# Treat the lungs, fool the brain and appease the mind: towards holistic care of patients who suffer from chronic respiratory diseases

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**Mindfulness-based cognitive therapy can improve well-being in COPD patients beyond usual therapeutic measures: this is additional evidence for a holistic approach to chronic breathlessness**
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In healthy people, breathing is the most natural thing in the world. No need to think about it. No need to be concerned about it. It is not even the object of conscious perception. But when breathing becomes difficult, when it produces suffering, nothing else matters[a]. Life discolours and shrinks around an act of breathing that has become elusive and uncertain, but pervasive. Disability ensues, which adds "a variety of adverse psychosocial, spiritual, or other consequences" to the respiratory-related physical limitations [1]. Respiratory suffering, be it called dyspnoea, breathlessness or by any other name, is therefore a major (and probably often the main) driver of impaired quality of life in patients afflicted with chronic respiratory diseases (and also cardiac diseases, neuromuscular diseases and severe obesity). To put things more bluntly, not being able to breathe freely is probably the worst thing that can happen to a human being. Dyspnoea has long been compared to pain [2] and has a lot of neurophysiological similarities with it [3, 4]. Yet in many ways dyspnoea is probably worse than pain. Indeed, acute dyspnoea goes hand in hand with fear, the fear of dying, which is not systematically the case with pain. And, not being a universal experience like pain, dyspnoea might be less susceptible than pain to induce reactions and empathy from those who witness it. Trained healthcare professionals dealing with respiratory distress on a daily basis fail to correctly evaluate the dyspnoea of their patients [5], and even though recent evidence suggests that vicarious dyspnoea does exist in a manner that resembles vicarious pain [6], the dyspnoea of chronic diseases tends to become invisible to caregivers [7]. This is perhaps because medical responses to dyspnoea

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[a]This text is derived from a passage in the foreword of the first edition of a document published in 2013 by the Forum of International Respiratory Societies, and this concept has become the "motto" of the French "Fondation du Souffle" (www.lesouffle.org).

are less codified and less efficient than responses to pain, but this phenomenon can only amplify the negative consequences of dyspnoea on the psychology of those experiencing it [7, 8]. Yet, as emphasised by Başoğlu [8] in a recent editorial, failure to enquire about, assess and properly treat breathlessness as outlined in specialist clinical guidelines is a breach of clinicians' ethical and legal duties to patients (see also [9]). On top of this clinical importance, respiratory suffering is the point of convergence and the final pathway of an array of diseases that at times have little in common and of which the specialists can have trouble understanding each other. In other words, dyspnoea is the "unifier" of respiratory medicine with all its diversity. For all these reasons, dyspnoea should be a foremost concern for all healthcare professionals, a primary criterion in clinical research, and the focus of specific multidisciplinary research efforts. Fortunately there are indications that this is becoming the case worldwide, and the European Respiratory Society (ERS) plays a significant role in this movement as attested to by a number of publications of all types in the *European Respiratory Journal* [1, 8, 10–14] and the *European Respiratory Monograph* series [15], and the endorsement by the ERS of the Dyspnea 2016 meeting organised by the International Dyspnea Society (www.dyspnea2016inparis.fr/sponsors/endorsement).

How can dyspnoea be addressed? Clearly, by correcting the physiological abnormalities resulting from the causative lung disease ("treat the lung"). There is a lot of research in this area, with a great many successes, but also a lot of frustration because many of the lesions and dysfunctions of the respiratory system are not fully reversible. Of note, the lung is not the only organ with which to target the correction of physiological abnormalities related to chronic respiratory diseases. For example, realising this with regards locomotor muscles has been instrumental in the development and success of rehabilitation as a component of the care of patients with chronic respiratory diseases. Of note also, there are still avenues to explore in the field of "pathophysiological" treatment, without needing new molecules or new discoveries, but through a bit of "lateral thinking". For example, insofar as increased respiratory impedance plays a major role in the pathogenesis of dyspnoea, reducing it by any means could be useful even though the chosen means are not disease-specific. Bronchodilators decrease respiratory impedance even in normal subjects: their putative benefits on dyspnoea in "non-bronchial diseases" are probably worth exploring [16].

