

# *Cortex modulation of gastric motor reflex activity*

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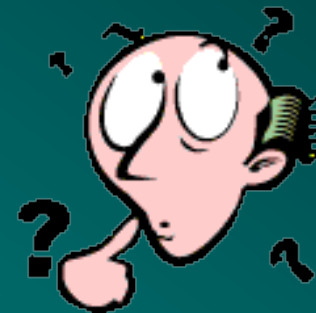
# Introduction

- ❖ No doubt now that psychological factors can influence autonomic functions.

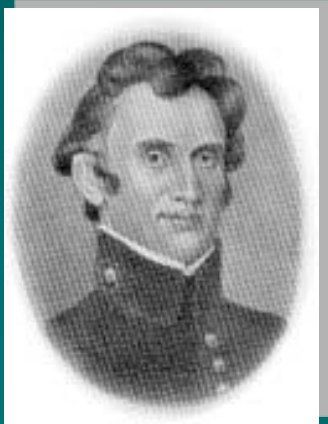
- ❖ Along with this, there is a continued interest in identify the cerebral regions that modulate autonomic functions in the hopes of understanding:

How “hight-level” brain mechanisms affect visceral functions, particularly in human deseases?

- ❖ This is one of the oldest questions in neuroscience and can be traced back to the beginning of 19th century.



## Historical notes



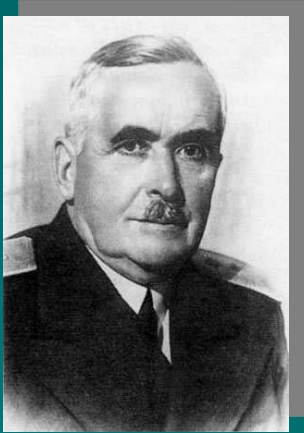
In 1833 U.S. army surgeon W. Beaumont had described his work with the Canadian voyageur that had a gunshot wound that resulted in a permanent hole in his abdomen. Through this hole W. Beaumont could observe stomach movement changes to food. He was the first who revealed that gastric motility depended on psychological state of the patient.

# Historical notes



In 1909 W.Cannon from Harvard University with using new to that time X-ray technique had shown that strong emotional reactions could alter the motor function of the alimentary canal.

# Historical notes



In 1924 Russian scientist K. Bykov had shown that many visceral functions, such as body heat, heart rate, blood pressure, gastrointestinal secretion and motility and etc can be changed with Pavlov's method of a conditioned reflexes.

Since that time with using an extirpation or stimulation of different cortex areas in different species, including human was shown that the most effective cortex areas to induce some visceral changes including gastrointestinal motility are located on medial and lateral surfaces of frontal lobe of the hemisphere.



Both of these now are involved into the **prefrontal cortex (PFC)** (*Ongur, Price, 2000*) and referred as:

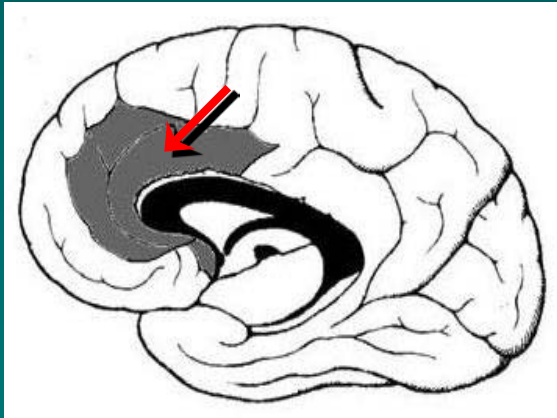
medial prefrontal cortex (mPFC)  
now is considered as  
"viscero-motor" area  
(*Terreberry, Neafsey, 1983*)



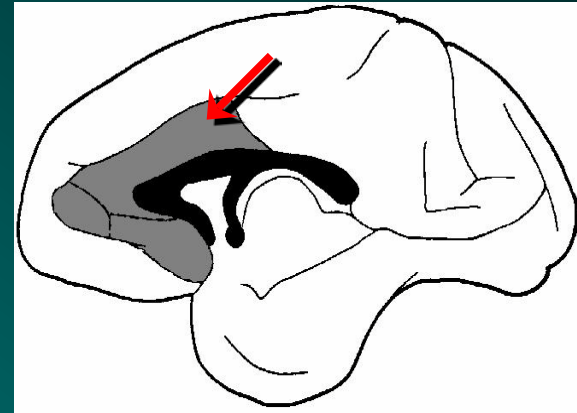
lateral prefrontal cortex (or insular)  
now is considered as  
"viscero-sensory" area  
(*Neafsey, 1990*)

# The approximate locations of the mPFC in different species

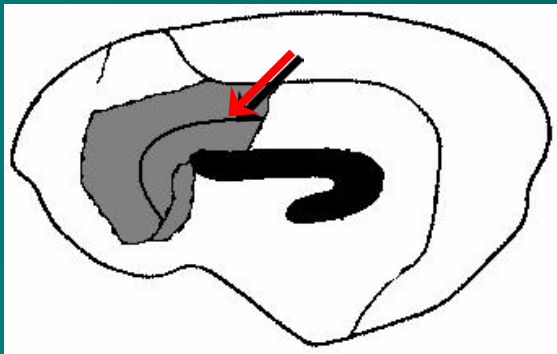
man



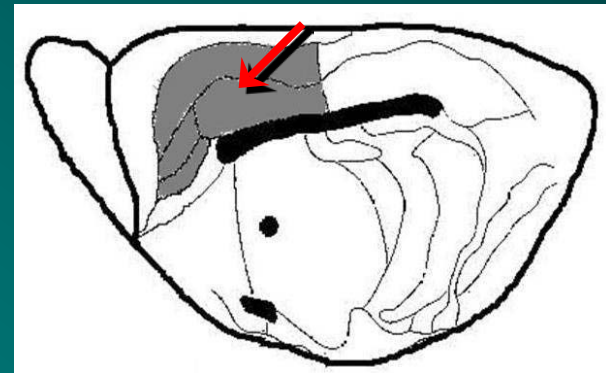
dog



cat

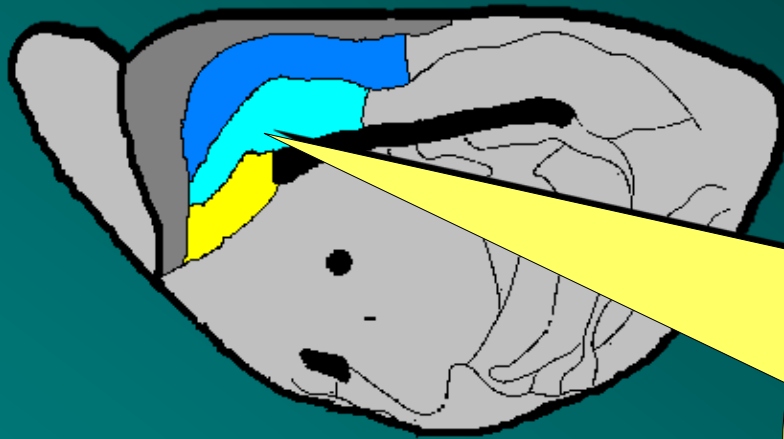


rat

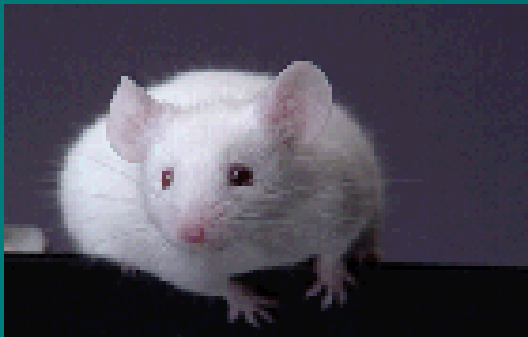




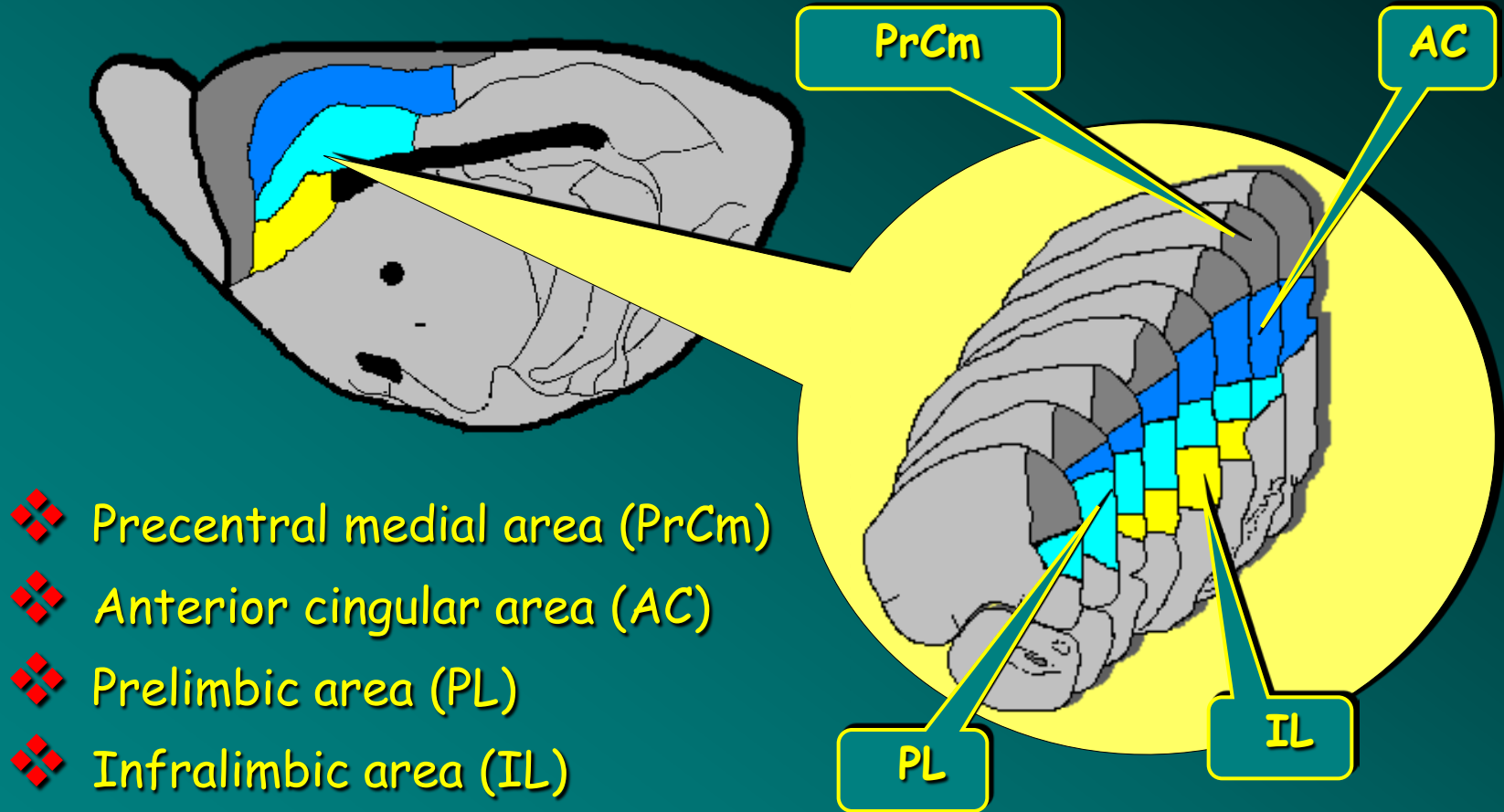
# The medial prefrontal cortex of the rat



medial wall  
of the hemisphere



# The medial prefrontal cortex of the rat



and is divided into at least four cytoarchitectonically distinct areas

The mPFC has been implicated in a variety of cognitive and executive processes such as:

