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Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: <www.elsevier.com/locate/scitotenv>

Climate change, environment pollution, COVID-19 pandemic and mental health

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HIGHLIGHTS

GRAPHICAL ABSTRACT

- Convergent evidence would indicate relationships between climate change, pollution and pandemics, like the current COVID-19
- These factors may provoke mental disorders "per se", however information on their possible reciprocal influences is scanty
- Literature review suggests that overall climate change, pollution and COVID-19 may increase the risk of mental disorders
- The prevention of pandemics and their mental consequences requires the promotion of global interventions to reduce climate change and air pollution

article info abstract

Article history: Received 30 October 2020 Received in revised form 10 January 2021 Accepted 11 January 2021 Available online 21 January 2021

Editor: Scott Sheridan

Keywords: Climate Change Environment Pollution Epidemics Pandemics COVID-19 Pandemic Mental Health

Converging data would indicate the existence of possible relationships between climate change, environmental pollution and epidemics/pandemics, such as the current one due to SARS-CoV-2 virus. Each of these phenomena has been supposed to provoke detrimental effects on mental health. Therefore, the purpose of this paper was to review the available scientific literature on these variables in order to suggest and comment on their eventual synergistic effects on mental health.

The available literature report that climate change, air pollution and COVID-19 pandemic might influence mental health, with disturbances ranging from mild negative emotional responses to full-blown psychiatric conditions, specifically, anxiety and depression, stress/trauma-related disorders, and substance abuse. The most vulnerable groups include elderly, children, women, people with pre-existing health problems especially mental illnesses, subjects taking some types of medication including psychotropic drugs, individuals with low socio-economic status, and immigrants.

It is evident that COVID-19 pandemic uncovers all the fragility and weakness of our ecosystem, and inability to protect ourselves from pollutants. Again, it underlines our faults and neglect towards disasters deriving from climate change or pollution, or the consequences of human activities irrespective of natural habitats and constantly increasing the probability of spillover of viruses from animals to humans.

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Review

In conclusion, the psychological/psychiatric consequences of COVID-19 pandemic, that currently seem unavoidable, represent a sharp cue of our misconception and indifference towards the links between our behaviour and their influence on the "health" of our planet and of ourselves. It is time to move towards a deeper understanding of these relationships, not only for our survival, but for the maintenance of that balance among man, animals and environment at the basis of life in earth, otherwise there will be no future.

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Contents

1. Introduction

According to the United Nations Framework Convention on Climate Change (UNFCCC), climate change is defined as "a change in the climate that is directly or indirectly attributable to human activities which alter the composition of the planetary atmosphere and add to the natural climatic variability observed on similar time intervals". It is evaluated by measuring systematic variations in the statistical quantities of meteorological variables calculated over a period of time of several decades, and usually at least thirty years [\(Sands, 1992](#page-14-0)). Therefore, in assessing climate change, natural climatic variability should be considered in relation to complex natural processes of the planet. Several objective evidences recorded in the last centuries revealed dramatic climate changes: increase in air and ocean temperatures, rise in sea level, widespread melting of glaciers, increase in frequency and intensity of extreme weather phenomena, variation in ocean salinity, wind patterns and annual distribution of rainfall, increase of hydrogeological, flood, drought and fire risks [\(Hughes,](#page-11-0) [2000\)](#page-11-0). Such phenomena provoke detrimental effects on natural, biological and anthropogenic systems [\(Steffen et al., 2015](#page-14-0); [Nogués-Bravo et al.,](#page-13-0) [2018\)](#page-13-0): changes in physiological responses and in phenology, modifications in individual species distribution and composition (i.e., migration, turnover of the ecological community, geographical reorganization, changes in population size, extinctions) [\(Müller et al., 2003](#page-13-0); [Tinner and](#page-14-0) [Kaltenrieder, 2005](#page-14-0); [Yasuhara et al., 2008](#page-15-0); [Peros et al., 2008](#page-13-0); [Ampel et al.,](#page-9-0) [2010;](#page-9-0) [Anderson et al., 2011;](#page-9-0) [Lothrop et al., 2011;](#page-12-0) [Jackson et al., 2014\)](#page-11-0), destruction of natural habitats, as well as variations in agricultural productivity and nutritional quality/capacity, and derangement of geopolitical, economical and social organizations [\(Botta et al., 2019\)](#page-10-0).

Environmental pollution is defined as the unfavorable alteration of the environment through the direct or indirect action of man ([Rai, 2016](#page-13-0)). It is considered the result of the urban-industrial and technologic revolution, with the rapid and ferocious exploitation of natural resources, and the huge increase in waste products [\(Hughes et al., 1980;](#page-11-0) [Brunekreef and](#page-10-0) [Holgate, 2002](#page-10-0); [Kampa and Castanas, 2008\)](#page-11-0). [Singh et al. \(1991\)](#page-14-0) defined it as "an unbalance condition from an equilibrium condition in any system". With no doubt, environment pollution is a global problem, common to both developed and developing countries attracting increasing attention for its severe long-term consequences [\(Hughes et al., 1980](#page-11-0); [Brunekreef and Holgate, 2002](#page-10-0); [Kampa and Castanas, 2008\)](#page-11-0). Air pollutants are gas or particles dispersed in the air, with different chemical and physical structures, and heterogeneous effects on air quality, climate and eventually human health [\(Hughes et al., 1980;](#page-11-0) [Brunekreef and Holgate, 2002](#page-10-0); [Kampa and Castanas, 2008](#page-11-0)). Some of these substances do not directly damage the air quality, but through the reactions with other substances present in the atmosphere. Carbon dioxide $(CO₂)$, methane $(CH₄)$, ozone (O_3) , nitrogen oxides (NO_x) , and fluorinated gases 3 are the main sources of gaseous pollutants deriving from industrial, agricultural, traffic and energy-producing sources, including buildings' heating [\(Hughes](#page-11-0) [et al., 1980](#page-11-0); [Brunekreef and Holgate, 2002](#page-10-0); [Kampa and Castanas, 2008](#page-11-0)). They are also called greenhouse gases, substances strengthening the earth's atmosphere's ability to capture long-wave radiation from the ground, and determining the phenomenon of global warming, the main cause of climate change [\(Botta et al., 2019\)](#page-10-0). The terms particulate matters (PMs) or aerosol particles describe condensed (solid or liquid) materials suspended in the atmosphere [\(Mukherjee and Agrawal, 2018\)](#page-13-0). They include crustal material, soot, combustion particles, nucleating clusters and biological material such as spores, but not by convention raindrops, hail or other hydrometeors [\(Mukherjee and Agrawal, 2018;](#page-13-0) [Mukherjee](#page-13-0) [and Agrawal, 2017](#page-13-0)). Primary PM is released into the atmosphere from sources such as incomplete combustion, dust and sea salts. Secondary PM is formed in the atmosphere from the condensation of low volatility gases, such as sulfuric acid, ammonia and organic compounds. Several airborne particles include both anthropogenic and natural components. Based on their aerodynamic equivalent diameter (AED), PMs of possible impact on human health are classified into: fine particles, with a diameter $< 2.5 \mu m$ (PM2.5), coarse particles, with a diameter between 2.5 and 10 μm (PM10-2.5), and ultra-fine particles, with diameters <0.1 μm. These particles have a potentially harmful effect on different parts of the respiratory tract: the upper respiratory tract is affected by PM10, while the pulmonary alveoli are affected by ultra-fine particles aerodynamic equivalent diameter (AED) [\(Mukherjee and Agrawal, 2018](#page-13-0); [Mukherjee and](#page-13-0) [Agrawal, 2017](#page-13-0); [Stanek et al., 2011;](#page-14-0) [El Morabet, 2018\)](#page-11-0).

