Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The SARS-CoV-2 and mental health: From biological mechanisms to social consequences

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A B S T R A C T

In December 2019, the first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, COVID-19) infection was reported. In only few weeks it has caused a global pandemic, with mortality reaching 3.4%, mostly due to a severe pneumonia. However, the impact of SARS-CoV-2 virus on the central nervous system (CNS) and mental health outcomes remains unclear. Previous studies have demonstrated the presence of other types of coronaviruses in the brain, especially in the brainstem. There is evidence that the novel coronavirus can penetrate CNS through the olfactory or circulatory route as well as it can have an indirect impact on the brain by causing cytokine storm. There are also first reports of neurological signs in patients infected by the SARS-Cov-2. They show that COVID-19 patients have neurologic manifestations like acute cerebrovascular disease, conscious disturbance, taste and olfactory disturbances. In addition, there are studies showing that certain psychopathological symptoms might appear in infected patients, including those related to mood and psychotic disorders as well as post-traumatic stress disorder. Accumulating evidence also indicates that the pandemic might have a great impact on mental health from the global perspective, with medical workers being particularly vulnerable. In this article, we provide a review of studies investigating the impact of the SARS-CoV-2 on the CNS and mental health outcomes. We describe neurobiology of the virus, highlighting the relevance to mental disorders. Furthermore, this article summarizes the impact of the SARS-CoV-2 from the public health perspective. Finally, we present a critical appraisal of evidence and indicate future directions for studies in this field.

1. Introduction

In December 2019, a first case of pneumonia, later known as novel coronavirus pneumonia was reported in Wuhan, Hubei Province, People's Republic of China. Experts from the Centers for Disease Control declared that it had been caused by a novel coronavirus (Huang et al., 2020a). The World Health Organization (WHO) named the disease COVID-19, and the International Committee on Taxonomy of Viruses named the virus the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Consequently, the global spread of SARS-CoV-2 contributed to enormous medical and social burden worldwide. The WHO has estimated the SARS-CoV-2 mortality rate at 3.4% (*WHO Director-General's opening remarks at the media briefing on COVID-19 - 3 March* 2020 - World Health Organization, 2020).

The SARS-CoV-2 is a novel coronavirus, which has a single-stranded positive sense RNA genome with an organization typical to other coronaviruses (CoVs), such as SARS and MERS (Zhu et al., 2020a). Genomic analyses have revealed that the SARS-CoV-2 also shares structural and biological similarity with other CoVs, such as MERS and SARS (Yu et al., 2020). However, the impact of the SARS-CoV-2 on the central nervous system and metal health remains unclear. Therefore, it may be relevant to refer to biology of other coronaviruses to understand the mechanisms underlying the consequences of SARS-CoV-2 infection. Besides viral structure, most coronaviruses share a similar infection pathway (Hulswit et al., 2016). There is evidence that neurotropism is one of common characteristics of CoVs (Li et al., 2012; Li et al., 2020a; Xu et al., 2005). Their presence has been demonstrated in the central nervous system (CNS) (Netland et al., 2008a) and in the cerebrospinal fluid (Marc et al., 2013). It is also important to note that patients with the SARS-CoV-2 infection can exhibit psychiatric symptoms, like insomnia, depressive mood, aggressive outbursts (Kim et al., 2018; Jeong et al., 2016). During the previous SARS and MERS epidemics, it has been shown that infected individuals commonly presented with symptoms of confusion (27.9%), depression (32.6%), memory impairment (34.1%) insomnia (41.9%) and occasionally steroid-induced mania and psychosis (0.7%). However, the same study indicated the long-term mental health effects, including depression, insomnia, anxiety, irritability, fatigue or even traumatic memories and Post-traumatic stress disorder (PTSD) (Rogers et al., 2020).

Nevertheless, the impact of the current pandemic goes far beyond direct brain damage. Increased panic, public restrictions, mass quarantine and overwhelming pressure on medical professionals might have a great impact on global mental health.

In this article, we provide a narrative review of studies investigating

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Table 1
Studies concerning neurological and psychiatric symptoms in COVID-19 patients and main findings included in the review.