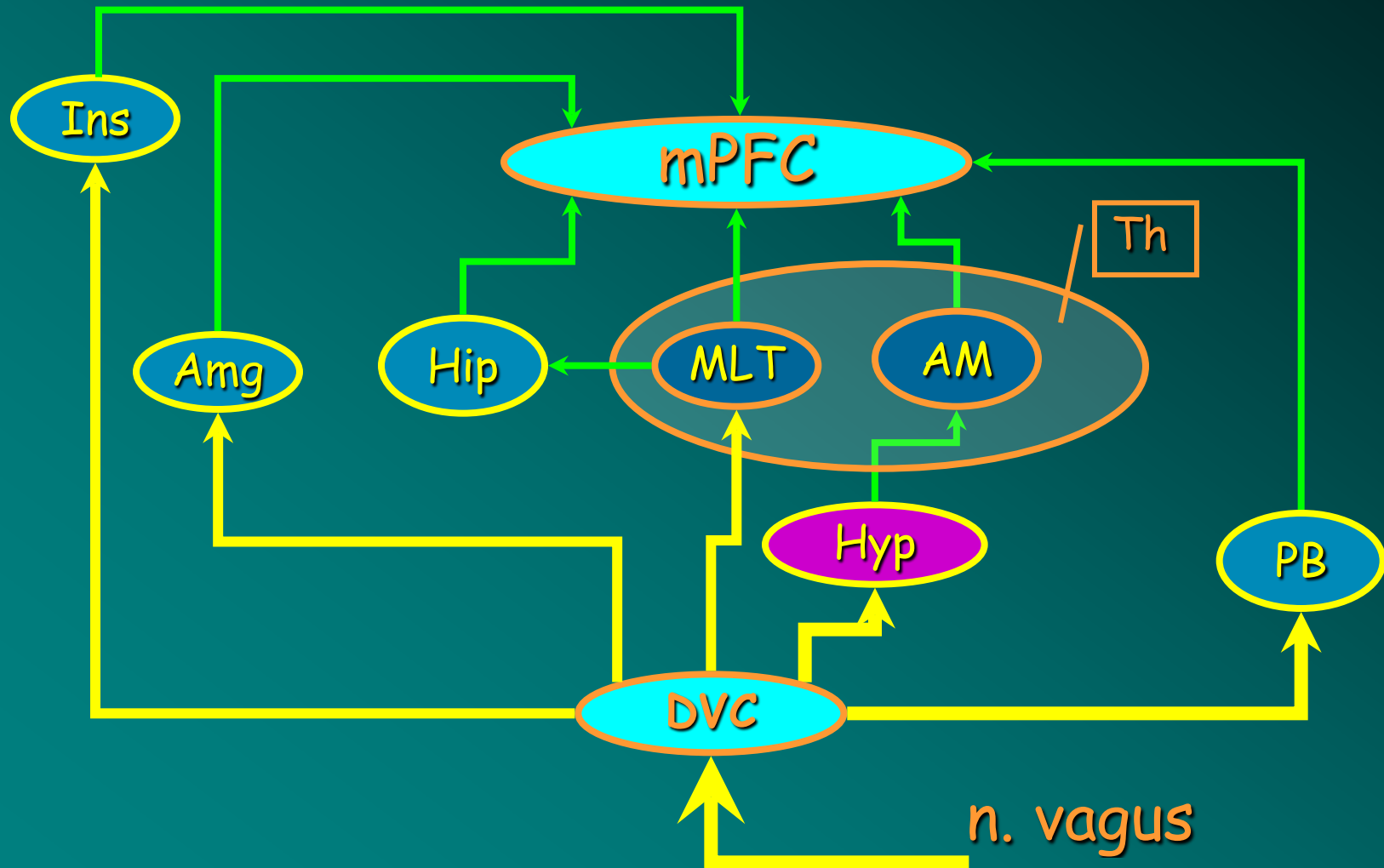
- ❖ attention, learning and working memory;
- ❖ fear, anxiety, stress and emotional related behaviour;
- ❖ arrangement of an autonomic tracking of integral behaviour - "viscero-motor" function.

From this point of view the mPFC can be considered as area providing an "interface" between cognition and behaviour and visceral sphere that is partly realized via dorsal vagal complex (DVC) that is located within low brainstem.

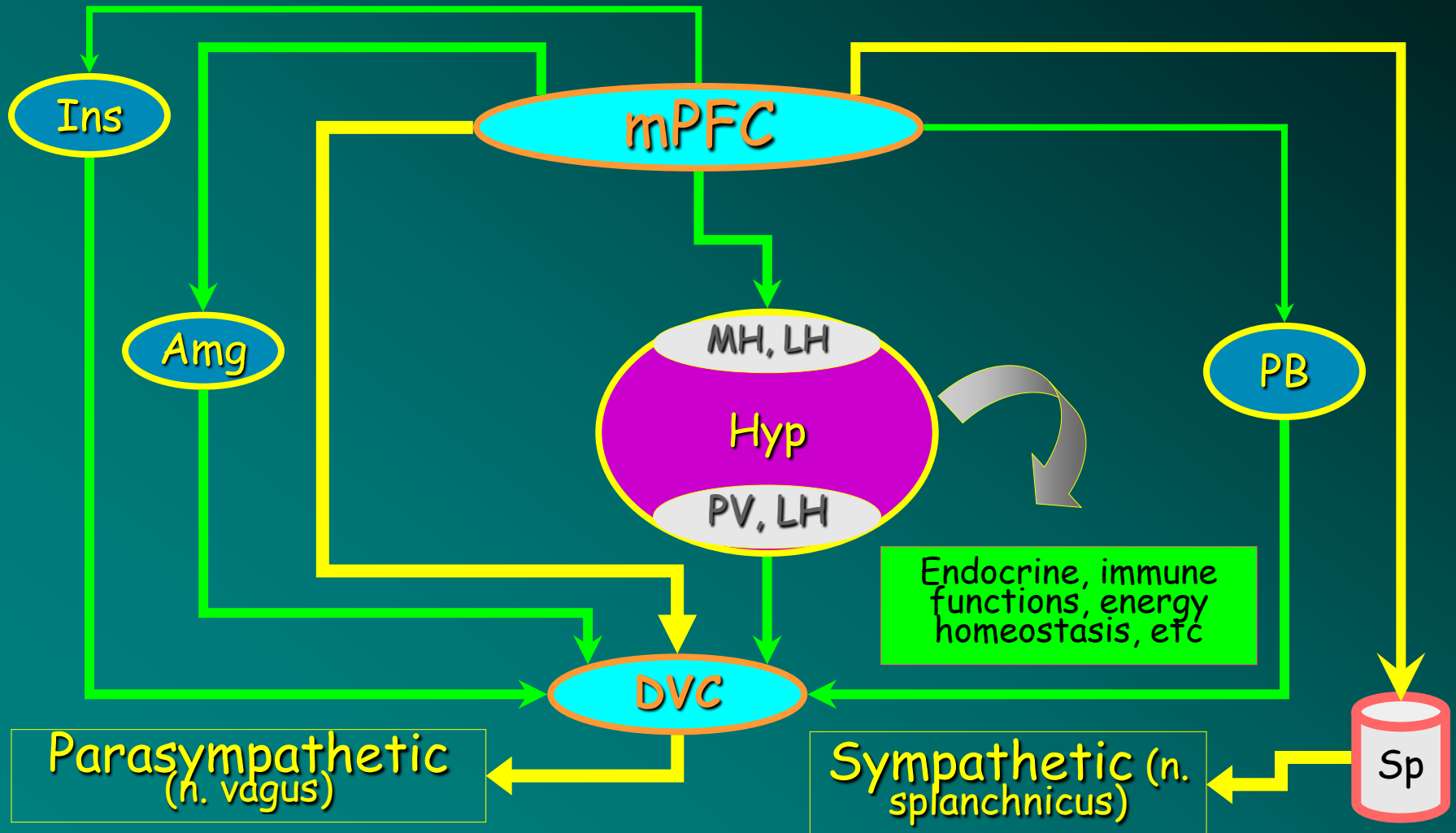


Which pathways are responsible for it?

Viscerosensory signals from DVC can reach the mPFC by indirect ways via:

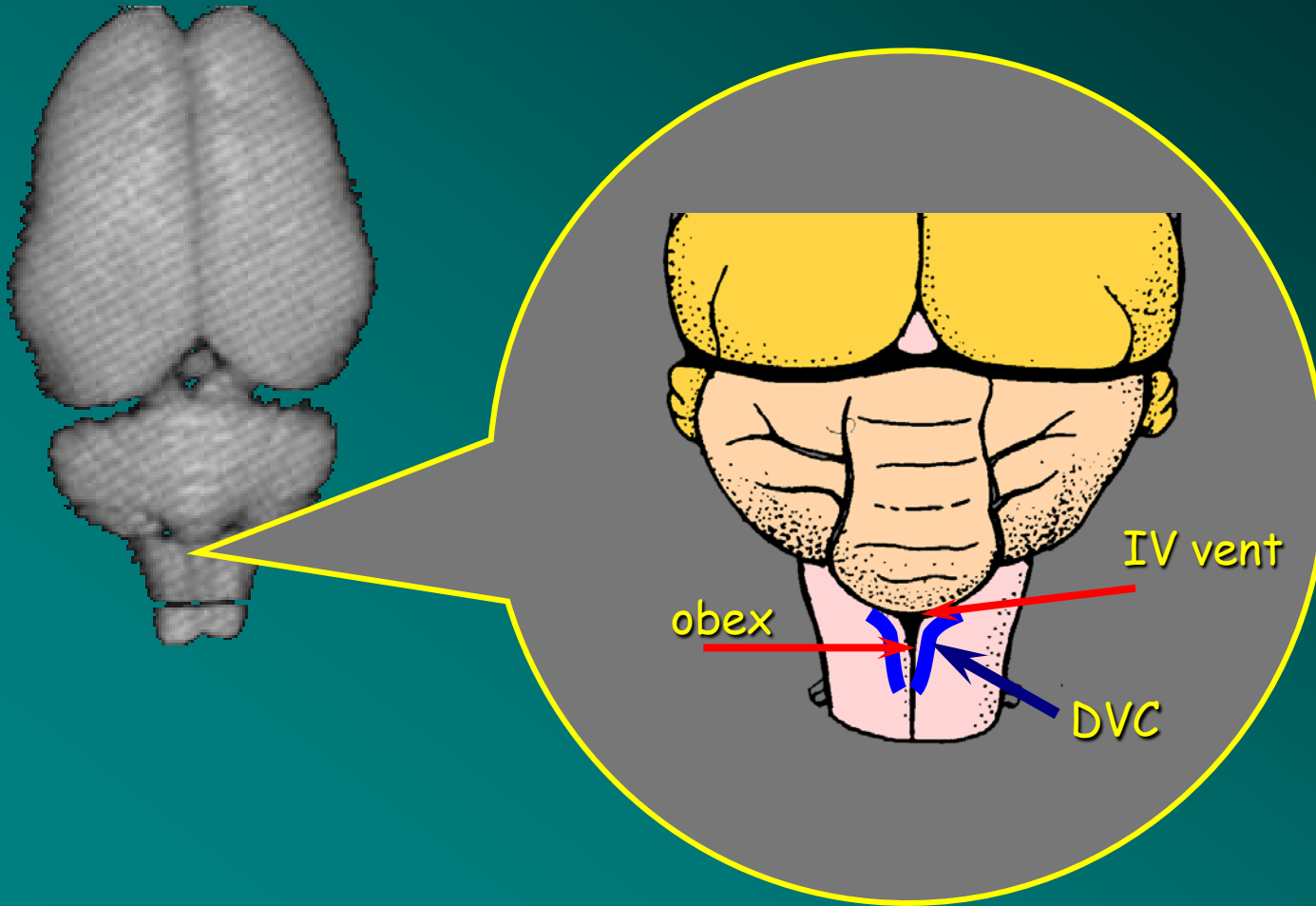


The mPFC realizes its "viscero-motor" functions via several descending ways:

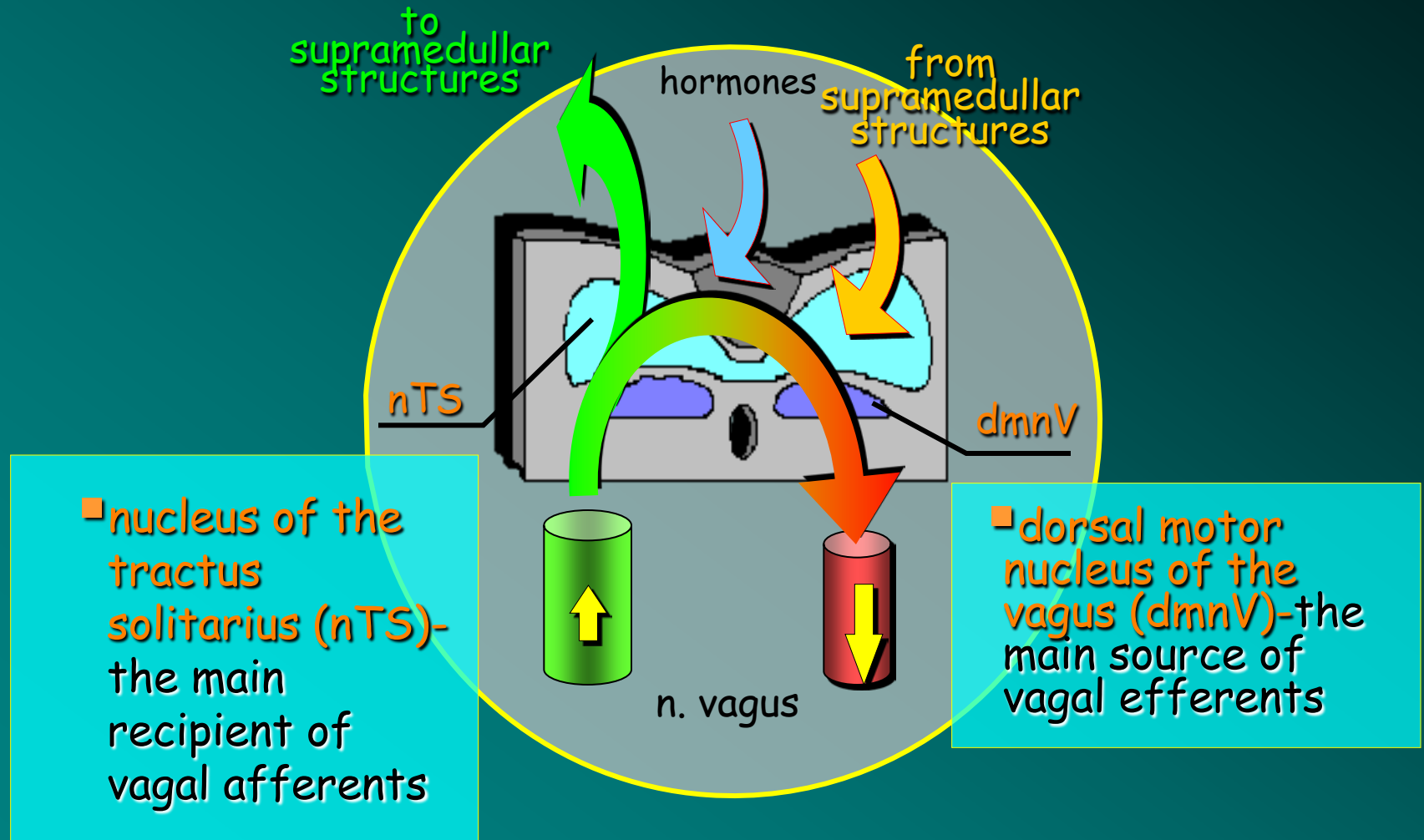




# The dorsal vagal complex (DVC)



# The DVC comprises three autonomic nuclei



# Background of the present study:

- The nTS is the main recipient of vagal afferent inputs from the proximal gastrointestinal tract (*Shapiro, Miselis 1985*).
- There are direct nTS connections to the dmV (*Rogers et al., 1980*).
- These nuclei participate in gastric motor vago-vagal reflex activity (*McCann and Rogers, 1992*).
- There are direct glutamate projections from the mPFC to nTS overlapping with those of vagal afferent endings (*Van der Kooy et al., 1984; Torrealba, Muller, 1999*).
- There is a good morphological basis for cortical modulation of vago-vagal reflexes which control gastrointestinal motor function (*Grundy, 1988*).

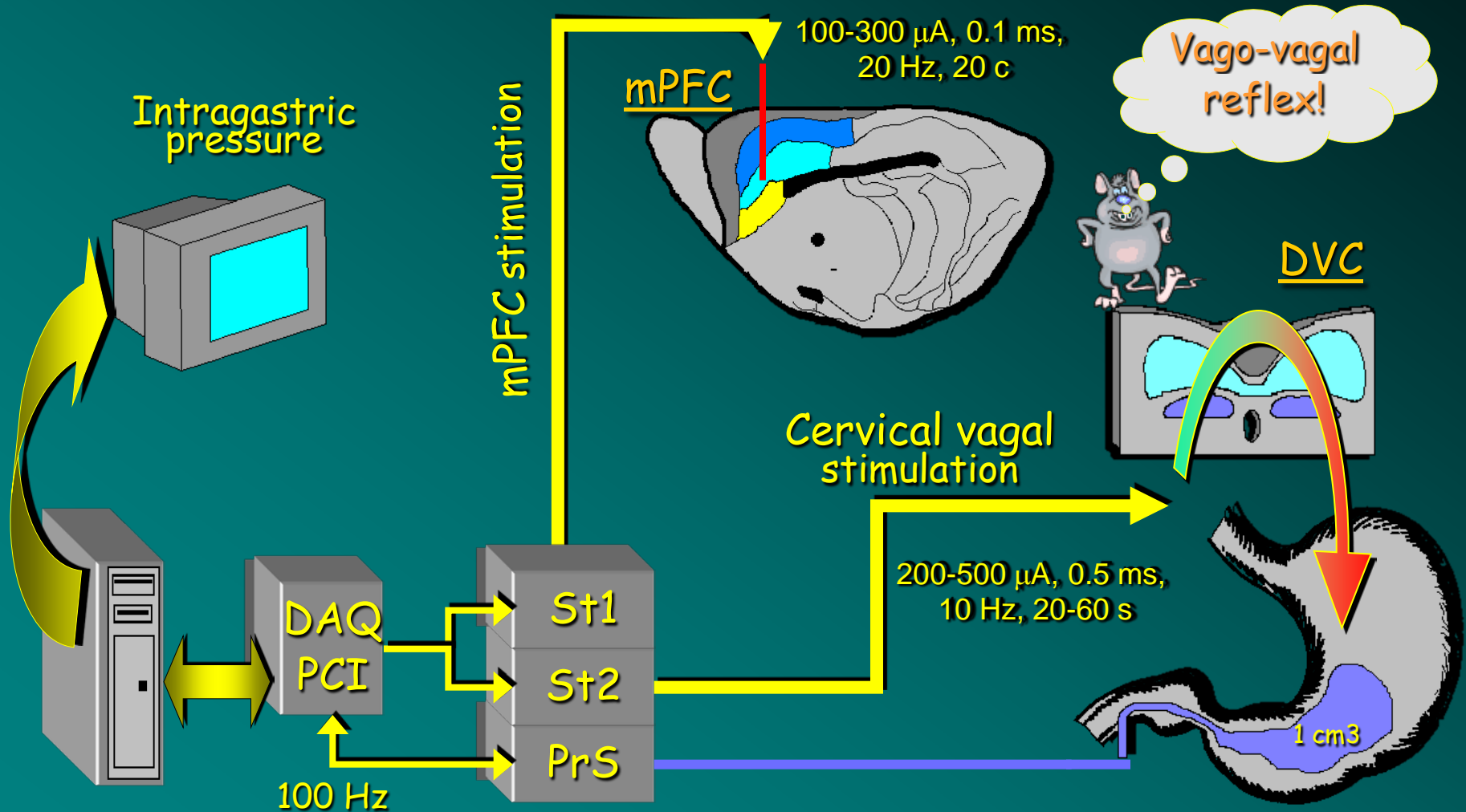
With using the model of cervical vagal stimulation are examined the hypothesis :

- The stimulation of the mPFC will modulate gastric motor function by influencing reflex transmission through vago-vagal reflexes.
- The stimulation of the mPFC will change the DVC neuron responses induced by vagal stimulation.

# *Methods and materials*

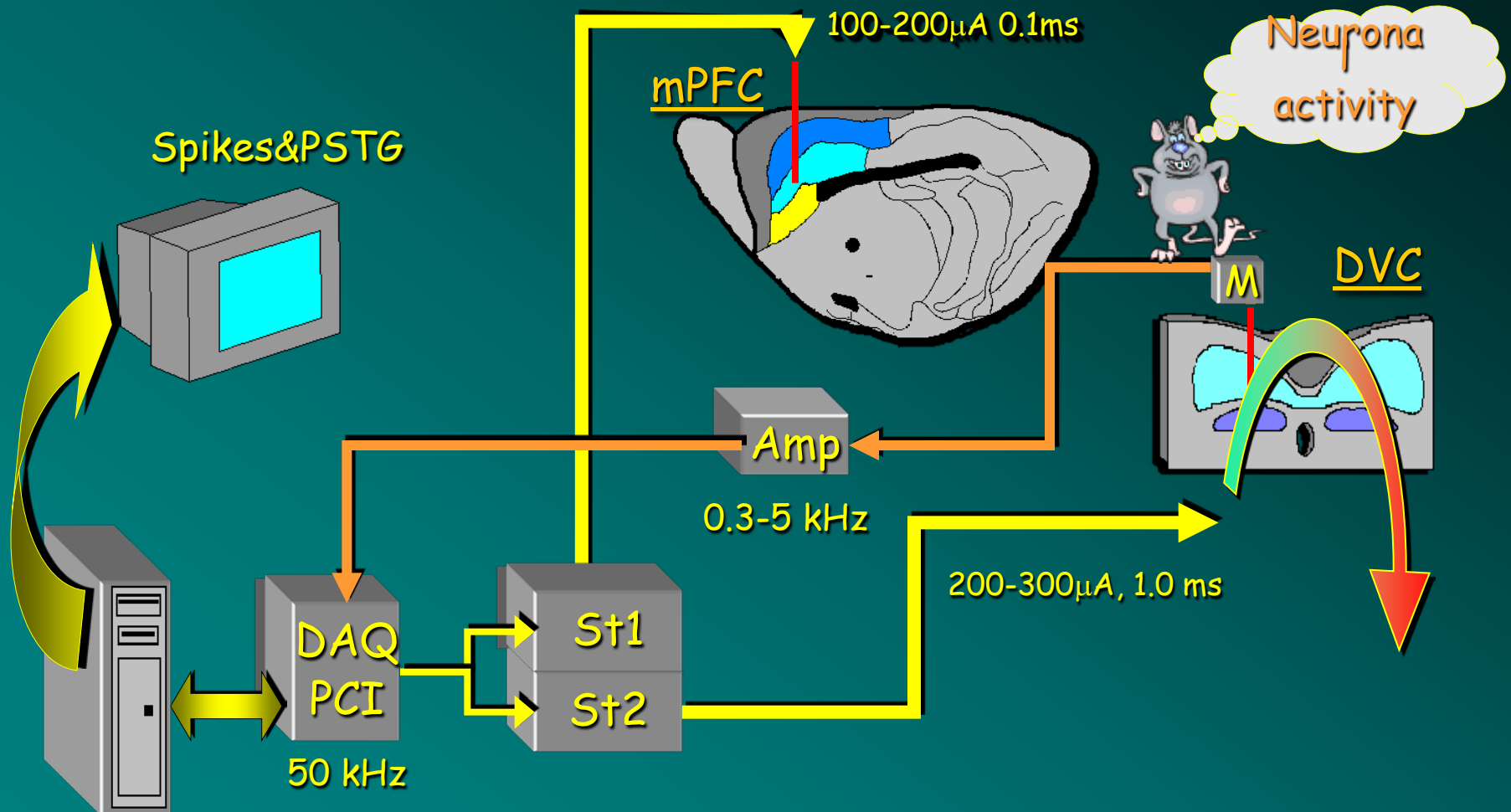
- Experiments: 35 Wistar rats (urethane, 1.2-1.5 g/ kg, i.p.).
- Cortical stimulation: tungsten electrodes (50  $\mu$ , 100 k $\Omega$ ).
- Cervical vagal stimulation: platinum hook electrodes.
- Registration of intragastric pressure: rubber balloon (1 cm<sup>3</sup>)
- Registration of unit activity: tungsten electrodes (5  $\mu$ , 3-8 M $\Omega$ ).
- Data acquisition and stimulation: custom made on-line computer system & software (*Panteleev et al., 1996*).
- Data analyses: Student's *t*-test or ANOVA with Origin 7.0
- Verification: DC, 100-200  $\mu$ A, 60 s, perfusion PAF, cryostat, 50  $\mu$ m, the rat's brain atlas (*Paxinos & Watson, 1982*).
- Drugs: atropine (0,1 mg/kg, iv), L-NAME (10-15 mg/kg, iv)

