

# **Carotid Baroreflex Physiology and Baroreflex Activation Therapy Mechanism of Action**

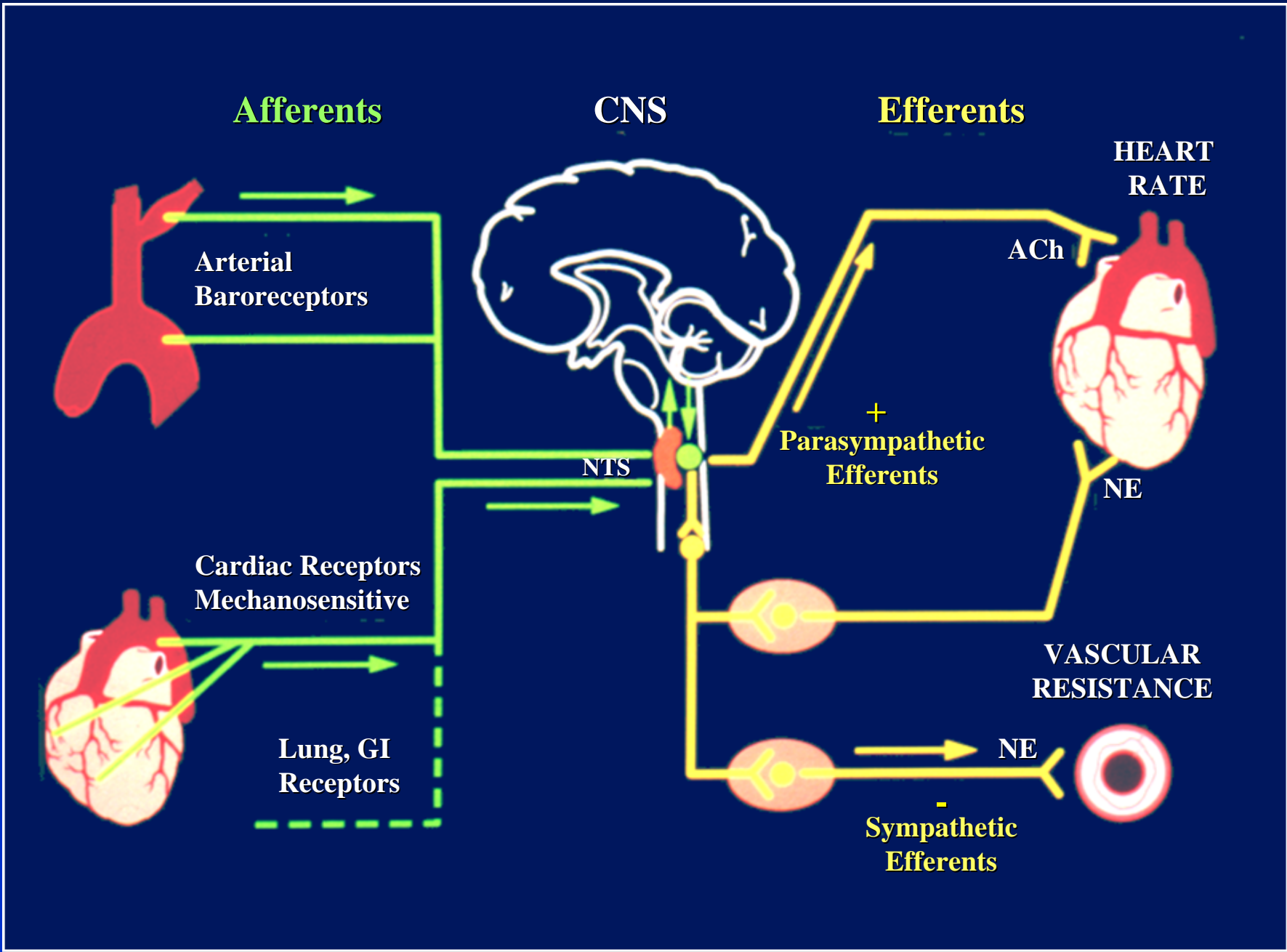
**Paris - ESC 30 August 2012**

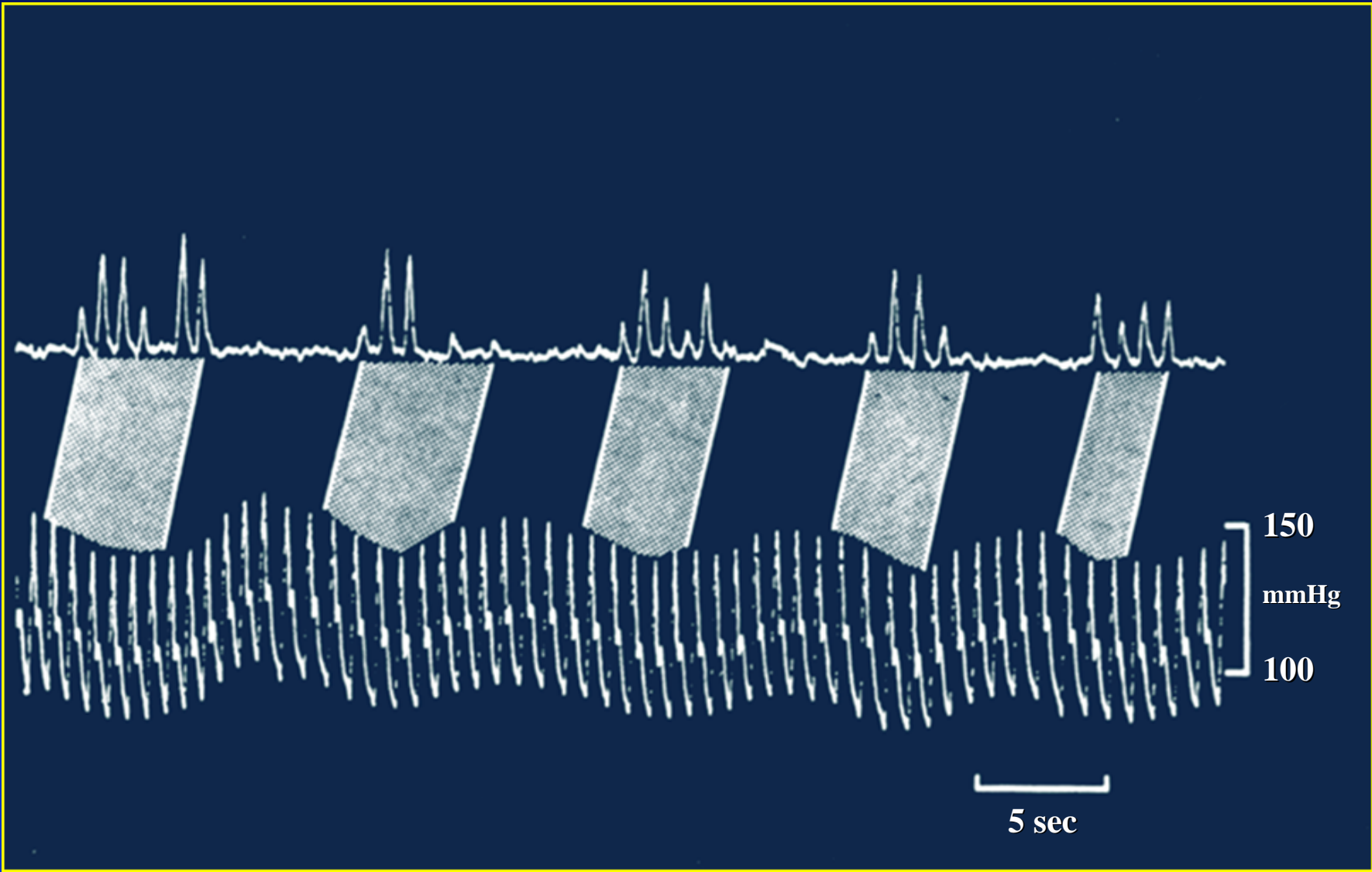
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*Milano, Italy*





