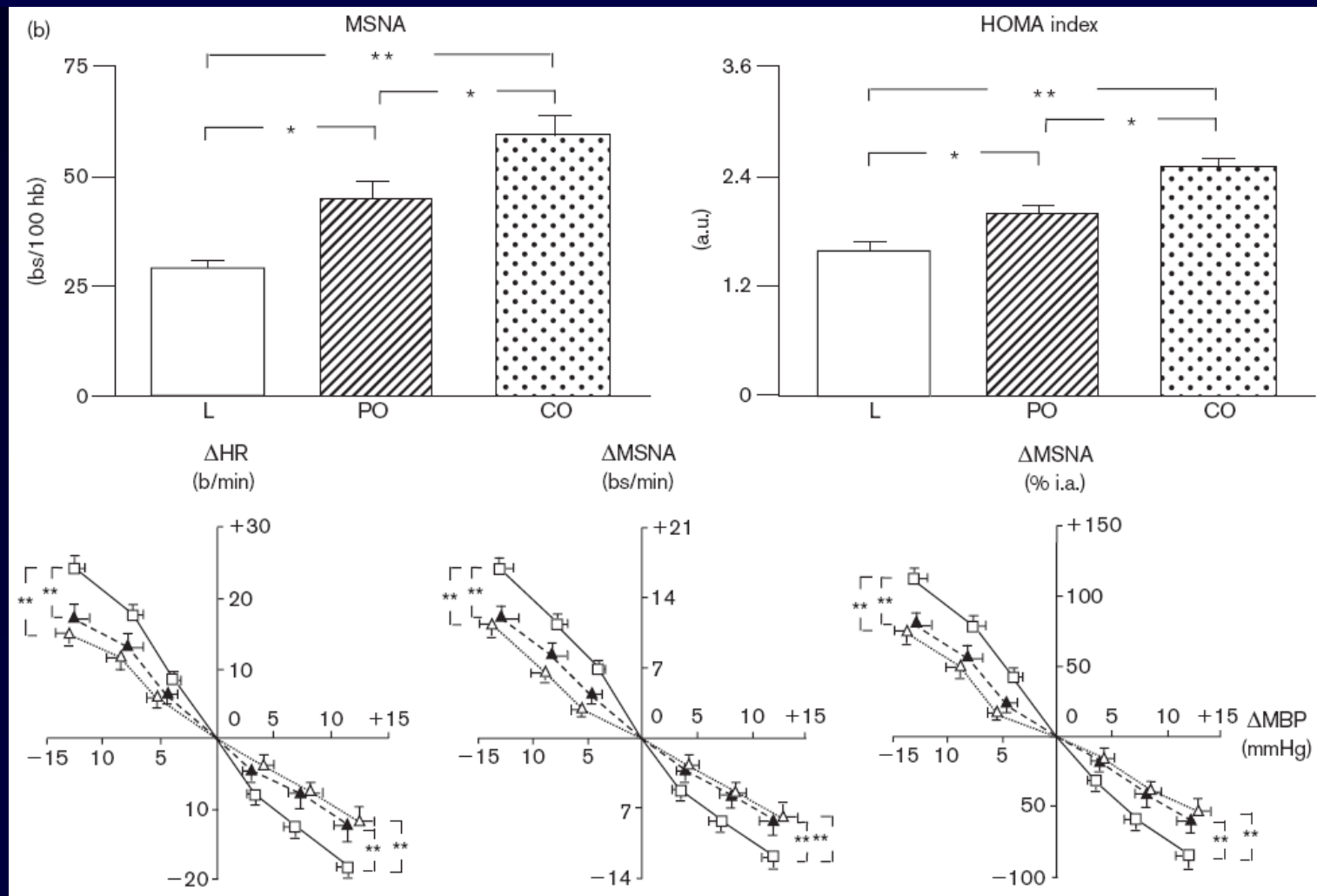
*Modified from Sharma.
Hypertension 2004*

