Janeczek, Piotr. COVID-19 pandemic: disease impact on nervous system, cognitive functioning and mental health. Journal of Education, Health and Sport. 2022;12(9):328-340. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2022.12.09.037
https://apcz.umk.pl/JEHS/article/view/39672
https://zenodo.org/record/7040520

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences). Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

Received: 15.08.2022. Revised: 20.08.2022. Accepted: 01.09.2022.

COVID-19 pandemic: disease impact on nervous system, cognitive functioning and mental health

Piotr Janeczek

Student of the Psychology at the Uniwersytet Jana Kochanowskiego w Kielcach

E-mail: piotrjaneczek99@gmail.com

ORCID: 0000-0003-3780-6983

Abstract

Introduction and purpose:

COVID-19, as an unknown disease until 2019, has posed and continues to pose a great challenge to the world of science and the people facing it. The purpose of this article is to present the possible consequences of experiencing COVID-19 disease and the pandemic itself in light of mental health and the organism functioning in the cognitive area, taking into account the impact of COVID-19 on the nervous system.

State of knowledge (brief description):

Coronaviruses are enveloped, positive single-stranded large RNA viruses. COVID-19 is a disease caused by the SARS-CoV-2 virus – its first case was reported in 2019 in Wuhan, China. Human coronaviruses can exhibit neuroinvasive, neurotropic and neurovirulent, SARS-CoV-2 also. In addition to symptoms and complications in the respiratory system, symptoms and complications are also encountered in the nervous system area; cognitive functioning may also be impaired. The pandemic as a phenomenon in itself and the outbreak of COVID-19 can carry very serious consequences from the mental health field. Among these are the problem of social isolation and its consequences or the impact of the disease and pandemic on well-being. Unfortunately, the time that has elapsed since the first cases of the disease and the amount of research does not allow a clear determination of the complications and consequences of the pandemic, but certain trends and phenomena are regularly studied and described.

Summary:

Existing research and the state of the art strongly underscore that COVID-19 and its pandemic could impinge on the mental health of people around the world. Changes in the nervous system and cognitive functioning are also observed as a result of contracting COVID-19. Science currently has no clear answers as to how long certain complications will persist and exactly what their genesis is – further research is recommended to explain them as precisely as possible.

Key words: COVID-19, mental health, nervous system, cognition, pandemics, socialization

Introduction and purpose

The COVID-19 pandemic is a time of new challenges not only for the world of science, but also for everyone in the world. The need for sudden changes and the emergence of a new reality undoubtedly could have put a strain on many people. The World Health Organization considers *"the spread of a new disease around the world"* to be a pandemic. In the case of COVID-19, we undoubtedly experienced such a phenomenon. COVID-19 is a disease that poses a threat not only to the respiratory system, but also to other areas of the organism functioning including mental health and – considering the seriousness of the disease and the actions associated with it to, for example, prevent its spread – in the consequences also of human functioning in society.

The main purpose of this article is to present the possible consequences of experiencing COVID-19 disease and the pandemic itself in light of mental health and the functioning of the body in the cognitive area, taking into account the impact of COVID-19 on the nervous system.

State of knowledge

Characteristics of coronaviruses

Coronaviruses are enveloped, positive single-stranded large RNA viruses first described in 1966 by Tyrell and Bynoe [1]. The name “coronavirus” comes from the spikes on their surface, noticeable by electron microscopy, which give the virus the appearance of a corona [2]. There are four subfamilies of coronaviruses: alpha, beta, gamma and delta with alpha and beta coronaviruses being derived from mammals (especially bats) and gamma and delta from pigs and birds [1]. Transmission of coronaviruses can occur from animal to human, human to animal, or animal to animal [3]. In animals, the virus mainly causes digestive, respiratory, and nervous system diseases – moreover, coronaviruses of animal and avian origin may have a higher mortality rate in infected animals than those of other origins [1, 4, 5]. The focus of researcher’s attention on coronaviruses came in 2002 and 2003 with the emergence of the coronavirus that causes severe acute respiratory syndrome (SARS-CoV) [5]. Until then, they had been treated as the backwater of virology because they did not cause serious disease in humans. In 2012, Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in Saudi Arabia, and bats were thought to be the source of both it and SARS-CoV, with confirmed zoonotic reservoirs for SARS-CoV and MERS-CoV being civet cats (for SARS-CoV) and dromedary camels (for MERS-CoV) [5]. Coronaviruses in humans are capable of causing both mild respiratory infections and, for example, acute respiratory distress syndrome (ARDS) [6]. The aforementioned coronaviruses SARS-CoV and MERS-CoV have a high mortality rate – for SARS CoV it is 10-50%, depending on the age of the infected person, while for MERS-CoV the mortality rate is approximately 35% [6, 7].