# The simplified scheme of the study of the intragastric pressure changes

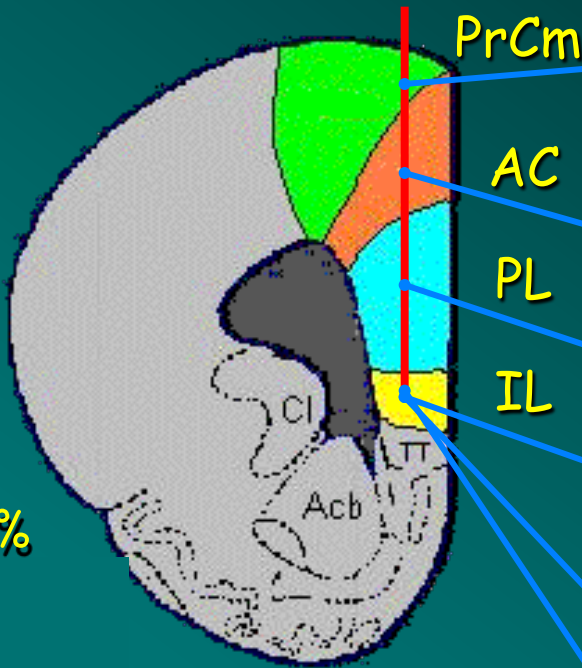




To study of neuronal activity of the nTS and dmNv the system was modified



# Gastric motor responses to mPFC stimulation



IGP, cm H<sub>2</sub>O

5

4

3

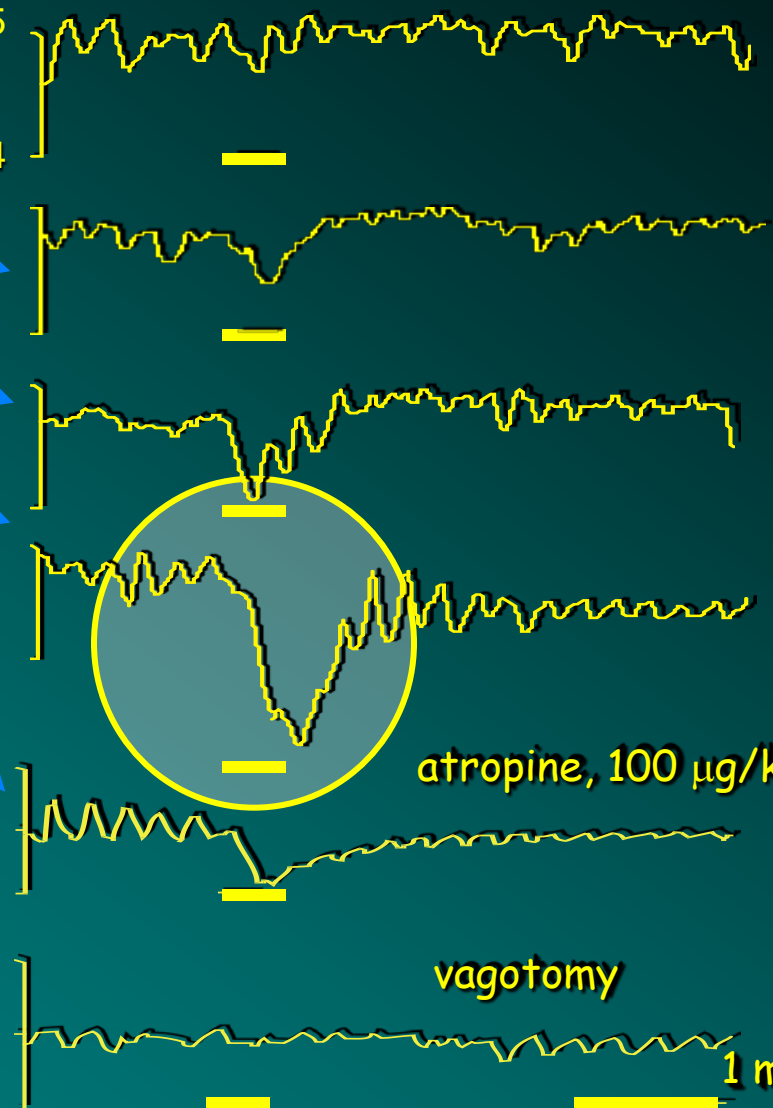
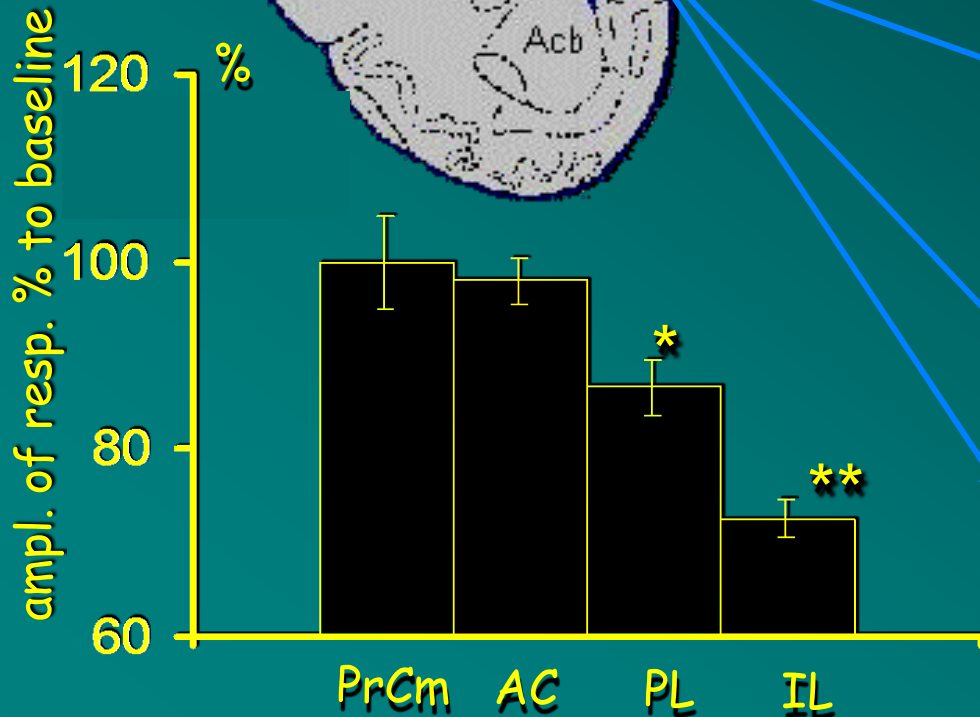
2

