Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Silent cognitive frailty at the interplay between delirium and COVID-19

Dear Editor,

We read with great interest the article by Banerjee and collaborators (Banerjee and Viswanath, 2020) providing a complete overview of neuropsychiatric manifestations of coronavirus disease 2019 (COVID-19) as well as pathogenic mechanisms. We would like to congratulate the authors for their interesting and complete review, and we would like to add some important points from a combination of geriatric and psychiatric points of view.

Delirium is a common geriatric syndrome defined as an abrupt change in the brain resulting from a homeostatic failure and characterized by inattention and acute cognitive dysfunction. It is has been demonstrated that delirium can be considered as the signature of the presentation of many diseases, particularly in frail and older persons, and it has been recognized as an independent risk factor for mortality (Kiely et al., 2009). From this perspective, delirium can be considered less a specifically as "brain" disorder, but a whole body organism failure (Martins and Fernandes, 2012). This point of view accommodates that delirium represents the balance between the fitness and frailty (defined as a status of high vulnerability to stress) of the person in whom it occurs. Thus, delirium is strongly related to the degree of the insult and substrate: a heavy insult is necessary to cause delirium in a very fit person, while a much light insult may cause delirium in a very frail person. In this context, homeostasis plays an important role and requires a coordinated response of physiological systems to correct any perturbation that disturbs the normal condition. The decline in such equilibrium or adaptive homeostasis, as happens during aging, may link COVID-19 to higher delirium susceptibility (Martins and Fernandes, 2012).

However, delirium is a frequent manifestation of COVID-19 affecting not only older (over 75 years old) but also adults and young old (55–75 years) persons (Helms et al., 2020). This could simply suggest a direct brain involvement rather than the worsening effect of a pre-existing condition of frailty. Many are the studies (as reported by authors) turning in such a direction, addressing the invasion of Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) in the central nervous system (CNS) and trying to discover the potential underlying neurotropic mechanisms used by such a virus. However, considering that persons experiencing the worst manifestation of COVID-19 are mainly those affected by type 2 diabetes, cardiovascular disorders and other comorbidities, delirium onset can be simply related to a misunderstood cognitive frailty, even in younger persons. However, autonomic dysfunction, by an anticholinergic effect, may also have an important role during COVID-19. Alterations in autonomic nervous system (ANS) activity in a condition of silent cognitive frailty may boost delirium during COVID-19. In fact, several cytokines upregulated in COVID-19 are strong activators of the hypothalamic-pituitary-adrenocortical (HPA) axis that by the activation of the autonomic nervous system leads to the release of norepinephrine and glucocorticoids (Coperchini et al., 2020), precipitant factors for the development of delirium. Indeed, in these patients the complex combination of hypoxemia, inflammation, sympathetic hyperactivity stress related, pain and anticholinergic drugs use, may further promote an autonomic unbalance leading to agitation, sedation or confusion. Such a hypothesis needs further attention and investigation considering that an early identification of subject at risk is essential for the management and recovery during COVID-19.

Declaration of Competing Interest

The authors report no declarations of interest.

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References

Banerjee, D., Viswanath, B., 2020. Neuropsychiatric manifestations of COVID-19 and possible pathogenic mechanisms: insights from other coronaviruses. Asian J. Psychiatr. 54. https://doi.org/10.1016/j.ajp.2020.102350.

Coperchini, F., Chiovato, L., Croce, L., Magri, F., Rotondi, M., 2020. The cytokine storm in COVID-19: an overview of the involvement of the chemokine/chemokine-receptor system. Cytokine Growth Factor Rev. https://doi.org/10.1016/j.cytogfr.2020.05.003.

Helms, J., Kremer, S., Merdji, H., Schenck, M., Severac, F., Clere-Jehl, R., Studer, A., Radosavljevic, M., Kummerlen, C., Monnier, A., Boulay, C., Fafi-Kremer, S., Castelain, V., Ohana, M., Anheim, M., Schneider, F., Meziani, F., 2020. Delirium and encephalopathy in severe COVID-19: a cohort analysis of ICU patients. Crit. Care 24, 491. https://doi.org/10.1186/s13054-020-03200-1.

Kiely, D.K., Marcantonio, E.R., Inouye, S.K., Shaffer, M.L., Bergmann, M.A., Yang, F.M., Fearing, M.A., Jones, R.N., 2009. Persistent delirium predicts greater mortality. J. Am. Geriatr. Soc. 57, 55–61. https://doi.org/10.1111/j.1532-5415.2008.02092.x.

Martins, S., Fernandes, L., 2012. Delirium in elderly people: a review. Front. Neurol. JUN. https://doi.org/10.3389/fneur.2012.00101.

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