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# THE NEUROLOGICAL CONSEQUENCES OF CONTRACTING COVID-19

## *The Lancet*'s COVID-19 Commission Mental Health Task Force

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## SUMMARY

Since the first confirmed case in Wuhan, China on December 31, 2019, the novel coronavirus (SARS-CoV-2) has spread quickly, infecting 165 million people as of May 2021. Since this first detection, research has indicated that people contracting the virus may suffer neurological and mental disorders and deficits, in addition to the respiratory and other organ challenges caused by COVID-19. Specifically, early evidence suggests that COVID-19 has both mild (e.g., loss of smell (anosmia), loss of taste (ageusia), latent blinks (heterophila), headaches, dizziness, confusion) and more severe outcomes (e.g., cognitive impairments, seizures, delirium, psychosis, strokes). Longer-term neurological challenges or damage may also occur. This knowledge should inform clinical guidelines, assessment, and public health planning while more systematic research using biological, clinical, and longitudinal methods provides further insights.

**Key words:** anosmia, ageusia, heterophila, headaches, dizziness, confusion, cognitive impairments, seizures, delirium, psychosis, strokes

# SYMPTOMS EXPERIENCED DURING COVID-19 INFECTION

A growing body of evidence suggests that COVID-19 is associated with neurological disorders and deficits (Bougakov et al., 2020; Solomon, 2021, Rogers et al., 2020). Some reported neurological symptoms associated with COVID-19 infection are anosmia (loss of smell), ageusia (loss of taste), heterophoria (latent squint; Belvis, et al, 2020), and headaches. Anosmia and ageusia appear quite common. In a sample of 417 patients with mild to moderate COVID-19 symptoms spanning 12 hospitals in Europe, 86% suffered olfactory dysfunction and 89% suffered gustatory dysfunction (Lechein et al, 2020). Other data collected from 214 individuals in Wuhan, China in January and February 2020 report that anosmia and ageusia may be some of the earliest symptoms, detectable in some individuals before respiratory difficulties emerge (Mao et al., 2020). Similar observations are noted in case studies as well (e.g., Zanin et al., 2020). Although olfaction tends to return upon COVID-19 recovery, gustatory deficiencies have been seen to persist beyond respiratory symptoms in over 70% of patients in some samples (Mao et al., 2020). A meta-analysis reporting on data from 3,598 cases suggests that headaches are also common symptom of COVID-19 infection, appearing in 12% of hospitalized patients (Borges do Nascimento et al., 2020), and among mild to moderate cases that rarely result in hospitalization (Belvis et al., 2020; Pinzon et al., 2020). A study of 917 people in Wuhan, China January to March 2020 indicate that these non-specific symptoms can all be caused by the condition related to the infection, while other neurological conditions may be due to sedation during ventilation (Xiong et al., 2020).

Psychological disruptions, including dizziness, confusion, delirium, and psychosis have also been reported. For instance, when an online network of researchers in the UK composed of neuroscientists, stroke physicians, psychiatrists, and intensive care doctors examined over 100 patient cases identified in April 2020, altered mental states were noted as the second most common presentation (Varatharaj et al., 2020). The majority (59%) of these patients displayed altered mental states that met criteria for diagnosis as determined by a psychiatrist or neuropsychiatrist. Importantly, nearly all of these cases (92%) were new diagnoses. Among the individuals showing altered mental states, the most common diagnoses were psychosis (43%), dementia-like syndromes (26%), and affective disorders (17%). While some symptoms were most common in older patients, nearly half (49%) of the patients with altered mental states were younger than 60 years of age. Experiences of delirium and mental disturbance may be compounded by the treatment of COVID-19 in hospitals, which often imposes social isolation, little or no physical contact with loved ones, and restricted movement from one's treatment space (Durkin et al., 2020; Kotfis et al., 2020; Nist et al., 2020).

Seizure and strokes have also been reported among COVID-19 patients. For instance, among 43 confirmed or likely cases of COVID-19 in the UK in March

2020, Paterson and all (2020) found that 8 (19%) had ischemic strokes. Similarly, of 125 patients presenting with a cerebrovascular event in the UK in April 2020, Varatharaj and colleagues (2020) found that 57 (74%) had ischemic strokes, 9 (12%) showed hemorrhaging in the brain, and 1 (1%) showing vasculitis (inflammation) in the brain and spinal cord, again consistent with swelling in the brain. Early case studies also report seizures (Moriguchi et al., 2020; Zanin et al., 2020).

# SYMPTOMS AFTER COVID-19 INFECTION

Even after recovering from COVID-19 infection, an individual may suffer from ongoing neurological challenges, which could be linked with what many call "long COVID" (Komaroff, 2020). For instance, a recent examination of cognitive test scores from 84,285 individuals in the UK, including those with confirmed or suspected COVID-19 infection as of May 2020, found that people who had recovered and were no longer symptomatic displayed significant cognitive deficits as compared to controls (Hampshire et al., 2020). This effect does not appear to be the result of individual characteristics that may distinguish cases and controls; differences remain when controlling for variables, such as age, gender, education, income, ethnicity, and previous medical disorders. Cognitive impairments when performing tests of semantic problem solving, spatial working memory, selective attention, and emotional processing were most severe for those who had been hospitalized, and larger for those who had been on a ventilator than for those who had not (Hampshire et al., 2020; ventilated: -0.57 SDs $n$ = 60 vs. not: -0.45SDs $n$ = 147). However, impairments were also detectable among individuals with confirmed cases without breathing impairment, suggesting that deficits may "scale with symptom severity" and impact a sizable portion of people who become infected. These findings are striking but require cautious interpretation because individuals were not followed over time with pre- and post-diagnosis assessments.

Perhaps as a result of swelling (associated with encephalitis) and hypoxia in the brain, there is some concern that COVID-19 may lead to long-term neurological or other challenges for survivors even after acute illness passes (Carfi et al., 2020; Goldberg et al., 2020; Tenforde et al., 2020), especially those who experienced numerous or severe symptoms during the disease (Bougakov et al., 2020). For instance, data from January 2020 from 62,354 people in the UK reveals that COVID-19 survivors with no history of psychiatric illness were approximately twice as likely to display a neuropsychiatric disorder, including insomnia and dementia, at three-month follow-up than people who experienced other health concerns, respiratory tract infections, influenza, or other health concerns (Taquet et al., 2020). Moreover, encephalitis, hypoxia, and strokes are well known causes of long-term and, in some cases, permanent neurocognitive damage. Consistent with this possibility, autopsies examining the brains of 18 individuals who died due to COVID-19 in April 2020 all showed signs of hypoxia (Solomon et al., 2020).

# CONCLUSION

In summary, evidence of the neurological impacts of COVID-19 is heterogeneous, tentative, and rapidly evolving. To date, the evidence suggests that COVID-19 very likely affects the brain and manifests in neurological symptoms, some of which may be long lasting. The mechanisms of the virus are still unclear, but some studies suggest that infection of the nervous system (Lucchese, 2020; Paniz-Mondolfi et al., 2020) or pathologies in the blood vessels and blood-brain barrier (Puccioni-Sohler et al., 2020) may be responsible. This knowledge should inform clinical guidelines, assessment, and public health planning while more systematic research using biological, clinical, and longitudinal methods provides further insights.

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