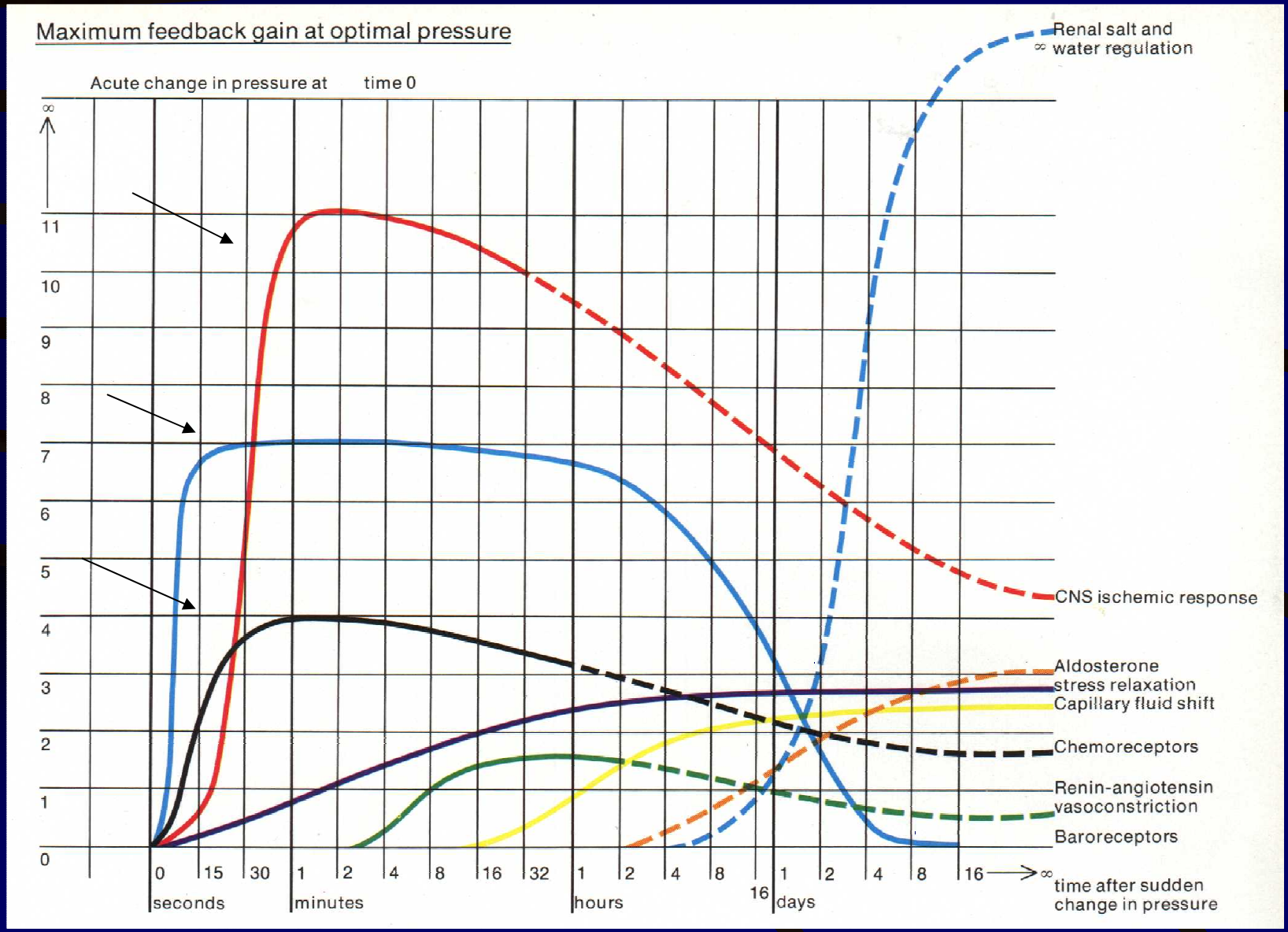
Les catécholamines et la tension artérielle

JM Krzesinski

Symposium Château de Jemeppe 5/5/2011

Mechanisms of acute Blood Pressure adaptations



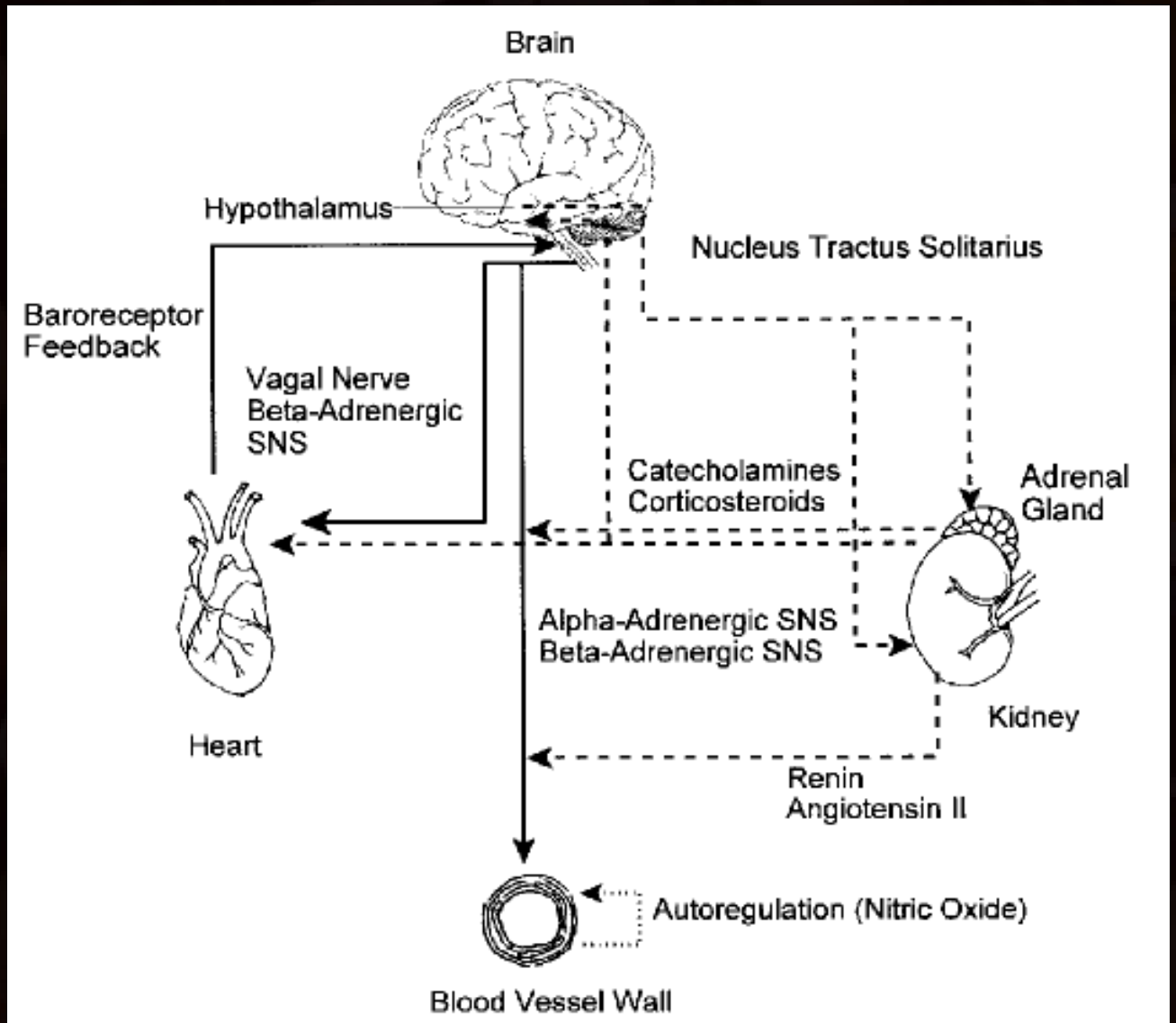


Figure 1.2. Major physiological systems involved in the regulation of blood pressure (dotted arrows represent local blood cell autoregulation; solid arrows represent neural influences; dashed arrows represent neuroendocrine influences; SNS = sympathetic nervous system).

History of HTA treatment (Chobanian NEJM 2009)

Table 1. Advances in the Treatment of Hypertension.

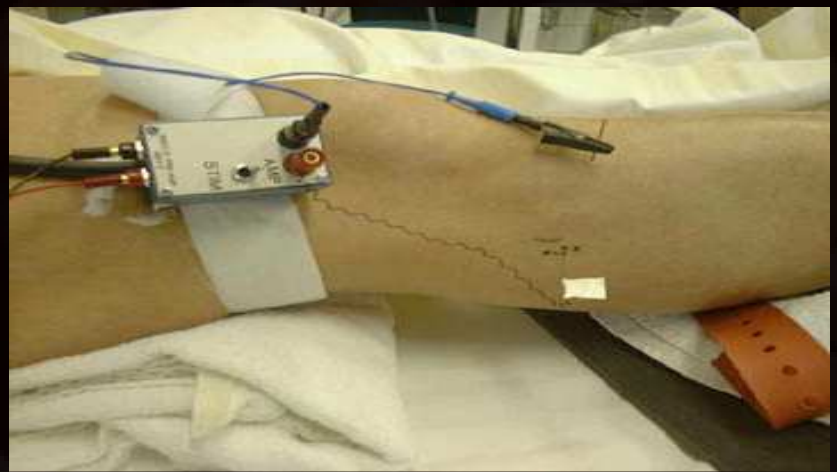
Decade and Therapy
1940s
Potassium thiocyanate
Kempner diet
Lumbodorsal sympathectomy
1950s
Rauwolfia serpentina
Ganglionic blockers
Veratrum alkaloids
Hydralazine
Guanethidine
Thiazide diuretics
1960s
α_2-Adrenergic–receptor agonists
Spironolactone
β-Adrenergic–receptor agonists
1970s
α_1-Adrenergic–receptor antagonists
Angiotensin-converting–enzyme inhibitors
1980s
Calcium antagonists
1990s
Angiotensin-receptor blockers
Endothelin-receptor antagonists*
2000s
Renin inhibitors

Traditional pharmacological therapies

- RAS inhibitors and Beta-receptor blockers slightly decrease central sympathetic outflow
- Diuretics and CCBl stimulate central sympathetic outflow
- Stimulation alpha 2 or imidazoline receptors within the central nervous system decreases central sympathetic activity: clonidine and moxonidine are used but frequent central side-effects are noted

Common clinical measures of whole-body SNSA

- Determination of venous plasma or urinary concentrations of NE
- Isotope dilution methodology (determination of NE spillover of individual organs) : regional patterns (central , cardiac, renal)
- Spectral analysis of spontaneous oscillations in heart rate or BP
- Microneurography technique (efferent postganglionic SNSA to the skeletal or skin)



The sympathetic nervous system in hypertension

Giuseppe Mancia

Journal of Hypertension 1997, 15:1553–1565

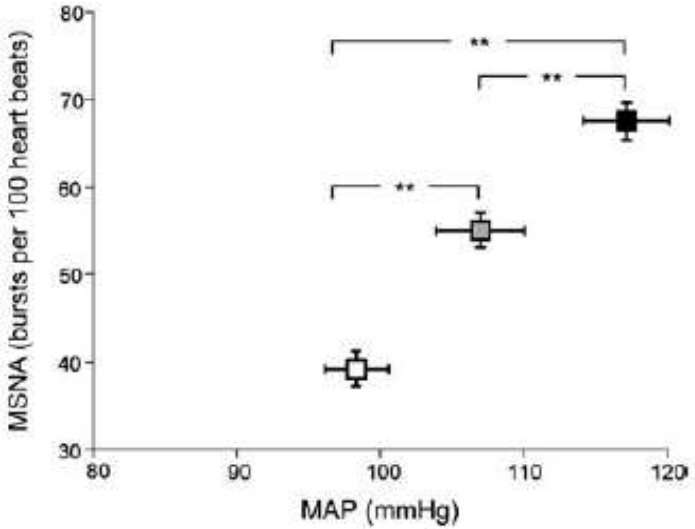


Figure 2. Progressive increase in muscle sympathetic nerve activity in normotensive control subjects (open square), mild-to-moderate (shaded square) and more severe essential hypertensive patients (filled square)
Abbreviations: MAP, mean arterial pressure; and MSNA, muscle sympathetic nerve activity. Data are shown as means ± S.E.M. ANOVA, $^{**}P < 0.01$ between groups. Data from Grassi *et al.* (1998*a*).

Table 1 **Resting values of mean arterial pressure (MAP) and muscle sympathetic nerve activity (MSNA) in age-matched normotensives, moderate and severe essential hypertensives and in secondary hypertensives**

	Normotensives (n = 15)	Moderate essential hypertensives (n = 14)	Severe essential hypertensives (n = 14)	Secondary hypertensives (n = 13)
MAP (mmHg)	98.4 ± 2.6	107.2 ± 1.7**	116.1 ± 4.5**	117.8 ± 4.4**
MSNA (bursts/ 100 heart beats)	40.3 ± 3.3	55.6 ± 4.1**	68.2 ± 4.1**	40.5 ± 6.7

Values are expressed as means ± SEM. $^{**}P < 0.01$.