It is now well known that environmental pollution and climate change might negatively impair several physiological systems and organs of individuals of all ages, possibly being involved in perinatal disorders, respiratory and cardiovascular disorders, allergies, cancer, and neurological and mental disorders [\(Kelishadi et al., 2009;](#page-11-0) [Miller, 2020](#page-13-0); [Kelishadi and Poursafa, 2010](#page-11-0); [Eze et al., 2014\)](#page-11-0).

In addition, the distribution, diffusion and transmission of diseases by water or vectors represent one of the most significant consequences of environment pollution and climate change [\(Lindahl and Grace,](#page-12-0) [2015](#page-12-0)). Indeed, infectious diseases, pollution and climate change seem to be connected in different ways, affecting each other, as there exist indications that variations of some meteorological parameters associated with climate change might favor the epidemics [\(Sajadi et al.,](#page-13-0) [2020;](#page-13-0) [Xie and Zhu, 2020;](#page-15-0) [Shi et al., 2020a](#page-14-0); [Wang et al., 2010;](#page-15-0) [Ruiz](#page-13-0) [et al., 2010](#page-13-0)). Moreover, even the destruction of wild animal habitats over time may thins the natural barrier between humans and wild animals containing pathogenic microorganisms, creating new contact areas (bits of forest near areas inhabited by humans) and the possibility of triggering spill over ([Ostfeld, 2009](#page-13-0); [Gibb et al., 2020\)](#page-11-0). This is particularly relevant in this historical period with humanity facing the severe pandemic of a coronavirus called severe acute respiratory syndrome coronavirus (SARS-CoV-2) that originated in the Chinese region of Hubei and soon spread all over the world [\(Gorbalenya et al., 2020](#page-11-0)). Again, a growing bulk of studies revealed an association between diffusion, incidence, morbidity and mortality of the current COVID-19 pandemic, caused by this virus, and air pollutants, especially air PM levels ([Petrosillo et al., 2020;](#page-13-0) [Tavella and Da Silva Júnior, 2020;](#page-14-0) [Conticini](#page-10-0) [et al., 2020;](#page-10-0) [Wu et al., 2020a\)](#page-15-0).

Moreover, increasing evidence suggests that climate change ([Berry](#page-9-0) [et al., 2010](#page-9-0); [Bourque and Willox, 2014\)](#page-10-0), environmental pollution ([Buoli et al., 2018;](#page-10-0) [Attademo and Bernardini, 2020](#page-9-0)), and pandemics ([Buoli et al., 2018](#page-10-0)), including the ongoing COVID-19 one ([Wang et al.,](#page-15-0) [n.d.;](#page-15-0) [Liu et al., 2020a\)](#page-12-0), might produce negative effects on mental health. It has long been known that air pollution and meteorological changes might induce psychopathological phenomena, such as meteoropathy ([Cianconi et al., 2020\)](#page-10-0), a term currently used to label any pathological dimension related to weather conditions ([Balsamo et al., 1992;](#page-9-0) [Zikic](#page-15-0) and Žikić[, 2018\)](#page-15-0). Furthermore, environmental pollutants, climate changes and SARS-CoV-2 infection have been associated with changes in the central nervous system (CNS) that could lead to mental and/or behavioral alterations through different physiopathological mechanisms: inflammatory processes, activation of the immune system, oxidative stress, damage to blood vessels, dysfunctions of neurotransmitter systems ([Costa et al., 2020a;](#page-10-0) [Chan et al., 2020;](#page-10-0) [Paniz-](#page-13-0)Mondolfi [et al., 2020](#page-13-0); [Steardo et al., 2020a](#page-14-0); [Calderón-Garcidueñas](#page-10-0) [et al., 2008a;](#page-10-0) [Calderón-Garcidueñas et al., 2011](#page-10-0); [Calderón-Garcidueñas](#page-10-0) [et al., 2012;](#page-10-0) [Guxens and Sunyer, 2012](#page-11-0); [Brockmeyer and D'Angiulli,](#page-10-0) [2016\)](#page-10-0). However, it is difficult to establish the specific cause-effect relationships of these phenomena on mental health, as they result from the interactions of two complex systems: the environment, with everything (biotic and abiotic elements) populating it, and human beings [\(Torres](#page-14-0) [and Casey, 2017](#page-14-0); [Gaddi et al., 2018\)](#page-11-0).

