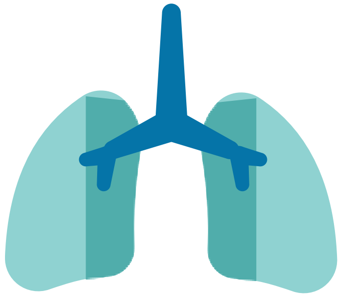
# Cardio-respiratory physiology




Valentin Ghibaudo

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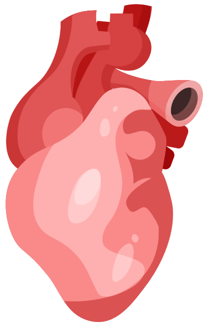
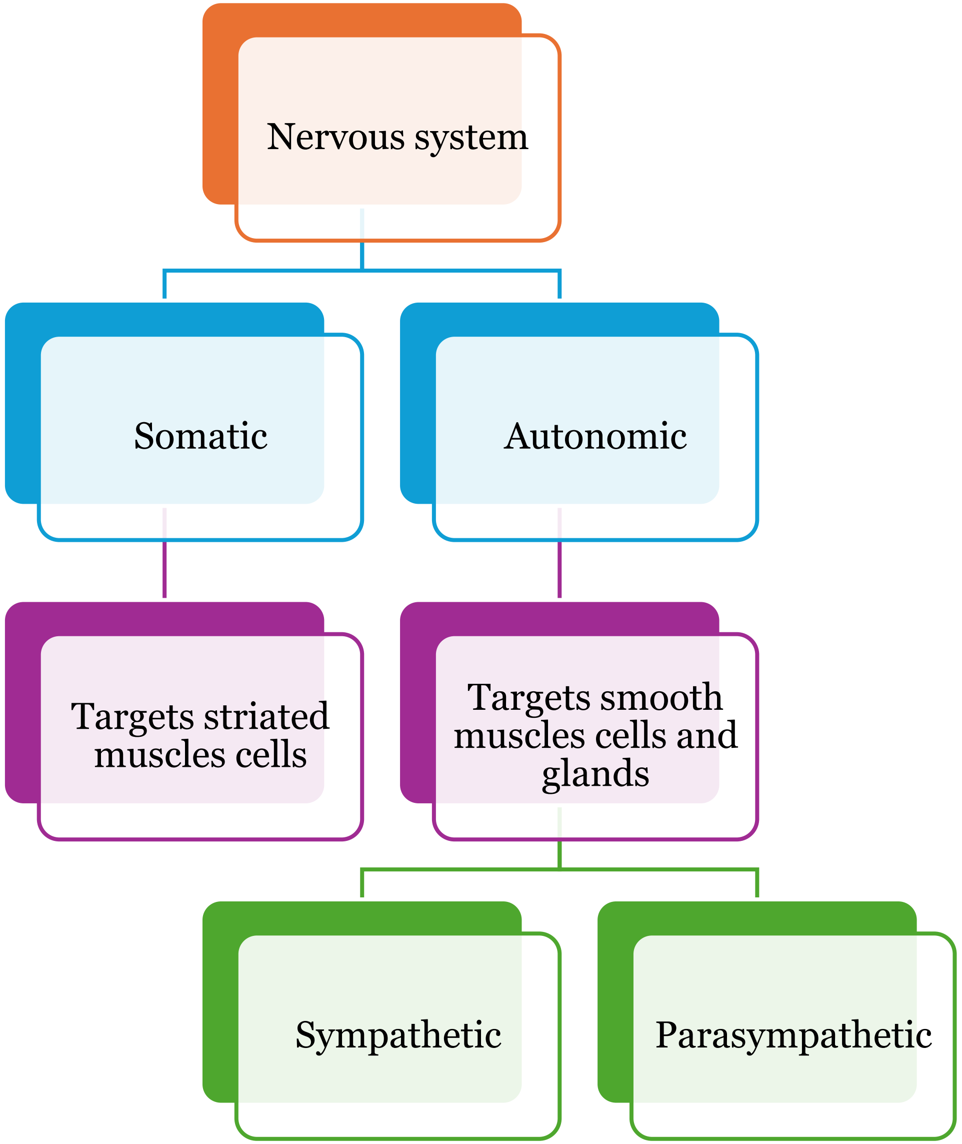


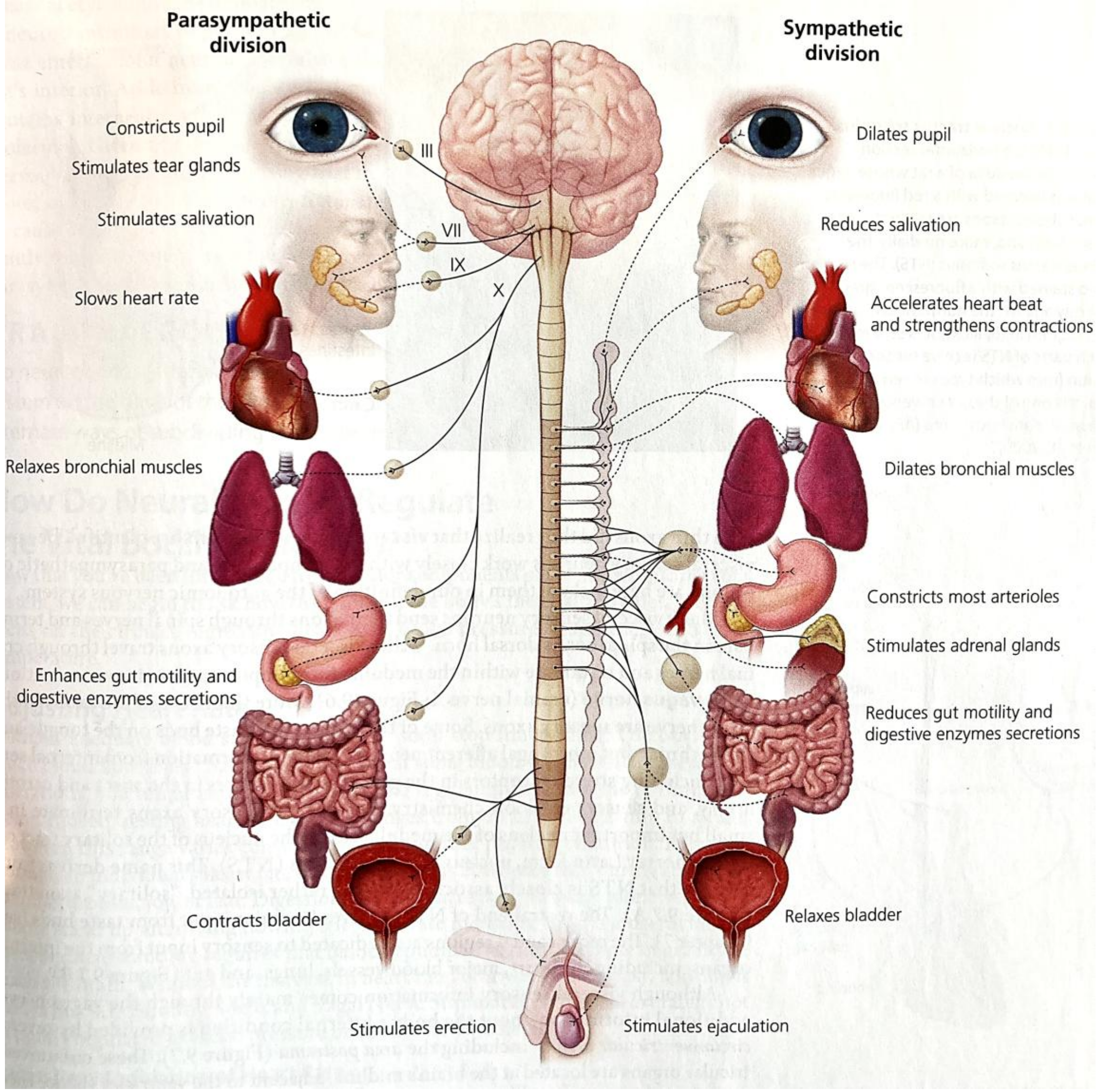
# Outline

- General introduction on the autonomic nervous system
- Genesis of the cardiac rhythm and heart rate derived metrics
- Genesis of the respiratory rhythm and respiratory rate derived metrics
- Cardio-respiratory coupling: Respiratory Heart Rate Variability
- Using cardio-respiratory related metrics to decipher psychological states, is it really possible ?

# General introduction on the autonomic nervous system

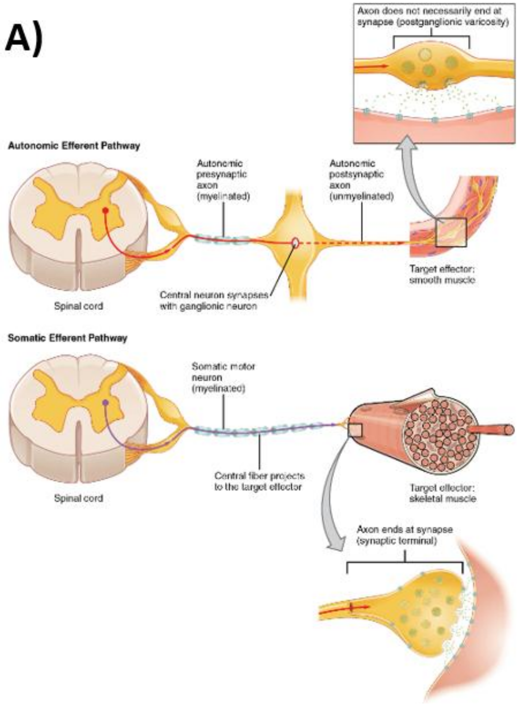


# General introduction on the autonomic nervous system




Striedter, 2016

A)

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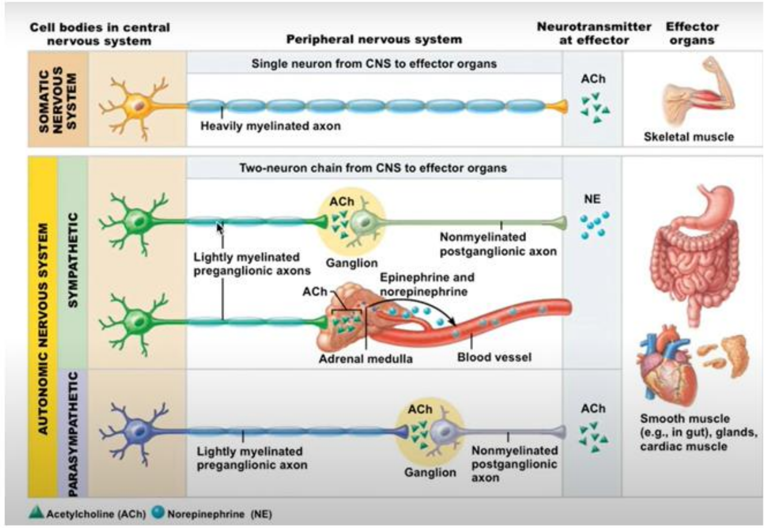
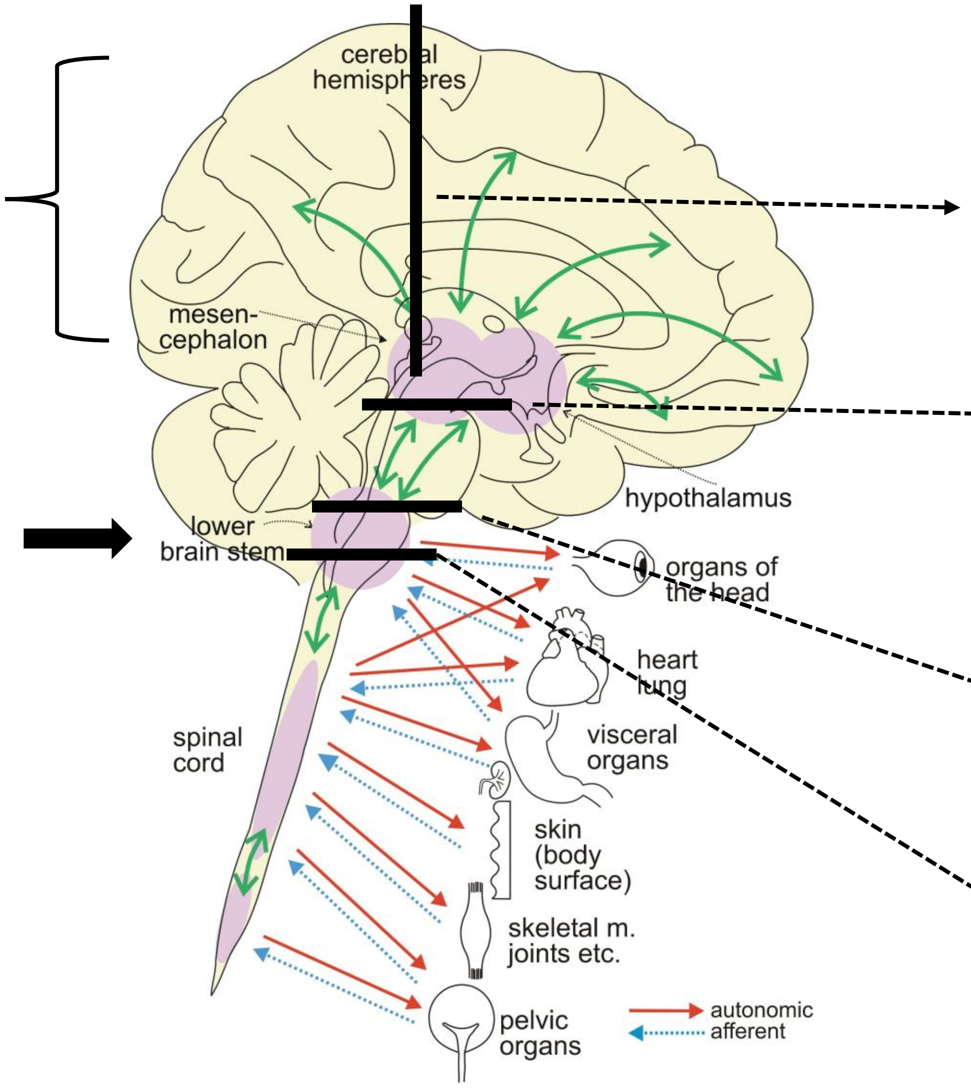



*A) Figure from "Comparison of Somatic and Visceral Reflexes" by OpenStax is licensed under CC BY 3.0 . B) Figure from BIO201 Anatomy & Physiology 1, WyzSci*

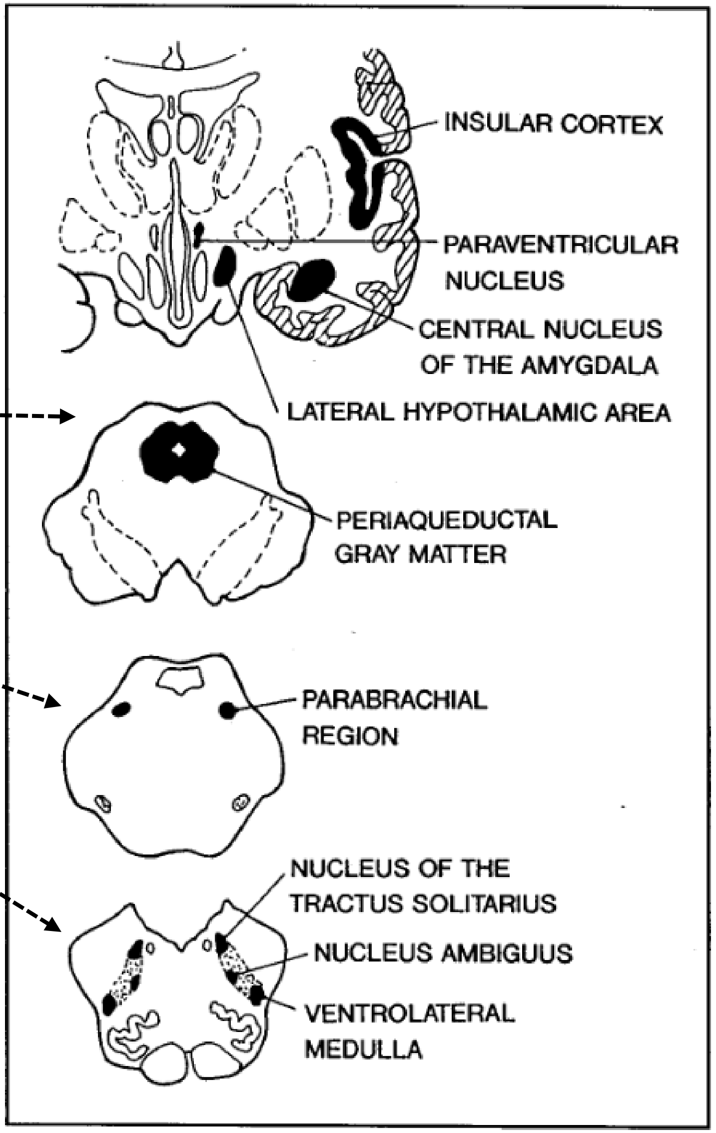
# General introduction on the autonomic nervous system

Telencephalon: a **minor** regulator of ANS

Medulla: The **MAJOR** regulator of ANS

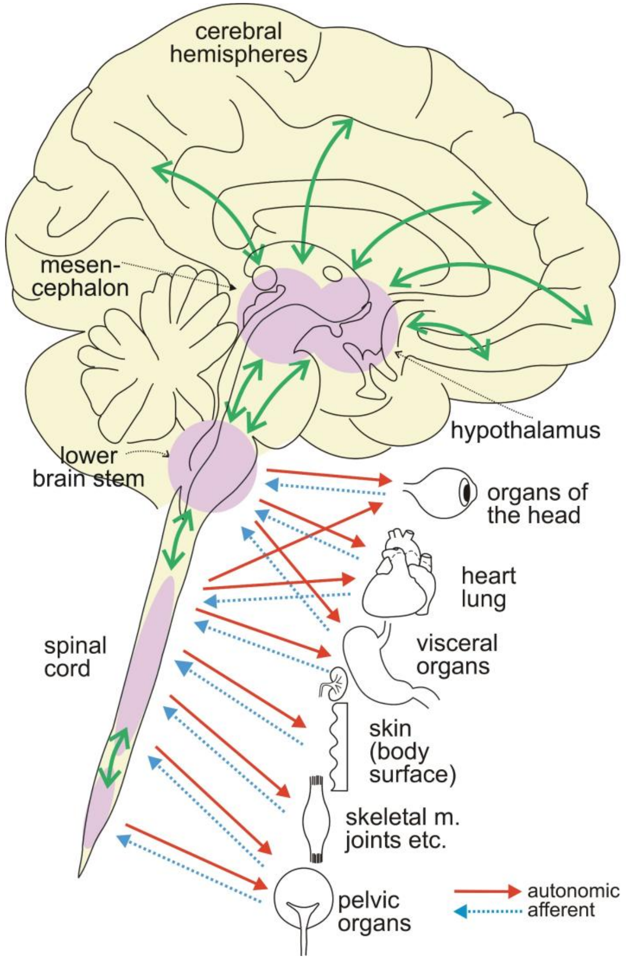


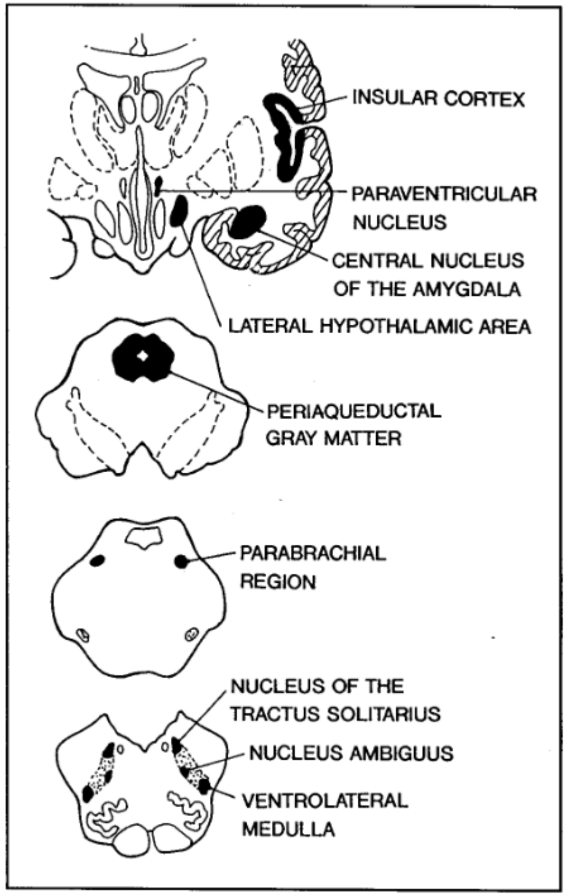

*Ref: https://www.physiologie.uni-kiel.de/en/research/autonomic-nervous-system-and-pain/research-interests*




