



**Universidade de São Paulo**  
**Disciplina: RFA-5706**  
**FARMACOLOGIA CARDIOVASCULAR**

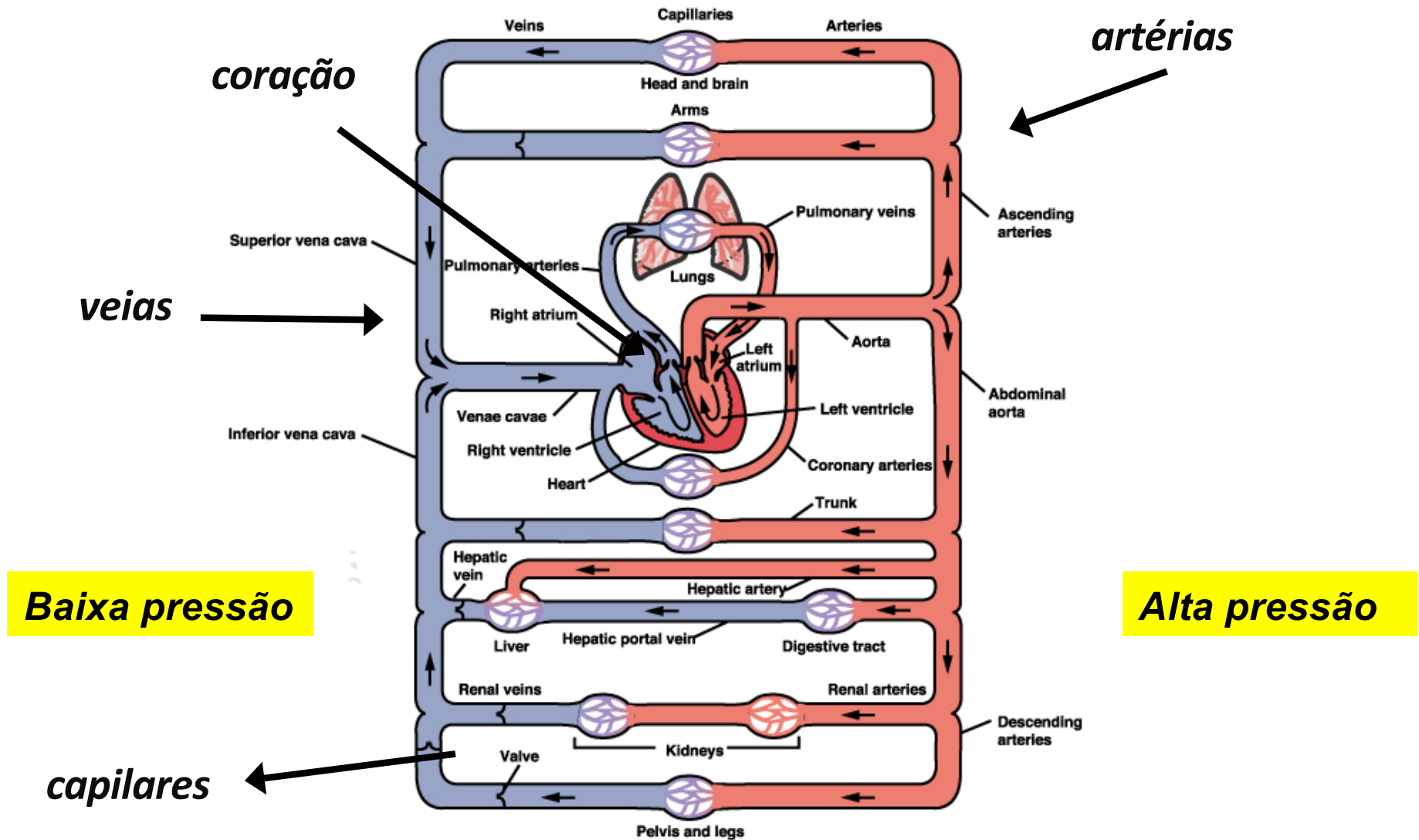


# **Mecanismos centrais que regulam o sistema cardiovascular**

**Mateus Ramos Amorim**

**Ribeirão Preto - 2020**

# Transporte e distribuição de oxigênio e nutrientes para os tecidos e remoção dos produtos do metabolismo



# Registro da pressão arterial (PA)

Stephen Hales



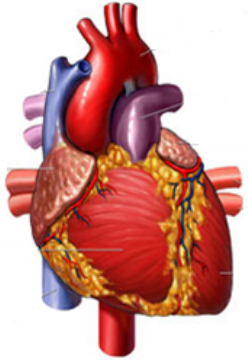
A.D.A.M



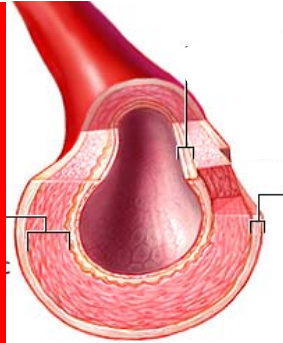
(<http://www.epi.umn.edu/cvdepi/photo.asp?id=523>)

# Roteiro da aula

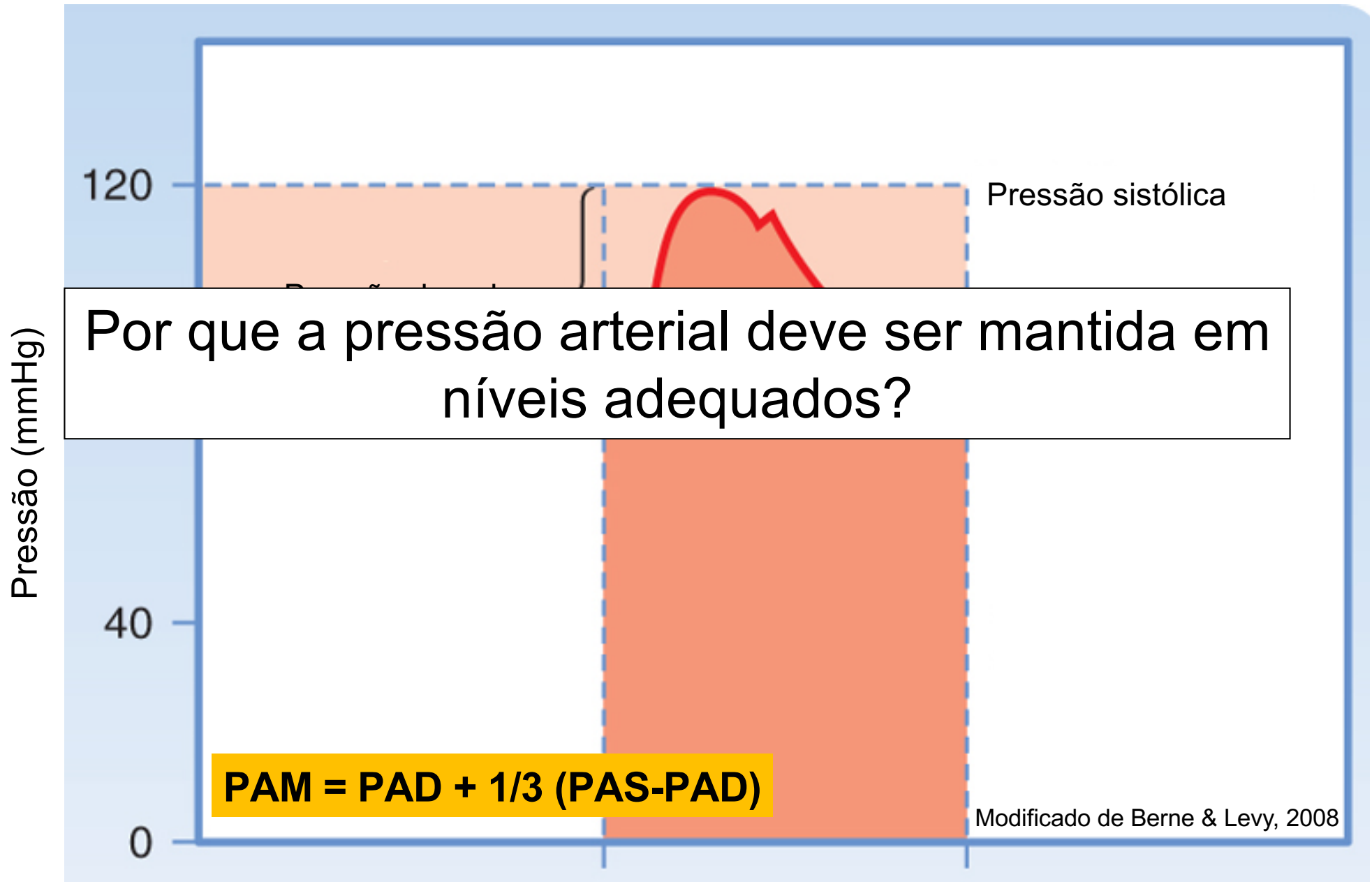
- Definição de pressão arterial (PA)
- Fatores que determinam a PA
- O barorreflexo
- Integração neural dos reflexos cardiovasculares
- Sistema nervoso simpático
- Sistema nervoso parassimpático
- O quimiorreflexo
- O reflexo cardiopulmonar
- Aplicando o conhecimento



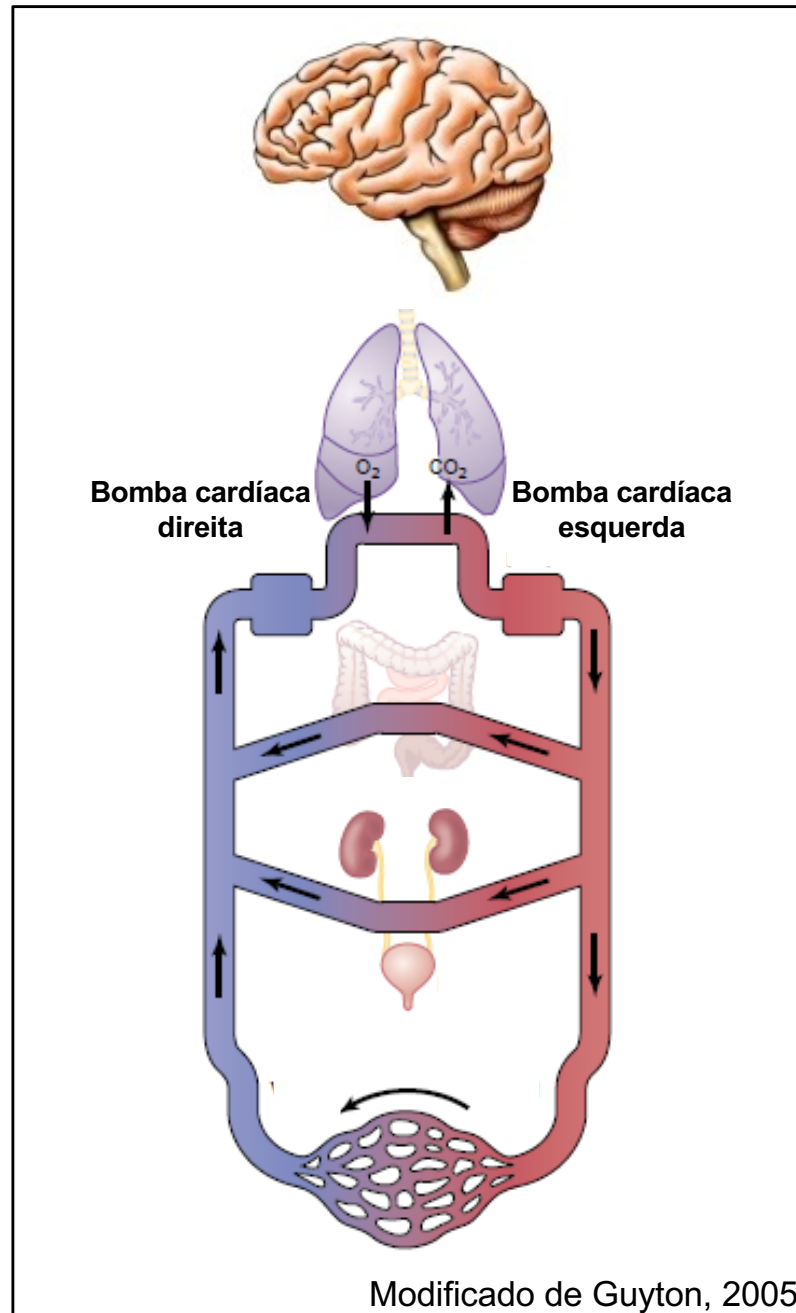
# Definição de PA



# Pressão arterial



# Perfusão de todos os órgãos e tecidos

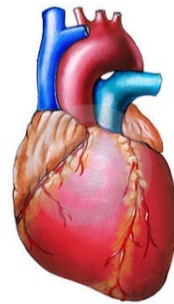


# O débito cardíaco e resistência periférica determinam a pressão arterial (PA)

## Pressão Arterial

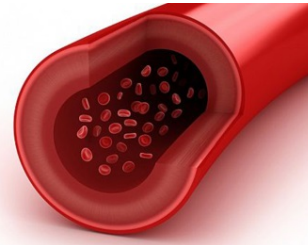


Modificado de McAadle, 2003



Débito cardíaco (DC)  
**4900 mL/min**

**X**



Resistência periférica (RP)

Frequência cardíaca (FC)  
**~ 70 bpm**

**X**

Volume sistólico (VS)  
**~ 70 mL**

$$PA = DC \cdot RP$$

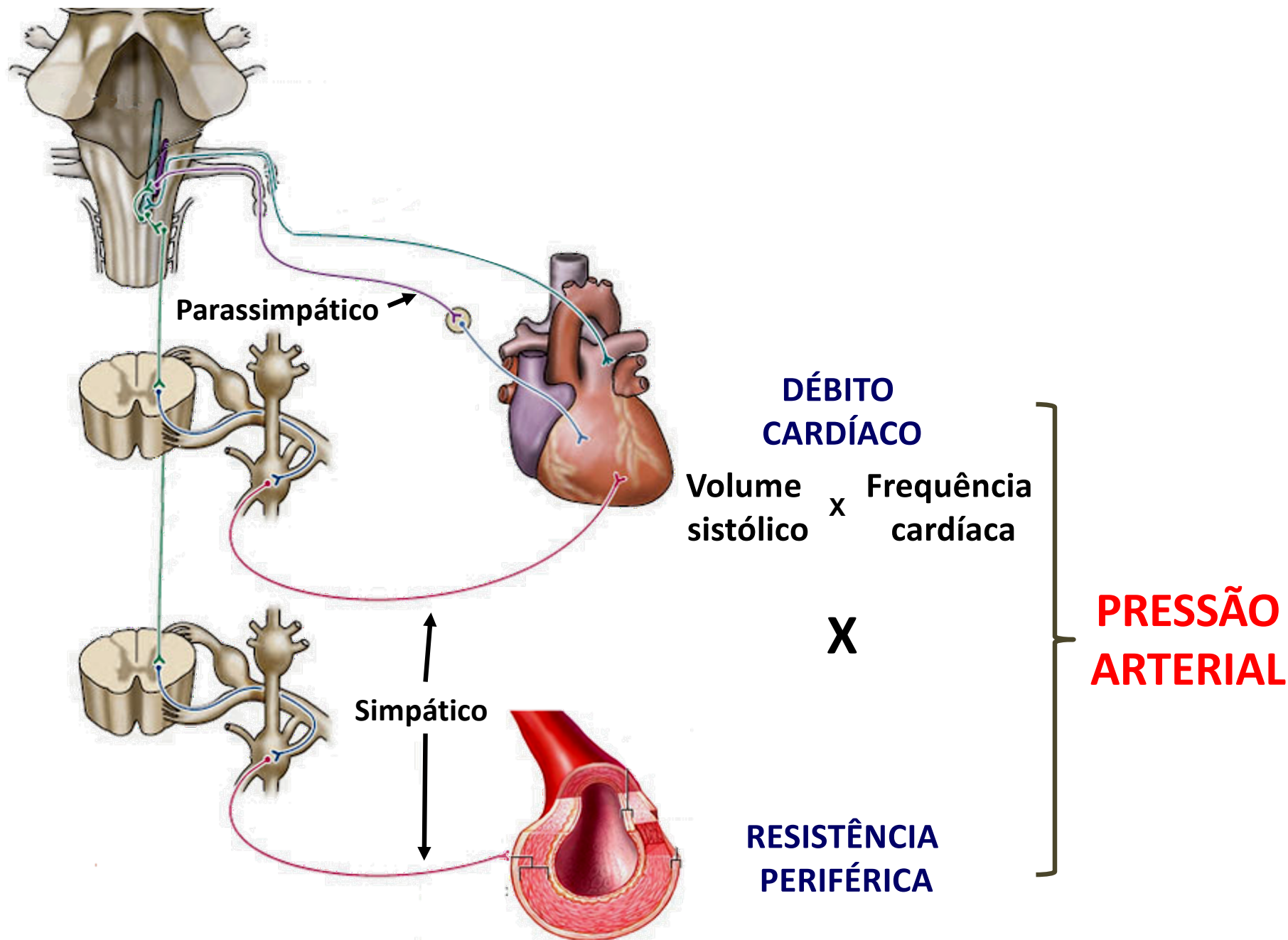
*FC* *VS*

<http://www.dreamstime.com/royalty-free-stock-photos-human-heart-image5130678>

[http://biofabris.com.br/pt/wp-content/uploads/2014/08/3d\\_print.jpg](http://biofabris.com.br/pt/wp-content/uploads/2014/08/3d_print.jpg)



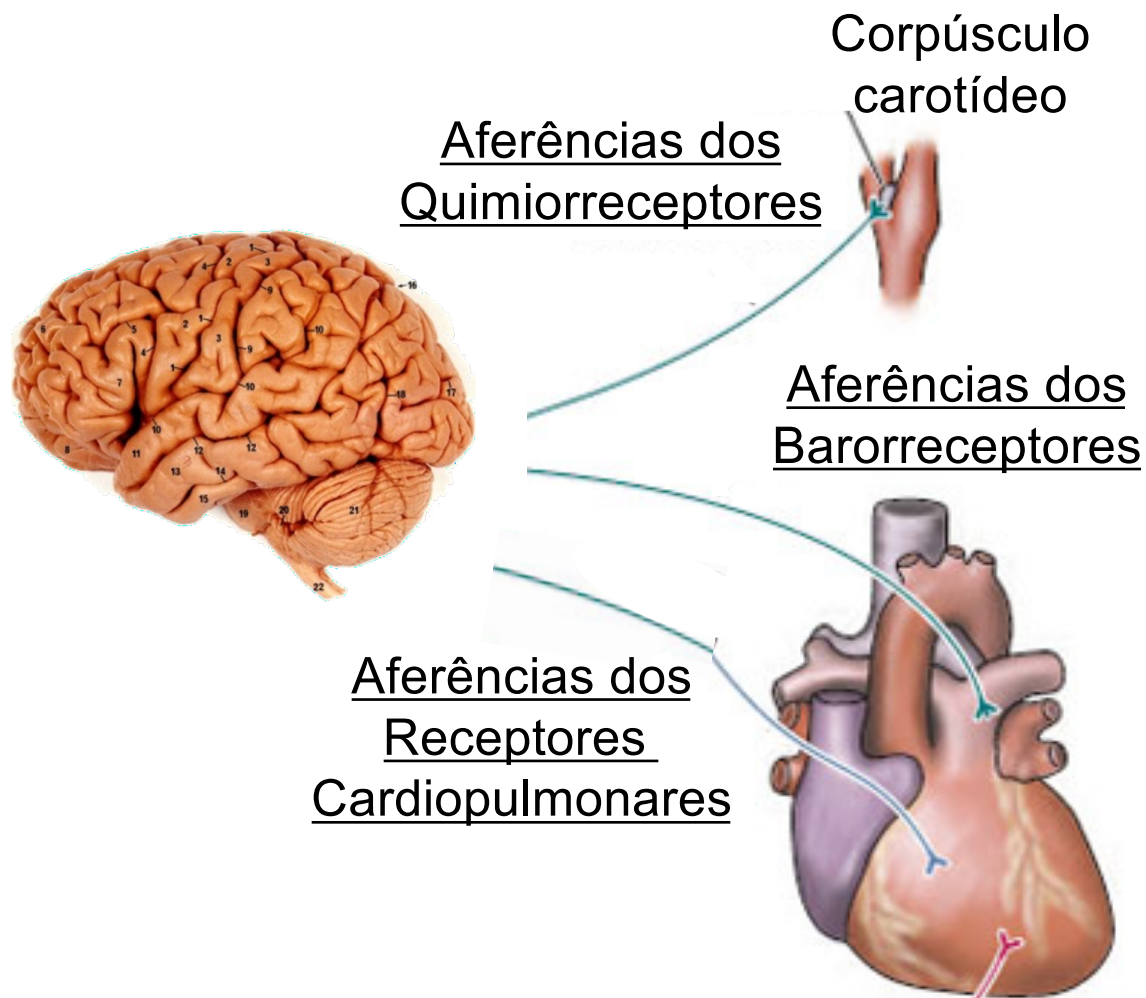
# Controle neural da pressão arterial

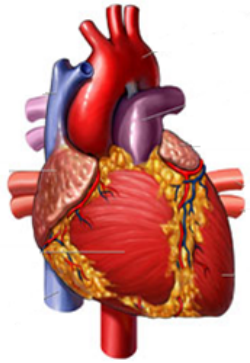


# Mecanismos de regulação da pressão arterial

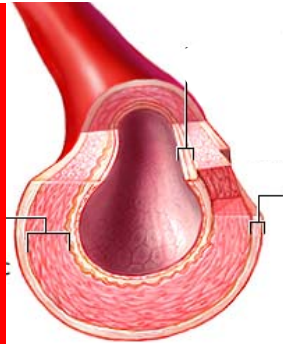
## REGULAÇÃO A CURTO PRAZO:

➤ Mecanismos neurais;

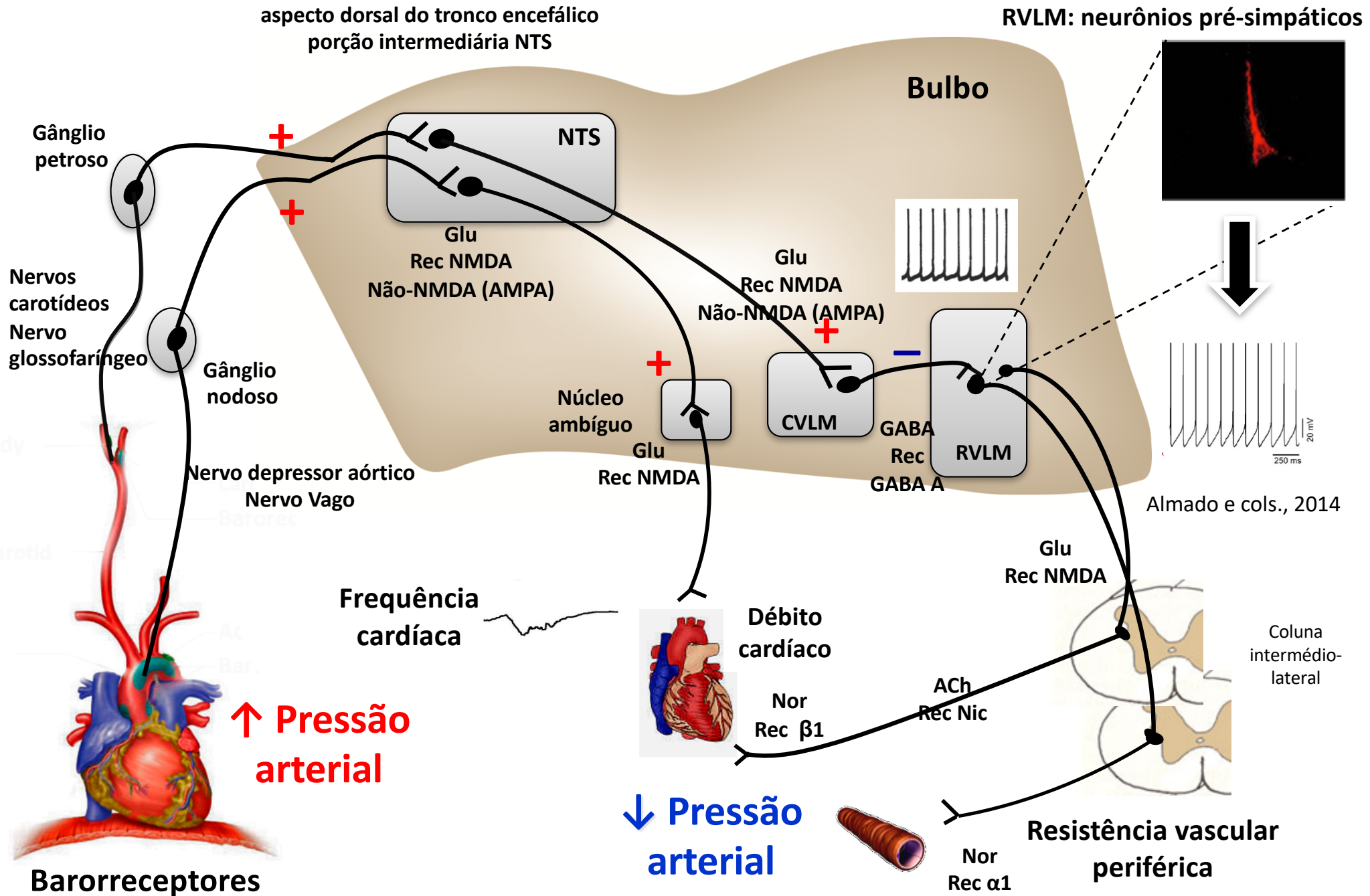




# O barorreflexo

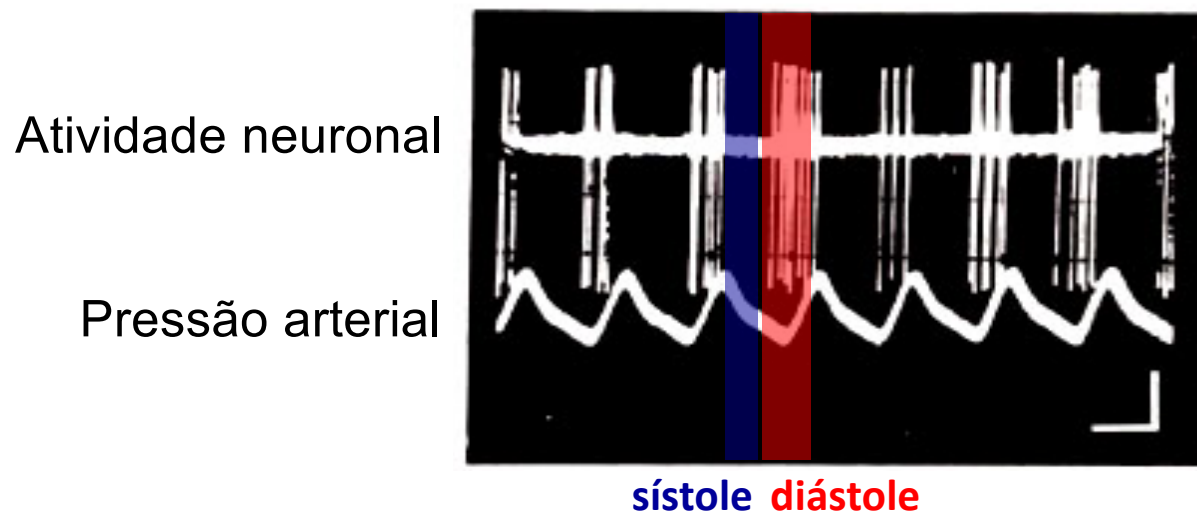
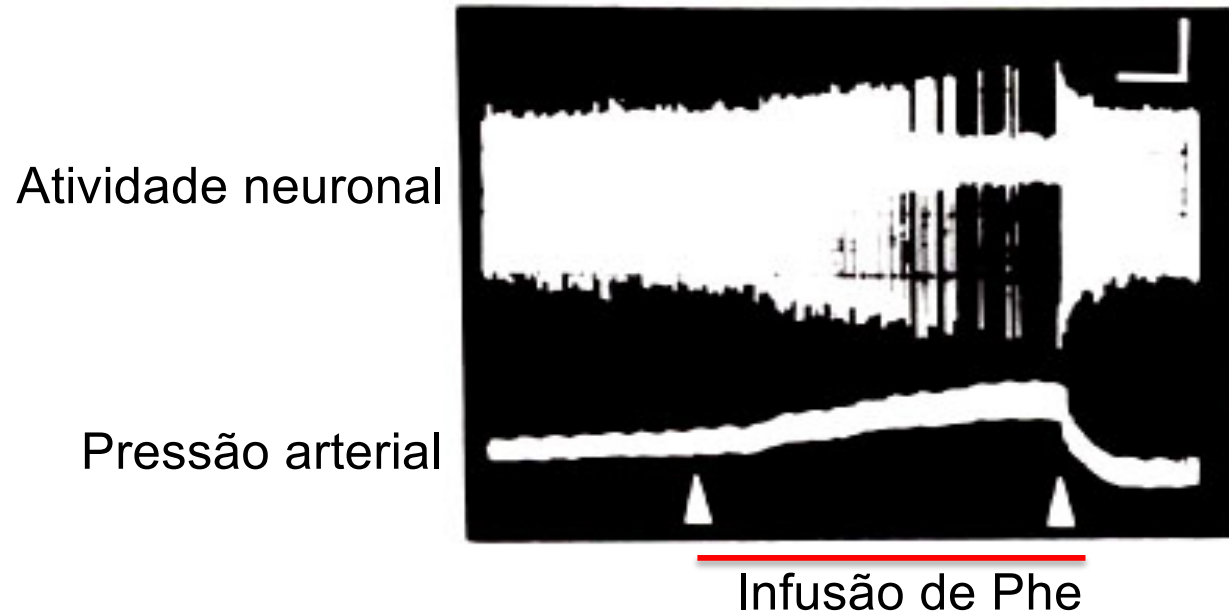