Therefore, the purpose of this paper was to review and comment on the scientific literature on the possible interactions between climate change, environmental pollution and COVID-19 pandemic, as well as their eventual synergistic effects on mental health.

2. Materials and methods

According to the PRISMA guidelines [\(Moher et al., 2009](#page-13-0)), the databases of PubMed, Scopus, Embase, PsycINFO and Google Scholar were accessed in order to research and collect articles that were published in English language only. Free text terms and MeSH headings were combined as it follows: "climate change OR environment pollution" AND "COVID-19 OR pandemics" OR "mental health". In the paper, human and animal studies were considered. Moreover, studies of all design types were included, from the cross-sectional to longitudinal studies, as well as brief reviews and communications. All the authors agreed to include in the review conference abstracts, posters and case reports if published in indexed journals.

All the authors equally contributed in identifying potential information specific to this topic among the titles and abstracts of the publications. The first selection excluded 45,740 titles because: a) duplicates; b) not concerning the scope of the paper; c) not informative enough. The second selection excluded 1322 abstracts after being read and reviewed, as the information reported did not fulfill the scope of our paper and/or the presented information did not seem relevant to the discussed topic. Subsequently, 937 more publications were excluded after being completely read and evaluated, as they did not provide enough information and/or resulted sufficiently in line with our review. Finally, 313 papers were included in the present review (Table 1).

2.1. Effect of climate change and environment pollution on COVID-19

The analysis of the global distribution of COVID-19 pandemic underlined that, at least in the first phase of the pandemic the proportion of cases to population per $10⁵$ (PCP) and proportion of death to population per 10^5 (PDP) were higher in northern areas of the world, including some parts of North America, Asia and Europe, all located in higher latitudes and with a colder climate and better socio-economic condition ([Sarmadi et al., 2020\)](#page-14-0). Several environmental and demographic factors have been associated with this distribution pattern ([Sarmadi et al., 2020](#page-14-0)). Certainly, a possible explanation might be in the different availability of diagnostic kits and health facilities between the north and south of the world [\(Bi et al., 2020](#page-9-0)). Furthermore, as for climate change, even for COVID19 urban slums with restricted living areas are at risk. Again, colder climates and higher population densities could also contribute to the greater spread of the disease [\(Sajadi et al., 2020](#page-13-0); [Xie and Zhu, 2020\)](#page-15-0).

Despite still inconclusive, several data highlighted an association between COVID-19 outbreak transmission and spread and different environmental factors, such as temperature, humidity and climate latitude ([Shi et al., 2020a](#page-14-0); [Poole, 2020;](#page-13-0) [Guo et al., 2020;](#page-11-0) [Chen et al., 2020a\)](#page-10-0). Indeed, it has long been known that weather significantly influence respiratory infections [\(Sajadi et al., 2020;](#page-13-0) [Wang et al., 2010;](#page-15-0) [Ruiz et al., 2010](#page-13-0); [Vandini et al., 2013\)](#page-15-0). Temperature, humidity, visibility, and wind speed can affect droplet stability in the environment, or affect survival of viruses, or impact epidemic transmission ([Chen et al., 2020a\)](#page-10-0). In China, temperature was proven to be an environmental driver of the COVID-19 outbreak. In particular, high temperature was observed to decrease the transmission rate of the infection and the incidence of new cases ([Shi et al., 2020a\)](#page-14-0). The authors also suggested that both lower and

Table 1 Article selection flow chart.

higher temperatures could be beneficial for decreasing the incidence of COVID-19 [\(Shi et al., 2020b](#page-14-0)). By contrast, no significant association between the incidence of COVID-19 and absolute humidity was reported ([Shi et al., 2020a\)](#page-14-0). In Indonesia, a study on Jakarta population led to similar results, showing that only temperature average was significantly correlated with COVID-19 spread [\(Tosepu et al., 2020](#page-14-0)). Another study based on data from Wuhan showed that COVID-19 basic reproduction number (R0), also called the basic reproduction ratio, an epidemiologic metric used to describe the contagiousness or transmissibility of infectious agents [\(Delamater et al., 2019](#page-10-0)), was negatively related to both temperature and humidity ([Guo et al., 2020\)](#page-11-0). Wang et al. (2020) confirmed that these two factors might reduce COVID-19 transmission ([Wang et al., 2020a](#page-15-0)). A study carried out in seven metropolitan cities and nine provinces from South Korea also supported the link of COVID-19 incidence with temperature ([Hoang and Anh, 2020\)](#page-11-0). In particular, a significantly non-linear association between daily temperature and COVID-19 confirmed cases was recorded, whereby each 1 °C increase in temperature was related with a 9% increase in COVID-19 confirmed cases, when the temperature was below 8 °C. In addition, even increases in $NO₂$, CO and $SO₂$ concentrations were associated with an increase in COVID-19 confirmed cases ([Hoang and Anh, 2020\)](#page-11-0). In Norway, normal and maximum temperature recorded during study period and low precipitation (rainfall) levels were positively associated with the incidence of COVID-19 pandemic [\(Menebo, 2020\)](#page-13-0). On the contrary, a Canadian study found no association of spread of COVID-19 and temperature and latitude [\(Jüni et al., 2020\)](#page-11-0).

As far as mortality rate is concerned, collecting data on daily deaths from COVID-19 and weather conditions in Wuhan, a study showed a positive association between COVID-19 mortality and daytime temperature, and a negative association between COVID mortality-19 and relative humidity [\(Ma et al., 2020\)](#page-12-0). A large study analyzed the associations between transmission and deaths caused by SARS-CoV-2 and meteorological variables worldwide. The results showed that an increase of one degree Fahrenheit in the mean daily temperature was related to a reduction in the number of COVID-19 cases. Moreover, a negative correlation between the mean temperature and number of COVID-19 cases, and a positive correlation between precipitation and SARS-CoV-2 transmission were reported. In addition, countries with higher rainfall showed an increased disease transmission, as compared with those with lower rainfall ([Sobral et al., 2020\)](#page-14-0).