Publication (year)	Tools	Group N	Results
Xu et al. (Xu et al., 2020a)	TTCGA and FANTOM5 CAGE dataset	695	ACE2 receptor is expressed on the mucosa of oral cavity.
Giacomelli et al. (Giacomelli et al., 2020)	A cross-sectional survey	59	One third of patients with COVID-19 reported taste or olfactory disorder.
Mao et al. (Mao et al., 2020)	Clinical data on neurological symptoms	214	Among COVID-19 patients, 36.4% had neurologic manifestations. Among the severe patients, 88% had neurologic manifestations.
Chen et al. (Chen et al., 2020a)	A retrospective study	21	Hypoxic encephalopathy occurred in 18.2% cases.
Moriguchi et al. (2020) (Moriguchi et al., 2020)	A case report	1	A case of meningitis/encephalitis in patient with coronavirus infection.
Helms et al. (Helms et al., 2020)	MRI, EEG, lumbar puncture	64	Larger leptomeningeal spaces in 62% of cases and recent asymptomatic ischemic stroke in 15% of cases in MRI. Non-specific in EEG. Oligoclonal bands (28%), elevated protein and IgG (14%) in cerebrospinal fluid analysis. Agitation reported in 69% of ICU patients. After discharge, 33% of patients had dysexecutive syndrome.
Debnath et al. (Debnath et al., 2020)	A retrospective study	40,469	Among the COVID-19 patients, 22.5% express neuropsychiatric symptoms, including headache (3.7%), insomnia (3.4%), encephalopathy (2.3%), cerebrovascular disease (1%), depression (3.8%) and suicidal ideation (0.2%).
Correa-Palacio et al. (Correa-Palacio et al., 2020)	A case report	1	A psychotic episode.
Chandra et al. (Chandra et al., 2020)	A case series	2	Two cases of psychotic episodes.
Mawhinney et al. (Mawhinney et al., 2020)	A case report	1	An acute manic episode.
Beach et al. (2020) (Beach et al., 2020)	A case series	4	Delirium as an only manifestation of COVID-19 infection.
Epstein et al. (Epstein et al., 2020)	A case report	1	Suicide attempt in patient with SARS-CoV-2 infection, who suffered from severe anxiety and insomnia.
Qi et al. (2020) (Qi et al., 2020b)	GHQ-12, PCL−C, SAS, SDS, FS-14, SSRS, SCSQ	41	PTSD symptoms occur among 12.2% of patients with COVID-19. The said group presented: high perceived stigmatization, fatigue (53.9%), anxiety and/or depression (26.8%).
Rohde et al. (Rohde et al., 2020)	Medical notes	11,072	Reported anxiety and PTSD in 8% of patients with COVID-19.
Kong et al. (Kong et al., 2020)	A metanalysis	976	Depression occurred in 35% and anxiety symptoms in 28% of patients with COVID-19
Yang et al. (Yang et al., 2020)	HAMD, HAMA	143	Anxiety and depression were more severe in COVID-19 patients than in general pneumonia group.
Chen et al. (Chen et al., 2020b)	A retrospective study	99	Confusion was reported in 9% of patients with novel coronavirus infection.
Huang et al. (2020) (Huang et al., 2020b)	A retrospective study	36	Consciousness disturbance was reported in 22.2% of COVID-19 patients on admission.
Qi et al. (Qi et al., 2020a)	A retrospective study	267	Severe patients presented confusion more often (20% vs 6.9%)
Leung et al. (Leung et al., 2020)	A retrospective study	50	Consciousness impairment was observed in 2% of SARS-CoV-2 patients.
Zhang et al. (Zhang et al., 2020a)	A retrospective study	82	Altered consciousness was reported in 21% COVID-19 patients, who subsequently died.

TTCGA: The Cancer Genome Atlas, FANTOM5 CAGE: Functional Annotation of The Mammalian Genome Cap, Analysis of Gene Expression, ACE2: Angiotensin-converting enzyme 2, PTSD: posttraumatic stress disorder, MRI: Magnetic Resonance Imaging, EEG: Electroencephalography, HAMA: Hamilton Anxiety Scale, HAMD: Hamilton Depression Scale. GHQ-12: General Health Questionnaire, PCL−C: PTSD Checklist – Civilian Version, SAS: Riker Sedation Agitation Scale, SDS: Sheehan Disability Scale, FS-14: Fatigue Scale, SSRS: Social Skills Rating System, SCSQ: Simple Coping Scale Questionnaire.

the impact of the SARS-CoV-2 on the CNS and mental health outcomes. We describe neurobiology of the virus, highlighting its relevance to mental disorders. Furthermore, this article summarizes the impact of the SARS-CoV-2 from the public health perspective. Finally, we provide a critical appraisal of evidence and indicate future directions for studies in this field.

2. Methods

In order to analyze the existing literature on neurological and psychiatric symptoms associated with the SARS-CoV-2, a review of the following databases was performed: the PubMed, the Scopus, the CINAHL and the Google Scholar. The following keywords were used in the search using the MeSH terminology: “SARS” or “coronavirus” or “COVID” and “brain” or “central nervous system” or “mental health” or “psychiatry”. Search strategy was limited to the publication period covering the years 2019–2020. A total of 1002 records was identified after removing duplicates. Finally, 47 original studies and 2 meta-analyses were included (Table 1, 2, 3). Additionally, this article was based on 22 non-original articles. A narrative review was structured around two main topics: 1) the impact of the SARS-CoV-2 on the CNS and 2) the impact of the SARS-CoV-2 from the public mental health perspective.