Gender-Selective Interaction Between Aging, Blood Pressure, and Sympathetic Nerve Activity

Krzysztof Narkiewicz, Bradley G. Phillips, Masahiko Kato, Dagmara Hering, Leszek Bieniaszewski and Virend K. Somers

Hypertension 2005;45:522-525; originally published online Mar 14, 2005;

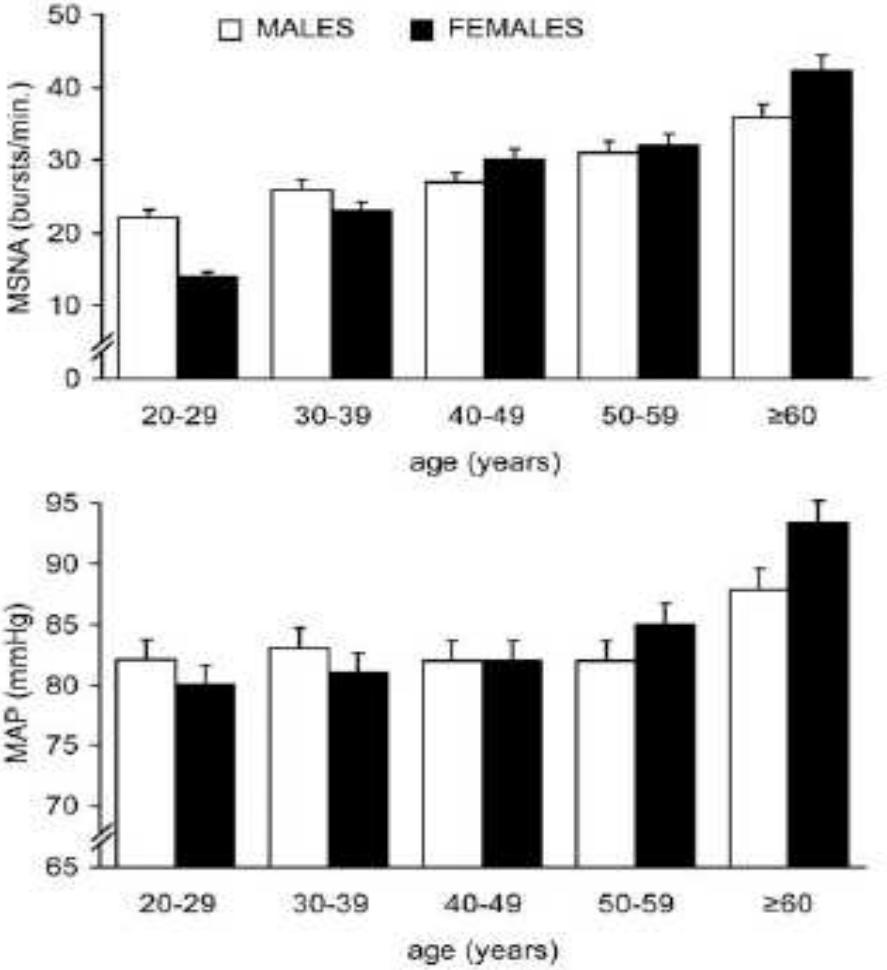


Figure 1. MSNA and mean arterial pressure (MAP) per decade and male and females subjects. Two-way ANOVA revealed that age influenced both MSNA ($P<0.0001$) and MAP ($P=0.005$). Gender had no significant effect on MSNA ($P=0.52$) or MAP ($P=0.59$). Gender and age had an interactive effect on MSNA ($P=0.01$), but not on MAP ($P=0.50$). In subjects aged 20 to 29, MSNA was lower in females than males ($P<0.01$ by pair-wise comparison with the use of Scheffé test).

Pathophysiology of Resistant Hypertension: The Role of Sympathetic Nervous System

Costas Tsioufis, Athanasios Kordalis, Dimitris Flessas, Ioannis Anastasopoulos, Dimitris Tsiachris, Vasilios Papademetriou, and Christodoulos Stefanadis

International Journal of Hypertension
Volume 2011, Article ID 642416, 7 pages
doi:10.4061/2011/642416

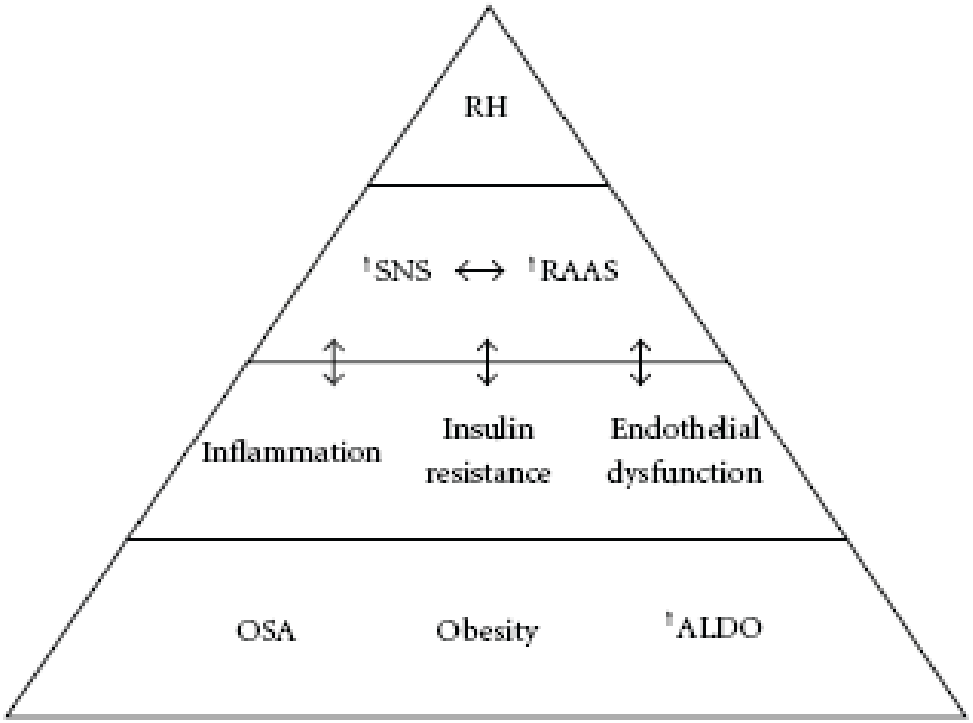


FIGURE 1: A proposed pathophysiologic pathway for the activation of SNS and the development of RH. Obesity, OSA and aldosterone excess are covering a great area of the mosaic of the phenotype of RH and are correlated with increased SNS activity, via multiple mechanisms. ↑ALDO: Aldosterone excess, OSA: Obstructive sleep apnea, ↑RAAS: Renin-Angiotensin-Aldosterone System activation, RH: Resistant hypertension, ↑SNS: Sympathetic nervous system hyperactivity.

Benefits from Treatment and Control of Patients with Resistant Hypertension

Michael Doumas,[1] Vasilios Papademetriou,[2] Stella Douma,[3] Charles Faselis,[1] Konstantinos Tsioufis,[2] Eugene Gkaliagkousi,[3] Konstantinos Petidis,[3] and Chrysanthos Zamboulis[3]

International Journal of Hypertension
Volume 2011, Article ID 318549, 8 pages
doi:10.4061/2011/318549

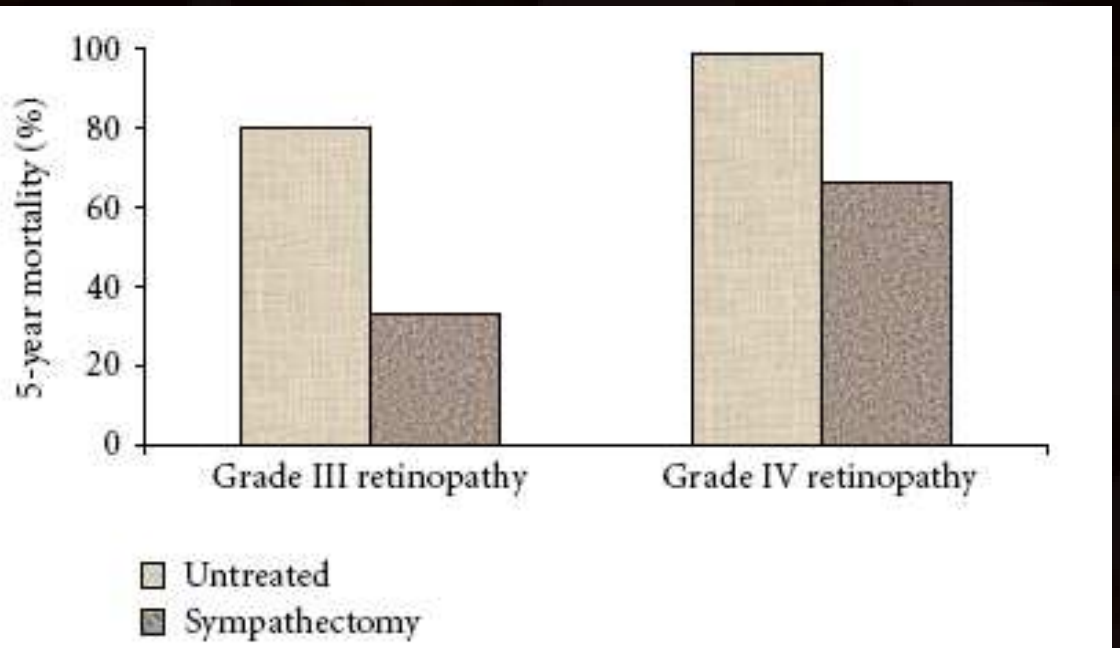


FIGURE 1: Five-year mortality rates (%) in untreated patients with malignant hypertension and Grade III or IV retinopathy compared to similar patients that underwent sympathectomy (modified from Keith et al. [25] and Peet et al. [26]).

1940

R. H. Smithwick and J. E. Thompson, "Splanchnicectomy for essential hypertension; results in 1,266 cases," *Journal of the American Medical Association*, vol. 152, no. 16, pp. 1501–1504, 1953.

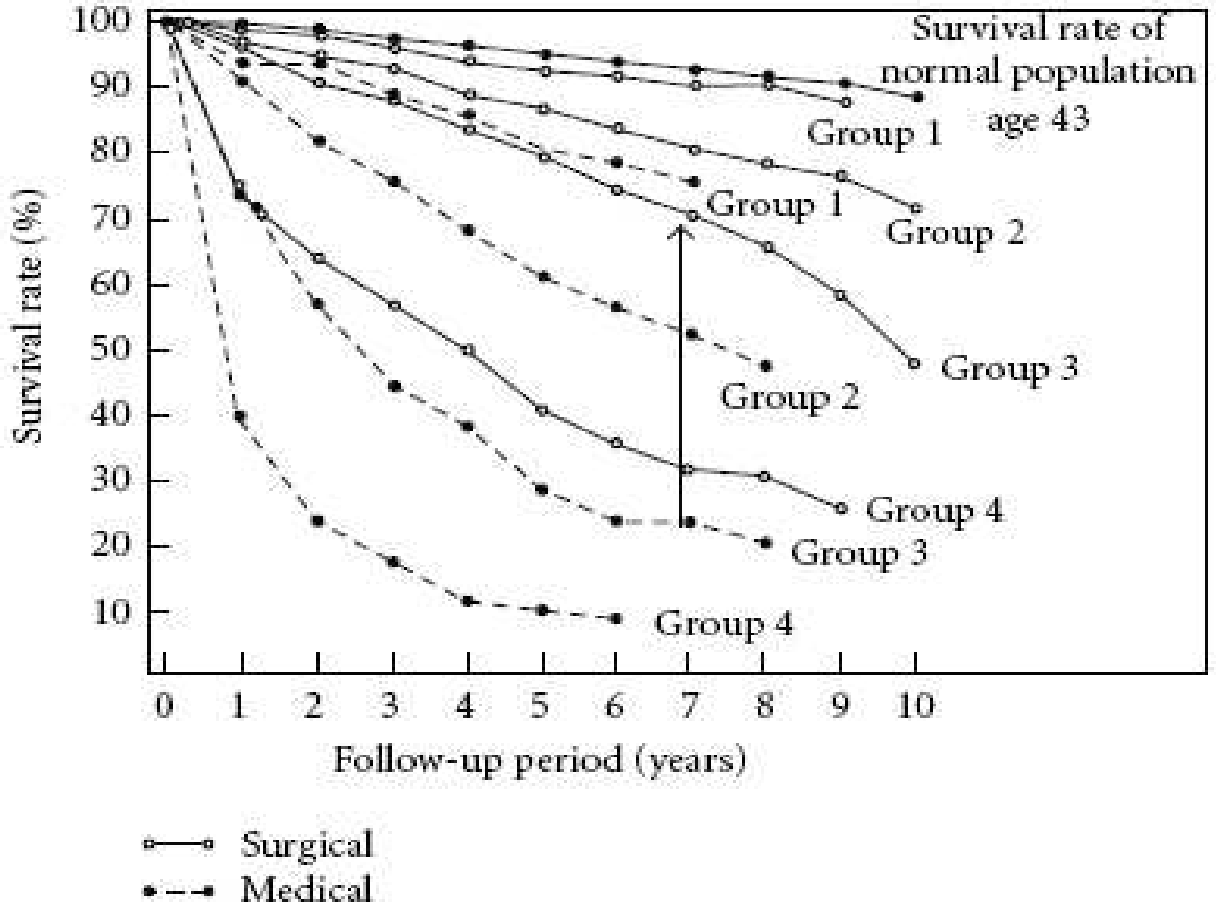


FIGURE 2: Survival rates in patients with malignant hypertension at various stages (Group 1–4) treated either medically or surgically

Complications of sympathetic activation in HTA

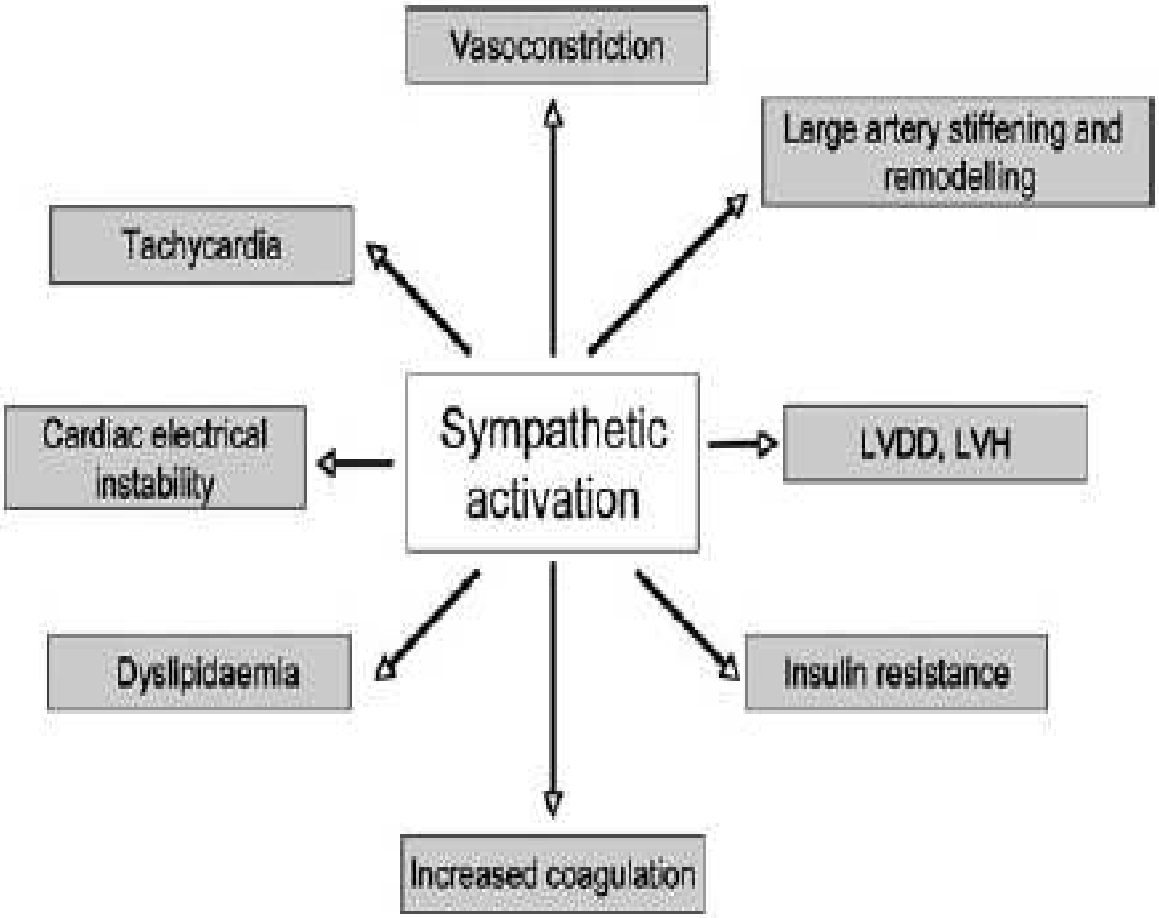


Figure 4. Schematic drawing of the adverse cardiovascular and metabolic effects of sympathetic activation in hypertension
Abbreviations: LVDD, left ventricular diastolic dysfunction; LVH, left ventricular hypertrophy.