As already mentioned, besides all these factors, the spread, the incidence and the mortality rates of COVID-19 seem have been associated with air pollution, especially PMs for their negative effects on health. Inhalable coarse particles with a diameter of between 2.5 and 10 μm, and inhalable fine particles, with a diameter of less than 2.5 μm seem to be the most dangerous PMs [\(Kim et al., 2015](#page-12-0)). Indeed, increased concentrations of PM2.5 and of pollutants, such as nitrogen dioxide and PM, were positively related to the number of infected individuals ([Coccia,](#page-10-0) [2020](#page-10-0)), as well as to the hospital admissions due to respiratory viruses [\(Carugno et al., 2018;](#page-10-0) [Glencross et al., 2020;](#page-11-0) [Nenna et al., 2017](#page-13-0); [Andree,](#page-9-0) [2020\)](#page-9-0). It was also suggested that this association could affect the progression and prognosis of the disease [\(Yao et al., 2020a](#page-15-0)). Wu et al. [\(Wu et al.,](#page-15-0) [2020a](#page-15-0)) concluded that even small increases in PM2.5 levels could worsen the progression and prognosis of the disease, and was linked to a significant increase (approximately 15%) of COVID-19 deaths. In fact, immune dysregulation is considered the major cause of a worse outcome in respiratory infections, including those provoked by SARS and COVID-19. Again, air pollution is one of the best-known factors of prolonged inflammation, ultimately leading to innate over-activation of the immune system ([Conticini et al., 2020](#page-10-0); [Wang et al., 2020b\)](#page-15-0). Some evidences showed that exposure to environmental pollution may be associated with high COVID-19 lethality rates in individuals living in polluted areas around the world [\(Cui et al., 2003](#page-10-0)). A systematic review on the relationship between air pollution and increased risk of morbidity for COVID-19, including 15 papers among 450, and carried out using an adaptation of the Cochrane rapid review methodology, concluded that the risk of morbidity

and mortality for COVID-19 increases with chronic and acute exposure to air pollution, especially particulate matter PM2.5 and PM10, and nitrogen dioxide [\(Félix-Arellano et al., 2020](#page-11-0)).

A recent report in China reported a substantial relationship between PM 2.5 and COVID-19 infection, which was revealed across 120 cities ([Xie and Zhu, 2020\)](#page-15-0). A study on the spatio-temporal spread of the COVID-19 epidemic in this country showed that the spread rate of the epidemic in Hubei province, and in general in economically more developed and more populated cities, was higher than in the rest of the China, and that the distribution of the epidemic areas tended to be stable over time. In addition, several factors, including the strength of economic connections, the population distribution, the accessibility to transport and medical facilities, as well as the average temperature [\(Xie et al.,](#page-15-0) [2020](#page-15-0)), have been shown to exert a certain influence on the epidemic. Subsequently, while exploring the temporal correlation between the case mortality rate (CFR) of COVID-19 and particulate matter (PM) in Wuhan, the most hit city in the Hubei province, higher CFR of COVID-19 was observed with increasing concentrations of inhalable PM10 and PM2.5 [\(Xie et al., 2020\)](#page-15-0).

In Italy, several researchers analyzed the relationship between COVID-19 pandemic and particulate pollution, starting from the observation that the course of the infection was very different throughout the country regions ([Setti et al., 2020a;](#page-14-0) [Setti et al., 2020b](#page-14-0)). Several data highlighted the possible association between elevated concentration of air pollutants and the high spread of COVID-19 in northern Italian regions ([Coccia, 2020](#page-10-0); [Martelletti and Martelletti, 2020](#page-12-0)). A first observational study based on initial epidemic diffusion reported a relationship between exceeding the legal limits of PM10 concentrations and the number COVID-19 cases ([Setti et al., 2020a](#page-14-0)). The analysis showed a direct relation between COVID-19 cases and PM10 pollution concentrations, in agreement with the previous literature on other viral infections ([Setti et al., 2020a\)](#page-14-0). An analysis conducted by the University of Bergamo concluded that SARS-CoV-2 RNA might be present in PM, suggesting it as a possible indicator of epidemic recurrence [\(Setti et al., 2020b\)](#page-14-0). Another study investigated the correlation between the degree of accelerated diffusion and lethality of COVID-19 and surface air pollution in the metropolitan area of Milan, the greatest city of northern Italy [\(Zoran](#page-15-0) [et al., 2020](#page-15-0)). The results showed that high levels of urban air pollution had a significant impact on increasing the rates of total cases of COVID-19, new daily cases and total deaths [\(Zoran et al., 2020\)](#page-15-0). In particular, daily PM mean levels were reported to influence the number of COVID-19 cases. Furthermore, still in Milan the average temperature correlated positively, while the relative humidity negatively with cases of COVID-19 [\(Zoran et al., 2020\)](#page-15-0).

The situations seem to be similar throughout the world. In USA an increase in PM2.5 concentrations was linked to a statistically significant increase in daily SARS-CoV-2 death rate (an increase of 1 μg/m3 of PM2.5 levels was associated with an 8% increase in the COVID-19 death rate) [\(Wu et al., 2020a\)](#page-15-0). Overlapping results were obtained in an analysis conducted on 355 municipalities in the Netherlands, where PM2.5 resulted to be a significant predictor of both the number of confirmed COVID-19 cases and related hospital admissions per 100,000 inhabitants ([Andree, 2020](#page-9-0)). There is also growing evidence of a positive correlation between PM2.5 levels and COVID-19 infection in India and Pakistan [\(Mehmood et al., 2020](#page-13-0)), two countries with the worst air pollution in the world [\(Lelieveld et al., 2015](#page-12-0); [Junaid et al.,](#page-11-0) [2018\)](#page-11-0), as recently, PM2.5 levels in these regions reached exceptionally high levels ([Junaid et al., 2018;](#page-11-0) [Li et al., 2018](#page-12-0)).

To summarize, although there are no conclusive results, some evidence would indicate that SARS-CoV-2 might use PM as a possible vector, while suggesting that countering air pollution might lead to a reduction in transmission and, therefore, in the spread of the disease ([Wu et al., 2020a;](#page-15-0) [Setti et al., 2020a\)](#page-14-0). Additionally, since particulate pollution has also been associated with increased COVID-19 morbidity and mortality, the reduction of environmental pollutants could theoretically produce a decline in consequent severe cases and deaths.