# Electrical Stimulation of Carotid Sinus Nerves in the Sixties

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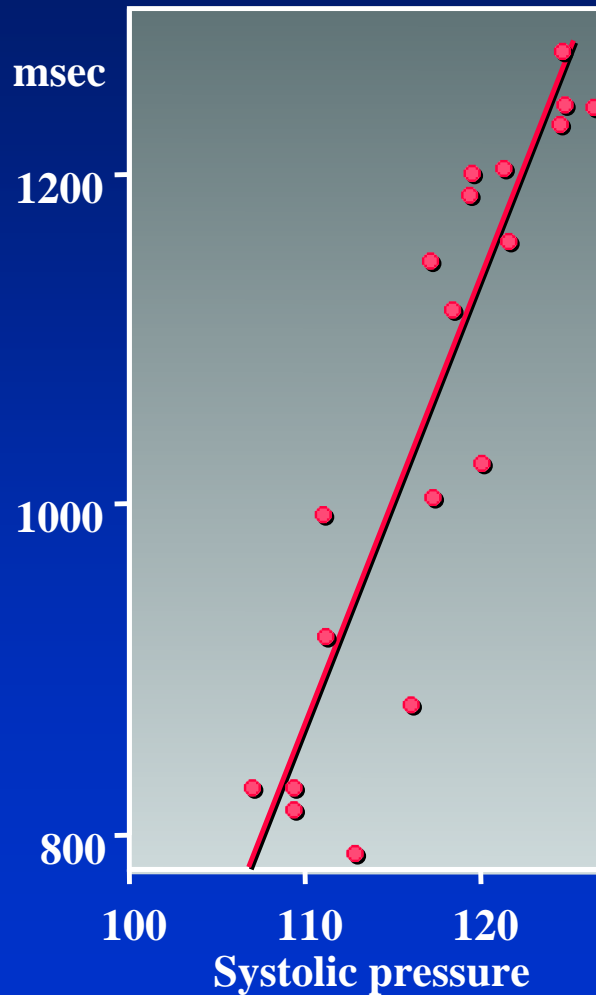
- Severe hypertension (vascular resistance ↓)
- Refractory angina pectoris
  - Bradycardia
  - ↓ Preload (venodilatation)
  - ↓ Afterload (arteriodilatation)
  - ↓ Myocardial contractility
  - ↓ Cardiac O<sub>2</sub> consumption
  - ↑ Coronary blood flow?
- Effects vanished after weeks
- Local disturbances from current spread to nearby tissues

# Reasons for Failure of Early Use of Carotid Baroreceptor Stimulation in Hypertension

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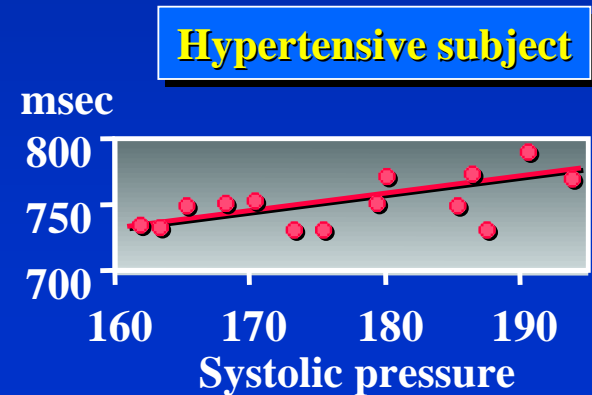
- **Effects typically short-lasting**
- **Opposition of aortic / cardiac mechano (baro) receptors**
- **Opposition by simultaneous carotid chemoreceptor stimulation**
- **Failure to increase stimulation parameters because of side effects**
- **In hypertension**
  - **Baroreceptor activation already maximal**
  - **Baroreflex impaired**