# O barorreflexo controla a atividade autonômica



# Os neurônios da RVLM são inibidos pelo barorreflexo

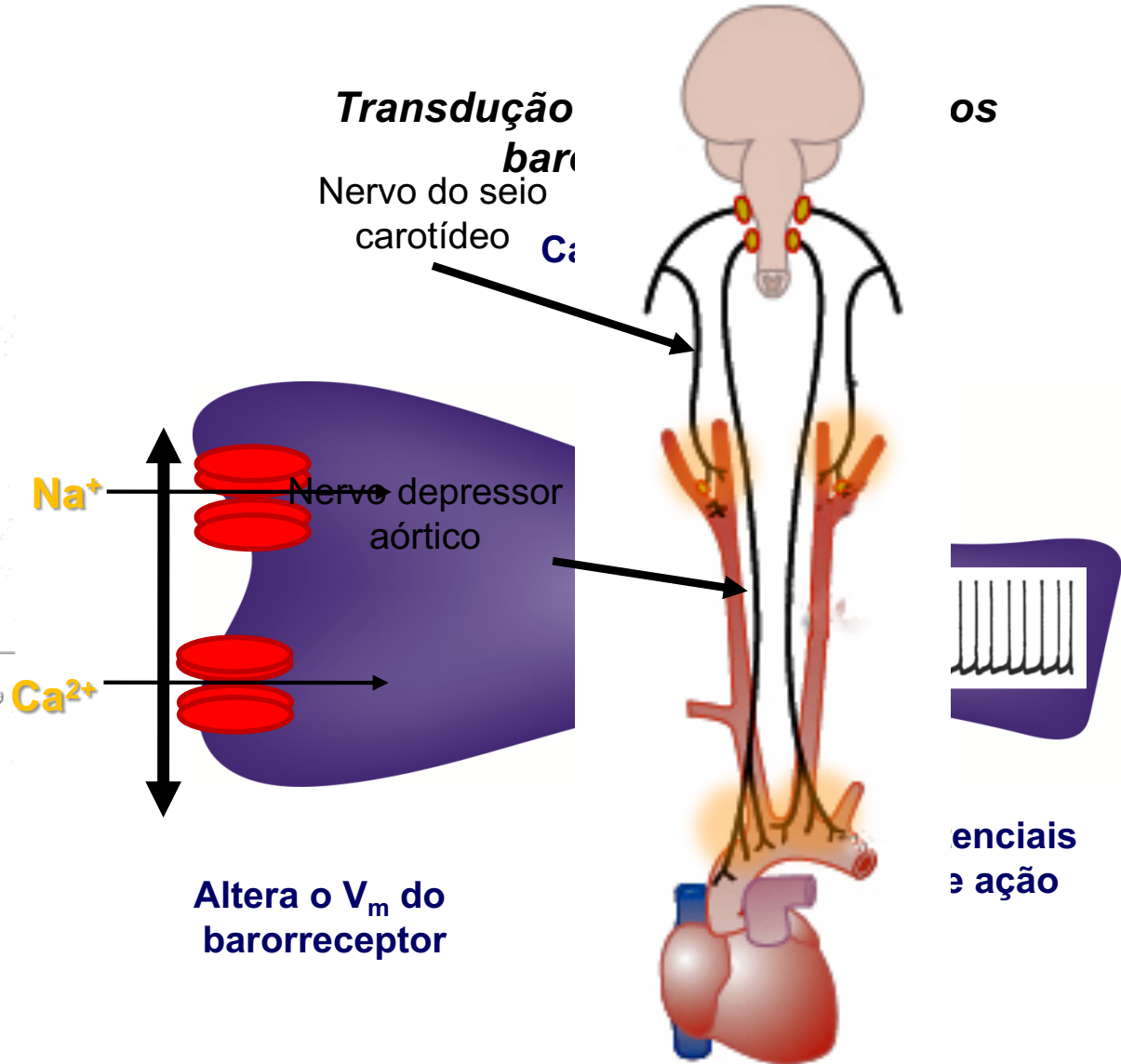
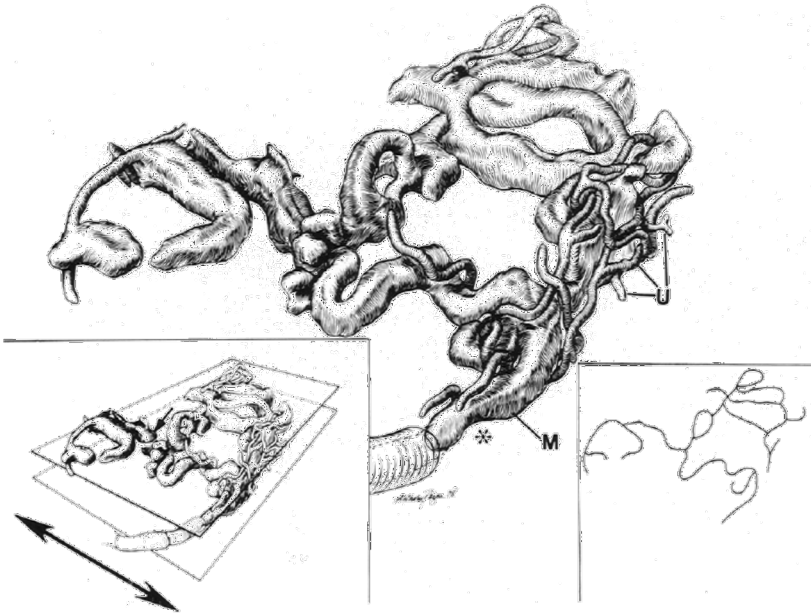
*A atividade dos neurônios da RVLM está associada ao nível de pressão arterial*



# Os barorreceptores são mecanorreceptores

## Os sensores e as aferências do barorreflexo

### Reconstrução tridimensional dos barorreceptores



Kraus, 1979

Baeado em Guyton, 2006

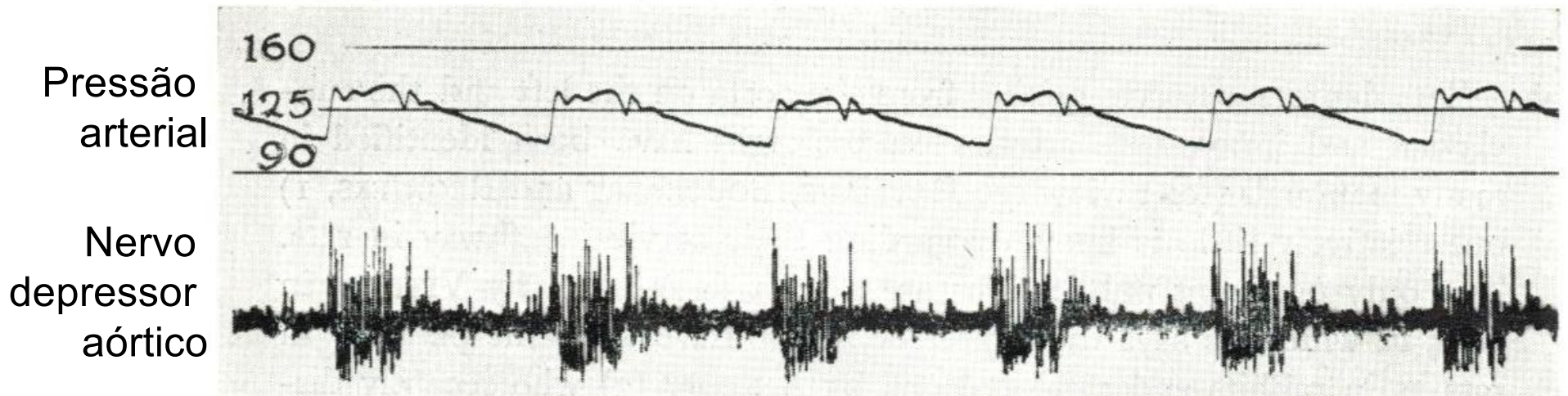
# A função dos barorreceptores em ratos

## AORTIC DEPRESSOR NERVES OF THE RAT\*

BY

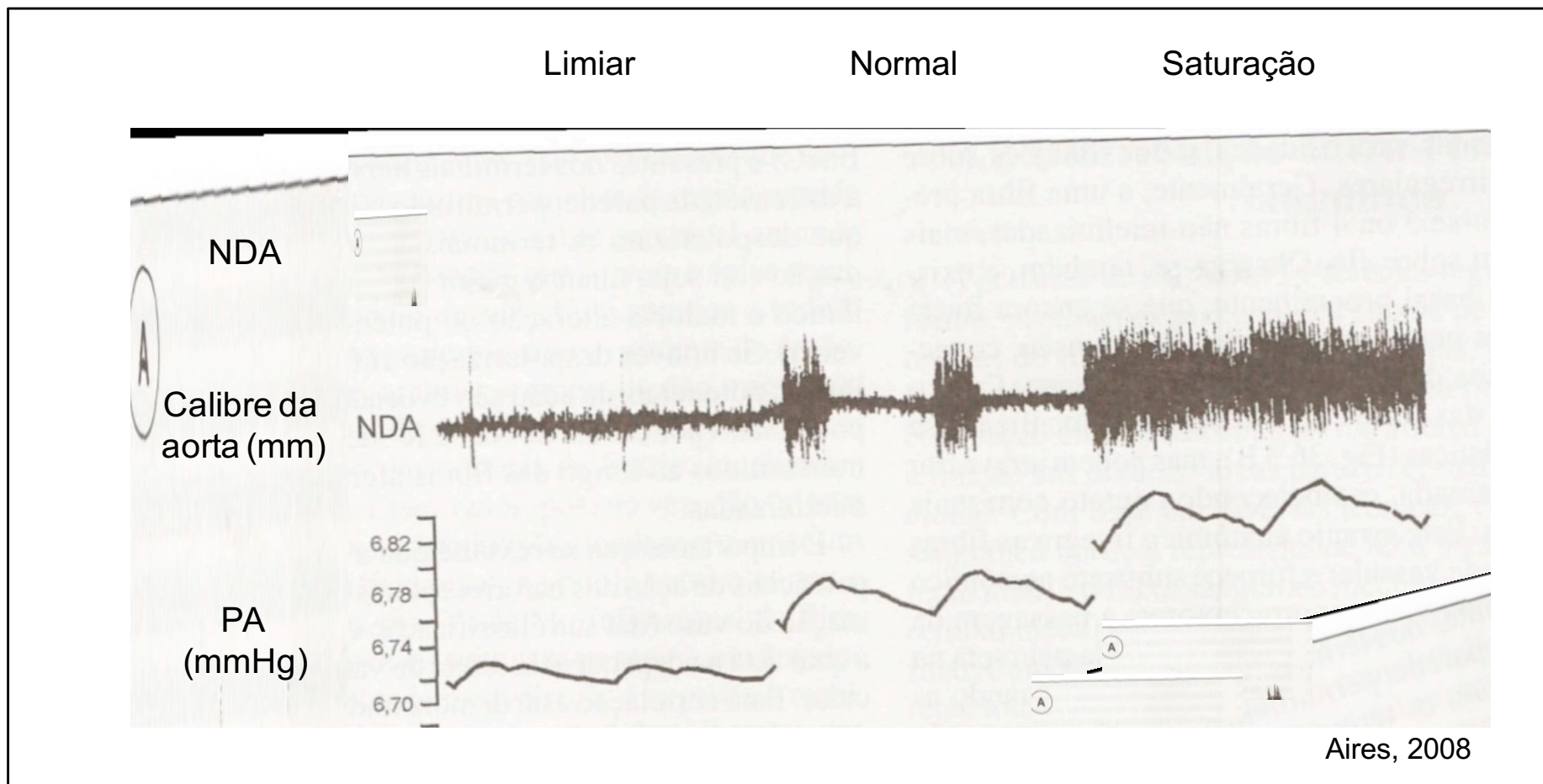
J. W. McCUBBIN, G. M. C. MASSON AND IRVINE H. PAGE

Arch. int. pharmacodyn., 1958, CXIV, No 3-4.



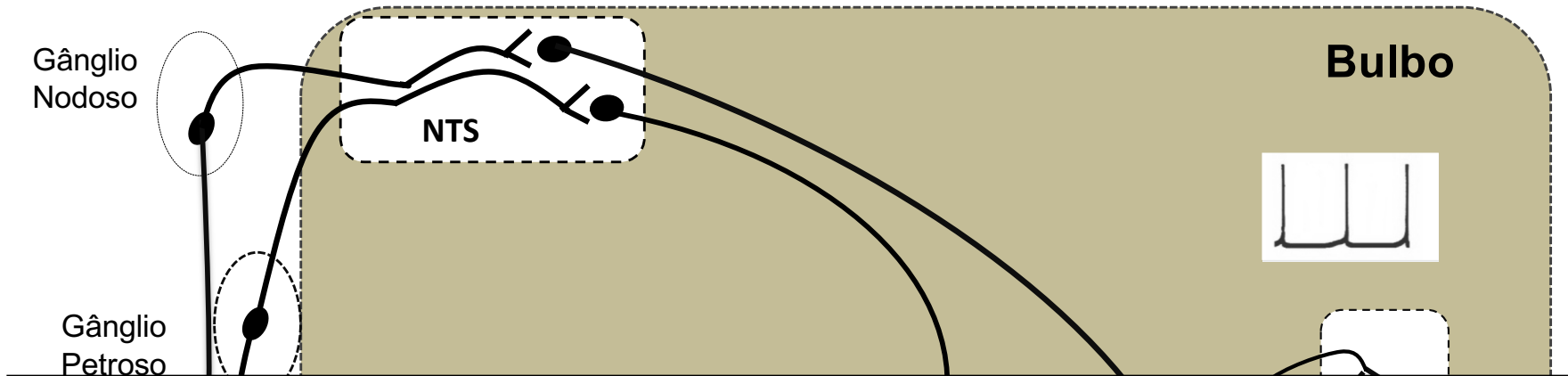
Modificado de McCUBBIN e cols., 1958

# Registros do nervo depressor aórtico, calibre da aorta e pressão arterial

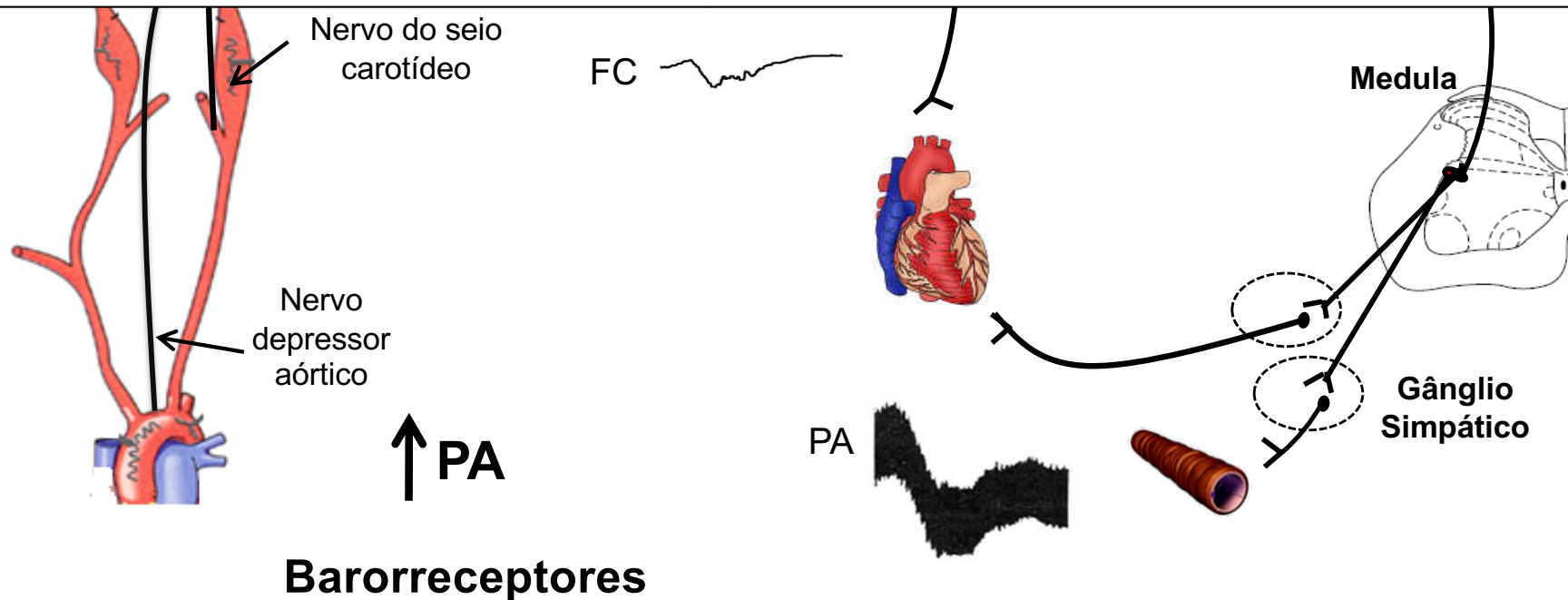




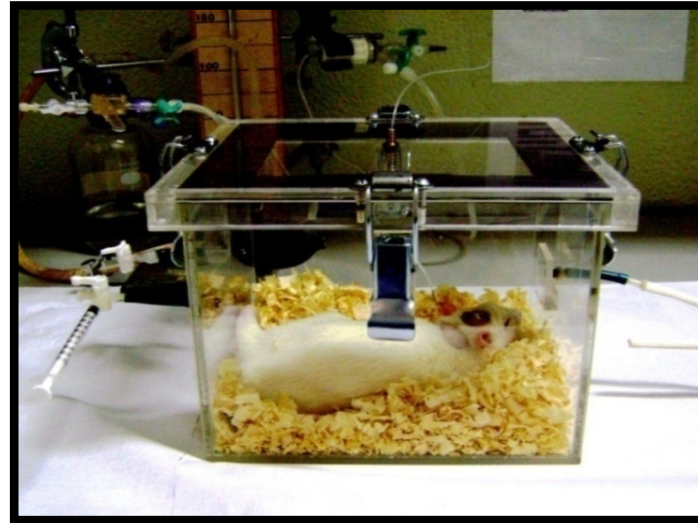
# Resposta do barorreflexo ao aumento da PA



**Redução do débito cardíaco e da resistência vascular periférica**



# Resposta do barorreflexo ao aumento da PA



Fenilefrina

Vasoconstrição

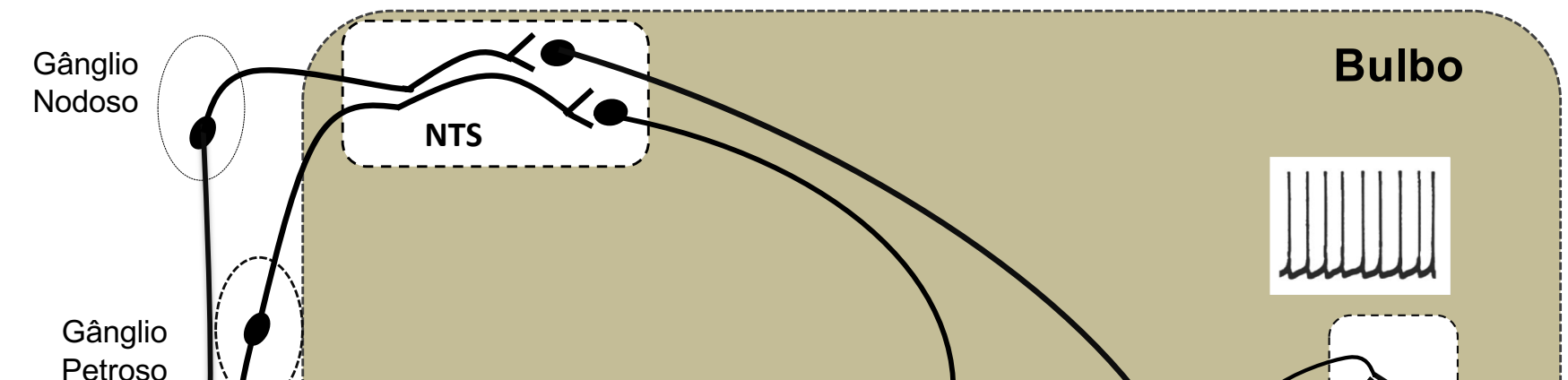
PAP

PAM

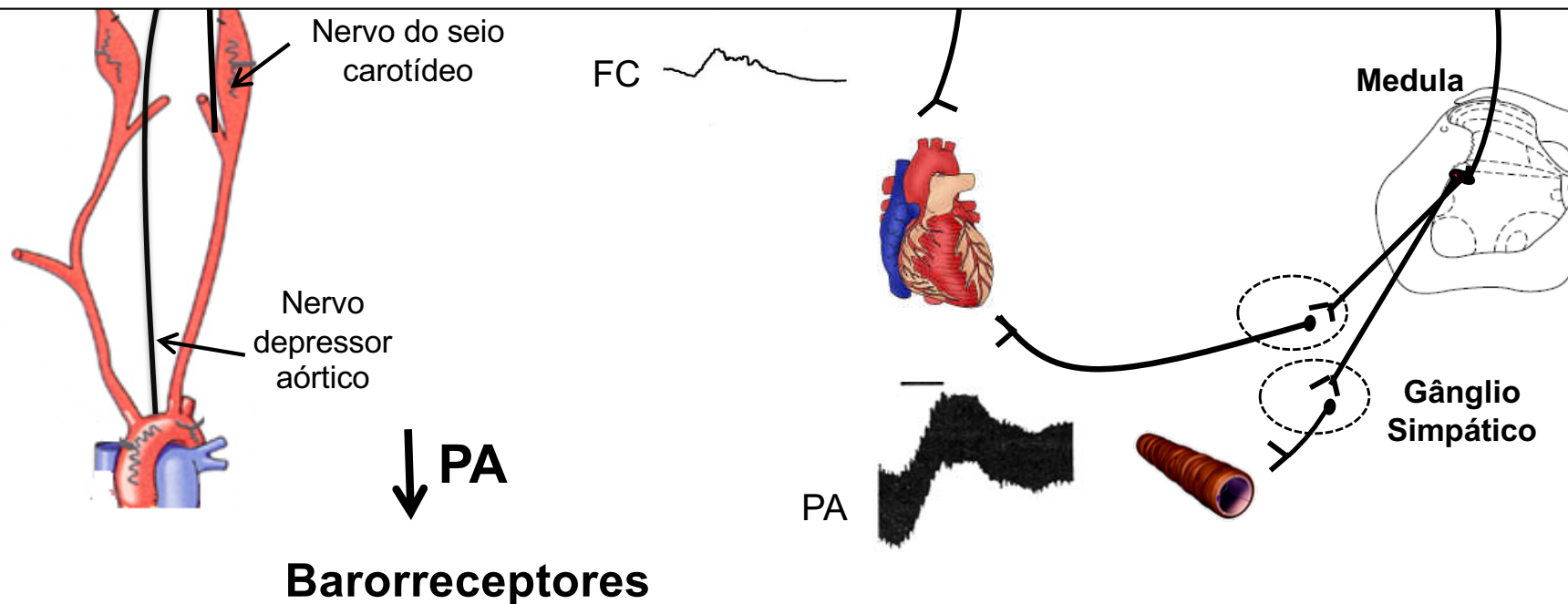
FC



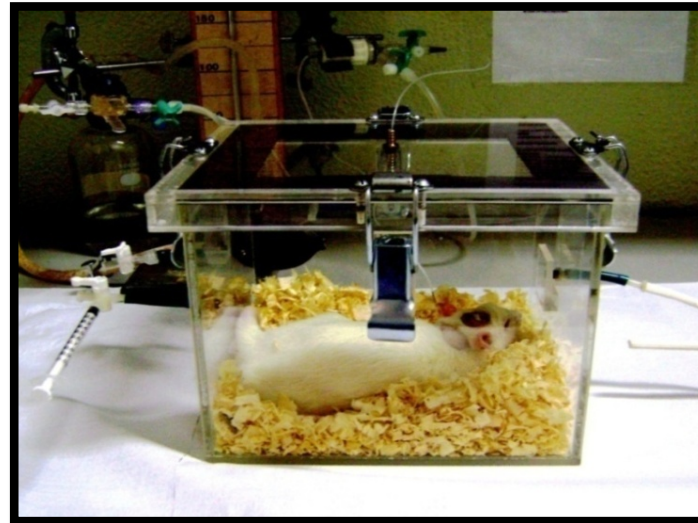
# Resposta do barorreflexo à redução da PA