2.2. Effects of climate change and air pollution on mental health

Climate change encompasses several environmental and weather modifications, including extreme natural events and gradual climate variations. Recently, there is a growing interest on the direct or indirect, short-term or long-term psychological/psychiatric consequences of climate change [\(Reifels et al., 2015\)](#page-13-0).

The available data would suggest that the impact of climate change on mental health might range from mild stress and distress symptoms to clinical disorders, mainly including anxiety, sleep disturbances, depression, and stress/trauma-related disorders ([Blanc et al., 2019](#page-9-0); [Hayes](#page-11-0) [et al., 2018;](#page-11-0) [Ursano et al., 2017\)](#page-15-0). Further, it is well known that extreme natural events (including any situation out of the ordinary and unpredictable, such as hurricanes, fires due to high temperatures, floods, tsunamis, tornadoes, and even the total confinement of a city, country or the whole world due to the spread of an infection) are more frequently associated with psychiatric disorders with acute onset than gradual environmental changes, as they have an immediate and direct impact on mental health [\(Cianconi et al., 2020](#page-10-0)). The loss of the normal routine generates psychological fragility, with the prevalence of negative thoughts and emotions, such as fear, anxiety, lack of hope and uncertainty about the future ([Cianconi et al., 2020;](#page-10-0) [U.S Global Change, R.P., 2016\)](#page-15-0). In a percentage ranging between 7 and 40% of predisposed and poorly resilient subjects, the psychological distress can easily become full-blown psychiatric disorders, specifically those related to stress and trauma (adaptation stress disorders, ASD, and post-traumatic stress disorder, PTSD) ([Salcioglu et al.,](#page-14-0) [2007](#page-14-0)), but also anxiety, depression, substance abuse, and suicidal thoughts, transient psychosis, and even relapse of Bipolar Disorder (BD) ([U.S Global Change, R.P., 2016](#page-15-0)). Different types of extreme weather events might be related to acute, sub-acute, and long-term effects on mental health ([Cianconi et al., 2020](#page-10-0)). In particular, long-term anxiety and depression, PTSD, aggression and suicide seem to be associated with floods (the most common disasters at global level) ([Ahern et al.,](#page-9-0) [2005\)](#page-9-0). Again extreme heat events were associated with increased aggression [\(Anderson et al., 2000](#page-9-0)), suicide and psychiatric admissions [\(Nitschke](#page-13-0) [et al., 2007\)](#page-13-0). Long periods of heat were linked to higher rates of criminal and aggressive behaviors ([Cheatwood, 1995](#page-10-0); [Cohn et al., 2004\)](#page-10-0), mood disorders, anxiety, somatoforms disorders, psychophysical exhaustion, and suicide [\(Hansen et al., 2008](#page-11-0); [Parsons, 2002;](#page-13-0) [Maes et al., 1994\)](#page-12-0). Even the decrease in temperatures is associated with increased aggression [\(Howarth and Hoffman, 1984\)](#page-11-0). High humidity rates have been associated with poor concentration and high fatigue [\(Howarth and Hoffman, 1984](#page-11-0)).

Unlike extreme weather events, the impact of gradual climate change on mental health, like the increase of temperatures and sea levels or precipitation pattern variations, is still unclear and more difficult to study, as it is less evident and essentially indirect ([Berry et al., 2008](#page-9-0)). In these situations, affection and possessions loss, community removal, and social connections reduction may cause or amplify the development of mental health problems [\(Coêlho et al., 2004\)](#page-10-0). The most frequent gradual climate changes are represented by long periods of extreme heat and/or drought, as several people are forced to migrate from their homeland ([Berry et al.,](#page-9-0) [2010\)](#page-9-0). Involuntary migration is known to be a relevant stressor with the potential to impair both physical and mental health ([Campbell and](#page-10-0) [Campbell, 2007](#page-10-0); [Huq et al., 2007](#page-11-0); [Schwerdtle et al., 2017](#page-14-0)). In areas at risk of drought, enhanced rates of anguish and depression were reported [\(Campbell and Campbell, 2007](#page-10-0); [Huq et al., 2007\)](#page-11-0), as well as high suicide rate among farmers living in these areas ([Kjellstrom, 2009](#page-12-0)). Additionally, the extinction of animal and plant species, as well as the destruction of the native environment and landscape, in the long term could cause more complex psychopathological disorders, such as dissociative symptoms, identity disorders, and personality changes ([Marshall et al., 2012](#page-12-0); [Woodbury, 2019;](#page-15-0) [Wei et al., 2017](#page-15-0)).

Albeit to a lesser extent, global climate change can also indirectly affect mental health. Even just the awareness of the ongoing climate change can induce negative emotional responses, including guilt, pain, anxiety and demoralization. In this case, the most affected subjects are those who already experienced high levels of stress due to other factors, so that, the additional stressful load could overwhelm their ability to recover [\(Brugha and Cragg, 1990\)](#page-10-0). Currently, there are no consistent and reliable objective tools for studying these responses, but several data showed a significant number of people reporting anxiety and stress associated with climate change ([Clayton, 2020](#page-10-0)).

Since mental disorders associated with climate change are novel and still poorly understood entities, new terms were coined to define some of them, which represent a latest challenge for clinicians. The term "solastalgia" labels a psychic state in which people do not recognize as familiar the environment where they live and are unable to adapt to it ([Albrecht et al., 2007\)](#page-9-0). The term "eco-anxiety", on the other hand, firstly denotes the stress that a subject experiences in perceiving nature as fragile and vulnerable, and secondly the frustration of not being able to face such a dramatic change ([Gifford and Gifford, 2016;](#page-11-0) [Arcanjo,](#page-9-0) [2019;](#page-9-0) [Lee et al., 2019](#page-12-0)).