# Slope of Linear Regression between Systolic Pressure induced by Angiotensin and Lengthening of R-R Interval



**Normal subject**

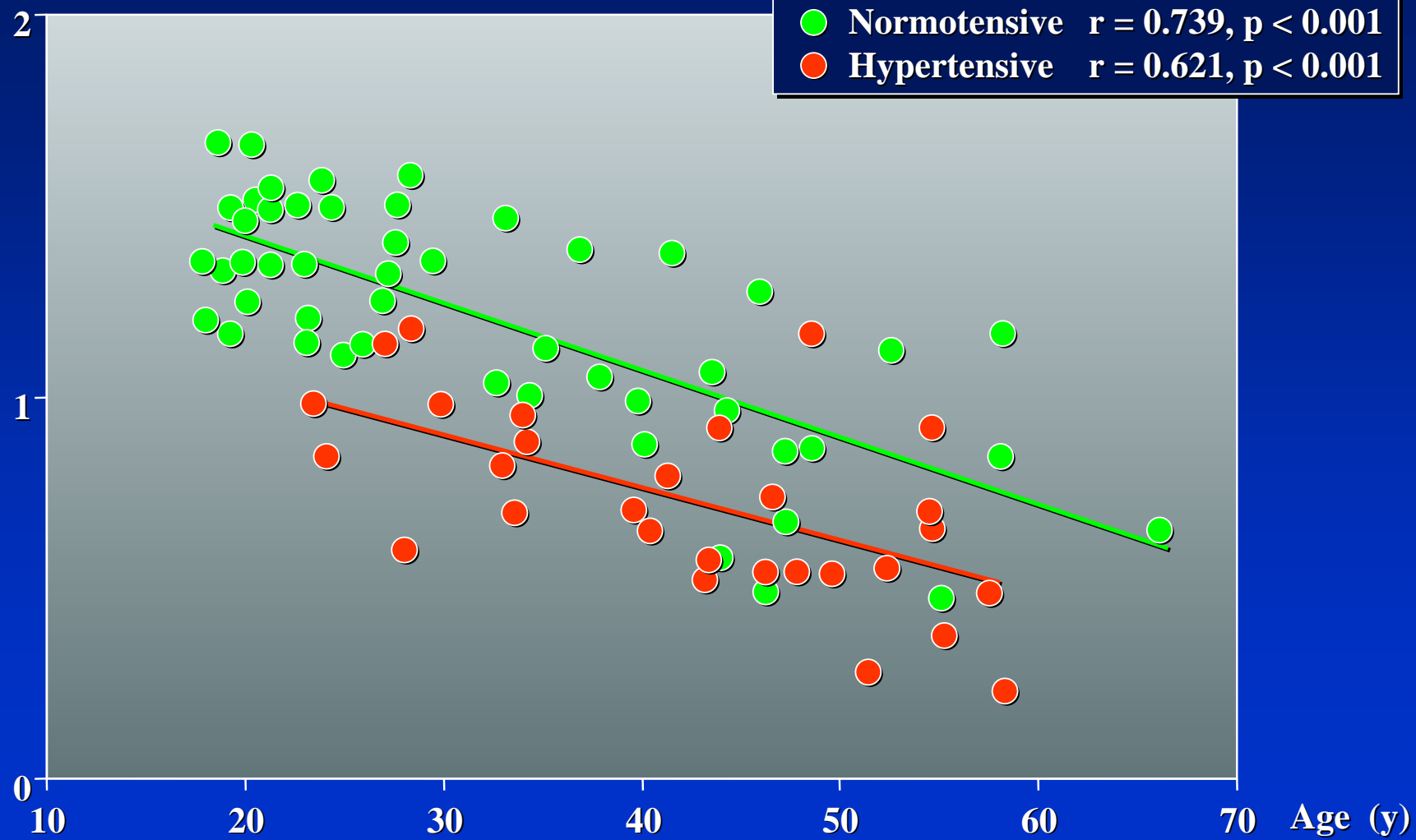
Slope = 27.3

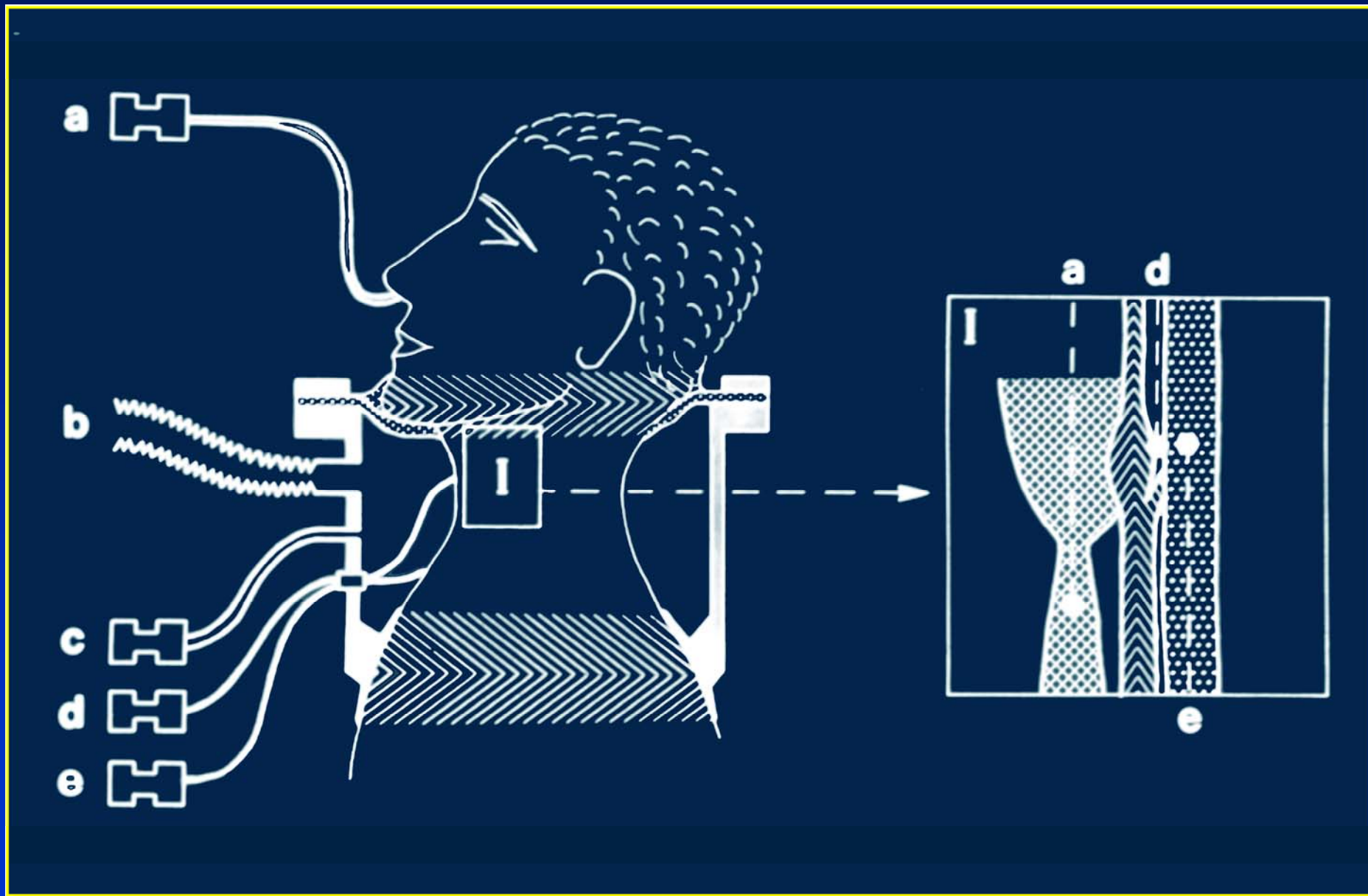


**Hypertensive subject**

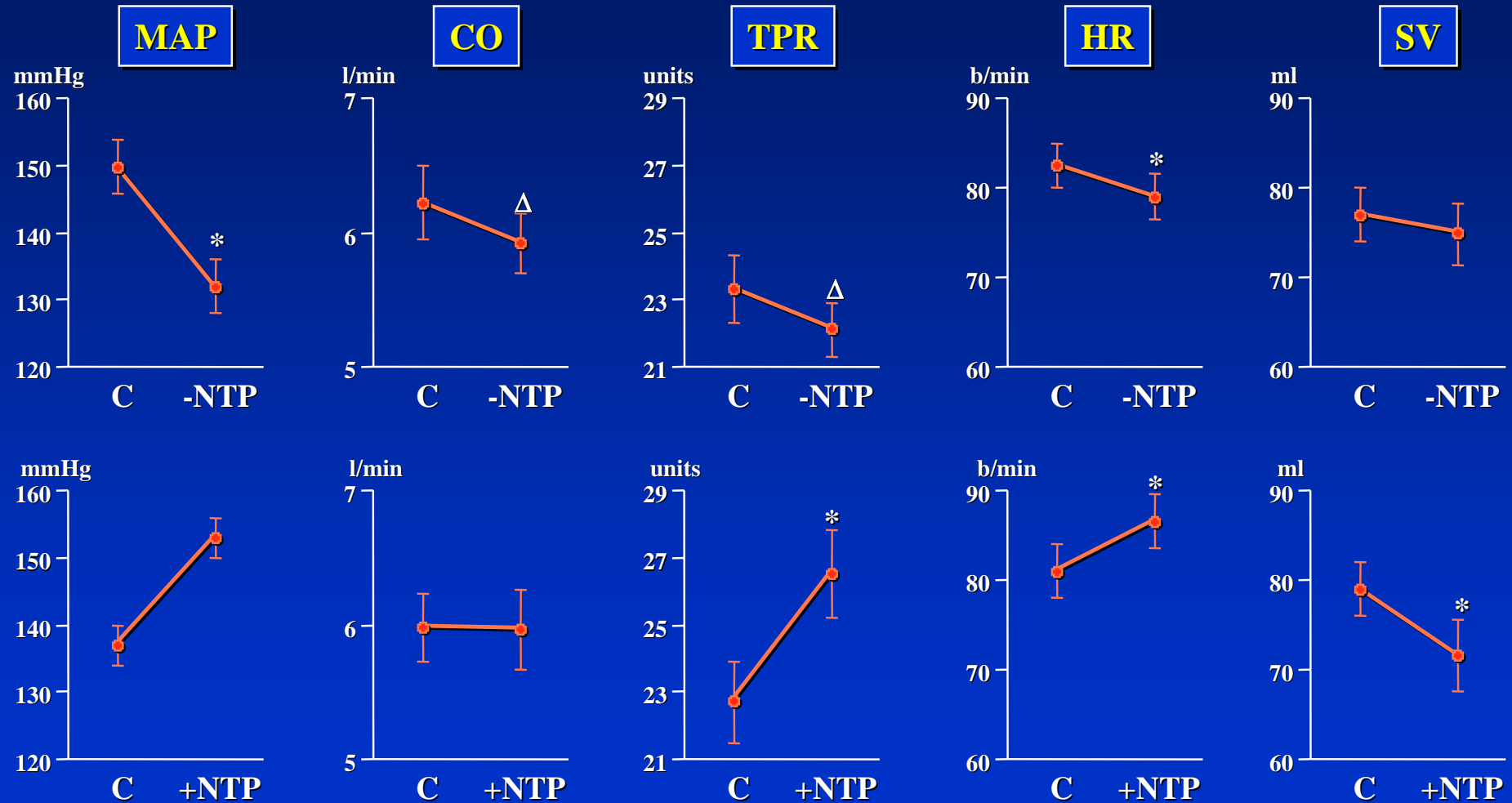
Slope = 1.6

Baroreflex sensitivity (log slope)