G. Grassi and others

Exp Physiol 95.5 pp 581–586

2009

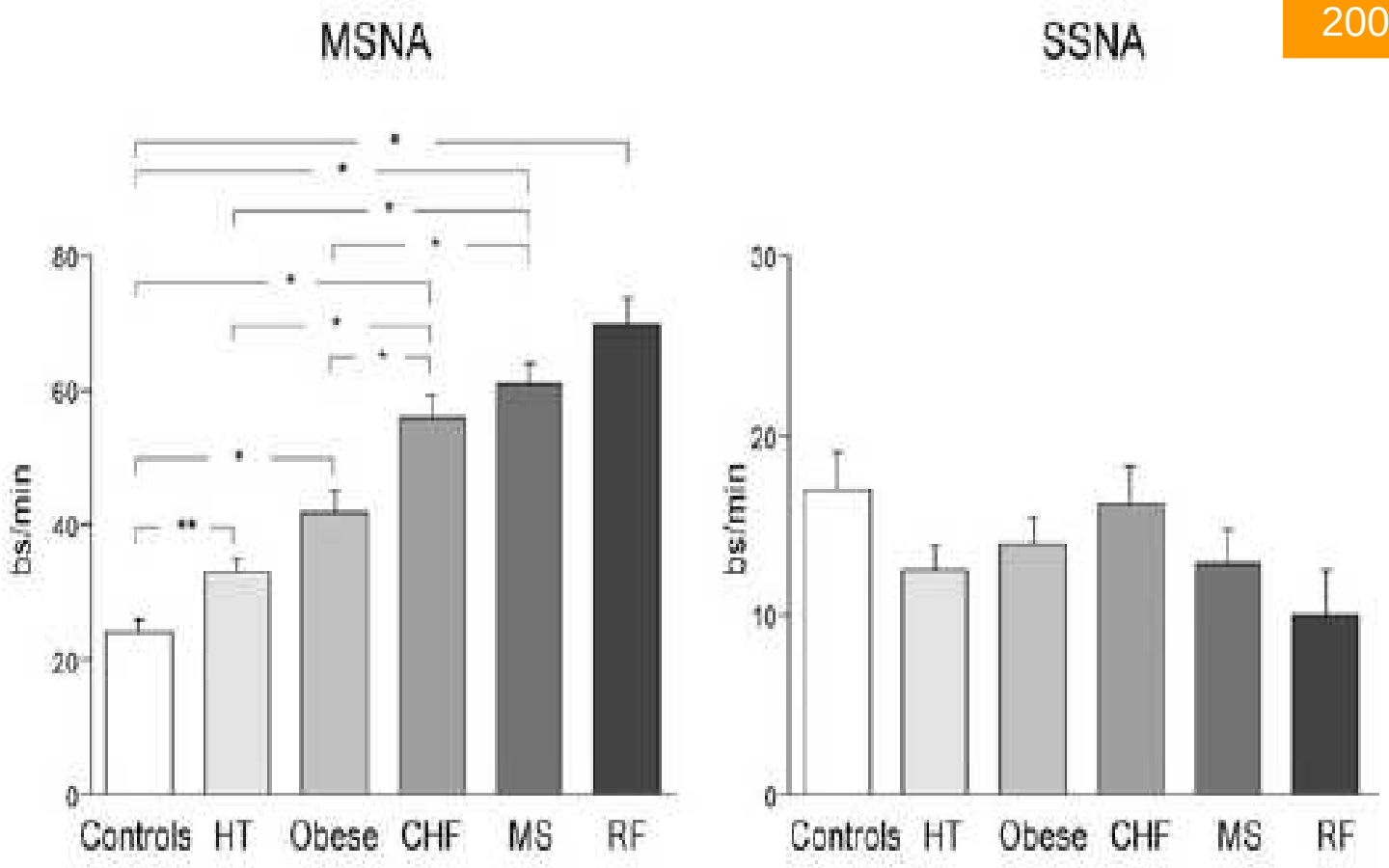
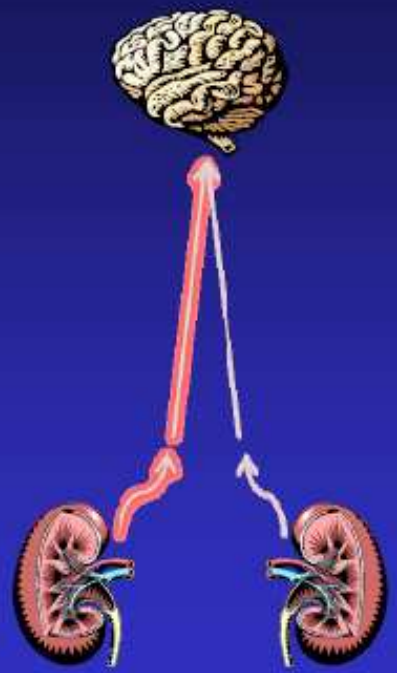


Figure 3. Behaviour of muscle (MSNA) and skin sympathetic nerve activity (SSNA) in healthy subjects and in patients with hypertension (HT), obesity (OB), congestive heart failure (CHF), metabolic syndrome (MS) or renal failure (RF)

Data are shown as means + S.E.M. ANOVA, $*P < 0.05$, $**P < 0.001$ between groups.

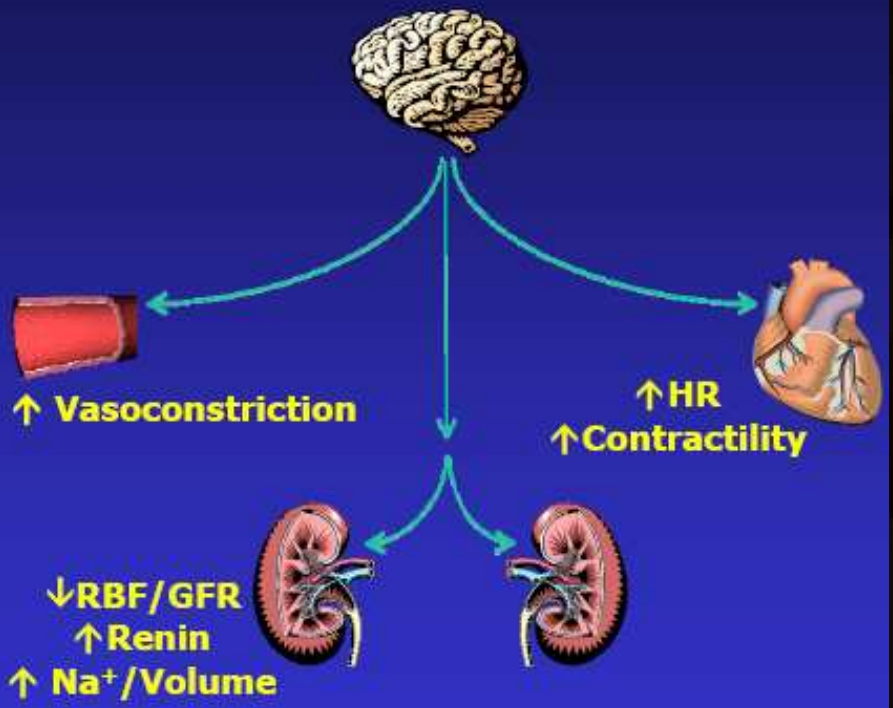
Renal Nerves and the SNS

Afferent Renal Sympathetics



The kidney is a source of central sympathetic drive in hypertension, heart failure, chronic kidney disease, and ESRD

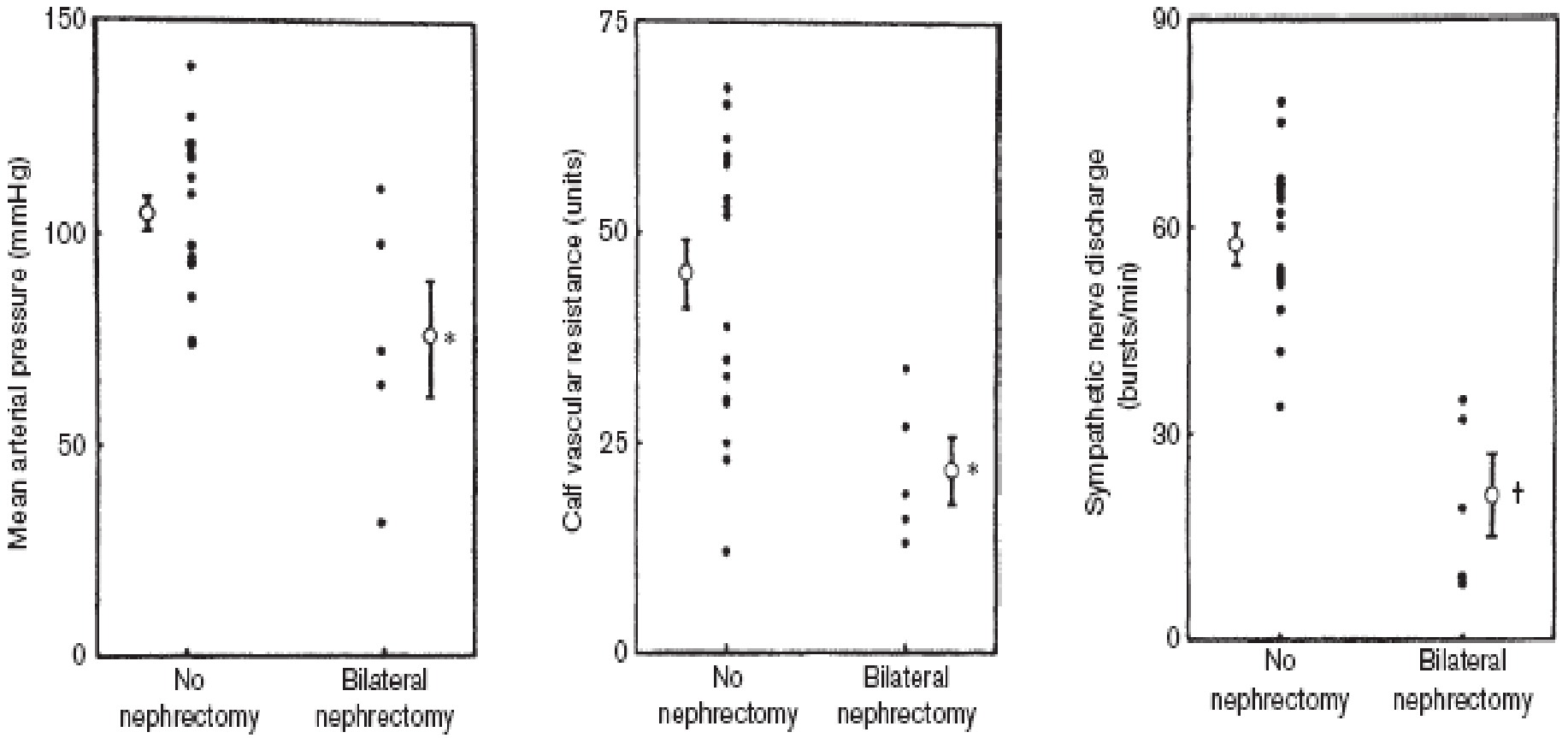
Efferent Sympathetic Activation



Patients cannot develop and/or maintain elevated BP without renal involvement

BIMM118

Importance of SNSA in CKD patients



Mean arterial pressure, vascular resistance in the calf and sympathetic nerve discharge in patients receiving hemodialysis who had undergone bilateral nephrectomy and in those who had not undergone nephrectomy. The solid circles are individual values, and the open circles and vertical bars are the mean ± SE values. The asterisks ($P < 0.05$) and dagger ($P < 0.01$) indicate a significant difference between the groups. (From Converse *et al.* [34] with permission. Copyright ©1992 Massachusetts Medical Society. All rights reserved.)