*Benarroch, 1993*

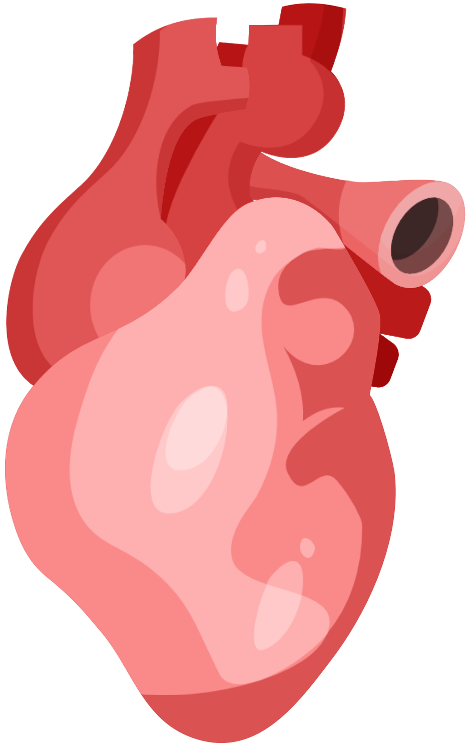
- Warnings about the old school view proposed in textbooks:
  - « Autonomic nervous system described only in peripheral nervous system » → **FALSE**
  - « Autonomic nervous system is only motor » → **FALSE**
    - 80% of autonomic nerves fibers are afferents to the central nervous system (= viscero-sensitive)
    - Organ → Viscero-sensitivity → Nucleus of the tractus solitarius
  - « Respiration is not part of the ANS » → I propose that **FALSE**




*Benarroch, 1993*

# Cardiac physiology



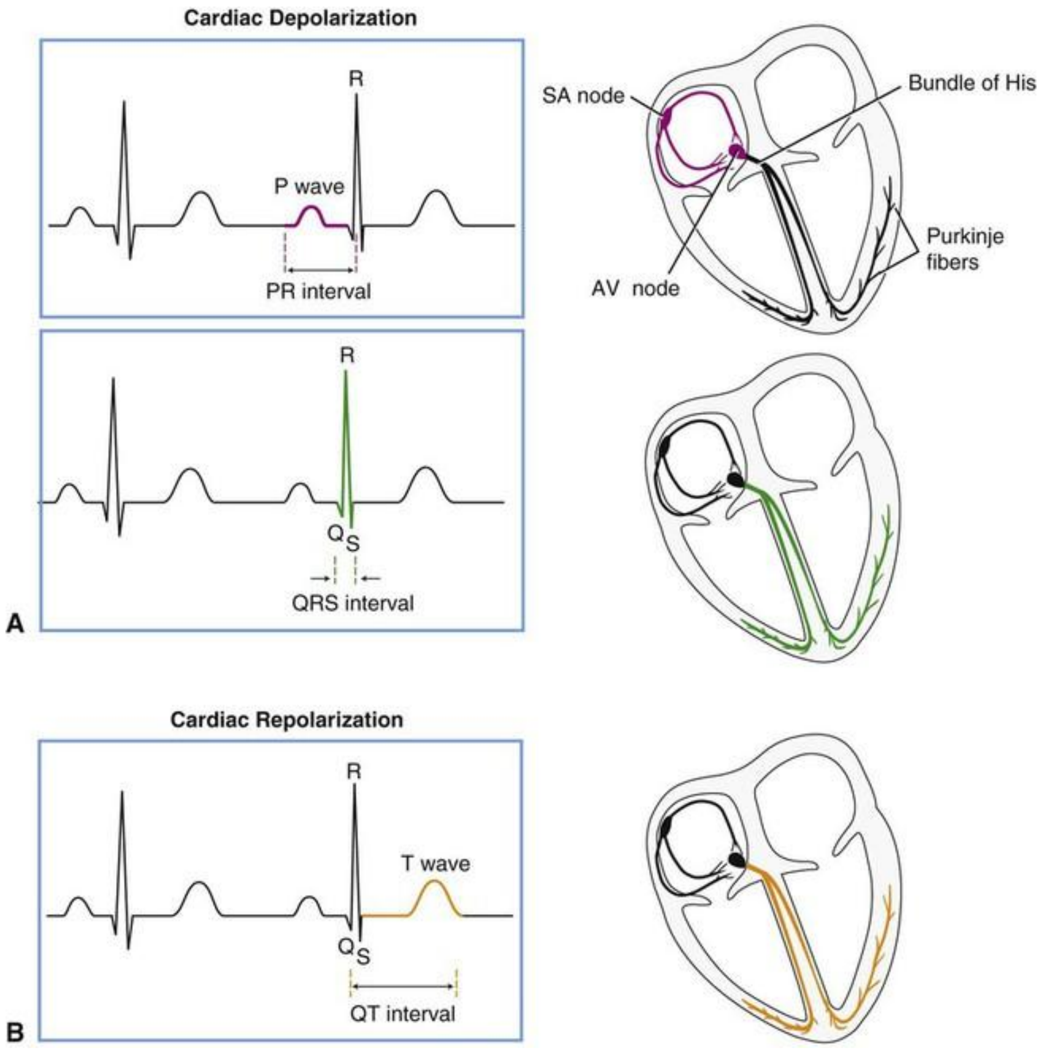
# Cardiac rhythm

- SA Node = Sinoatrial node
  - The pacemaker of the heart
  - Spreading depolarizing wave accross the myocardium through heart conduction system

- PQRST complex = 1 heartbeat
  - P = Atrial activation
  - QRS = Ventricular activation
  - T = Ventricular inactivation
    - atrial inactivation occurs at the same time than QRS

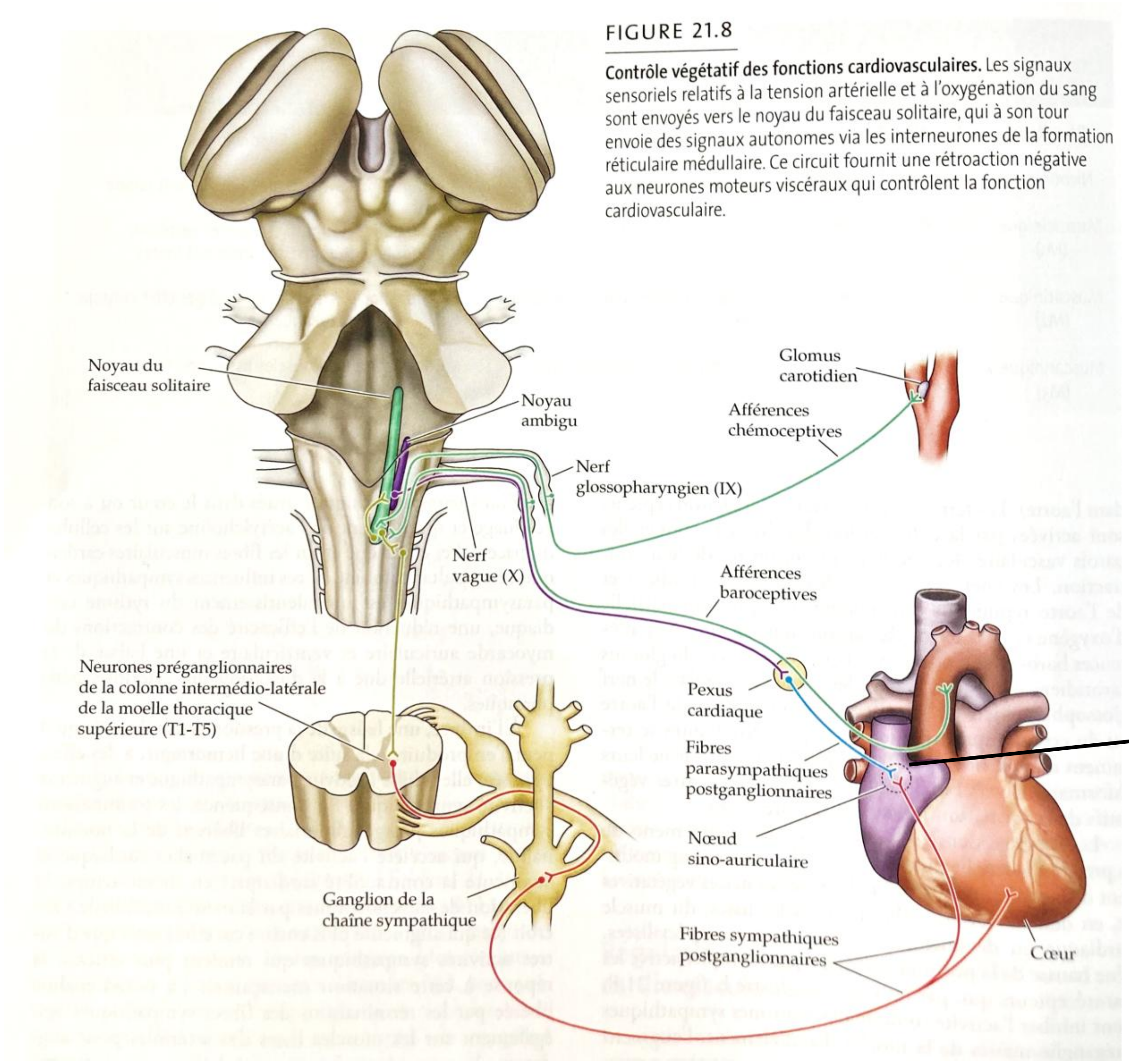
- Has its own rhythm = ~110 bpm

- Under the influence of parasympathetic and sympathetic nerves



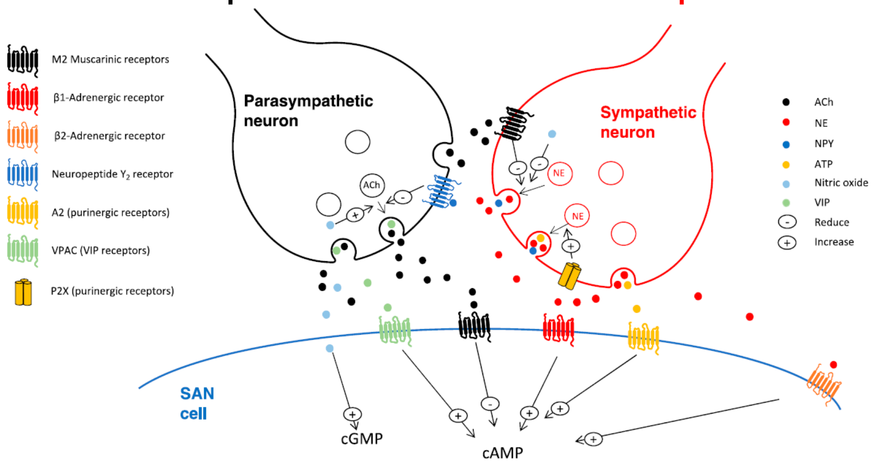

https://thoracickey.com/electrocardiogram-identification/

# Cardiac regulation: sympathetic and parasympathetic



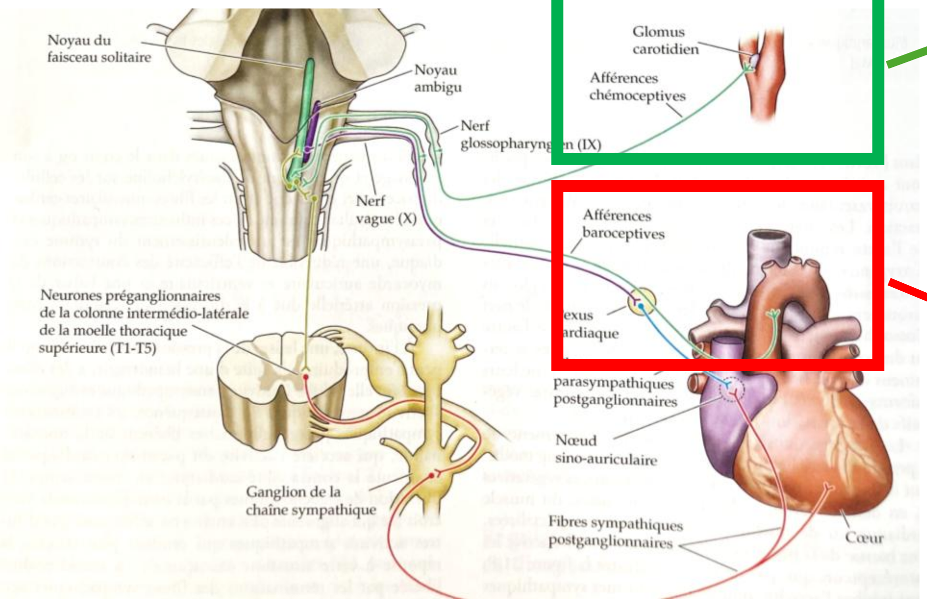

*Purves et al., 2015*

| **VAGUS NERVE (Cranial Nerve n° X)** | **CARDIAC NERVES (From paravertebral sympathetic chain)** |
|---|---|
| <u>Parasympathetic</u><br>• Hyperpolarizing<br>• ~ Inhibition<br>• ~ Lower heart rate | <u>Sympathetic</u><br>• Depolarizing<br>• ~ Excitation<br>• ~ Higher heart rate |




*Fedele & Brand, 2020*

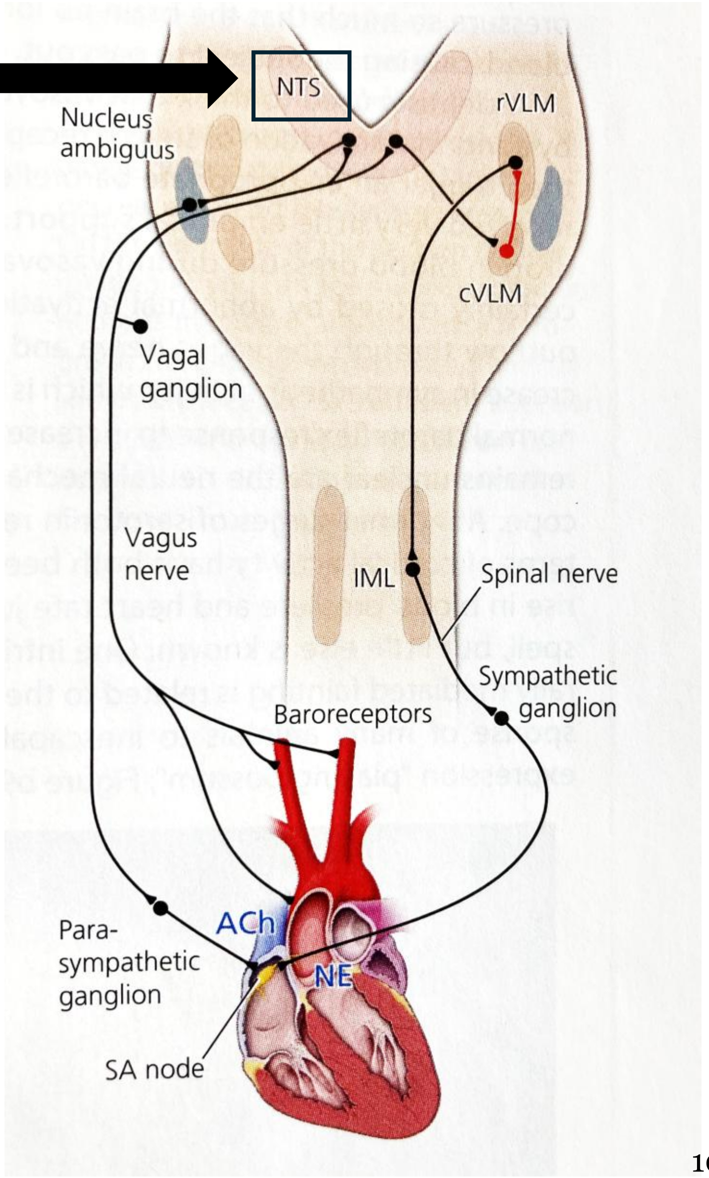
# Cardiac regulation: Brainstem




*Purves et al., 2015*

**BaroReflex**
=
Blood pressure stabilisation
*Ex: I move…*

**ChemoReflex**
=
Gas pressure stabilisation
*Ex: I run…*



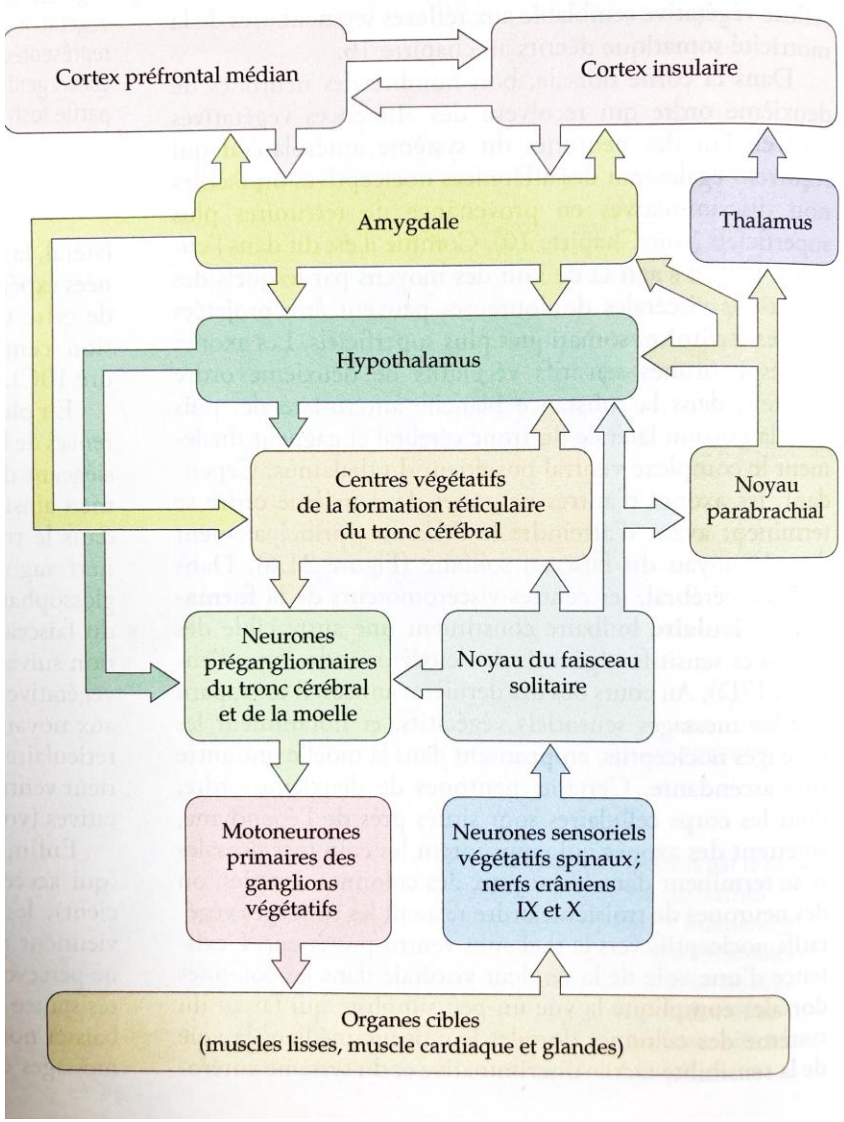

*Striedter, 2016*

**<u>BaroReflex and ChemoReflex = The Two major regulators of the heart rate</u>**

Way before psychological influences…

# Cardiac regulation: Higher center influences → Still highly debated

- Brainstem
  - Baro and Chemo R → « Homeostatic heart » !
- Hypothalamus
  - « Circadian heart » ☺
  - Hormones (hypohyse)
- Amygdala
  - « Emotional heart » ?
- Insular Cortex
  - « Somatosensory integrator heart » ??
- ?
  - « Conscious heart » ???