**Aumento do débito cardíaco e da resistência vascular periférica**



# Resposta do barorreflexo à redução da PA



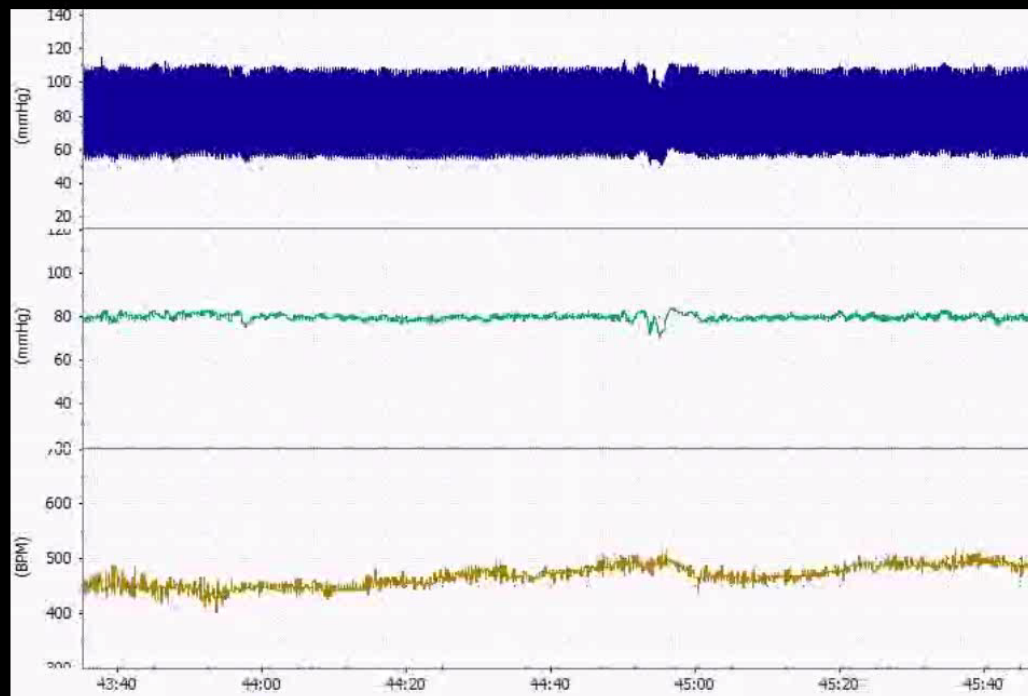
Nitroprussiato  
de sódio

Vasodilatação

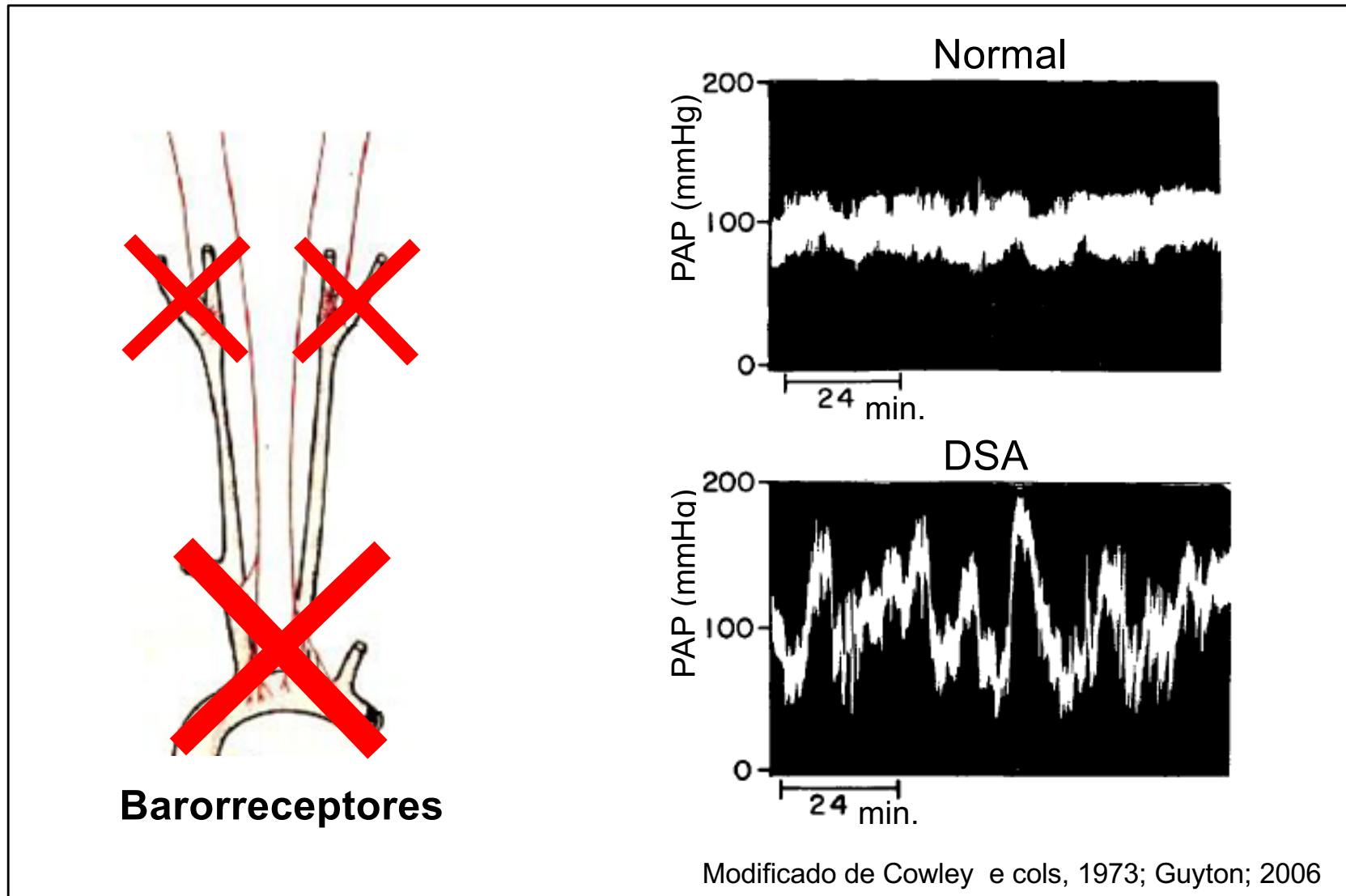
PAP

PAM

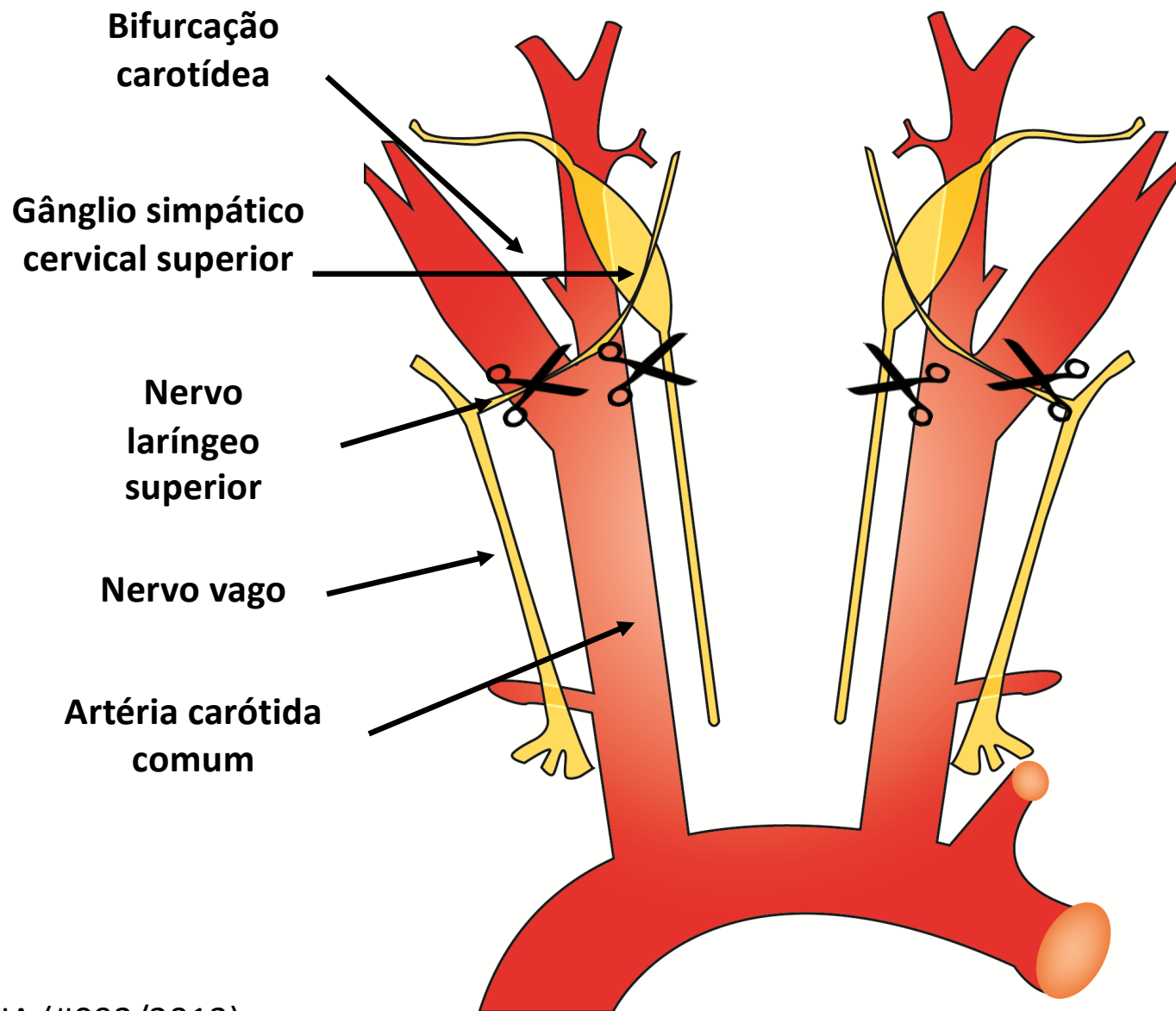
FC

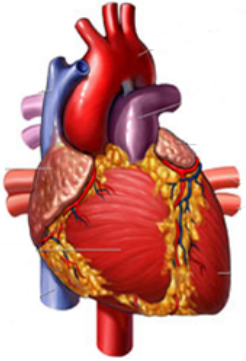


# A função essencial dos barorreceptores e a desnervação sino-aórtica (DSA)

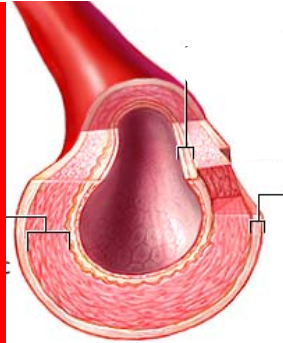


# Desnervação sino-aórtica (DSA) em ratos





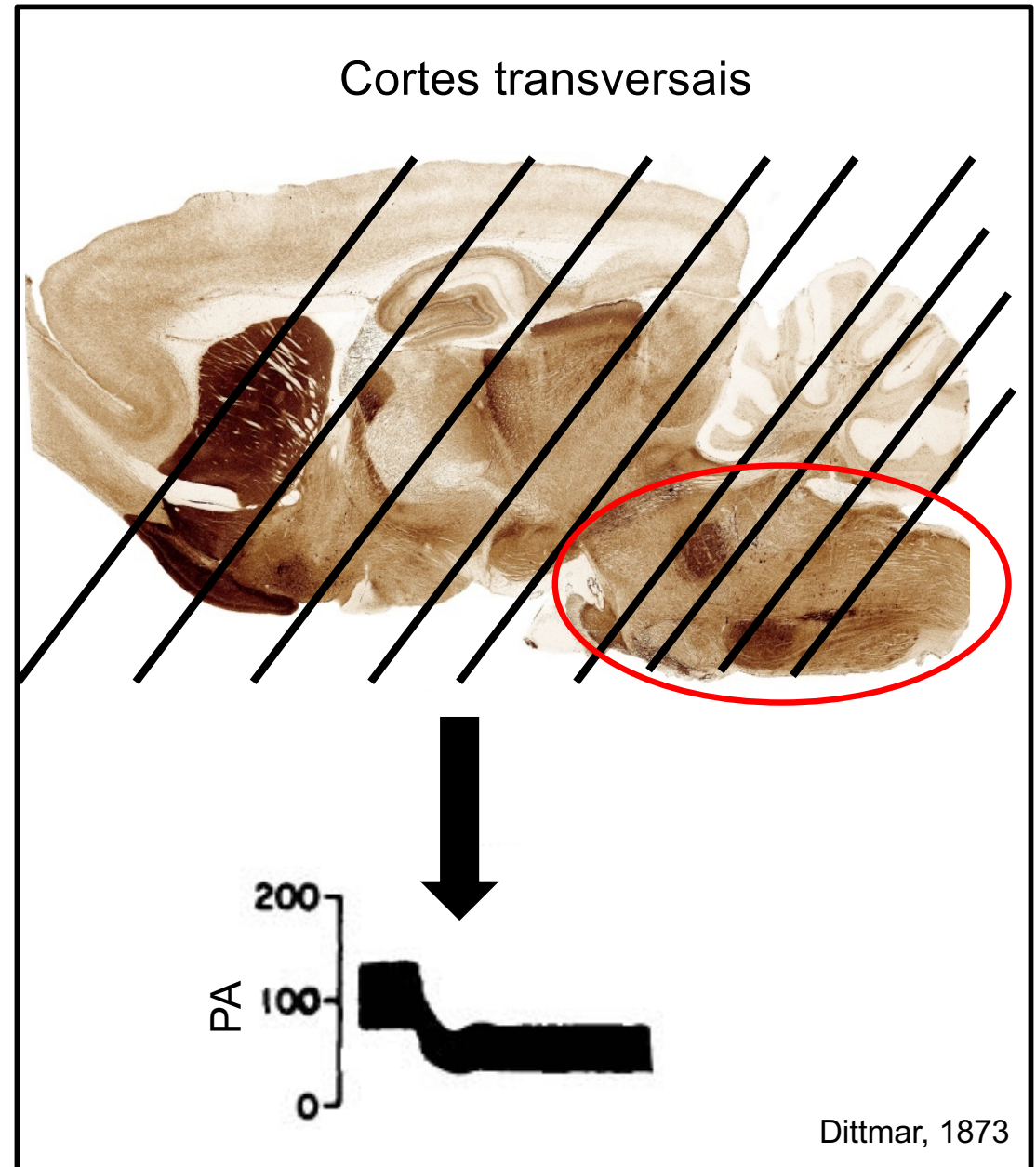
# Integração neural dos reflexos cardiovasculares



# O sistema nervoso central na regulação da PA



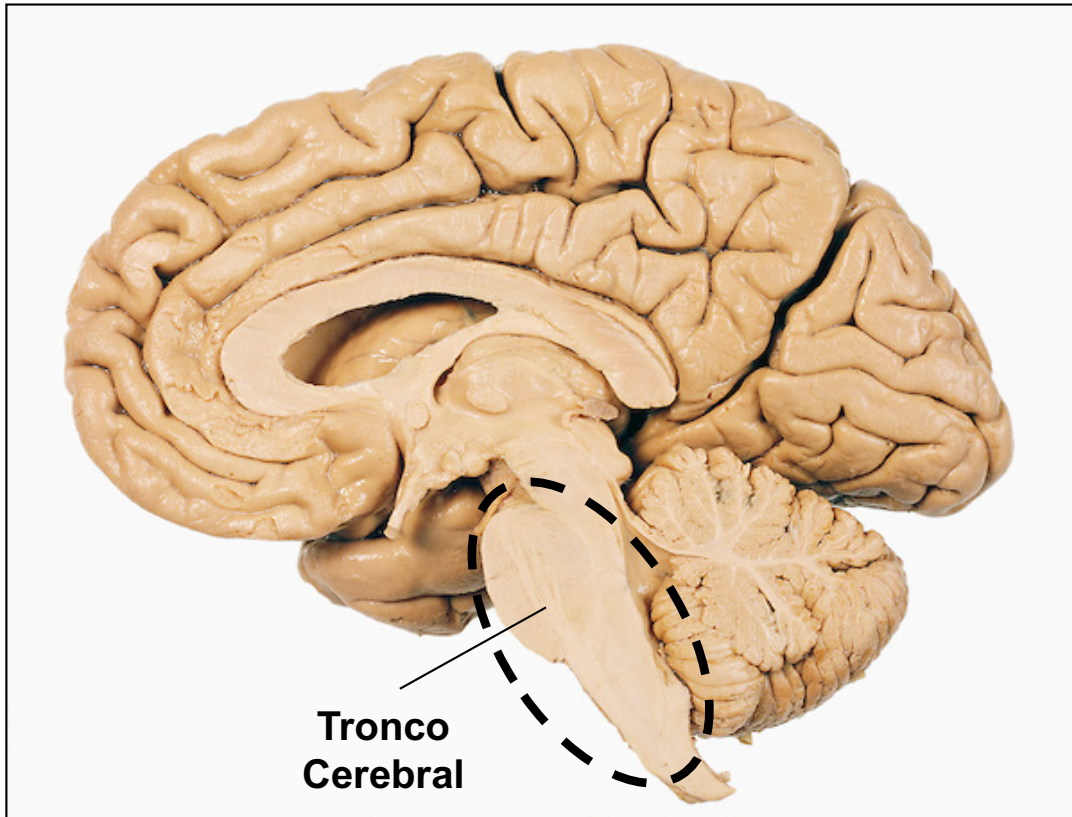
Claude Bernard (1851)