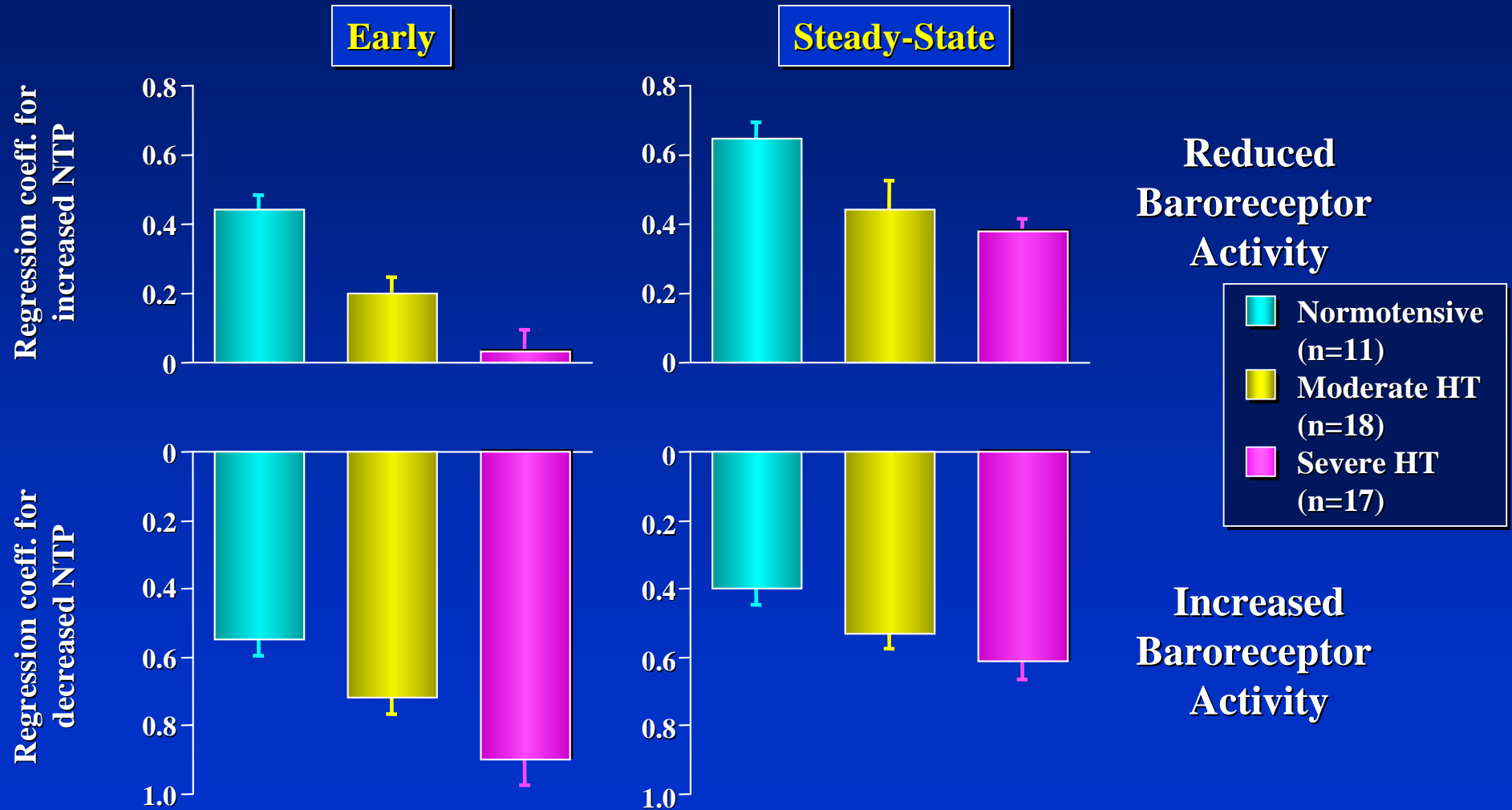


# Hemodynamic Responses to Activation of the Carotid Baroreceptors by Application of Negative (-35 ± 1 mmHg) or Positive (+33 ± 1 mmHg) Pressures within a neck Chamber in 27 Subjects