1

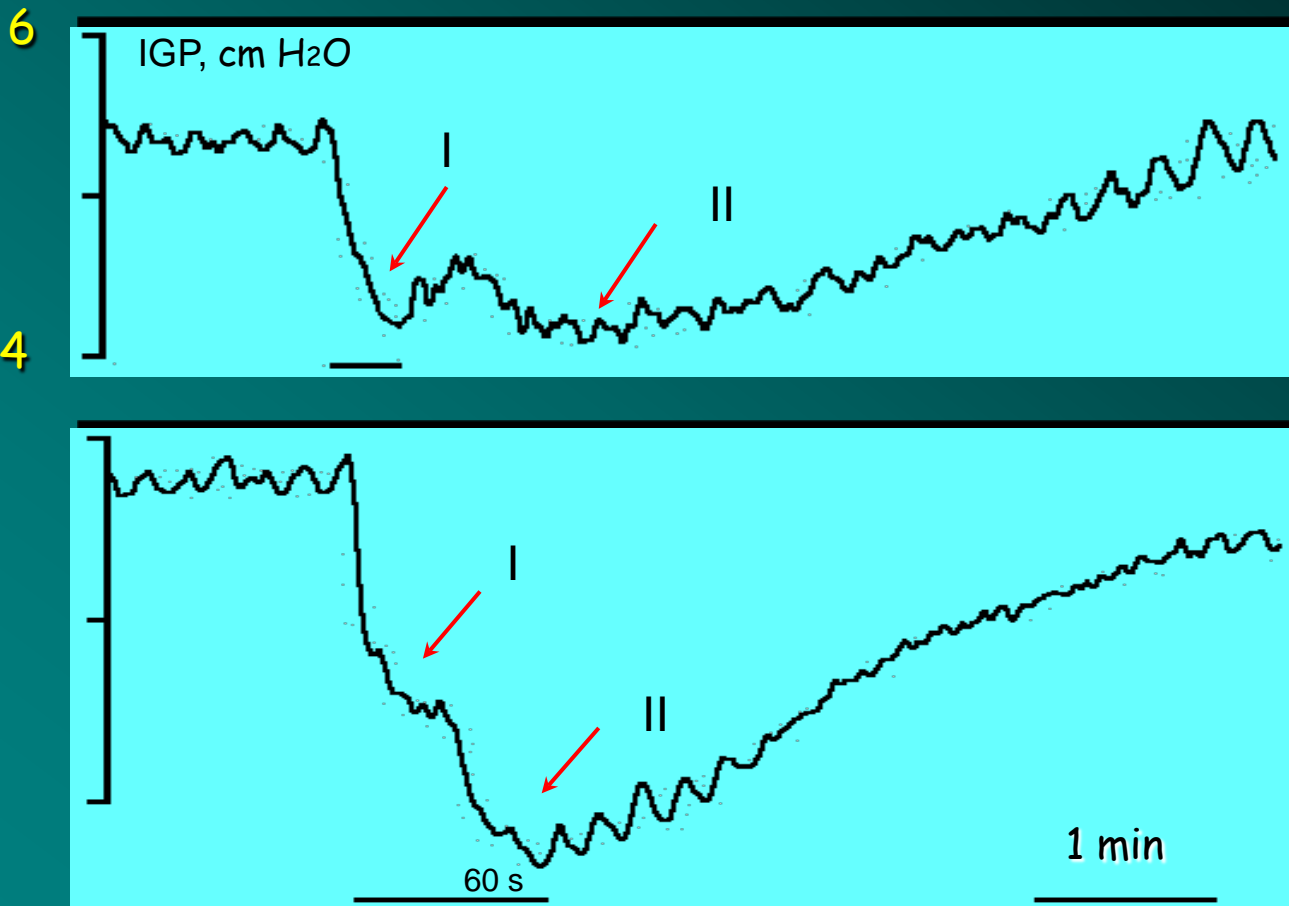
0

-1

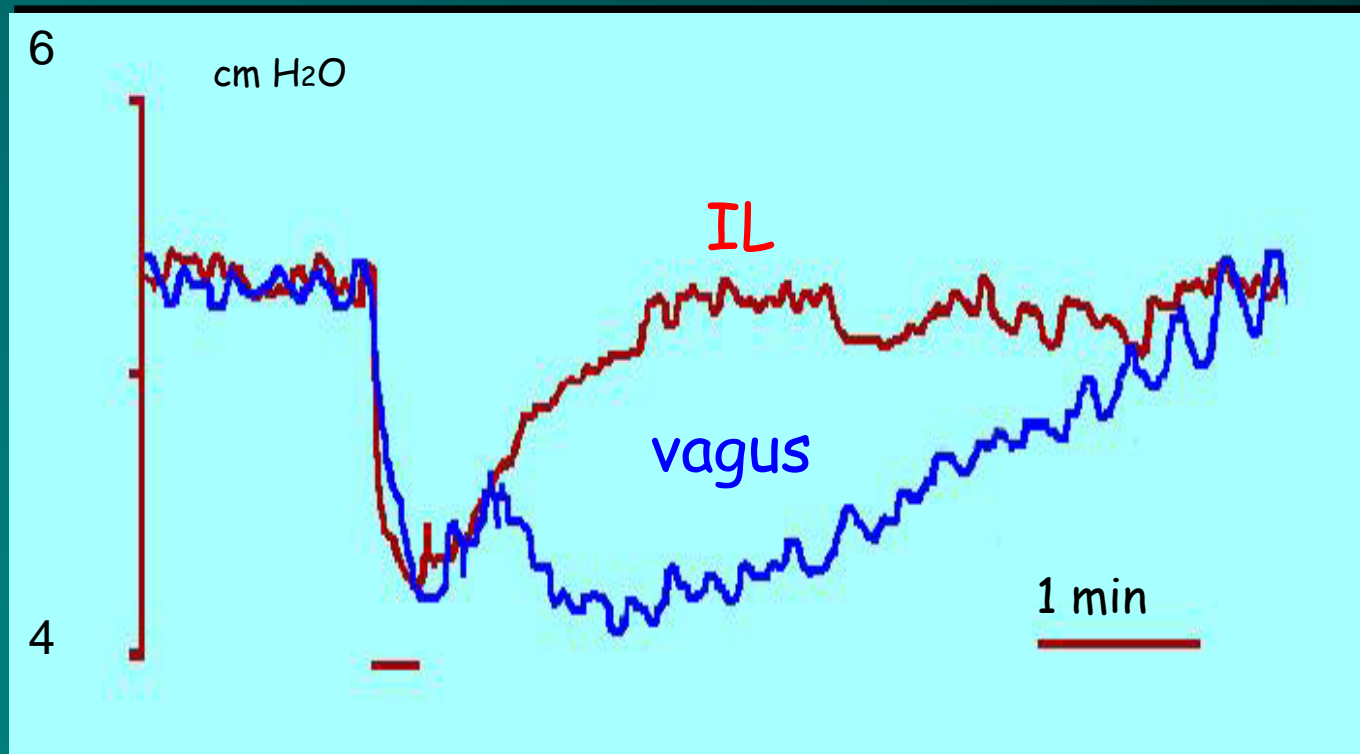
-2



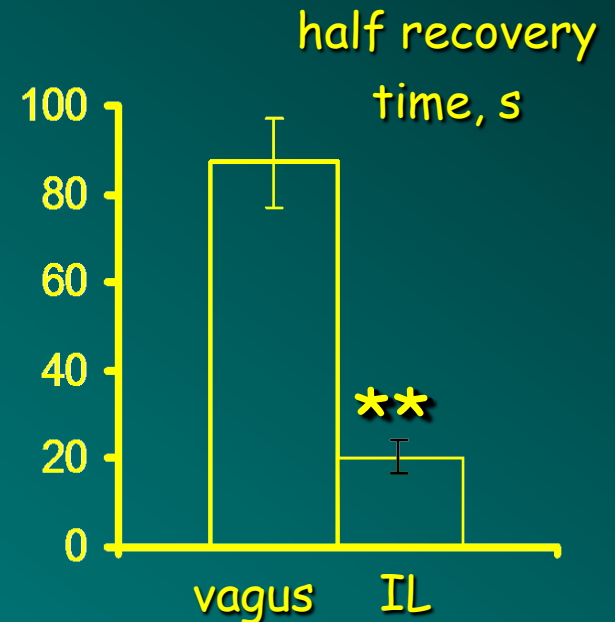
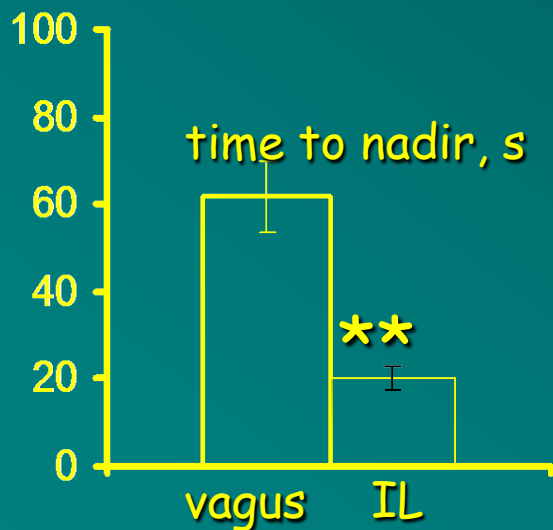
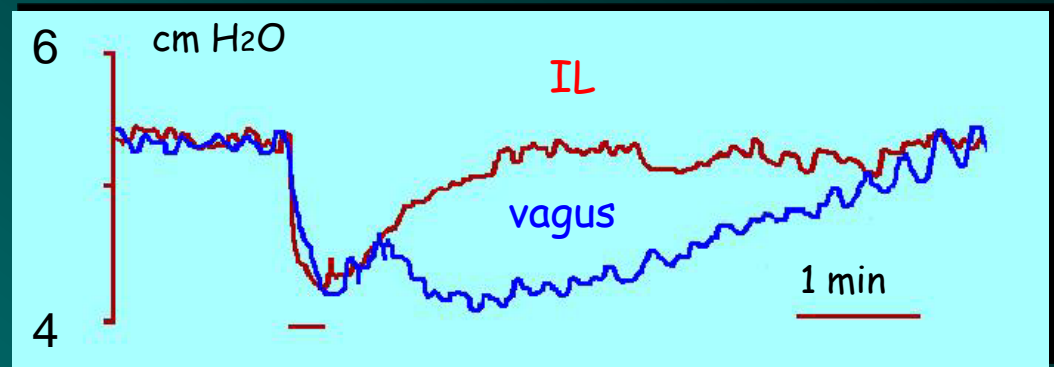
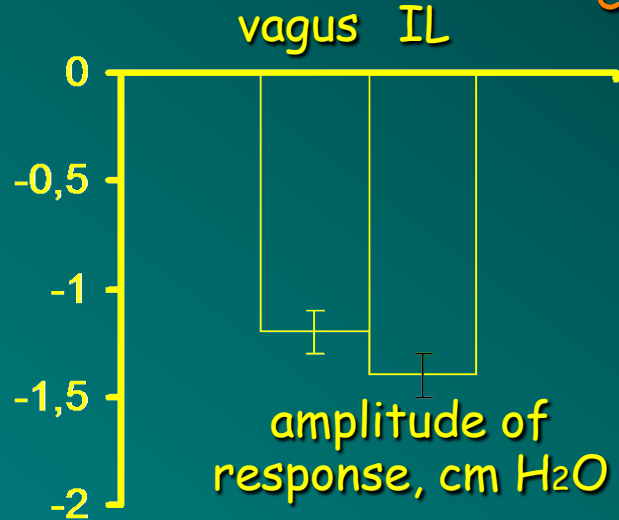
Stimulation of the cervical vagus (CV) also resulted in a predominantly inhibitory gastric motor responses, a like relaxation



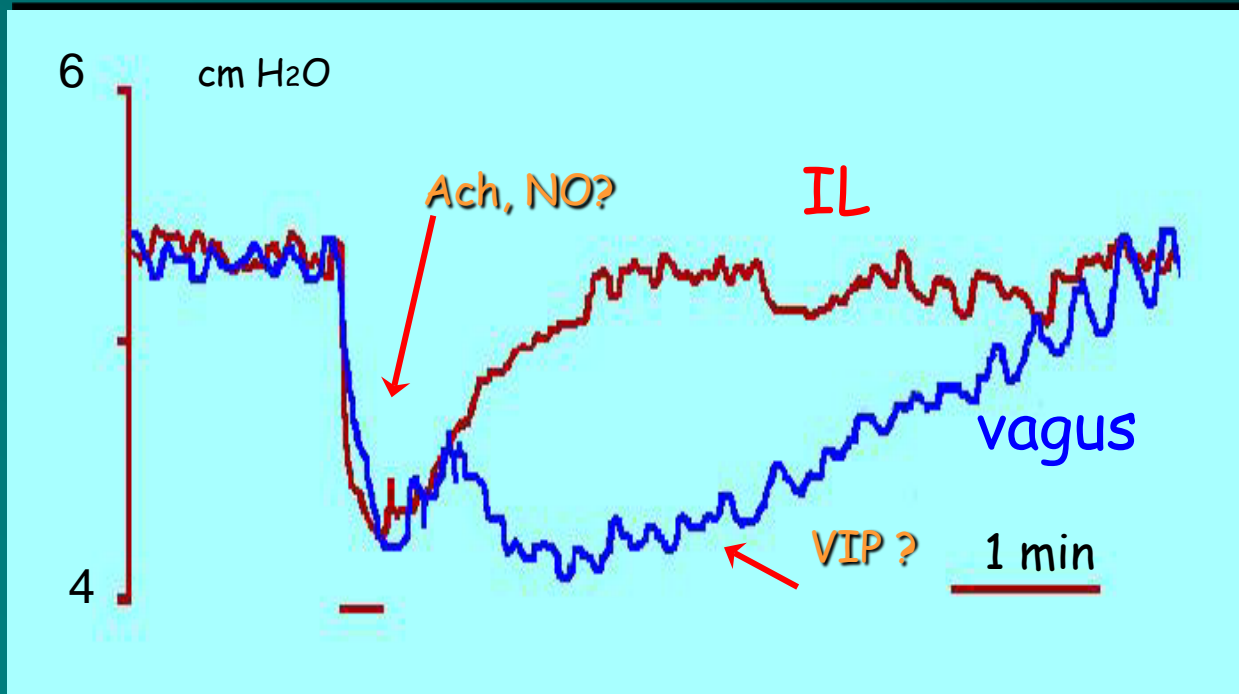
At comparable amplitudes the gastric relaxations to vagal and IL stimulation showed very different time courses.



The the mean data for amplitude, time to nadir and half recovery time of gastric responses to CV (blue columns) and IL cortex (yellow columns) stimulation



The comparison of gastric relaxations showed that initial phase of CV induced response is very similar to gastric response to IL stimulation.