*Purves et al., 2015*

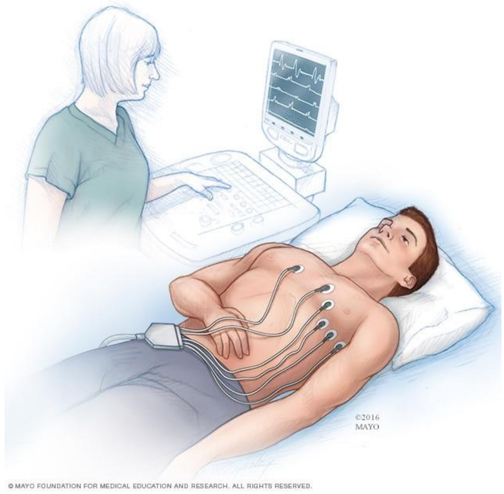
# Measuring cardiac activity and computing heart rate features

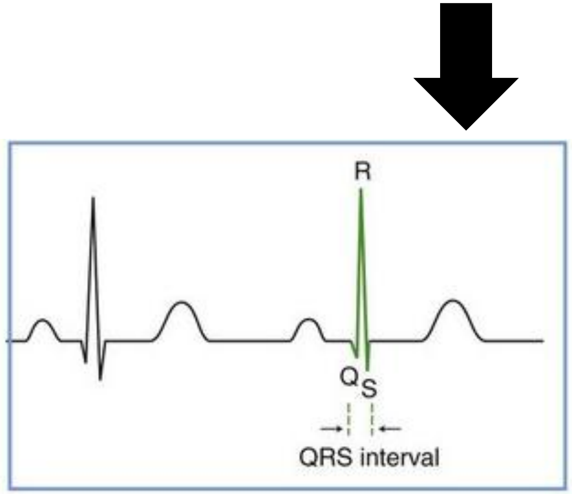
- Electrocardiogram

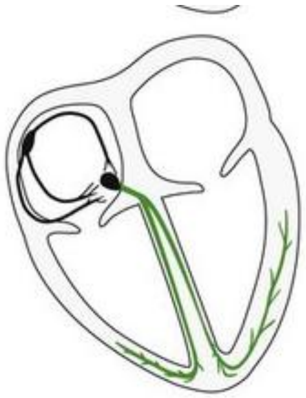
  - Only 3 electrodes is enough…

  - … to get R peak timing = used as a proxy of each heartbeat

  - … if enough sampling rate
    - > 100 Hz for heart rate
    - > 250 Hz for « simple » heart rate variability
    - > 1000 Hz for « more precise » heart rate variability

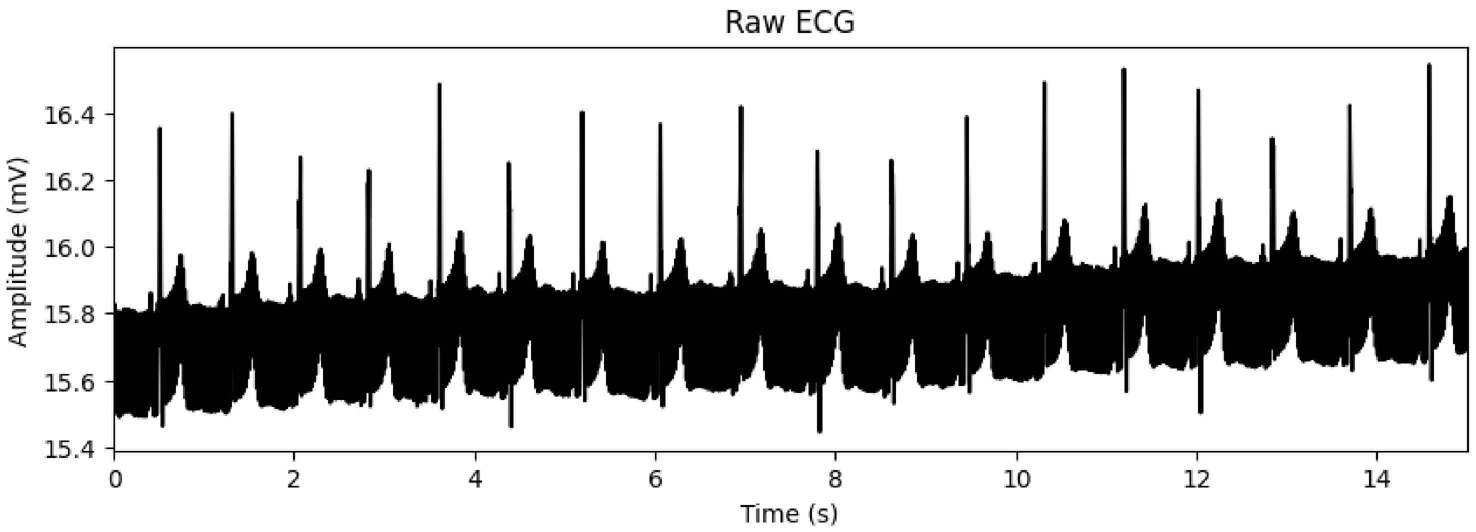


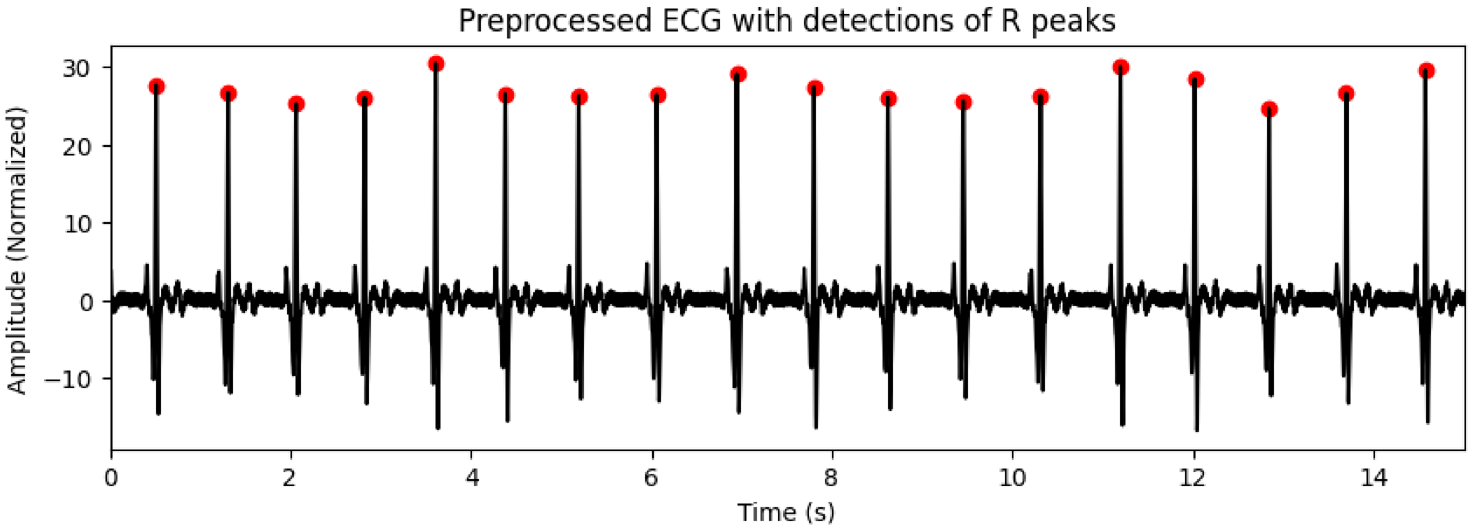



# Measuring cardiac activity and computing heart rate features

- From raw ECG …




- To R peaks detected



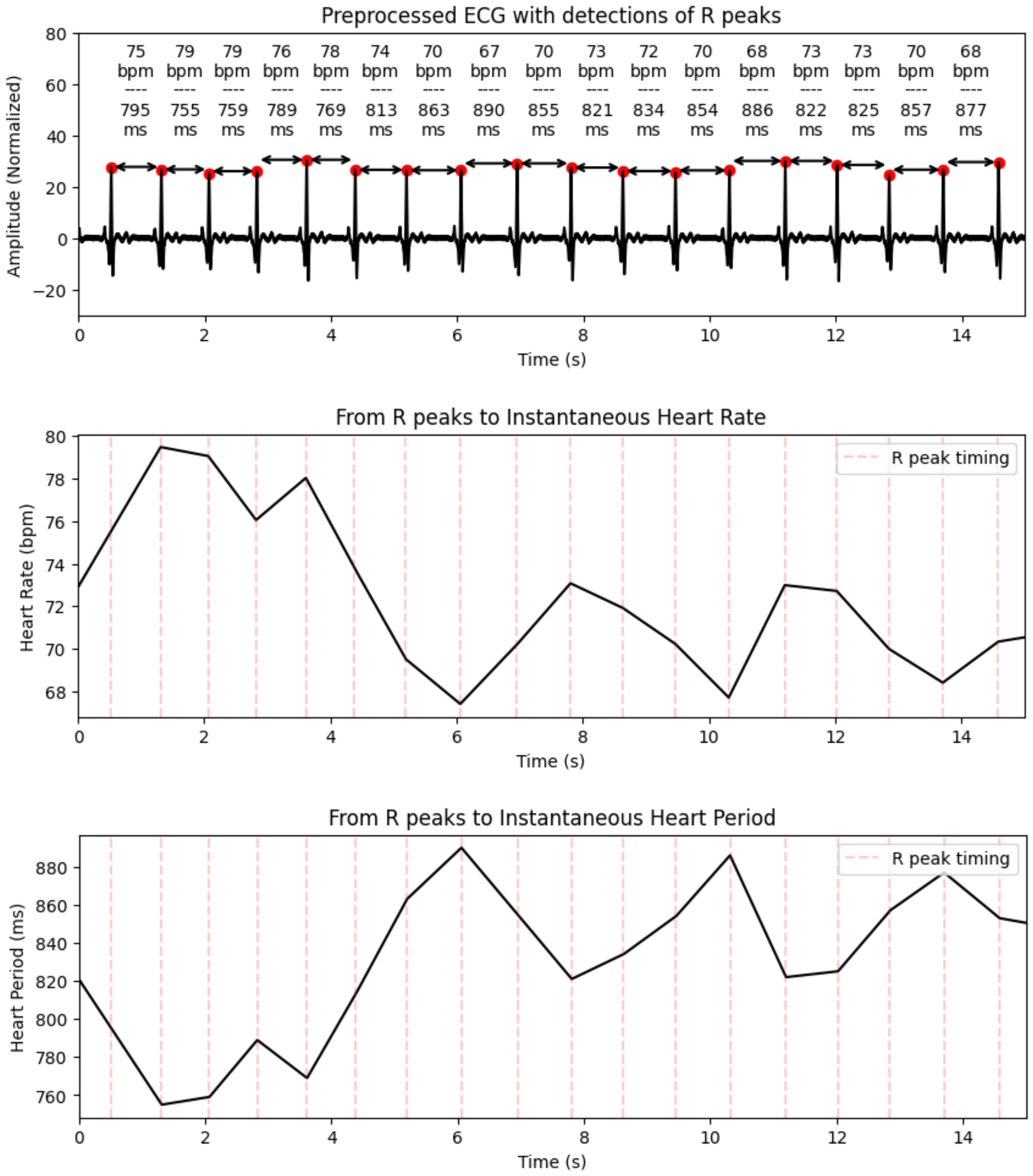
# Measuring cardiac activity and computing heart rate features

- From R peaks …

- … to Heart Rate / Heart Period

  - R to R interval (RRi) = Heart period (s or ms)

  - 60 / RRi (s) = Heart Rate (bpm)

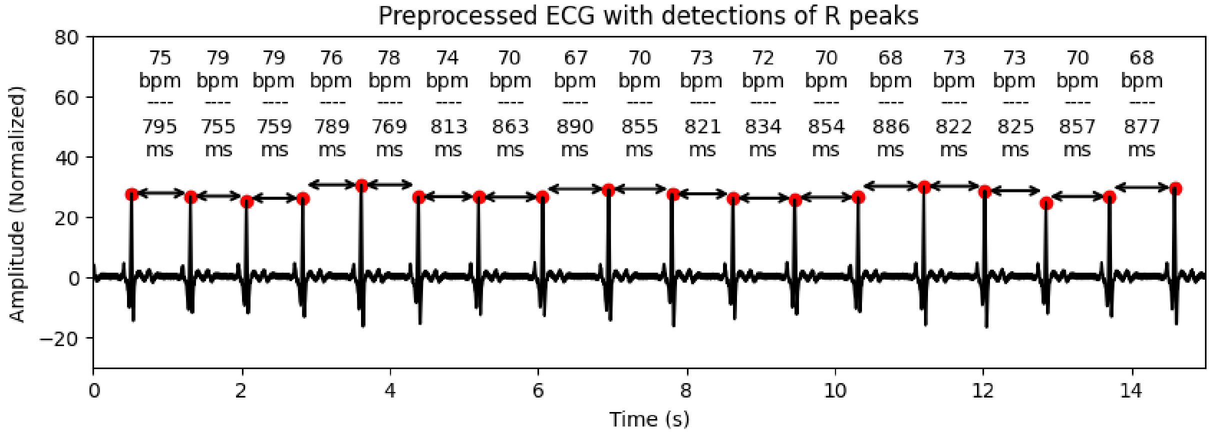


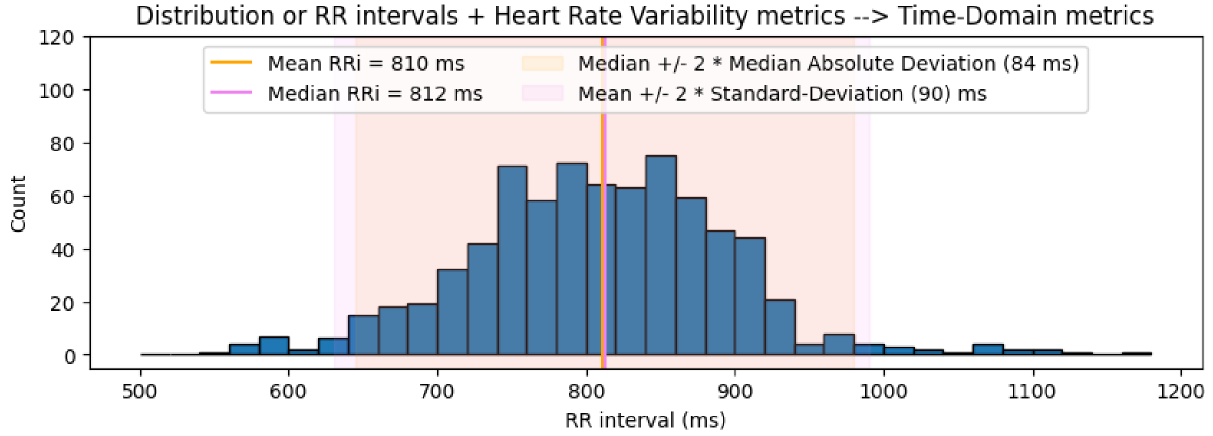
# Measuring cardiac activity and computing heart rate features

- From RR intervals to time-domain metrics

  - Mean / Median RRi → Statistical position of the distribution ~ Heart Rate

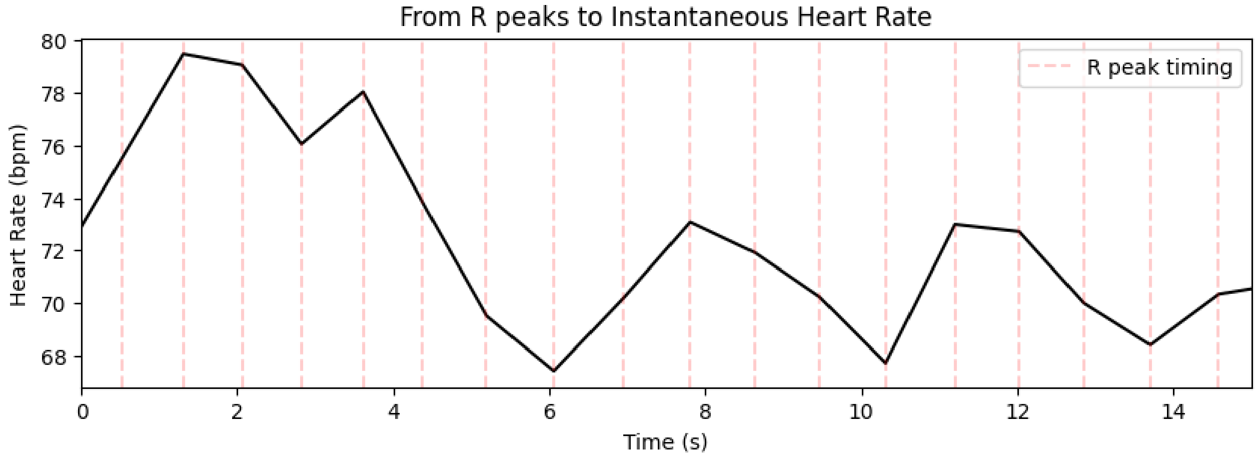
  - SD / MAD RRi → Statistical dispersion of the distribution ~ Heart Rate Variability