3. The SARS-CoV-2 impact on the central nervous system

3.1. Central nervous system penetration

There are only few pathways of CNS invasion by CoVs that have been confirmed. It has been shown that CoVs may first invade peripheral nerves, and then enter the CNS via a synapse route (Li et al., 2013; Andries and Pensaert, 1980). Experimental studies have revealed that other CoVs, when given intranasally, could access the brain through the olfactory bulb, and then spread to specific brain regions (Netland et al., 2008a; Netland et al., 2008b). Another well-known pathway of neural invasion is through systemic circulation (Baig et al., 2020). Among the brain areas that should be regarded as invloved, the brainstem seems to be the major target for the SARS-CoV (Netland et al., 2008b). There are two crucial nuclei in the brainstem: the nucleus of the solitary tract and the nucleus ambiguus. The former nucleus receives sensory information from receptors in the respiratory tract, and the latter one together with the nucleus of the solitary tract provide innervation to airway glands, smooth muscles, and blood vessels. Such neuroanatomic interconnections indicate that the death of infected patients may be due to the dysfunction of the cardiorespiratory center in the brainstem (Li et al., 2020a).

It has been found that the angiotensin converting enzyme 2 receptor (ACE2) is crucial for penetrating cells by the SARS-CoV and the SARS-CoV-2 (Wrapp et al., 2020; Zhao et al., 2020). It plays a role in cardiovascular disease and is widely present in multiple human organs,

Table 2
Studies concerning impact of SARS-CoV-2 pandemic on mental health in global population.

Publication (year)	Tools	Group N	Results
Liu et al. (Liu et al., 2020a)	PCL-5, PSQI	285	PTSS occured in 7% of population in the most affected areas. Bad sleep quality was linked to PTSS.
Zhang et al. (Zhang and Ma, 2020)	IES	263	Half of general population felt fear due to the COVID-19 pandemic but in general, it had a mild stressful impact
Junling et al. (2020) (Junling et al., 2020)	WHO-5, GAD-7	4872	Prevalence of depression and anxiety among public in China was 48%, and was connected to social media exposure.
Li et al. (Li et al., 2020b)	Machine-learning analysis of social media posts	17,865	After the outbreak of the pandemics, negative emotions and sensitivity to social risks arouse, while the scores of positive emotions and life satisfaction fell. Active social media users were concerned more about their health and family, and less about leisure and friends.
Zhang et al. (Zhang et al., 2020b)	SF12, K6, SWLS	369	As many as 38% of people had to work from home due to pandemic. A group accounting for 25% stopped working and had worse mental and physical health distress level. Physically active people were more vulnerable to wellbeing issues.
Cao et al. (Cao et al., 2020)	GAD-7	7143	As many as 0.9% of college students experienced severe, 2.7% moderate, and 21.3% mild anxiety.
Zhong et al. (Zhong et al., 2020)	An online questionnaire	6910	People with better knowledge on the COVID-19 had more positive attitudes and more often used preventive measures.
Roy et al. (Roy et al., 2020)	An online questionnaire	662	Public opinion on preventive measures was generally positive. People reported anxiety, worries about getting infected and sleep problems during the COVID-19 pandemic. Above 80% of people thought that they needed mental health help during outbreak.
Zulkifli et al. (Zulkifli et al., 2020)	Case report	1	The first case report on psychotic episodes related to pandemic outbreak.
Qiu et al. (Qiu et al., 2020)	A self reported questionnaire	52,730	As many as 35% of people in quarantine experienced psychological distress. Women, individuals with higher education and older people were much more vulnerable to develop PTSD, in contrast to young people.
Xiao et al. (Xiao et al., 2020a)	PSCI-16, SAS, SASR, PSQI	170	Low social capital was associated with increased anxiety and stress; higher social capital was positively associated with good quality of sleep.

PCL-5: Checklist for DSM-5, PSQI: Pittsburgh Sleep Quality Index, PTSS: Posttraumatic stress symptoms, IES: Impact of Event Scale, WHO-5: WHO-Five Well-Being Index, GAD-7: Generalized Anxiety Disorder Scale, SF12: The Short Form-12, K6: the six-item Kessler Psychological Distress Scale, SWLS: Satisfaction With Life Scale, PSCI-16: Personal Social Capital Scale 16 questionnaire, SAS: Self-Rating Anxiety Scale, SASR: Stanford Acute Stress Reaction questionnaire, SAS: Self-Rating Anxiety Scale.

including the nervous system and skeletal muscles (Hamming et al., 2004). The ACE2 is also expressed by the epithelial cells of oral cavity (Xu et al., 2020a), which would support the concept of olfactory route of the CNS invasion by a novel coronavirus (Table 1). Indeed, it has been shown that around one third of patients with COVID-19 report taste or olfactory disorder (Giacomelli et al., 2020). Moreover, based on epidemiological data on COVID-19, the average time from the first symptoms to hospital admission is 7 days, and to the intensive care is 8 days. Therefore, the latency period may be enough for the virus to enter and destroy neurons (Wang et al., 2020a). On the other hand, it has been proposed that the novel coronavirus can reach the ACE2 receptors within CNS also through the systemic circulation (Baig et al., 2020). However, there is still a lack of studies confirming this pathway.