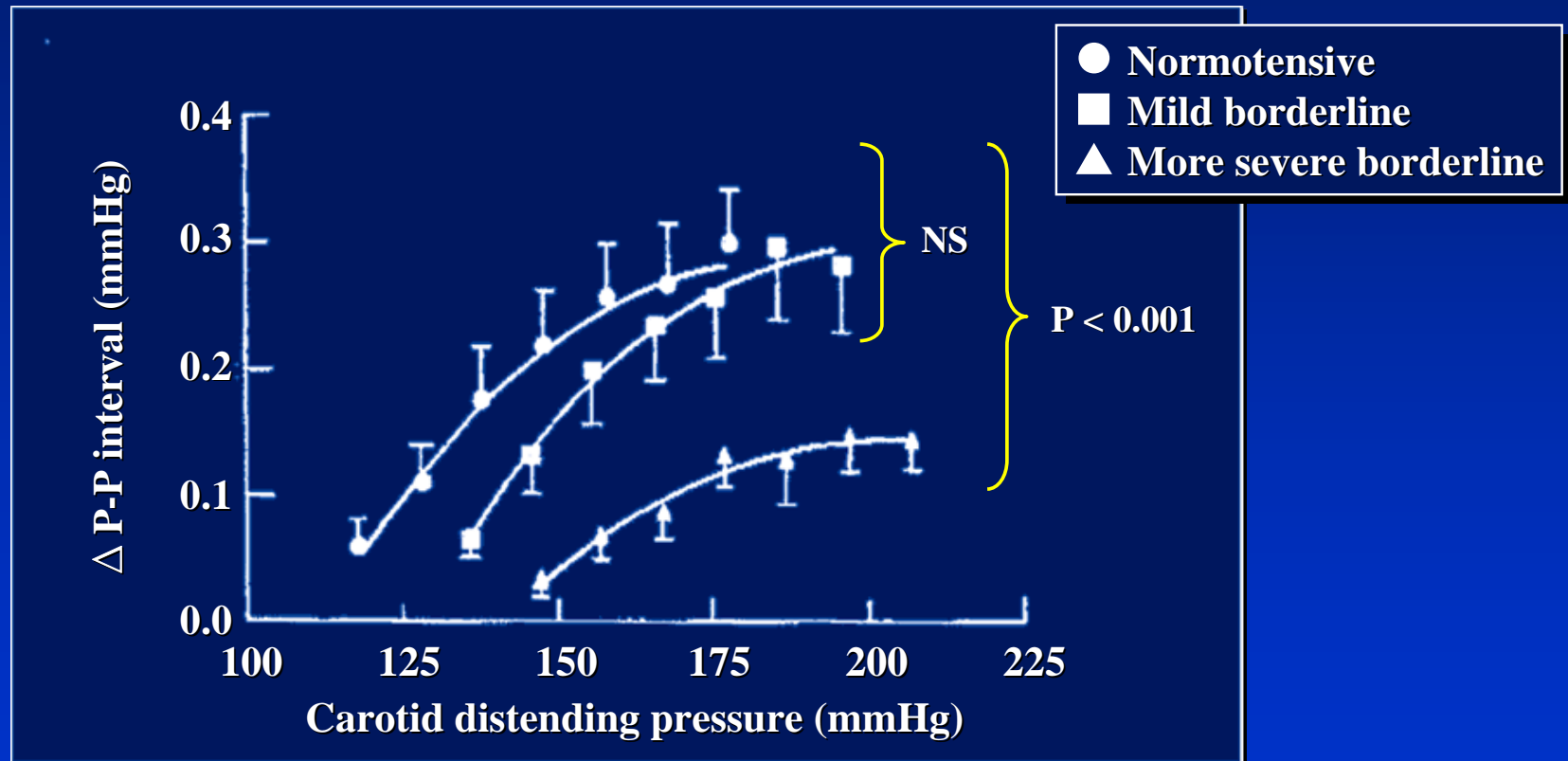


\* p 0.001; Δ p < 0.002

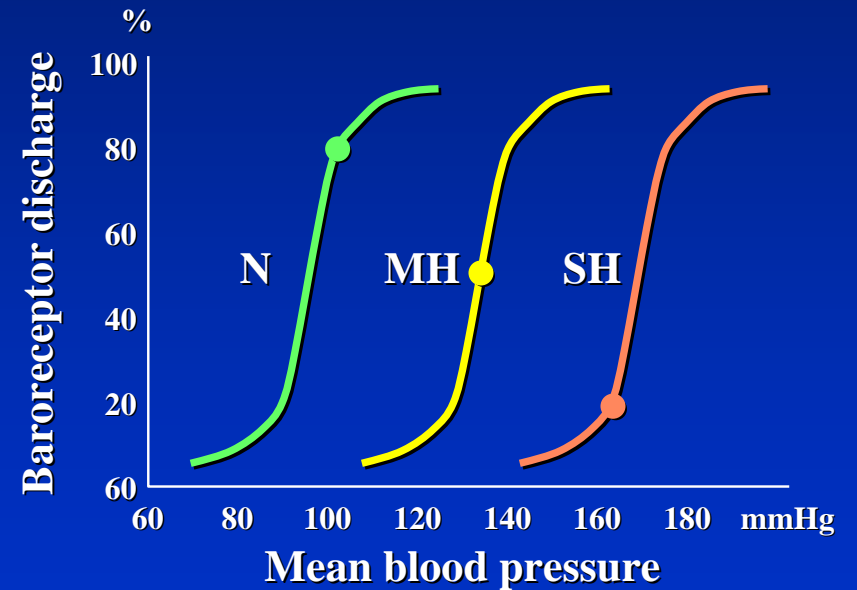
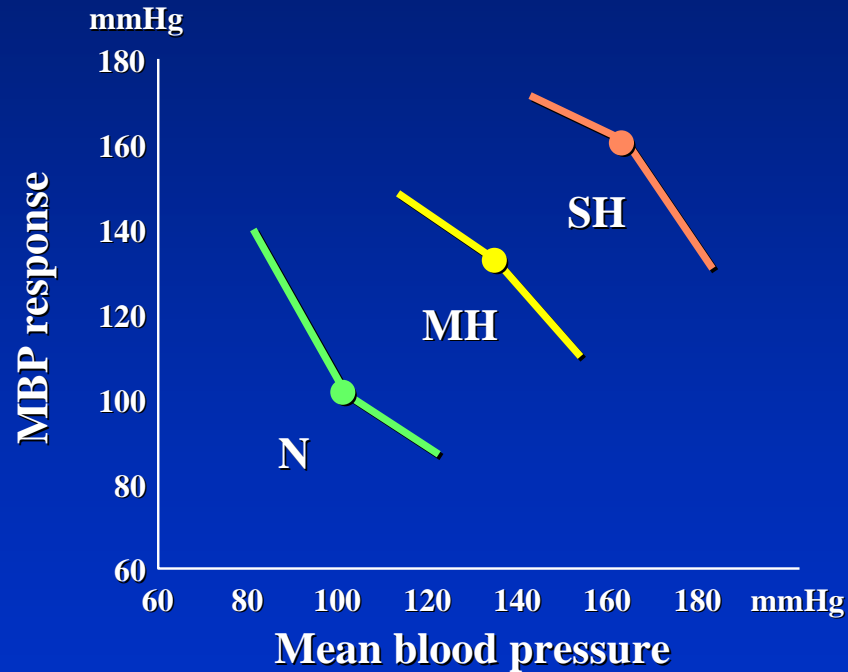
# MAP (i.a. measurements) Responses to Carotid Baroreceptor Deactivation and Stimulation in Normotension and Hypertension



# Increases in P-P Interval induced by Distending the Carotid Sinuses through Application of 