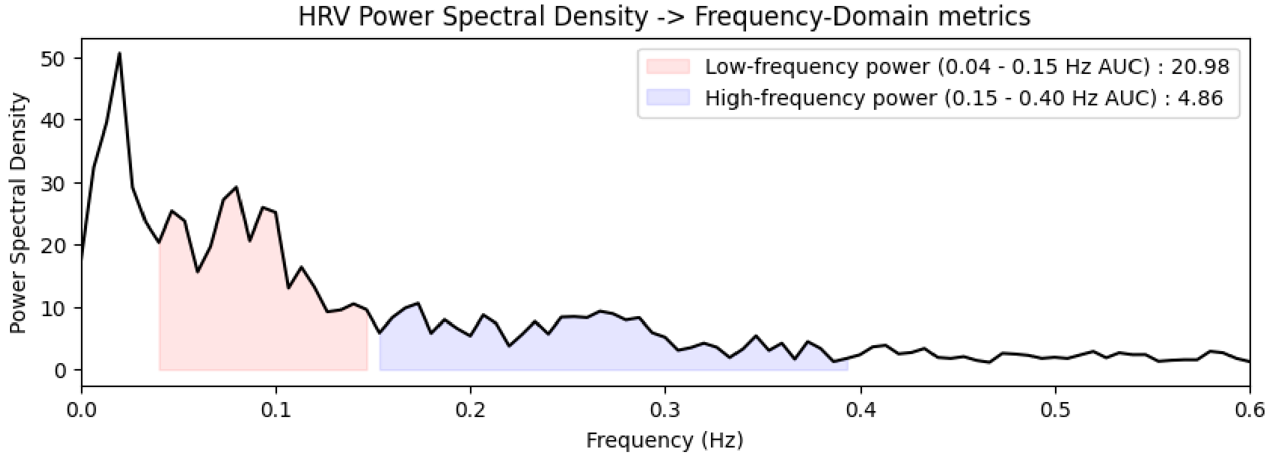


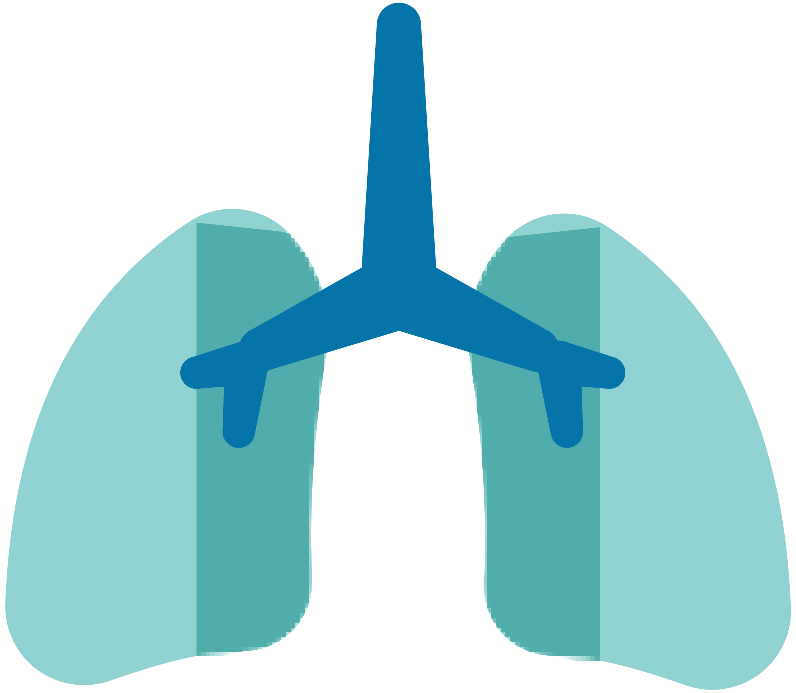
# Measuring cardiac activity and computing heart rate features

- From instantaneous heart rate to frequency-domain metrics
  - Fourier Transform needs regular sampling → interpolation step
  - Power in some frequency bands, ex:
    - LF (low-frequency) : 0.04 to 0.15 Hz
    - HF (high-frequency) : 0.15 to 0.40 Hz
- Warnings :
  - Need enough recording duration
  - HF and LF highly depends on respiratory frequency



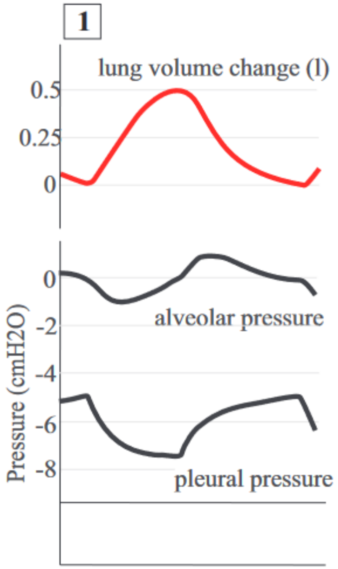



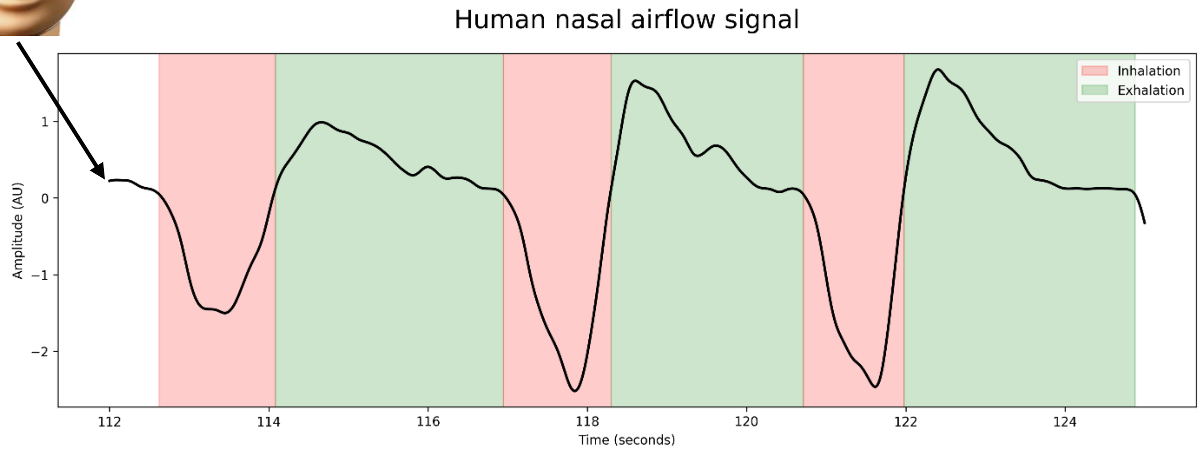
# Respiratory physiology

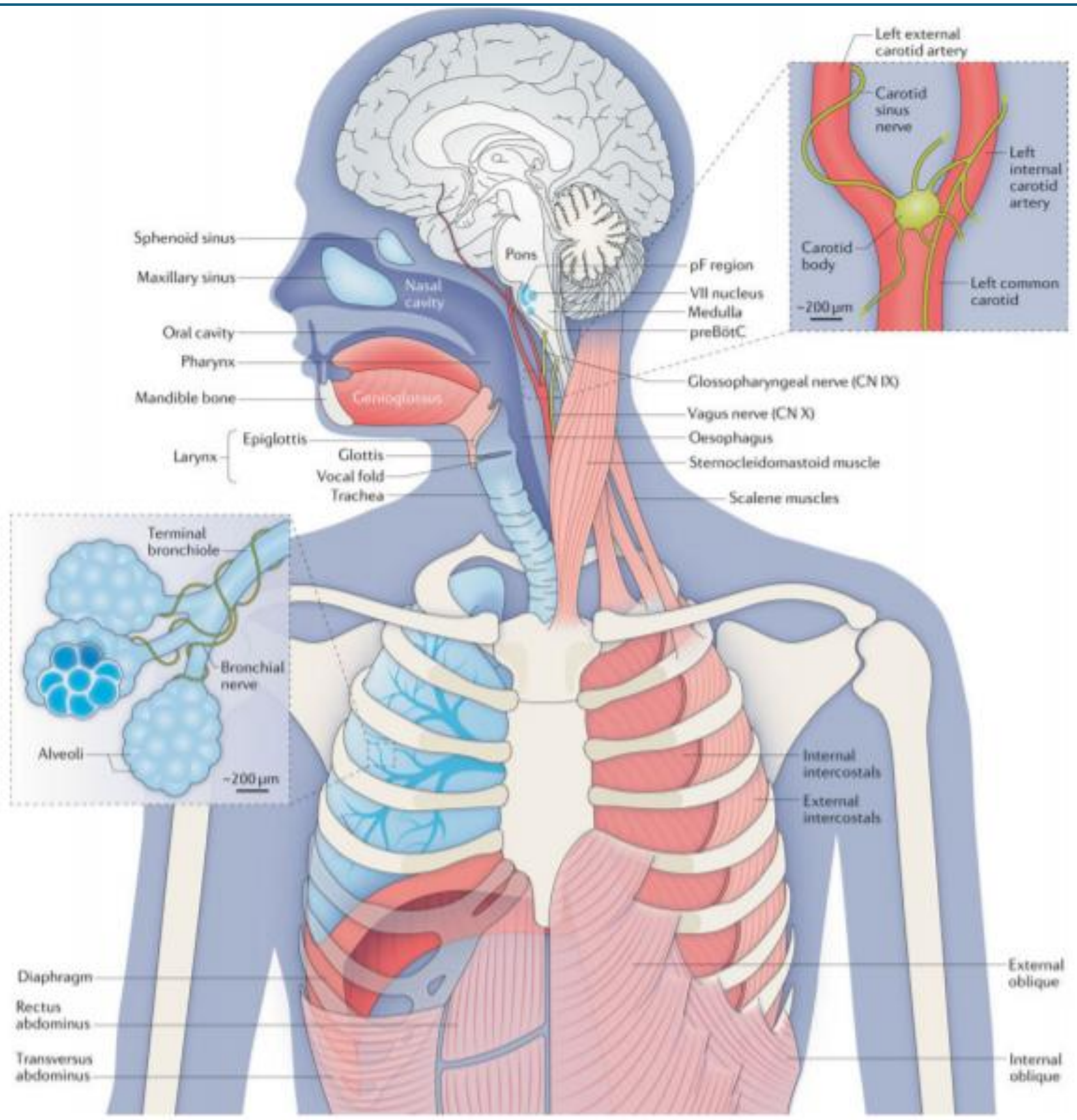


# Respiratory rhythm

- Respiratory system
  - Airways
    - Superior
    - Middle
    - Inferior
  - Muscles (+ bones)
    - **Diaphragm**
    - Intercostal
    - Neck
  - Neurons
    - Somatic → Thorax muscles
    - Autonomic → Bronchis



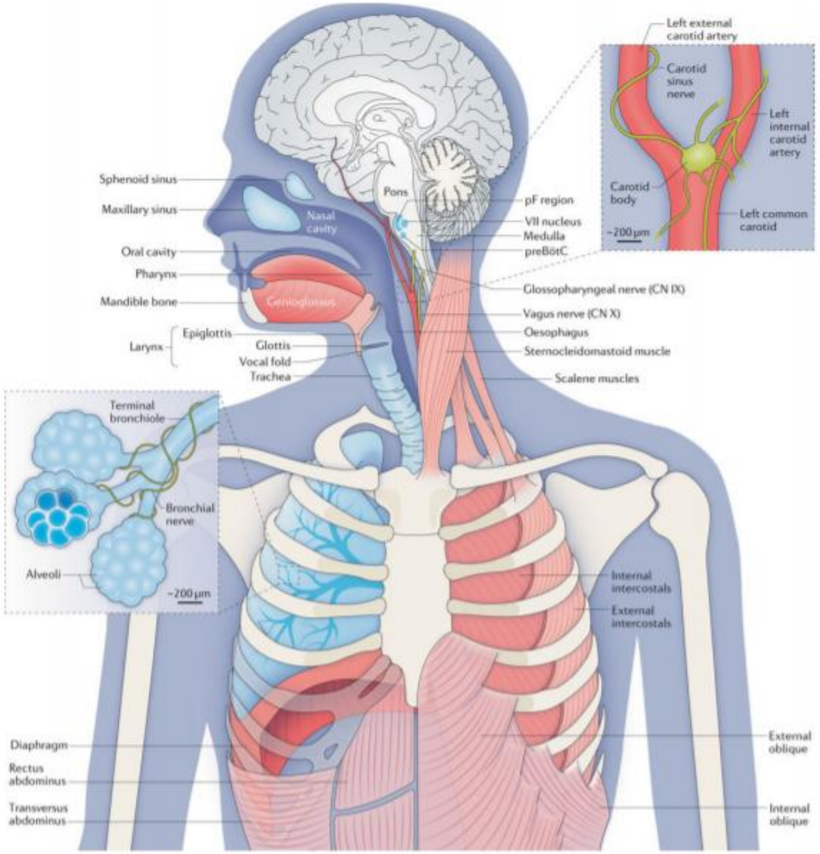

*Del Negro et al., 2018*

# Respiration: Neural command

- **Automatic command**

- Target = Smooth muscles
  - Bronchis

- Nerves = Viscero- motor and sensitive
  - Parasympathetic = Vagal nerve (X)
  - Sympathetic = from paravertebral chain




*Del Negro et al., 2018*

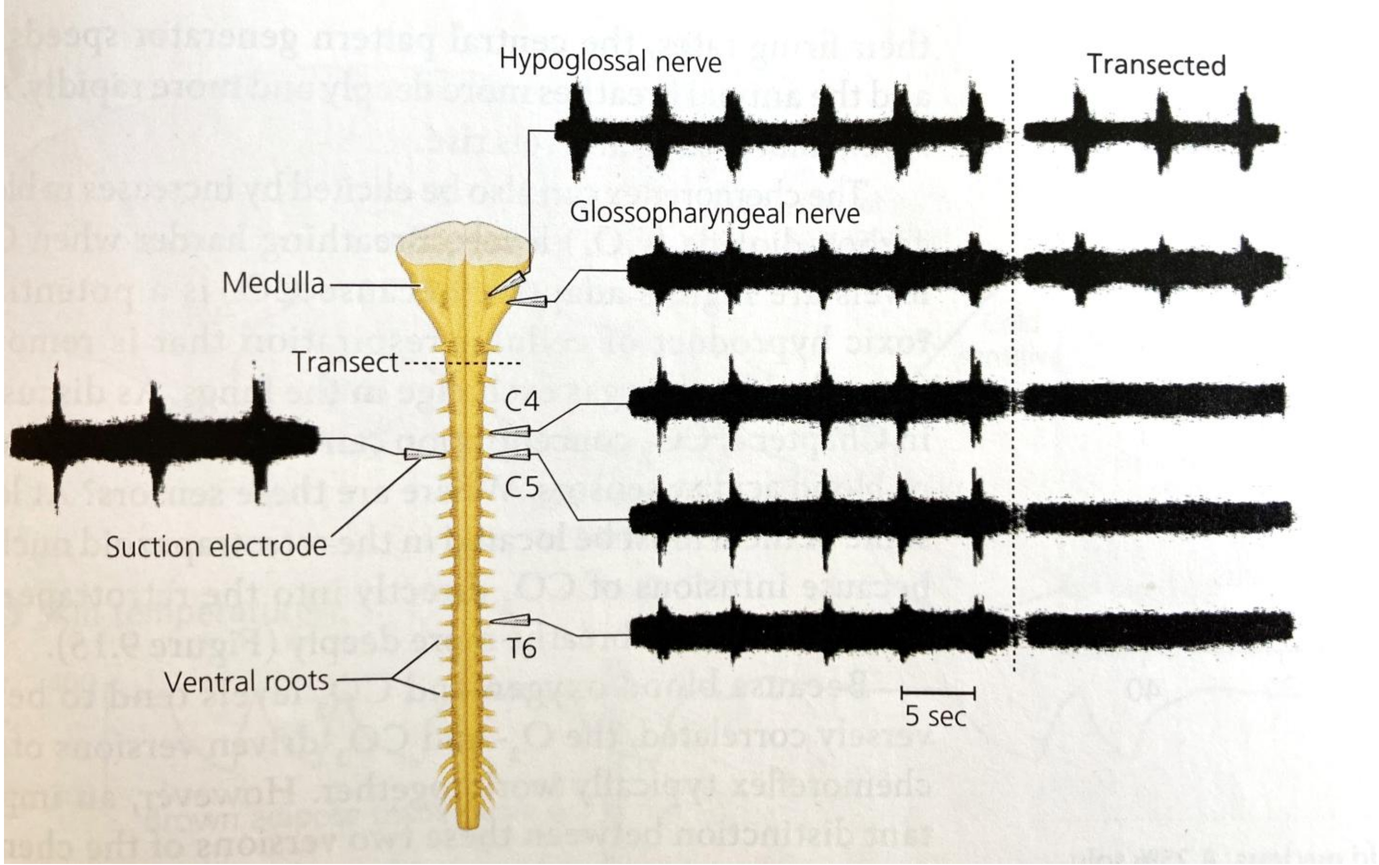
- **Semi-automatic command**
  - Automatically regulated by brainstem
  - But can be volitionally controlled in some species

- Target = Striated muscles
  - Diaphragm + Intercostal + Neck / Mouth

- Nerves = Somato-motors
  - Phrenic nerve
    - diaphgram
  - Intercostal nerves
    - intercostal muscles
  - Cranial nerves (IX, X, XII, XII)
    - Neck and mouth muscles

# Respiration: Spinal command

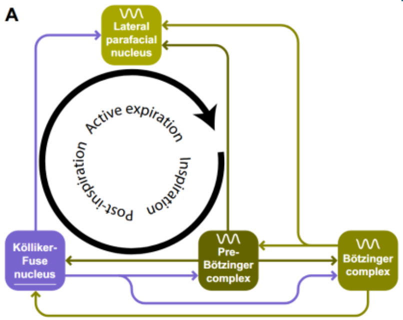
- Semi-automatic
  - Phrenic nerve
    - C3-C4-C5 myelomeres
  - Intercostal nerves
    - T1 to T12



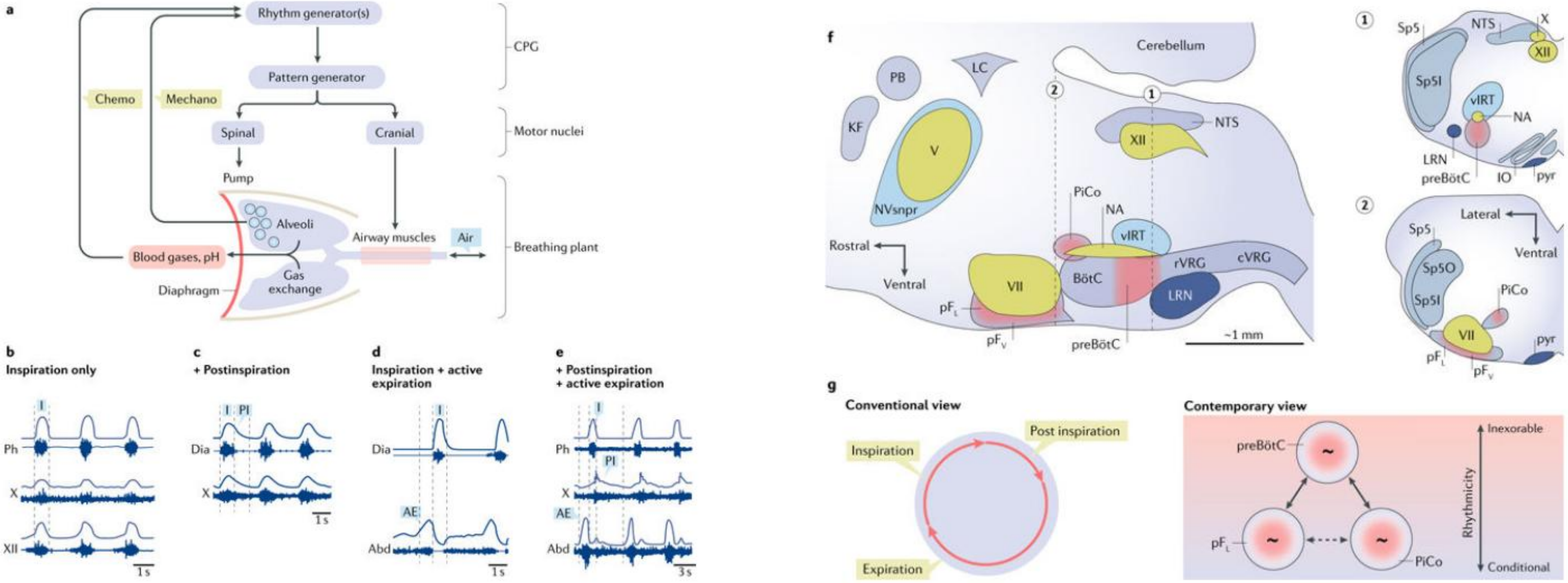

*Striedter, 2016*

# Respiration: Brainstem regulation

- ChemoReflex (cf Heart) + MechanoReflex (Stretch R)
  - NTS → **PreBötzinger Complex**