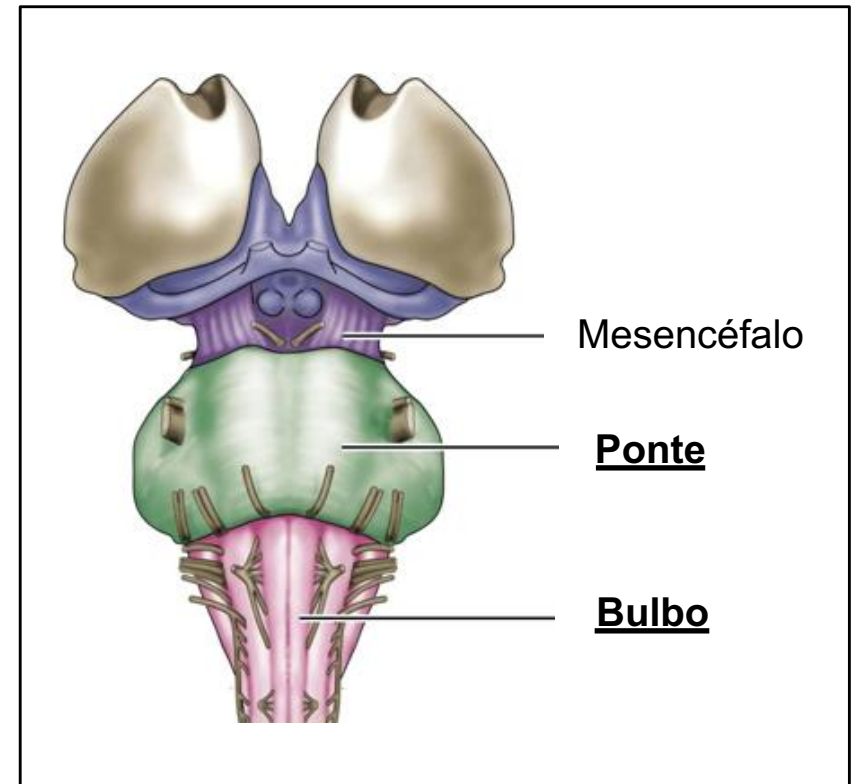


# Integração neural da função cardiovascular

Corte sagital



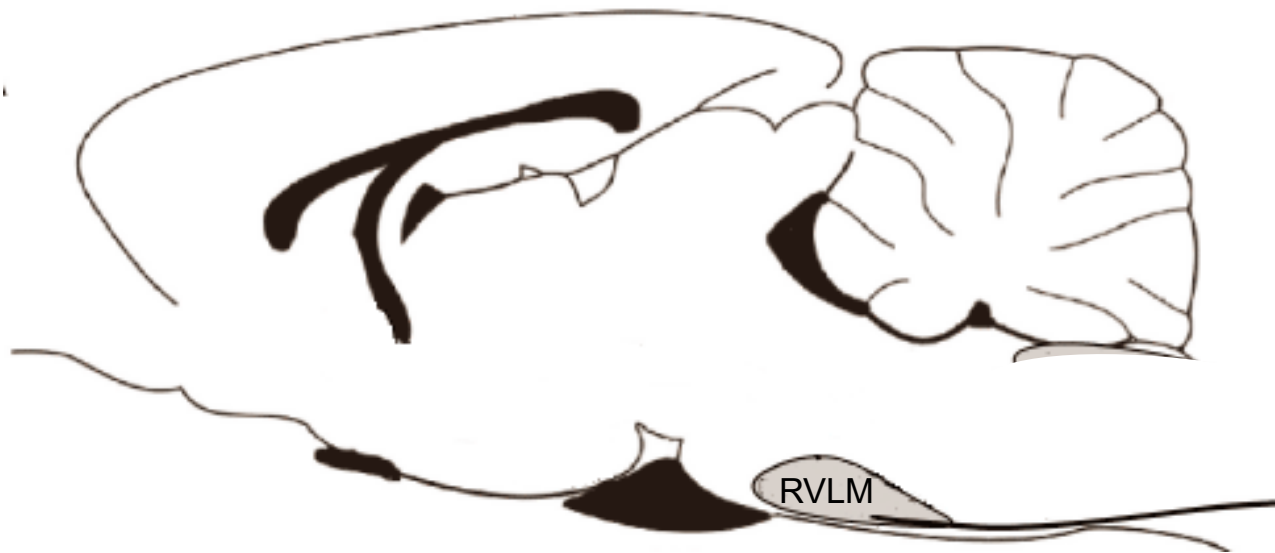
Visão ventral



O tronco cerebral regula a função cardiovascular

# Rostral Ventrolateral Medulla (RVLM)

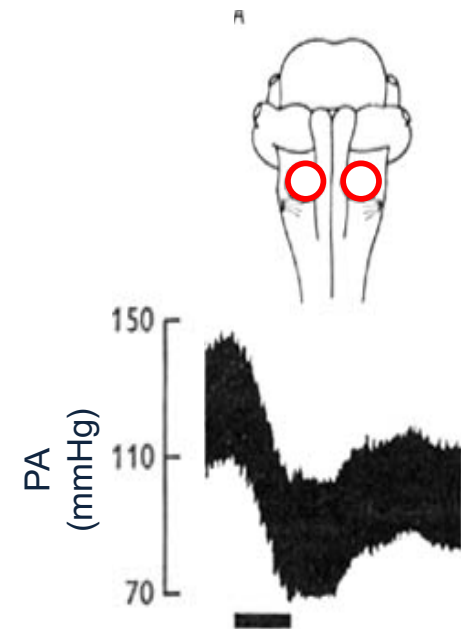
Corte sagital



Modificado de Cravo e cols, 2009

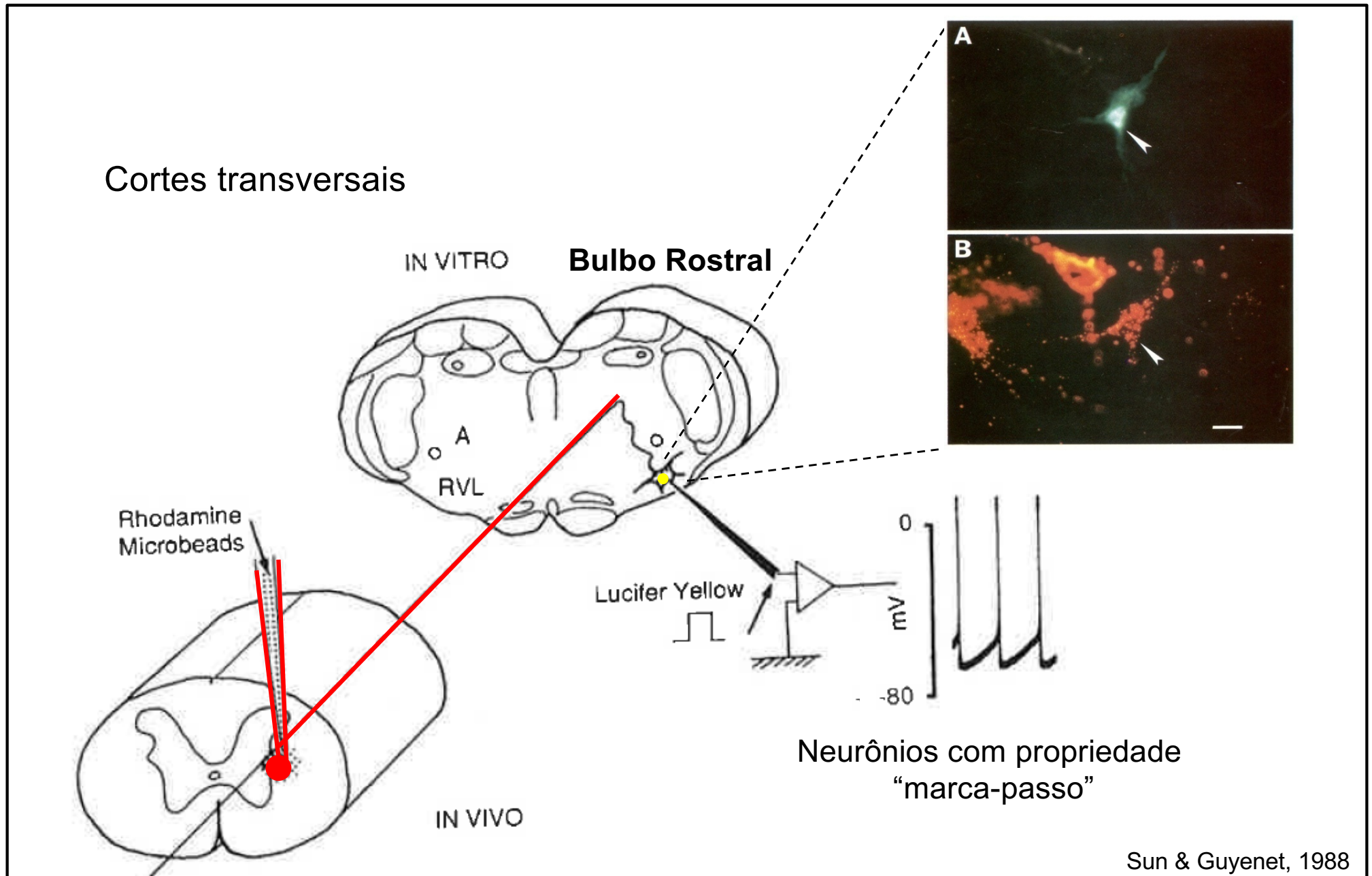
Inibição da região rostral do bulbo

Visão ventral

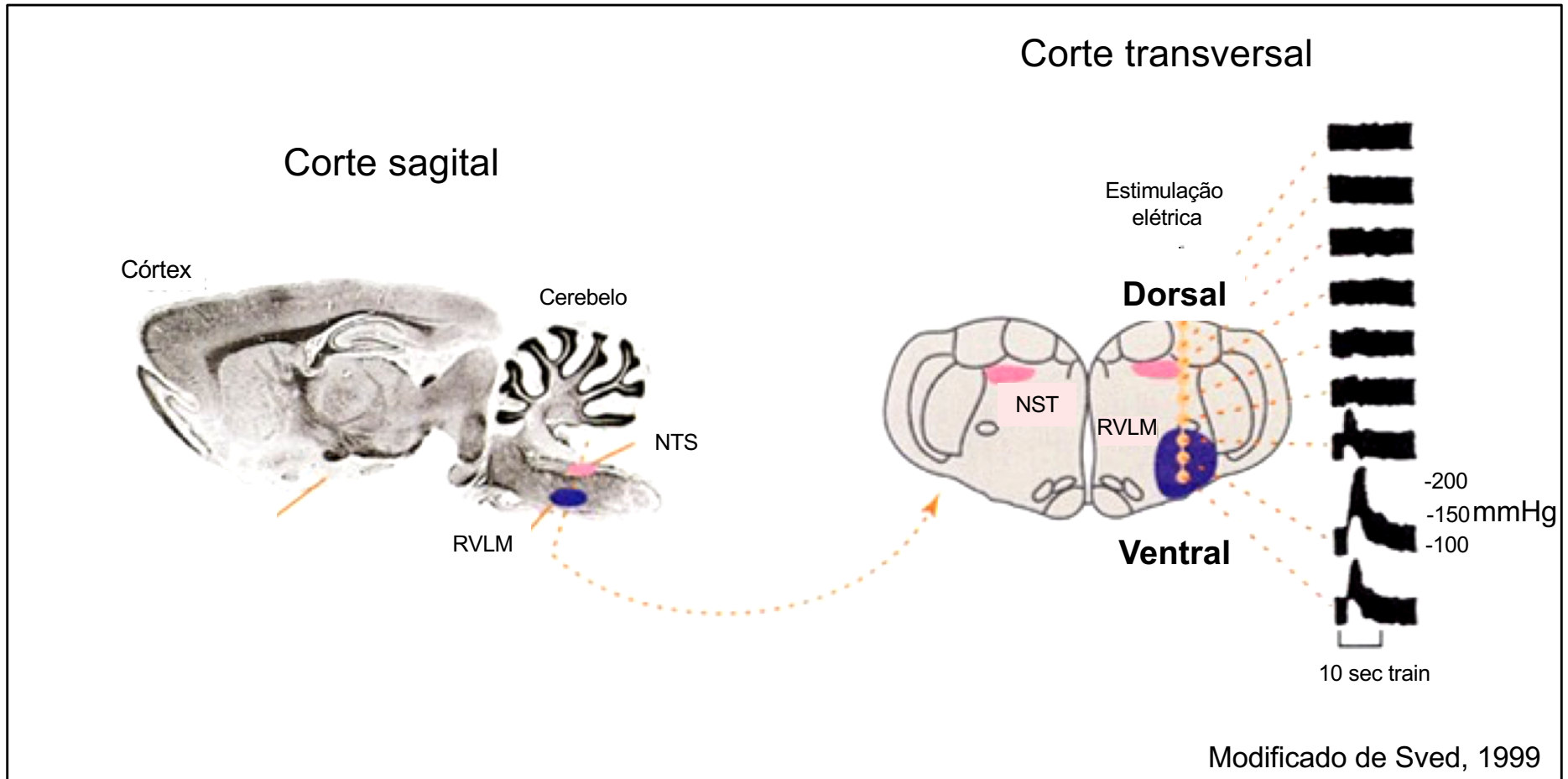


Modificado de Guertzstein & Silver, 1974

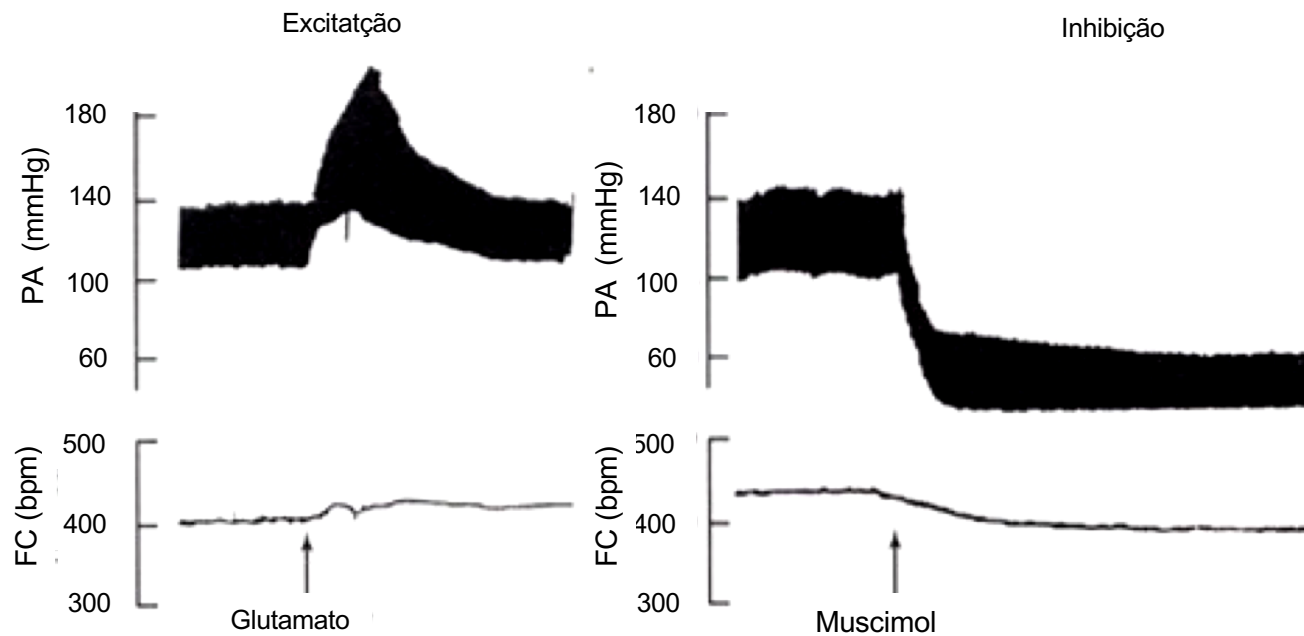
# Neurônios do RVLM que se projetam para IML



# Efeitos cardiovasculares da estimulação do RVLM

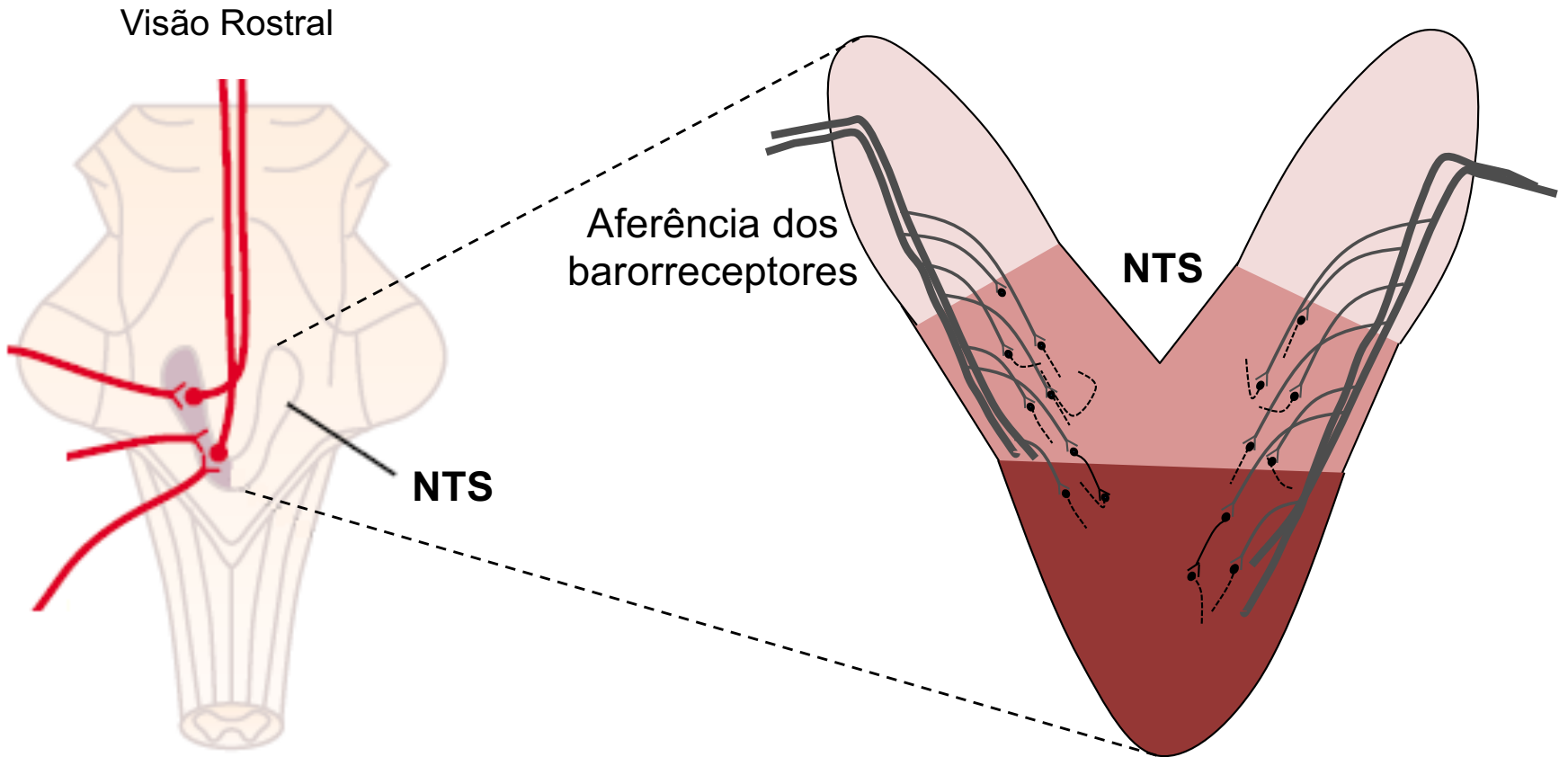


# Efeitos da excitação ou inibição do RVLM



Modificado de Sved, 1999

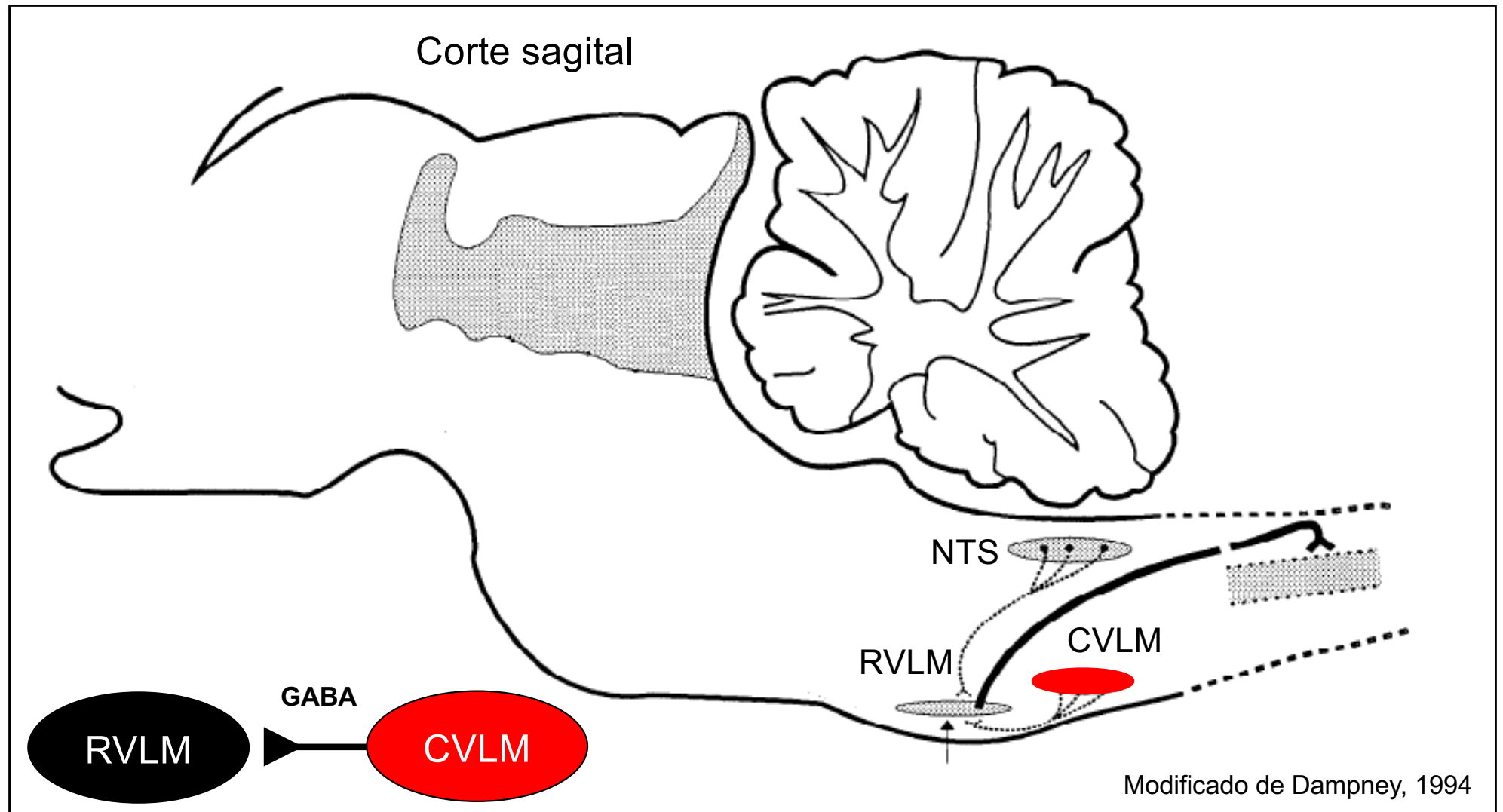
# Núcleo do trato solitário (NTS)



Modificado de Guyton., 2006

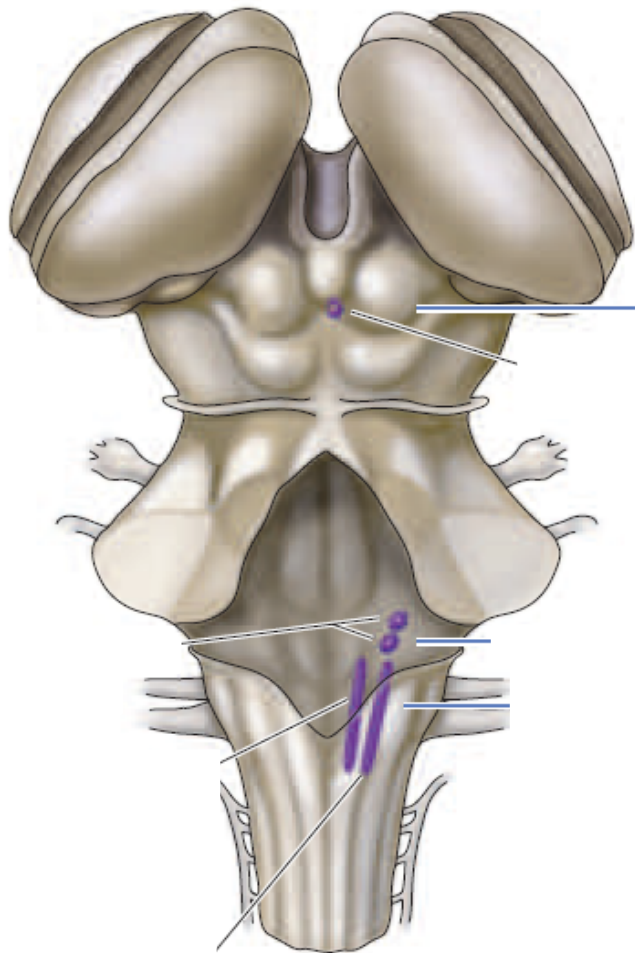
Machado e cols., *in press*

# Caudal Ventrolateral Medulla (CVLM)



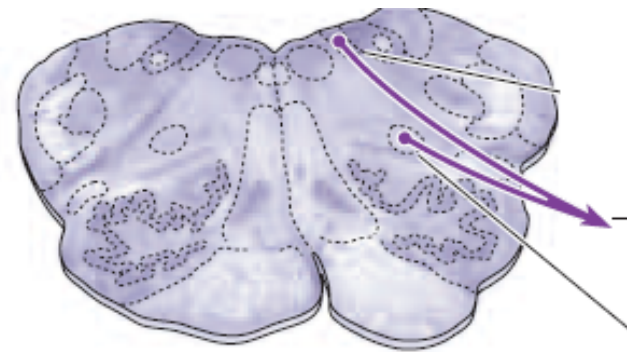
# Núcleo ambíguo (NA)

Visão Rostral



Núcleo ambíguo

Neurônios pré-ganglionares  
parassimpáticos para o coração

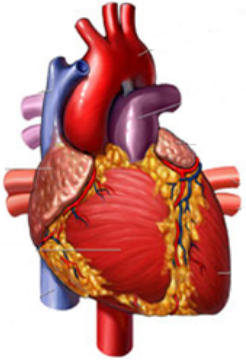


Nervo Vago (X)

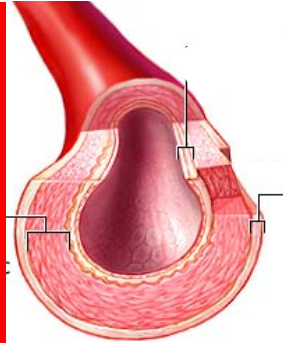
Núcleo ambíguo

Modificado de Purves ,2004

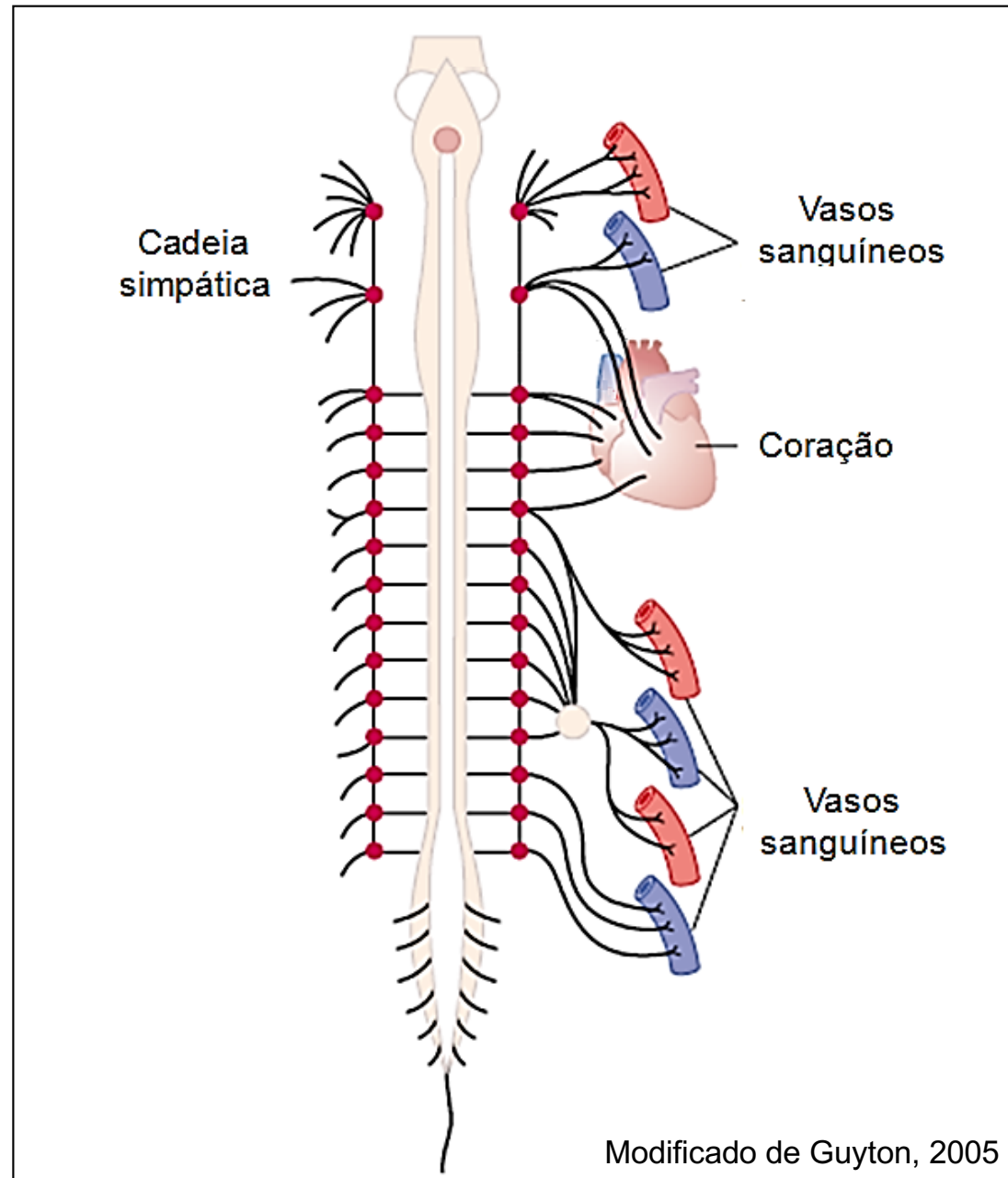




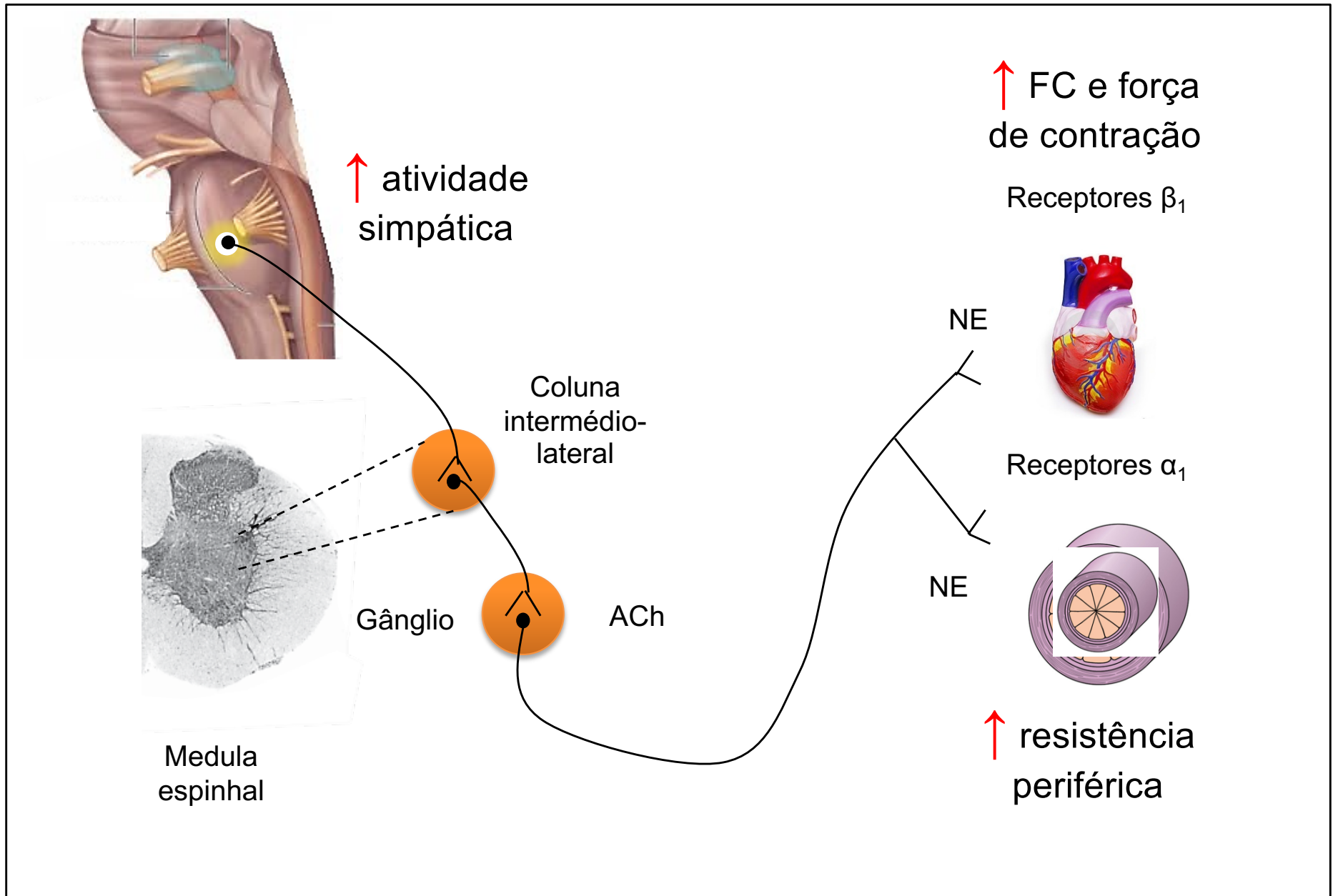
# Sistema nervoso simpático



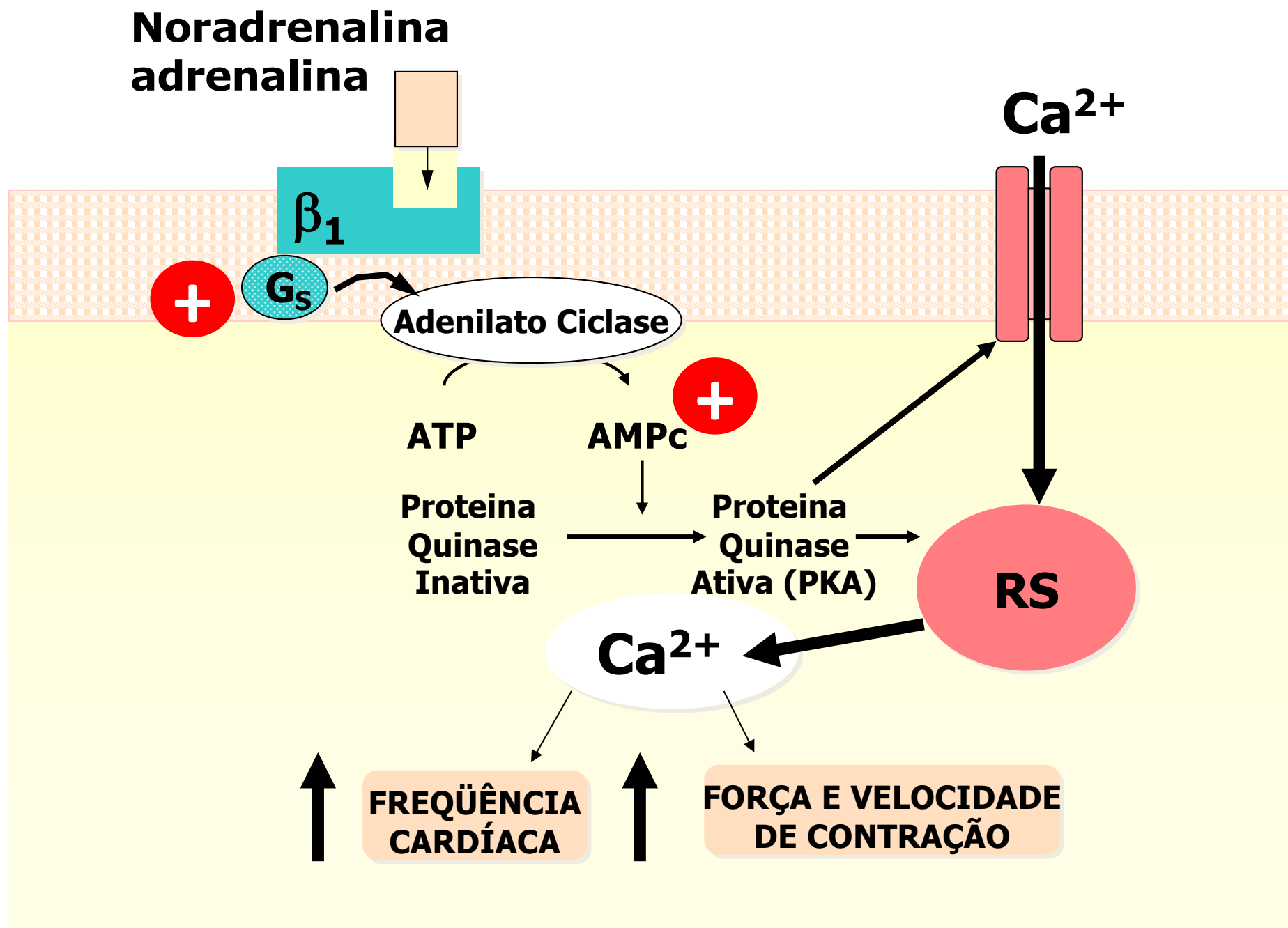
# Inervação simpática para o sistema cardiovascular



