Lack of dyspnea in patients with Covid-19: another neurological conundrum?

B. Bertran Recasens[a], J. M. Martinez-Llorens[b], J. J. Rodriguez-Sevilla[c] and M. A. Rubio[a]

[a]*Neuromuscular Unit, Neurology Department, Hospital del Mar, Barcelona,* [b]*Pneumology Department, Hospital del Mar, Barcelona, and* [c]*Hematology Department, Hospital del Mar, Barcelona, Spain*

Correspondence: M. A. Rubio, Neuromuscular Unit, Neurology Department, Hospital del Mar, Barcelona, Spain (tel.: +34 93 248 32 35; fax: +34 93 248 32 36; e-mail: MARubio@parcdesalutmar.cat).

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One relevant feature of the Covid-19 disease is the absence of dyspnea, described as 'shortness of breath' or 'an unpleasant urge to breathe'. The lack of dyspnea is observed even in the most severe cases, in which subjects present tachypnea and tachycardia. In the Wuhan cohort, 62.4% of severe cases and 46.3% of those who ended up intubated, ventilated or dead did not present dyspnea [1,2].

Similar findings have been reported in the severe acute respiratory syndrome coronavirus (SARS-CoV) infection where only 34.8% of critical patients reported dyspnea. These data differ significantly from other viral pulmonary infections where the presence of dyspnea is much more frequent, i.e. 69% in Severe acute respiratory syndrome—middle East respiratory syndrome, 95% in respiratory syncytial virus and 82% in influenza [3].

Dyspnea is a multidimensional cognitive construct of respiratory sensation, resulting from peripheral afferences and processed through the brainstem to subcortical and supratentorial structures. Peripheral afferent fibers are located in the lungs and airways; they respond to chemical and mechanical stimuli and drive physiological responses such as cough, tachypnea and dyspnea. The afferent fibers that appear to play the most relevant role in dyspnea are the pulmonary C-fibers, which are predominantly located below the alveolar membrane. The chemical activation of these C-fibers (histamine, adenosine, prostaglandine E2 or lobeline) causes dyspnea or intensifies it and their inhibition (inhaled furosemide) suppresses it.

Although local changes in viral pneumonia could stimulate C-pulmonary fibers, the cytokine storm syndrome (which is rather characteristic of Covid-19) could damage these neurons and therefore explain a total or partial loss of their function. However, this hypothesis collides with the fact that some viral respiratory infections induce an upregulation of receptors from these afferent sensory fibers [4].

For many viruses, the olfactory bulb is the gateway to the central nervous system. In particular, hyposmia has been observed in patients with Covid-19 [5]. Furthermore, experimental findings show that SARS-CoV enters the central nervous system via the olfactory bulb. It rapidly spreads to other regions, causing neuronal death and affecting the nucleus of the solitary tract (where pulmonary C-fibers are projected) on the fourth day since the onset of the infection [6]. It is important to point out that there are other structures that participate in the sensory perception of dyspnea that are affected before the involvement of the nucleus of the solitary tract (i.e. thalamus, insula and limbic system).

However, whereas other neurological manifestations of the central nervous system [5] have been described, such as dizziness, we must be cautious in attributing those symptoms to a direct neurotoxic effect of the virus rather than a systemic response in the infectious context.

The emerging situation of a global epidemic of Covid-19 has presented many challenges in a wide variety of disciplines from science to the economy. Neurologists should not ignore the questions raised by this novel coronavirus and we must be prepared to answer them. This is why now, more than ever, what Gandalf once (almost) said remains valid: "A neurologist is never late, nor is he early, he arrives precisely when he means to."

Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

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