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Review

# Understanding dyspnea as a complex individual experience☆

Anja Hayen*, Mari Herigstad, Kyle T.S. Pattinson

*Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, Oxford, OX3 9DU, United Kingdom*

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ABSTRACT

Dyspnea is the highly threatening experience of breathlessness experienced by patients with diverse pathologies, including respiratory, cardiovascular, and neuromuscular diseases, cancer and panic disorder. This debilitating symptom is especially prominent in the elderly and the obese, two growing populations in the Western world. It has further been found that women suffer more strongly from dyspnea than men. Despite optimization of disease-specific treatments, dyspnea is often inadequately treated. The immense burden faced by patients, families and the healthcare system makes improving management of chronic dyspnea a priority.

Dyspnea is a multidimensional sensation that encompasses an array of unpleasant respiratory sensations that vary according to underlying cause and patient characteristics. Biopsychological factors beyond disease pathology exacerbate the perception of dyspnea, increase symptom severity and reduce quality of life. Psychological state (especially comorbid anxiety and depression), hormone status, gender, body weight (obesity) and general fitness level are particularly important. Neuroimaging has started to uncover the neural mechanisms involved in the processing of sensory and affective components of dyspnea.

Awareness of biopsychological factors beyond pathology is essential for diagnosis and treatment of dyspnea. Increasing understanding the interactions between biopsychological factors and dyspnea perception will enhance the development of symptomatic treatments that specifically address each patient's most pressing needs at a specific stage in life. Future neuroimaging research can provide objective markers to fully understand the role of biopsychological factors in the perception of dyspnea in the hope of uncovering target areas for pharmacologic and non-pharmacologic therapy.



**Contents**

1. Introduction ..... 45
2. Perception of dyspnea ..... 46
3. The impact of emotions on dyspnea perception ..... 46
4. Dyspnea and cognitive processing ..... 47
5. Challenges for dyspnea management ..... 48
6. Conclusion ..... 49
Contributors ..... 49
Competing interest ..... 49
Funding ..... 49
Provenance and peer review ..... 49
References ..... 49

## 1. Introduction

Dyspnea is the highly distressing experience of breathlessness that makes simple everyday activities like playing with the grandchildren, going to the shops or simply getting dressed in the morning a major challenge. This chronic debilitating burden affects an increasingly large group of patients with respiratory diseases



* Corresponding author. Tel.: +44 1865 234544; fax: +44 1865 234072.
*E-mail address:* anja.hayen@ndcn.ox.ac.uk (A. Hayen).

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like chronic obstructive pulmonary disease (COPD) and asthma, heart failure and terminal cancer [1] and is a main symptom of panic disorder [2]. Dyspnea is a strong predictor of mortality in patients with COPD and heart failure and amongst the most common causes for emergency department visits [3,4]. Due to its chronicity, costly long-term treatment of dyspnea is necessary in many patients. For example, the annual direct treatment costs of COPD, the fifth biggest killer disease in the UK with over 30,000 annual deaths, were estimated at £820 per patient with an additional £820 of secondary economic costs, accumulating to a total societal cost of over £2.1 billion [5]. Similar figures are reported from the USA [6].

Dyspnea itself often influences the course of disease and symptoms often persist after medical treatment options have been exhausted [7]. Dyspnea can lead to early cessation of exercise, and fear of dyspnea might discourage patients from engaging in daily activities, resulting in reduced cardiovascular fitness and muscle strength, which again increase the feeling of dyspnea, thus initiating and perpetuating a spiral of decline [3]. Patients, family and friends endure great emotional suffering when facing loss of independence and increasing physical distress [8]. Many patients, especially those who have smoked, are obese or do not engage in regular exercise, feel that they have brought their symptoms upon themselves, which makes them feel guilty and less likely to seek appropriate medical help [9].

This review will highlight variations in perception and treatment success of dyspnea that present challenges for dyspnea management. Evidence from clinical and laboratory studies will be reviewed to show how emotions affect the perception of dyspnea and how understanding the neural mechanisms behind these modulations can aid dyspnea management. The challenges of managing dyspnea in older people, obese people and women, three populations particularly vulnerable to dyspnea, will be highlighted and we will suggest how future research can help to understand the neural mechanisms involved in the perception of dyspnea in order to better target treatment. Increased understanding of the neural mechanisms behind dyspnea will allow us to individually address the most important aspects of dyspnea suffering in each patient. While research on the neural mechanisms of dyspnea is still in its infancy, it can reveal important directions for improvements of dyspnea therapy and future research.