Angiotensinogen mRNA in subcutaneous vs visceral fat



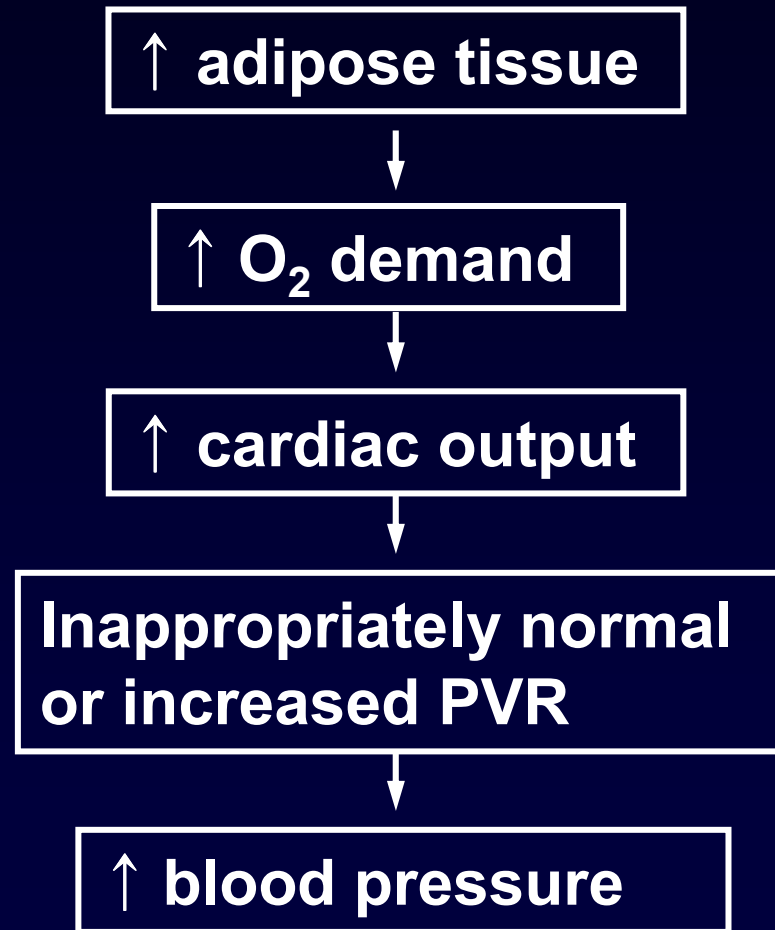
Dussere et al. Biochimica et Biophysica Acta 2000