COVID-19 is a disease caused by the SARS-CoV-2 virus – its first case was reported in 2019 in Wuhan, China [8]. By the end of 2019, 44 cases of it had been registered there, while the first case in Europe was reported in January 2020 [9]. Studies have shown homology with the bat SARS-like coronavirus (BatCoV RaTG13) at 96.3%, which may indicate that bats are the natural host of COVID-19 [10]. It is assumed that the virus originated from a mutation of viruses common among animals and spread to humans at one of the wet markets – the presence there was a common point among the first infected with SARS-CoV-2. Unfortunately, the current state of knowledge on the source of SARS-CoV-2 does not allow to unequivocally confirm this assumption [11].

SARS-CoV-2 is a highly mutation-prone virus, and there are many variants. Among the variants of concern to the WHO are the alpha, beta, gamma, delta and omicron variants [12]. COVID-19 is a highly contagious disease – the SARS-CoV-2 virus is capable of droplet transmission, through bioaerosols, as well as direct contact with infected material [13, 14]. Symptoms of COVID-19 are varied and dependent on the virus variant. The most common symptoms include fatigue, headache, fever, cough, shortness of breath, muscle aches, decreased nasal patency, rhinorrhea, loss of smell, taste disturbances, sore throat, nausea, vomiting, and diarrhea [15, 16, 17]. There is no uniform clinical picture of COVID-19. It can occur both asymptomatically and with symptoms while they can be both mild and very severe thus potentially leading to death. An asymptomatic course of the disease is potentially able to significantly increase viral transmission, which is a significant obstacle to trying to control transmission [18]. A 2021 meta-analysis of 16 studies showed that the pooled incidence of asymptomatic cases was 48.2% [19]. It was also shown that children and women were more likely to be asymptomatic COVID-19 patients as a result of which they could be invisible carriers of SARS-CoV-2. Infection of others can also occur before the first symptoms appear in an infected person. It is estimated that pre-symptomatic transmission can occur 1-3 days before the first symptoms appear in source patients [20]. The incubation period of the virus depends on its variant, while it is considered to range from 2 to 14 days [21]. Although COVID-19 spreads faster than SARS-CoV and MERS-CoV, it has a lower mortality rate [22]. In the 2020 WHO report, the mortality rate for COVID-19 was about 2.5% – the worse prognosis mainly affects the elderly and patients with comorbidities [22, 23]. Based on previous statistics, it has been shown that more than 80% of COVID-19 deaths were in people over 60 years of age; at the same time, more than 75% of those who died had comorbidities such as diabetes, cardiovascular disease, or cancer [22]. Gender has also been shown to matter, with a higher risk of death in men [24].

SARS-CoV-2 as a neuroinvasive, neurotropic and neurovirulent virus and its impact on nervous system and cognitive functioning

Human coronaviruses can exhibit neuroinvasive (ability of the virus to enter the nervous system), neurotropic (the propensity of a pathogen to infect cells within the nervous system), and neurovirulent (the capacity of pathogens to cause disease of the nervous system) effects, which in summary means that when they invade the human body, they are able to penetrate the central nervous system and infect neurons and contribute to neurological diseases [25, 26, 27]. The virus is able to enter the nervous system through blood-borne spread or neuronal retrograde spread. This is no different for the SARS-COV-2 virus – based on the studies, it is concluded that SARS-CoV-2 has the potential to penetrate the central nervous system [28, 29]. Although SARS-CoV-2 is implicitly associated with its classification as a respiratory pathogen when COVID-19 is severe, numerous neurological complications can be encountered – orientation problems, stroke onset or neuromuscular disorders [30]. Although this phenomenon is not new to science, as neurological changes have already been described for other viruses affecting the respiratory system including coronaviruses, the neurological

symptoms and complications encountered with COVID-19 have been common and severe enough (both short-term and long-term) to garner the attention of scientists and non-scientists alike [31]. A study conducted by Matschke and colleagues in 2020 on people who died from severe COVID-19 showed that SARS-CoV-2 virus was detected in the brains of more than half of the patients examined [32]. A study by Emmi and colleagues in 2022 based on analysis of neuropathological changes in patients who died from COVID-19 and juxtaposing them with a control group provide a kind of confirmation of the neuroinvasiveness of the virus [33]. Neuroinvasion can lead to the death of nerve cells and brain ischemia, among other things. The virus uses the ACE2 receptor to get inside the cells. The research team of Baig, Khaleeq, Ali, Syeda in 2020, after analyzing data on ACE2 expression in neural tissue, linked this to the neurotropic effects of the virus [34]. Reports from other researchers also point to this feature of the virus. The neurovirulent potential of the SARS-CoV-2 virus is capable not only of causing neurological diseases or increasing the risk of neurodegenerative diseases, but also of exacerbating conditions already present in the body; examples of the neurovirulent effects of SARS-CoV-2 include meningitis and encephalitis that occur in patients [36, 37, 38].