The most likely:

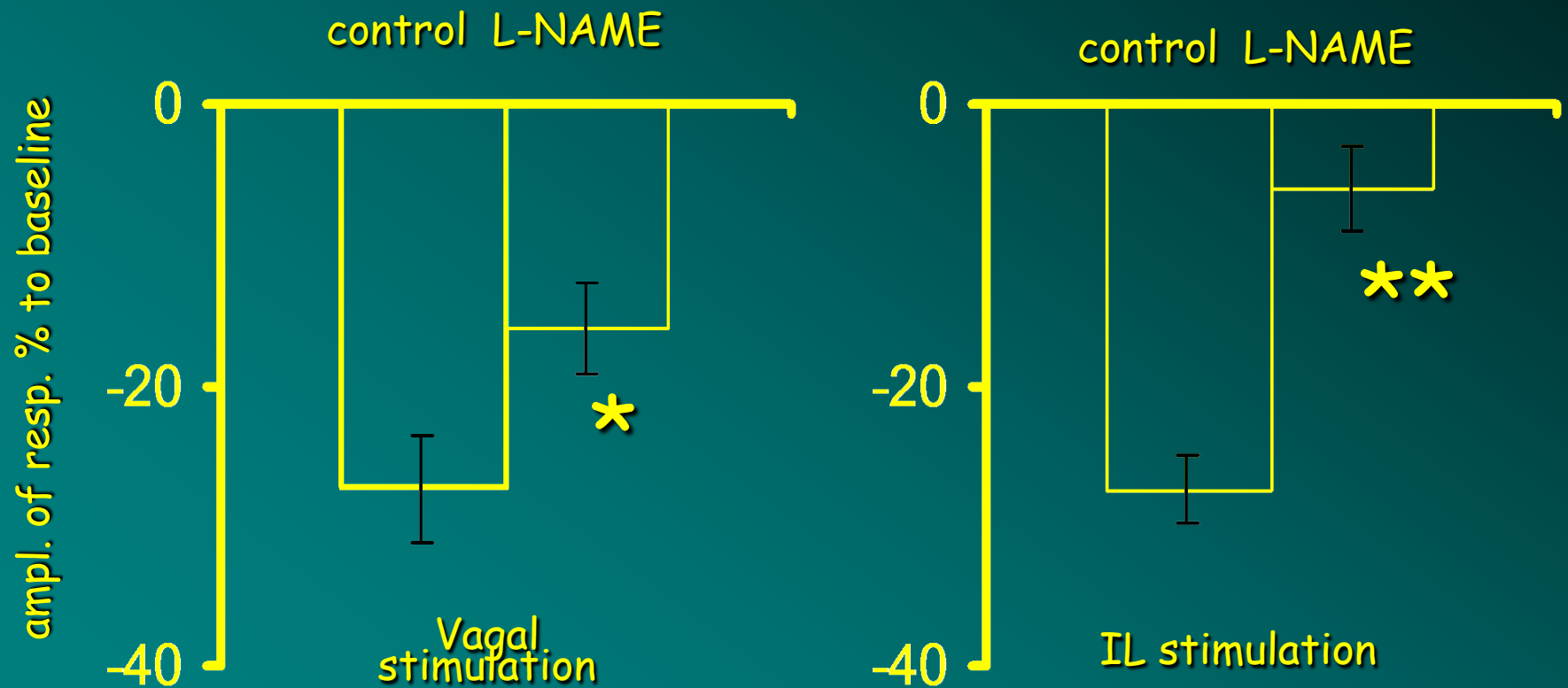
I - phase is related to Ach, NO-ergic mechanisms

II - phase is, probably, related to VIP-ergic mechanism

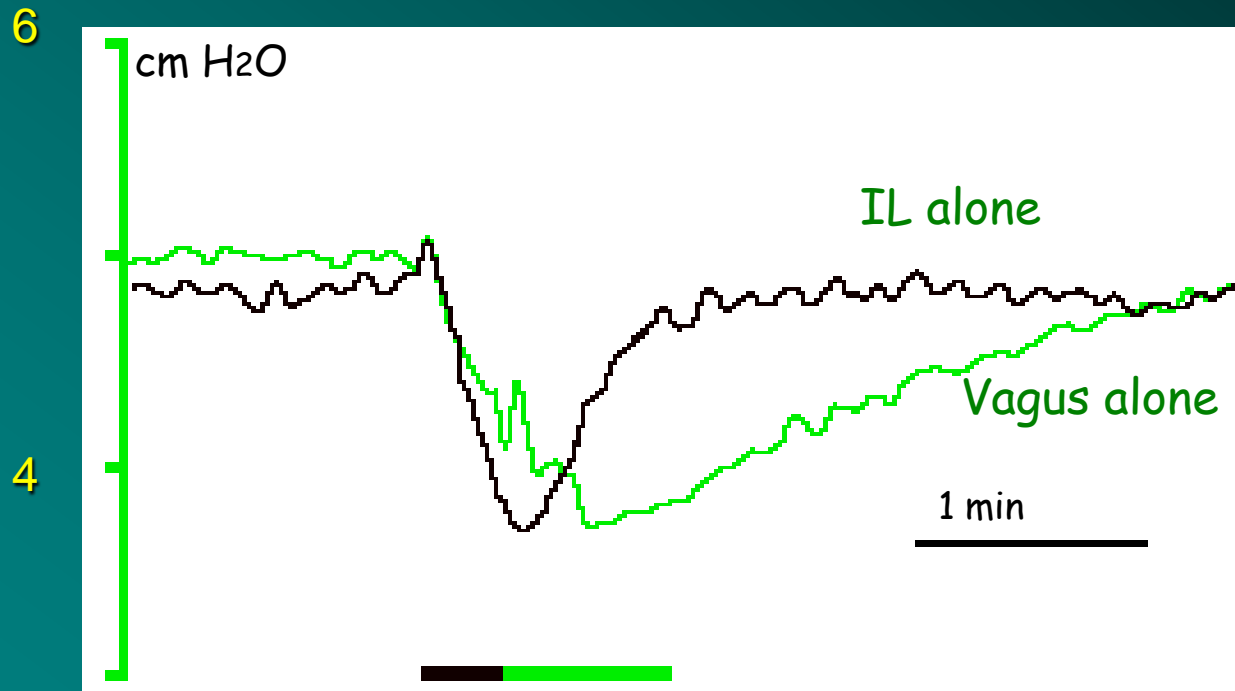
*(Grundy et al., 1993)*



The mean data for amplitude of gastric responses to CV (blue columns) and IL stimulation (yellow columns) before and after L-NAME administration (10 mg/kg, iv).

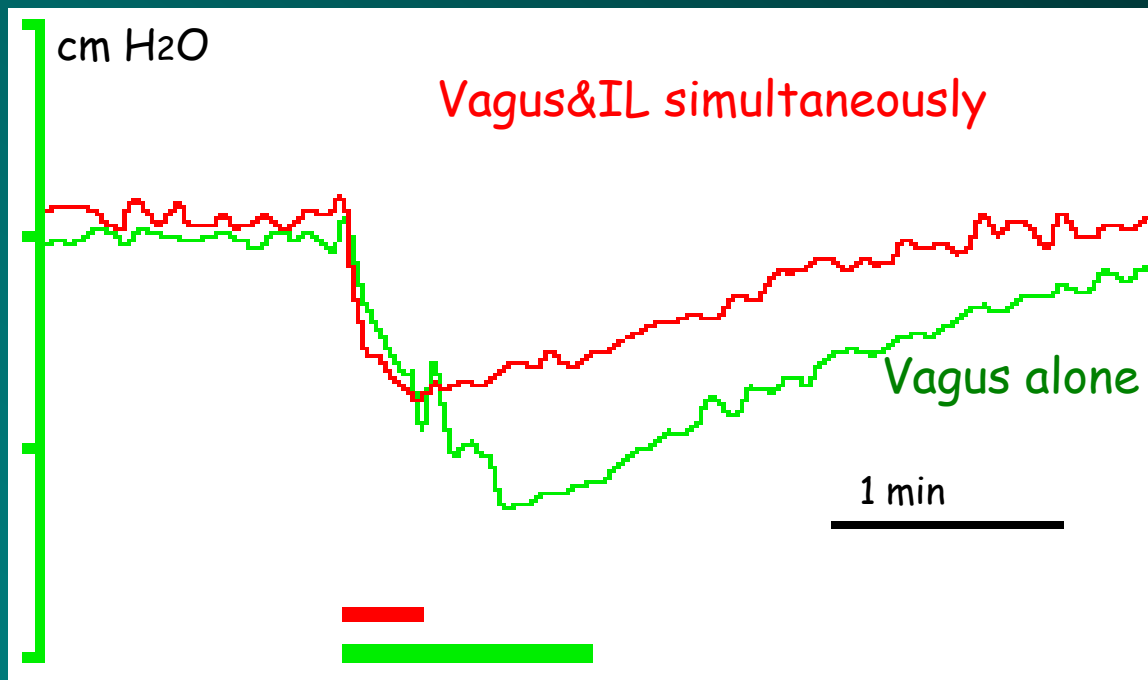


The superposition of gastric responses to IL (black line) and CV (green line) stimulation obtained from one animal



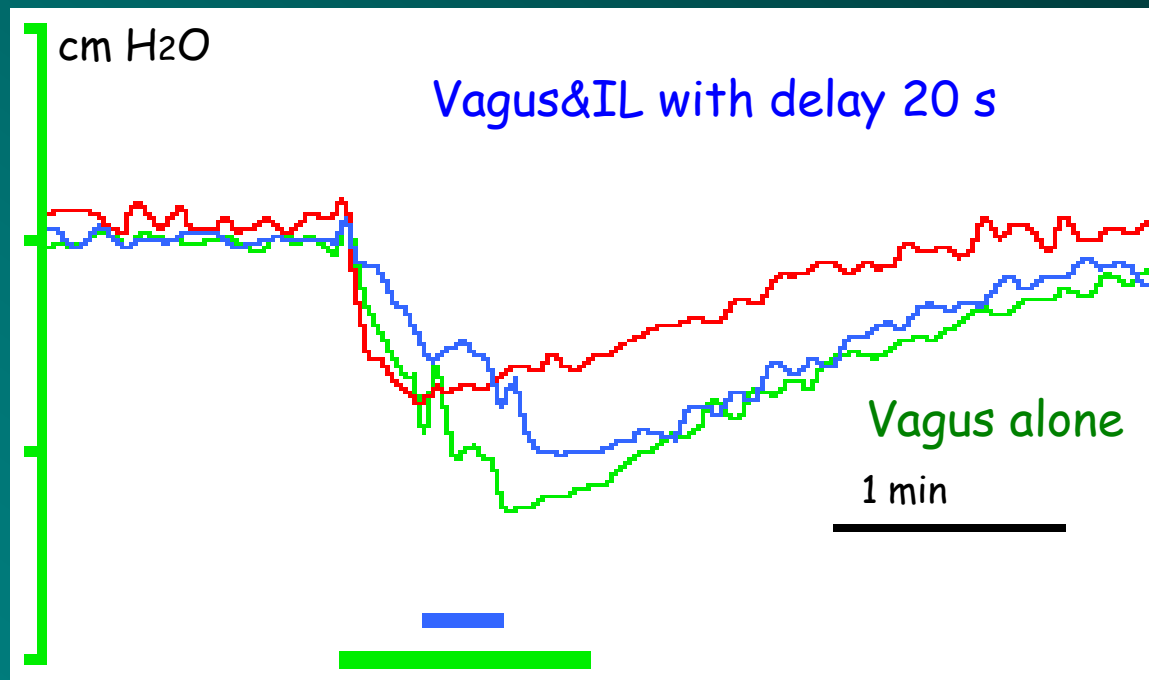
# The superposition of gastric responses to simultaneously applied IL&CV (red line) versus CV (green line) stimulations

