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AIR POLLUTION NANOPARTICLES EXPOSURE AND NEUROLOGICAL COMPLICATIONS CAUSED BY COVID-19

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ABSTRACT

Some of the recent researches show that air pollutants such as particulate matter (PM), including fine particles (PM<2.5µm, PM2.5) and very fine particles (PM <0.1µm, PM 0.1) can reach the brain and affect CNS health. Neurological complications with Coronavirus Disease 2019 (COVID-19) have been observed. The aim of this review the relationship between air pollutants exposure and COVID-19 was focused on the role of airborne aerosols particles in the prevalence of the disease, as well as the neurological effects of COVID-19. It is not yet clear how the virus is transmitted from one sick person to another and why it is so transmissible. Viruses can be probably transmitted through speech and exhalation aerosols. Findings show that SARS-CoV-2 aerosol transmission is possible. Spike (S) proteins of SARS-CoV-2 determine tissue tropism using an angiotensin-converting enzyme receptor type2 (ACE-2) to bind to the cells. ACE-2 receptor is found in the tissues of the nervous system. Neurological disorders that occur with COVID-19 can have many pathophysiological backgrounds. Some are the result of a direct viral attack on tissues of the nervous system, others appear to be an autoimmune process post-viral, and still others appear to be the result of systemic and metabolic complications associated with critical illness.

Introduction

A body of evidences that support the involvement of CNS in path physiology of the COVID-19 is increasing. Though COVID-19 mainly affects the respiratory and cardiovascular systems, the recent reports suggest that it can cause certain the neurological symptoms including hypoglycemia, dizziness, headache, encephalitis, encephalopathy, acute cerebrovascular events, disorder of consciousness, skeletal muscle injury, and poly Neuritis that can the even precede common features such as cough and fever [1]. Furthermore, the recovered COVID-19 patients without specific neurological manifestations during the acute stage also showed brain damages even three months after discharged [2]. Mechanically, have been proposed the several pathways in which SARS-CoV-2 led to neurological complications such as direct damage to specific receptors and neurons, secondary hypoxia, cytokine-related damage and reversal travel along fibers of the nerve [3]. In any case, the exact mechanisms of COVID-19 neurological manifestations are largely unattainable. Generally, neurological dysfunction can be a result of systemic disease, direct viral injury and /or systemic inflammation [4]. The virus can interact with the brainstem pathways, thus in addition to direct lung damage, leading to indirect respiratory dysfunction. The coronavirus uses the ACE2 receptor to enter cells and circulate. Because also these receptors are found in the brain glial cells and the spinal neurons, they can attach to, multiply and damaged the neuronal tissue [1]. Some studies indicate that particles and aerosols in the air reach the brain and affect CNS health, with changes in the BBB or leakage and transmission along the olfactory nerve to the OB and active Microglia are the main components [5-8].

COVID-19 associated Brain Disorders and Central Nervous System

SARS-CoV-2 is a respiratory pathogen, there are reports of neurological appearances, such as encephalitis and epileptic seizures that will recommend a CNS inclusion of the disease [9]. Encephalitis may be the result of infection or the entry of viral proteins into the brain. SARS-CoV-2 mRNA has been recuperated from cerebrospinal fluid and can therefore cross the BBB [10, 11]. SARS-CoV-2 can contaminate nerve cells in a brain Sphere model [12]. SARS-CoV-2 may cause certain changes in the CNS without crossing the BBB, as COVID-19 is associated with cytokine storms and large numbers of cytokines cross the BBB to affect CNS function [13]. The SARS-CoV-2 spike protein can directly affect the BBB obstruction work, which gives more in-depth information on COVID-19-related neuropathology. Most likely, the interaction between SARS-CoV-2 and BBB is multifocal and involves reversible activation at more than one receptor or signaling cascade [14]. Convincing evidence suggests that SARS-CoV binds to the cell layer by binding to HACE2, which is now too well known to be a useful SARS-CoV-2 receptor [15]. Studies on human tissue have shown that these receptors are not as large as the epithelium of the lungs and small intestine, but in arterial and venous endothelial cells and arterial smooth muscle in all organs considered, counting the brain [16]. Compared to HCoV-OC-43, in vivo manifestations of SARS-CoV disease indicate that the infection enters the brain through the olfactory bulb and then causes trans-neuronal expansion [17]. Brain tissue samples from patients with SARS-CoV were examined under a microscope which showed neuronal degeneration, necrosis, edema, extensive glial cell hyperplasia, and cellular infiltration of vascular dividers by monocytes and lymphocytes [18]. It is also suggested that prolonged expression of ACE2 with central glial and ventricular material may provide another potential route for SARS-CoV-2 or SARS-CoV to enter the CSF and/or spread around the brain [19]. SARS-CoV particles are found mainly in neurons with brain tests from SARS patients [20].