Relation of body fat distribution to SNS, baroreflex and HOMA index



Grassi et al. J Hypertens 2004

Adiposity and hemodynamic alterations

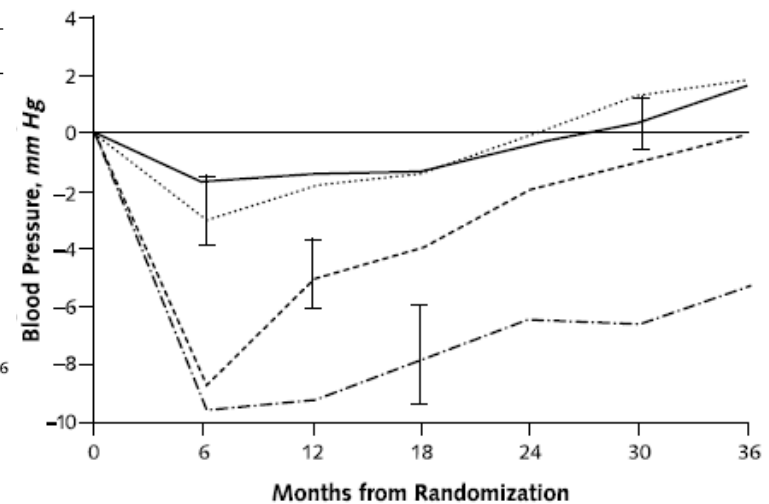
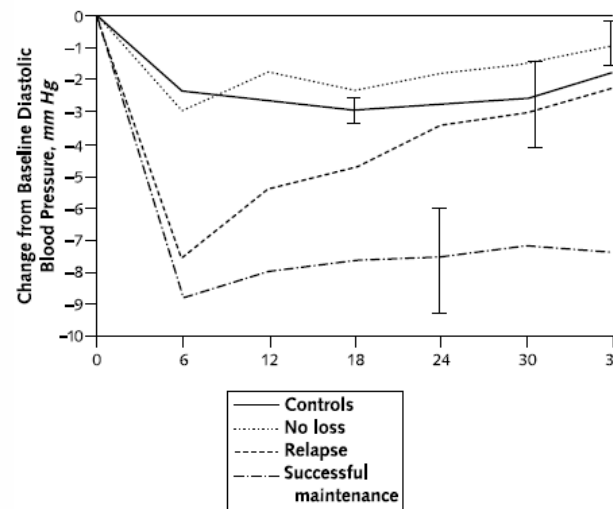
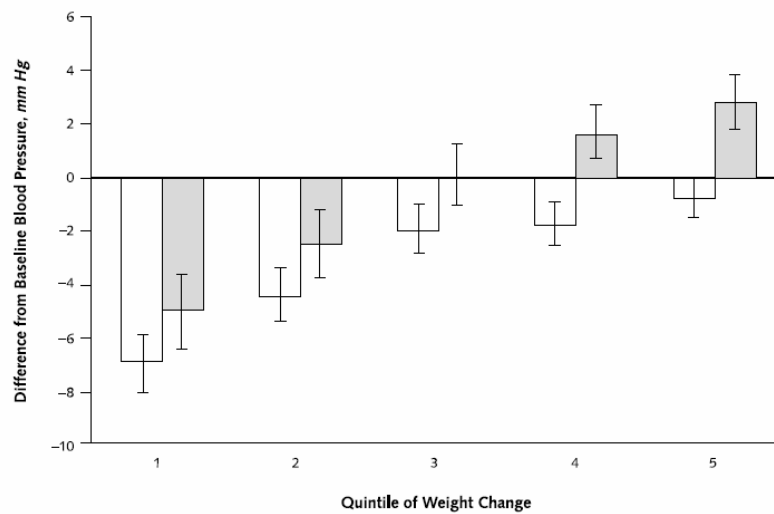


*Poirier et al.
Circulation 2006*

Treatment of Obese Hypertensive Patients

Long-Term Weight Loss and Changes in Blood Pressure: Results of the Trials of Hypertension Prevention, Phase II

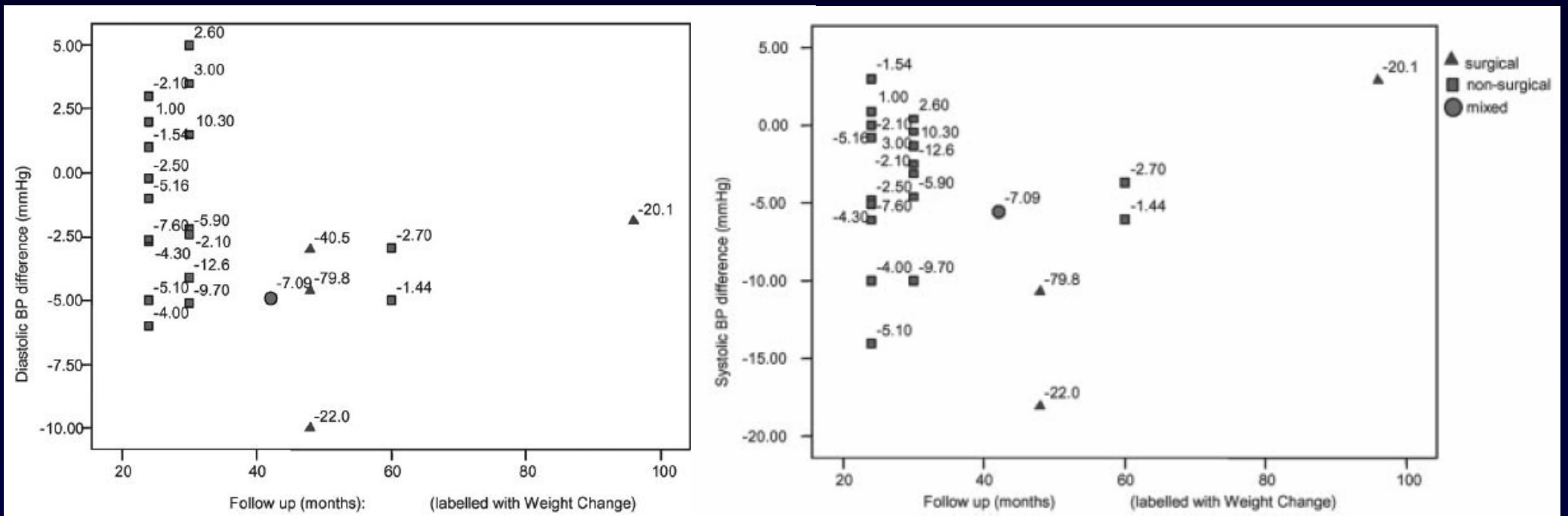
Victor J. Stevens, PhD; Eva Obarzanek, PhD; Nancy R. Cook, ScD; I-Min Lee, MD, ScD; Lawrence J. Appel, MD, MPH; Delia Smith West, PhD; N. Carole Milas, MS, RD; Mildred Mattfeldt-Beman, PhD; Lorna Belden, MS, RD; Charlotte Bragg, MS, RD; Marian Millstone, MS; James Raczynski, PhD; Amy Brewer, MS, RD; Bali Singh, MS, RD; and Jerome Cohen, MD, for the Trials of Hypertension Prevention Research Group



