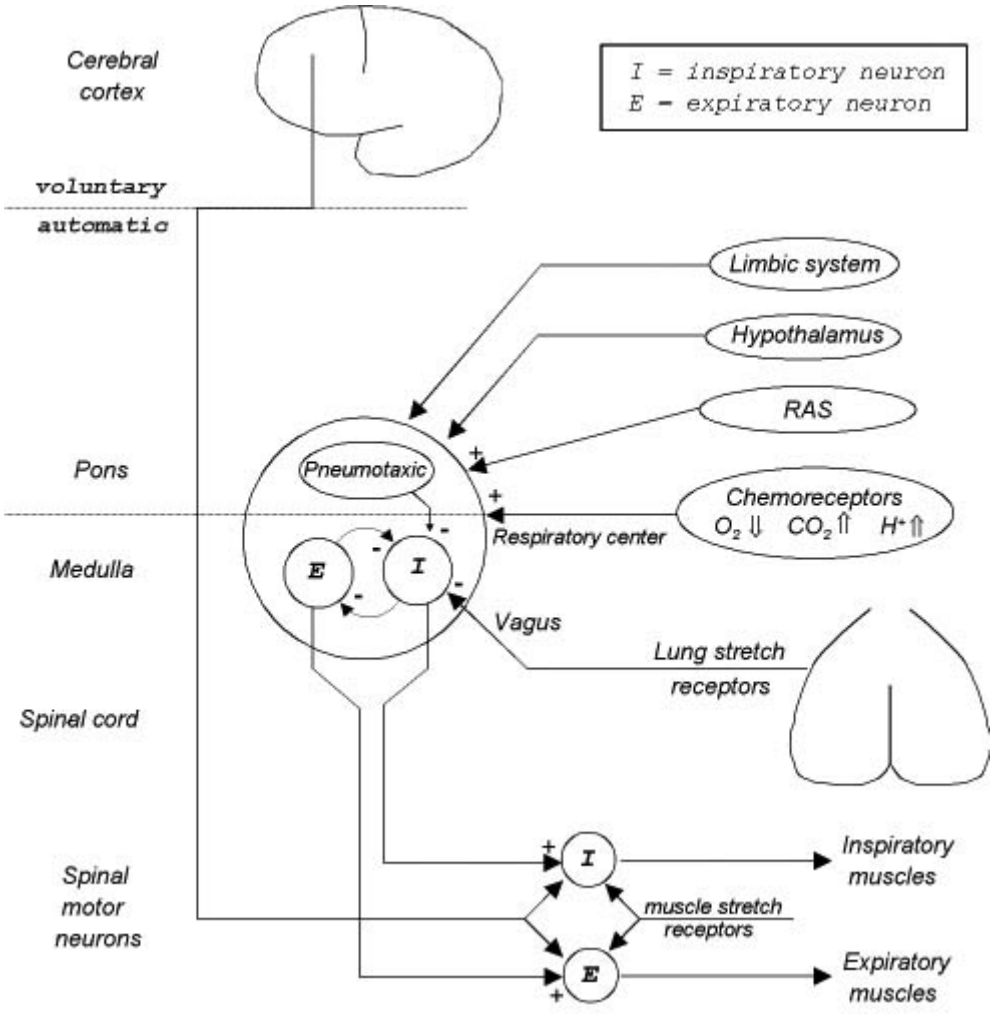
NEUROGENESIS OF RESPIRATION

A. Introduction

1. Neurogenesis define: function of CNS structures responsible for establishing the basic respiratory rhythm

2. Terms:

apnea	no ventilation
hyperpnea	high frequency of ventilation
hypoventilation	insufficient ventilation for metabolic needs; indicated by $P_{A\text{-}CO2} > 42$ mmHg
hyperventilation	excess ventilation in relation to metabolic needs; indicated by $P_{A\text{-}CO2} < 38$ mmHg
dyspnea	subjective sensation of difficulty in breathing; generally indicates the physiological demand for ventilation exceeds the person's ability to respond



NEUROGENESIS OF RESPIRATION

A. Introduction (continued)

3. Two neurogenic systems (both CNS)

a. involuntary (automatic): involve medulla, pons, limbic system (emotional responses), hypothalamus (temperature regulation), and other subcortical structures

b. voluntary: involve cerebral cortex

Note 1: systems independent
Note 2: both systems require intact innervation of respiratory muscles (alpha motoneurons)
Note 3: the muscles of respiratory ventilation are controlled by the somatic motor system, not the autonomic system (the autonomic system controls airway smooth muscle contraction and secretion)