0.6-S Negative Pressures within a Neck Chamber



# Schematic Drawing of the Stimulus-response Curves Relating Arterial BP and Carotid Baroreceptor Firing at Different BPs and the Concomitant Migration of the Reflex Set-point



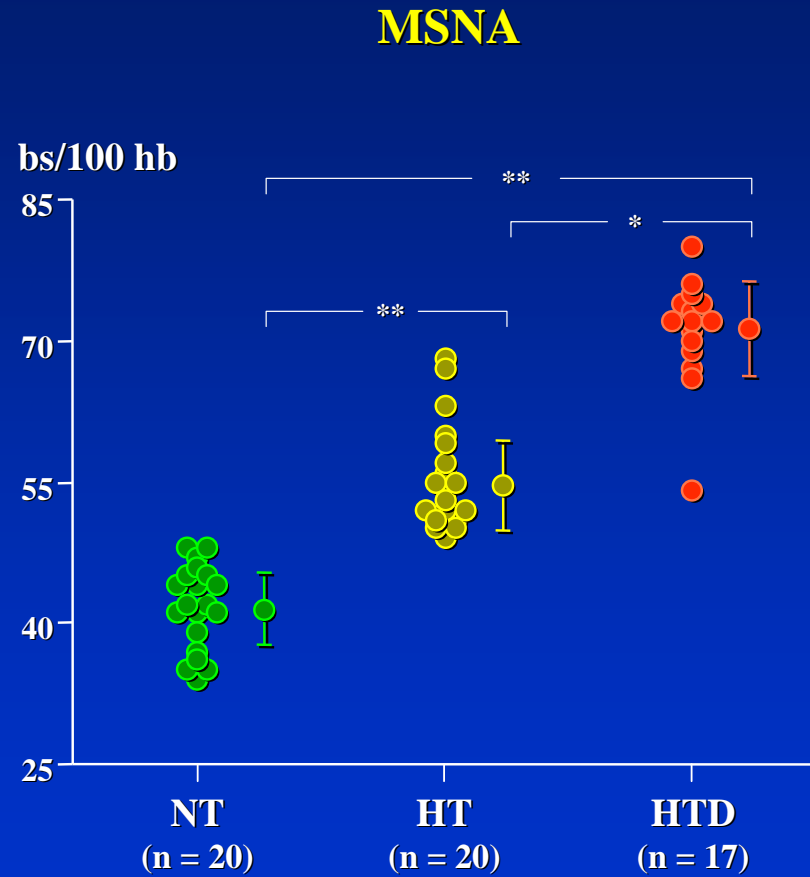
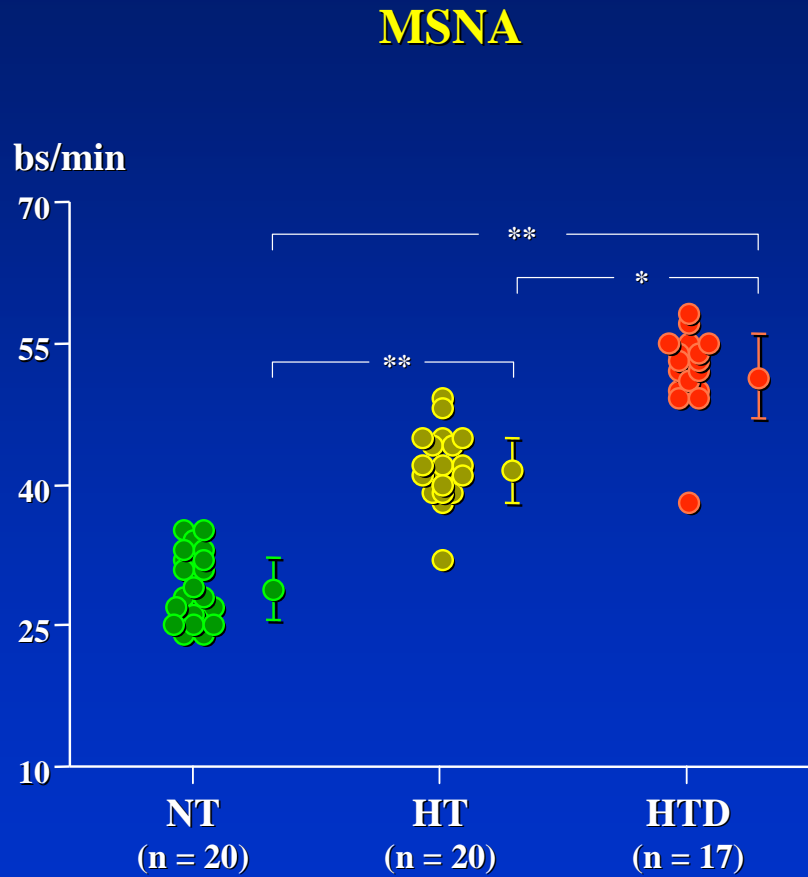
# Differential Baroreflex Control of Cardiovascular Targets