Stevens et al. Ann Intern Med 2001

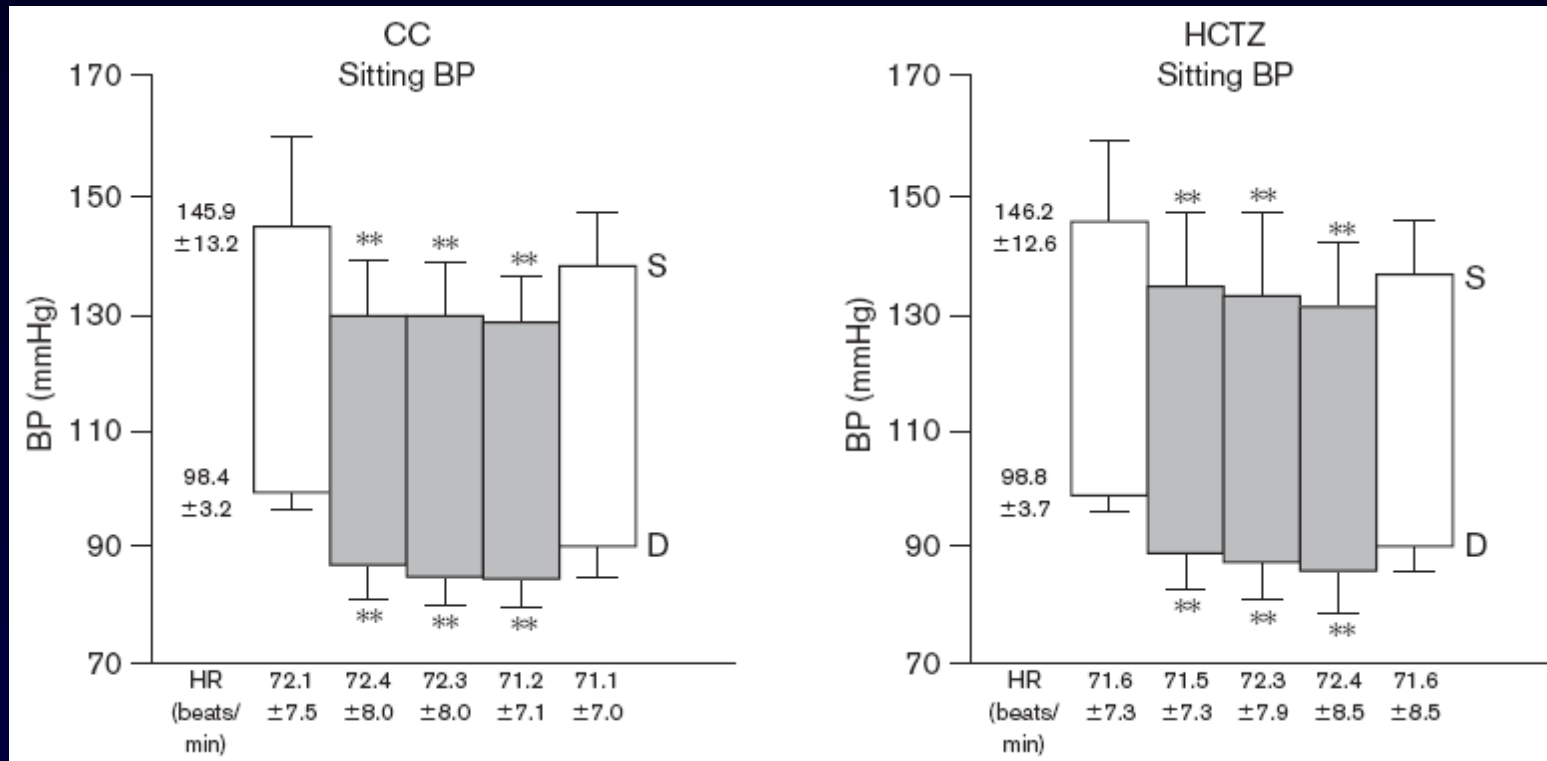
Effect of weight loss on long-term hypertension outcomes

