The severe form of COVID-19 tends to be associated with neurological deficits. Among patients with acute respiratory distress syndrome (ARDS), who comprised two standardised test batteries. Patients, resolved in six of them (P5–P7, P10, P11, P13) or subsided to a great extent (P12).

The neuropsychological evaluation comprised two standardised test batteries. The Montreal Cognitive Assessment (MoCA; https://www.mocatest.org), which covers main cognitive functions, revealed normal cognitive performances in four patients (table 1; P1–P4), mild deficits in four (P5–P8) and moderate to severe deficits in five (P9–P13). MoCA subtests revealed selective cognitive pattern with lower performances in executive functions for patients with normal MoCA scores and more extensive cognitive impairment in executive, memory, attentional and visuospatial functions, with relatively preserved orientation and language, for patients with mild to severe MoCA deficits.

The Frontal Assessment Battery (FAB; www.psychdb.com/cognitive-testing/fab) revealed executive dysfunction in eight patients (table 1; P6–P13). Among the FAB subtests, the most affected was lexical fluency, impaired in all patients except in one (with normal MoCA: P3).

Pearson (r) and Spearman (rho) correlation analyses were conducted. MoCA and FAB scores were correlated (r=0.88; p=0.001). Mental fatigue and cognitive slowness, assessed with observational scales, correlated with MoCA (respectively: rho=−0.67; p=0.012; rho=−0.74; p=0.004) and FAB scores (respectively: rho=−0.85; p<0.001; rho=−0.72; p=0.006). Age correlated with FAB (r=−0.591; p=0.033) but not with MoCA scores. There was no significant correlation between MoCA or FAB scores and the following measures: gender, length of ICU stay, duration of mechanical ventilation, delay between ICU discharge and cognitive assessment, mood and anxiety disturbances. Mood disturbance, assessed in self-report, was considerable (table 1; ≥5/10) in 38% of patients and 23% reported anxiety about breathing difficulties, fear of dying or reminiscences of intensive care. Seven patients presented ICU delirium (table 1); its occurrence was correlated with MoCA score (rho=−0.619; p=0.024) and cognitive slowness (rho=0.585; p=0.036), but not with FAB, length of ICU stay, duration of mechanical ventilation, delay between ICU discharge and cognitive assessment, age, gender, mental fatigue, mood and anxiety disturbances.

Eleven patients had brain imaging. None of them sustained acute stroke or ischemic damage; among the eight patients who had MRI-based morphometry, focal brain atrophy was, however, present in patients with normal (table 1; P1) or deficient performance at MoCA (P10–P13) as it was absent in patients with normal (P3, P4) or deficient performance at MoCA (P7). Four patients had lumbar puncture, revealing enhanced proteinorachia (P3, P11, P13) and barrier index (P11, P13) or normal values (P12).

Two cognitive profiles characterise the post-critical acute phase of severe COVID-19: (1) normal score at MoCA, but tendency for lower performances

<table>
<thead>
<tr>
<th>Patients</th>
<th>MoCA mean (0–30)</th>
<th>MoCA mean subtest scores (0–6)</th>
<th>FAB mean subtest scores (0–3)</th>
<th>Cognitive slowness (0–3)</th>
<th>Mental fatigue (0–3)</th>
<th>Mood (0–10) and anxiety* (0–30)</th>
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<td>P1</td>
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<td>2.00</td>
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</tr>
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</table>

**Table 1** Patient (P1–P13) characteristics and performance in cognitive tests

**Patients were rated from highest to lowest performing at MoCa test. Three patients had a CT scan, which was within normal range (P9, P11, P13); right patient had an MRI-based morphometry, which was within normal range in three patients (P1, P4, P7) and showed signs of atrophy, in four others (P1, P5, P7, P12). ICU delirium was rated 1 (no delirium) or 2 (with delirium). Scores at MoCA and FAB performance within normal limits in its italic, deficit in bold. For the MoCA, the maximum score is 30 and deficit score below 26 (‘MoCa: Montreal Cognitive Assessment; FAB, frontal assessment battery; Mo, male; Fe, female; IC, intelligence; Co, concentration; Fl, fluency; At, attention; Ex, executive function; Fl, fluency; Co, concentration’). **MoCA** deficits.

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Two cognitive profiles characterise the post-critical acute phase of severe COVID-19: (1) normal score at MoCA, but tendency for lower performances
in executive than in other cognitive functions; (2) mild to severe deficits at MoCA with extensive cognitive impairment in executive, memory, attentional and visuospatial functions, but relatively preserved orientation and language, executive dysfunction being confirmed by the FAB score. These cognitive profiles together with mood and anxiety disturbances, which we observed in the acute stage, in the absence of stroke, are reminiscent of those reported in the aftermath of ARDS of other aetiologies, where up to 70% of ARDS survivors had presented at hospital discharge cognitive deficits, affecting predominantly attention, mental processing speed, memory and executive functions, with a high prevalence of depression and anxiety.

Furthermore, cognitive impairment in severe COVID-19, as in ARDS of other aetiologies, may not correlate with length of mechanical ventilation or length of ICU stay and thus severity of the acute illness. However, the occurrence of ICU delirium tends to be associated with poorer cognitive performance.

Structural damage, such as ischaemic or hypoxic encephalopathies of the hippocampus, basal ganglia or cerebellum lesions as well as brain atrophy (in particular hippocampal) or disruption of functional connectivity, which occur frequently in ARDS survivors, may contribute to cognitive dysfunction. In the context of COVID-19, stroke and perfusion abnormalities have been reported, but were excluded here in all 11 patients, who had brain imaging during the acute stage.

Prior brain atrophy may confer worse outcome as shown for the risk to develop delirium and cognitive disorders in ARDS of other aetiologies. Patchy grey and/or white matter atrophy was present in five patients (of the eight who had MRI), most likely reflecting a prior condition; it was associated with cognitive impairment in four patients. However, brain atrophy did not always induce cognitive impairment and conversely, cognitive impairment was also present without imaging abnormalities, as in previous non-COVID-19 studies.

Our sparse data on cerebrospinal fluid suggest that increased blood–brain barrier permeability may contribute to neurological symptoms, as previously described for mild central nervous system inflammation in ICU patients.

In conclusion, pattern of cognitive deficits, present during the acute stage in our 13 patients without history of cognitive, psychiatric or neurological disorders, is probably linked to critical illness as part of ARDS due to COVID-19, since it is very similar to those reported in ARDS of other aetiologies. Further investigations are needed to determine predictive factors and underlying neural mechanisms, and clarify with a long-term follow-up whether patients will completely recover.

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Contributors SC participated in study conception and design, interpretation and draft of the manuscript. VB participated in study conception and design, performed neuropsychological data acquisition and interpretation, and draft of the manuscript. SC-H performed statistical analysis, interpretation and draft of the manuscript. VB performed radiological data acquisition and interpretation, and draft of the manuscript. RB-V performed neurological data acquisition and interpretation, and draft of the manuscript. JV, RDP and P-AB participated in elaborating the large scale of this study and performed critical revision of the manuscript.

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References