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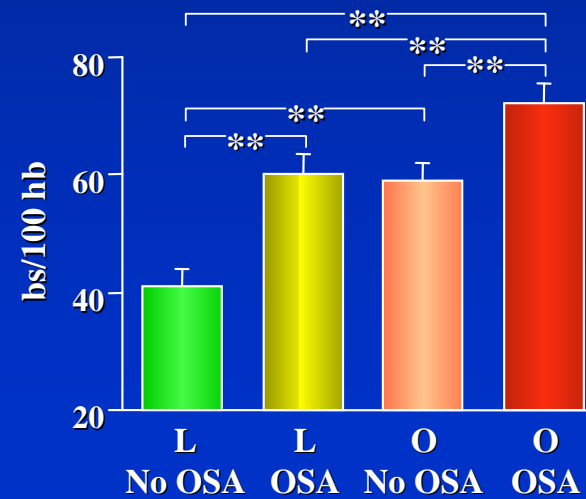
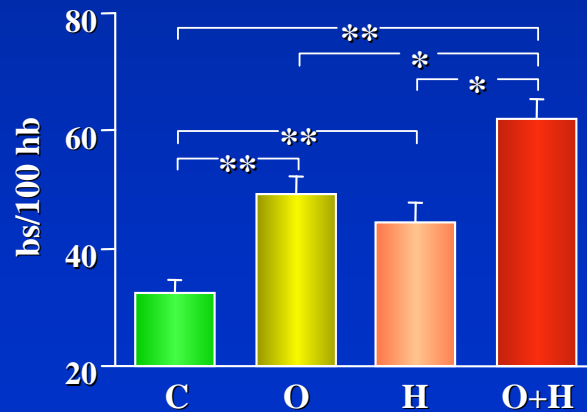
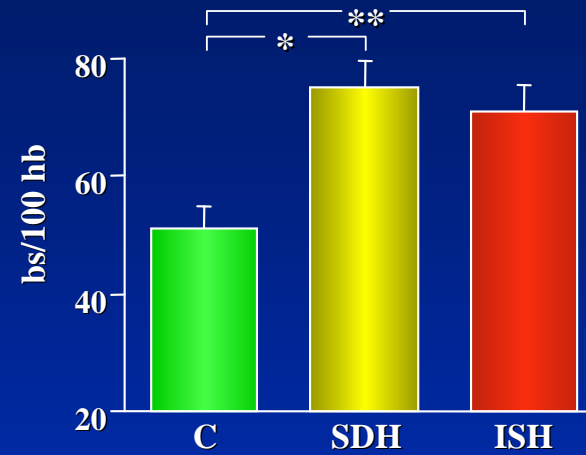
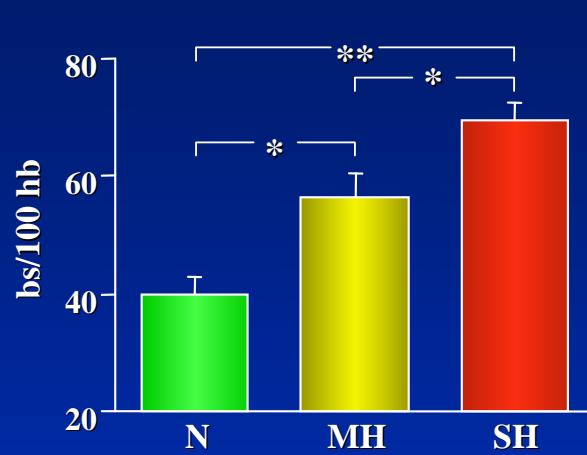
## *Arterial baroreflex control of BP and HR in Hypertension*

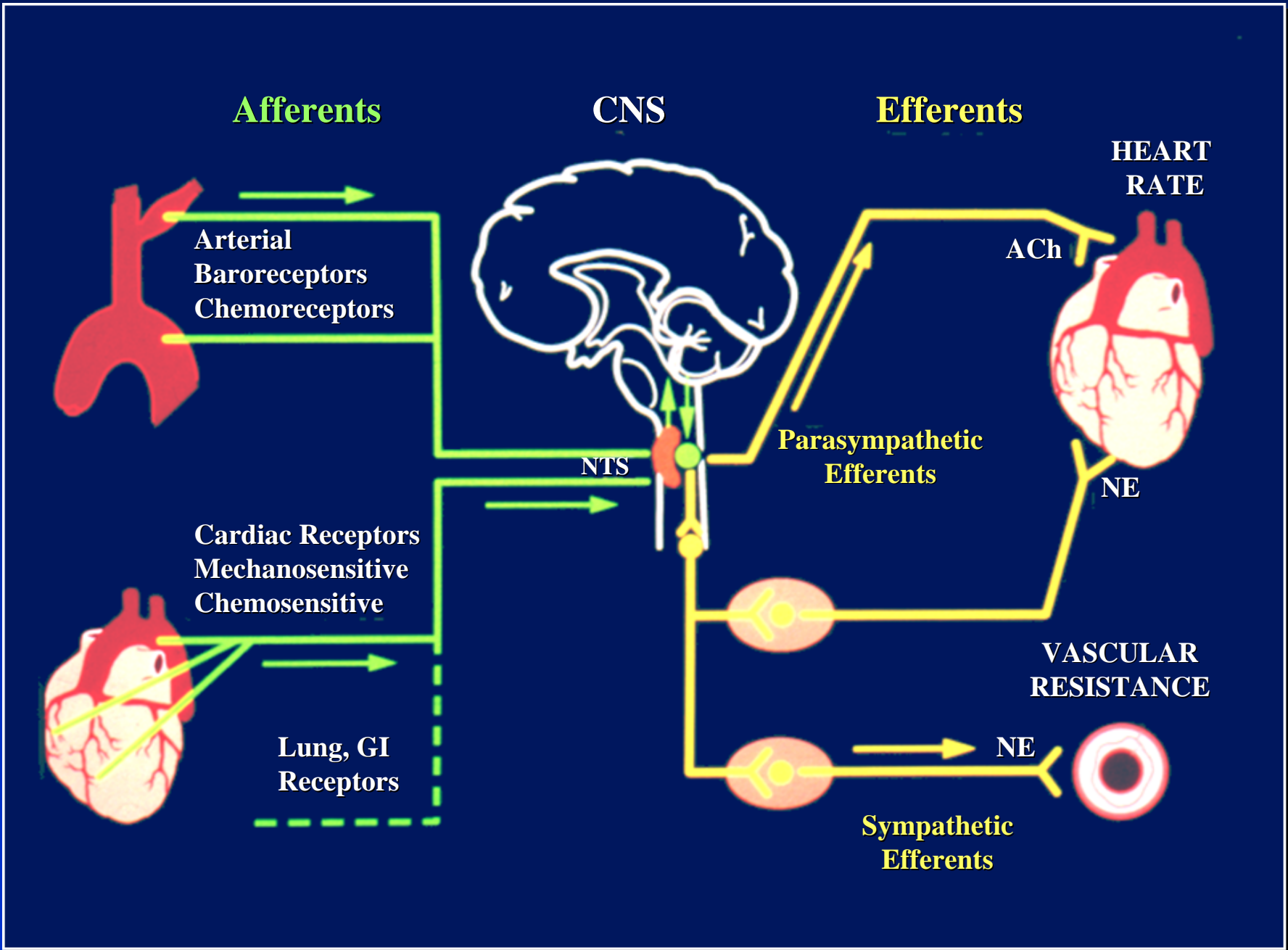
- **Impaired baroreflex control of HR**
- **Preserved (with resetting) baroreflex control of BP and MSNA**