Besides the effects caused by climate change, air pollution by itself might also influence mental health, although this is topic just at its dawn, given the difficulties in establishing a causal relationship ([Buoli](#page-10-0) [et al., 2018\)](#page-10-0). In any case, in the last few years, growing evidence suggested a link between environmental pollution and mental disorders ([Buoli et al., 2018;](#page-10-0) [Khan et al., 2019\)](#page-12-0). Some studies on healthy people highlighted an association between high concentrations of PM2.5 and greater psychological distress ([Sass et al., 2017](#page-14-0)) or impaired cognitive performance [\(Shehab and Pope, 2019](#page-14-0)). Long-term exposure to high concentrations of PM10, $NO₂$, CO, and sulfur dioxide was positively associated with the prevalence of stress, poor quality of life, diagnosis of depression and suicidal ideation [\(Shin et al., 2018;](#page-14-0) [Bernardini et al.,](#page-9-0) [2020\)](#page-9-0). Exacerbation of psychiatric disorders, increased number of emergency access for the onset of psychiatric symptoms, and suicidal ideation and behaviors were also reported in periods of the year and in geographic areas with higher levels of atmospheric pollutants [\(Lee](#page-12-0) [et al., 2019;](#page-12-0) [Szyszkowicz, 2007](#page-14-0); [Yackerson et al., 2014](#page-15-0); [Szyszkowicz](#page-14-0) [et al., 2010](#page-14-0); [Kim et al., 2010;](#page-12-0) [Lin et al., 2016](#page-12-0); [Oudin et al., 2018](#page-13-0); [Zhang](#page-15-0) [and Zhou, 2020;](#page-15-0) [Bernardini et al., 2019](#page-9-0); [Duan et al., 2018](#page-11-0); [Szyszkowicz et al., 2018](#page-14-0); [Wang et al., 2018](#page-15-0); [Gao et al., 2017](#page-11-0); [Strahilevitz et al., 1979;](#page-14-0) [Kim et al., 2019](#page-12-0); [Bai et al., 2019](#page-9-0); [Song et al.,](#page-14-0) [2018](#page-14-0); [Chen et al., 2018;](#page-10-0) [Szyszkowicz et al., 2016;](#page-14-0) [Szyszkowicz, 2010](#page-14-0); [Szyszkowicz et al., 2009;](#page-14-0) [Qiu et al., 2019](#page-13-0); [Cho et al., 2015\)](#page-10-0). Interestingly, recent data showed an association between air pollutants levels and emergency access for psychiatric symptoms even in relatively lowpolluted geographic areas such as Umbria (Italy) and Göteborg (Sweden) ([Bernardini et al., 2019\)](#page-9-0).

Again, an association was noted between pollutants and psychotic disorders, in particular schizophrenia ([Attademo and Bernardini, 2017](#page-9-0); [Attademo et al., 2017](#page-9-0)). Interestingly, extreme hot environment temperature, birth in winter or early spring, air pollution especially with PM10, PM2.5, SO₂, NO₂, lead, and tetrachlorethylene exposure have been related to the onset of schizophrenia [\(Agustina and Wulandari, 2019\)](#page-9-0). Moreover, urbanicity (urban birth and current city living) has been described as one of the risk factors for the onset of psychosis [\(Heinz et al., 2013;](#page-11-0) [Fett et al.,](#page-11-0) [2019;](#page-11-0) [Krabbendam and van Os, 2005;](#page-12-0) [Radua et al., 2018](#page-13-0)). Social stress, exposure to environmental pollutants, and disease agents were proposed as potential mechanism that might underlie this association [\(Attademo and](#page-9-0) [Bernardini, 2017;](#page-9-0) [Heinz et al., 2013;](#page-11-0) [Radua et al., 2018](#page-13-0); [Kirkbride et al.,](#page-12-0) [2007\)](#page-12-0). It is interesting to note that air pollution could be a potential mediator of the association between urbanicity and the risk of both schizophrenia and viral epidemics or pandemics ([Attademo and Bernardini,](#page-9-0) [2017;](#page-9-0) [Neiderud, 2015\)](#page-13-0).

Several evidence revealed higher depression and anxiety rate among subjects exposed to air pollutants; in particular, increased risk of depressive symptoms were associated with high levels of $NO₂, O₃, PM10$, and PM2.5 [\(Vert et al., 2017;](#page-15-0) [Lim et al., 2012;](#page-12-0) [Kioumourtzoglou et al.,](#page-12-0) [2017\)](#page-12-0). Subjects exposed to high concentrations of PM10 and PM2.5 were more likely to suffer from significant anxiety symptoms [\(Power](#page-13-0) [et al., 2015;](#page-13-0) [Pun et al., 2017\)](#page-13-0).

Different studies suggest that air pollution may contribute to the pathophysiology of neurodevelopmental disorders, while highlighting the association between air pollution and attention/deficit hyperactivity disorder (ADHD) ([Saez et al., 2018](#page-13-0)), although a recent systematic review concluded that this association is weak ([Donzelli et al., 2019\)](#page-10-0). Again, autism spectrum disorders (ASD) were associated with trafficrelated air pollution [\(Volk et al., 2011](#page-15-0); [Volk et al., 2013\)](#page-15-0), diesel exhaust (DE) [\(Roberts et al., 2013\)](#page-13-0), PM ([Jung et al., 2013;](#page-11-0) [Talbott et al., 2015;](#page-14-0) [Jo](#page-11-0) [et al., 2019](#page-11-0); [Kaufman et al., 2019\)](#page-11-0), O₃ ([Kaufman et al., 2019](#page-11-0); [McGuinn](#page-13-0) [et al., 2020\)](#page-13-0). However, negative findings are also available ([Youse](#page-15-0)fian [et al., 2018\)](#page-15-0).