## 2. Perception of dyspnea

Dyspnea is not one experience, but encompasses a whole range of sensations (e.g. air hunger, feeling of increased effort, rapid breathing) that are highly subjective. Individual variation between patients in dyspnea perception and resulting impairment is large and reaches beyond the underlying cause [10]. Treatment of the primary cause of dyspnea is essential, but despite optimum treatment, patients often continue to suffer from dyspnea and the associated decrease in quality of life [7]. In conjunction with disease-specific treatments, symptomatic treatments can help to manage dyspnea. To improve and optimally target these treatments, a better understanding of the mechanisms underlying dyspnea is necessary because “one size does not fit all”.

One model of dyspnea perception describes a primary sensory component (intensity) and a primary affective component (unpleasantness) [11]. These components can vary independently [12]. These primary components are followed by a secondary, more cognitive affective component that leads to long-term emotional responses (suffering) that affect future dyspnea-related behavior [11]. Dyspnea is a subjective experience and while animal models have given us insight into mechanisms behind specific pathologies, it is difficult to derive information about the subjective experience of dyspnea from animal models; these models are ill equipped

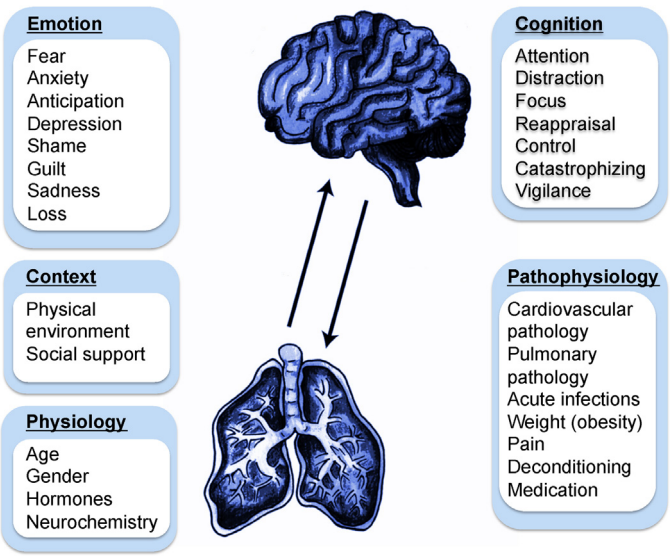


**Fig. 1.** Dyspnea is a multidimensional set of experiences that is closely linked to almost every aspect of a patient's physiological and psychological state. The brain is the main relay station integrating these complex internal and external experiences with physiological respiratory signals.

to study the mechanisms underlying dyspnea perception. Much research on dyspnea mechanisms has hence been performed in healthy individuals exposed to laboratory dyspnea. Replicating the emotional component of dyspnea in a laboratory environment is difficult as laboratory dyspnea does not cause the existential fears dyspnea sufferers encounter in daily life, hence patient studies will be necessary in order to fully comprehend all aspects of dyspnea.

Neuroimaging research has confirmed the important role of emotional processing in the perception of dyspnea. There is evidence for a common emotion-related human brain network that underlies the perception of aversive bodily sensations such as dyspnea and pain [13]. When respiratory stimuli are applied to healthy volunteers in a non-threatening laboratory context, they primarily activate somatomotor areas [14]. When laboratory dyspnea is evoked, the limbic system, an array of brain structures involved in emotional processing, and paralimbic areas like the insula (implicated in interoception, emotion and cognition) are activated [15]. This research hints at different neuronal networks being responsible for the different aspects of dyspnea perception, but future research in clinical populations is necessary to disentangle the neuronal processes implicated in the sensory and affective processing of chronic dyspnea.

## 3. The impact of emotions on dyspnea perception

Based on the concept of total pain proposed by Dame Cicerly Saunders in the 1960s, a model of total dyspnea has highlighted the vicious circle in which dyspnea affects and is affected by physical, psychological, spiritual and social aspects of a patient's life [16]. While an array of potential modulators for the perception of dyspnea is presented in Fig. 1, this review will focus on the impact of negative emotions, and the challenges that age, obesity and gender present to dyspnea management and research.

An individual's emotional disposition, current mood, level of general anxiety and anticipation of dyspnea, as well as the increased attention paid to one's respiration can all influence how dyspnea is perceived. Depression and anxiety are two major comorbidities of respiratory disease (e.g. approx. 40% of patients with COPD suffer from depression [17] and approx. 30% have comorbid anxiety disorders [18]) and have been shown to almost double mortality