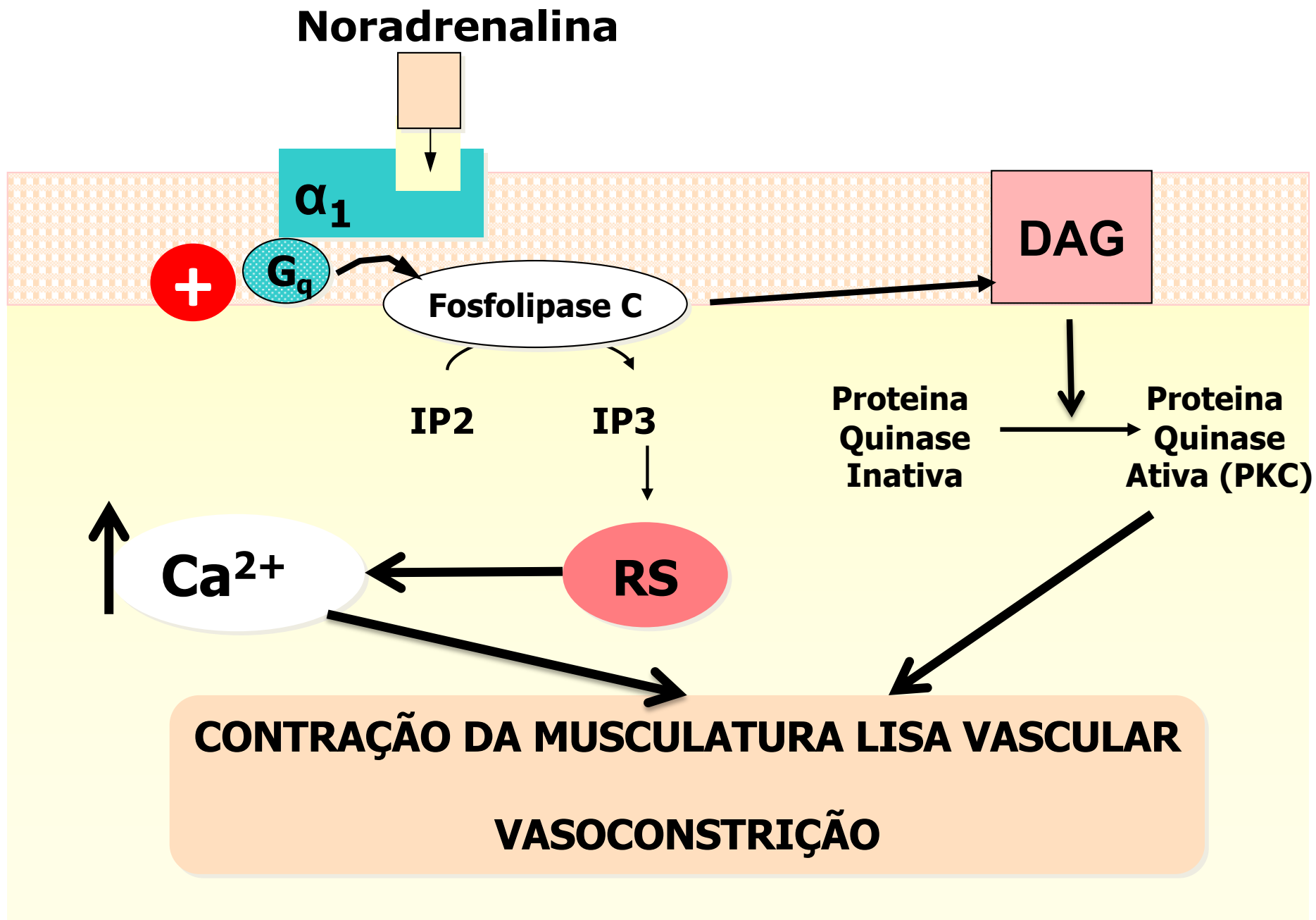
# Inervação simpática para o sistema cardiovascular

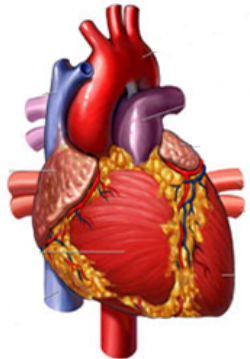


# Ativação simpática: Coração

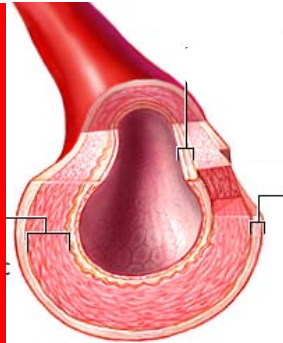


# Sistema nervoso simpático: Tônus vasomotor

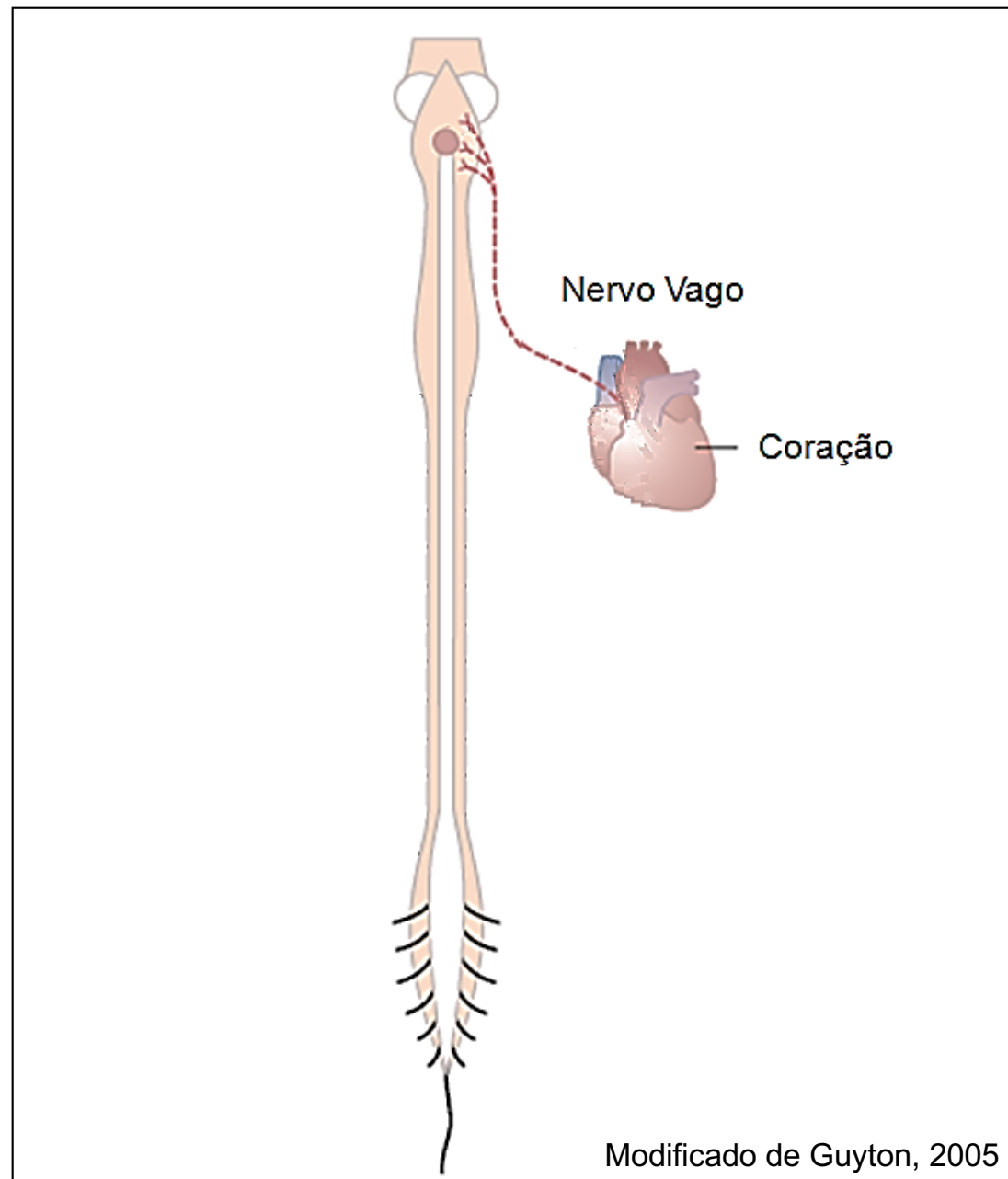




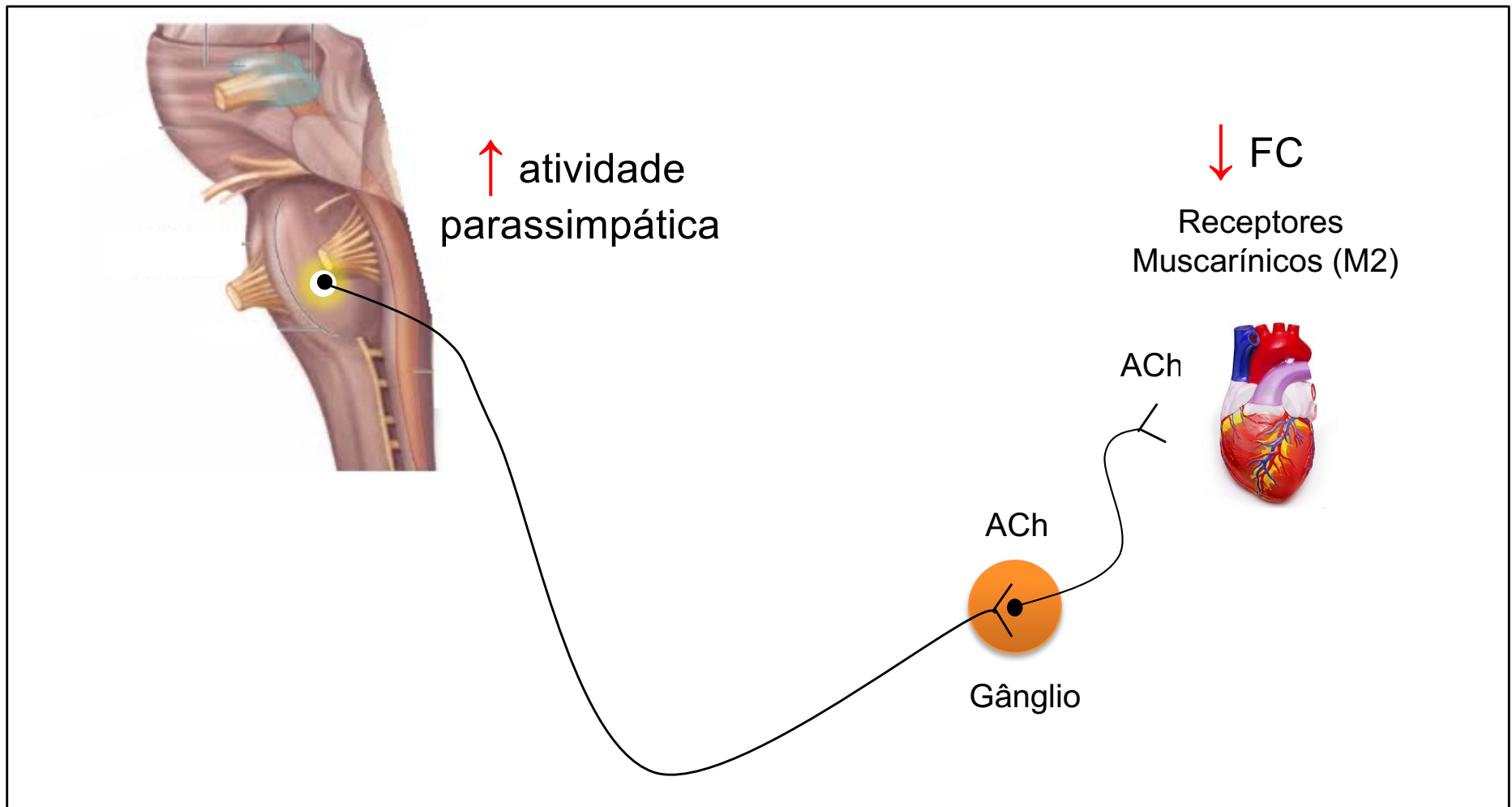
# Sistema nervoso parassimpático



# Inervação parassimpática para o sistema cardiovascular

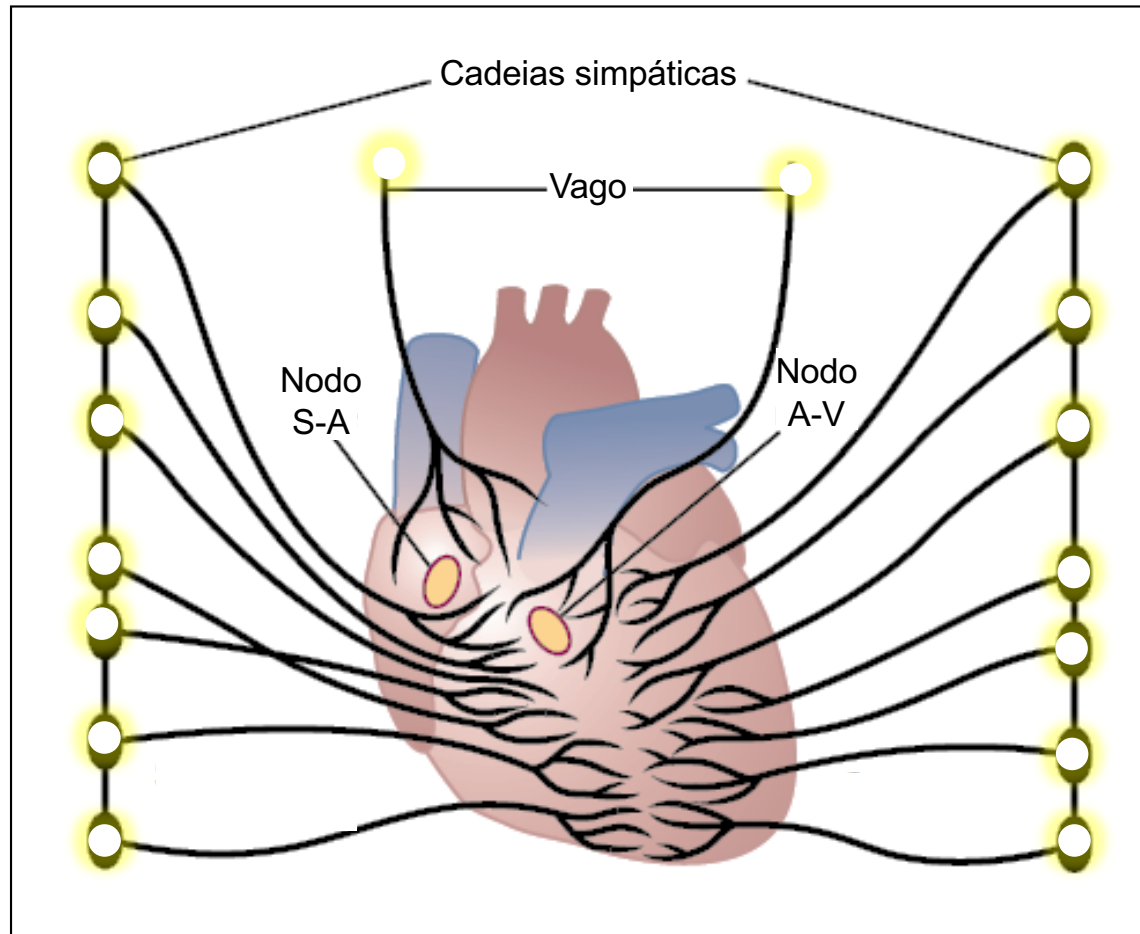


# Inervação parassimpática para o sistema cardiovascular

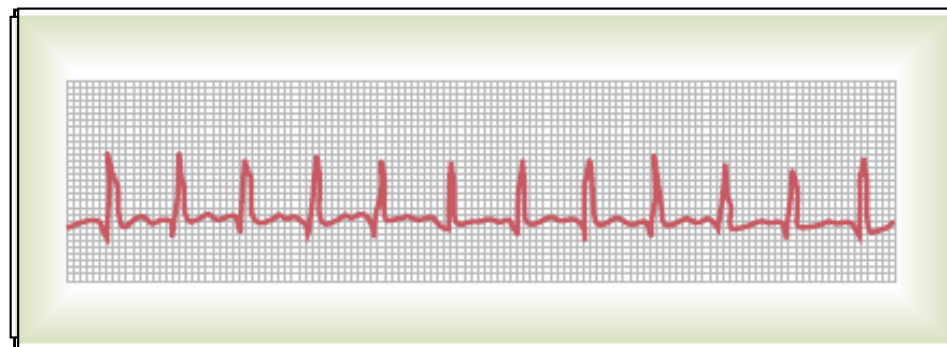




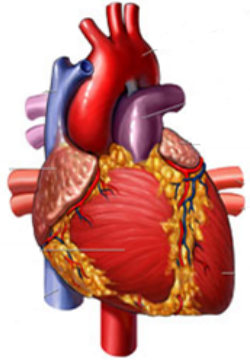
# Nervos cardíacos simpáticos e parassimpáticos



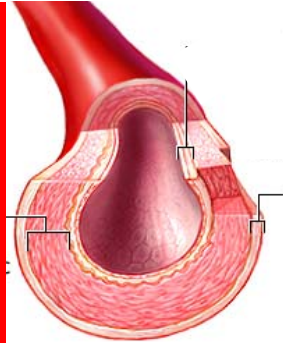
ECG



↑ FC e  
força de  
contração  
↓ FC normal



# O quimiorreflexo

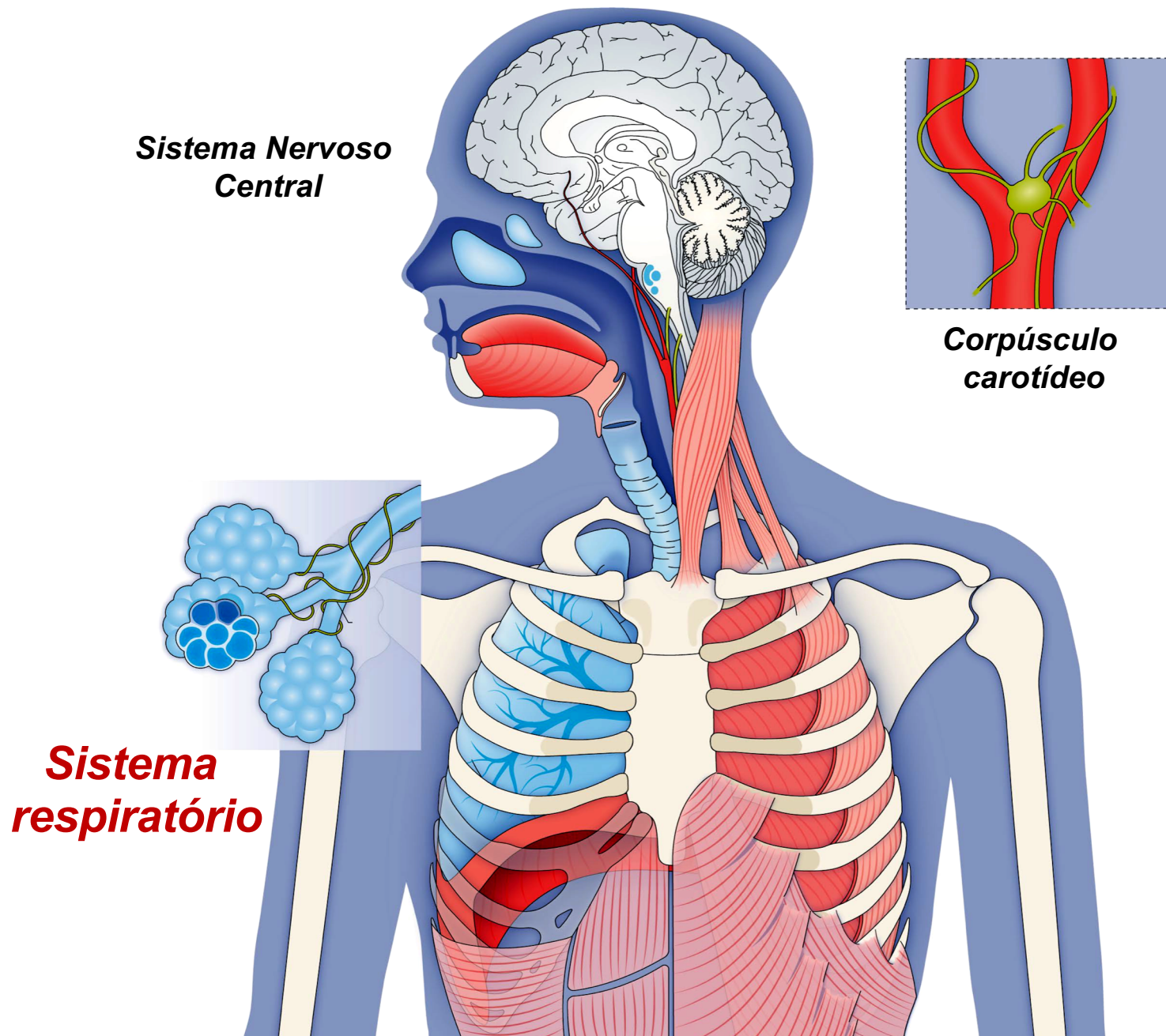


# Quimiorreflexo

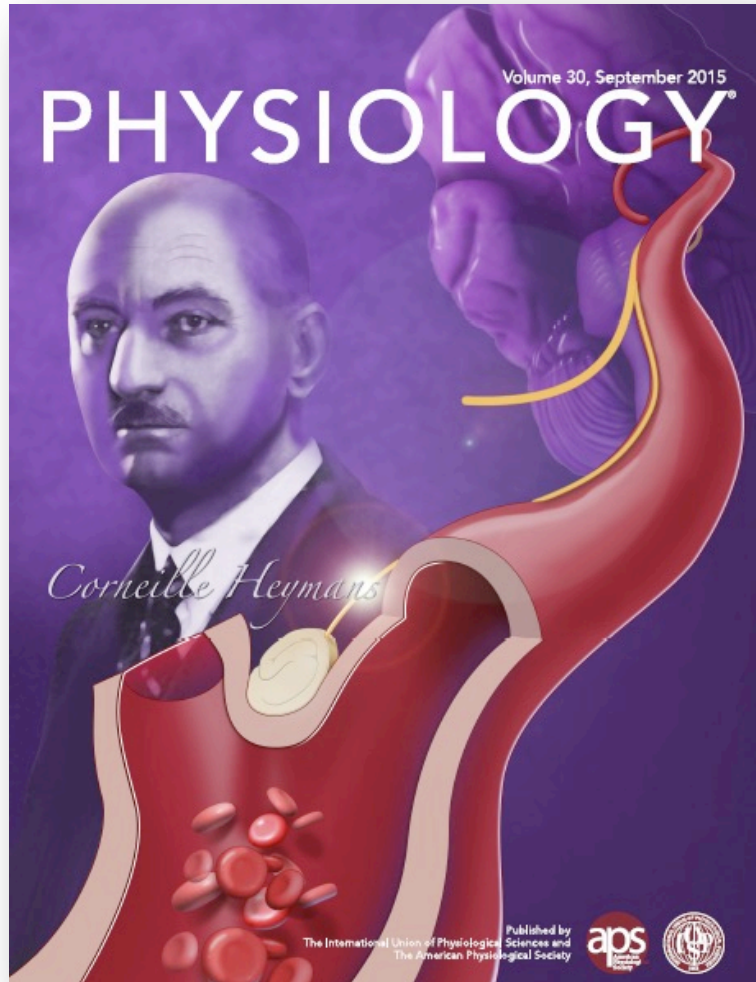


**Alterações cardiovasculares**

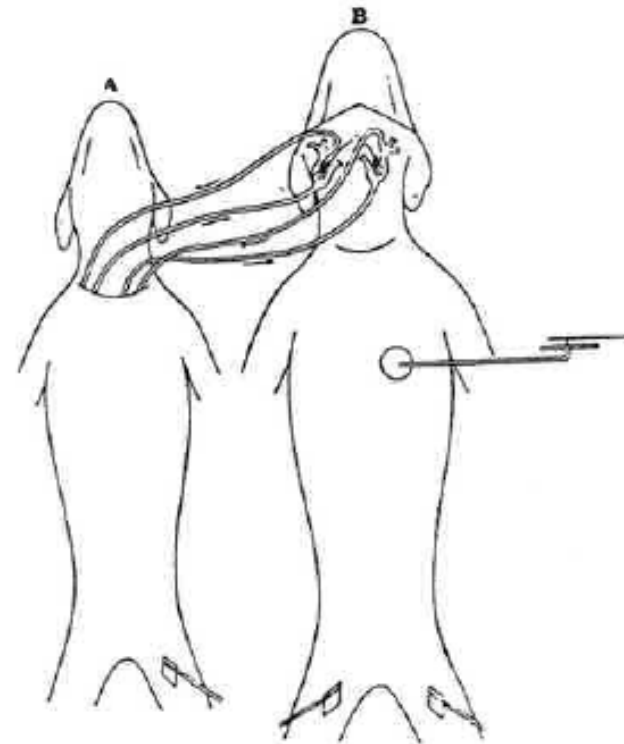
# Controle neural da ventilação



# Quimiorreceptores periféricos



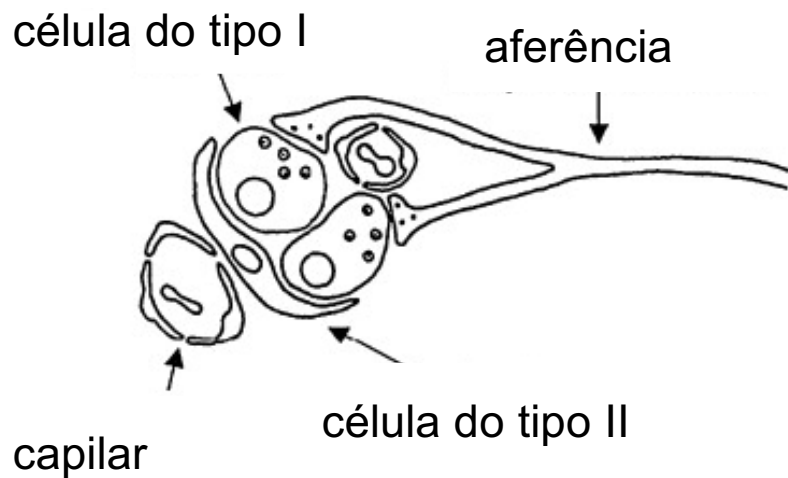
The Nobel Prize in Physiology or Medicine 1938  
Corneille Heymans



The Nobel Prize in Physiology or Medicine 1938 was awarded to Corneille Heymans "for the discovery of the role played by the sinus and aortic mechanisms in the regulation of respiration".