In addition, pollutants were associated with increased expression of markers of neurodegenerative diseases, such as alpha-synuclein or beta-amyloid, and suggested to contribute to the pathophysiology of Alzheimer's (AD), Parkinson's diseases and multiple sclerosis [\(Costa](#page-10-0) [et al., 2020a;](#page-10-0) [Chen et al., 2017](#page-10-0)). Epidemiological studies reported that exposure to air pollution was associated with cognitive decline and pathological changes in the brain [\(Calderón-Garcidueñas et al., 2008a](#page-10-0); [Chen et al., 2017;](#page-10-0) [Wilker et al., 2015](#page-15-0); [Chen et al., 2015;](#page-10-0) [Clifford et al.,](#page-10-0) [2016](#page-10-0)). In the Framingham Offspring study the brain volume of elderly subjects without dementia and stroke decreased with increasing PM2.5 concentration [\(Wilker et al., 2015](#page-15-0)). In the Women's Health Initiative Memory Study (WHIMS), not only the total brain volume, but also the white matter volume of subjects exposed to high concentration of PM2.5 was found reduced [\(Chen et al., 2015\)](#page-10-0). In fact, the Lancet Commission for the prevention and treatment of dementia included air pollution in the list of potential risk factors for cognitive decline ([Landrigan](#page-12-0) [et al., 2018;](#page-12-0) [Livingston et al., 2017](#page-12-0)). However, as highlighted by a recent systematic literature review, the evidence for this association is considered still inconclusive ([Peters et al., 2019](#page-13-0)).

Further, animal and human studies suggest that air pollution may cause neurotoxicity [\(Calderón-Garcidueñas et al., 2008a](#page-10-0); [Calderón-](#page-10-0)[Garcidueñas et al., 2011;](#page-10-0) [Calderón-Garcidueñas et al., 2012;](#page-10-0) [Guxens](#page-11-0) [and Sunyer, 2012](#page-11-0); [Freire et al., 2010;](#page-11-0) [Guxens et al., 2014\)](#page-11-0). In animal studies, exposure to air pollutants produced neuro-inflammatory responses ([Brockmeyer and D'Angiulli, 2016;](#page-10-0) [Calderón-Garcidueñas](#page-10-0) [et al., 2016;](#page-10-0) [Block and Calderón-Garcidueñas, 2009\)](#page-9-0). In particular, exposure to O_3 and PM2.5 has been related to neurovascular to the damage and the production of autoantibodies against neural proteins ([Brockmeyer and D'Angiulli, 2016](#page-10-0); [Calderón-Garcidueñas et al., 2016](#page-10-0); [Block and Calderón-Garcidueñas, 2009\)](#page-9-0). Experimental and animal studies revealed that PM inhalation increased reactive oxygen species and activated inflammatory processes in the brain, as well as it was associated with amyloid beta protein (Aβ) and alpha-synuclein aggregates ([Costa et al., 2020a](#page-10-0)), disruption of the blood-brain barrier, and microglial activation [\(Calderón-Garcidueñas et al., 2008b;](#page-10-0) [Levesque](#page-12-0) [et al., 2011](#page-12-0); [Block et al., 2004](#page-9-0)). Elevated levels of neuro-inflammatory markers were found in the brain of children exposed to high air pollution ([Calderón-Garcidueñas et al., 2011;](#page-10-0) [Calderón-Garcidueñas et al.,](#page-10-0) [2008b](#page-10-0); [Calderón-Garcidueñas et al., 2013](#page-10-0)). Given the evidence indicating the presence of neuro-inflammation in some psychiatric disorders, it has been also speculated that pollutants might be involved in these processes. It is worth noting that neuro-inflammation processes seem particularly relevant in severe COVID-19 patients [\(Buemann et al., 2020\)](#page-10-0).

However, to date results remain inconclusive, since other studies reported no consistent evidence for an association between air pollution and mental disorders [\(Buoli et al., 2018;](#page-10-0) [Zijlema et al., 2016](#page-15-0); [Wang](#page-15-0) [et al., 2014\)](#page-15-0). Wang et al. found no association between depressive symptoms with both long-term exposure to traffic pollution and short-term changes in pollutant concentrations [\(Wang et al., 2014\)](#page-15-0). Similar results were obtained in an analysis of four cohorts of the European general population ([Zijlema et al., 2016\)](#page-15-0).

To summarize, although different findings would suggest that climate change and environmental pollutions might provoke detrimental effects on mental health, reliable data are a few. However, with no doubt, this is an intriguing and emerging field requiring to be deepened in the future by controlled studies in larger and heterogeneous populations that might better reflect the clinical reality.

2.3. Effects of SARS-CoV-2 on mental health

Growing evidence showed the negative influence of SARS-CoV-2 pandemic on the worldwide population's psychological wellbeing, due to both biological and psychosocial factors [\(Xiang et al., 2020;](#page-15-0) [Galea](#page-11-0) [et al., 2020](#page-11-0); [Pfefferbaum and North, 2020](#page-13-0); [Reger et al., n.d.;](#page-13-0) [Brooks](#page-10-0) [et al., 2020\)](#page-10-0). The imprecision about how many people have caught the disease, the fear of becoming infected and/or infecting family members, the fatality rate, the uncertainty about the effectiveness of treatments, generated a sense of bewilderment and insecurity in the whole world population ([Xiang et al., 2020;](#page-15-0) [Galea et al., 2020;](#page-11-0) [Pfefferbaum and](#page-13-0) [North, 2020](#page-13-0); [Reger et al., n.d.;](#page-13-0) [Brooks et al., 2020\)](#page-10-0). On the other hand, even the countermeasures taken to contain the spread of the infection, and the resulting socio-economic collapse, had an important impact on the overall mental health [\(Xiang et al., 2020](#page-15-0); [Galea et al., 2020](#page-11-0); [Pfefferbaum and North, 2020](#page-13-0); [Reger et al., n.d.](#page-13-0); [Brooks et al., 2020\)](#page-10-0). In addition, the impact of fake rumors or news should not be underestimated. Indeed, the absence of clear messages increases fear and prompts people to seek information from less reliable sources ([Yao, 2020;](#page-15-0) [Marazziti and Stahl, 2020\)](#page-12-0). Intense media exposure to COVID-19 news was associated with an even higher prevalence of depressive symptoms, anxiety and sleep disturbances [\(Peretti-Watel](#page-13-0) [et al., 2020\)](#page-13-0). The World Health Organization (WHO) defines this flow of misinformation as "infodemic" ([World Health, O, 2020](#page-15-0)), underling the negative effect that bad information can have on world population psychology ([Zarocostas, 2020\)](#page-15-0).

