



Dyspnea in cancer patients

Session 17: Dyspnea: Novel strategies for evaluation and management

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Faculty Disclosure

Nothing to disclose

Dyspnea: Outline

1. Definitions and impact of dyspnea in cancer
2. Mechanisms of dyspnea
3. Causes of dyspnea in cancer

Dyspnea

- 20-40% of cancer patients present with dyspnea at diagnosis and up to 70% cancer patients experience dyspnea in the last 6 weeks of life.¹
- Definition: a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity and derives from the interaction among physiological, psychological, social, and environmental factors.²

1. Hui, D. 2012 *J Pall Med*; 16(3):274-280

2. ATS consensus statement. 1999 *AJRCCM*; 159:321-340

Subtypes of dyspnea

Subtype	Mechanisms	Examples	Possible treatment
Work of Breathing	Activity of cerebral motor cortex (corollary activation)	Pleural effusion Neuromuscular disease	Drainage NIV
Tightness	Stimulation of airway receptors	COPD/ asthma/ Malignant airway obstruction	Bronchodilators Steroid Airway stent
Air hunger Insufficient respiration	Chemoreflex activity	Pneumonia Pneumonitis Hyperinflation	Antibiotics Steroids? NIV
Tachypnea	Stimulation of pulmonary C fibers	Vascular congestion Interstitial lung disease	Opioids HF oxygen