J Am Soc Nephrol 15: 524–537, 2004

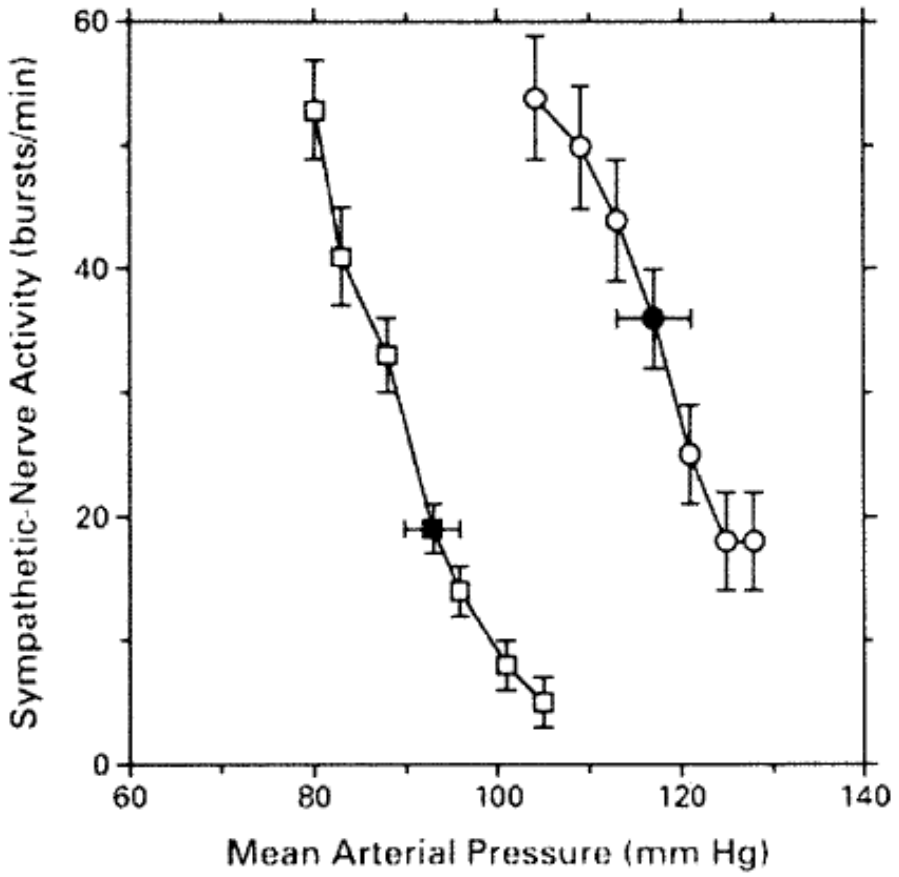


Figure 2. Baroreflex sensitivity assessed by changes in MSNA during acute pharmacologic variation of BP. In comparison with healthy subjects (squares), patients with CRF (circles) show a higher resting sympathetic activity and a curve shift to a higher BP level. However, baroreflex sensitivity is unchanged, because in the operating range (the area surrounding the baseline position; closed symbols), any change in BP causes comparable changes in MSNA in both groups.

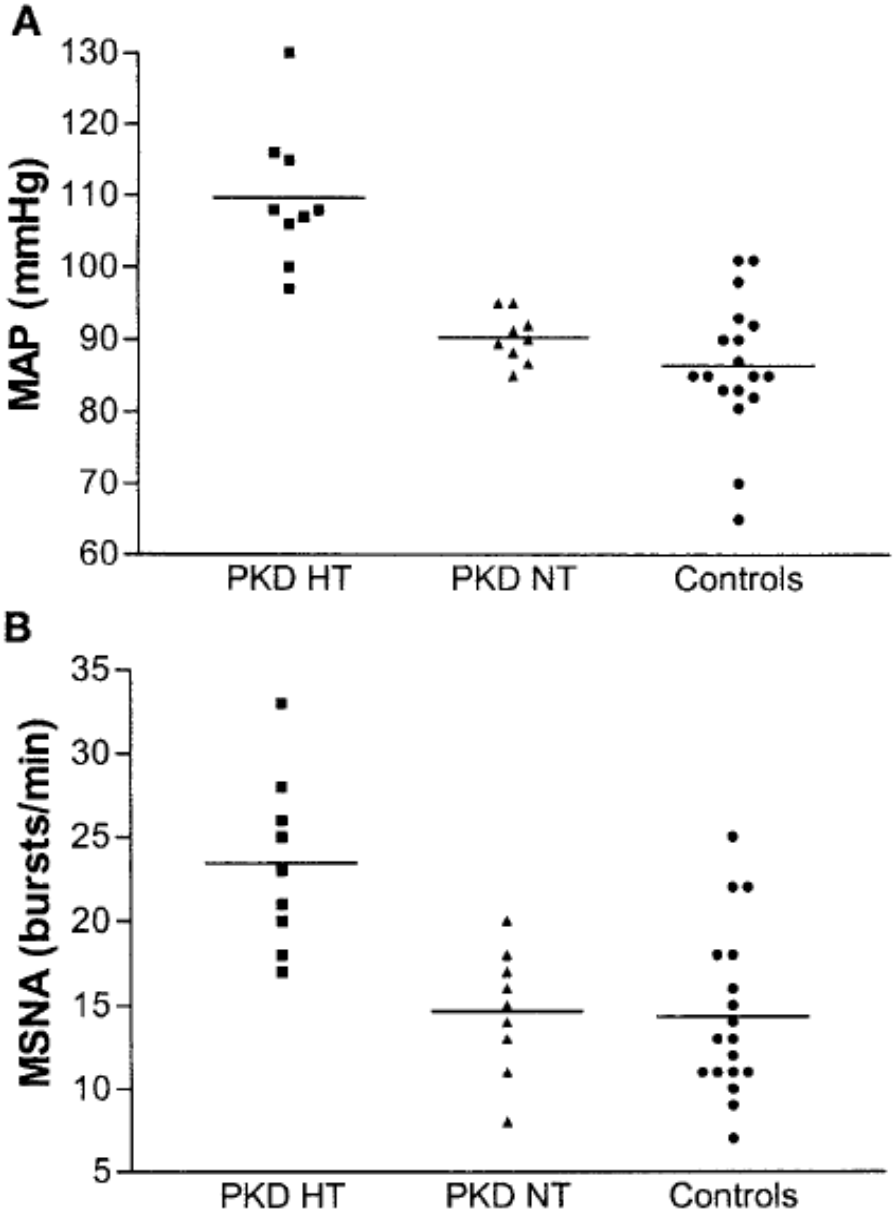


Figure 3. MSNA and mean arterial pressure (MAP) in patients with polycystic kidney disease (PKD) and healthy control subjects. MSNA is elevated only in the hypertensive (HT) patients, and not in the normotensive (NT) patients. The patients have early PKD, and GFR is still normal. Reprinted from reference 23, with permission.

Early Sympathetic Activation in the Initial Clinical Stages of Chronic Renal Failure

Guido Grassi, Fosca Quarti-Trevano, Gino Seravalle, Francesca Arenare, Marco Volpe, Silvia Furiani, Raffaella Dell'Oro and Giuseppe Mancia

Hypertension published online Feb 7, 2011;

Table 1. Demographic, Anthropometric, Biochemical, Hemodynamic, Echocardiographic, Neurohumoral, and Microneurographic Characteristics of Control Patients and Patients With Renal Failure

Variable	Control Patients (n=31)	Renal Failure Patients (n=42)
Sex, men/women	28/3	32/10
Age, y	56.6±1.3	60.7±1.8
BMI, kg/m^2	26.1±0.6	27.2±0.6
Waist circumference, cm	91.1±1.8	94.8±1.9
Waist:hip ratio	0.93±0.02	0.96±0.02
Estimated glomerular filtration rate, mL/min per 1.73 m^2	85.2±2.4	40.7±1.7*
Hemoglobin, g/dL	14.0±0.9	13.9±1.3
Sphygmomanometric BP, S/D, mm Hg	142.3±2.1/77.7±1.8	143.6±2.5/73.2±1.4
Heart rate, bpm	69.1±1.3	74.4±2.0*
Plasma NE, pg/mL	259.3±21.3	350.8±47.7
LVEDD, mm	50.9±1.0	49.8±0.5
LVMI, g/m^2	111.4±2.4	117.4±1.8
LVEF, %	61.3±1.0	59.6±0.8
Proteinuria, g/24 h	0.04±0.01	1.6±0.2†
MSNA, bursts per minute	31.5±1.4	43.8±1.4‡
MSNA, bursts per 100 heartbeats	45.7±2.0	60.0±2.1‡

Data are shown as mean±SEM unless otherwise indicated. BMI indicates body mass index; S, systolic; D, diastolic; NE, norepinephrine.

*$P<0.05$ refers to the statistical significance between renal failure patients and controls.

†$P<0.001$ refers to the statistical significance between renal failure patients and controls.

Table 2. Subgroups of Patients According to Estimated Glomerular Filtration Rate (Modification of Diet in Renal Disease Quartiles)

		Estimated Glomerular Filtration Rate, mL/min per 1.73 m^2	
Quartile	Subjects (n)	Mean±SEM	Range
I	18	95.4±1.6	106–75
II	17	67.6±1.7	74–55
III	18	47.5±1.2	54–41
IV	20	31.4±1.8	40–17

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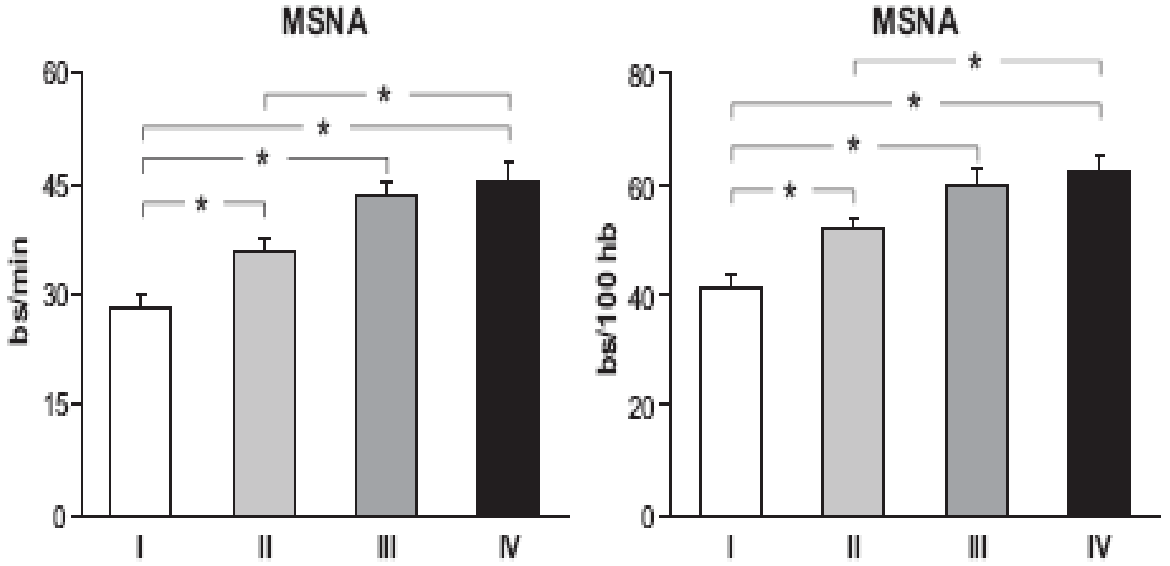


Figure 2. MSNA expressed as burst incidence over time (bursts per minute, left) or as burst incidence corrected for heart rate (bursts per 100 heartbeats, right) in the subjects of the study grouped according to quartiles of estimated glomerular filtration rate. Asterisks (*$P<0.05$) refer to the statistical significance between quartiles. Data are shown as mean±SEM.

Beta blockers in the management of chronic kidney disease

GL Bakris[1], P Hart[2] and E Ritz[3]

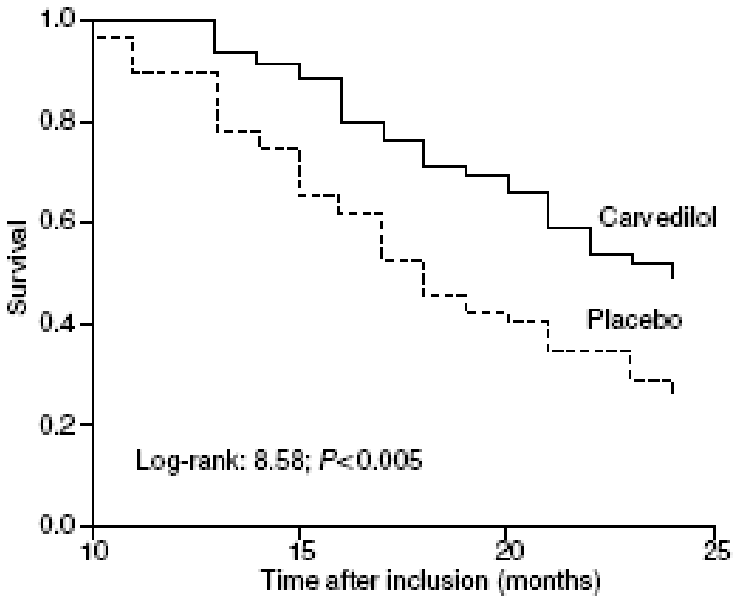
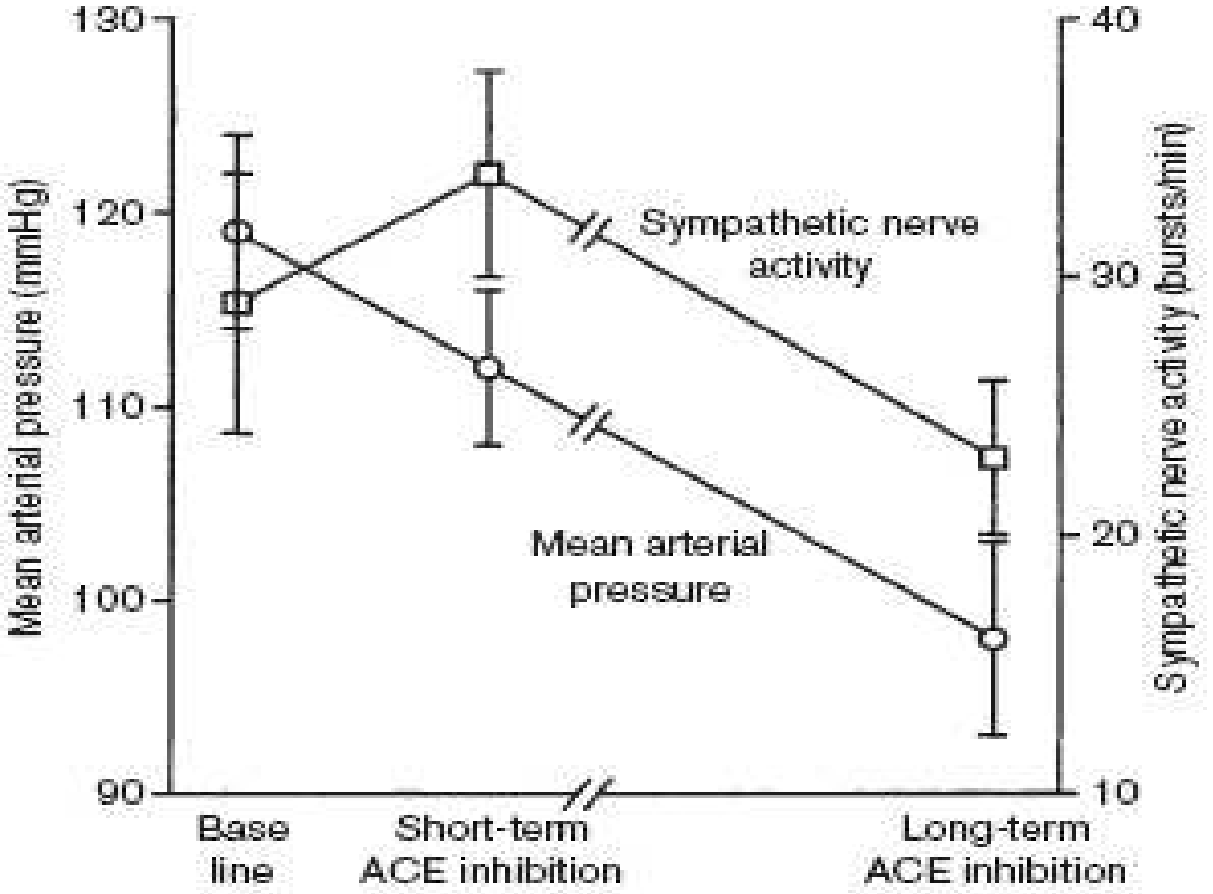


Figure 1 | Kaplan–Meier curve for all-cause mortality during 24-month follow-up in hemodialysis patients with cardiomyopathy according to the use of carvedilol. Used with permission.[12]

The sympathetic nervous system modulates renal function through its receptors namely β_1 (cardiac output and renin release), α_1 (systemic and renovascular constriction), and β_2 renovascular dilation. Sympathetic overactivity is commonly seen in chronic kidney disease (CKD) and is an important contributor to increasing the risk of cardiovascular events as well as increasing renal disease progression. Recent

It is apparent that greater use of this drug class for blood pressure control would further enhance reduction of risk of heart failure, the most common cause of death in the first year of starting dialysis.