With the release from the intensive care unit (ICU), one-third of patients have a behavioral disorder, which involves careless confusion or unorganized development in response to the command [21]. A few patients who recovered from COVID-19 develop psychological problems. These include sadness, discomfort, and PTSD. Long-term effects can include the progression of Alzheimer's or Parkinson's disease [22].

Air pollution exposure and neurological complications of COVID-19

The SARS-CoV-2, which resembles the UFPs, can reach a brain through an olfactory nerve and OB [23]. Viral binding to BBB endothelial cells through ACE2 expression further disrupts the BBB and facilitates viral entry into CNS. Pulmonary viral invasion causes systemic inflammation (through increased levels of IL-6, IL-12, IL-15, and TNFα), leading to a CNS pro-inflammatory state through glial cell activation [3, 5]. Local and systemic effects of the lung alveolar together cause severe hypoxia and ultimately lead to cerebrovascular dysfunction [3]. Recently, the examining

relationship between corona virus mortality and prolonged NO2 exposure showed that air pollution exposure may be a major contributor to COVID-19-related mortality [24, 25].

The SARS-CoV-2 known pathophysiology and other Coronaviruses provide clues as to the possible mechanisms of CNS damage. Now it has been shown that SARS-CoV-2, like other HCoV of which the SARS-CoV-2 virus group is a member, can attack the CNS. The SARS-CoV-2 attack is thought require both cell surface receptor to viral spike protein binding and S protein priming by cell proteases. In particular, SARS-CoV-2 uses ACE2 as the input receptor and the cell protease of TMPRSS2 for the S protein primer [26]. Cross surveys on ACE2 and the TMPRSS2-positive cells on human tissue found these proteins the expression in the nasal goblet and the ciliated epithelial cells and also oligodendrocytes [27]. Co-expression of ACE2/TMPRSS2 in oligodendrocytes can be one method of CNS proliferation or infiltration. During the SARS-CoV pandemic, encephalitis acute cases were reported with the virus detected in the patient CSF [9, 28]. Some of pathological studies reported that infectious virus and viral RNA identified in the brain tissue. In post-mortem four SARS-CoV patients examination and four individuals control, found SARS-CoV RNA and antigen in the cerebellum of people infected with SARS-CoV [29]. Other Coronaviruses have already been found in autopsy studies in the brain: OC43 and HCoV 229E strains were identified in 44 of the 90 brain donors determined by RT-PCR [30]. OC43 prevalence in patients with the MS was significantly higher than the control group. Beside, another study showed MCP-1 chemokine mRNA increase in the astrocyte cell lines due to infection of HCoV-OC43 [31]. Elevation in MCP-1 is associated with increased BBB permeability [32]. Therefore, these results indicate that HCoV infection can exacerbate the neuropathology of MS, raising the possibility that the coronavirus infection can interact with preexisting neuropathology or coexisting, leading to neurological or chronic complications create. Coronaviruses can invade the CNS through a transneuronal or hematopoietic pathway. The early SARS-CoV-2 neuroinvasion may be via the OB [33]. Air pollution nanoparticles transport from nasal epithelium to olfactory nerve and then HI has been shown in mice models [5, 34]. HCoV transport also from nasal epithelium to olfactory nerve and then CNS has been shown in rat models. Only three days after HCoV-OC4 intranasal inoculation, the transgenic mice had cells containing specific viral antigens in OB. During the seven days postinoculation, at the same time as a fatal clinical encephalitis, the virus spread throughout the whole brain. In mice, like HCoV-OC43, following experimental nasal inoculation, SARS-CoV has been found in CNS. Within over 1-2 weeks after infection, approximately eight-fold increase in density of SARS-CoV-positive cells was observed in the CNS, mainly accumulated in the HI [33]. Clinically SARS-CoV is associated with encephalitis cases, viral particles, and ischemic changes in the neurons and genome sequencing has been detected in human autopsy in the brain [35]. Although the genomic identities of SARS-CoV and SARS-CoV-2 are up to 82% similar, SARS-CoV-2 have unique genetic traits, particularly encoding proteins that can contribute to both virus replication and pathogenicity [36]. The significance and implications of genetic differences are still unclear. Coronaviruses may be cross into CNS through the BBB that is compromised by inflammatory mediators, endotheliitis or endothelial injury, transmigration of virus-carrying macrophages, or direct endothelial cells infection themselves [27, 30, 37].