*Krohn et al., 2023*

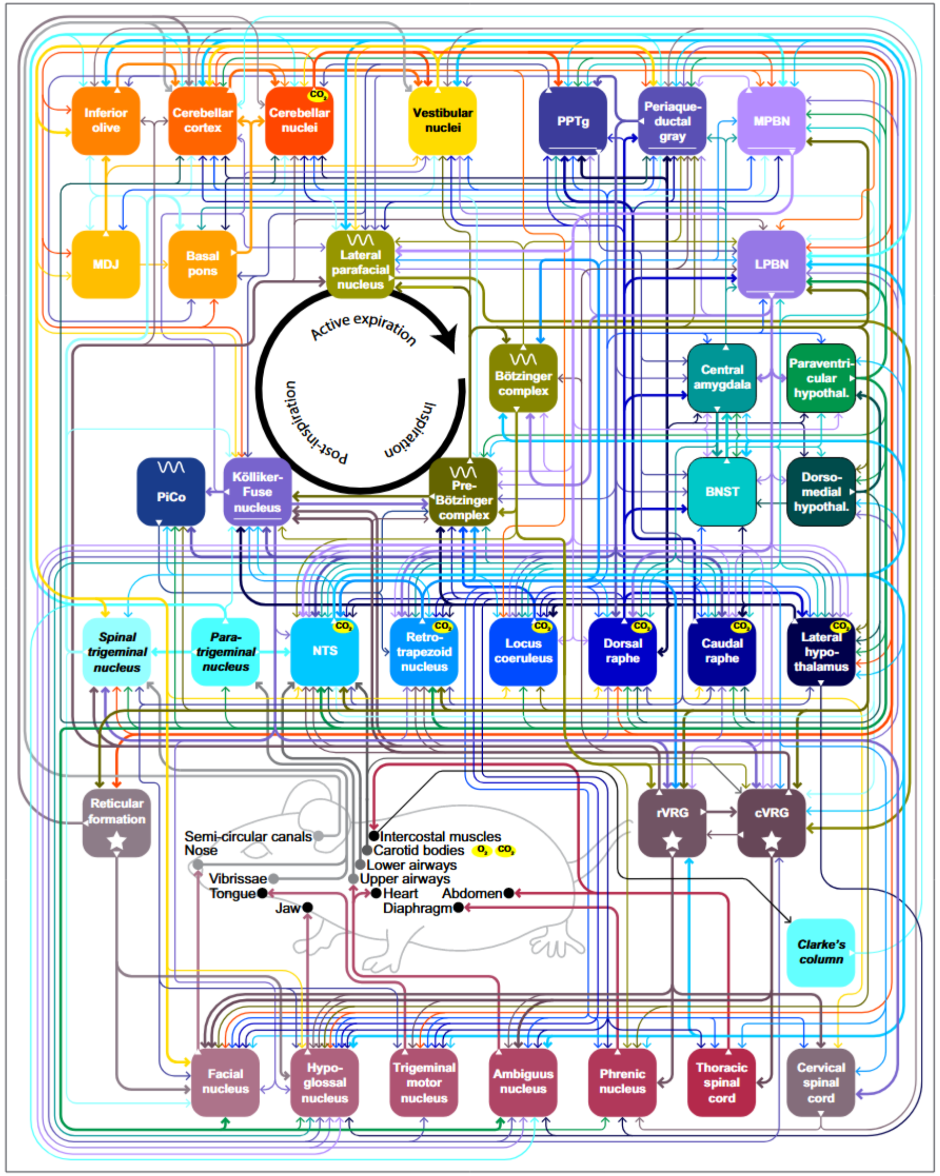


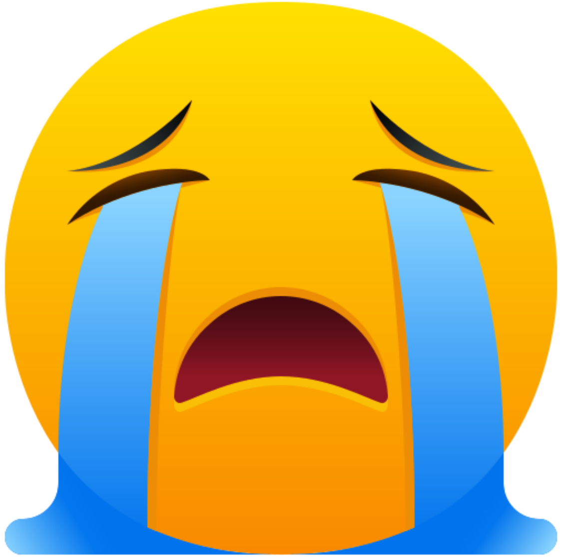



*Del Negro et al., 2018*

# Respiration: Higher centers influences

*Krohn et al., 2023*



# Respiration: Higher centers influences on CPG Respi

- **(Pre)motor frontal cortex**
  - **Vocalizations**
- Amygdala
  - « Emotional breathing »
- ?
  - « Cognitive breathing »

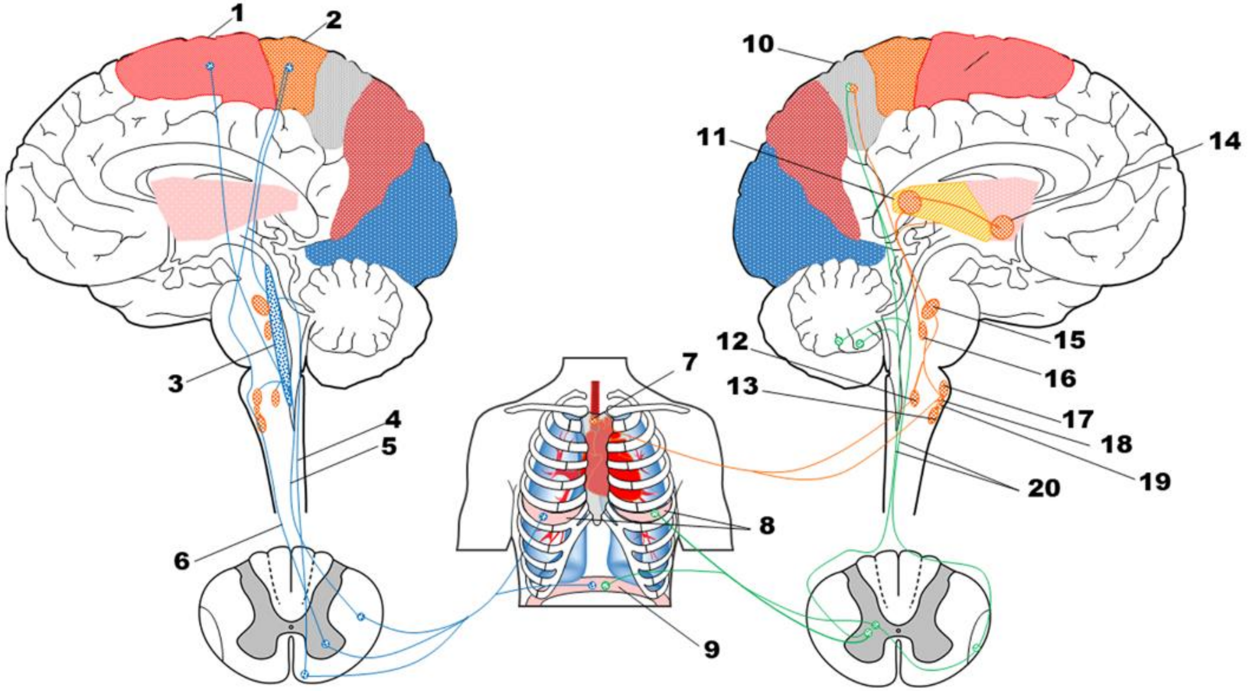
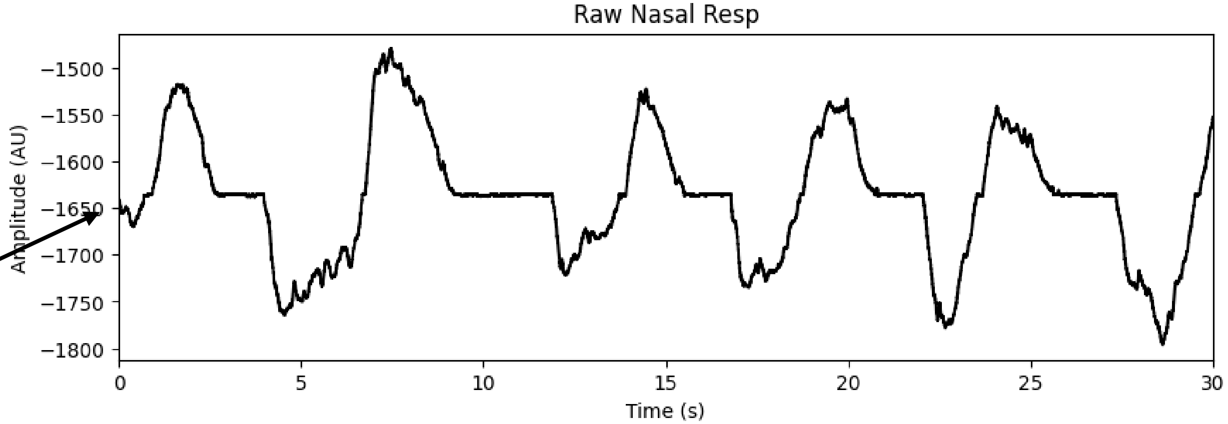


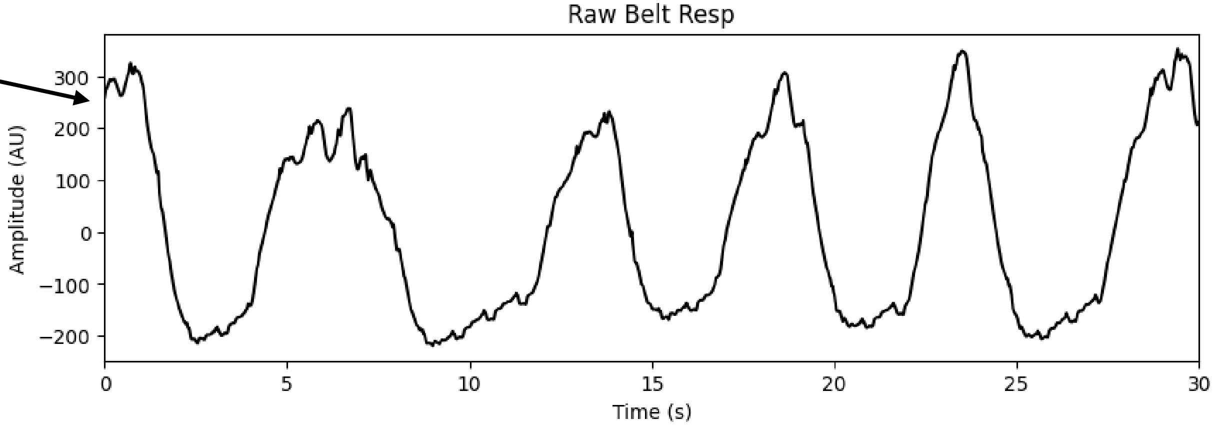

**Fig. 1.** Schematic representation of the efferent (left) and afferent (right) breathing pathways. 1 = Supplementary motor area; 2 = Motor cortex (M1); 3 = Reticular formation; 4 = medial reticular tract; 5 = Dorsal reticulospinal tract; 6 = Lateral corticospinal tract; 7 = Peripherical chemoreceptors; 8 = Intercostal muscles; 9 = diaphragm; 10 = Primary somatosensory cortex (S1); 11 = Posterior insula; 12 = Dorsal Respiratory Group; 13 = Ventral Respiratory Group; 14 = Anterior insula; 15 = Parabrachial/Kölliker-Fuse complex (Pneumotaxic center); 16 = Apneustic center; 17 = the parafacial respiratory group/retrotrapezoid nucleus; 18 = pre-Bötzinger complex; 19 = Bötzinger complex; 20 = ventral and dorsal spinocerebellar tracts.

*Betka et al., 2022*

# Measuring respiratory activity

- Various strategies
  - Nose
    - Pressure sensor / Airflow
    - Thermic sensor
  - Thorax / Belly
    - Diameter sensor
      - Mechanical
      - Piezo-electric sensor
  - Plethysmography
  - Others…

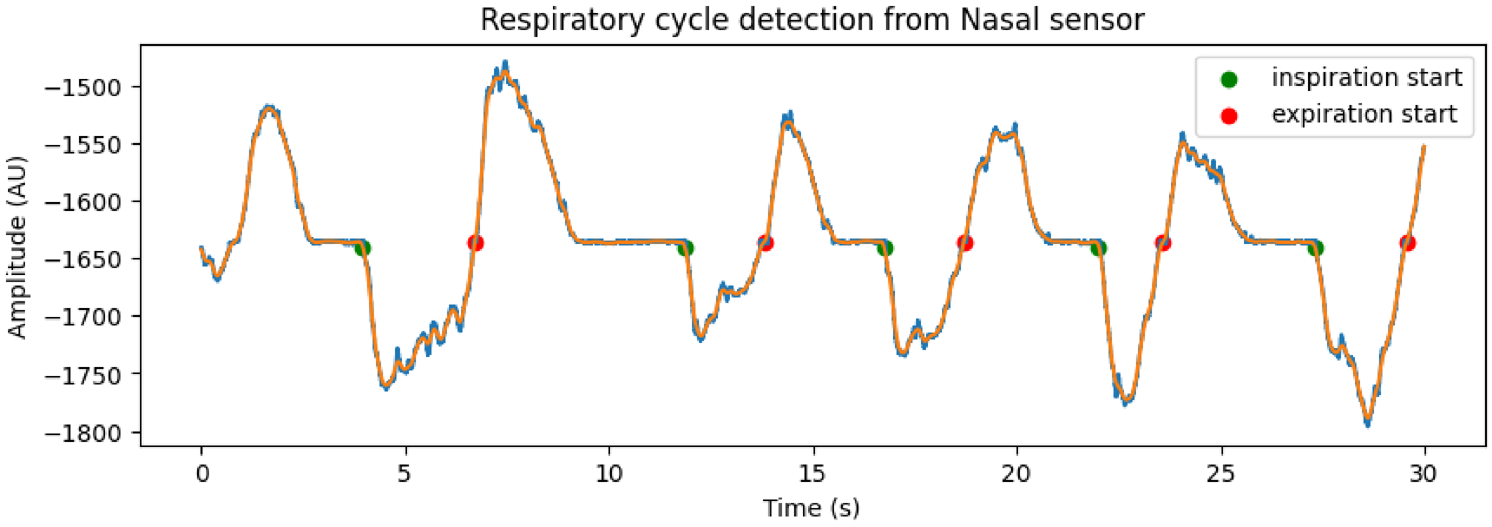


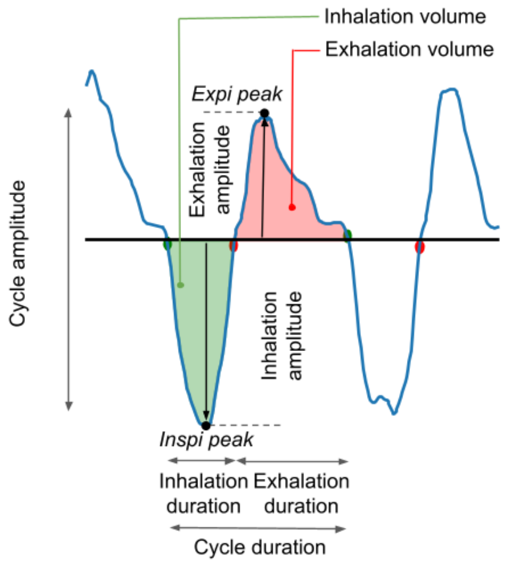



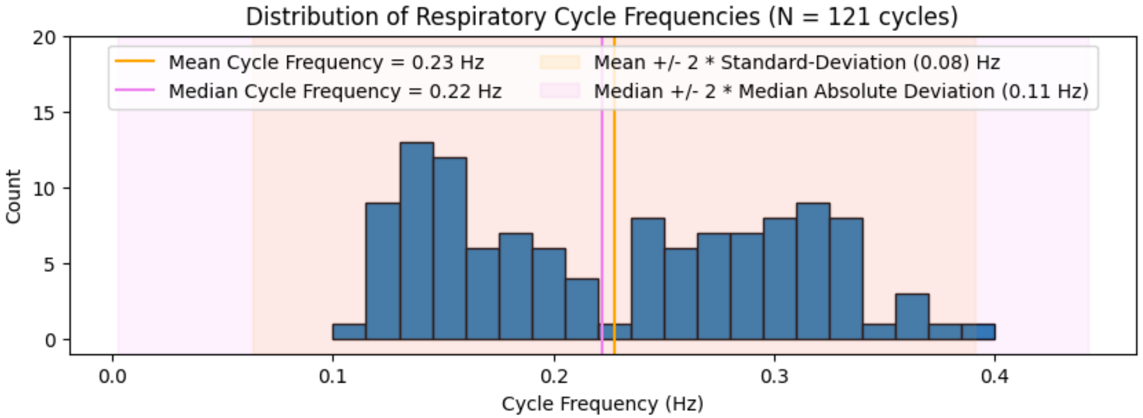

**Warning: Quality of Belt (thorax / belly) recordings highly depends on morphology of participants… sometimes unusable !**

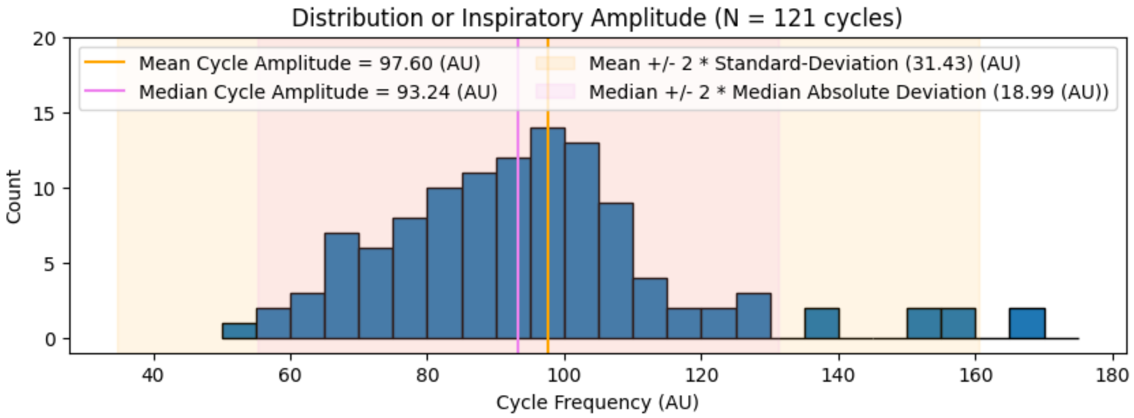
# Detecting respiratory cycles and computing features on each cycle

- Good quality signal = signal on which inspi-expi / expi-inspi transitions are clearly appearing