3.2. Neuroinflammation

The SARS-CoV-2 can also affect the brain tissue by causing a cytokine storm, which is believed to have an impact on neurological and psychiatric symptoms (Clark and Vissel, 2017). It has been reported that high cytokine release, characterized by increased production of interleukin (IL)-2, IL-7, granulocyte-colony stimulating factor, interferon-γ inducible protein 10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1-α, and tumor necrosis factor-α, is associated with a severity of COVID-19 (Huang et al., 2020a). In other studies, the authors have found that the release of IL-1b and IL-6 was triggered by the novel coronavirus infection (Conti et al., 2020). Additionally, a retrospective, multicentric study of 150 COVID-19 cases in Wuhan revealed that elevated levels of ferritin and IL-6 might serve as predictors of mortality (Ruan et al., 2020). Authors proposed that chronic low-grade inflammatory response might be crucial in the neuropsychiatric manifestation of the SARS-CoV-2 infection (Debnath et al., 2020). However, it remains questionable whether the SARS-CoV-2 infection has an impact on inflammation and mental health independently (Wang et al., 2020b), or if it is a causal process (Troyer et al., 2020). The aforementioned issue needs to be addressed by future studies (Horn et al., 2020).

Overall, there are several potential mechanisms that may be responsible for the effect of COVID-19 on the CNS. Direct viral invasion of the brain causing encephalitis, neuroinflammation, peripheral organ dysfunction and cerebrovascular changes can separately, or all combined cause neuropsychiatric symptoms (Heneka et al., 2020).

3.3. Neurological manifestation of the SARS-CoV-2 infection

There are first reports showing that the SARS-CoV-2 can damage CNS, causing viral encephalitis, hypoxic encephalopathy (Chen et al., 2020a), meningitis-encephalitis (Moriguchi et al., 2020), infectious toxic encephalopathy and acute cerebrovascular disease (Wu et al., 2020). An autopsy report of deceased patients showed brain tissue edema and partial neuronal degeneration (Xu et al., 2020b). Moreover, athe first case of viral encephalitis caused by the SARS-CoV-2 was confirmed in March 2020. However, only few studies on neurological signs of patients infected by the SARS-CoV-2 have been conducted so far. One of such studies showed that 36.4% of COVID-19 patients had neurological manifestations. Severely affected patients were more likely to develop neurological symptoms (88%), especially acute cerebrovascular disease, conscious disturbances and muscle injury (Mao et al., 2020). Moreover, the authors also found that the lymphocyte counts were lower with D-dimer levels higher in patients with CNS symptoms, what can explain why the patients with severe manifestation develop cerebrovascular disease. In another study, the authors reported that one third of patients infected by the SARS-CoV-2 had symptoms from peripheral nervous system, namely taste or olfactory disturbances; 20.3% of them had symptoms before hospital admission, while 13.5% experienced the symptoms during the hospitalization (Giacomelli et al., 2020). The study analyzed MRI images of 13 infected patients, as well as EEG and cerebrospinal fluid. MRI showed larger leptomeningeal spaces in 62% and recent asymptomatic ischemic stroke in 15% of cases. EEG changes were non-specific, but cerebrospinal fluid analysis demonstrated the presence of oligoclonal bands (28%) and elevated

Table 3
Studies concerning impact of the SARS-CoV-2 pandemic on mental health in healthcare professionals.