- Review of 13 studies with 5000 patients



Aucott et al. Hypertension 2005

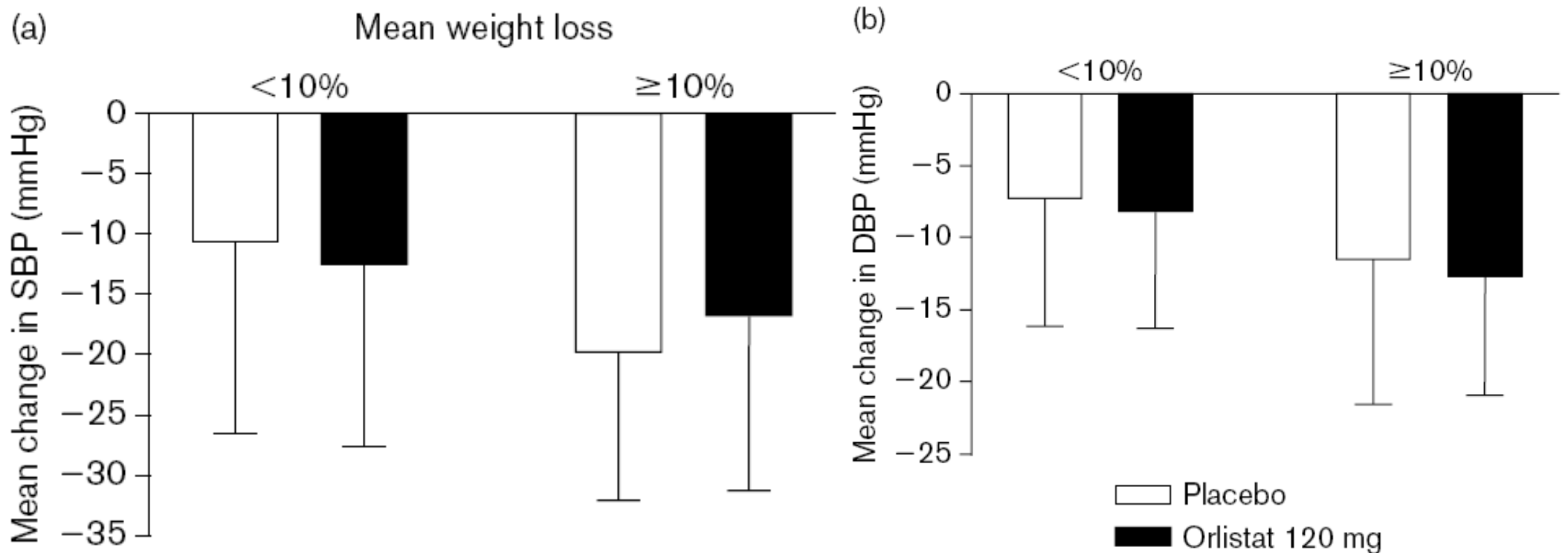
Candesartan vs HCTZ in obese hypertensive patients