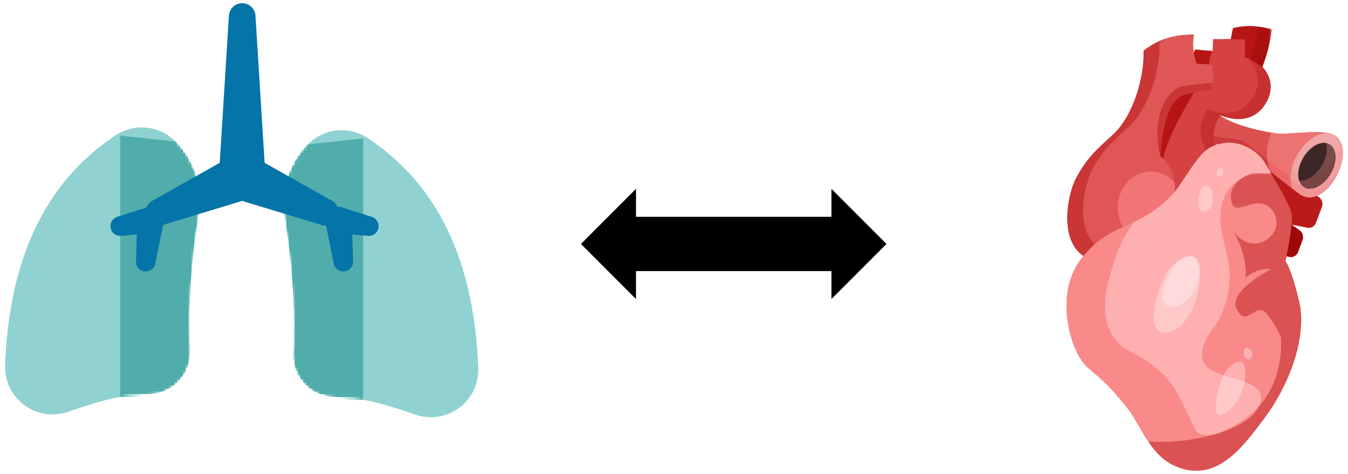


# Cardio-respiratory coupling: Respiratory Heart Rate Variability



# Respiratory Heart Rate Variability

- Respiratory Heart Rate Variability = RespHRV

- Recently renamed from Respiratory Sinus Arrhythmia = RSA

nature reviews cardiology https://doi.org/10.1038/s41569-025-01160-z



Expert recommendation

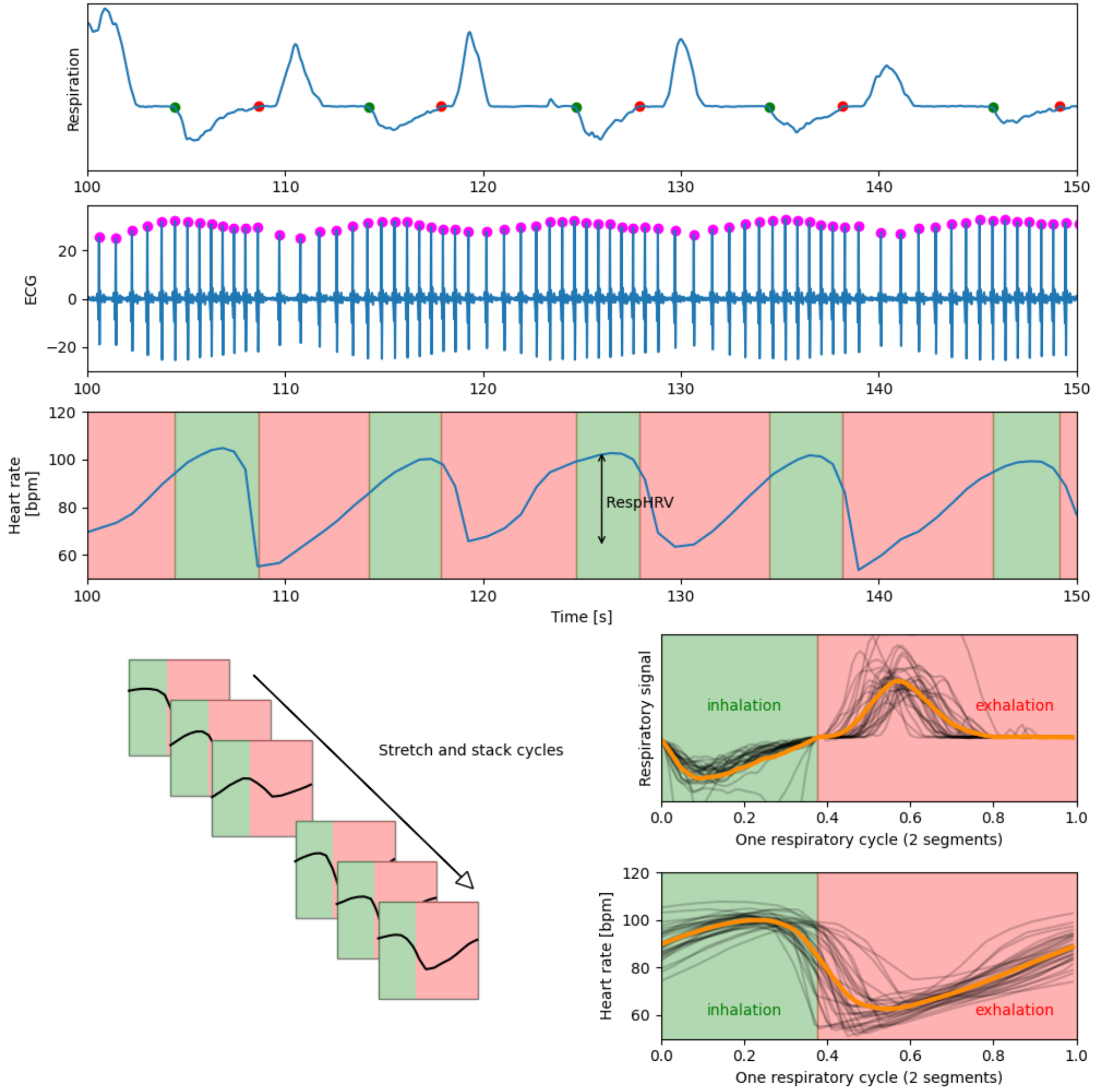
Check for updates

## Redefining respiratory sinus arrhythmia as respiratory heart rate variability: an international Expert Recommendation for terminological clarity

Clément Menuet[1], Alona Ben-Tal[2,3], Ambre Linossier[1], Andrew M. Allen[4], Benedito H. Machado[5], Davi J. A. Moraes[6], David G. S. Farmer[7], David J. Paterson[8], David Mendelowitz[9], Edward G. Lakatta[10], Edwin W. Taylor[11], Gareth L. Ackland[12], Irving H. Zucker[13], James P. Fisher[3], James S. Schwaber[14], Julia Shanks[3], Julian F. R. Paton[3], Julie Buron[15], K. Michael Spyer[16], Kalyanam Shivkumar[17], Mathias Dutschmann[18,19], Michael J. Joyner[20], Neil Herring[8], Paul Grossman[21], Robin M. McAllen[22], Rohit Ramchandra[3], Song T. Yao[4], Thomas Ritz[23] & Alexander V. Gourine[16]

# RespHRV: Our heart rate depends on respiration

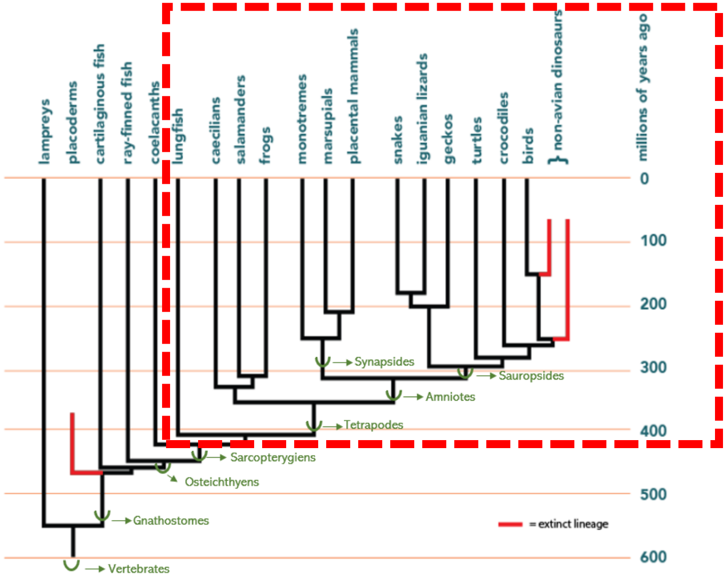
- Heart rate increases during inspiration
- Heart rate decreases during expiration



# When RespHRV has evolved ?

- In the first air-breathing vertebrates

*Lungfish (Dipneuste)*




***RespHRV***
***=***
***Air-breathing vertebrates***

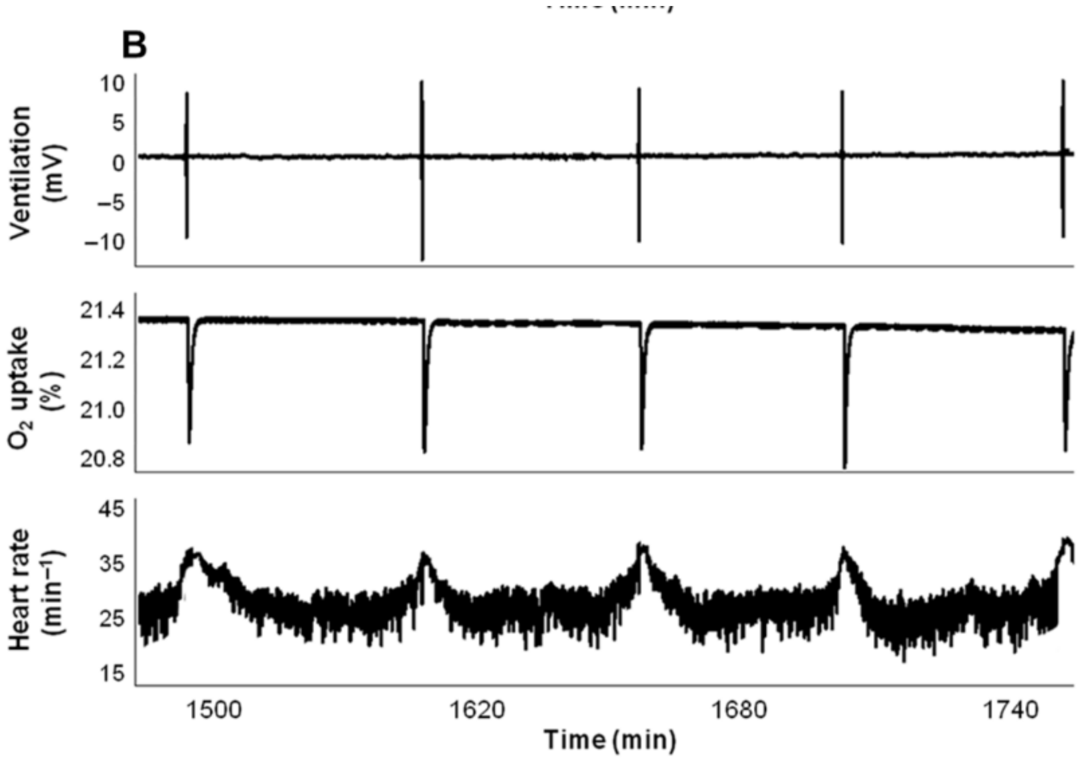
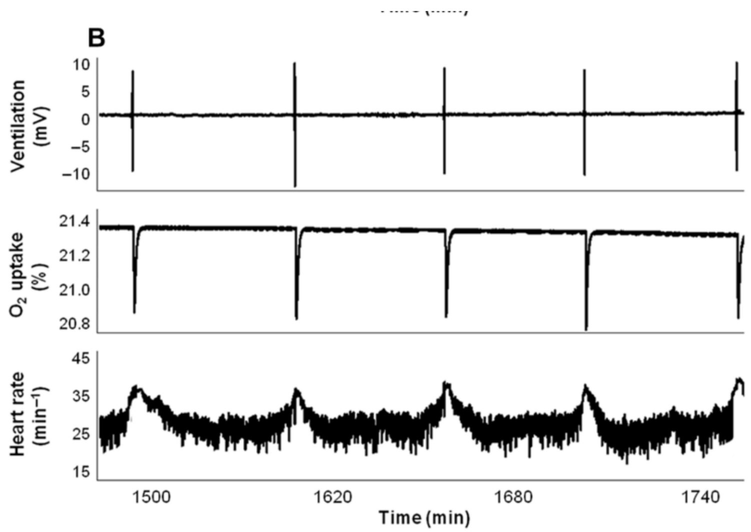



**Fig. 1. Cardiorespiratory and metabolic recordings from a lungfish, *L. paradoxa*, at 25°C.** Recordings of ventilation [recorded as surfacing events (mV)], oxygen uptake (measured as changes in $\%O_2$), and heart rate ($min^{-1}$) during consecutive air-breathing cycles in a single lungfish (220 g). Recordings from 1 to 4 hours after surgery (**A**) and in the recovered, undisturbed animal 24 hours after instrumentation (**B**).

*Monteiro et al., 2018*

# Why RespHRV ?

- Several theories
- The main :
  - Saving energy while optimizing gaz exchange
    - = Heartbeats mainly during maximal inflation

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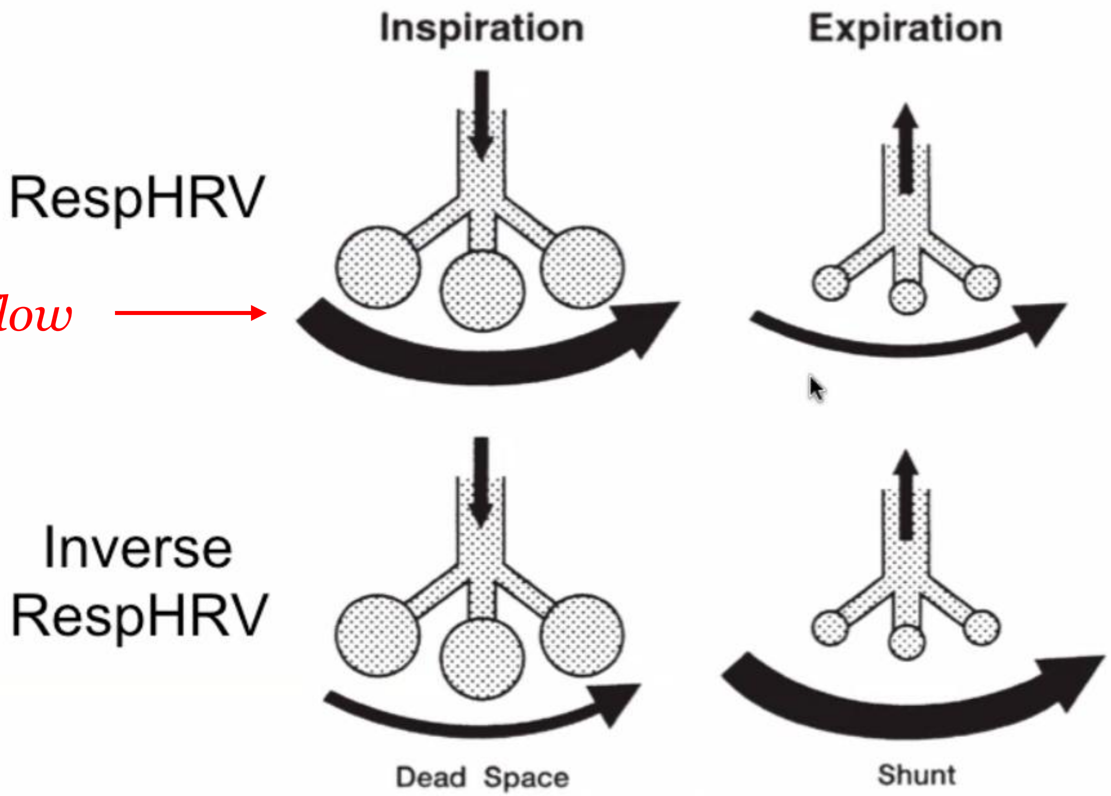
*Monteiro et al., 2025*

*Blood flow*




*Hayano et al., 1996*

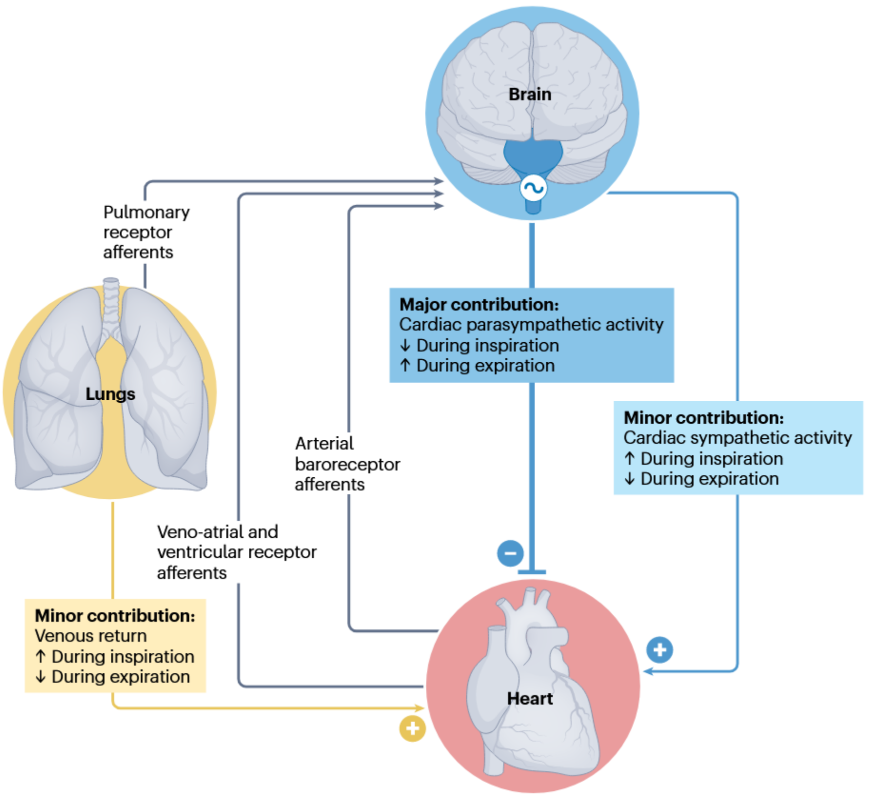
# How RespHRV is generated ?

- Main contributor = PreBötzinger !