Publication (year)	Tools	Group N	Results
Mo et al. (Mo et al., 2020)	SOS, SAS	180	Nurses who fight against COVID-19 are under stress. Being only children, working long hours per week, and anxiety are concerned to be the risk factors.
Bo et al. (Bo et al., 2020)	PCL-C	730	As many as 96.2% of the COVID-19 patients in stable condition experience significant posttraumatic stress symptoms. Half of them find the psycho-educational services helpful.
Shi et al. (Shi et al., 2020)	33-item survey questionnaire	311	As many as 89.51% of psychiatrists have extensive knowledge of the COVID-19 and 77.17% of them want to treat psychiatric patients with the SARS-CoV-2 virus infection.
Pappa et al. (Pappa et al., 2020)	A metanalysis	33,062	Anxiety was reported by 23.2%, depression by 22.8% and insomnia by 38.9% of medical workers in the analyzed papers. Female professionals and nurses have more prominent affective symptoms.
Kang et al. (Kang et al., 2020)	PHQ-9, GAD-7, ISI, IES-R	994	As many as 22.4% of medical and nursing staff working in Wuhan had moderate, and 6.2% severe disturbances in the wake of the epidemic, especially young women. As many as 17.5% had to participate in counseling or psychotherapy.
Lai et al. (Lai et al., 2020)	PHQ-9, GAD-7, ISI, IES-R	1257	Depression occurs in 50.4% of health care workers, anxiety in 44.6%, insomnia in 34.0%, and distress concerns 71.5% of them. The risk is higher for women, those with seniority titles and for workers at the center of the epidemic.
Lu et al. (Lu et al., 2020)	NRS, HAMA, HAMD	2299	Front line medical staff who have close contact with infected patients have higher fear, anxiety and depression scores in comparison to administrative staff.
Sun et al. (Sun et al., 2020)	Colaizzi's phenomenological method, interviews conducted face-to-face or by telephone	20	Nurses report, that fatigue, discomfort, and helplessness are caused by work, anxiety, and concern for infecting other people. Self-coping styles include: psychological and life adjustment, team support, altruistic acts and rationalization.
Xiao et al. (Xiao et al., 2020b)	SAS, GSES, SASR, PSQI, SSRS	80	Social support is associated with better self-efficacy and sleep quality, as well as with lower degree of anxiety and stress among medical staff that treated patients with COVID-19 infection.
Du et al. (Du et al., 2020)	BDI-II, BAI	134	Depression was reported by 12.7% and anxiety by 20.1% of medical workers.
Guo (Guo et al., 2020)	SAS, SDS	11,118	As many as 31% of healthcare workers reported depression and 17% of them declared anxiety during the pandemic.
Liu et al. (Liu et al., 2020b)	SAS	512	As many as 12.5% of medical stuff working with COVID-19 patients reported anxiety.
Qi (Qi et al., 2020c)	AIS, PSQI	1306	Almost half of all medical workers (45.5%) suffer from insomnia.
Tan et al. (Tan et al., 2020)	DASS-21	470	Depressive symptoms were present in 8.9% of healthcare professionals and anxiety in 14.5% of them.
Zhang et al. (Zhang et al., 2020d)	GAD-7 ISI PHQ-9	1563	Half of medical professionals suffers from depression, 45% from anxiety and 36% from insomnia.
Zhang et al. (Zhang et al., 2020e)	ISI GAD-2 PHQ-2	2182	Sleep disturbance was reported by 33.9% of healthcare workers. As many as 10% suffered from anxiety and depression.
Zhu et al. (Zhu et al., 2020b)	GAD-7 PHQ-9	5062	As many as 24% of medical stuff experience anxiety, and 13.5% depression symptoms during pandemic.

PTSD: posttraumatic stress disorder, PCL-5: Checklist for DSM-5, PSQI: Pittsburgh Sleep Quality Index, PTSS: Posttraumatic stress symptoms, GAD-7: Generalized Anxiety Disorder Scale, SAS: Self-Rating Anxiety Scale, SASR: Stanford Acute Stress Reaction questionnaire, SOS: Stress Overload Scale, SAS: Self-Rating Anxiety Scale, PHQ-9: Patient Health Questionnaire, ISI: 7-item Insomnia Severity Index, IES-R: the 22-item Impact of Event Scale-Revised, NRS: a numeric rating scale on fear, HAMA: Hamilton Anxiety Scale, HAMD: Hamilton Depression Scale, GSES: the General Self-Efficacy Scale, SASR: the Stanford Acute Stress Reaction questionnaire, SSRS: the Social Support Rate Scale, BDI-II: Beck Depression Inventory, BAI: Beck Anxiety Inventory, AIS: Athens Insomnia Scale, DASS-21: Depression, Anxiety and Stress Scale.

levels of protein and IgG (14%) (Helms et al., 2020).

A large study of 40,469 patients diagnosed with the COVID-19 infection showed that 22.5% of them expressed neuropsychiatric symptoms, including headache (3.7%), insomnia (3.4%), encephalopathy (2.3%), cerebrovascular disease (1%), depression (3.8%) and suicidal ideation (0.2%) (Nalleballe et al., 2020).

3.4. Mental health and SARS-CoV-2 infection

The first studies that have already been carried out, confirm that the novel coronavirus pandemic can also severely affect mental health of infected individuals.

There are case reports of first-episode psychosis in people with SARS-CoV-2 infection (Correa-Palacio et al., 2020; Chandra et al., 2020). However, it is unclear, whether the etiology is related to the virus itself, to the stress related to pandemic, or to treatment with the use of corticosteroids or hydroxychloroquine (Correa-Palacio et al., 2020). Unfavorable mental health outcomes were reported also as one of the first signs of the novel coronavirus infection in a patient with acute manic episode (Mawhinney et al., 2020). Another paper showed 4 cases of delirium in older patients, as the only clinical manifestation of the COVID-19 (Beach et al., 2020).