Changes in mean arterial pressure and muscle sympathetic nerve activity during an intravenous infusion of enalaprilat and during long-term treatment with enalapril in nine patients with chronic renal failure. The mean arterial pressure was decreased by both long-term treatment with enalapril ($P < 0.001$) and short-term infusion of enalaprilat ($P = 0.007$). Muscle sympathetic nerve activity was decreased by long-term treatment with enalapril ($P < 0.001$) and increased by a short-term infusion of enalaprilat ($P = 0.005$). Values are means ± SE. ACE denotes angiotensin converting enzyme. (From Ligtenberg *et al.* [60] with permission. Copyright ©1999 Massachusetts Medical

Sympathetic hyperactivity in haemodialysis patients is reduced by short daily haemodialysis

Oliver Zilch[a,b], Pieter F. Vos[a,b], P. Liam Oey[c], Maarten-Jan M. Cramer[d], Gerry Ligtenberg[b], Hein A. Koomans[b] and Peter J. Blankestijn[b]

2007

Table 1 Dialysis, neurohumoral, and haemodynamic parameters in 11 patients during conventional haemodialysis and at 6 months after conversion to short daily haemodialysis

	CHD	SDHD
Plasma urea pre-dialysis (mmol/l)	28.6 ± 6.0	25.7 ± 6.6*
Plasma urea post-dialysis (mmol/l)	12.3 ± 3.0	14.8 ± 4.1*
Single-pool Kt/V urea per week	3.6 ± 0.4	4.6 ± 1.2*
Dry weight (kg)	67.6 ± 10.9	68.9 ± 11.6
Ultrafiltration volume per dialysis (l)	2.4 ± 1.0	1.5 ± 0.6*
Ultrafiltration volume per week (l)	7.0 ± 3.0	8.8 ± 3.6*
ECFV (ml/kg)	380 ± 55	361 ± 51
PRA (fmol/l per second)[a]	280 (115–1527)	810 (177–1805)
MSNA (bursts/min)	39 ± 19	28 ± 15*
Heart rate (beats/min)[b]	81 ± 16	78 ± 17
Stroke volume (ml)	59 ± 16	62 ± 12
Cardiac output (l/min)	4.6 ± 1.0	4.7 ± 0.9
Mean arterial pressure (mmHg)	113 ± 11	98 ± 9*
Total peripheral resistance (mmHg/min per l)	25.4 ± 6.4	21.2 ± 3.2*

CHD, Conventional haemodialysis; ECFV, extracellular fluid volume (ml/kg lean body mass); MSNA, muscle sympathetic neural activity; PRA, plasma renin activity; SDHD, short daily haemodialysis. [a] Median and 25–75% interquartile range. [b] Heart rate average over 24 h. * $P \leq 0.05$.

Table 2 Ambulant interdialytic blood pressure data (during 2 days) in 11 patients during conventional haemodialysis and at 6 months after conversion to short daily haemodialysis

	CHD		
	Day 1	Day 2	SDHD
MAP diurnal (mmHg)	111 ± 12	111 ± 12	104 ± 13*
MAP nocturnal (mmHg)	102 ± 11	102 ± 12	90 ± 13*
Day–night difference (%)	8.7 ± 6.6	7.8 ± 5.8	13.5 ± 6.4*
SBP diurnal (mmHg)	148 ± 17	148 ± 18	141 ± 21
SBP nocturnal (mmHg)	139 ± 15	138 ± 19	127 ± 19*
Day–night difference (%)	6.3 ± 4.5	7.0 ± 4.2	9.8 ± 4.6*
DBP diurnal (mmHg)	91 ± 9	90 ± 10	85 ± 10*
DBP nocturnal (mmHg)	82 ± 9	83 ± 9	72 ± 13*
Day–night difference (%)	8.8 ± 5.7	7.4 ± 6.2	15.7 ± 7.4*

CHD, Conventional haemodialysis; DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure; SDHD, short daily haemodialysis. * $P \leq 0.05$ compared with CHD.

Sympathetic hyperactivity in haemodialysis patients is reduced by short daily haemodialysis

Oliver Zilch[a,b], Pieter F. Vos[a,b], P. Liam Oey[c], Maarten-Jan M. Cramer[d], Gerry Ligtenberg[b], Hein A. Koomans[b] and Peter J. Blankestijn[b]

Table 3 Neurohumoral and haemodynamic parameters in seven patients during conventional haemodialysis, at 6 months after conversion to short daily haemodialysis, and at 2 months after switching back to conventional haemodialysis

	CHD	SDHD	CHD
Dry weight (kg)	69.9 ± 13.6	71.5 ± 14	71.4 ± 14.6
ECFV (ml/kg)	376 ± 44	387 ± 47	376 ± 55
MSNA (bursts/min)	32 ± 19	24 ± 11*	33 ± 18**
Mean arterial pressure (mmHg)	115 ± 11	98 ± 10*	106 ± 18
Cardiac output (l/min)	4.9 ± 1.3	4.7 ± 1.2	4.4 ± 0.8
Total peripheral resistance (mmHg/min per l)	24.8 ± 5.9	21.1 ± 3.2*	24.8 ± 5.5**

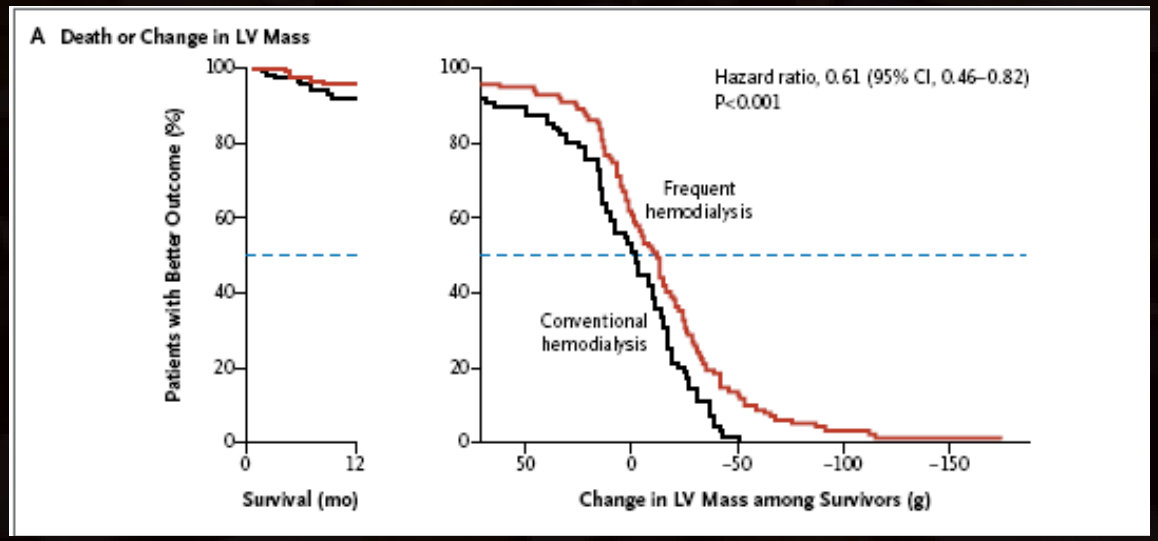
CHD, Conventional haemodialysis; ECFV, extracellular fluid volume (ml/kg lean body mass); MSNA, muscle sympathetic neural activity; SDHD, short daily haemodialysis. *$P \leq 0.05$ compared with CHD; **$P \leq 0.05$ compared with SDHD.

Conclusion The study shows that sympathetic hyperactivity in haemodialysis patients is reduced by increasing the frequency of treatment sessions. This is probably because of the decrease in number or magnitude of the fluid fluctuations. *J Hypertens* 25:1285–1289 © 2007

In-Center Hemodialysis Six Times per Week versus Three Times per Week

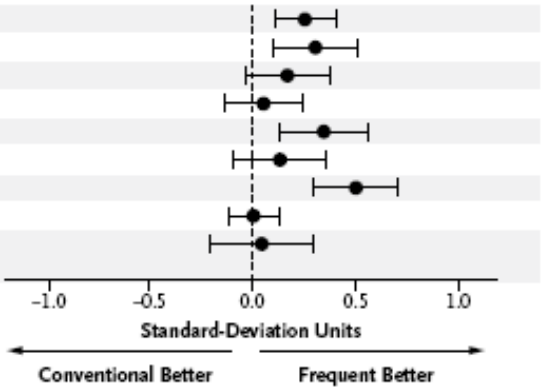
N Engl J Med 2010;363:2287-300.

The FHN Trial Group*

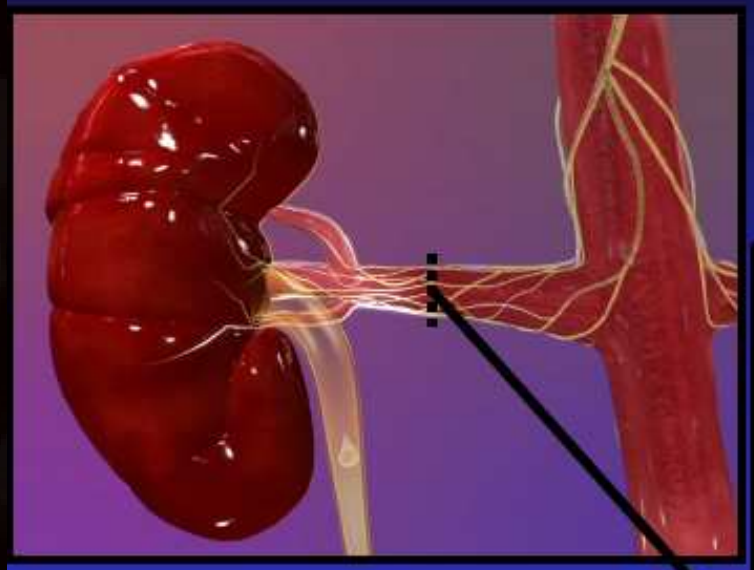


C Main Secondary Outcomes

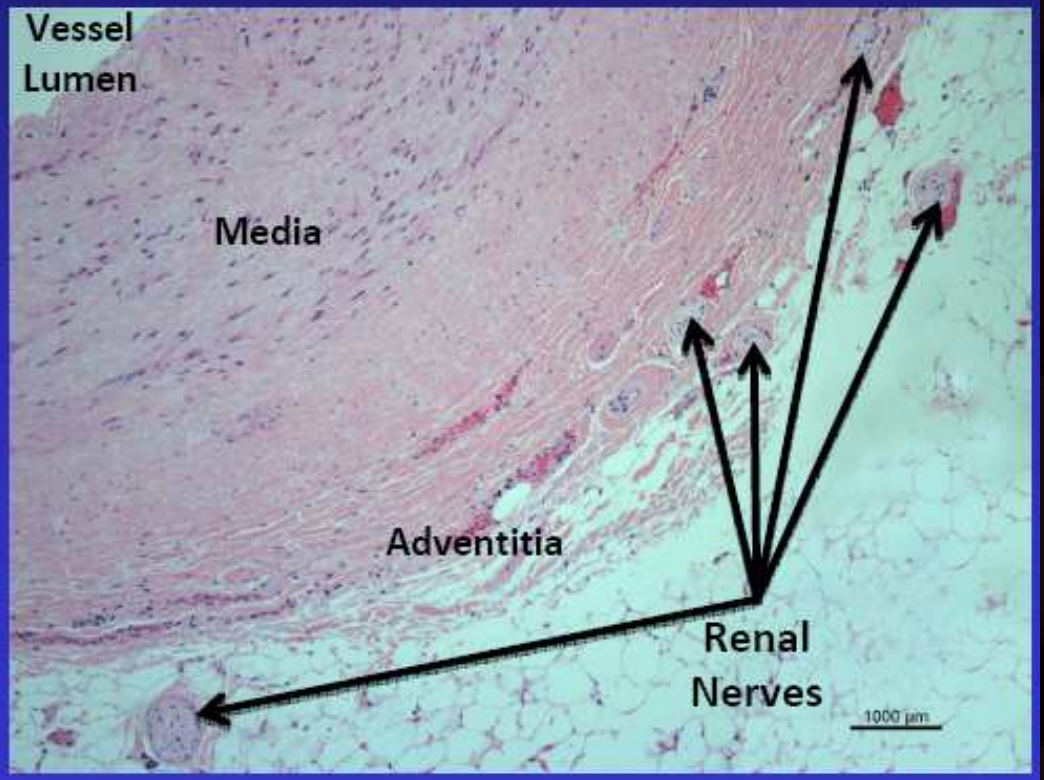
Outcome	Effect Measure
LV mass	Mean decrease
Physical-health composite score	Mean increase
Beck Depression Inventory score	Mean decrease
Predialysis albumin	Mean increase
Predialysis phosphorus	Mean decrease
ESA dose	Mean decrease in log
Predialysis systolic blood pressure	Mean decrease
Trail Making Test Part B	Negative log relative risk
Death or hospitalization unrelated to vascular access	Negative log hazard ratio