As already mentioned, the SARS-CoV-2 virus can cause both long-term consequences and those acute symptoms shortly after infection. Among the many studies on SARS-CoV-2, many classifications of symptoms can be found, one of which is to classify them based on central nervous system, peripheral nervous system, musculoskeletal and psychiatric symptoms [39]. The occurrence of neurological abnormalities with COVID-19 may be associated with a cytokine storm – this is a hyperinflammatory state caused by a sudden increase in cytokines (proteins that stimulate other immune system cells to respond in specific ways) in the body. Their symptoms include fatigue, high fever, and nausea [40]. Stimulation of the immune system and its overactivity is capable of leading to organ damage and neurological symptoms with an increased risk of death for hospitalized patients [41, 42].

Central nervous system neurological disorders include headaches, strokes, cerebral hemorrhages, acute encephalopathy, epileptic seizures, acute cerebrovascular disease, and meningitis [42, 43, 44, 45, 46, 47, 48]. Manifestations from the peripheral nervous system take the form of chronic pain, taste and smell sensory disturbances, and Guillain-Barré syndrome may also occur; musculoskeletal symptoms (myalgia, joint pain) may also occur [49, 50, 51, 52, 53].

Brain fog (also commonly referred to as covid fog) is also among the reported complications after COVID-19. Symptoms include memory problems, difficulty concentrating and focusing, and lack of mental clarity [39]. The current state of knowledge is that brain fog can occur with long COVID-19 syndrome (symptoms lasting longer than 12 weeks that cannot be explained by another diagnosis) or post-COVID syndrome [54]. A 2021 study found that 62.4% of the patients experienced long COVID-19 syndrome with 7.2% of them struggling with brain fog [55]. Hugon and colleagues suggest that this may be related to dysfunction in the cortex of the cingulate gyrus [56]. Cognitive problems after COVID-19 infection are common. The 2021 Delgado-Alonso study examined 50 patients who underwent COVID-19, and they performed worse than healthy subjects in areas such as divided attention, selective attention, executive function, visuospatial processing, working memory and episodic memory [57]. The genesis of cognitive problems is not fully understood, but there are several hypotheses according to which cognitive dysfunction may, among other things, result from: direct invasion of the brain centers in question by the virus; from hypoxia resulting from the virus invading the lungs and bronchi, and subsequently the brain; from stroke and meningitis; from inflammation due to SARS-CoV-2 virus infection [58, 59, 60, 61]. Among those infected with the virus, inflammatory changes in blood vessels and arteriovenous problems can occur, which can

impinge on the occurrence of cognitive dysfunction [62]. Ventilation and high doses of sedative drugs are also capable of causing cognitive impairment [63, 64].

Psychological and social aspects of the pandemic and mental health problems in people who were affected by COVID-19

Globality and longevity are characteristic features of pandemics compared to other types of disasters If we look at history, we will be able to see that pandemics were able to cause serious mental health consequences [65]. This can be due to a number of aspects, some of which include illness-related health problems, unemployment, social distance or a change in past habits. The COVID-19 pandemic is no different. The SARS-CoV-2 virus has infected millions of people, and while originally the eyes of the world were mainly on the symptoms and consequences associated with respiratory failure, research on COVID-19 has shown that there are far more consequences and effects of becoming infected [66]. The uncertainty, especially in the first year of the pandemic, also could have placed a very heavy burden on people around the world – among its factors are the risk of infection or sudden lifestyle changes caused by strict restrictions in many countries to prevent the spread of the virus.

The aforementioned social isolation can have a significant impact on health and well-being. Social isolation can be defined as inadequate, insufficient interactions with other people, including those interactions at the individual, group and community levels [68, 69, 70, 71]. It should be noted that social isolation in the subject of measurability is a moving concept. Some measures refer to external isolation which refers to the frequency of contact or interactions with other people, while others focus on internal or perceived social isolation noting a person's perception of loneliness, trust and relationship satisfaction [67]. The different perspectives from which one looks at the phenomenon of social isolation are important and necessary because everyone feels and experiences given events and experiences uniquely – one can feel a sense of isolation even having frequent contact with other people, and conversely, despite limited contact with others, one may not feel isolated [72]. Until the pandemic, most of the existing studies were conducted on groups of elderly people; this was due to the fact that old age is a developmental period in a person's life in which, among other things, retirement occurs, so there is a far greater risk of external isolation [73]. During the pandemic, the phenomenon of isolation was a common and very intense one. In many countries, at one point only medical personnel and representatives of certain professions were allowed to leave their homes regularly – this phenomenon has affected all age groups. In studies on social isolation, results show that increased social isolation is associated with decreased life satisfaction, higher levels of depression, and lower levels of psychological well-being [74, 75, 76, 77]. A study conducted in 2020 to determine the relationship between communication ratings (frequency and quality) and feelings of loneliness and life satisfaction during the SARS-CoV-2 pandemic found that ratings of frequency of contact with others were the most significant for both loneliness and life satisfaction [78]. As the authors of the study explain, this may be due to the fact that interpersonal contacts define a person's participation in the life of a particular social group and are a determinant of the social network to which that particular individual belongs. At the same time, the need for affiliation is then satisfied, which may translate into a greater sense of satisfaction with life and a better sense of its quality. Looking at the phenomenon of social isolation from a different perspective, it is also worth mentioning that social isolation and poor well-being can result from dissatisfaction with the place where one lives, from lack of resources (for example, food) and problems with work [71]. Also, studies conducted on people who were quarantined showed that psychological stress reactions may emerge from the experience of physical and social isolation [79]. Among the effects of quarantine may be negative symptoms such as confusion, anger or symptoms of post-traumatic stress disorder.