A meta-analysis of 12 studies considering a combined number of 976 patients with the SARS-CoV-2 infection has shown that depressive symptoms occurred in 35% and anxiety in 28% of them (Kong et al., 2020). One of the studies that have been performed, compared the COVID-19 patients with individuals suffering from other forms of pneumonia (Yang et al., 2020). It has revealed more severe anxiety and depression symptoms in the SARS-CoV-2 patients. Unfavorable outcome due to severe anxiety was reported in one patient, who consequently attempted suicide (Epstein et al., 2020). Four other studies described high prevalence of confusion and consciousness impairment among the COVID-19 patients (2%- 22%) (Chen et al., 2020b; Huang et al., 2020b; Qi et al., 2020a; Leung et al., 2020). Altered consciousness could be associated with more severe progress of the disease, as it had been reported in 21% COVID-19 patients, who subsequently died (Zhang et al., 2020a). A paper elaborated in France, reported agitation in 69% of patients, however it was caused by drugs withdrawal (Helms et al., 2020). As far as 33% of patients from this study had dysexecutive syndrome with attention and movements impairment at the day of discharge. Moreover, a report concerning 730 COVID-19 patients who were in a stable condition, demonstrated that 96.2% of them

experienced symptoms meeting the criteria of PTSD. Although all the patients were provided with psycho-educational support, only half of them claimed that those interventions were helpful (Bo et al., 2020). On the other hand, different authors suggest much lower percentage of PTSD in this group (8%) (Rohde et al., 2020). Another paper also has shown a high prevalence of PTSD among patients with the COVID-19 (12.2%). Authors highlighted high perceived stigmatization in this group, alongside fatigue (53.9%), anxiety and/or depression (26.8%) (Qi et al., 2020b).

It is also important to mention that psychiatric patients can be more susceptible to the SARS-CoV-2 infection (Yao et al., 2020). Due to their mental health, poor self-control, self-care, and lack of insight, they may be incapable of practicing infection control, therefore being vulnerable to the COVID-19 and its complications (Kim and Su, 2020). On the other hand, patients with obsessive compulsive disorder can be more exposed to stress, which would lead to exacerbation of their symptoms (Fineberg et al., 2020). However, the survey of 311 psychiatrists showed that 89.51% of them obtained extensive knowledge on the COVID-19 and 77.17% of them wanted to treat patients with mental disorders and comorbid SARS-CoV-2 infection (Shi et al., n.d.). Still, it is important to address this point in order to apply new strategies, especially considering a lack of adequate training in internal medicine among psychiatrists in some countries (Xiang et al., 2020a).

4. The impact of the SARS-CoV-2 from the public mental health perspective

4.1. A global perspective

Pandemic should especially be considered in terms of global social phenomena. During the pandemic, public mental health can be affected for multiple reasons (Table 2). Media reporting the escalating numbers of new cases and deaths, public restrictions and mass lockdown are likely to raise anxiety, which may have serious implications for global mental health (Rubin and Wessely, 2020). For instance, it has been estimated that the prevalence of posttraumatic stress symptoms was 7% in most affected areas in China (Liu et al., 2020a). Similar results have been obtained by other authors, who indicated that half of general population feel horrified due to the COVID-19 pandemic, however in general, it had a mild stressful impact (Zhang and Ma, 2020). In contrast, it has been suggested that depression or anxiety symptoms could affect almost 50%. One of the potential risk factors for the occurrence of psychopathological symptoms may be the frequent social media exposure (Junling et al., 2020). For the sake of reference, a recent study in which machine learning techniques have been used, analyzed posts of more than 17 thousand social media users who lived in China, in regions affected by the pandemics. It was found that the level of negative emotions and sensitivity to social risks increased, while the scores of positive emotions and the level of life satisfaction decreased during the pandemic (Li et al., 2020b).

Several regulations that affect daily activities, have been implemented in order to stop the spread of the virus. Most of them are focused on maintaining physical isolation and social distance, which so far are the only effective methods to reduce the possibility of further transmission of coronavirus. However, despite the great need to introduce these restrictions, they can have a negative impact on the mental health of many people. In many countries, non-essential workers have been forced to work at home. It has been estimated that 38% of people had to stop going to their workplace due to the pandemic in China; 25% stopped working at all and experienced high levels of psychological distress. In addition, wellbeing of people who until now have been physically active appeared to be deteriorated (Zhang et al., 2020b). Closing schools and universities was one of first decisions made in many countries facing the coronavirus pandemic, what has also negatively affected most students. In a survey conducted among 7143 college students, it was found that 0.9% of them experienced severe, 2.7% moderate, and 21.3% mild anxiety. Furthermore, the authors found that having relatives or acquaintances with COVID-19, impaired daily life activities. Additionally, delays in academic activities constituted risk factors for experiencing anxiety symptoms (Cao et al., 2020).

However, it should be noted that despite of all these negative emotional consequences, researchers have shown, that public opinion is generally positive with regard to the implemented preventive actions (Zhong et al., 2020). Nevertheless, people still report anxiety, worries about getting infected and sleep problems during the COVID-19 pandemic, which is also reflected by a recent study showing that the increased demand of psychiatric support is reported by 80% of study participants (Roy et al., 2020). Unfortunately, the scenario of global mental health crisis is very likely to occur, which is confirmed in first case reports of psychotic episodes related to pandemic outbreak (Zulkifli et al., 2020).