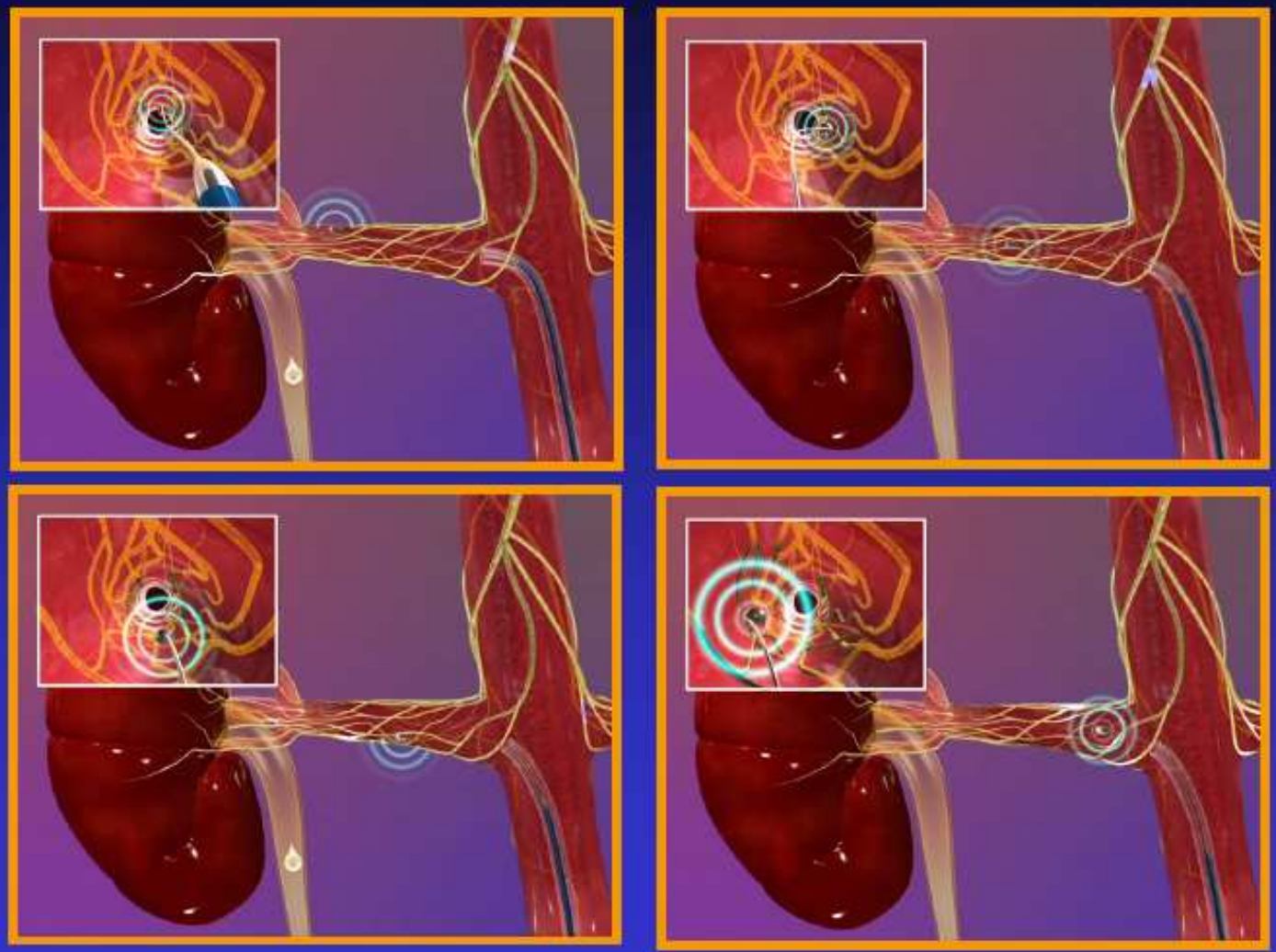
Renal Sympathetic Nerves as Therapeutic Target



- Arise from T10-L1
- Follow the renal artery to the kidney
- Primarily lie within the adventitia



Treatments



Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study

Symplicity 1

www.thelancet.com Vol 373 April 11, 2009

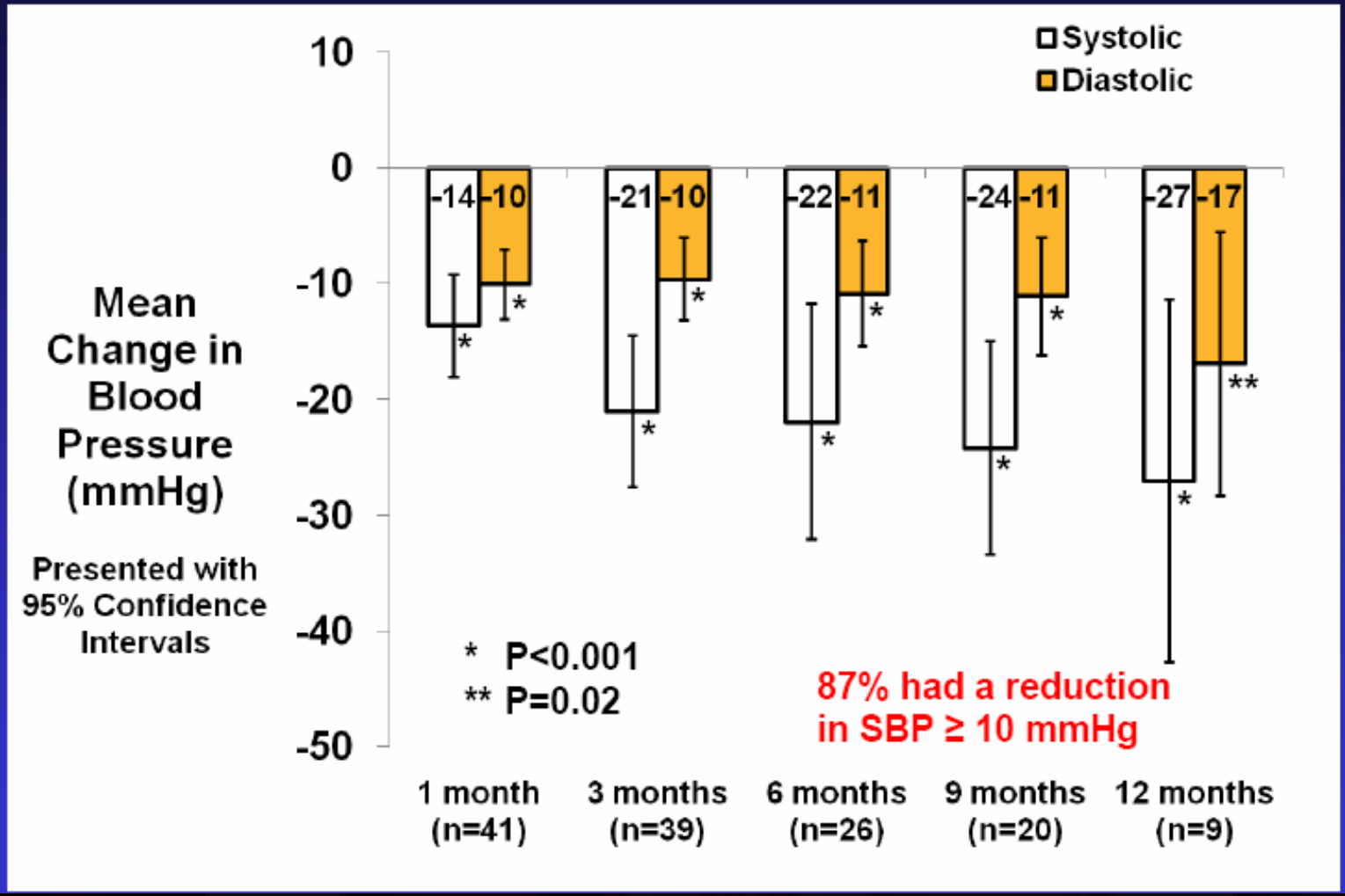
Henry Krum, Markus Schlaich, Rob Whitbourn, Paul A Sobotka, Jerzy Sadowski, Krzysztof Bartus, Boguslaw Kapelak, Anthony Walton, Horst Sievert, Suku Thambar, William T Abraham, Murray Esler

	All patients (N=50)	Patients undergoing procedure (N=45)	Patients not eligible for procedure (N=5)
Age (years)	57 (9)	58 (9)	51 (8)
Sex (female)	21 (42%)	20 (44%)	1 (20%)
Ethnic origin (non-white)	2 (4%)	2 (4%)	0
Type 2 diabetes mellitus	16 (32%)	14 (31%)	2 (40%)
CAD	11 (22%)	10 (22%)	1 (20%)
Hyperlipidaemia	34 (68%)	29 (64%)	5 (100%)
eGFR (mL/min/1·73 m^2)	83 (22)	81 (23)	95 (15)
Heart rate (bpm)	73 (11)	72 (11)	79 (9)
Blood pressure (mm Hg)	177/100 (19/14)	177/101 (20/15)	173/98 (8/9)
Number of antihypertension drugs	4·7 (1·4)	4·7 (1·5)	4·6 (0·5)
ACE or ARB	47 (94%)	43 (96%)	4 (80%)
β blocker	39 (78%)	34 (76%)	5 (100%)
Calcium-channel blocker	36 (72%)	31 (69%)	5 (100%)
Vasodilator	8 (16%)	8 (18%)	0%
Diuretic	46 (92%)	43 (96%)	3 (60%)

Data are mean (SD) or number (%). ACE=angiotensin-converting enzyme inhibitor. ARB=angiotensin II receptor blocker. bpm=beats per minute. CAD=coronary artery disease. eGFR=estimated glomerular filtration rate.

Table: Baseline patient characteristics

Results: Blood Pressure Reduction



Results: Procedure

- Procedure Time
  - Median 38 minutes
  - Interquartile range: 34-48 min
- Renal denervation effectiveness
  - Mean renal noradrenaline spillover (N=10) decrease was 47% (95% CI: 28-65%; p=0.0003)
- Ablation accompanied by pain
  - Managed by intravenous narcotics and/or sedatives
  - Pain did not persist beyond the RF energy application

Results: Vascular Safety

- Treatment delivered without complication in 96% (43/45)
  - 1 renal artery dissection during catheter delivery (before RF energy application), stented without further sequelae
  - 1 femoral pseudoaneurysm, manually reduced without further sequelae
- No long-term vascular complications observed
  - 18 patients with angiograms 14-30 day follow-up angiograms
  - 14 patients with 6-month MRA

Results: Subset with ABPM

- 12 patients had paired ABPM at baseline & >30 days post bilateral treatment
- Change in office SBP correlated with change in systolic ABPM (r^2=0.62, p=0.002)
- 67% were either non-dippers or reverse-dippers at baseline, whereas 33% remained non-dippers or reverse-dippers after the intervention

Results: Medication Changes

- Mean of 4.7 ± 1.5 anti-hypertensives at baseline, which was unchanged at the latest follow-up visit (p=NS)
- 3 patients required reduction of medications after normalization of BP

Results: Renal Safety

- Paired baseline & 6-month eGFR (MDRD) data available on 25 patients:
  - Baseline eGFR was 79 ± 21 mL/min/1.73m^2
  - 6-month follow-up eGFR was 83 ± 25 mL/min/1.73m^2
  - 6 had an improvement in eGFR of ≥ 20%
  - 1 had a reduction of eGFR of ≥ 20%
    - Associated with substantial decrease BP and addition of ARB and HCTZ

Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial

*Symplicity HTN-2 Investigators**

Lancet 2010; 376: 1903–09

	Renal denervation group (n=52)	Control group (n=54)
Baseline systolic blood pressure (mm Hg)	178 (18)	178 (16)
Baseline diastolic blood pressure (mm Hg)	97 (16)	98 (17)
Age (years)	58 (12)	58 (12)
Sex (female)	18 (35%)	27 (50%)
Race (white)	51 (98%)	52 (96%)
Body-mass index (kg/m²)	31 (5)	31 (5)
Type 2 diabetes	21 (40%)	15 (28%)
Coronary artery disease	10 (19%)	4 (7%)
Hypercholesterolaemia	27 (52%)	28 (52%)
eGFR* (mL/min per 1·73 m²)	77 (19)	86 (20)
eGFR* 45–60 mL/min per 1·73 m²	11 (21%)	6 (11%)
Serum creatinine (µmol/L)	91 (25)	78 (18)
Urine albumin-to-creatinine ratio (mg/g)†	128 (363)	109 (254)
Cystatin C (mg/L)‡	0·9 (0·2)	0·8 (0·2)
Heart rate (bpm)	75 (15)	71 (15)
Number of antihypertension medications	5·2 (1·5)	5·3 (1·8)
Patients on hypertension medication for more than 5 years	37 (71%)	42 (78%)
Patients on five or more medications	35 (67%)	31 (57%)