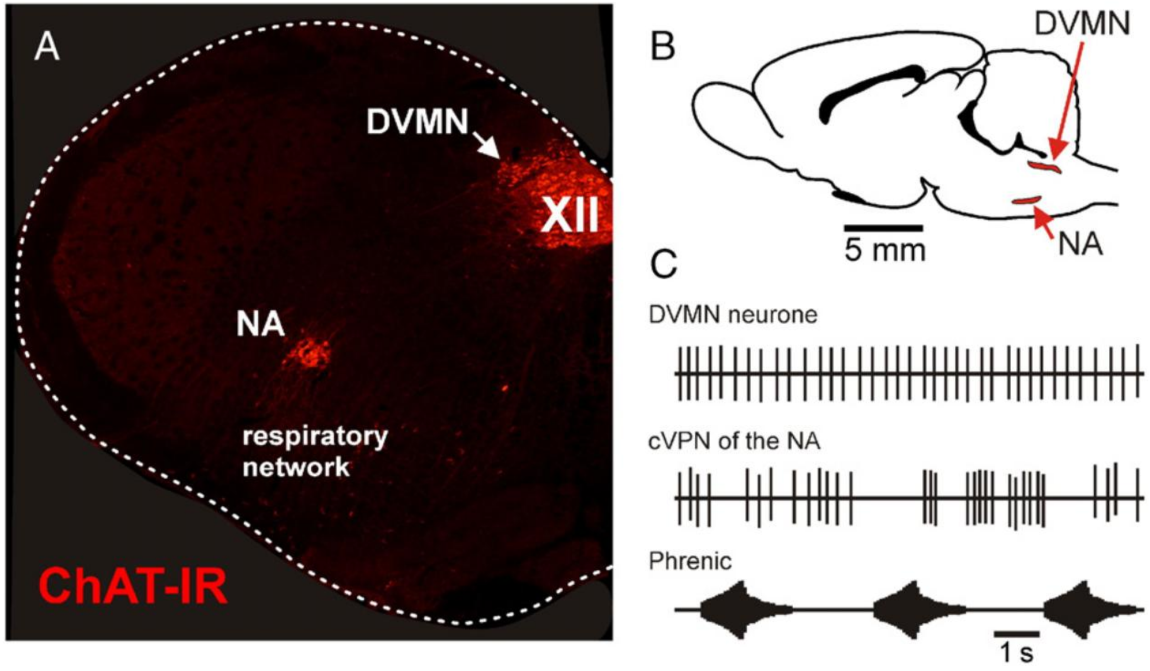
**PreBötzinger complex neurons drive respiratory modulation of blood pressure and heart rate**

Clément Menuet[1,2]*, Angela A Connelly[1], Jaspreet K Bassi[1], Mariana R Melo[1], Sheng Le[3], Jessica Kamar[1], Natasha N Kumar[4], Stuart J McDougall[5], Simon McMullan[3], Andrew M Allen[1,5]*

*Menuet et al., 2020*



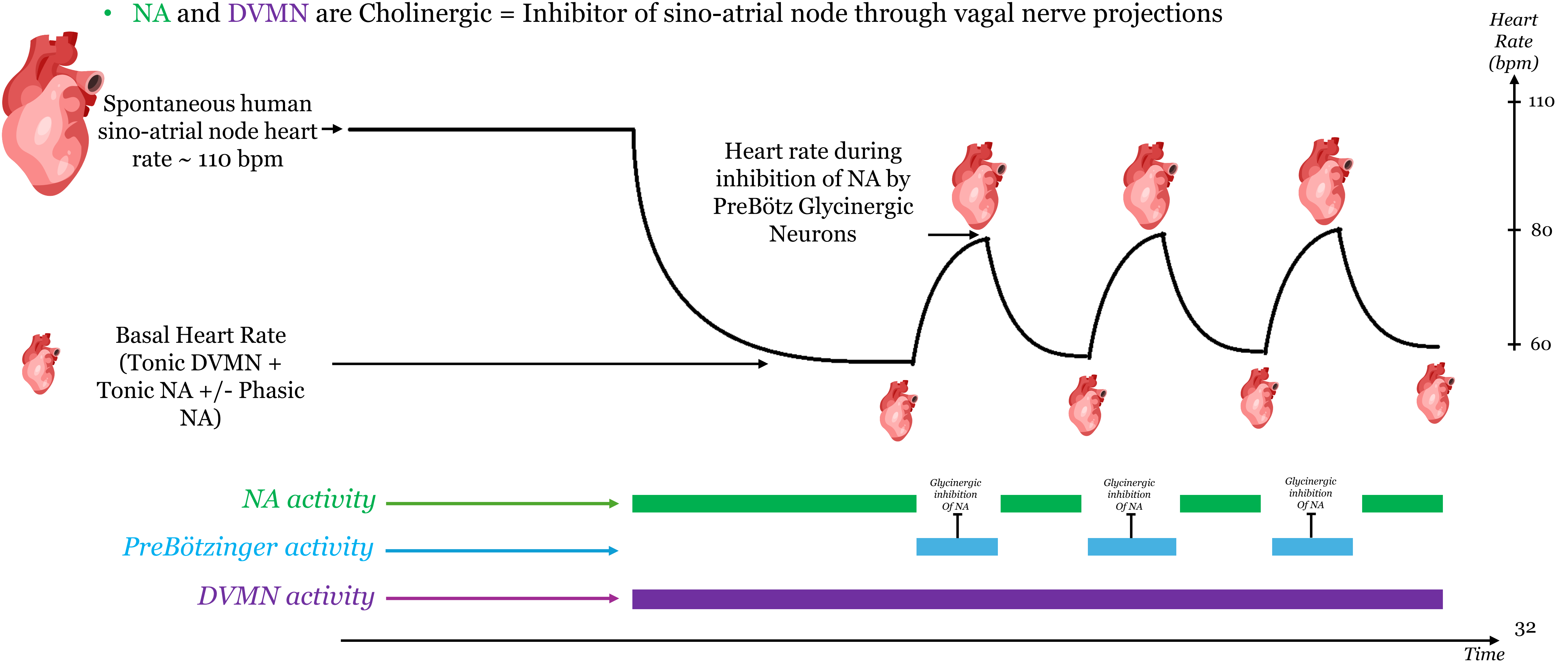

*Menuet et al., 2025*



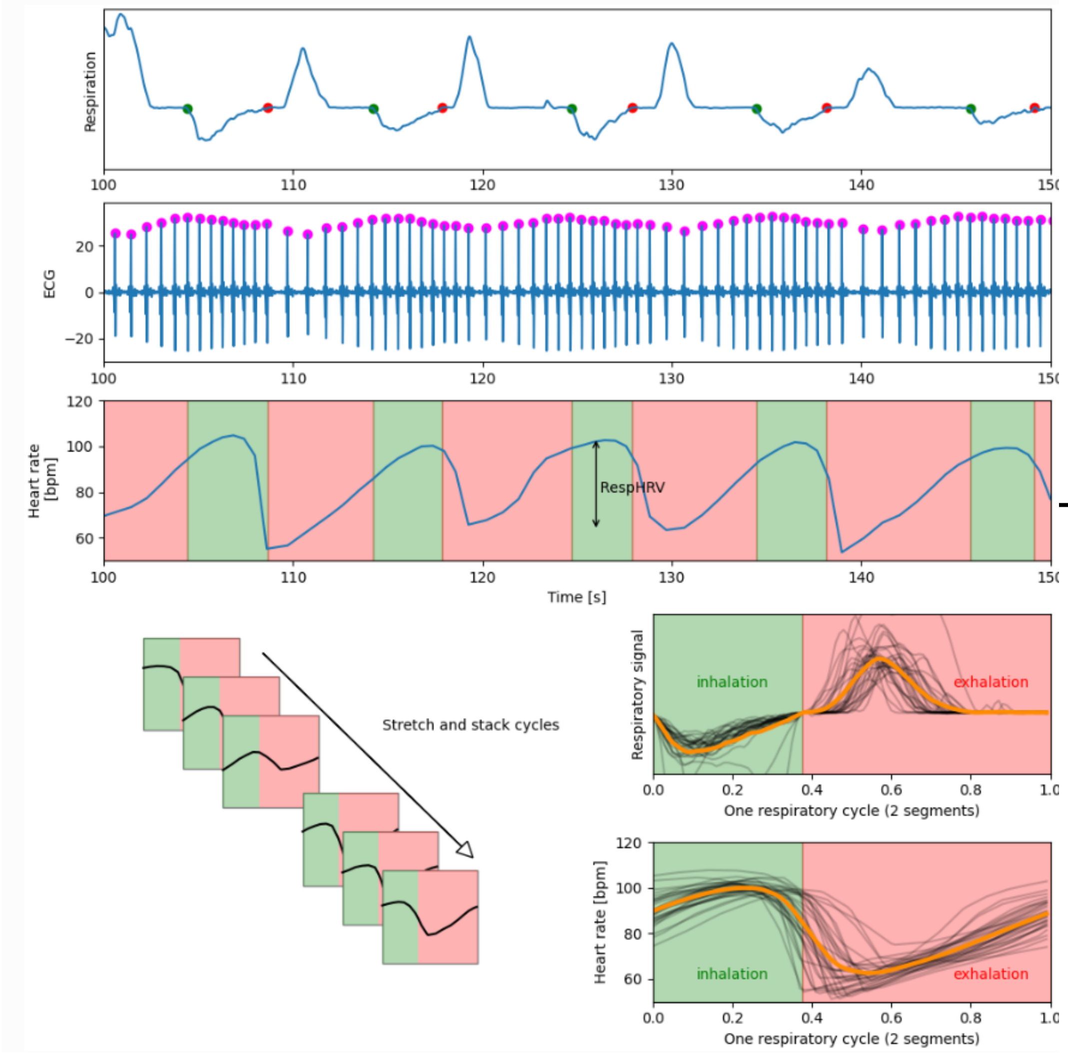

*Gourine et al., 2016*

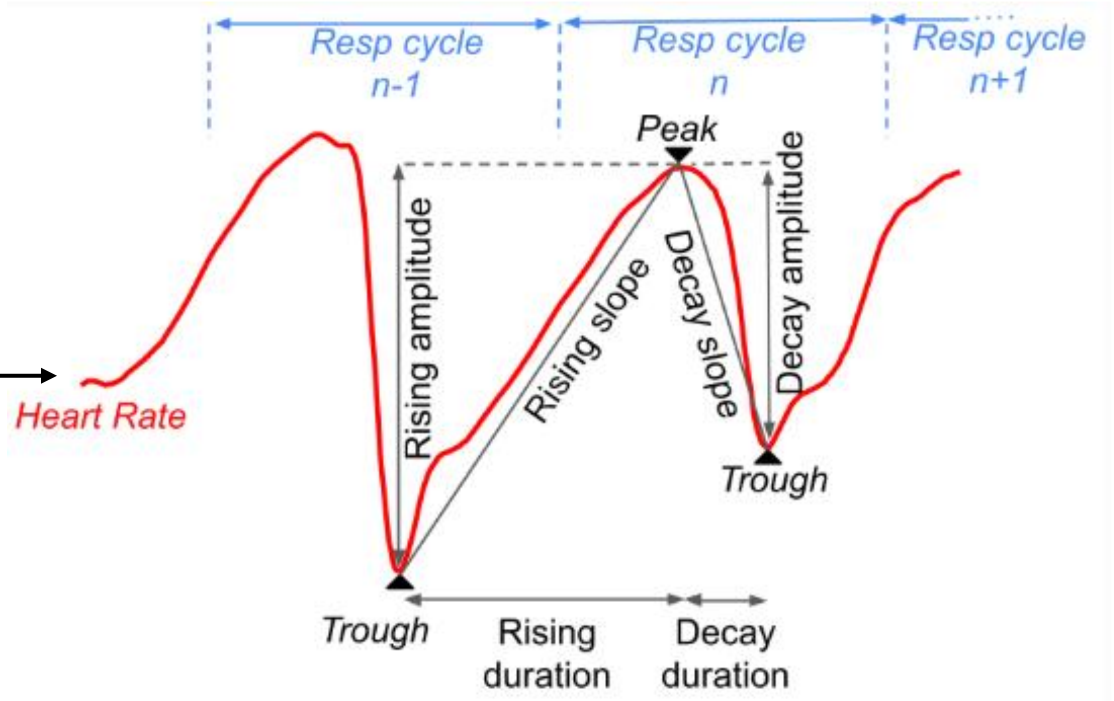
# A schematic and simple view of central generation of RespHRV

- An interplay between Nucleus Ambigus (NA) and PreBötzinger Neurons (Inspi) under the constant pressure of Dorsal Motor Nucleus of the Vagus Nerve (DVMN)
  - NA and DVMN are Cholinergic = Inhibitor of sino-atrial node through vagal nerve projections



# Computing RespHRV features during each respiratory cycle

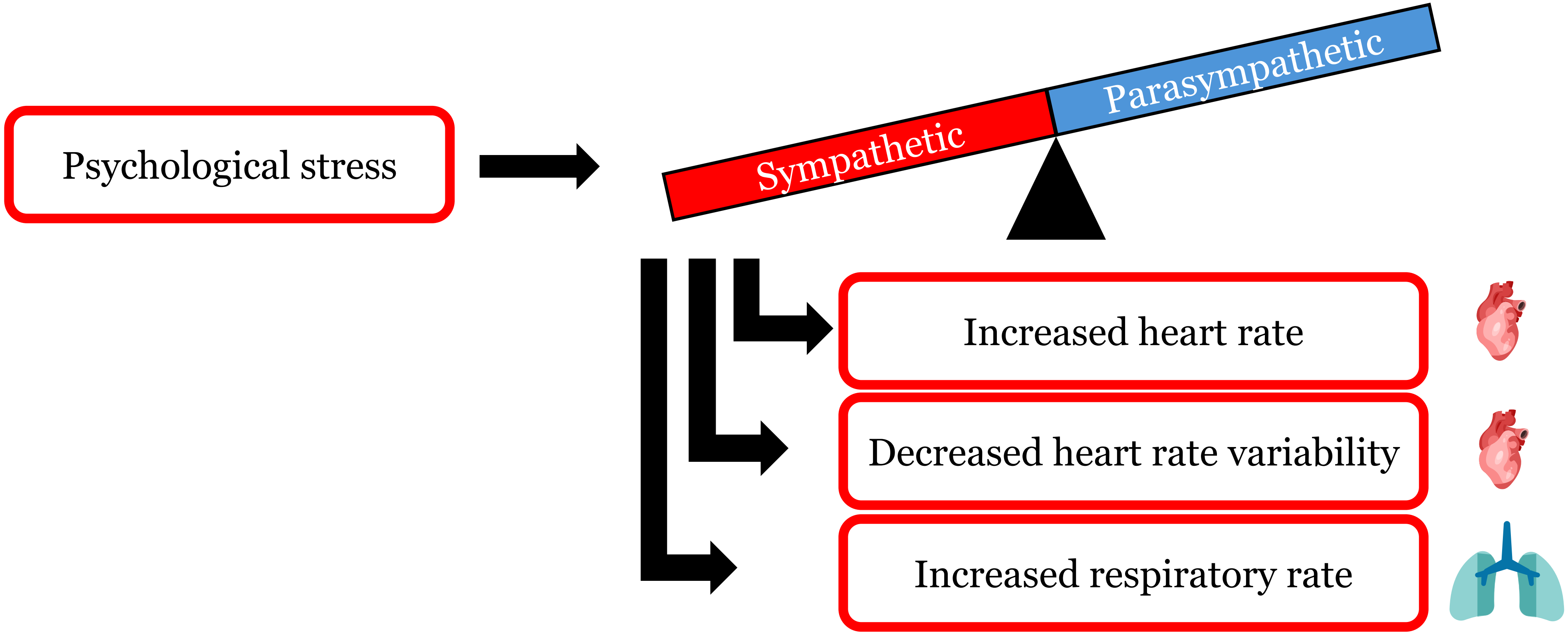


# Using cardio-respiratory related metrics to decipher psychological states, is it really possible ?

# Using cardio-respiratory related metrics to decipher psychological states, is it really possible ?

- The way too much simple way of interpreting heart / respi rate +- variability



# Using cardio-respiratory related metrics to decipher psychological states, is it really possible ?

- Because of high impact of one publication from North America
  - Heart Rate Variability : Standards of Measurement, Physiological Interpretation, and Clinical Use, 1996
  - Misinterpreted by literature
  - Good to read but carefully !

**Summary and Recommendations for Interpretation of HRV Components**

Vagal activity is the major contributor to the HF component.

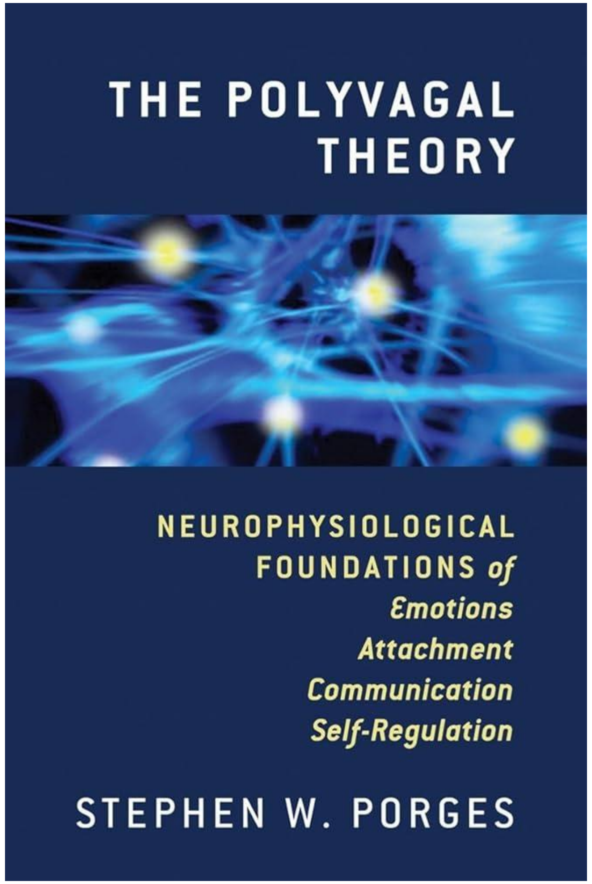
Disagreement exists in respect to the LF component. Some studies suggest that LF, when expressed in normalized units, is a quantitative marker of sympathetic modulations; other studies view LF as reflecting both sympathetic activity and vagal activity. Consequently, the LF/HF ratio is considered by some investigators to mirror sympathovagal balance or to reflect the sympathetic modulations.

Physiological interpretation of lower-frequency components of HRV (that is, of the VLF and ULF components) warrants further elucidation.

This is partially wrong !

# Using cardio-respiratory related metrics to decipher psychological states, is it really possible ?

- And because of Stephen W. Porges




This is wrong !