The COVID-19 pandemic, as already mentioned, triggered the need for many changes in people's lives. One area that had to adapt very quickly to the new reality was education. In order to prevent backlogs and discontinuity in learning, technology has proven to be a major ally in trying to reduce the transmission of the virus, the use of which has made remote learning possible. The use of computer technology and the Internet is considered to be the main element of remote learning (e-learning) [80]. The way in which the Internet and the computer were used varied from one institution to another, as each could use different programs and applications in different ways, but the common feature of e-learning is undoubtedly the commitment that both parties had to show [81]. It turns out, however, that although e-learning in the context of the pandemic and reducing virus transmission has proven to be a very important alternative to the traditional form of education, students nevertheless prefer a form of classroom learning that allows them to acquire knowledge face-to-face. This is mentioned, among other things, in a study conducted in late 2020 and early 2021 on a group of 604 students [81]. Among the advantages of e-learning mentioned by the students were the lack of the need to commute or save time, but among the disadvantages were mentioned, for example, the lack of interaction or the lack of opportunities for practical classes which, in the case of universities or technical schools, is a significant obstacle to the effectiveness of learning and preparation for a profession. In addition to e-learning as a way of teaching and its effects and results, it is worth mentioning that attending educational institutions also plays a socialization role. This, too, was taken into account by the students in the studies cited above. Although e-learning offers a kind of human interaction, these are interactions with specific characteristics. One can refer here to the social isolation mentioned in earlier paragraphs where the intensity and quality of contacts (of course, taking into account personal preferences and perceptions of social isolation) played an important role for the well-being of the individual. Learning from home is a significant obstacle to making new friends, maintaining existing relationships, and creating and carrying out new or existing initiatives. Studies have shown that students studying remotely via e-learning during the COVID-19 pandemic experienced high levels of stress and depressive symptoms [82]. Also, the percentage of students who reported suicidal thoughts at the time is alarming. Students also stressed that their motivation to learn was lower, and that e-learning itself had a negative impact on their level of knowledge. Socialization plays a very important role not only in psychological terms, but also in the implementation of joint activities and goals such as, for example, creating and implementing projects together [83]. The results of a study focused on the psychological and academic effects of studying from the home published in 2021 also note that universities should take special care to foster peer communication in online learning – as the authors note, this can be done, for example, by promoting group work and collaborative learning, or by developing social structures [84]. Discussion groups that allow for discussion and sharing of experiences can be helpful.

The COVID-19 pandemic affected the well-being of people around the world [85]. A group of people who were particularly exposed to the virus were medical workers. As a result, medical personnel at the time were exposed to a myriad of psychological stressors – among them are, for example, fears of contracting the virus, putting their loved ones at risk, or the stress of unfavorable patient outcomes or death [86, 87]. These factors pose a potential threat to mental health by potentially causing depression, post-traumatic stress disorder, experiencing psychological distress and other mental health difficulties [85]. An international study found a link between the availability of personal protective equipment, the provision of staff training and the provision of mental health support in the workplace and mental health during COVID-19 [88]. Data compiled in this study from more than 2,500 people in 41 countries around the world indicated high levels of emotional distress. The fact of feeling depressed or hopeless at least some of the time was reported by more than 60%, and one in six people

reported experiencing these feelings frequently or all the time [88]. What's more, according to the study, those claiming not to have received adequate personal protective equipment were more than twice as likely to experience depressive thoughts. Emotional distress with higher levels was found in the UK and the US, with nearly a third of respondents reporting regular depressive thoughts. There are also studies that report that nurses are at risk of achieving worse mental health than doctors [89, 90, 91]. The results of a study in China report that nurses are at significantly higher risk for severe depression and anxiety than doctors [91]. In contrast, another study found that nurses experienced greater financial concerns and anxiety compared to other groups [92].

In the face of the SARS-CoV-2 pandemic, science and the world are faced with a very important question – how the pandemic, the COVID-19 infection and all the changes that occurred during the pandemic affected and will affect our mental health. The COVID-19 pandemic resembles the SARS-CoV and MERS-CoV pandemic in its course and psychopathological picture [93]. Therefore, based on these, researchers speculate on the likelihood of established physical and mental health disorders in COVID-19 survivors. Considering the available knowledge, patients in whom susceptibility to persistence of mental health disorders after COVID-19 treatment can be observed are those treated in the intensive care unit (especially intubated patients). In this group, symptoms of depression, PTSD, anxiety disorders, sleep disorders, symptoms of pain syndrome and chronic fatigue syndrome are more frequently diagnosed [93]. Considering the possibility of SARS-CoV-2 penetrating into the central nervous system, it may contribute to the induction of neurological and psychiatric symptoms, among other things: headaches, loss of consciousness, inappropriate sensation of stimuli, delirium, and cerebrovascular disease may be present [94]. The sudden need to change previous behavioral patterns may also not go unnoticed – this can impinge on the weakened functioning of the central nervous system. Unfortunately, it is currently too early to talk reliably about the long-term effects of the pandemic. Also, the number of methodologically correct studies is currently too small to make reliable conclusions. Based on the science so far in this area, it is possible to talk about some predictions and trends, as cited above, but it is important to remember that only by addressing this topic in future studies will it be able to tell us more about the actual effects of COVID-19 disease and the pandemic.