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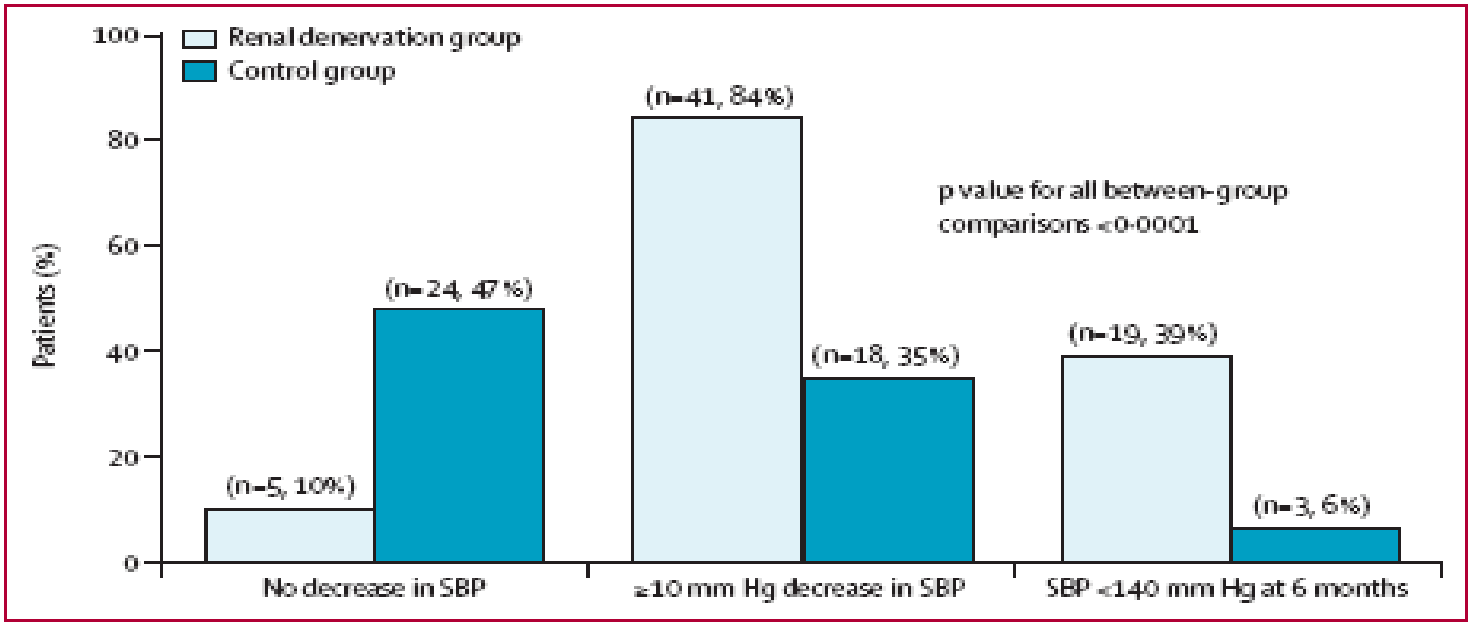


Figure 3: **Proportion of patients in the renal denervation and control groups that at 6 months had no decrease in systolic blood pressure, a 10 mm Hg or greater decrease in SBP, or achieved a SBP of less than 140 mm Hg**

SBP=systolic blood pressure.

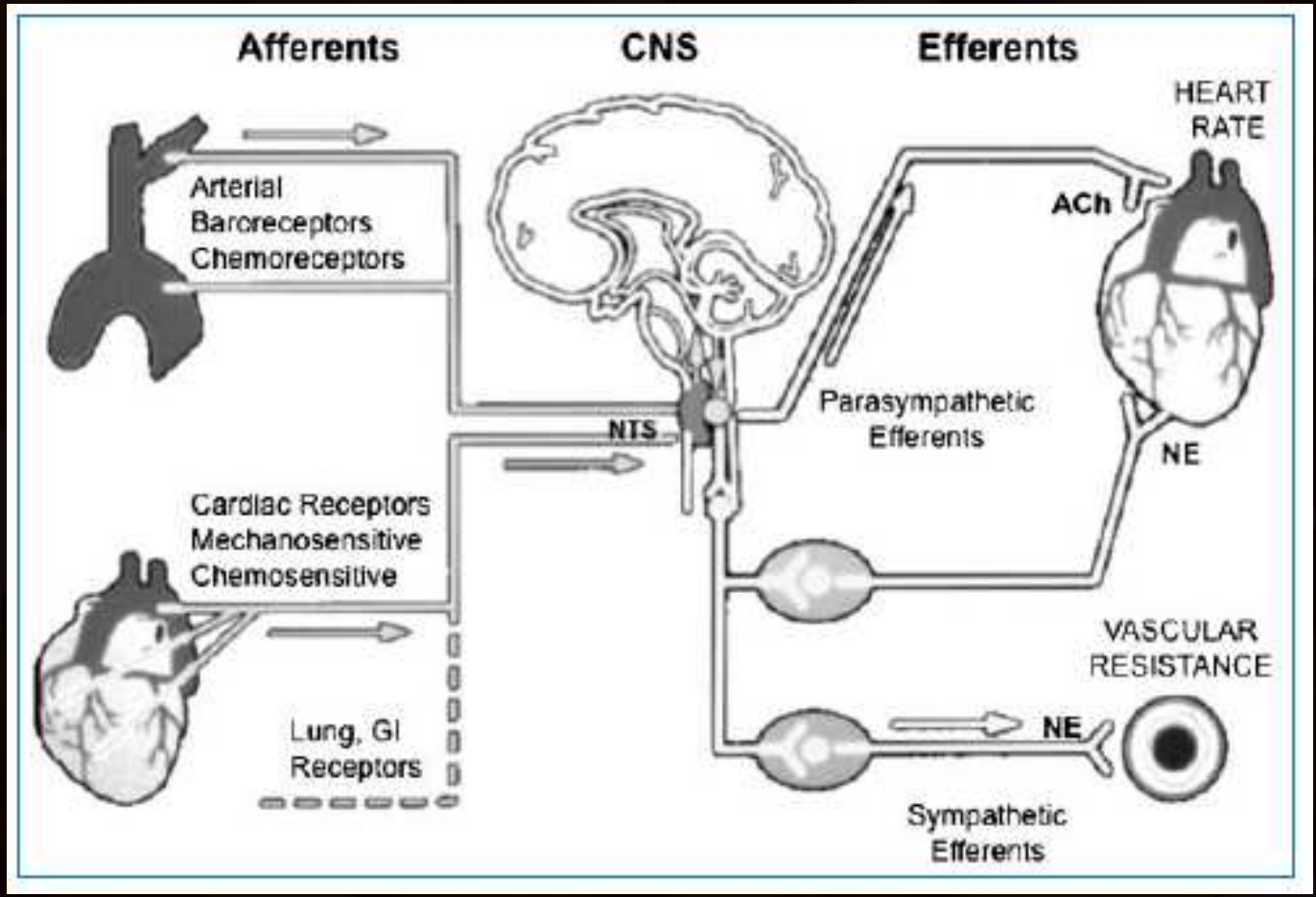
	Renal denervation group		Control group		Difference in mean change (95% CI)	p value
	Patients (n)	Mean change (SD)	Patients (n)	Mean change (SD)		
eGFR* (mL/min per 1·73 m²)	49	0·2 (11)	51	0·9 (12)	−0·7 (−5·4 to 3·9)	0·76
Serum creatinine (μmol/L)	49	0·2 (17·6)	51	−1·1 (10·3)	1·3 (−4·5 to 7·0)	0·67
Cystatin C (mg/L)	37	0·1 (0·2)	40	0·0 (0·1)	0·0 (0·0 to 0·1)	0·31

eGFR=estimated glomerular filtration rate. *Calculated on the basis of Modification of Diet in Renal Disease Study criteria.[22]

Table 2: **Baseline, change from baseline to 6 months, and difference in change in measured concentrations of eGFR, serum creatinine, and cystatin C for renal denervation and control groups**

Resistant Hypertension Treatment through Carotid Baroreceptor Stimulation

APJOC 2010; 000:(000). Month 2010



Electrical Carotid Baroreceptor Stimulation in Resistant Hypertension

Giuseppe Mancia, Gianfranco Parati and Alberto Zanchetti

Hypertension 2010;55;607-609; originally published online Jan 25, 2010;
DOI: 10.1161/HYPERTENSIONAHA.109.147306

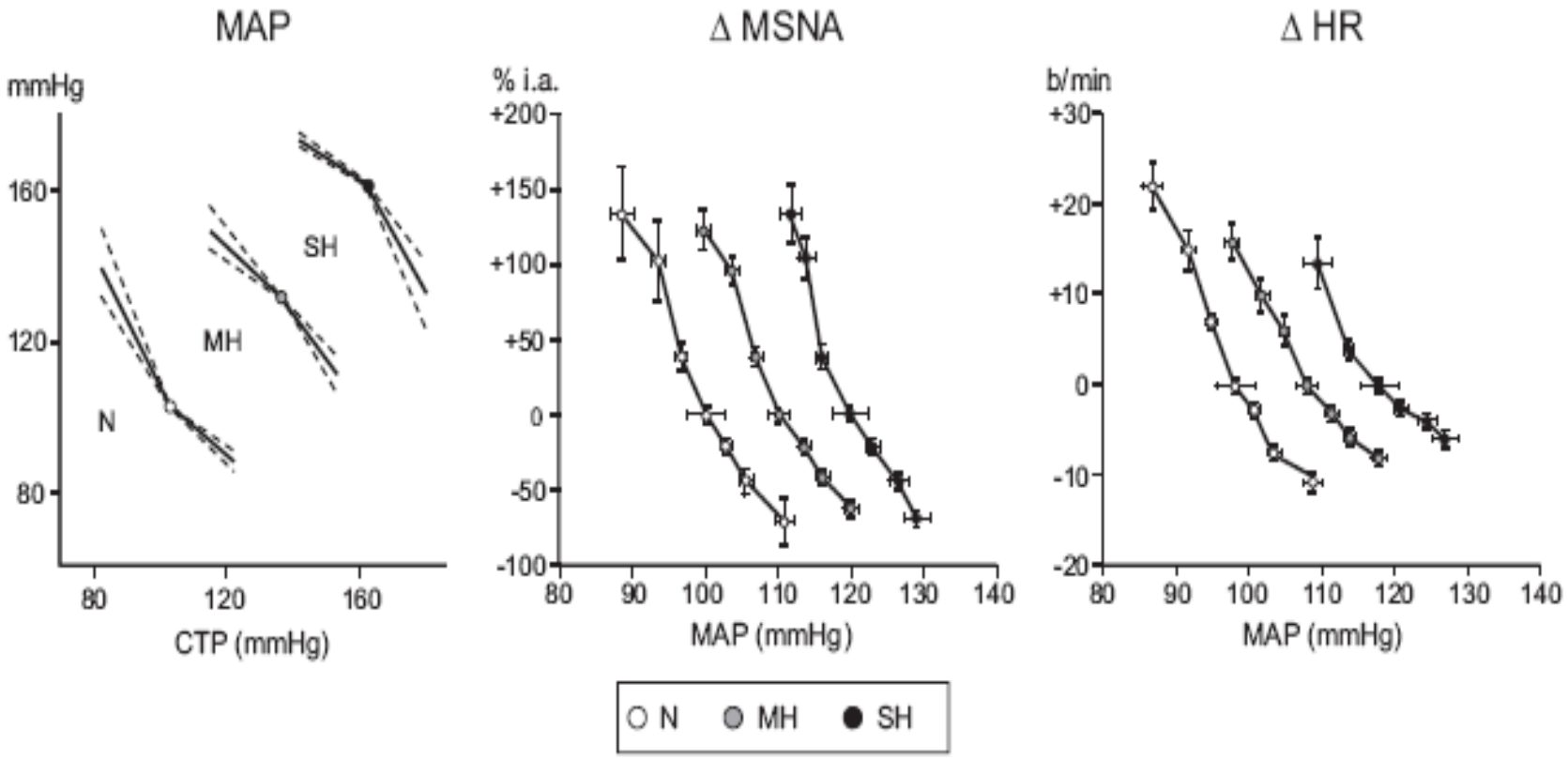
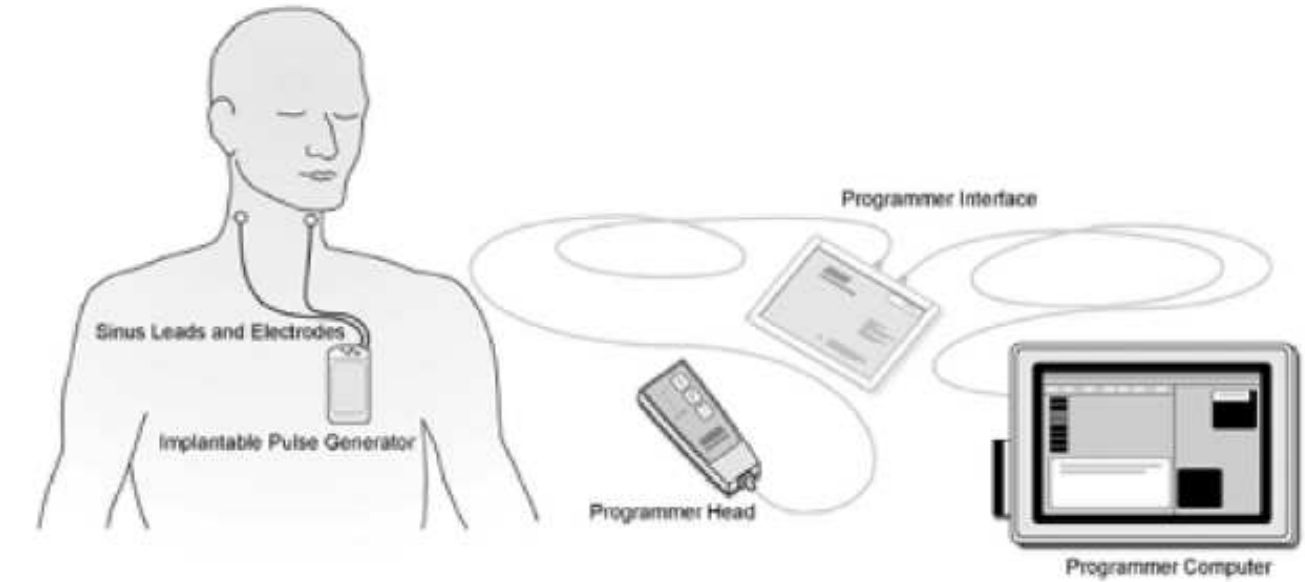


Figure. Left, Progressive reductions and increases in mean arterial pressure (MAP; intra-arterial measurements) in response to progressive increases and reductions in carotid transmural pressure (CTP) obtained via a neck chamber device. The central and right panels show the reductions and increases in muscle sympathetic nerve activity (MSNA) and heart rate (HR) in response to increases and reductions in MAP obtained via infusion of phenylephrine and nitroprussiate. Data refer to mean regression line or mean values (±SE) from normotensive subjects (N), moderate essential hypertensive subjects (MH), and severe essential hypertensive subjects (SH). Data



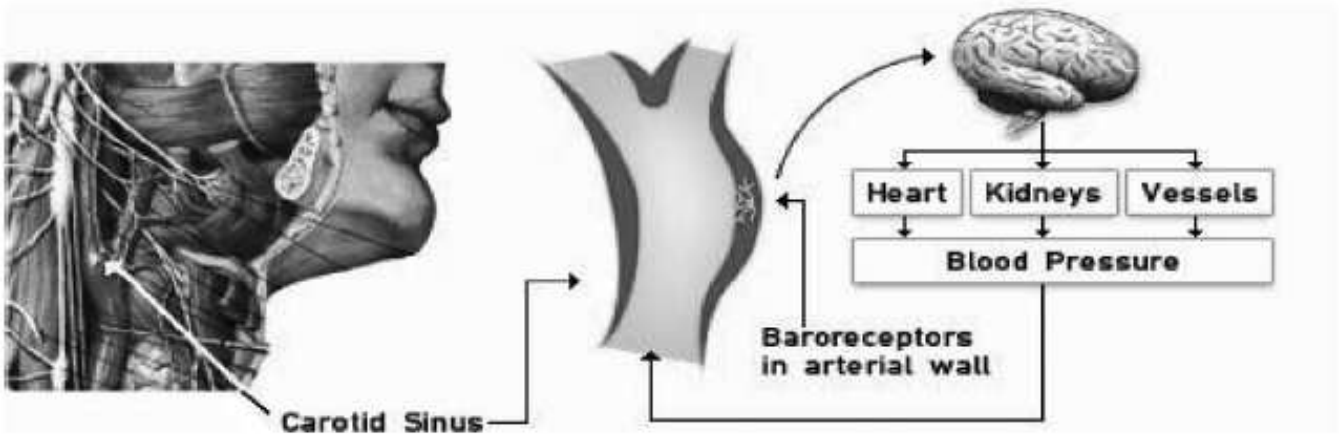


Figure 6. Representation of Rheos system (CV Rx) of carotid sinus stimulation.