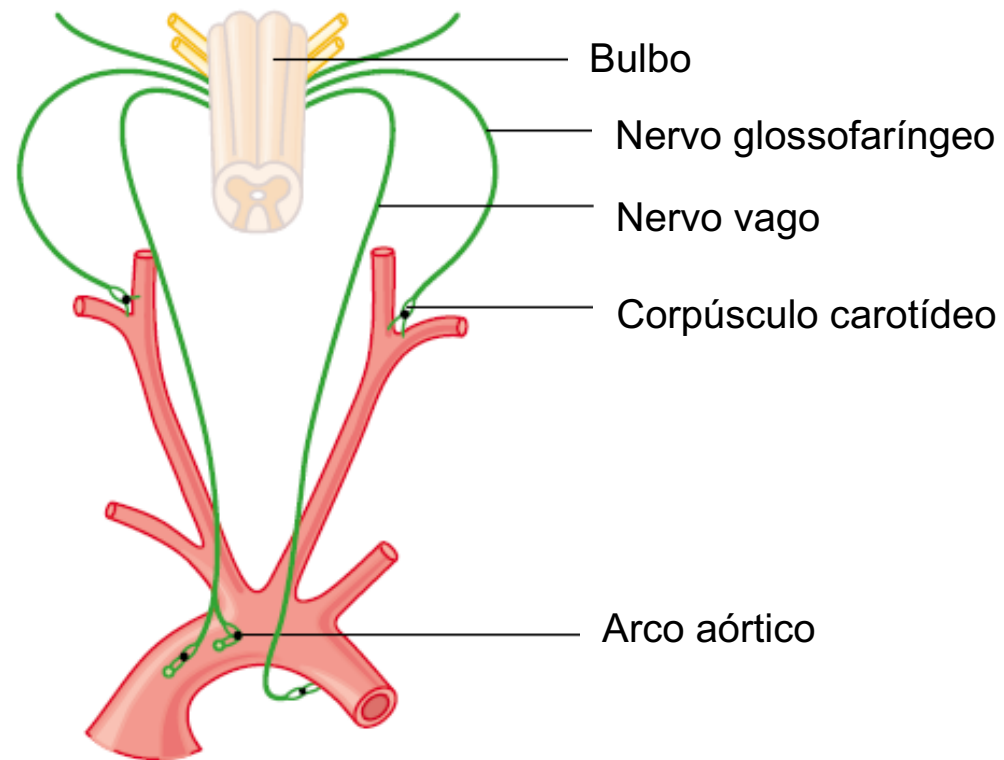
# Quimiorreceptores periféricos

## Estrutura do corpúsculo carotídeo



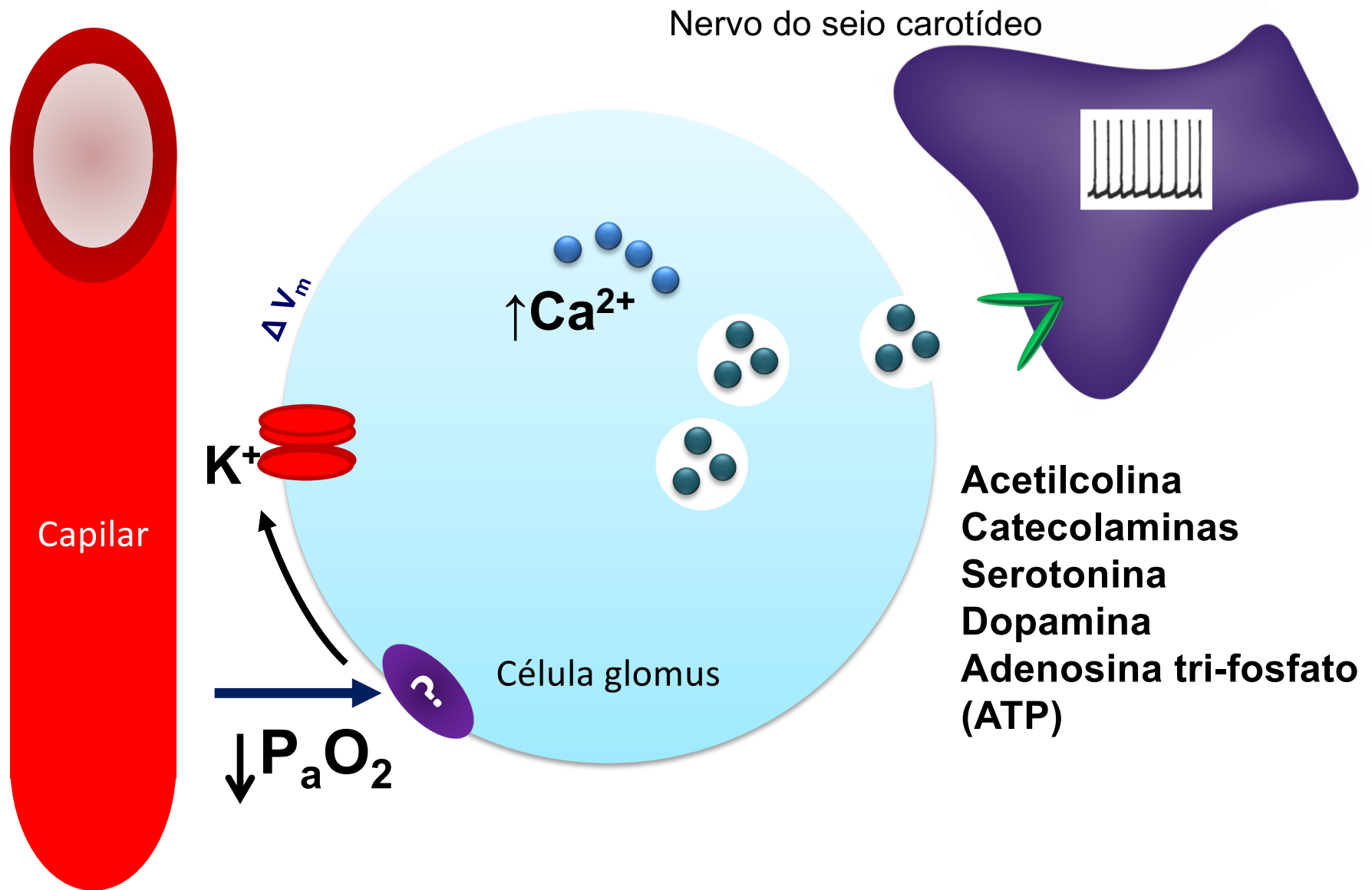
Modificado de Peers e cols, 2010

## Aferência dos quimiorreceptores

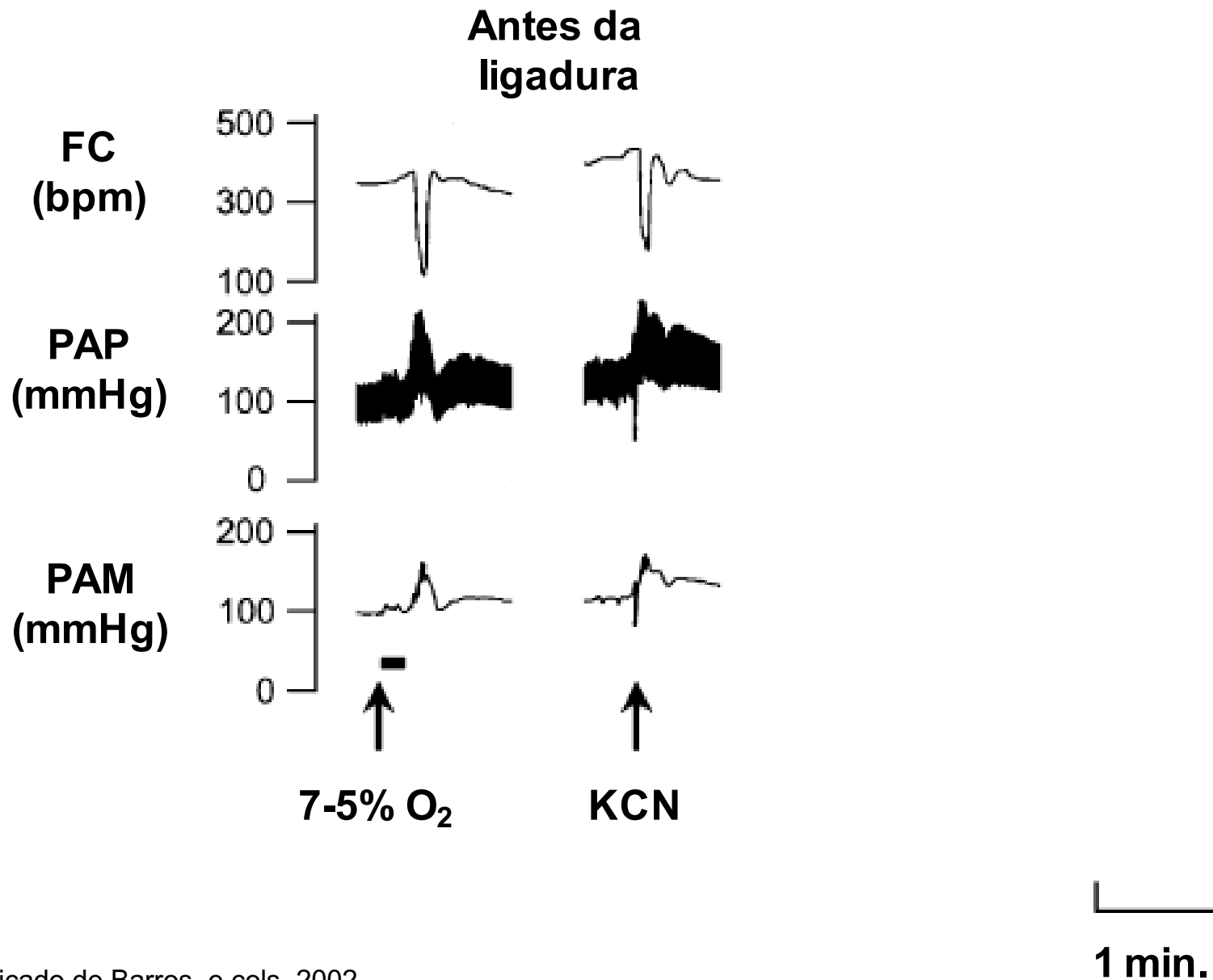


Modificado de Guyton, 2006

# Detecção da diminuição da $P_{aO_2}$ pelo corpúsculo carotídeo

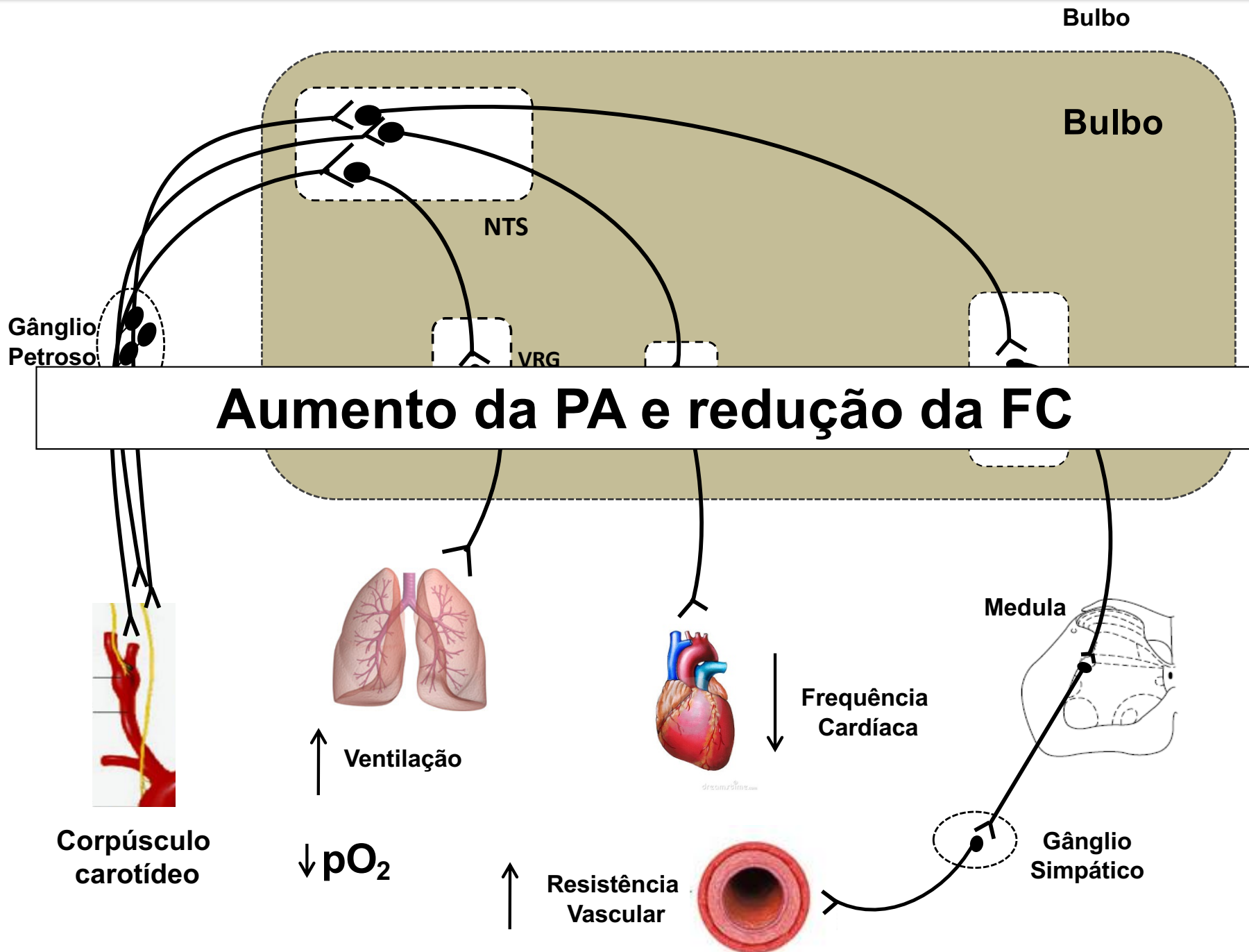


# Os quimiorreceptores no controle da PA



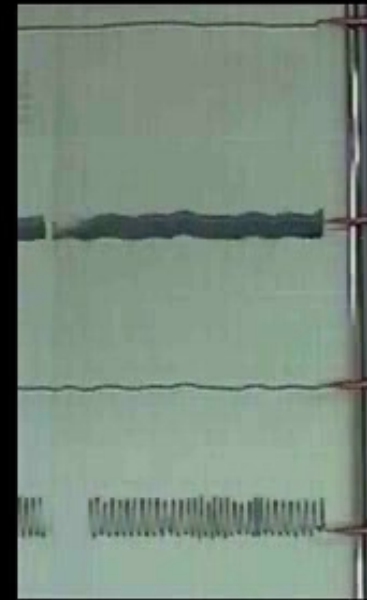


# Quimiorreflexo



# Resposta do quimiorreflexo no rato

KCN  
(i.v.)



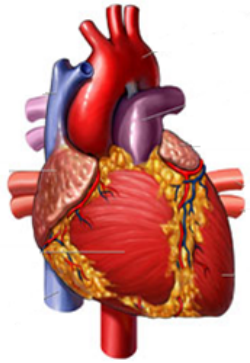
FC

PAP

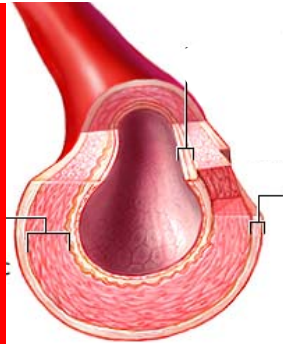
PAM

Laboratório de controle autonômico e respiratório

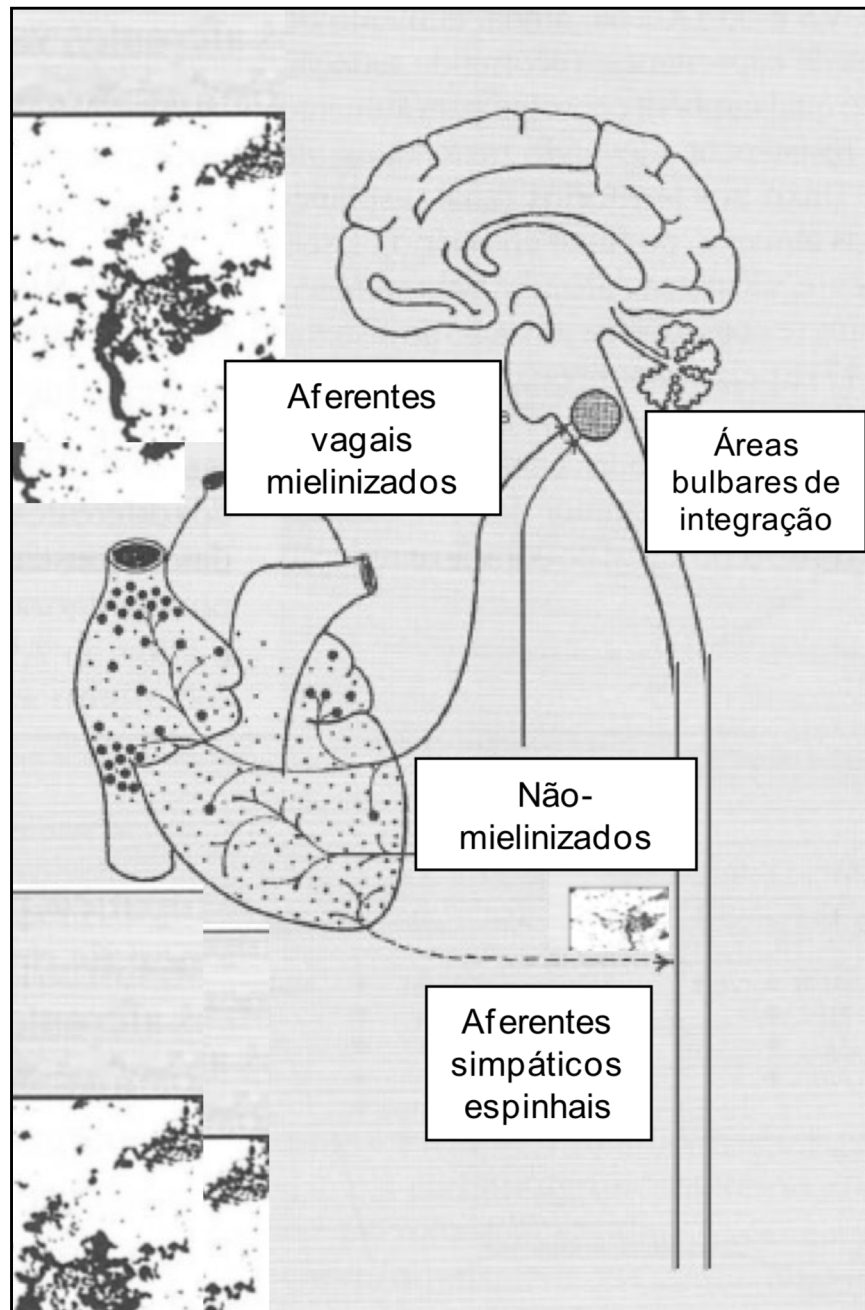
A bradicardia do quimiorreflexo não é secundária a resposta  
pressora



# O reflexo cardiopulmonar Bezold-Jarisch



# Receptores cardiopulmonares

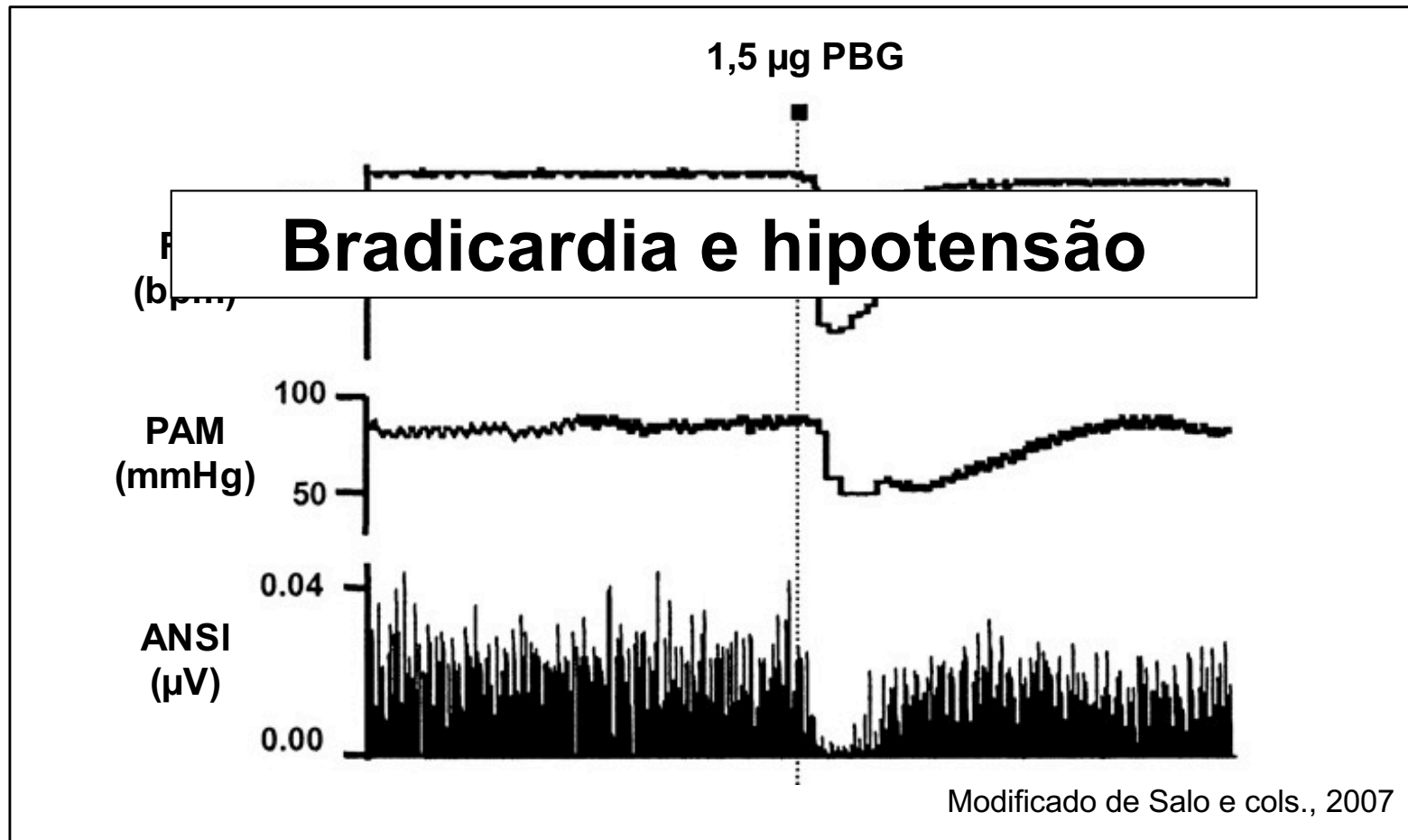


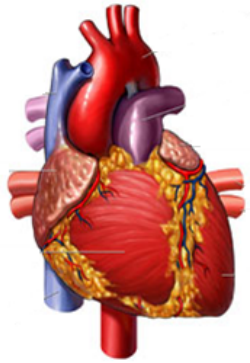
➤ Receptores de estiramento.

➤ Alterações de volume de sangue.