Summary

The COVID-19 pandemic changed the lives of the entire world in a very short period. The need to change, to adapt quickly to the new reality undoubtedly left its mark on the lives of many people. In medical and psychological terms, COVID-19 turned out to be a disease that projected not only on the respiratory system, but also on many other areas of the human body. Among them is the nervous system and cognitive functioning. As a result of the pandemic, the mental health of those who contracted COVID-19 was also damaged, although it should be emphasized that the peculiarities of the pandemic phenomenon may also have caused mental problems in those who did not contract COVID-19. Reliable, methodologically correct research will certainly yield many answers as to what the consequences of COVID-19 and its pandemic are, but unfortunately, the current state of knowledge and the time that has passed since the first cases of the disease do not allow definite conclusions to be drawn.

References

[1] Velavan TP, Meyer CG. The COVID-19 epidemic. Tropical medicine & international health. 2020;25(3):278.

[2] Singhal T. A review of coronavirus disease-2019 (COVID-19). The indian journal of pediatrics. 2020;87(4):281-6.

[3] Graham RL, Baric RS. Recombination, reservoirs, and the modular spike: mechanisms of coronavirus cross-species transmission. Journal of virology. 2010;84(7):3134-46.

[4] Pyrć K. Ludzkie koronawirusy. Postępy Nauk Medycznych. 2015;28(4B).

[5] Ng LF, Hiscox JA. Coronaviruses in animals and humans. British Medical Journal Publishing Group; 2020.

[6] Graham RL, Donaldson EF, Baric RS. A decade after SARS: strategies for controlling emerging coronaviruses. Nature Reviews Microbiology. 2013;11(12):836-48.

[7] Middle East respiratory syndrome coronavirus (MERS-COV) [Internet]. World Health Organization. World Health Organization; 2019 [cited 2022Aug30]. Available from: https://www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers#tab=tab_1

[8] Novel coronavirus (2019-ncov): Situation report, 1 [Internet]. World Health Organization. World Health Organization; 2020 [cited 2022Aug30]. Available from: https://apps.who.int/iris/handle/10665/330760

[9] Stoecklin SB, Rolland P, Silue Y, Mailles A, Campese C, Simondon A, et al. First cases of coronavirus disease 2019 (COVID-19) in France: surveillance, investigations and control measures, January 2020. Eurosurveillance. 2020;25(6):2000094.

[10] Huang X, Wei F, Hu L, Wen L, Chen K. Epidemiology and clinical characteristics of COVID-19. Archives of Iranian medicine. 2020;23(4):268-71.

[11] Coronaviruses [Internet]. National Institute of Allergy and Infectious Diseases. U.S. Department of Health and Human Services; 2021 [cited 2022Aug30]. Available from: https://www.niaid.nih.gov/diseases-conditions/coronaviruses

[12] Tracking sars-COV-2 variants [Internet]. World Health Organization. World Health Organization; [cited 2022Aug30]. Available from: https://www.who.int/activities/tracking-SARS-CoV-2-variants/

[13] Carlos AJ, Ha DP, Yeh D-W, Van Krieken R, Tseng C-C, Zhang P, et al. The chaperone GRP78 is a host auxiliary factor for SARS-CoV-2 and GRP78 depleting antibody blocks viral entry and infection. Journal of Biological Chemistry. 2021;296.

[14] Cheng Q, Yang Y, Gao J. Infectivity of human coronavirus in the brain. EBioMedicine. 2020;56:102799.

[15] Clinical characteristics of COVID-19 [Internet]. European Centre for Disease Prevention and Control. 2022 [cited 2022Aug30]. Available from: https://www.ecdc.europa.eu/en/covid-19/latest-evidence/clinical

[16] Stokes EK, Zambrano LD, Anderson KN, Marder EP, Raz KM, El Burai Felix S, Tie Y, Fullerton KE. Coronavirus Disease 2019 Case Surveillance - United States, January 22-May 30, 2020. MMWR Morb Mortal Wkly Rep. 2020 Jun 19;69(24):759-765

[17] Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. PloS one. 2020;15(6):e0234765.

[18] Kronbichler A, Kresse D, Yoon S, Lee KH, Effenberger M, Shin JI. Asymptomatic patients as a source of COVID-19 infections: A systematic review and meta-analysis. International journal of infectious diseases. 2020;98:180-6.