B. Medulla (Respiratory Center)

1. anatomy: two groups of cells
   a. inspiratory (I) neurons; control muscles of inspiration
   b. expiratory (E) neurons; control muscles of expiration

2. necessary for respiration: destruction leads to immediate and permanent cessation of automatic respiration

3. sufficient for respiration: even when isolated from other neural inputs (by section of higher structures and vagus nerve), can support a relatively normal pattern of ventilation

4. the inspiratory and expiratory neurons exhibit reciprocal innervation (mutually inhibitory)

5. deficits of the isolated respiratory center in controlling ventilation include

ataxic (irregular) breathing

poor adjustment to varying body needs

C. Lung Stretch Receptors

1. afferent endings (mechanoreceptors) in airway smooth muscle; stimulus is lung volume increase

2. associated with a variety of reflexes, the best studied of which is:

3. Hering-Breuer Reflex

a. initiated by increasing lung volume

b. afferent pathway is via the vagus nerve

c. action: inhibit further inspiration

d. role: aid in establishing uniform pattern of respiration, particularly in deep inspiration

NEUROGENESIS OF RESPIRATION (continued)

D. Pneumotaxic Center

1. Located in the pons (rostral to the medulla)

2. Appears to inhibit “I” neurons of the respiratory center

3. Function of pneumotaxic center: aid in establishing the normal respiratory rhythm; prevents apneustic breathing (sustained inhalation with occasional expiratory gasps)

E. Reticular Activating System (RAS)

1. Located in the reticular system of the brain stem; activity associated the “awake” or “conscious” state

2. When active, simulates respiratory ventilation

3. When RAS activity is reduced, as during sleep, ventilation is reduced and $P_{A\text{-}CO2}$ increases by a few mmHg

   a. Sleep Apnea: in some individuals, ventilation ceases temporarily (10+ seconds) during sleep

   b. types of sleep apnea

      1) central apnea: reduced CNS respiratory drive

      2) obstructive apnea: increased upper airway resistance (laryngospasm and/or bronchospasm)

   c. in infants, can lead to SIDS (Sudden Infant Death Syndrome)

4. RAS may be an important drive in individuals with decreased spontaneous Respiratory Center activity (drug overdose, Ondine's Curse)

F. Other Neural Structures

1. Hypothalamus: change in respiration associated with temperature regulation (not important in humans)

2. Limbic System: respiratory changes in emotion

3. Cerebral cortex: voluntary control (limited), learning

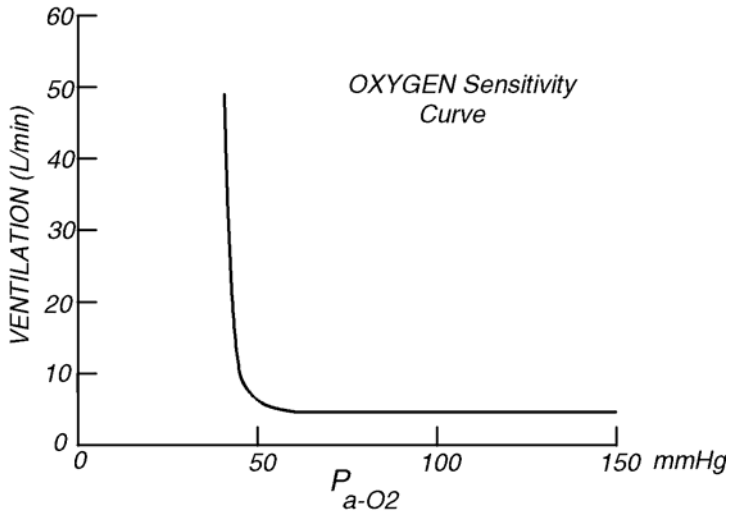
4. Irritant receptors: airway receptors responding to inhaled irritating substances; cause hyperpnea and bronchoconstriction

5. Respiratory muscle spindle receptors and joint receptors; may contribute to respiratory drive in exercise

CHEMICAL REGULATION OF VENTILATION (Note: examples of homeostasis by negative feedback)

A. Oxygen

1. Response as a function of P_{a-O2}



a. relatively small effect in the normal range (P_{a-O2} > 70 mmHg)