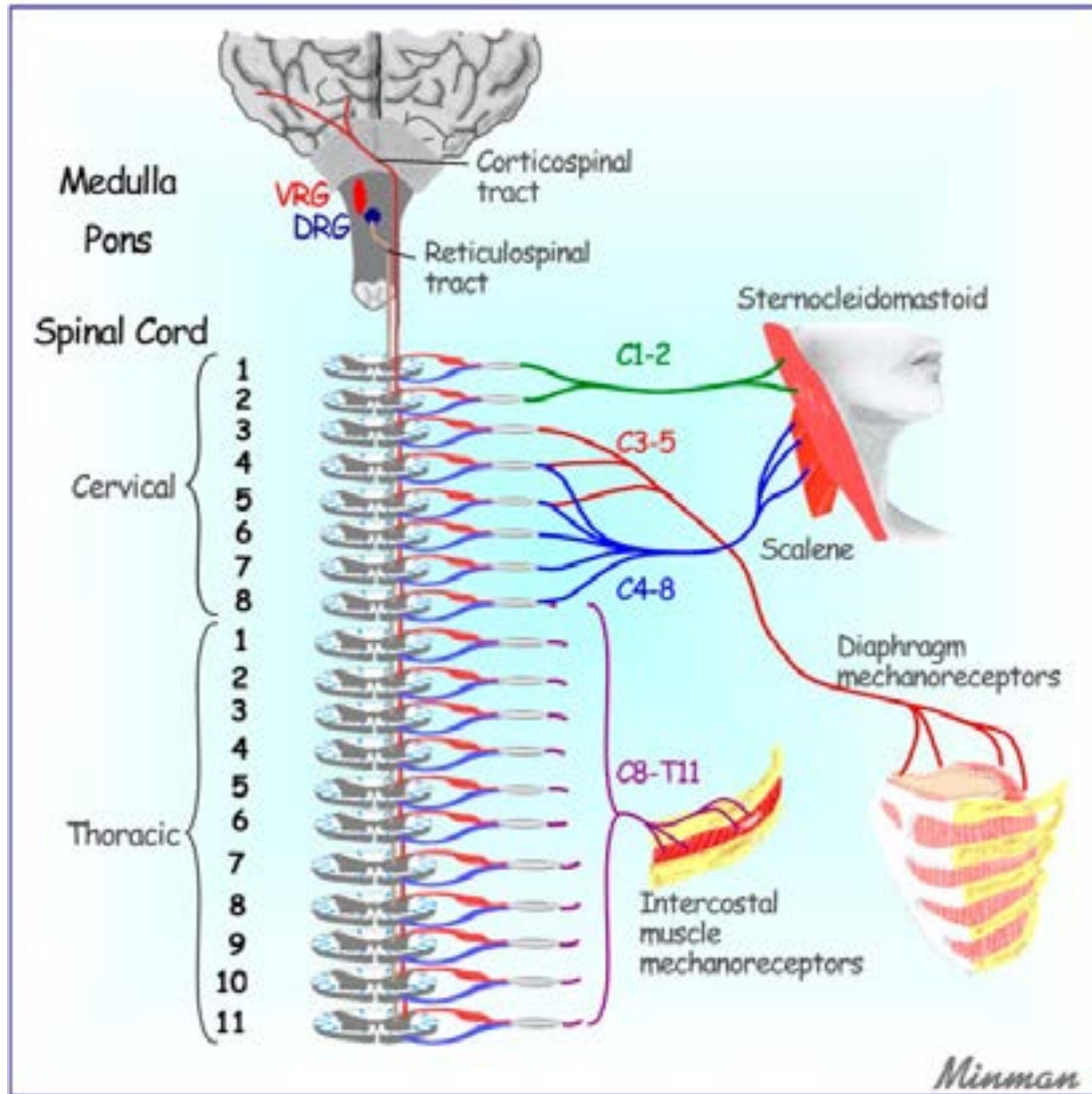
Dyspnea

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- Definition: a subjective experience of breathing discomfort that consists of qualitatively distinct sensation that vary in intensity and derives from interaction among physiological, psychological, social, and environmental factors.²
- Leads to physical impairment and adversely affects quality of life and mortality.