6

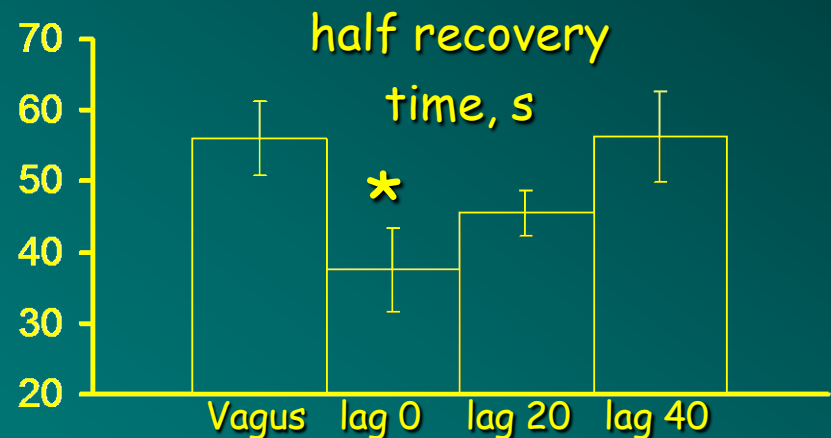
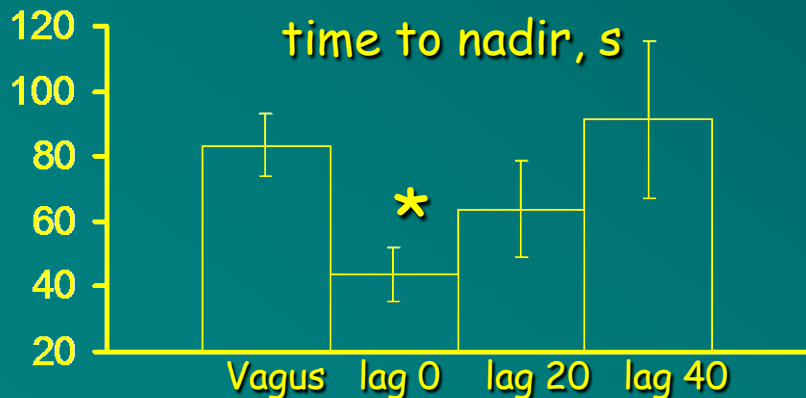
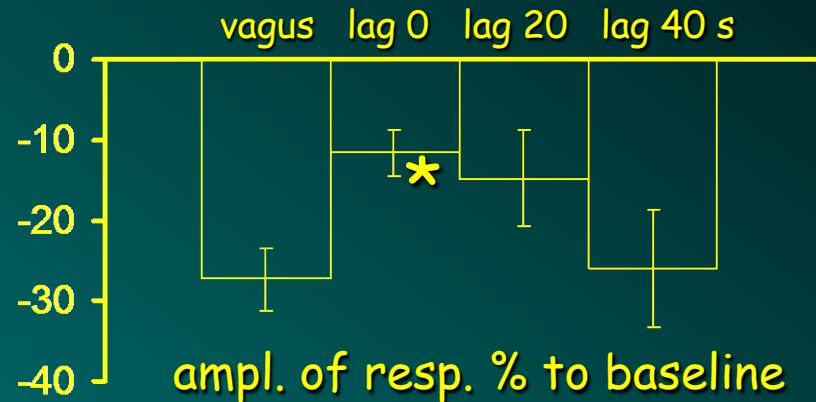
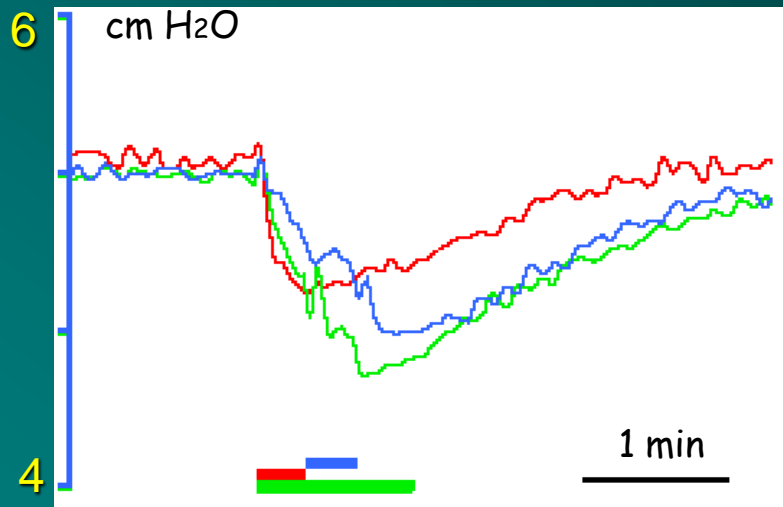


# The superposition of gastric responses to delayed IL&CV (blue line) versus CV (green line) stimulations

6



The mean data for amplitude, time to nadir and half recovery time of gastric responses during simultaneous stimulation of CV and IL cortex.



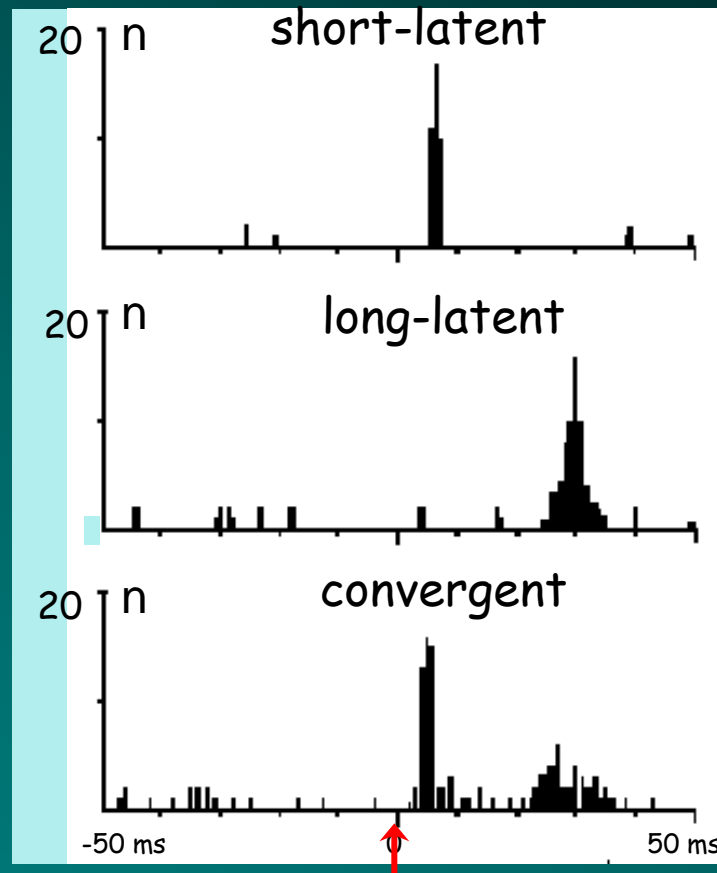
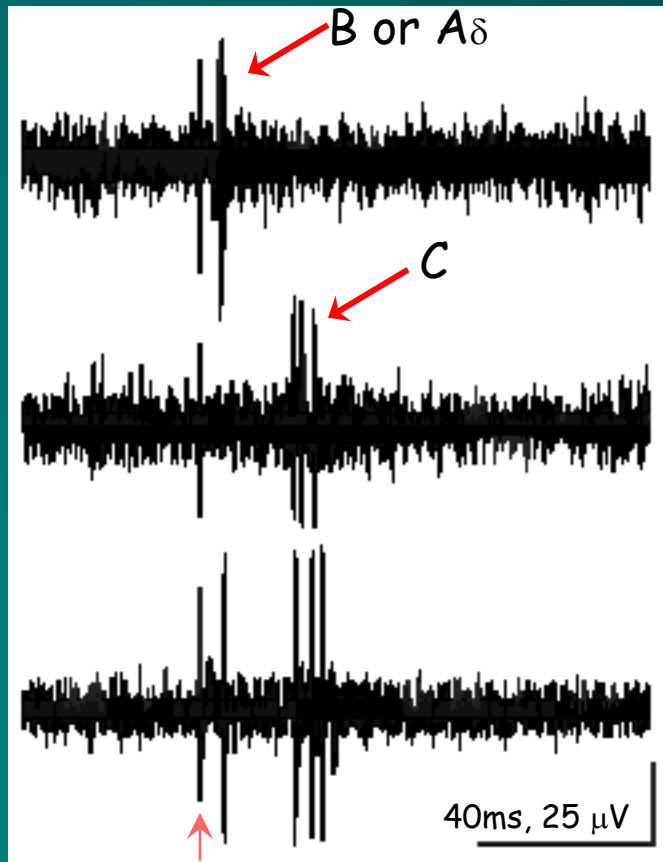
## In summary:

- ✓ The most profound intragastric pressure changes are induced by IL stimulation.
- ✓ Gastric responses to both stimuli are mediated by vagus nerve and include cholinergic and NO-ergic components.
- ✓ Vagal and IL stimulation evoke different profiles of intragastric pressure response.
- ✓ IL stimulation exerts an inhibitory influence of vago-vagal reflexes, probably via NO-dependent ways
- ✓ The more profound IL action to CV induced gastric relaxation was observed when onsets both of stimuli were simultaneous.



