

Post-COVID Cognitive, EEG Changes Persist Up to 10 Months

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Patients who recover from COVID-19 show interrelated cognitive, EEG, and MRI abnormalities 2 months after hospital discharge — with some "disturbances" persisting as long as 10 months later, new research suggests.

In a cohort of patients admitted to the emergency department (ED) with a diagnosis of COVID-19, who also underwent follow-up neuropsychological assessment and an EEG, more than half showed cognitive disturbances mainly affecting memory and attention 2 months after discharge.

At 10-month follow-up, there was a significant amelioration of cognitive impairment. However, some cognitive deficits and disturbances in mood were still evident in a little over a third of patients. EEG findings showed slowing of cortical activity, which was only partially ameliorated at month 10.

"Cognitive and psychopathological disturbances are associated with COVID-19 infection within 2 months from hospital discharge, partially persist in the post-COVID phase, and are associated with electroencephalographic alterations," senior author Massimo Filippi, MD, full professor of neurology, Vita-Salute San Raffaele University, Milan, Italy, told *Medscape Medical News*.

"Whether these alterations are directly linked with the infection itself or with its related consequences is still to be determined, as well as whether they are completely reversible or part of a neurodegenerative process," added Filippi, who is also chair of the Neurology Unit, Neurorehabilitation Unit, and director of the Neurophysiology Service and Neuroimaging Research Unit.

The findings were [published online](#) March 6 in the *Journal of Neurology*.

Useful Tool

COVID-19 survivors report neurologic sequelae, including cognitive impairments, which have been "amply described" in research conducted between 1 and 6 months after recovery, the investigators write.

However, few studies to date have "explored cognitive involvement through structured neuropsychological assessments, with most observing a short follow-up and involving only few patients," they add.

After having COVID, individuals also experience a "wide range of persistent psychiatric disturbances," including depression, posttraumatic stress disorder (PTSD), and anxiety.

Several neuroimaging studies have shown neuropathologic changes in COVID patients. A previous EEG study conducted by Filippi's group showed that EEG alterations "might represent a useful tool to evaluate early cerebral involvement in COVID-19," the investigators note.

They found in their cohort an "anterior prevalence of slow waves, correlating with metabolic and hypoxic alterations."

No previous studies have used EEG analysis after infection resolution. "Considering the lack of longitudinal studies with long follow-up and with structured neuropsychological and EEG assessments, we aimed at exploring longitudinal cognitive and concomitant EEG features" in COVID survivors up to 10 months after hospital discharge, the researchers write.

"The evidence of persisting neurocognitive complaints in a relevant proportion of COVID-19 survivors at the 1-month follow-up neurological evaluation, together with the lack of long-term studies with structured neuropsychological, neurophysiological, and neuroradiological assessments, were the main drivers of our study," Filippi added.

Investigators assessed adult patients admitted to the ED with a COVID diagnosis. Those who reported subsequent cognitive complaints underwent neuropsychological assessment and 19-channel EEG within 2 and 10 months after hospital discharge (baseline, n = 49; follow-up, n = 33). At baseline, 36 patients also underwent a brain MRI. Patients were compared to healthy matched controls.

The researchers estimated EEG regional current densities and linear lagged connectivity values and measured brain and white matter hyperintensity (WMH) volumes. They evaluated clinical and instrumental data between patients and controls at baseline

in the patient group and in those with/without dysgeusia/hyposmia over time.

Of all participants, most (85.7%) were treated as inpatients, roughly one quarter (26.5%) required noninvasive mechanical ventilation, and 4.1% required orotracheal intubation. Almost three quarters (73.5%) experienced neurologic manifestations, notably dysgeusia (59.2%) and hyposmia (44.9%).

Although acute neurologic symptoms were resolved in most patients at baseline, 26.5% continued to report asthenia.

Clinical Monitoring

At baseline, 53% of patients showed an impairment in at least one cognitive domain, primarily executive functions. In addition, 16%, 6%, and 6% of patients showed pure executive, memory, and visual-spatial impairment, respectively.

One quarter of participants showed a multidomain impairment — with 23% involving, among others, the executive domain.

Additionally, 28% of patients presented with psychopathologic disturbances, including depressive symptoms (10%), PTSD features (12%), or both (6%).

Participants performed more poorly in all the investigated cognitive domains, compared to the healthy controls group; and the executive dysfunctions correlated with acute-phase respiratory distress.

On EEG, patients showed higher regional current density and connectivity at delta band, which correlated with executive performance, compared with their healthy peers. Their MRIs also showed greater total, right frontal, and right parieto-occipital WMH volumes in comparison with the healthy control group, which correlated with verbal memory deficits.

Although a reduction in cognitive impairment and delta band EEG connectivity was observed over time, the psychopathologic symptoms persisted. In particular, patients who had experienced acute dysgeusia/hyposmia showed lower improvement at memory tests compared with patients who had not experienced those symptoms.

Lower EEG delta band at baseline predicted worse cognitive functioning at follow-up.

"Clinical monitoring is crucial to prevent symptoms from worsening, and when the symptoms are present, cognitive stimulation trainings either at the hospital or at home through telemedicine or through dedicated apps are needed," Filippi noted.

He also recommended outdoor physical exercises or long walks to "benefit physical and mental health, since physical recovery is important for the body, including the brain."

Confounding Effects?

Commenting for *Medscape Medical News*, Jacqueline Becker, PhD, clinical neuropsychologist and assistant professor of medicine, Icahn School of Medicine at Mount Sinai, New York City, said, "The finding that cognitive impairment, particularly in executive functioning, was present following COVID-19 recovery in hospitalized patients is consistent with prior research," including [a study](#) conducted by Becker's group.

However, "while it was reassuring that the authors found improvements in some cognitive domains 10 months later, the study did not take several factors into account that may confound these results," said Becker, who was not involved with the current research.

For example, practice effects from taking the same neuropsychological tests in a short time frame "would result in a natural improvement in scores," she said.

Given that the study did not find abnormalities in brain volume on MRI, as prior studies have shown, "it is also possible that the cognitive impairment in this cohort was primarily due to the comorbid psychological symptoms reported and less a reflection of neurologic involvement from COVID-19," she noted.

"Nevertheless, the study will hopefully prompt larger longitudinal investigations into the cognitive and neurophysiological consequences of COVID-19," Becker said.

Filippi is editor-in-chief of the Journal of Neurology and associate editor of Human Brain Mapping, Neurological Sciences, and Radiology. He has received compensation for consulting services and/or speaking activities from Almiral, Alexion, Bayer, Biogen, Celgene, Eli Lilly, Genzyme, Merck-Serono, Novartis, Roche, Sanofi, Takeda, and Teva Pharmaceutical Industries; and receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Teva Pharmaceutical Industries, Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, and ARiSLA (Fondazione Italiana di Ricerca per la SLA). Becker has reported no relevant financial relationships.

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