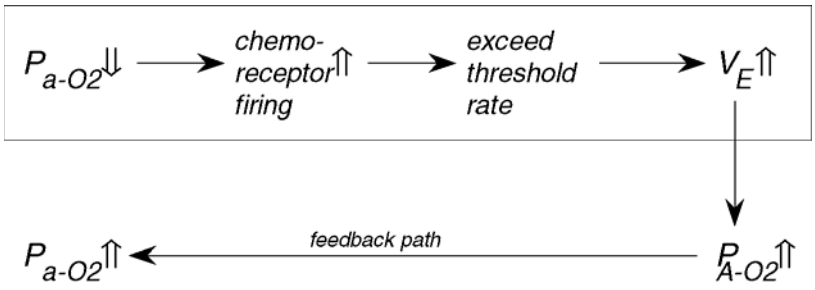
b. only important in pronounced hypoxemia (P_{a-O2} < 60 mmHg)

c. high P_{a-O2} does not depress ventilation (except for chronic hypercapnia – high blood CO2)

2. Receptors: carotid (mainly) and aortic oxygen-sensitive chemoreceptors in carotid and aortic bodies

3. Stimulus: $P_{a-O2} \downarrow$

4. Regulation schematic:



5. Physiological significance

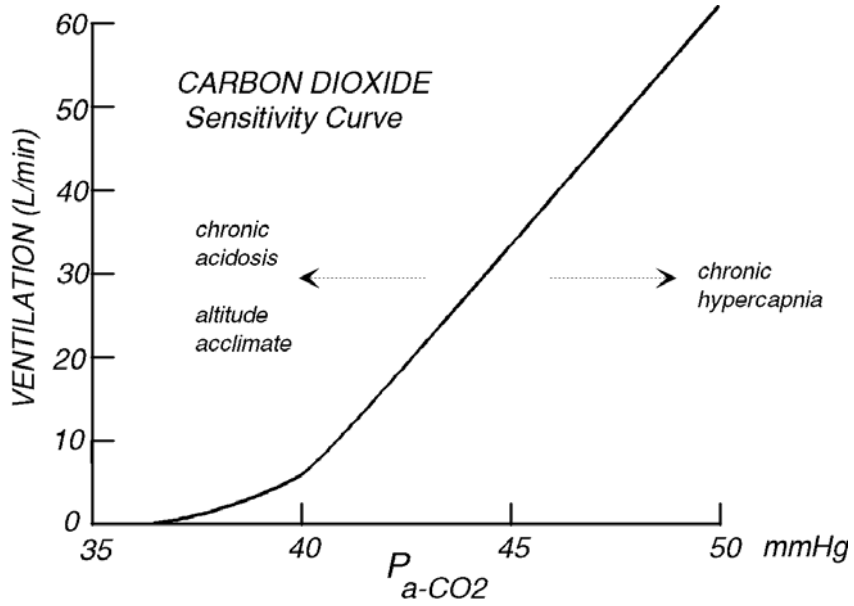
a. homeostatic: helps maintain P_{a-O2} in conditions of severe hypoxia

b. remains when other chemostimulation is lost (e.g. deep anesthesia)

CHEMICAL REGULATION OF VENTILATION (continued)

B. Carbon Dioxide

1, Response as a function of $P_{a\text{-}CO2}$



a. very large effect

b. sensitive in the normal range (≅ 40 mmHg)

c. low $P_{a\text{-}CO2}$ depresses ventilation

d. very high CO_2 is a respiratory depressant

2. Afferent receptors

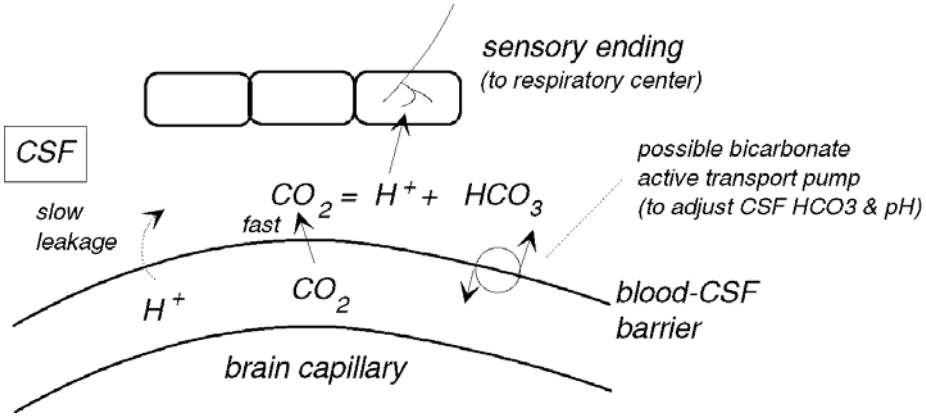
In the CNS near the ventral surface of the medulla, close to the respiratory center; affected by cerebro-spinal fluid (CSF)