SARS-CoV, the SARS responsible virus, after deployment in the CNS, has been shown that to be rapidly capable of the transneuronal proliferation and infected neurons death in models of transgenic mice that express human ACE2 receptors [17]. Some of the infected mice with HCoV-OC43, the human coronavirus causing common cold, develop a neurological infection and acute encephalitis or may survive the acute infection and behavioral changes of develop chronic encephalitis and OC43 virus persistence indicate that neurons were affected [38]. Infection of cortical neurons and hippocampal by HCOV-OC43 in the tissue culture have shown that the death of cells may occur due to apoptosis of the infected, neighboring and non-infected cells [38]. Previous findings have shown that TNF-α, a known stimulant for apoptosis, is released by the infected cells and can be involved in uninfected cells apoptosis and in microglia infiltration and activation [39]. Both SARS-CoV-2 and the SARS-CoV enter the host cells via ACE2 receptors, but the phylogenetic data and complex receptor analysis at the atomic level suggest that coronavirus can recognize the human ACE2 with greater efficiency [40, 41]. In one study that introduced soluble hrsACE2 at the clinical grade in the engineered human tissue, the hrsACE2 was capable of effectively inhibit the virus and prevent it from attaching to cells [42]. ACE2, which is high levels expressed in the various tissues including brain endothelial cells, type2 alveolar cells, glial cells and neurons [16, 43, 44], renin-angiotensin system regulates by opposing ACE signaling via production of vasodilator peptide angiotensin [45-47]. Has been shown SARS-CoV to reduce the ACE2 levels in mice lungs without detectable altering in the ACE expression [48]. By reducing ACE2 regulation expression, the SARS-CoV-2 can upset the ACE/ACE2 cerebrovascular control delicate balance, that may lead to excessive vasoconstriction, unopposed ACE signal, or impaired cerebral autoregulation. It has previously been shown that SARS-CoV infection with the high levels of the cytokines, including TNFα, IL-6, IL12, IL-1β and INFγ, is phenomenon Known as the "cytokine storm" [45, 49], these pre-inflammatory cytokines high levels are associated with poor outcomes. The SARS-CoV-2 has such pathogenicity because the severity of COVID-19 is now associated with increased the levels of TNFα, INFγ, IL-17, IL-10, IL-8, IL-7, IL-6, IL-2, IL-1β, INFγ-inducible protein-10, MCP1 and G-CSF [45, 50, 51]. Elevated IL-6 and ferritin, hyper inflammation markers, have previously been associated with mortality in the COVID-19 [45, 52]. Cytokine storms can contribute to neurotoxicity and acute lung injury; the mice infected with the influenza A virus showed a significant increase in cytokines IL-1β, IL-6 and TNF-α with excessive vascular permeability in the lungs and also brain within the 6 days of the inoculation [53]. The BBB integrity can be disrupted by immune-mediated toxicity and cytokine-induced damage in absence of the direct viral spread and or attack. Findings suggest that ANE, for example, may be caused by the cytokine toxicity [54]. Also cytokines can be directly neurotoxic, mediating or even inhibiting CNS cell injury either acting alone or synergistically [55]. The methods in which observed highly activated signaling of cytokine in infection of SARS-CoV-2 may affect neuronal outcome via altering neuro-inflammatory pathways are not known [56].

Conclusion

Scientific studies on exposure can help transmit the virus via aerosol, how to use personal protective equipment in personal exposure, source of entry into the receptor pathways, the survival of the virus at different levels, in various environments conditions and meteorological including temperature, ultraviolet radiation, humidity [57, 58]. Extreme heat and or the arrival of the cold season and decreasing air temperature and the occurrence of temperature inversion, especially in crowded cities, can interfere with the dispersion of air pollutants on the ground level and increase the concentration of pollutants and the health damage. Because of money related troubles and social segregation due to COVID-19, numerous mental issues can emerge. They can be postponed by months. There is an increment in "passing of lose hope" from substance mishandle or suicide. The hazard is more prominent among people with dementia, mental sickness, and extreme invertedness [59].

Declaration of interest

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