Carotid Baroreceptor Stimulation, Sympathetic Activity, Baroreflex Function, and Blood Pressure in Hypertensive Patients

Karsten Heusser, Jens Tank, Stefan Engeli, André Diedrich, Jan Menne, Siegfried Eckert, Tim Peters, Fred C.G.J. Sweep, Hermann Haller, Andreas M. Pichlmaier, Friedrich C. Luft, Jens Jordan

Table 3. Individual Changes in Hemodynamic Variables

Identification No.	ΔSBP, mm Hg	ΔDBP, mm Hg	ΔHR, bpm	ΔMSNA				Stimulation, V
				Bursts per min	Bursts per 100 Heartbeats	au/min	10^{-3} au per Burst*	
1	−12	−5	−1	−0.8	+0.8	−0.37	−4.85	5.5
2	−7	−4	−3	+3.0	+5.9	+0.58	6.66	5.0
3	+7	+2	−1	+1.8	+3.4	+0.08	2.62	6.0
4	+1	−1	−1	−6.6	−9.2	−0.26	1.83	5.0
5	−88	−32	−13	−1.2	+5.0	−0.12	−2.50	4.0
6	−22	−16	−4	−2.2	+0.6	+0.58	11.23	6.0
7	−24	−9	0	−4.2	−6.9	−0.29	−2.58	7.0
8	−27	−15	−6	−10.5	−11.2	−0.97	−16.89	4.5
9	−54	−35	−10	−9.5	−1.6	−0.50	−1.94	7.0
10	−9	−1	−3	+1.0	+2.0	0.00	−0.98	7.0
11	−35	−14	−14	…	…	…	…	6.0
12	−108	−45	+1	−16.5	−28.1	−1.56	−18.02	5.0

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; au, arbitrary unit; …, no data.

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renin concentration decreased 20±8% ($P<0.05$). Electric field stimulation of carotid sinus baroreflex afferents acutely decreased arterial blood pressure in hypertensive patients, without negative effects on physiological baroreflex regulation. The depressor response was mediated through sympathetic inhibition. (***Hypertension*. 2010;55:619-626.**)

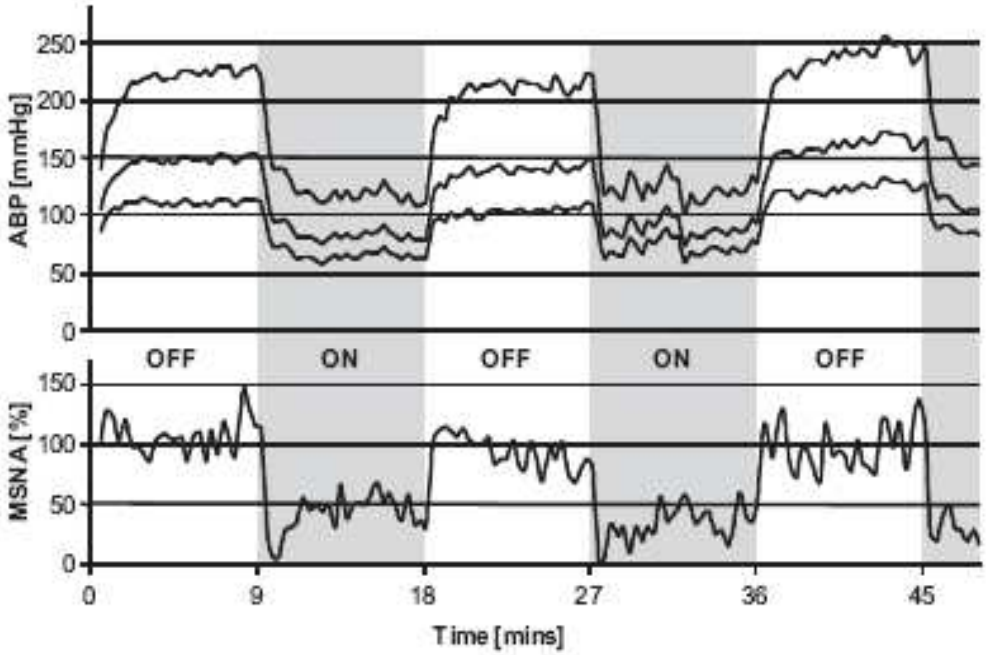
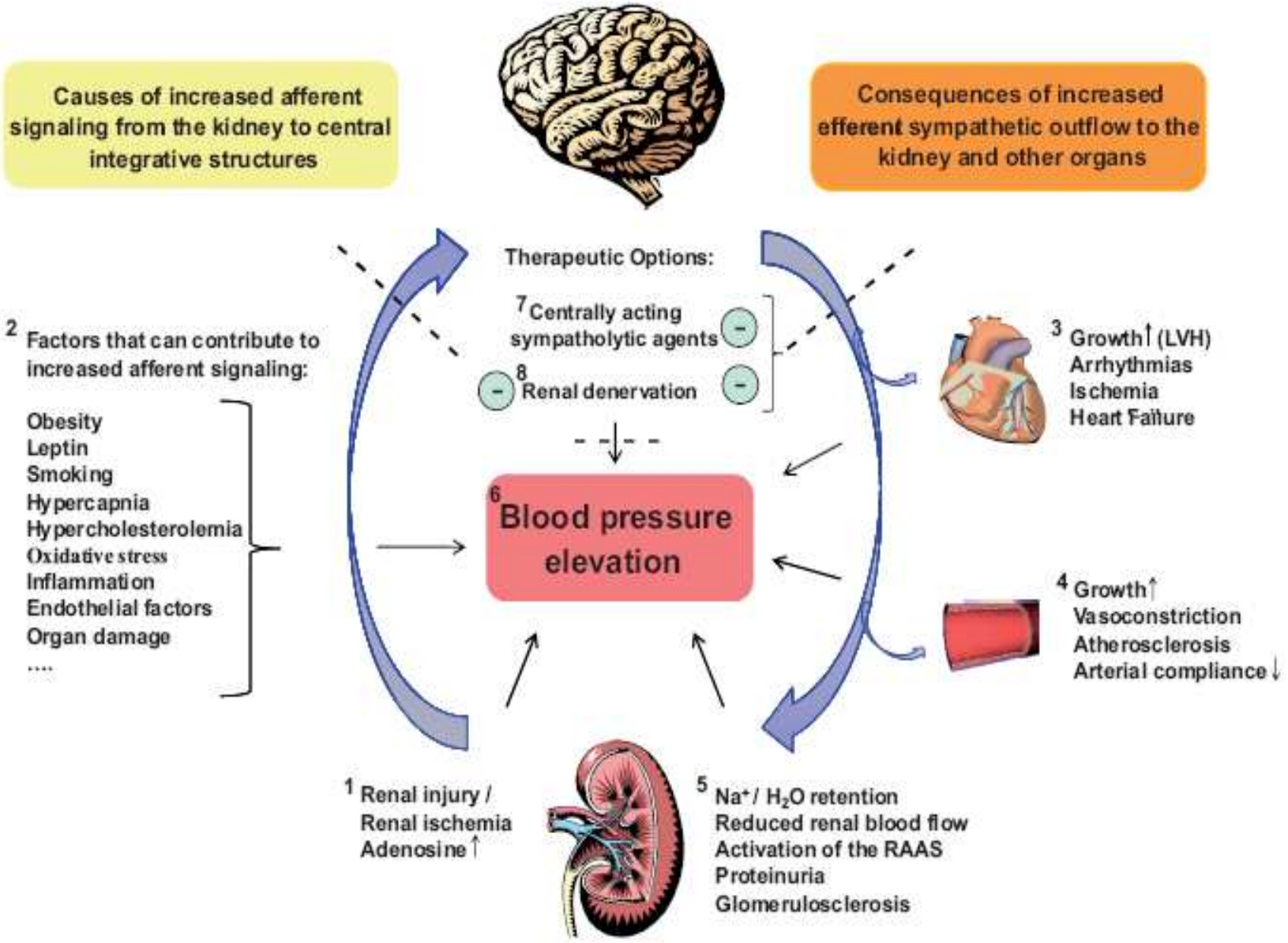


Figure 2. Response repeatability: systolic, mean, and diastolic arterial blood pressure (ABP) and relative total MSNA over time in patient 12. Each time the stimulator was switched on, ABP and MSNA decreased acutely and remained suppressed throughout the stimulation period.


Causes of increased afferent signaling from the kidney to central integrative structures
Consequences of increased efferent sympathetic outflow to the kidney and other organs
Therapeutic Options:
7 Centrally acting sympatholytic agents
8 Renal denervation
2 Factors that can contribute to increased afferent signaling:
Obesity
Leptin
Smoking
Hypercapnia
Hypercholesterolemia
Oxidative stress
Inflammation
Endothelial factors
Organ damage
....
6 Blood pressure elevation
3 Growth↑ (LVH)
Arrhythmias
Ischemia
Heart Failure
4 Growth↑
Vasoconstriction
Atherosclerosis
Arterial compliance↓
1 Renal injury /
Renal ischemia
Adenosine↑
5 Na+ / H2O retention
Reduced renal blood flow
Activation of the RAAS
Proteinuria
Glomerulosclerosis

Therapeutic strategies for targeting excessive central sympathetic activation in human hypertension

James P. Fisher[1] and Paul J. Fadel[2]

Resistant essential HTA, CKD ?

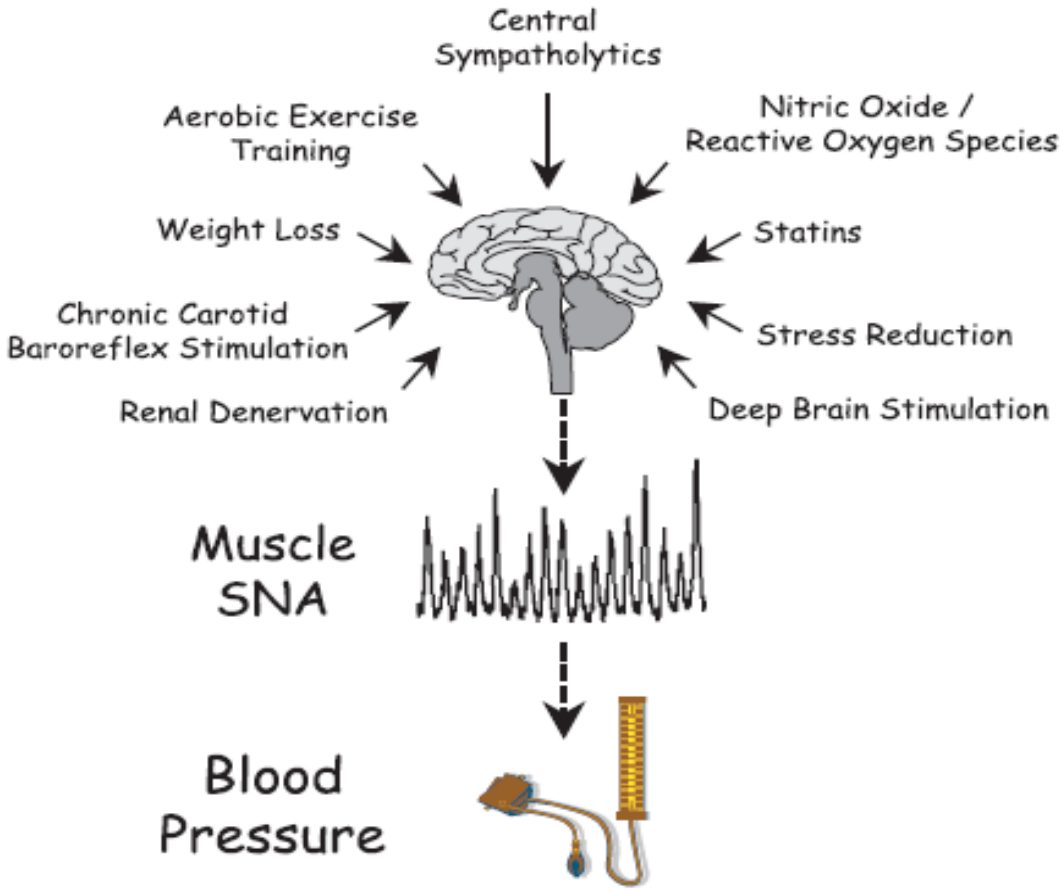


Figure 2. A schematic representation of the current therapeutic strategies and targets for reducing excessive central sympathetic nerve activity in hypertension
The sympathetic nervous system constitutes an important putative drug target in hypertension. As noted in the main text of this review, traditional pharmacological approaches for the management of essential hypertension appear ineffective in reducing central sympathetic outflow. This schematic diagram depicts several novel and promising therapeutic strategies for targeting neurogenic hypertension in the future. SNA, sympathetic nerve activity.