# The nTS neurons showed to CV stimulation three types of responses

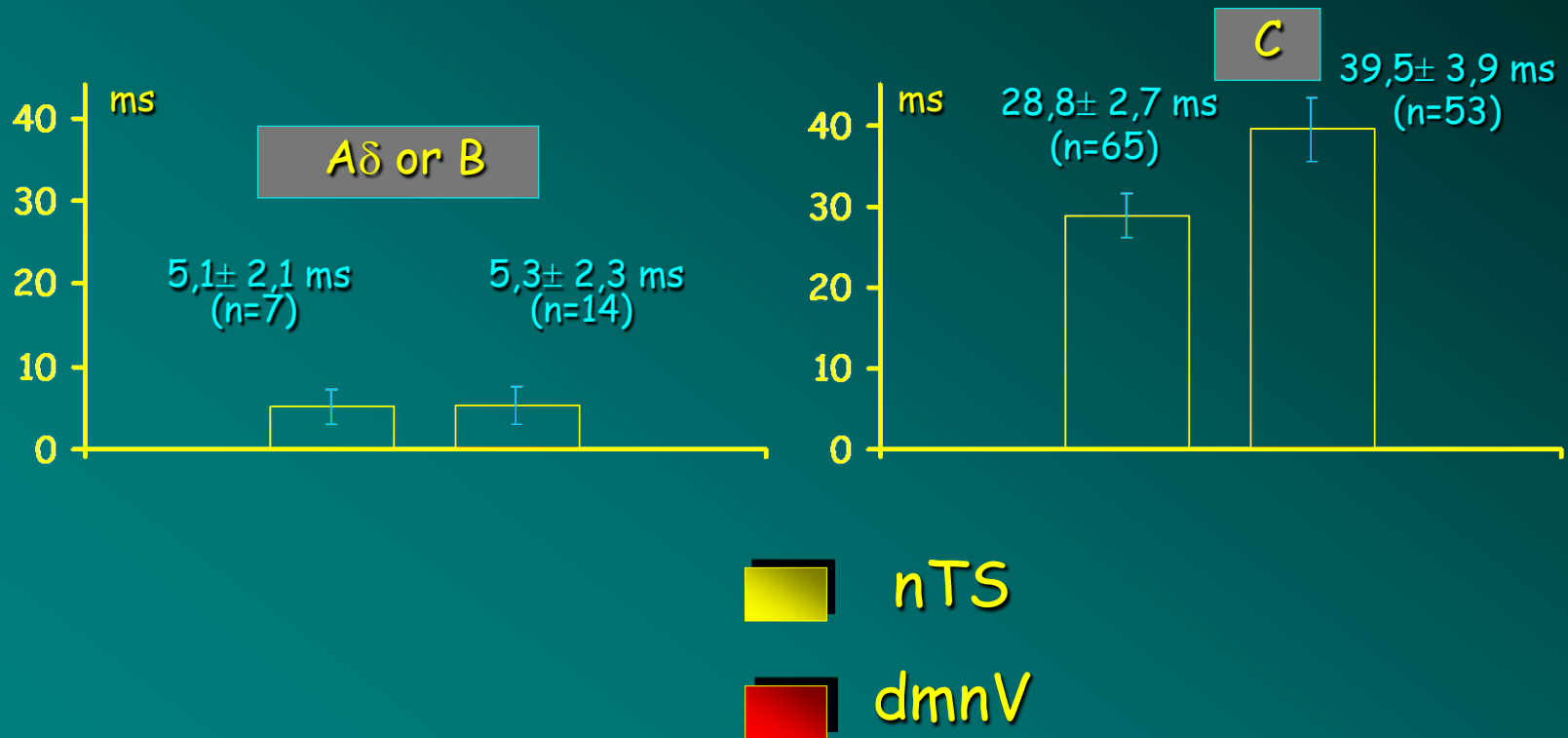
Correspond to  
conduction  
velocity



$3,1 \pm 0,5$   
m/s

$0,6 \pm 0,1$   
m/s

# The mean latencies of the nTS and dmV neuron responses to CV stimulation

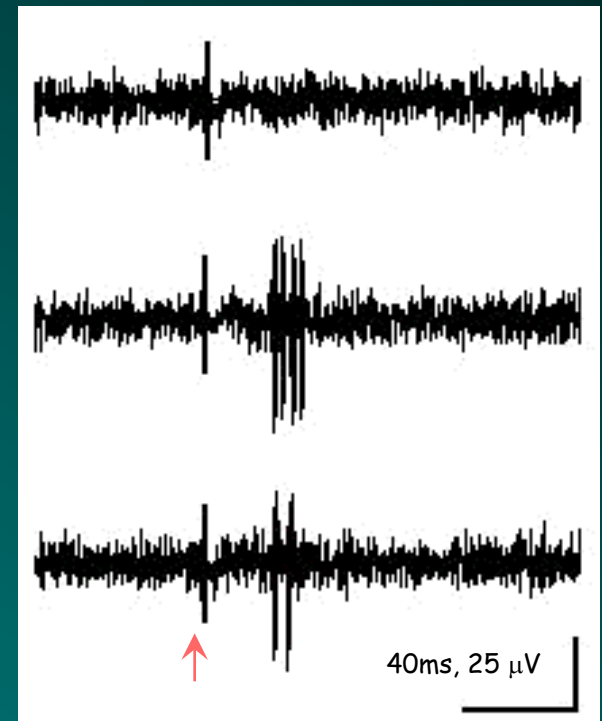


# The IL stimulation can facilitate and inhibit the nTS neuron responses to CV stimulation

IL  
vagus  
IL&vagus

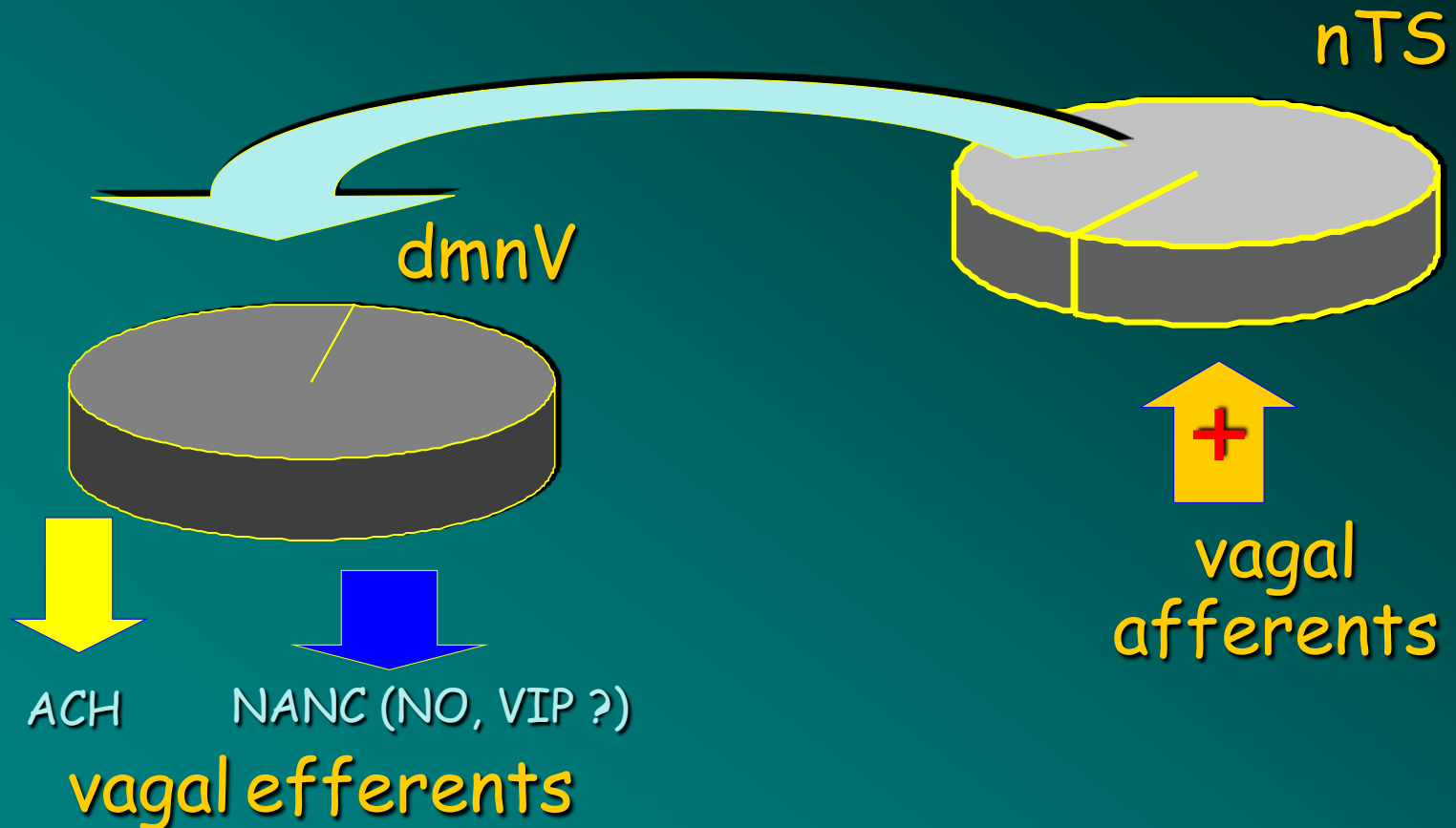


facilitation

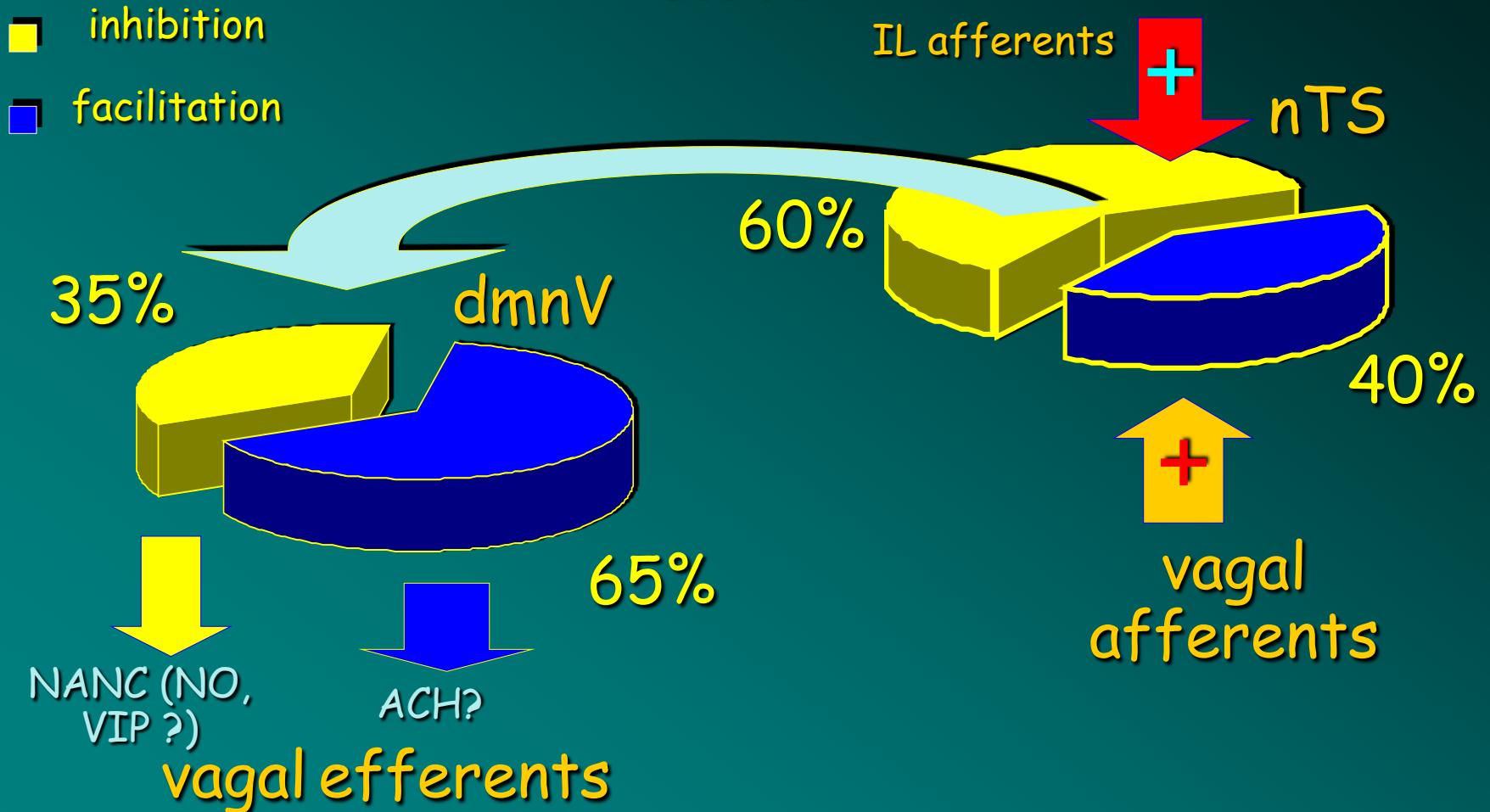


inhibition

# The simplified scheme of the possible mechanism of gastric vago-vagal reflexes modulation by IL cortex



# The simplified scheme of the possible mechanism of gastric vago-vagal reflexes modulation by IL cortex



# Summary

- Descending nervous pathways from IL cortex influence transmission through vagal reflex pathways at the level of the nTS and dmV
- The characteristics of gastric relaxatory responses reflect the individual patterns of preganglionic input to the enteric nervous system via cholinergic and non-cholinergic vagal pathways
- Due to interaction between corticofugal and vagal inputs to nTS neurones, the pattern of efferent output can be changed to produce a different end-organ response.