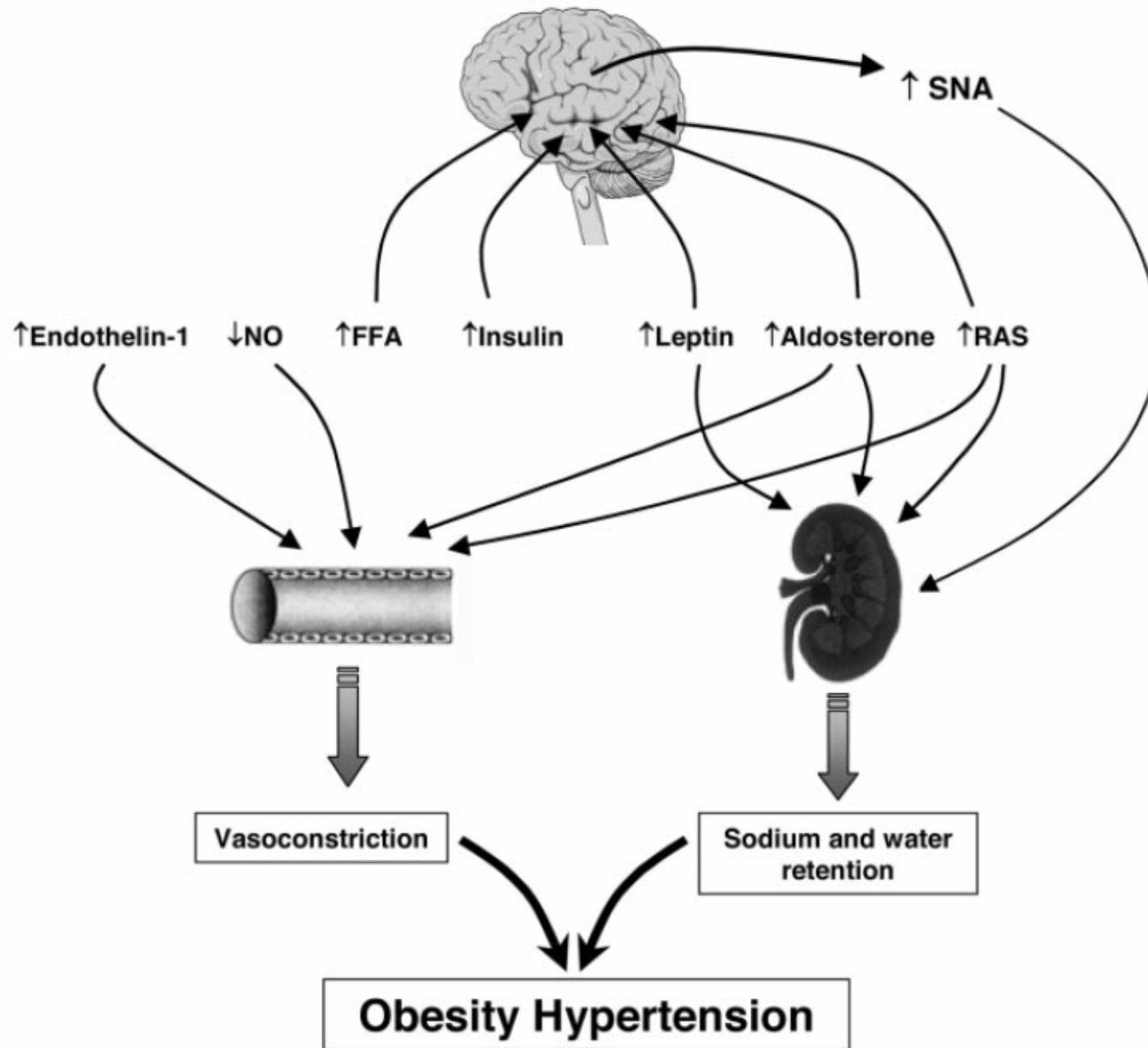
Grassi et al. J Hypertens 2003

Orlistat-induced weight loss and blood pressure

- A meta-analysis of 628 patients in 5 RCTs



Sharma et al. J Hypertens 2002



*Rahmouni et al.
Hypertension 2005*

***Thank You for
Your Attention***