# Sympathetic and Baroreflex Cardiovascular Control in Hypertension-related Left Ventricular Dysfunction



# Sympathetic Activity (Peroneal Nerve) in Different Clinical Conditions





# Difficulties in Antagonizing Sympathetic Hyperactivity with Drugs

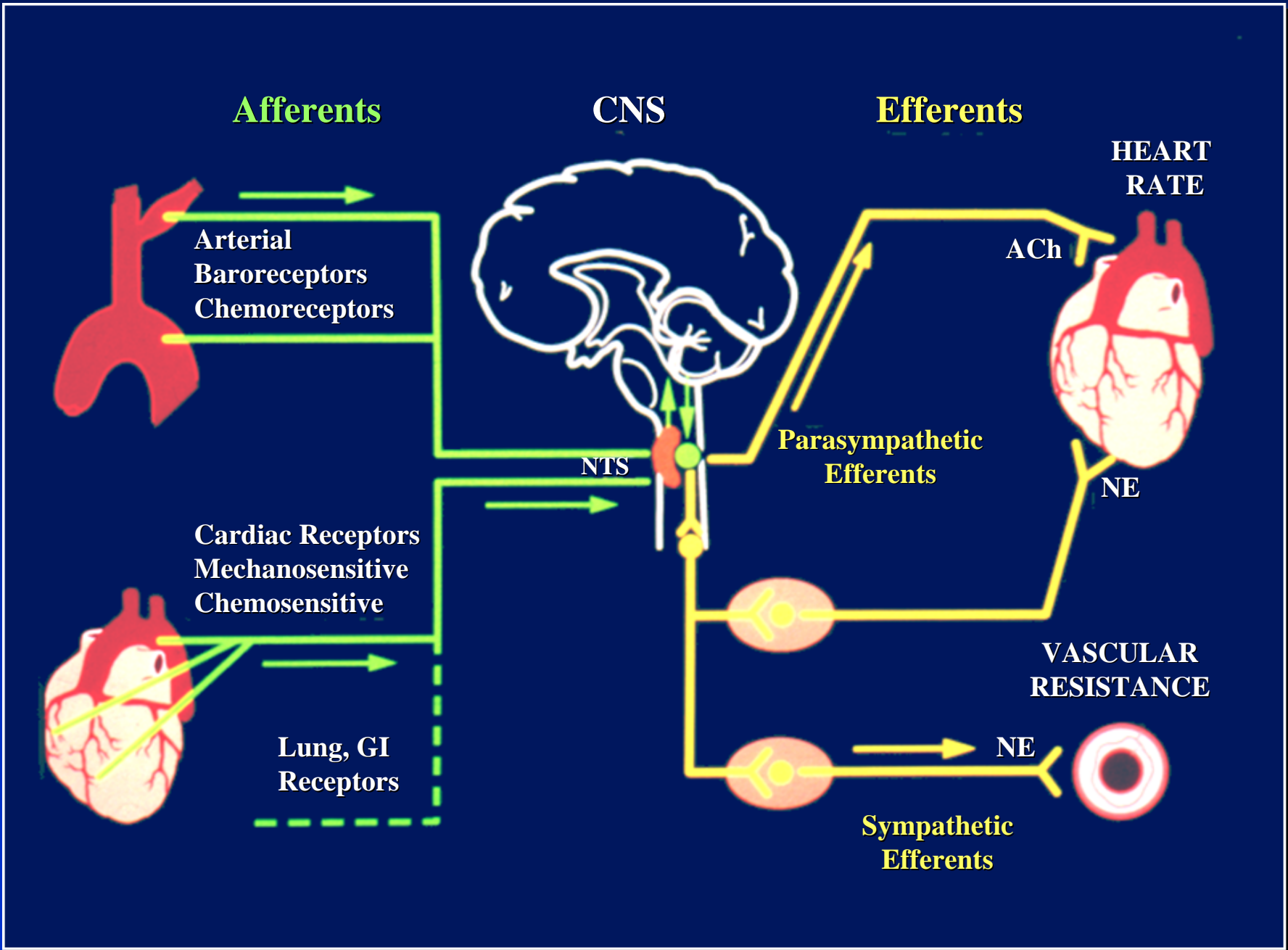
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## Peripheral Blockade

- **Ganglion blockers: indiscriminate blockade of sympathetic and parasympathetic activity ; ileus, impotence, orthostatic hypotension**
- **Blockers of post-ganglionic neuron endings: failure to ejaculate, orthostatic hypotension**
- **Alpha-adrenergic receptor blockers: orthostatic hypotension**

## Modulation of Central Control

- **Reserpine, methyldopa, clonidine: difficulty to dissociate blood pressure lowering from other centrally induced phenomena (sleepiness, dry mouth, depression)**



**Afferents**

**CNS**

**Efferents**

**HEART RATE**

Arterial  
Baroreceptors  
Chemoreceptors

Cardiac Receptors  
Mechanosensitive  
Chemosensitive

Lung, GI  
Receptors

NTS

Parasympathetic  
Efferents

ACh

NE

VASCULAR  
RESISTANCE

NE

Sympathetic  
Efferents

# The First Generation CVRx Rheos<sup>®</sup> System