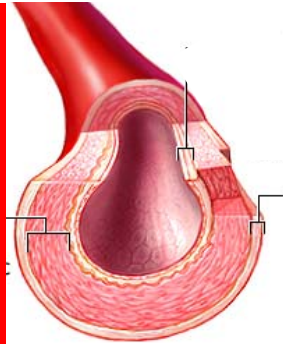
# Resposta do reflexo cardiopulmonar

Reflexo Bezold-Jarisch – Fenilbiguanida (PBG)

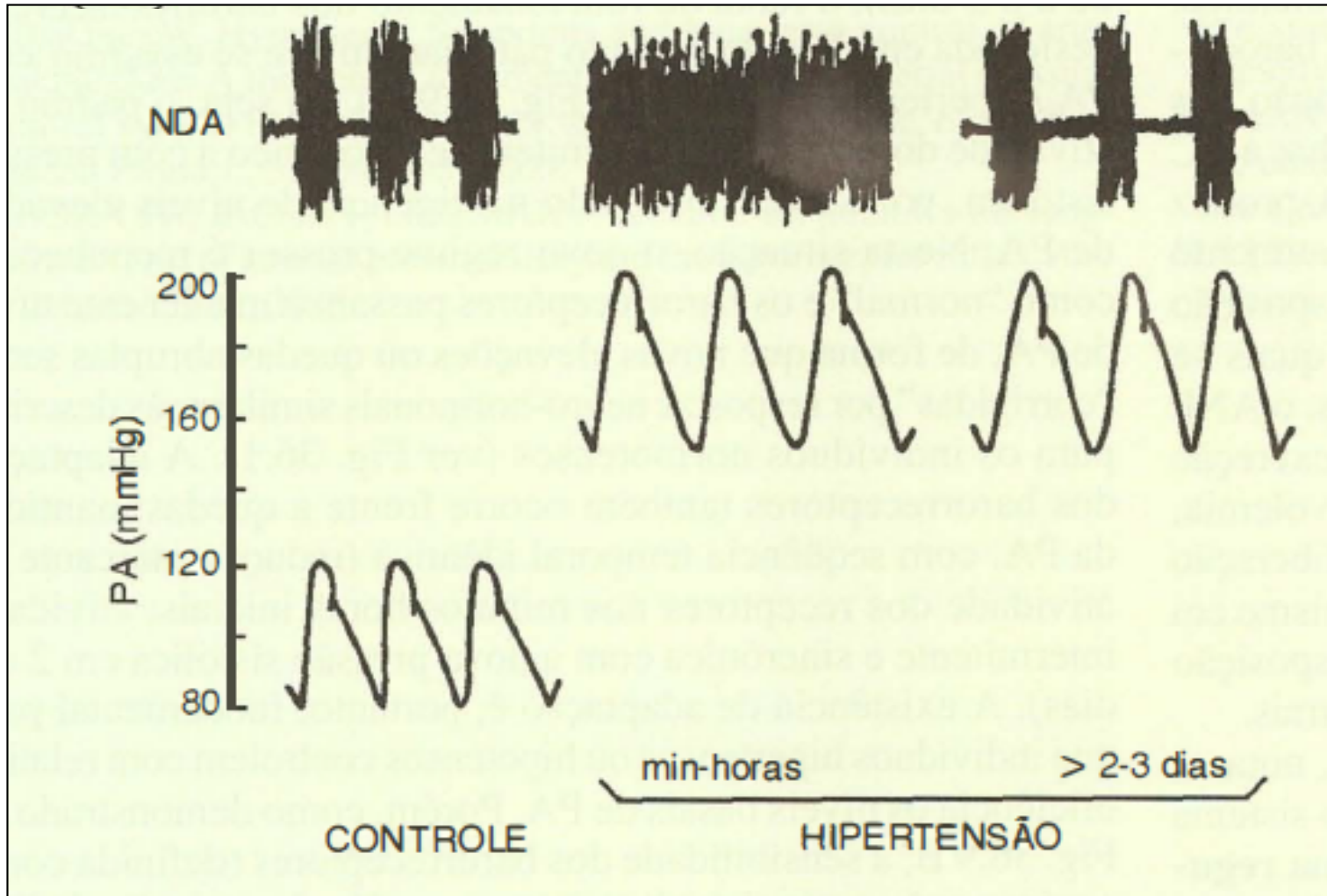




# Aplicando o conhecimento



# Adaptação dos barorreceptores na hipertensão



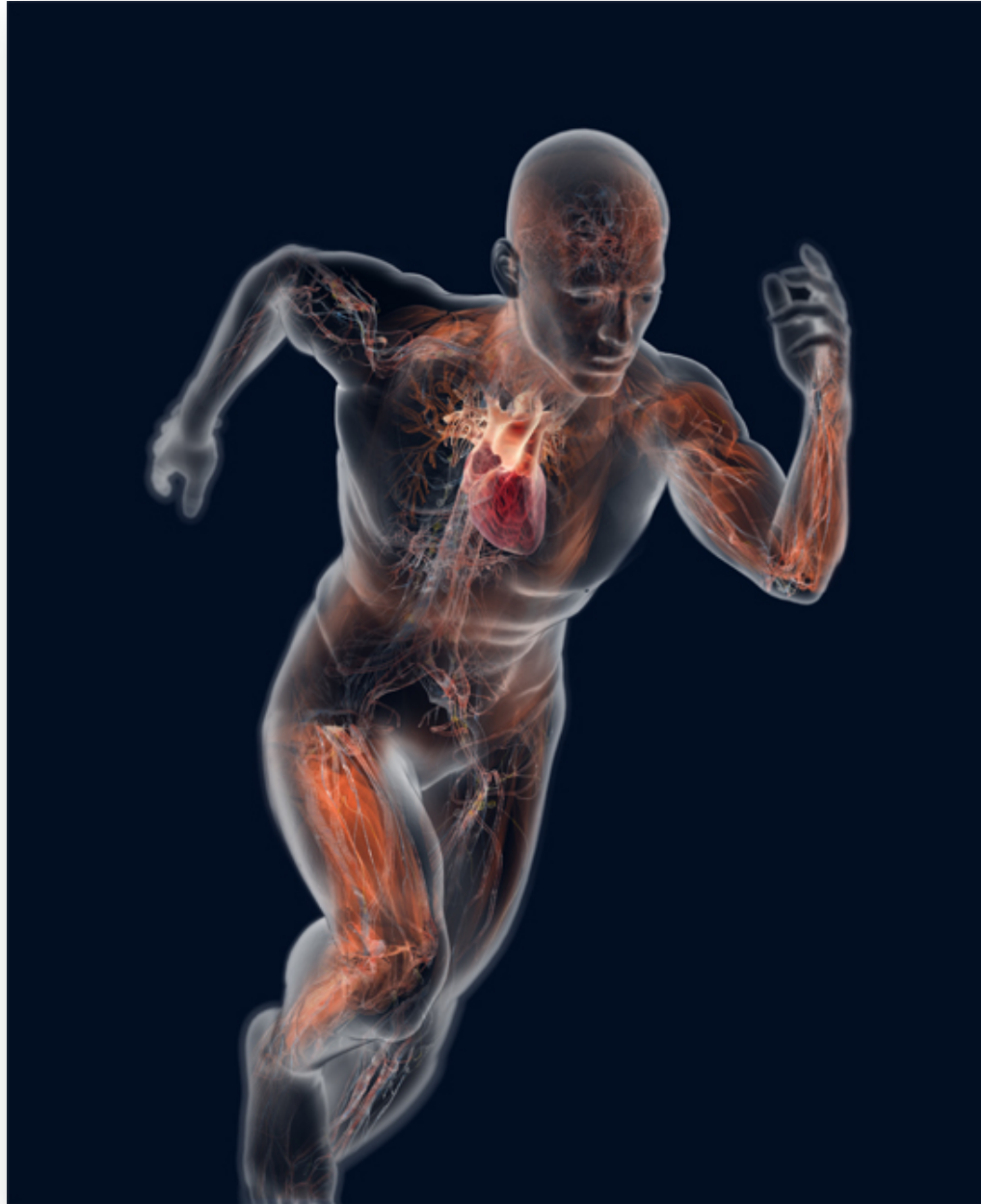
# O estresse ortostático



Modificado de Lanier e cols; 2011

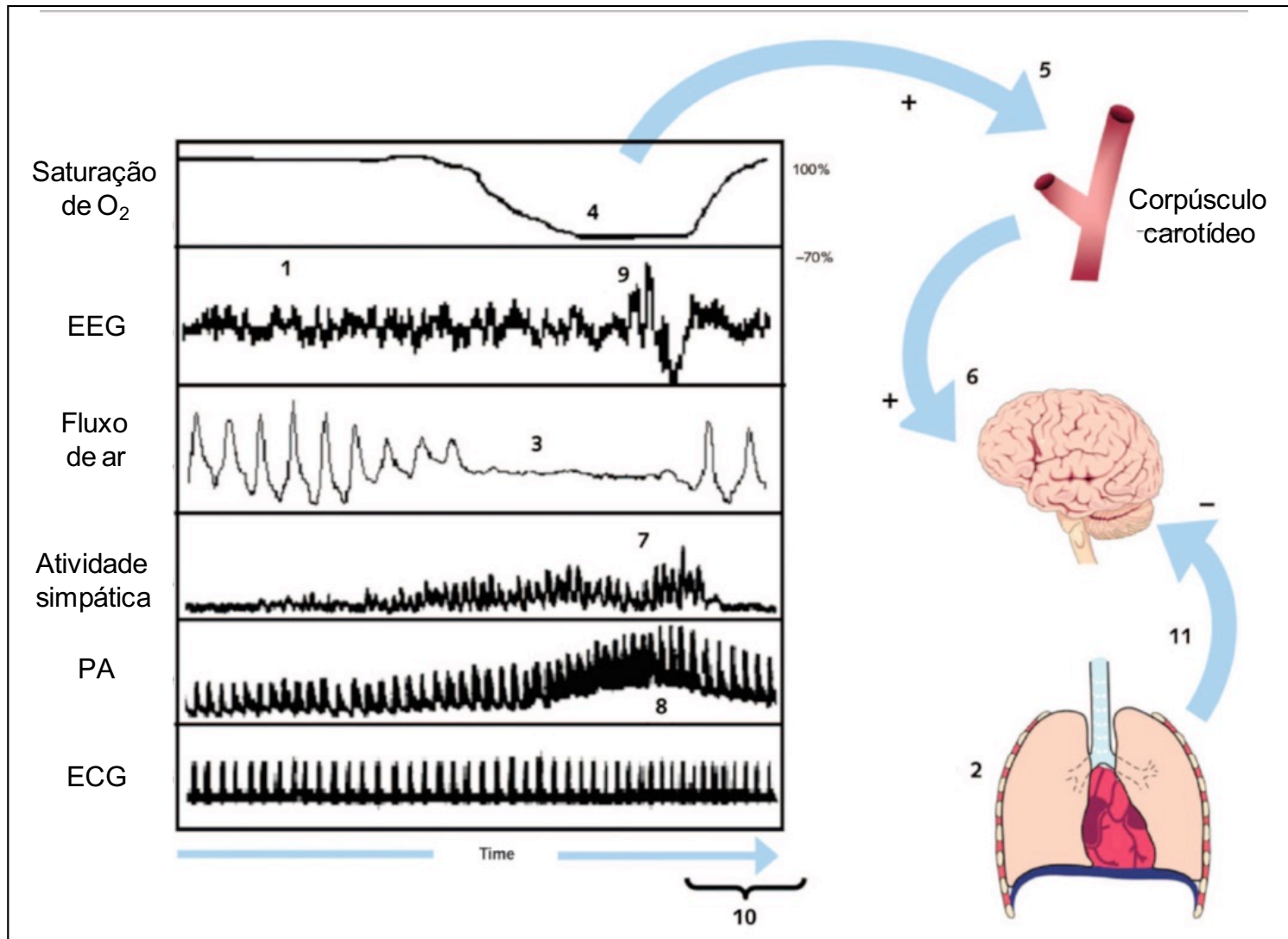


# Comportamento da PA durante o exercício físico



Smith e cols., 2005

# Hipóxia em humanos



Caples e cols., 2005

# Doenças cardio-respiratórias são problemas de saúde pública

## Estimativa de mortes no mundo (2004):

1. Problemas Cardio-respiratórios 35,8%
2. Doenças infecciosas e parasitárias 23,0%
3. Câncer 12,5 %
4. Traumas 6,2 %



World Health Organization

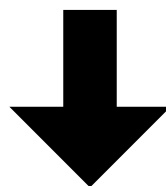
# Hipertensão arterial: Quais são os mecanismos?

Na maioria dos pacientes hipertensos, a causa é:



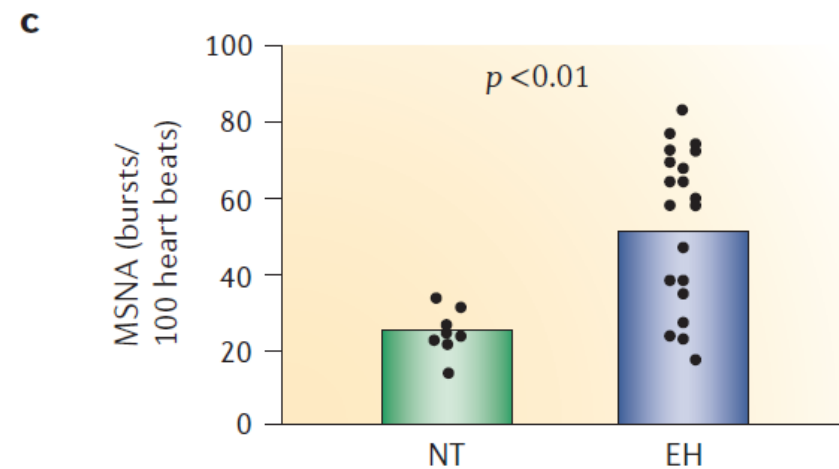
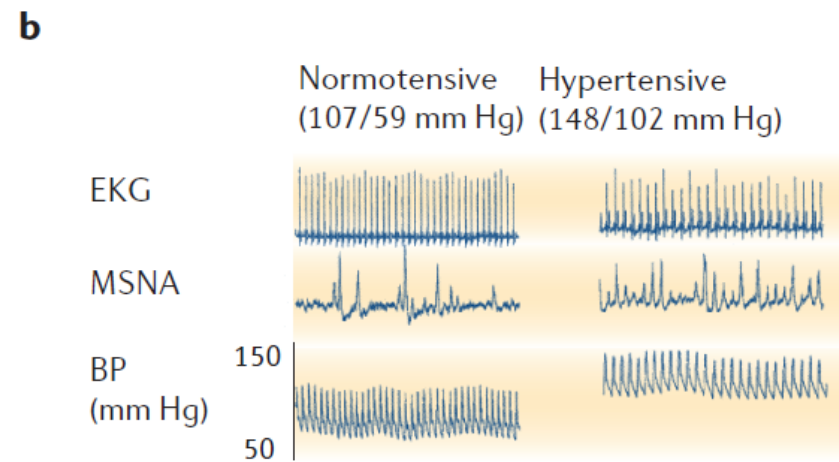
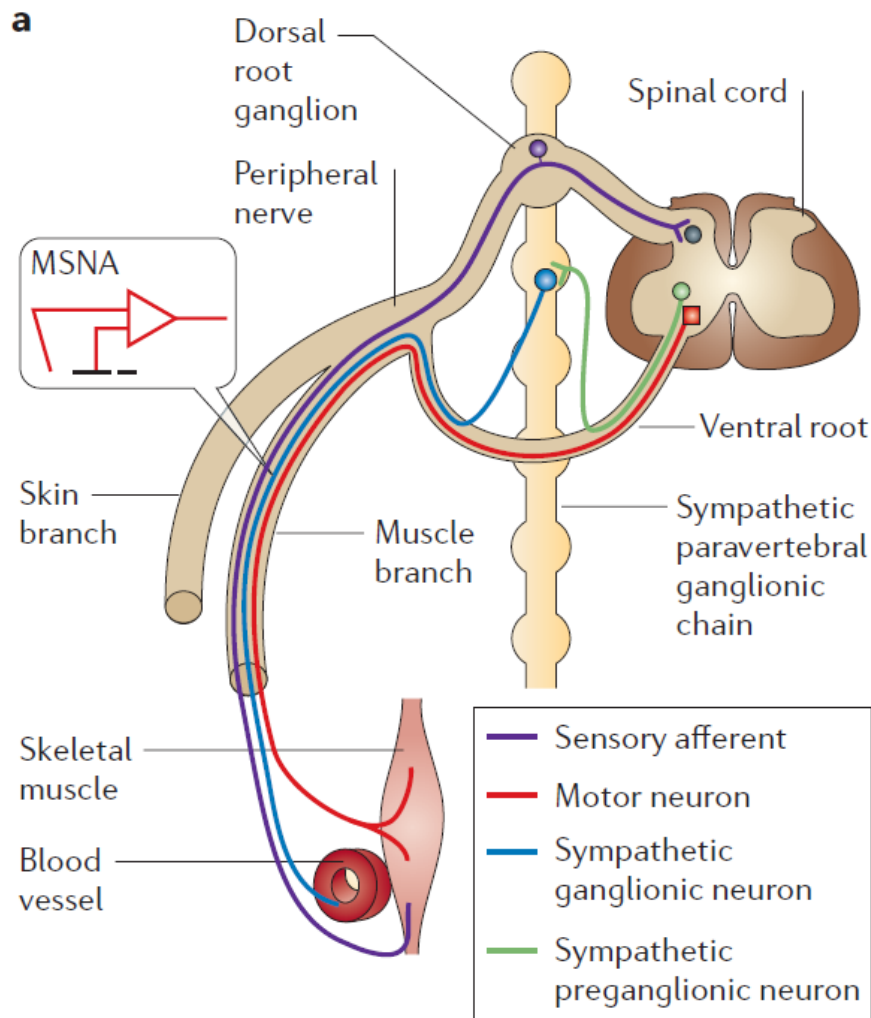
**DESCONHECIDA**

Cerca de 50 % dos  
pacientes hipertensos  
têm sua pressão  
arterial normalizada

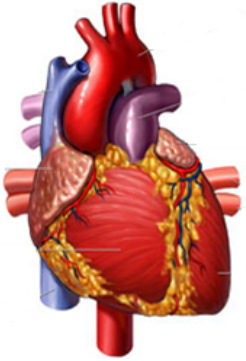


Alterações nos mecanismos neurais que controlam a função cardiovascular

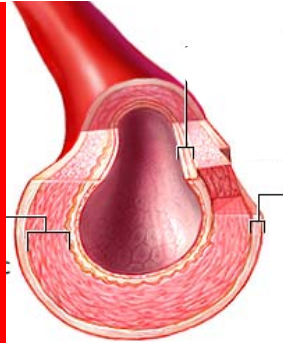
# Hipertensão e Hiperatividade Simpática



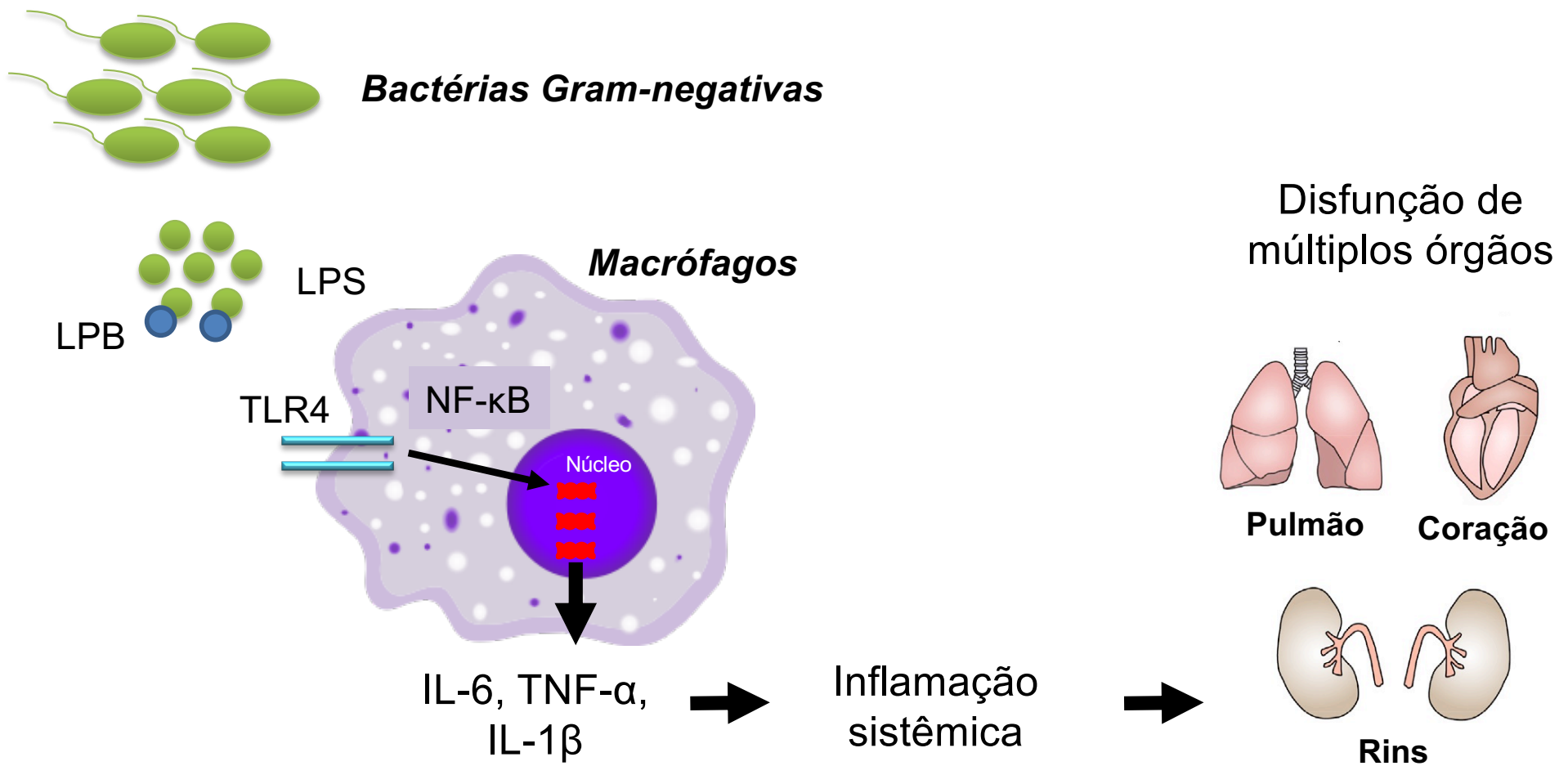
Guyenet, *Nat. Neurosc.*, 2006



# Controle neural da PA durante a inflamação sistêmica

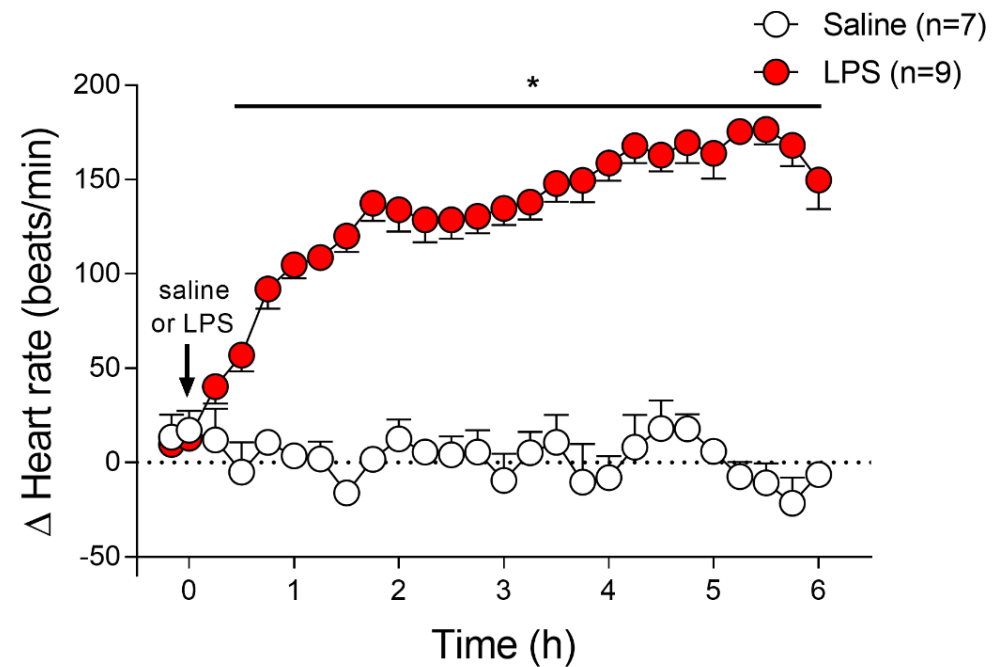
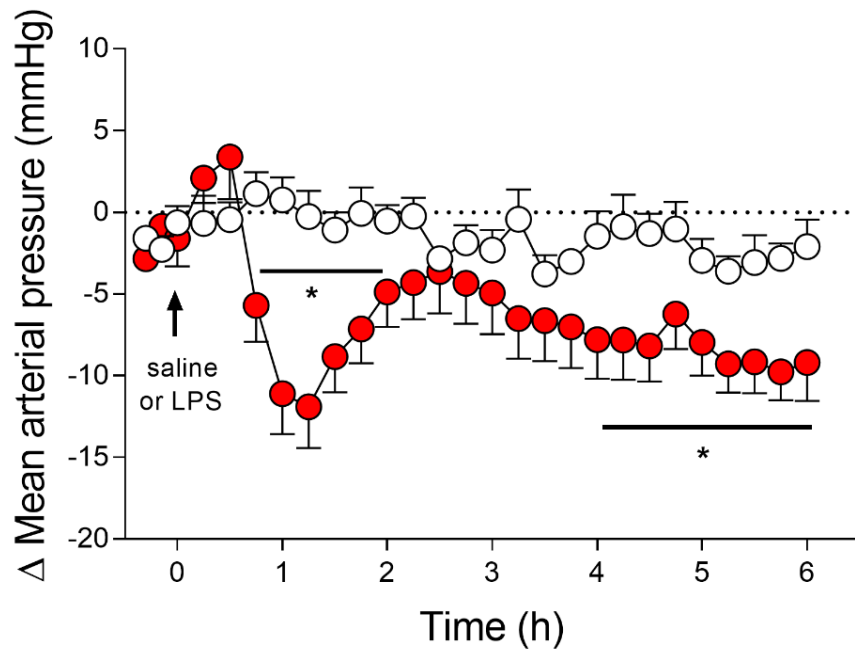


# Reconhecimento do lipopolissacarídeo (LPS)



# Alterações durante a inflamação sistêmica induzida por LPS

LPS (1.5 mg/kg)