Dyspnoea can also be addressed by targeting the brain. After all, no brain, no dyspnoea. So, when respiratory system physiological abnormalities have been corrected or cannot be further corrected ("chronic breathlessness" [1] or "persistent dyspnoea" [17]), it is logical to turn to the brain ("fool the brain"). Benefits can be achieved pharmacologically through direct action on brain receptors involved in the pathogenesis of dyspnoea. Opioids are currently the only such approach of somewhat proven efficacy [18], although there is some controversy (summarised in [19]) and the corresponding evidence needs strengthening. As recently emphasised in an editorial published in the *European Respiratory Journal* (*ERJ*) [20], it is also possible to alleviate dyspnoea by pharmacological or non-pharmacological interventions aimed at rebalancing the respiratory-related brain efferent output with the corresponding afferent input (load-capacity balance/corollary discharge theory [21]). Likewise, nebulised furosemide is thought to relieve dyspnoea [22] by enhancing the afferent traffic from the respiratory system through direct stimulation of tracheobronchial slowly adapting stretch receptors [23]. There are many research avenues in this direction, from simple actions (stimulation of trigeminal afferents by use of portable fans [24]) to more sophisticated ones (inducible respiratory neuroplasticity [25] by analogy with an approach that has proven useful in certain types of pain [26, 27]).

But "treating the lung" and "fooling the brain" can, in the current state of our research and knowledge, fail to relieve dyspnoea sufficiently to make life acceptable again. This is true for the dyspnoea that stems from chronic diseases with identified lesions or organ dysfunction, but is also true for certain unexplained dyspnoeas (*e.g.* in patients with the chronic hyperventilation syndrome, where there is no organic disorder to correct but that still qualifies as a disease and a disability according to World Health Organization principles). Are there other approaches, and are they available today? In this issue of the *ERJ*, Farver-Vestergaard *et al.* [28] present the results of a cluster randomised controlled trial of mindfulness-based cognitive therapy in chronic obstructive pulmonary disease (COPD). The primary objective of this study was to test the efficacy of a combined mindfulness and cognitive therapy approach on psychological distress as assessed using the hospital anxiety and depression scale (HADS). This is in line with the currently accepted multidimensional model of dyspnoea [29] from which it is clear that anxiety and depression are the ineluctable consequences of dyspnoea when the behavioural changes that it induces fail to correct or to prevent it. The rationale behind the choice of intervention stemmed from data showing that psychosocial interventions can be effective in COPD patients [30–32], particularly when they incorporate a cognitive dimension [33], and from data pointing at the putative interest of meditative techniques in the same context [34]. The combination of mindfulness with a cognitive approach (building on data suggesting the interest of cognitive behavioural therapy [35]) was therefore logical. Farver-Vestergaard *et al.* [28] found that mindfulness-based cognitive therapy as an add-on to