- Treat reversible causes and palliate those that are irreversible

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Mechanisms of Dyspnea



Afferent information from the respiratory muscles

Stretch/ muscle tension
Lung volume

Transferred back through the anterior horn cells in the spinal cord to the pontine/medullar respiratory center and to the somatosensory cortex.

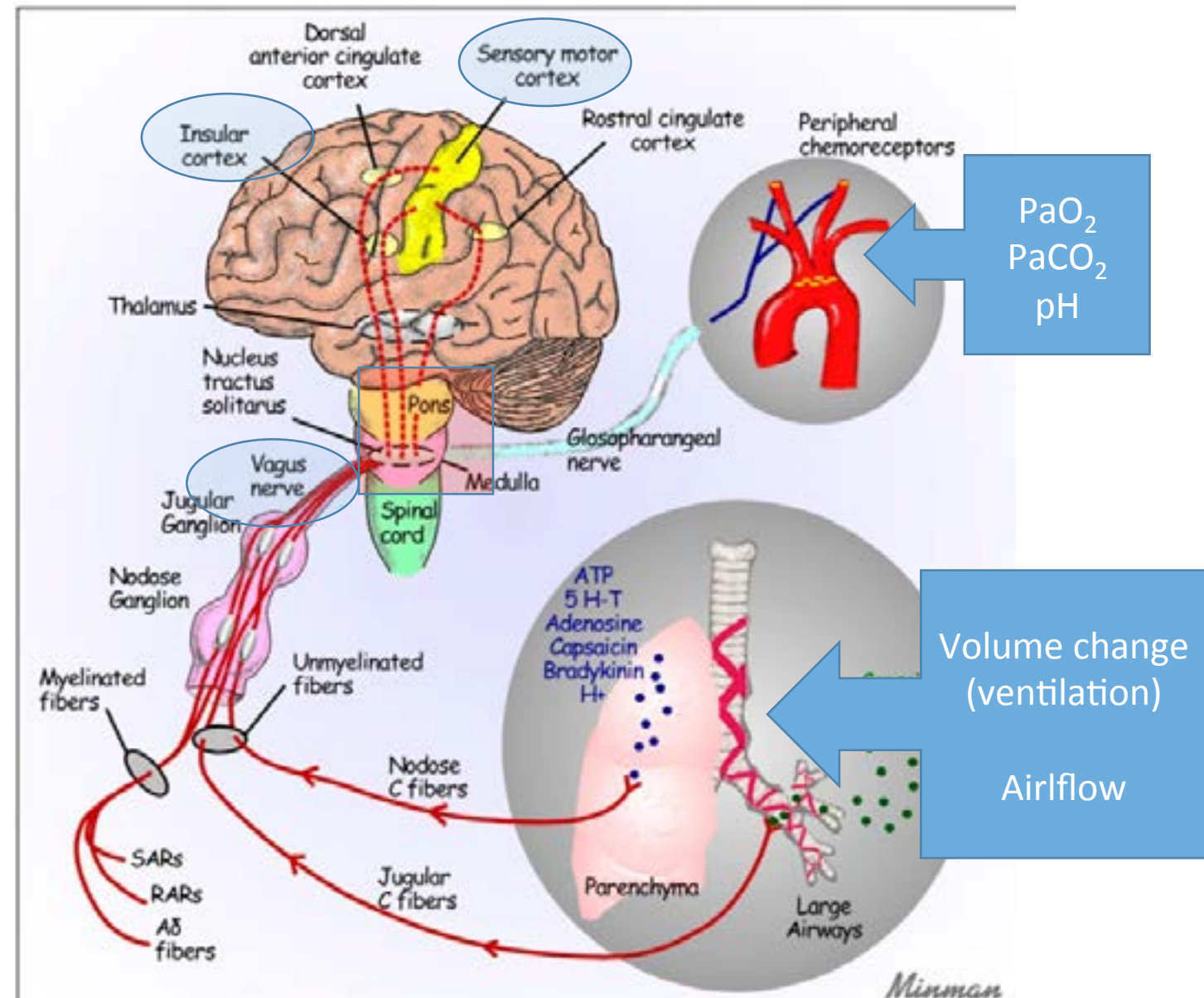
Measure effort (work of breathing)