4.2. Mental health of quarantined people

Restrictions that have been taken to decrease the transmission of the SARS-CoV-2 increase the intensity of anxiety, depression, feelings of loneliness and perceived threat in the society (*World Health Organization. Mental health and psychosocial considerations during the COVID-19 outbreak, 18 March* 2020. No. WHO/2019-nCoV/MentalHealth/2020.1, 2020). These recommendations and the necessary social isolation can have far-reaching negative consequences and might be associated with limiting the continuation of providing tailored care, support and treatment. Some populations might be particularly vulnerable to such restrictions. These include people suffering from dementia (Armitage and Nellums, 2020), chronical diseases, mental illness and young children who may feel distressed and need parent-child closeness (Jiloha, 2020). The global spread of the SARS-CoV-2 and its disproportionate impact on the aforementioned groups can cause even greater disparities in the access to services they need and their further marginalization. In addition, it is important to emphasize the fact that pandemic is a crisis for everyone. People who have not experienced psychopathological symptoms so far, can react negatively to the new reality by presenting with adjustment disorders in the form of anxiety or depressive symptoms. People who are quarantined loose the possibility to meet face-to-face and access to traditional social help, what is a stressful phenomenon itself (Zhang et al., 2020c). According to the Chinese nationwide study carried out on 52,730 quarantined individuals, almost 35% of them experienced psychological distress. Women, people with higher education and those at older age were much more vulnerable to react with intensive stress and were more prone to develop symptoms meeting the criteria of PTSD, in contrast to young people. However, the distress level was influenced by the availability of local medical resources, efficiency of the regional public health system, as well as by preventive and control measures taken against the epidemic situation (Qiu et al., 2020). In another Chinese study, authors found that low levels of social capital were linked to increased levels of anxiety and stress, and good social situation was positively associated with better quality of sleep (Xiao et al., 2020a).

The most recent review of studies investigating the impact of quarantine reported that negative psychological effects of quarantine could cause adverse mental health outcomes. These included the symptoms of PTSD, depression, anxiety, sleep problems, increased fear, stigmatization, low self-esteem and a lack of self-control (Hossain et al., 2020). The mental health deterioration risk factors which were deemed as significant were: longer quarantine duration, boredom, infection concerns, frustration, inadequate supplies and information, financial loss, and possible stigma. It has been suggested that the pandemic might exert long-lasting adverse psychological effects (Brooks et al., 2020). It is worth noting that not unloaded angry and emotional tension in combination with deficits in individual coping strategies during the social isolation can lead to increased domestic violence (Xiang et al.,

2020b). It has further been indicated that also people working long hours, and those experiencing higher levels of anxiety are at substantial risk of mental health deterioration (Mo et al., 2020).

4.3. Medical workers

Health professionals, especially those exposed to the COVID-19, are at high risk of psychopathological symptoms caused by the infection. It is a case because of they had been put in dilemma, in which they had to decide to work combining a real fear of being infected and spreading the virus to their close ones (Xiang et al., 2020b). Moreover, they were faced with an unprecedented situation, being forced to make difficult decisions on how to provide care for all severely unwell patients with constrained resources, and how to work under extreme pressures. This can cause some of them to experience moral injury or mental health problems (Greenberg et al., 2020).

A recent study conducted among Chinese medical staff, demonstrated that 22.4% of them had moderate, and 6.2% experienced severe disturbances in the wake of the epidemic. A considerable number of professionals claimed that they have sought counseling or psychotherapy (Kang et al., 2020) (Table 3). A survey that was carried out among 1257 medical workers in Wuhan (China) found that almost 80% of participants reported distress, half of them declared symptoms of depression, 44.6% experienced anxiety, and one third suffered from insomnia. Especially nurses, women, professionals with more seniority titles, frontline health care workers, and those working in the center of epidemic reported more severe consequences to their mental health. Furthermore, those engaged in a direct care of patients with the COVID-19 were at higher risk of depression, anxiety, insomnia, and distress (Lai et al., 2020). Similar results were obtained by the authors of another Chinese study, which showed that medical staff who had a close contact with infected patients had higher fear, anxiety and depression scores (Lu et al., 2020). Seven other studies indicated the severity of depressive and anxiety symptoms among healthcare professionals working with the COVID-19 patients, with the range of 8.9%–50% and 10%–45%, respectively (Du et al., 2020; Guo et al., 2020; Liu et al., 2020b; Tan et al., 2020; Zhang et al., 2020d; Zhang et al., 2020e; Zhu et al., 2020b). Likewise, the research papers revealed high prevalence of sleep disturbances in this group, ranging from 33.9% to 45.5% (Qi et al., 2020c; Zhang et al., 2020f). Another study conducted among nurses used Colaizzi's phenomenological method, which focuses on the emotions and experience, showing shared patterns. Participants complained on severe fatigue, discomfort, and feeling helplessness caused by working conditions, alongside with fear and anxiety, caused by the concern of infecting other people. Most common self-coping styles incorporated psychological and life adjustment, team support, altruistic acts and rationalization. Despite that, professional caregivers of the COVID-19 patients experienced personal growth, including increased affection and gratefulness, feeling of professional responsibility, and self-reflection (Sun et al., 2020).