**A administração de LPS em ratos induz hipotensão e taquicardia similares ao seres humanos com sepse.**



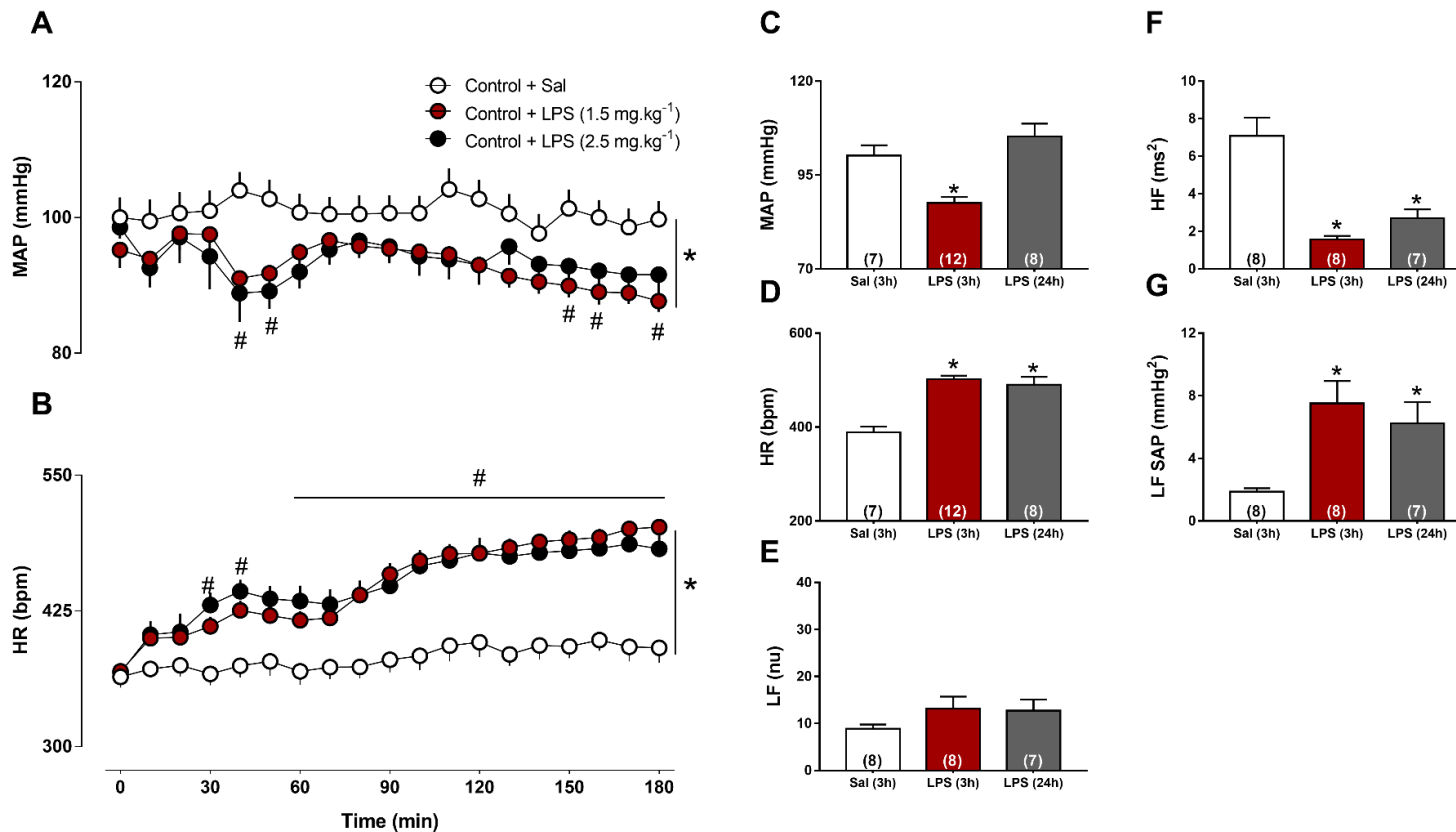
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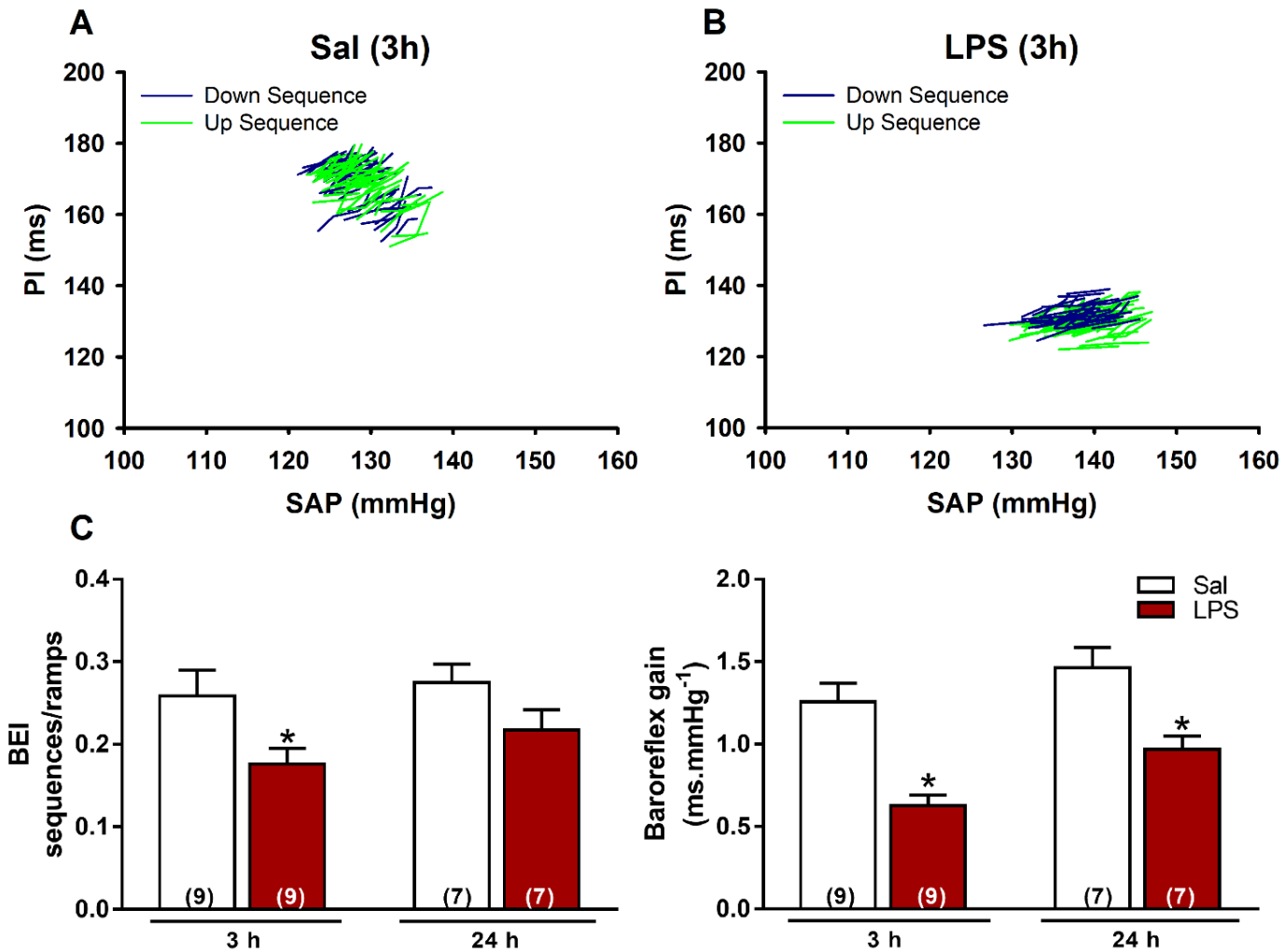
# Neuroinflammation in the NTS is associated with changes in cardiovascular reflexes during systemic inflammation



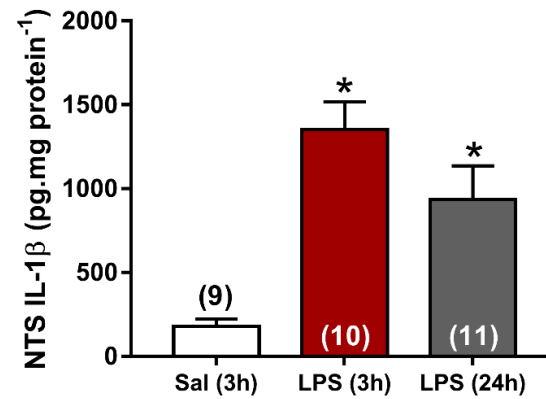
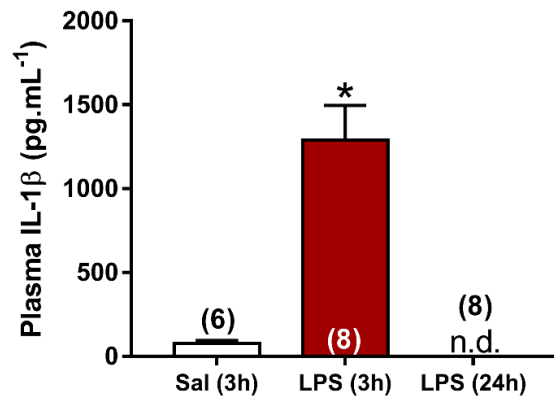
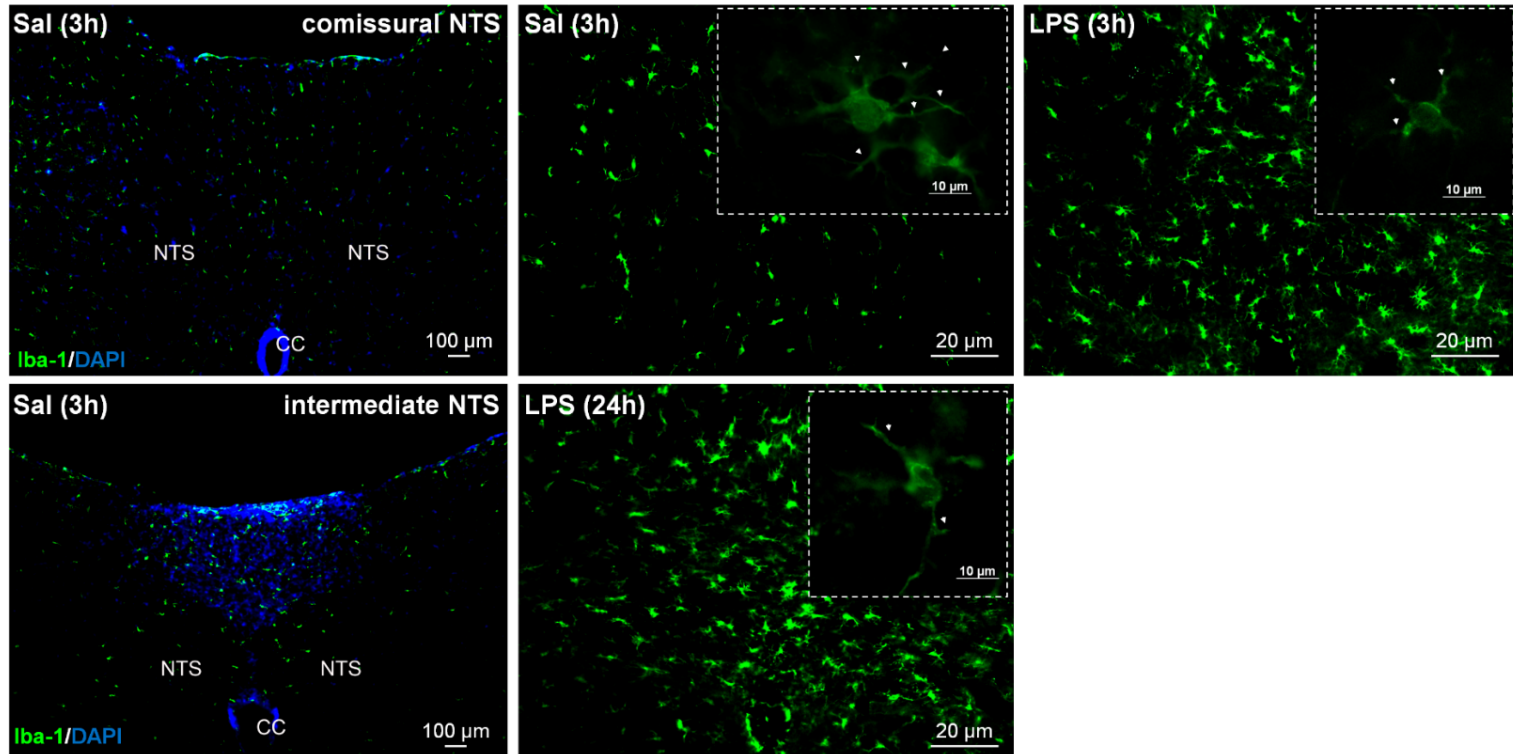
Mateus R. Amorim<sup>1</sup>, Júnia L. de Deus<sup>2</sup>, Rafael A. Cazusa<sup>3</sup>, Clarissa M. D. Mota<sup>2</sup>, Luiz E. V. da Silva<sup>2</sup>, Gabriela S. Borges<sup>2</sup>, Marcelo E. Batalhão<sup>4</sup>, Evelin C. Cárnio<sup>4</sup> and Luiz G. S. Branco<sup>1\*</sup>



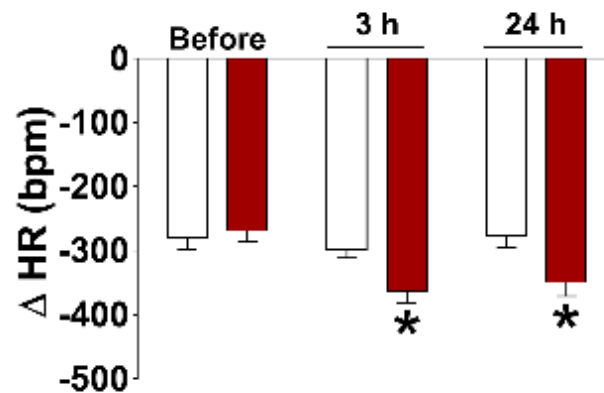
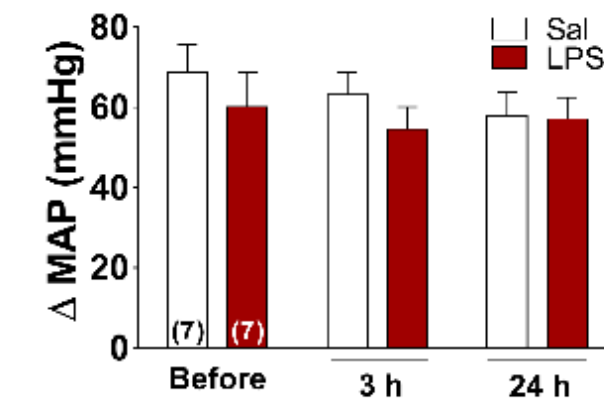
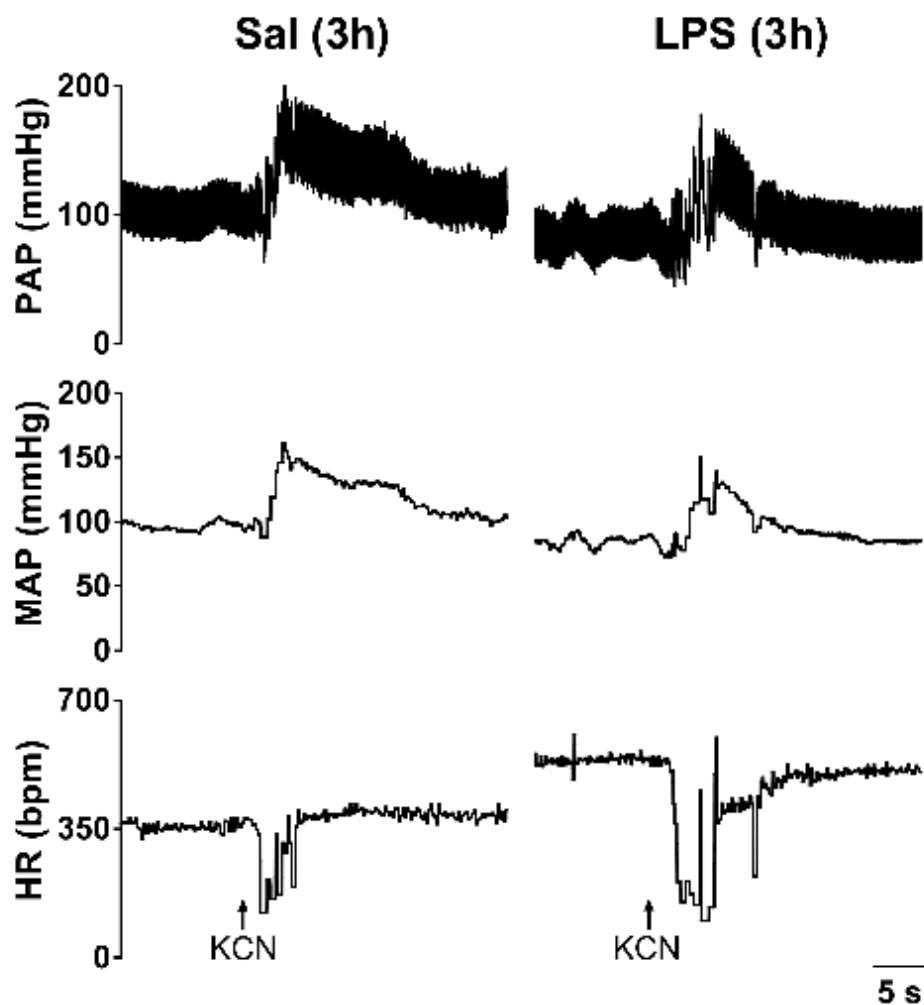
# Barorreflexo durante a inflamação sistêmica



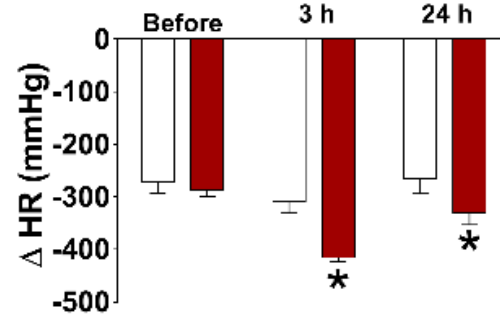
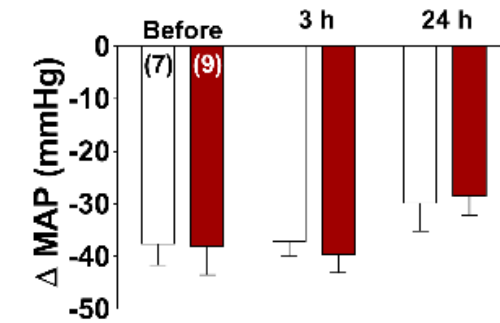
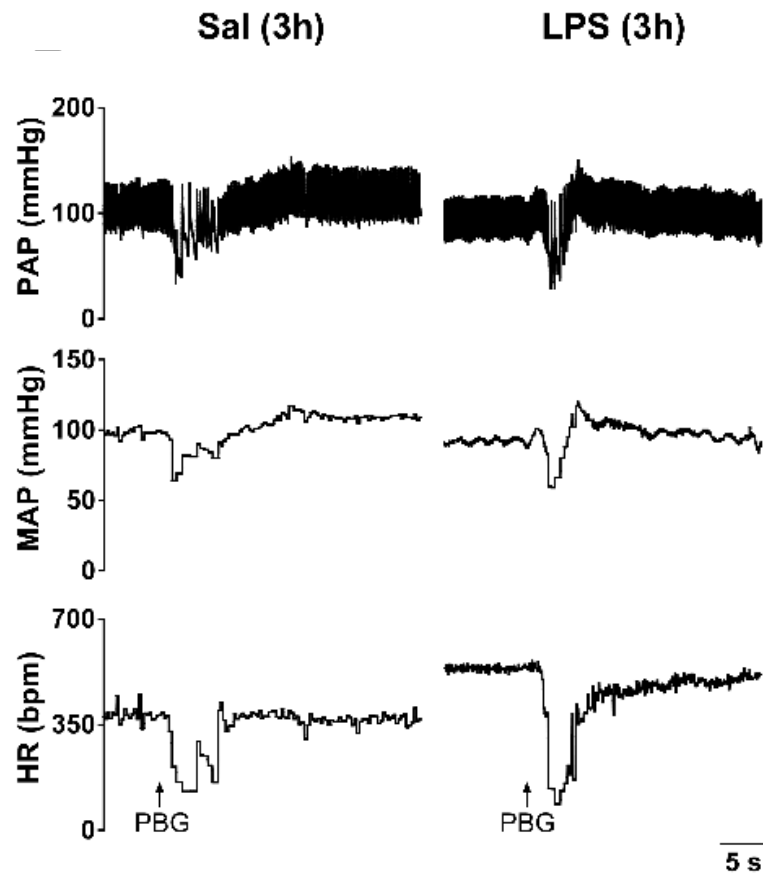
# Inflamação sistêmica



# Quimiorreflexo durante a inflamação sistêmica

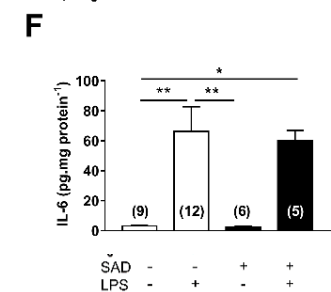
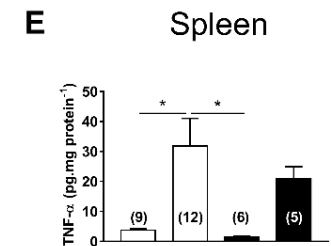
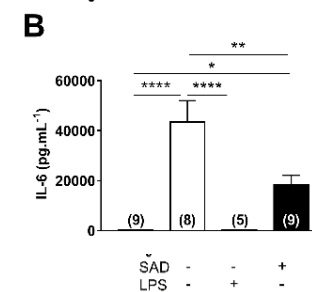
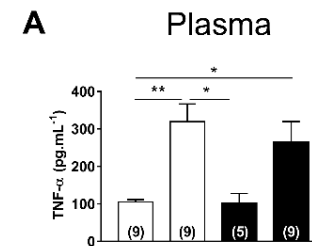
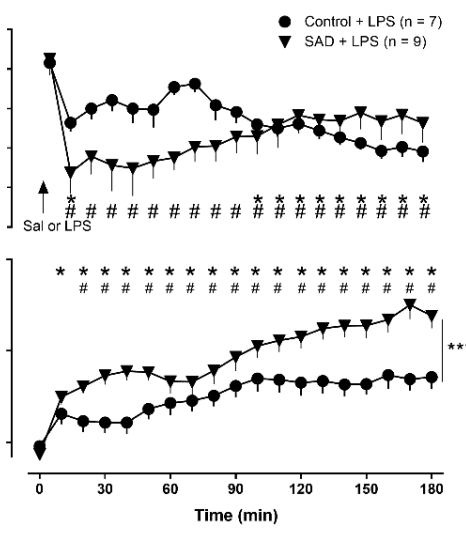
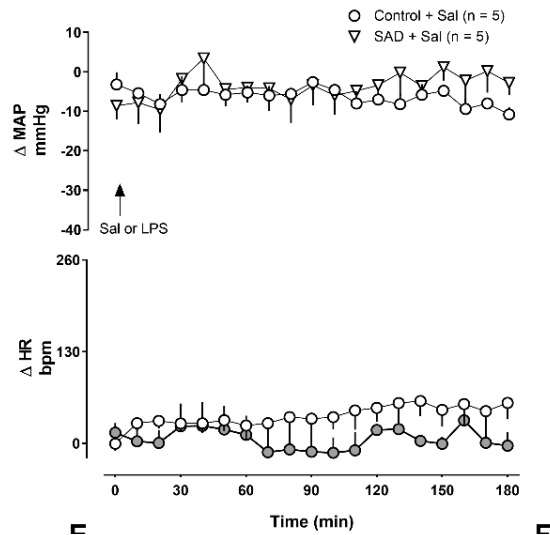


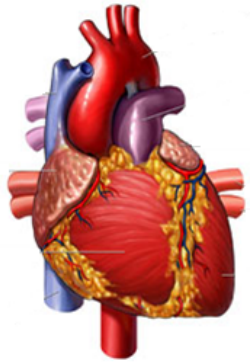
# Reflexo de Bezold-Jarish durante a inflamação sistêmica



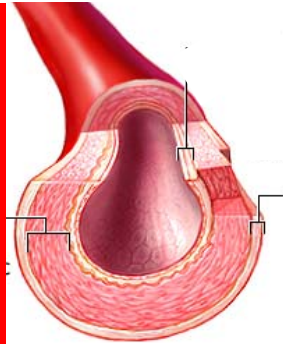
OPEN **Baroreceptor denervation reduces inflammatory status but worsens cardiovascular collapse during systemic inflammation**

Mateus R. Amorim<sup>1</sup>, Júnia L. de Deus<sup>1</sup>, Camila A. Pereira<sup>2</sup>, Luiz E. V. da Silva<sup>2</sup>, Gabriela S. Borges<sup>2</sup>, Nathanne S. Ferreira<sup>2</sup>, Marcelo E. Batalhão<sup>3</sup>, José Antunes-Rodrigues<sup>2</sup>, Evelin C. Carnio<sup>3</sup>, Rita C. Tostes<sup>2</sup> & Luiz G. S. Branco<sup>1,2</sup>



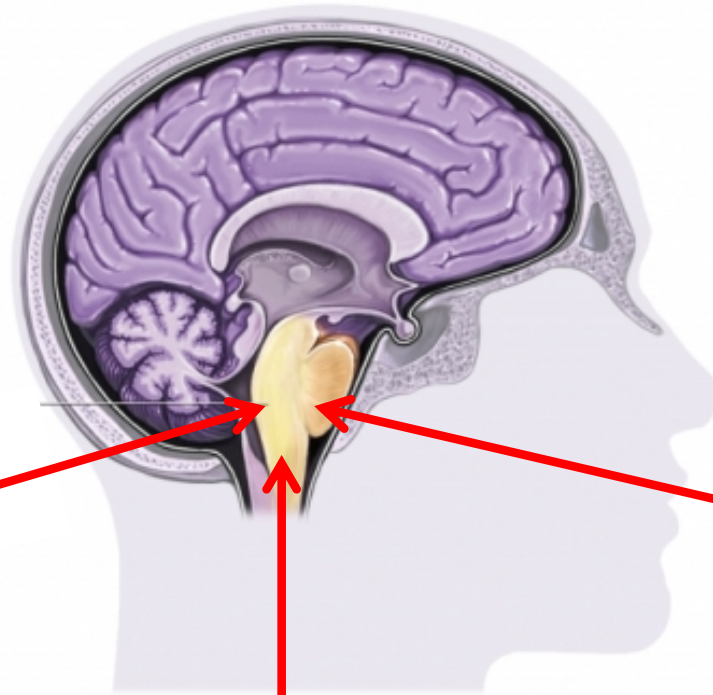


# Considerações finais



# Considerações finais

Sistema nervoso central



**Barorreceptores**

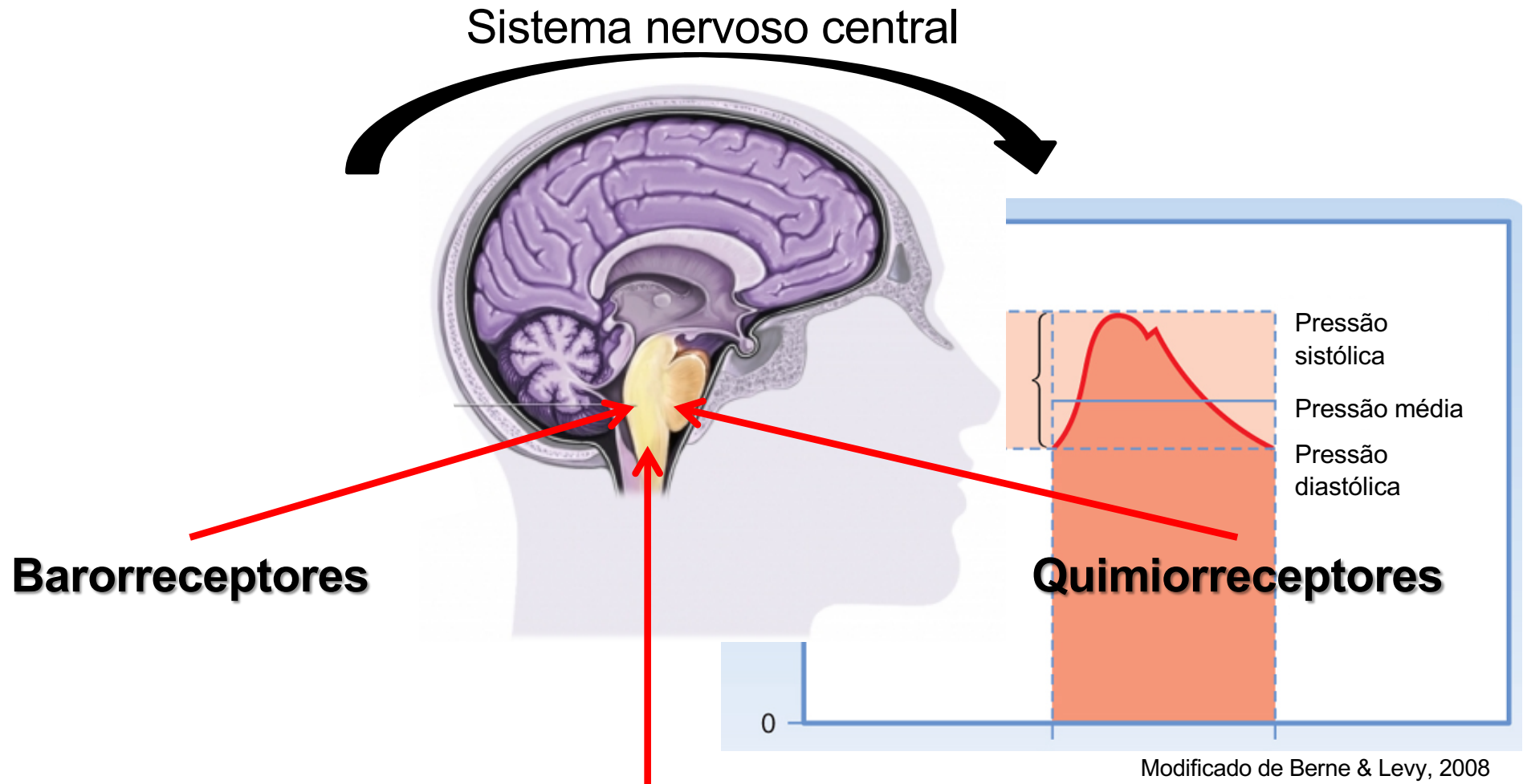
**Quimiorreceptores**

**Receptores cardiopulmonares**

Sistema nervoso periférico



# Considerações finais



**Receptores cardiopulmonares**

Sistema nervoso periférico