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Letter to the Editor

Assessing post-ICU cognitive dysfunction in ventilated COVID-19 patients requires consideration of contributing factors

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We read with interest the article by Pernille *et al.* on dynamic impairment of cognitive functions shortly after discharge from the intensive care unit (ICU) and three months later in COVID-19 patients requiring mechanical ventilation^[1]. Application of the MMSE, FAB, oral naming test, Dubois five words test, and MADRS in 13 COVID-19 patients on the ICU revealed that all patients had cognitive impairment at baseline but all improved three months later on two of the five global tests^[1]. It was concluded that ventilated COVID-19 patients experience acute and short-term cognitive impairment that improves after three months^[1]. The study is appealing but raises concerns that should be discussed.

The main limitation of the study is that no cerebral imaging of the included patients was generally not performed^[1]. Although the included patients were admitted because of respiratory deterioration, it cannot be ruled out that these patients developed cerebral complications during their stay on the ICU. COVID-19 can be complicated by a number of cerebral complications including stroke, intracerebral bleeding, venous sinus thrombosis, encephalopathy, acute disseminated encephalomyelitis (ADEM), multiple sclerosis (MS) myelin oligodendrocyte glycoprotein (MOG)-associated encephalomyelitis, acute, hemorrhagic leucoencephalitis (AHLE), immune encephalitis, seizures, cerebellitis, or hypophysitis^[2]. All these conditions can impair cognitive functions. Some of them may not be detected unless actively searched for. Before assessing cognitive functions in COVID-19 patients it is crucial to know whether or not these patients had involvement of the brain. In addition, we should be informed how many of 13 patients had delirium acute respiratory distress syndrome (ARDS), cardiac arrest, sepsis, or renal insufficiency during stay in the ICU.

Another limitation is that no EEGs were recorded. Because any disorientation, delirium or dizziness could be the manifestation of non-convulsive status epilepticus (NCSE), it is critical that NCSE is appropriately ruled out on the EEG in each patient.

A further limitation is that it is unclear which medications the included patients were taking during stay in the ICU or at the time the first test series was carried out. Since a number of drugs affect cognitive performance, it is crucial to include this information in the analysis and interpretation of the generated data. Particularly sedatives, analgesics, antidepressants, neuroleptics, anti-seizure drugs, and anesthetics are known to impair cognitive performance^[3]. We should be told how many hours after extubation or weaning the neuropsychological tests were performed.

In the results section it is mentioned that none of the patients had a cognitive complaint pre-ICU^[1]. However, the absence of cognitive dysfunction can only be confirmed by conducting appropriate neuropsychological tests, since, as mentioned in the discussion, cognitive dysfunction can go undetected by the patients themselves,.

The latency between extubation and neuropsychological test was 6 days (median latency)^[1]. Because cognitive functions can change significantly over this period, the current data may not represent cognitive functionality immediately after extubation.

Overall, the interesting study has some limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study.

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