[19] Syangtan G, Bista S, Dawadi P, Rayamajhee B, Shrestha LB, Tuladhar R, et al. Asymptomatic people with SARS-CoV-2 as unseen carriers of COVID-19: A systematic review and meta-analysis. 2020.

[20] Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ. Presymptomatic transmission of SARS-CoV-2. Morbidity and Mortality Weekly Report. 2020;69(14):411.

[21] Symptoms of COVID-19 [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022Aug30]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html

[22] Dymecka J. Psychosocial effects of the COVID-19 pandemic. Neuropsychiatria i Neuropsychologia/Neuropsychiatry and Neuropsychology. 2021;16(1):1-10. doi: 10.5114/nan.2021.108030.

[23] Coronavirus disease (covid-19) situation reports [Internet]. World Health Organization. World Health Organization; [cited 2022Aug30]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

[24] Ye Q, Wang B, Mao J, Fu J, Shang S, Shu Q, et al. Epidemiological analysis of COVID-19 and practical experience from China. Journal of medical virology. 2020;92(7):755-69.

[25] Arbour N, Day R, Newcombe J, Talbot PJ. Neuroinvasion by human respiratory coronaviruses. Journal of virology. 2000;74(19):8913-21.

[26] Giraudon P, Bernard A. Inflammation in neuroviral diseases. Journal of neural transmission. 2010;117(8):899-906.

[27] Wei L, Wang Z, Huang Y, Schwarz G, Wheelock V. COVID-19: Neuro-invasiveness, neurotropism and neurovirulence. Journal of Neurology and Experimental Neuroscience. 2020;6(S1):S24-S31.

[28] Lima M, Siokas V, Aloizou A-M, Liampas I, Mentis A-FA, Tsouris Z, et al. Unraveling the possible routes of SARS-COV-2 invasion into the central nervous system. Current treatment options in neurology. 2020;22(11):1-15.

[29] Solomon IH, Normandin E, Bhattacharyya S, Mukerji SS, Keller K, Ali AS, et al. Neuropathological features of Covid-19. New England Journal of Medicine. 2020;383(10):989-92.

[30] Spudich S, Nath A. Nervous system consequences of COVID-19. Science. 2022;375(6578):267-9.

[31] Bergmann CC, Lane TE, Stohlman SA. Coronavirus infection of the central nervous system: host–virus stand-off. Nature Reviews Microbiology. 2006;4(2):121-32.

[32] Matschke J, Lütgehetmann M, Hagel C, Sperhake JP, Schröder AS, Edler C, et al. Neuropathology of patients with COVID-19 in Germany: a post-mortem case series. The Lancet Neurology. 2020;19(11):919-29.

[33] Iadecola C, Anrather J, Kamel H. Effects of COVID-19 on the nervous system. Cell. 2020;183(1):16-27. e1.

[34] Song E, Zhang C, Israelow B, Lu-Culligan A, Prado AV, Skriabine S, et al. Neuroinvasion of SARS-CoV-2 in human and mouse brain. Journal of Experimental Medicine. 2021;218(3).

[35] Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host–virus interaction, and proposed neurotropic mechanisms. ACS chemical neuroscience. 2020;11(7):995-8.

[36] Pyne JD, Brickman AM. The Impact of the COVID-19 Pandemic on Dementia Risk: Potential Pathways to Cognitive Decline. Neurodegenerative Diseases. 2021;21(1-2):1-23.

[37] Huang YH, Jiang D, Huang JT. SARS-CoV-2 detected in cerebrospinal fluid by PCR in a case of COVID-19 encephalitis. Brain, behavior, and immunity. 2020;87:149.

[38] Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. International journal of infectious diseases. 2020;94:55-8.

[39] Cascella M, De Blasio E. Features and Management of Acute and Chronic Neuro-Covid: Springer; 2022.

[40] Mahmudpour M, Roozbeh J, Keshavarz M, Farrokhi S, Nabipour I. COVID-19 cytokine storm: The anger of inflammation. Cytokine. 2020;133:155151.

[41] Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020;584(7821):430-6.

[42] Chou SH-Y, Beghi E, Helbok R, Moro E, Sampson J, Altamirano V, et al. Global incidence of neurological manifestations among patients hospitalized with COVID-19 - A report for the GCS-NeuroCOVID consortium and the ENERGY consortium. JAMA network open. 2021;4(5):e2112131-e.

[43] Kacem I, Gharbi A, Harizi C, Souissi E, Safer M, Nasri A, et al. Characteristics, onset, and evolution of neurological symptoms in patients with COVID-19. Neurological Sciences. 2021;42(1):39-46.

[44] Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. New England Journal of Medicine. 2020;382(23):2268-70.

[45] Asadi-Pooya AA, Simani L, Shahisavandi M, Barzegar Z. COVID-19, de novo seizures, and epilepsy: a systematic review. Neurological Sciences. 2021;42(2):415-31.

[46] Khedr EM, Shoyb A, Mohammaden M, Saber M. Acute symptomatic seizures and COVID-19: Hospital-based study. Epilepsy Research. 2021;174:106650.