A very recent metanalysis of 13 papers, including 33,062 participants in total has found, that during the COVID-19 pandemic, anxiety, depression and insomnia symptoms were present in 23.2%, 22.8% and 38.9% of healthcare workers respectively (Pappa et al., 2020).

Hopefully, some interventions are proved to be helpful for medical professionals dealing with mental problems. One study found that social support for the medical staff improves self-efficacy and sleep quality, as well as decreases the level of anxiety and stress (Xiao et al., 2020b).

5. Conclusions and future perspectives

Although there is still a limited number of studies on the SARS-CoV-2, current evidence strongly suggests its deteriorating impact on the CNS. It is especially important for future studies, as patients, who develop neurological symptoms in the course of the COVID-19, are more likely to have severe progression of the disease. The presence of the novel coronavirus in the brain can also manifest in psychiatric symptoms. It has been documented that the SARS-CoV-2 can pass through the blood-brain barrier, or it can reach the brain via the olfactory bulb. Although it has been shown that the virus can interact with the ACE2 receptors, the exact mechanisms underlying its deleterious effects on the CNS remain unknown. To date, various biological alterations associated with the coronavirus infection have been identified, and some of them, especially those related to the activation of microglia (Li et al., 2004) and cytokine signaling (Qing et al., 2020), might be of relevance to specific mental health outcomes. More and more often, cytokine alterations are being recognized as common findings in mood and psychotic disorders (Misiak et al., 2020; Frydecka et al., 2018; Misiak et al., 2019); however, causal associations are poorly established and their perception as downstream effectors of the underlying pathology cannot be ruled out. Similarly, microglia activation has also been demonstrated in severe mental disorders (Enache et al., 2019). Apart from the potential contribution of the SARS-CoV-2 to the development of mood and psychotic disorders, the awareness of adverse psychiatric effects of medications used in the treatment of the SARS-CoV-2 infection should be taken into consideration. For instance, it has been reported that psychotic symptoms might be the consequence of the treatment with chloroquine and hydroxychloroquine (Mascolo et al., 2018; Kwak and Kim, 2020).

It is important to note that previously known CoVs have been associated with certain mental disorders. Indeed, significantly higher rates of seropositivity for CoVs has been found in patients with a history of mood disorders (Okusaga et al., 2011). Similarly, Severance et al. (Severance et al., 2011) reported increased seropositivity for CoVs in patients with recent-onset psychosis. The concept of prenatal and perinatal infections as causative factors for various neurodevelopmental disorders has gained particular attention. Although, according to the available reports, pregnant women are at low risk of unfavorable outcomes of the SARS-CoV-2 infection, these conclusions might be premature (Sominsky et al., 2020). At this point, it is of great importance that non-specific maternal immune activation might also be associated with impaired neurodevelopmental trajectories in the offspring (Boulanger-Bertolus et al., 2018).

The outbreak and its media coverage also shape individual attitudes, stress responses and health literacy behaviors. Maintaining appropriate public information might also be of great importance in preventing stress-related mental health outcomes (Depoux et al., 2020). Patients, health professionals, and the general public are under a great psychological stress, which may lead to the development of various psychiatric symptoms and maladaptive responses, such as anxiety, fear, depression, and insomnia. As it has been shown, providing accurate information, professional counseling as well as social support can significantly help in dealing with these issues. Moreover, psychiatric and psychological services also play a pivotal role in the overall disease control (Li et al., 2020c). In times of global lockdown, mental health services should focus on providing help through telemedicine approaches (Zhou et al., 2020). Many psychiatric hospitals and psychological centers have already launched hotlines to provide psychological counseling services for people in need (Bao et al., 2020). However, it is important to stress that this negative impact can last longer than the coronavirus pandemic. In a 3-year follow-up study of the SARS outbreak in 2003, 23% of health care workers still reported moderate or greater depressive symptoms (Liu et al., 2012).

Although our knowledge on biology and long-term clinical outcomes of the SARS-CoV-2 infection is largely limited, approaching the pandemic based on lessons learnt from previous outbreaks of infectious diseases and biology of other CoVs provide the only grounds for developing public mental health strategies. Translation of therapeutic strategies that improve stress coping responses might contribute to alleviate the burden driven by the pandemic. Longitudinal studies will be the basis for further insights into potential consequences of the

outbreak. Animal model studies might also be important to extend early insights into neurobiology of the SARS-CoV-2.

Declaration of Competing Interest

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