Cf : Paul Grossmann, 2023

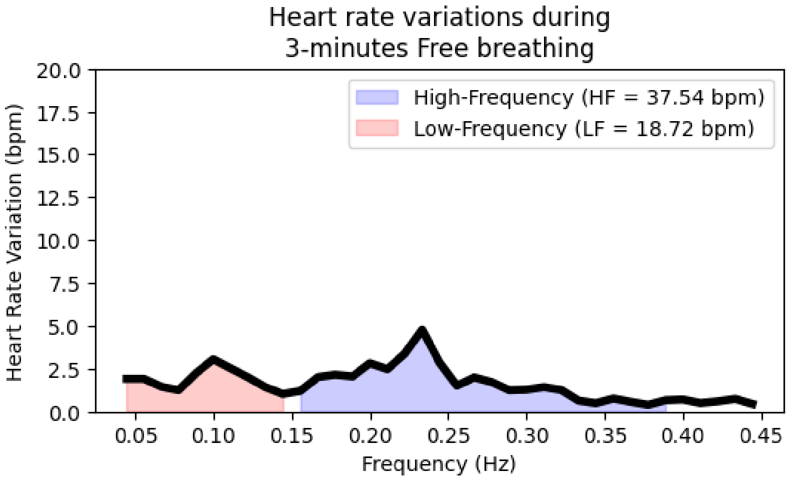
Review

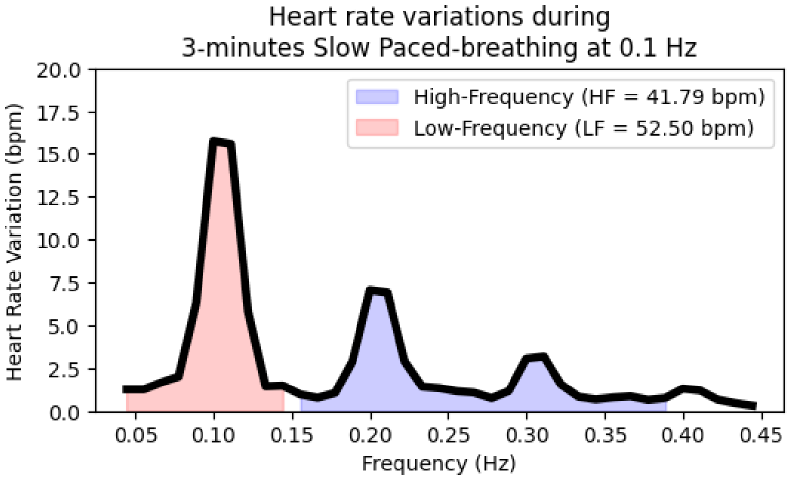
Fundamental challenges and likely refutations of the five basic premises of the polyvagal theory

Paul Grossman

# Challenging frequency-domain HRV metrics

- Spectral power between 0.04 and 0.15 Hz = « Low Frequency Power »
- Spectral power between 0.15 et 0.40 Hz = « High Frequency Power »
- Why 0.15 Hz à 0.40 Hz ? → Expected respiratory frequency of a human
  - **What if it is not True ???**



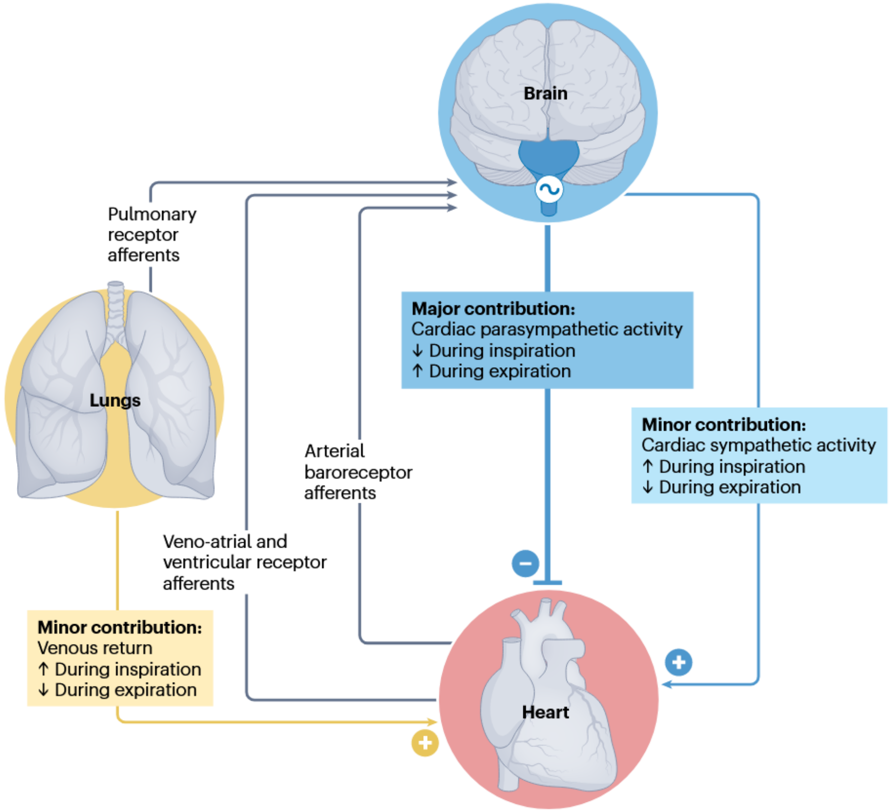
# Challenging HF power band

Is it true ? ➡

**Summary and Recommendations for Interpretation of HRV Components**

Vagal activity is the major contributor to the HF component.

- Very partially
  - 1) RespHRV ~ HF and not depends only on vagal activity




*Menuet et al., 2025*

# Challenging HF power band

Is it true ?

**Summary and Recommendations for Interpretation of HRV Components**

Vagal activity is the major contributor to the HF component.

- Very partially
  - 1) RespHRV ~ HF and not depends only on vagal activity
  - 2) RespHRV ~ HF and highly depends on respiratory frequency (and amplitude)

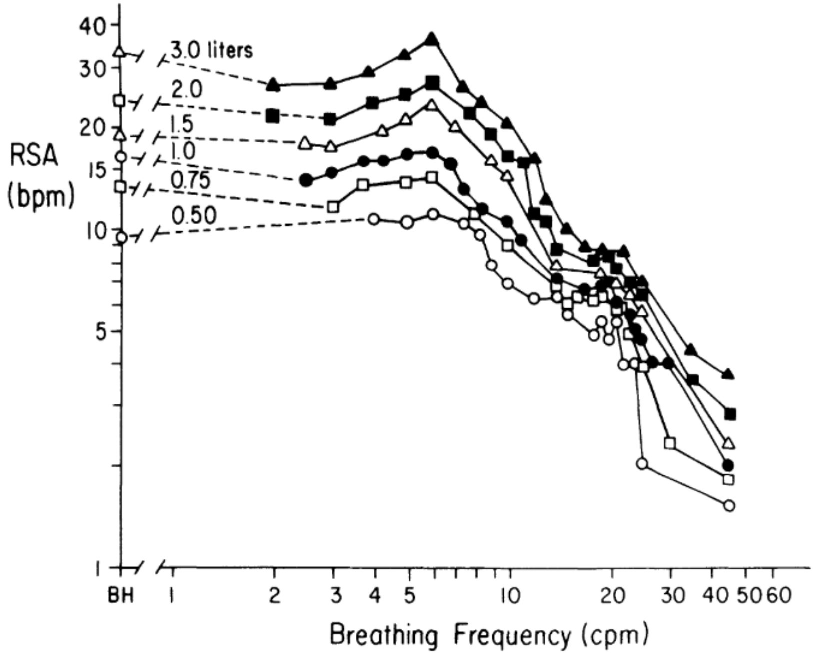



FIG. 4. Log respiratory sinus arrhythmia (RSA) vs. log breathing frequency for 6 different tidal volumes (0.5–3.0 liters). *Subject 5* breathing air.

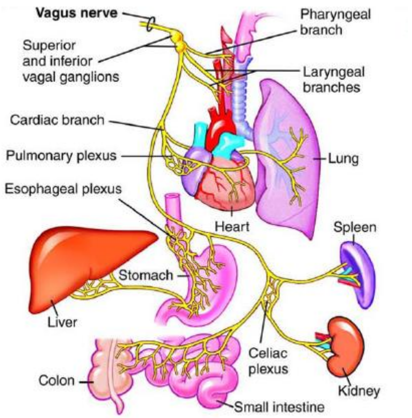
*Hirsh & Bishop, 1981*

# Challenging how we see « vagal » / « parasympathetic system »

- Classical description
  - *“The sympathetic system activates the body for action, while the parasympathetic system restores it to calm and recovery”*

- But the two work in synchrony
  - *“hypothesis that enhanced vagal activity optimizes HR responses to sympathetic stimulation”*

- Vagal nerve is just a highway of neurons targeting many organs




https://www.byondhealthcare.com/hs-fs/hubfs/Vagus%20Nerve%20Pathway.png?width=413&height=415&name=Vagus%20Nerve%20Pathway.png

**Immediate and sustained increases in the activity of vagal preganglionic neurons during exercise and after exercise training**


Alla Korsak[1], Daniel O. Kellett[1], Qadeer Aziz [1,2], Cali Anderson[3], Alicia D’Souza[3], Andrew Tinker [2], Gareth L. Ackland[4], and Alexander V. Gourine [1]*

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Time of primary review: 40 days

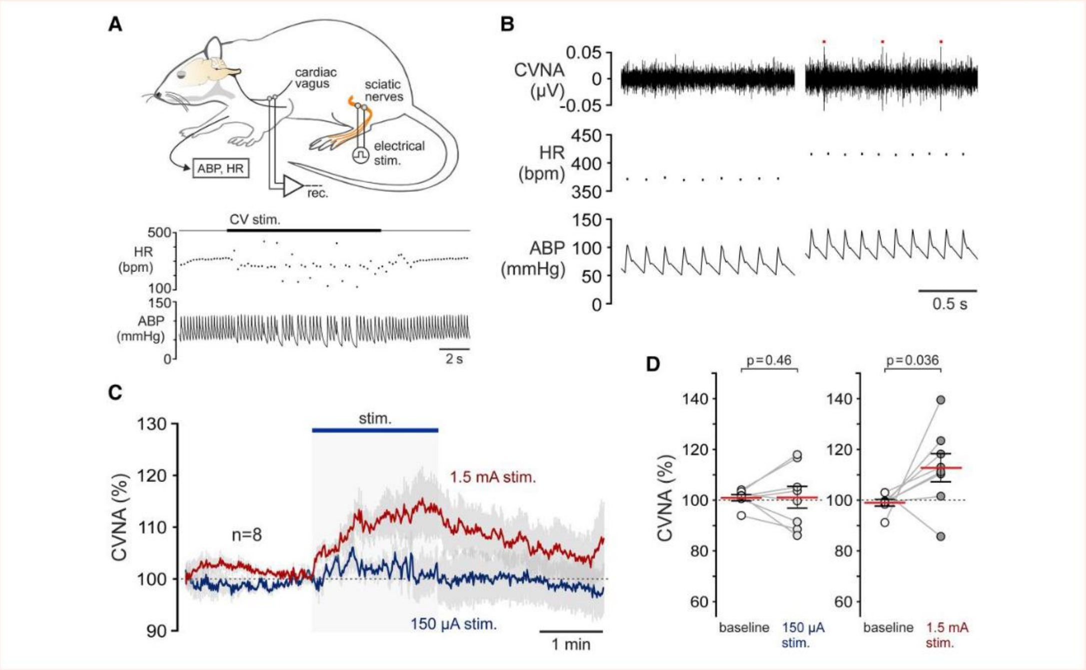



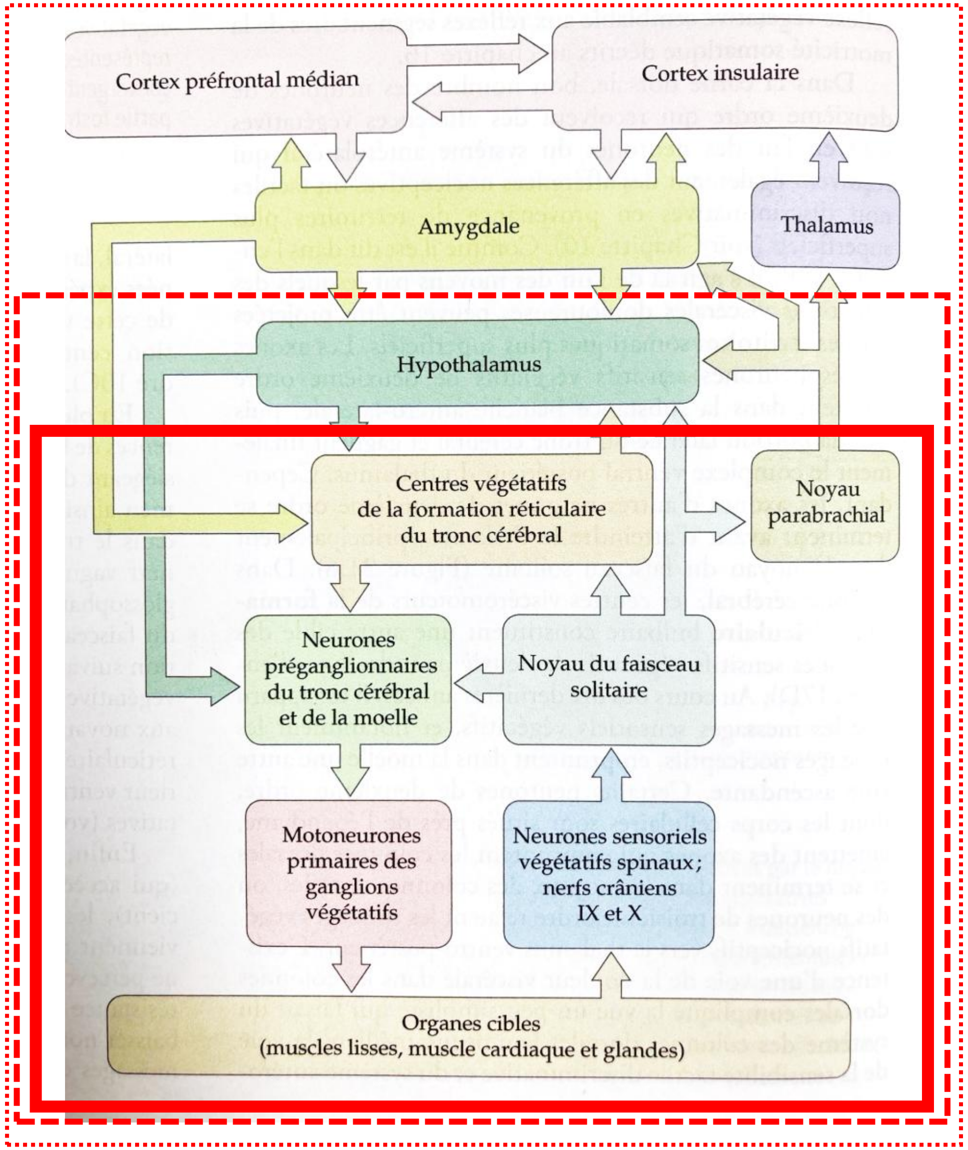

**Figure 6** Exercise increases the cardiac vagal nerve activity (CVNA). (*A*) A diagram of the experimental setup in anaesthetized rats instrumented for the recordings of the activity of the cardiac branch of the vagus nerve, ABP, and HR (illustrated on this figure as instantaneous frequency). Electrical stimulation of sciatic nerves was applied to mimic bouts of acute exercise. Representative recordings of HR and ABP responses to electrical stimulation (1 mA, 1 ms pulses, 10 Hz) of the CV are shown; (*B*) Stretches of representative recordings illustrating increases in CVNA in response to high-intensity sciatic nerve stimulation. Three dots above the recording mark stimulus artefacts; (*C*) Averaged activity profiles illustrating changes in CVNA in response to low- and high-intensity exercise; (*D*) Summary data illustrating relative changes in CVNA in response to low- and high-intensity exercise. *P* values, paired *t*-test.

# So… what is heart rate (variability) ?

- Heart rate variability is primarily an adaptation to physiological demands, like **respiration**, baro- and chemo-reflex!

- So, to interpret regarding physiology … and **respiration** of the subject

- So, record **respiration** when you record the heart




*Purves et al., 2015*

# Two lights into the darkness

- 1. Respiration is semi-automatic…
  - Volitional control … to communicate … Emotions !

*Betka et al., 2022*

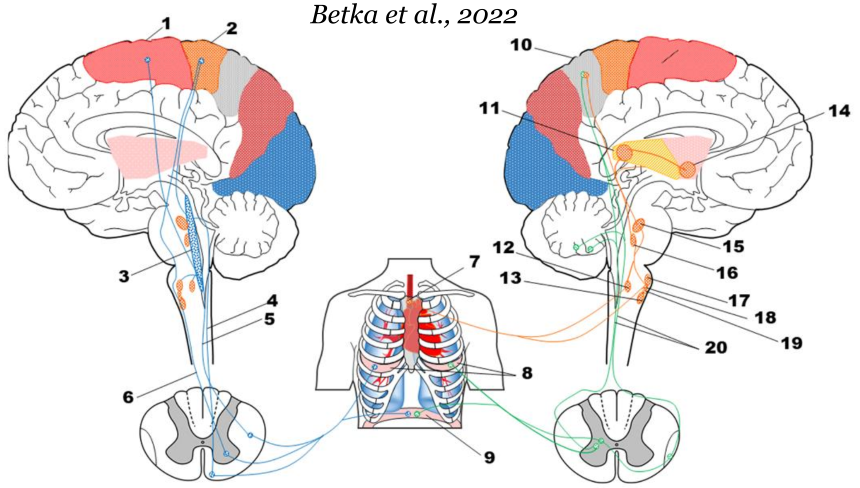



**Fig. 1.** Schematic representation of the efferent (left) and afferent (right) breathing pathways. 1 = Supplementary motor area; 2 = Motor cortex (M1); 3 = Reticular formation; 4 = medial reticular tract; 5 = Dorsal reticulospinal tract; 6 = Lateral corticospinal tract; 7 = Peripherical chemoreceptors; 8 = Intercostal muscles; 9 = diaphragm; 10 = Primary somatosensory cortex (S1); 11 = Posterior insula; 12 = Dorsal Respiratory Group; 13 = Ventral Respiratory Group; 14 = Anterior insula; 15 = Parabrachial/Kölliker-Fuse complex (Pneumotaxic center); 16 = Apneustic center; 17 = the parafacial respiratory group/retrotrapezoid nucleus; 18 = pre-Bötzinger complex; 19 = Bötzinger complex; 20 = ventral and dorsal spinocerebellar tracts.

- 2. Buron et al., 2025

nature neuroscience

Article https://doi.org/10.1038/s41593-025-02074-2

**Oxytocin modulates respiratory heart rate variability through a hypothalamus–brainstem–heart neuronal pathway**

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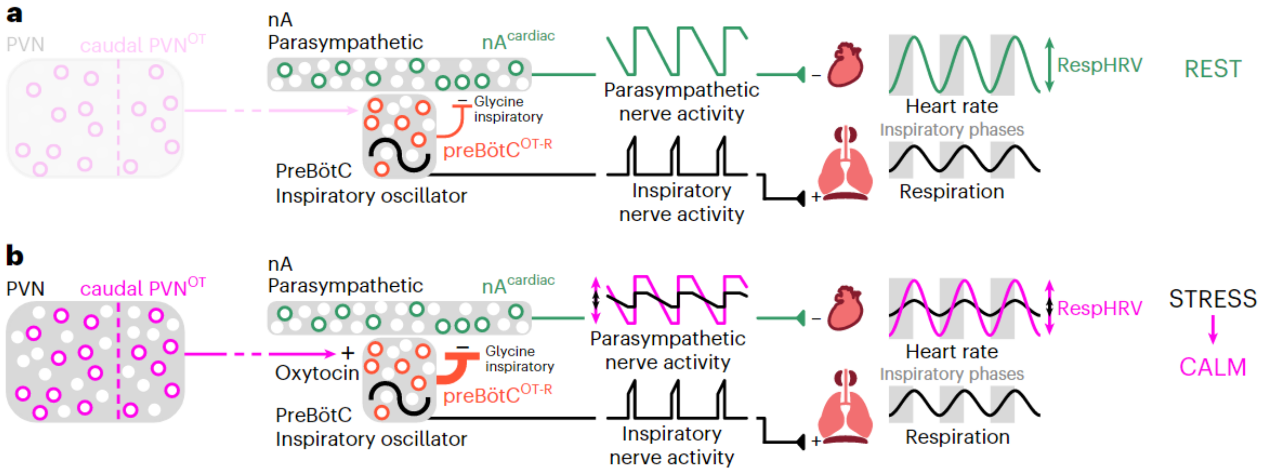
Julie Buron[1,3], Ambre Linossier[1], Christian Gestreau[1], Fabienne Schaller[1], Roman Tyzio[1], Marie-Solenne Felix[1], Valéry Matarazzo[1], Muriel Thoby-Brisson[2], Françoise Muscatelli[1] & Clément Menuet[1]




*Buron et al., 2025*

# Thanks… let's pratice

- Contact: vaghibaudo@gmail.com
- physio
  - https://github.com/samuelgarcia/physio

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