[47] Garg RK, Paliwal VK, Gupta A. Encephalopathy in patients with COVID-19: a review. Journal of Medical Virology. 2021;93(1):206-22.

[48] Bridwell R, Long B, Gottlieb M. Neurologic complications of COVID-19. The American journal of emergency medicine. 2020;38(7):1549. e3-. e7.

[49] Jiang F, Yang W-L, Wang J-W, Zhu Z, Luo C, Arendt-Nielsen L, et al. Pain during and after coronavirus disease 2019: Chinese perspectives. Pain Reports. 2021;6(1).

[50] Vittori A, Lerman J, Cascella M, Gomez-Morad AD, Marchetti G, Marinangeli F, et al. Coronavirus Disease 2019 Pandemic Acute Respiratory Distress Syndrome Survivors: Pain After the Storm? Anesthesia and analgesia. 2020.

[51] Finsterer J, Scorza FA. Guillain-Barre syndrome in 220 patients with COVID-19. The Egyptian journal of neurology, psychiatry and neurosurgery. 2021;57(1):1-7.

[52] Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. Clinical infectious diseases. 2020;71(15):889-90.

[53] Nepal G, Rehrig JH, Shrestha GS, Shing YK, Yadav JK, Ojha R, et al. Neurological manifestations of COVID-19: a systematic review. Critical Care. 2020;24(1):421.

[54] Overview: Covid-19 rapid guideline: Managing the long-term effects of covid-19: Guidance [Internet]. NICE. 2020 [cited 2022Aug30]. Available from: https://www.nice.org.uk/guidance/ng188

[55] Asadi-Pooya AA, Akbari A, Emami A, Lotfi M, Rostamihosseinkhani M, Nemati H, et al. Long COVID syndrome-associated brain fog. Journal of medical virology. 2022;94(3):979-84.

[56] Hugon J, Msika E-F, Queneau M, Farid K, Paquet C. Long COVID: cognitive complaints (brain fog) and dysfunction of the cingulate cortex. Journal of Neurology. 2022;269(1):44-6.

[57] Delgado-Alonso C, Valles-Salgado M, Delgado-Álvarez A, Yus M, Gómez-Ruiz N, Jorquera M, et al. Cognitive dysfunction associated with COVID-19: A comprehensive neuropsychological study. Journal of Psychiatric Research. 2022;150:40-6.

[58] Vanderlind WM, Rabinovitz BB, Miao IY, Oberlin LE, Bueno-Castellano C, Fridman C, et al. A systematic review of neuropsychological and psychiatric sequalae of COVID-19: implications for treatment. Current opinion in psychiatry. 2021;34(4):420.

[59] Kashani KB, editor Hypoxia in COVID-19: sign of severity or cause for poor outcomes. Mayo Clinic Proceedings; 2020: Elsevier.

[60] Spence JD, De Freitas GR, Pettigrew LC, Ay H, Liebeskind DS, Kase CS, et al. Mechanisms of stroke in COVID-19. Cerebrovascular Diseases. 2020;49(4):451-8.

[61] Magalhaes RC, Pimenta LP, Barbosa IG, Moreira JM, de Barros JL, Teixeira AL, et al. Inflammatory molecules and neurotrophic factors as biomarkers of neuropsychomotor development in preterm neonates: a systematic review. International Journal of Developmental Neuroscience. 2018;65:29-37.

[62] Koralnik IJ, Tyler KL. COVID-19: a global threat to the nervous system. Annals of neurology. 2020;88(1):1-11.

[63] Girard TD, Thompson JL, Pandharipande PP, Brummel NE, Jackson JC, Patel MB, et al. Clinical phenotypes of delirium during critical illness and severity of subsequent long-term cognitive impairment: a prospective cohort study. The Lancet Respiratory Medicine. 2018;6(3):213-22.

[64] Hopkins RO, Jackson JC. Long-term neurocognitive function after critical illness. Chest. 2006;130(3):869-78.

[65] Han RH, Schmidt MN, Waits WM, Bell AK, Miller TL. Planning for mental health needs during COVID-19. Current psychiatry reports. 2020;22(12):1-10.

[66] Aknin LB, De Neve J-E, Dunn EW, Fancourt DE, Goldberg E, Helliwell JF, et al. Mental health during the first year of the COVID-19 pandemic: A review and recommendations for moving forward. Perspectives on psychological science. 2022;17(4):915-36.

[67] Clair R, Gordon M, Kroon M, Reilly C. The effects of social isolation on well-being and life satisfaction during pandemic. Humanities and Social Sciences Communications. 2021;8(1):1-6.

[68] Nicholson NR. A review of social isolation: an important but underassessed condition in older adults. The journal of primary prevention. 2012;33(2):137-52.

[69] Smith BJ, Lim MH. How the COVID-19 pandemic is focusing attention on loneliness and social isolation. Public Health Res Pract. 2020;30(2):3022008.

[70] Umberson D, Karas Montez J. Social relationships and health: A flashpoint for health policy. Journal of health and social behavior. 2010;51(1):S54-S66.