3. Stimulus:

H^+ of CSF, which is in turn controlled by P_{CO2} of blood, and, to a smaller extent, blood pH

CHEMICAL REGULATION OF VENTILATION (continued)

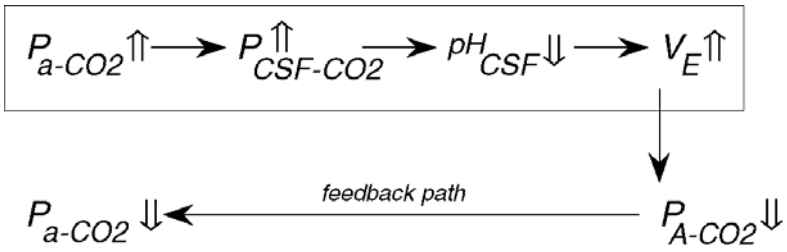
B. Carbon Dioxide (continued)



Note 1: blood-brain (and blood-CSF) barrier permits CO_2 to equilibrate rapidly but is only slowly permeable to H^+

Note 2: CO_2 response due mainly to changes in CSF pH but changes in arterial pH also contribute due to the effect of P_{CO2} on blood pH (see next section)

4. Regulation schematic:



5. Physiological significance

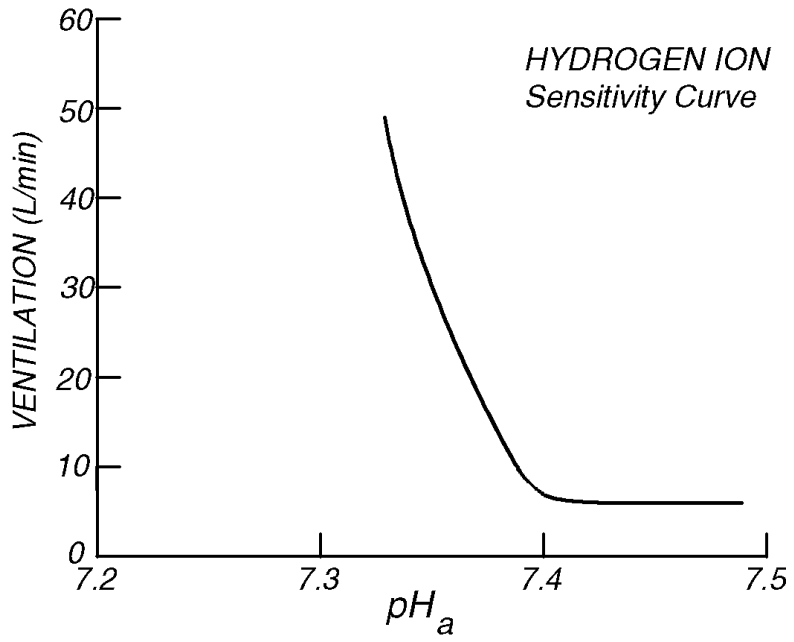
   a. homeostatic: maintains $P_{a\text{-}CO2}$ within the normal range (38-42 mmHg), thus

   b. helps maintain brain pH constant

CHEMICAL REGULATION OF VENTILATION (continued)

C. Hydrogen Ion

1. Response as a function of pH_a



   a. appreciable effect

   b. especially marked at acid pH

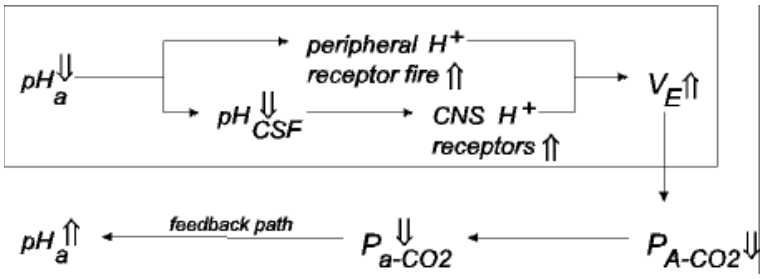
2. Afferent endings

   a. carotid body and aortic body H^+ sensitive receptors (rapid response)

   b. CNS medullary H^+ receptors (slow H^+ leakage across the blood-brain barrier, so slow response)

3. Stimulus: pH_a (and pH_{CSF})

4. Regulation schematic



5. Physiological significance

   a. Contributes to maintaining blood pH in the normal range through control of respiratory ventilation