Mechanisms of Dyspnea

Peripheral and central chemoreceptors. Project to the ponto-medullary respiratory centers (PMRC)

Pulmonary C fibers carry information from the lung parenchyma, airways and pulmonary vasculature via the vagus nerve to the PMRC and via the thalamus the sensory motor cortex and insular cortex.

The imbalance between central neural output which does not produce the expected result (airflow or ventilation) monitored by the receptors in the muscles and pulmonary system generates the sensation of dyspnea



Mechanisms of dyspnea: fMRI

Insular cortex

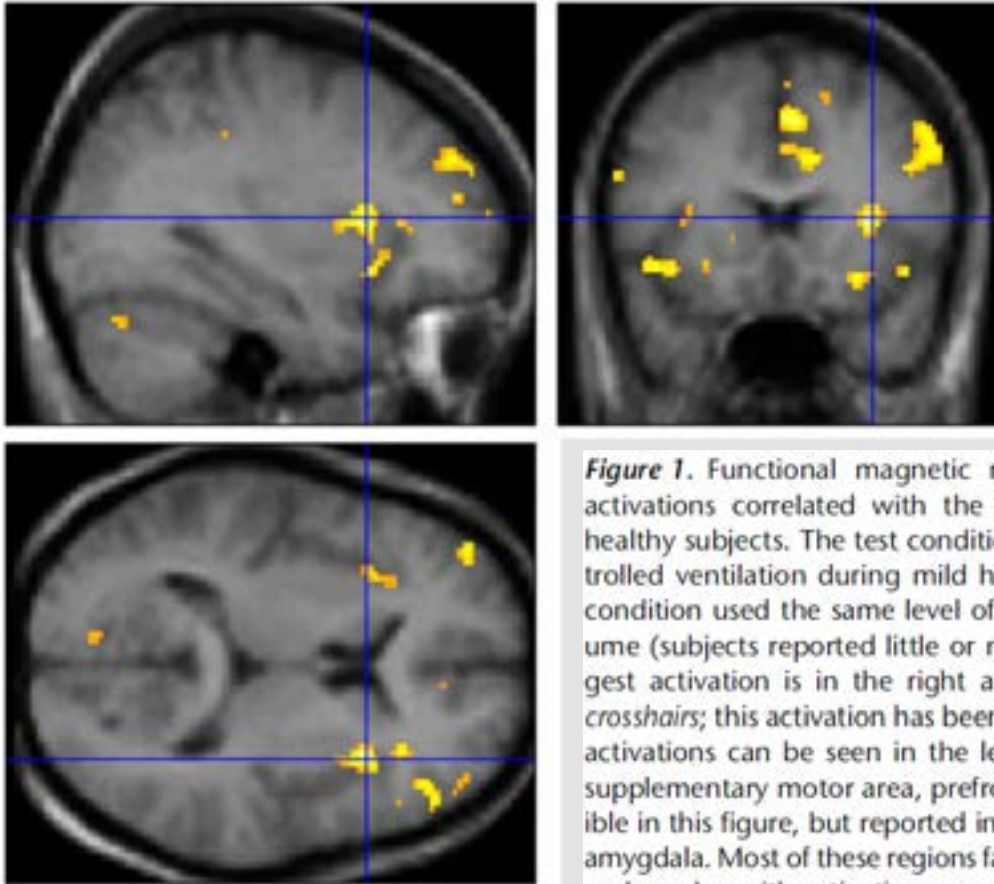


Figure 1. Functional magnetic resonance images showing cerebral activations correlated with the experience of strong air hunger in healthy subjects. The test condition consisted of low tidal volume controlled ventilation during mild hypercapnia; the baseline comparison condition used the same level of hypercapnia but with high tidal volume (subjects reported little or no discomfort at baseline). The strongest activation is in the right anterior insula, indicated by the *blue crosshairs*; this activation has been shown in a number of studies. Other activations can be seen in the left anterior insula, anterior cingulate, supplementary motor area, prefrontal cortex, and cerebellum. Not visible in this figure, but reported in the same study was activation of the amygdala. Most of these regions fall in the category of limbic/paralimbic, and overlap with activations seen during pain, thirst, fear, and hunger. Reproduced and adapted with permission from Reference 137.

The dyspneic patient: COPD

Tightness

Increased work of breathing

Tachypnea

Air hunger

Distress

Increased effort due to airway resistance and disadvantaged chest wall geometry lead to afferent feedback

Deconditioning of muscles leads to increase metabolic byproducts (lactate breath)

As ventilatory drive increases and outweighs capacity, the patient is no longer able to meet respiratory demands. Receptors (chemoreceptors, proprioceptors) signal air hunger.

Input to/from the limbic system increase anxiety and emotional responses and over time, chronic symptoms impact quality of life

The dyspneic patient: COPD

Tightness

Increased work of
breathing

Tachypnea

Air hunger

Distress

Interplay of neurophysiological mechanisms

Interplay and overlap between subtypes

Individual considerations

Multifaceted approach

Domains of dyspnea

Domains of dyspnea measurement

Domain	Definition
Sensory–perceptual experience	Measures of what breathing feels like to the patient or research subject.
Affective distress	Measures of how distressing breathing feels. Focus can be either immediate (e.g. unpleasantness) or evaluative (e.g., judgments of meaning or consequences).
Symptom impact or burden	Measures of how dyspnea/ breathlessness affects functional ability, employment (disability), quality of life, or health status.

Causes of dyspnea in cancer patients

Directly related to cancer	Related to cancer therapy
Primary/metastatic parenchymal lung involvement Airway obstruction (intrinsic or extrinsic tumor) Carcinomatous lymphangitis Pleural tumor Malignant pleural effusion Pericardial effusion Superior vena cava syndrome Tumor microemboli Phrenic nerve paralysis Atelectasis Tracheal-oesophageal fistula Chest-wall invasion (carcinoma en cuirasse) Pathological chest-wall fractures	Surgery (after lobectomy or pneumonectomy) Radiation pneumonitis Chemotherapy-induced pulmonary fibrosis Chemotherapy-induced cardiomyopathy
Indirectly related to cancer	Unrelated to cancer
Pneumonia Cachexia Anaemia Electrolyte abnormalities Pulmonary embolus Paraneoplastic syndromes	Chronic obstructive pulmonary disease Asthma Congestive heart failure Cardiac ischaemia Arrhythmias Pulmonary vascular disease Obesity Neuromuscular disorders Aspiration Anxiety Pneumothorax Interstitial lung disease Psychosocial/spiritual pain

Causes of dyspnea

Potential causes of dyspnea^b

Airway lesion	24 (8)
Lung parenchymal metastasis	125 (42)
Lymphangitic carcinomatosis	25 (8)
Pulmonary embolism	12 (4)
Pneumonia	145 (48)
Pleural effusion	166 (56)
Heart failure	8 (3)
Tamponade	2 (1)
Anemia (<11 g/L)	232 (78)
Metabolic acidosis	3 (1)
Atelectasis	121 (41)
Pericardial effusion	26 (9)
Chronic obstructive pulmonary disease	29 (10)
Pneumothorax	7 (2)
Pulmonary fibrosis	7 (2)
Others	9 (3)

Airway

Parenchymal

Pleural/ Chest wall

Neuromuscular

Vascular

Metabolic

Hemoglobin

Reversible or

Irreversible?