[71] Zavaleta D, Samuel K, Mills CT. Measures of social isolation. Social Indicators Research. 2017;131(1):367-91.

[72] Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT. A short scale for measuring loneliness in large surveys: Results from two population-based studies. Research on aging. 2004;26(6):655-72.

[73] Nyqvist F, Victor CR, Forsman AK, Cattan M. The association between social capital and loneliness in different age groups: a population-based study in Western Finland. BMC public health. 2016;16(1):1-8.

[74] Cacioppo JT, Cacioppo S. Social relationships and health: The toxic effects of perceived social isolation. Social and personality psychology compass. 2014;8(2):58-72.

[75] Courtin E, Knapp M. Social isolation, loneliness and health in old age: a scoping review. Health & social care in the community. 2017;25(3):799-812.

[76] Dahlberg L, McKee KJ. Social exclusion and well-being among older adults in rural and urban areas. Archives of gerontology and geriatrics. 2018;79:176-84.

[77] Harasemiw O, Newall N, Mackenzie CS, Shooshtari S, Menec V. Is the association between social network types, depressive symptoms and life satisfaction mediated by the perceived availability of social support? A cross-sectional analysis using the Canadian Longitudinal Study on Aging. Aging & mental health. 2019;23(10):1413-22.

[78] Mróz J, Kosowski P. Ocena komunikacji a poczucie samotności i satysfakcji z życia w czasie pandemii. Kwartalnik Naukowy Fides et Ratio. 2020;42(2):214-26. doi: 10.34766/fetr.v42i2.284.

[79] Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. The lancet. 2020;395(10227):912-20.

[80] Aboagye E, Yawson JA, Appiah KN. COVID-19 and E-learning: The challenges of students in tertiary institutions. Social Education Research. 2021:1-8.

[81] Gherheș V, Stoian CE, Fărcașiu MA, Stanici M. E-learning vs. face-to-face learning: Analyzing students' preferences and behaviors. Sustainability. 2021;13(8):4381.

[82] Rutkowska A, Cieślik B, Tomaszczyk A, Szczepańska-Gieracha J. Mental Health Conditions Among E-Learning Students During the COVID-19 Pandemic. Frontiers in Public Health. 2022;10.

[83] Adnan M, Anwar K. Online Learning amid the COVID-19 Pandemic: Students' Perspectives. Online Submission. 2020;2(1):45-51.

[84] Wilczewski M, Gorbaniuk O, Giuri P. The psychological and academic effects of studying from the home and host country during the COVID-19 pandemic. Frontiers in Psychology. 2021;12:644096.

[85] Greenberg N, Weston D, Hall C, Caulfield T, Williamson V, Fong K. Mental health of staff working in intensive care during Covid-19. Occupational Medicine. 2021;71(2):62-7.

[86] Greenberg N, Tracy D. What healthcare leaders need to do to protect the psychological well-being of frontline staff in the COVID-19 pandemic. Bmj Leader. 2020.

[87] Williamson V, Greenberg N, Bowden G, Rothenfluh D, Nnadi C, Reynolds J. The mental health impact of providing spine care during COVID-19. The Spine Journal. 2020;20(9):1363-6.

[88] Khajuria A, Tomaszewski W, Liu Z, Chen J-h, Mehdian R, Fleming S, et al. Workplace factors associated with mental health of healthcare workers during the COVID-19 pandemic: an international cross-sectional study. BMC health services research. 2021;21(1):1-11.

[89] Cai H, Tu B, Ma J, Chen L, Fu L, Jiang Y, et al. Psychological impact and coping strategies of frontline medical staff in Hunan between January and March 2020 during the outbreak of coronavirus disease 2019 (COVID-19) in Hubei, China. Medical science monitor: international medical journal of experimental and clinical research. 2020;26:e924171-1.

[90] Cao J, Wei J, Zhu H, Duan Y, Geng W, Hong X, et al. A study of basic needs and psychological wellbeing of medical workers in the fever clinic of a tertiary general hospital in Beijing during the COVID-19 outbreak. Psychotherapy and psychosomatics. 2020:1.

[91] Lai J, Ma S, Wang Y, Cai Z, Hu J, Wei N, et al. Factors associated with mental health outcomes among health care workers exposed to coronavirus disease 2019. JAMA network open. 2020;3(3):e203976-e.

[92] De Kock JH, Latham HA, Leslie SJ, Grindle M, Munoz S-A, Ellis L, et al. A rapid review of the impact of COVID-19 on the mental health of healthcare workers: implications for supporting psychological well-being. BMC public health. 2021;21(1):1-18.

[93] Makara-Studzińska M, Załuski M, Lickiewicz J. Czy ozdrowieńcy COVID-19 to przyszli pacjenci psychiatrów i psychologów? Szybki przegląd literatury naukowej. Psychiatria. 2021;18(2):140-51.

[94] Sinanović O, Muftić M, Sinanović S. COVID-19 pandemia: neuropsychiatric comorbidity and consequences. Psychiatria Danubina. 2020;32(2):236-44.