pulmonary rehabilitation resulted in a statistically and clinically significant improvement of the HADS score and more specifically of its "depression" dimension. Strikingly, the effect was durable and still present after 6 months. These are very important results that should raise hope in our capacity to improve the well-being of patients that have often lost hope and feel helpless. To speak bluntly again, these results tell us that there is still hope after "optimal bronchodilation". As always, the study by FARVER-VESTERGAARD *et al.* [28] has limitations, which are clearly discussed in the article. The evolution of inflammatory markers before and after the interventions in the two treatment arms are not easy to interpret (*e.g.* the significant increase in tumour necrosis factor-α in the group that underwent pulmonary rehabilitation only and lack thereof in the group that underwent pulmonary rehabilitation and mindfulness-based cognitive therapy). The results are at variance with previous studies of mind–body interventions in COPD that failed to show benefits [36, 37], which is somewhat troubling but reasonably explained by the authors. How this study will translate in practice remains to be seen. How to select the patients who will benefit most from this or other mind–body approaches will be a challenge to determine. Indeed, to the neophyte it is easy to put every type of mind–body or psychosocial intervention into the same pot, but there are significant differences between them (not only between mindfulness-based cognitive therapy and mindfulness-based stress reduction [28], but even more obviously when cognitive behavioural therapy, hypnosis, coping skills therapy or other approaches are considered): caution will be needed in evaluating and then choosing the best approaches. Nevertheless, the major merit of this study is that it introduces a novel approach in the care of COPD patients with persistent dyspnoea, and we do need novelties in this field. Of note, FARVER-VESTERGAARD *et al.* [28] provide the full treatment manual used in their study as an online supplement to their article. This is a remarkable document that will be of major use for those willing to follow suit.

Did the mindfulness-based cognitive therapy approach used by FARVER-VESTERGAARD *et al.* [28] help the patients enrolled in the trial with their dyspnoea? This was not specifically assessed, but there was no significant improvement in the COPD assessment test. It would have been of the utmost interest to know what the effects of the therapeutic intervention under scrutiny were on a multidimensional assessment of dyspnoea like the Multidimensional Dyspnoea Profile or the Dyspnoea-12 [10, 38, 39]. In COPD outpatients, it has been shown that the affective dimension of dyspnoea was more marked in patients exhibiting signs of depression [13]. It is, therefore, possible that reducing psychological distress through a mind–body type of approach could also improve dyspnoea through the "affective" pathway; or that improving the affective dimension of dyspnoea could attenuate psychological distress; or both. At any rate, and for those keen to relate the effects of a therapeutic intervention to observable effects, there is a logic to using mind–body approaches to treat dyspnoea. Indeed, the pathogenesis of dyspnoea heavily involves brain networks comprising the insular cortex. The insula is among the brain regions strongly activated during sustained experimental dyspnoea induced by carbon dioxide stimulation [40] and inspiratory mechanical loading [41]. It is activated as soon as breathing is made difficult by experimental loading (and actually from the first breath on, see [42]). It is activated in patients with chronic respiratory diseases by the mere anticipation of dyspnoea [43, 44]. Yet mindfulness training has been associated with modulation of the activity of the insula in response to an aversive respiratory stimulus [45], which may explain its success in certain situations with a probable "respiratory component" [46]. We do not know if the mindfulness-based cognitive intervention modulated the functioning of the insula in the patients studied by FARVER-VESTERGAARD *et al.* [28], and it seems that these patients did not experience dyspnoea relief. But they did feel better. They were less depressed. They could live better with their dyspnoea. They had gained control. Their mind was appeased even though their body had not experienced dramatic improvements [47]. And this is a major result.

In conclusion, it becomes increasingly clear that the approach to the chronically or persistently dyspnoeic patient needs to be multifaceted, multidisciplinary and multidimensional: in other words holistic [48] (see also the recent correspondence from FAULL *et al.* [49] in the *ERJ*). The encouraging results obtained by the "breathlessness intervention service" approach (improved quality of life, reduced symptom impact, lessened carers burden [50]) attests to the validity of this postulate, as does the efficacy of integrating supportive care to the therapeutic project way before the "end of life" context [51, 52]. Integrated approaches are efficient regarding "classical" outcomes, but they also positively impact dignity [53], a fundamental element of humanity that should never be denied to sick patients because of their sickness. The study of FARVER-VESTERGAARD *et al.* [28] shows that, in this perspective, it is important to integrate the care of the mind in the care of dyspnoea, and therefore to treat the person as a whole and not only his/her lungs or his/her brain. In other words, consider chronic or persistent breathlessness not only as a symptom, not only as a syndrome, but, in the end, as a self-contained all-encompassing condition warranting our undivided and "primary" attention.

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