Since the outbreak of the pandemic, there was an increase of psychological distress, feelings of anguish and uncertainty, fear of death, demoralization, anxiety, insomnia, distorted perceptions, dangerous behaviors including increased use of alcohol and abuse substances, as well as internet addiction conducts, among a large part of adults, children and adolescents everywhere [\(Wang et al., n.d.;](#page-15-0) [Liu et al., 2020a;](#page-12-0) [Peretti-Watel et al.,](#page-13-0) [2020;](#page-13-0) [World Health, O, 2020;](#page-15-0) [Tang et al., 2020;](#page-14-0) [Tian et al., 2020;](#page-14-0) [McGinty](#page-12-0) [et al., 2020;](#page-12-0) [Holmes et al., 2020](#page-11-0); [Finlay and Gilmore, 2020;](#page-11-0) [Sun et al.,](#page-14-0) [2020\)](#page-14-0). It was also noted that people living in areas with a high risk of infection were at greater risk for high psychological distress than those living in non-infected areas [\(Taylor et al., 2008](#page-14-0)).

Several data have been accumulated on the effects of confinement on mental health. Mass quarantine, a countermeasure applied in several countries to reduce the spread of the pandemic, was likely to increase community anxiety, as it increased perception of danger, reduced the sense of security and certainty, caused feelings of loneliness, unpredictability, and lack of control over one's life [\(Peretti-Watel et al., 2020\)](#page-13-0). Furthermore, forced isolation imposed a drastic change in lifestyle, with the loss of habits, leisure and pleasure activities, social bonds, and some individuals with the loss of employment became more prone to boredom, frustration and failure [\(Peretti-Watel et al., 2020\)](#page-13-0). Some of the first studies on effect of confinement showed an increased prevalence of psychiatric symptoms and disorders, especially depressive symptoms, anxiety and insomnia, as well as increased need of psychological support ([Peretti-Watel et al., 2020\)](#page-13-0). Woman and young adults resulted the most affected people by psychological distress, in accordance with previous research that concluded that these population groups are the most vulnerable to stress and more prone to develop PTSD [\(Peretti-Watel et al., 2020](#page-13-0); [Marazziti et al., 2020](#page-12-0)). These findings on quarantine psychological distress were confirmed by many recent studies carried out worldwide, from China to USA ([Qiu et al., 2020](#page-13-0); [Lee, 2020;](#page-12-0) [Richardson et al., 2020](#page-13-0)). Furthermore, lockdown was associated with an increased risk of eating disorders, including overweight and obesity ([Siddiqui and Jakaria, 2020\)](#page-14-0), as a result of depression, anxiety, loneliness, but also of fewer economic resources, that lead people to less healthy nutrition [\(Hamer and Stamatakis, 2008](#page-11-0)). This outcome was associated with a higher risk for COVID-19 infection and mortality, but also with a higher probability of a second wave of the COVID-19 pandemic [\(Siddiqui and Jakaria, 2020\)](#page-14-0). Indeed, several studies observed that obesity is the second highest comorbid condition among COVID-19 patients ([Siddiqui and Jakaria, 2020](#page-14-0)), while increasing the risk COVID-19 infection and mortality, as it is associated with systemic inflammation and over-activation of the immune system, and, as such, it might contribute to the damage of the lungs and of other organs [\(Ryan and](#page-13-0) [Caplice, 2020\)](#page-13-0). In addition, fatty tissue can act as a virus reservoir, resulting in a greater spread of the virus [\(Wilker et al., 2015\)](#page-15-0).

Rising data reports the highest incidence of anxiety and depression in quarantined individuals, COVID-19 patients and their affections, as well as frontline workers [\(Xiang et al., 2020;](#page-15-0) [Peretti-Watel et al.,](#page-13-0) [2020;](#page-13-0) [Qiu et al., 2020;](#page-13-0) [Kisely et al., 2020\)](#page-12-0). Different cross-sectional studies using self-report instruments on China ([Lai et al., 2020](#page-12-0)) and Italy ([Rossi et al., 2020a](#page-13-0)) health care workers exposed to COVID-19, reported a variety of psychiatric symptoms, from moderate to severe, the most common of which were anxiety, depression, insomnia and traumatic distress. This result was not verified in another cross-sectional study assessing on healthcare professionals exposed to COVID-19 in Singapore [\(Tan et al., 2020\)](#page-14-0), maybe due to their previous experience with the SARS epidemic. In line with the data gathered from other natural disasters [\(Torales et al., 2020](#page-14-0)), the prevalence of ASD/PTSD symptoms in the general population during the COVID-19 pandemic seems to range from 7% to 53.8% [\(Benfante et al., 2020;](#page-9-0) [Fekih-Romdhane](#page-11-0) [et al., 2020;](#page-11-0) [Rossi et al., 2020b;](#page-13-0) [Shevlin et al., 2020;](#page-14-0) [Alshehri et al.,](#page-9-0) [2020;](#page-9-0) [Xiong et al., 2020](#page-15-0)), with the highest rates reported in subjects directly exposed to the trauma of acute illness and loss, including COVID-19 patients, their family members, and frontline and health care workers [\(Liu et al., 2020a;](#page-12-0) [Tang et al., 2020;](#page-14-0) [Lai et al., 2020](#page-12-0); [Torales](#page-14-0) [et al., 2020\)](#page-14-0). There are many factors that might increase the risk of developing such conditions: female sex, lower socioeconomic status, interpersonal conflicts, frequent social media use and lower resilience and social support. Furthermore, it is important to consider that such dramatic situations can trigger relapses of pre-existing mental disorders, such as chronic mood or anxiety disorders and suicidal tendencies (Ćosić [et al., 2020;](#page-10-0) [Shah et al., 2020](#page-14-0); [Thome et al., 2020\)](#page-14-0).

Some studies, primarily in small series, investigated neuropsychiatric symptoms and/or disorders directly in COVID-19 patients. Data on SARS reported that during acute epidemics approximately 20–40% of patients suffered from neuropsychiatric symptoms, including delirium, insomnia, anxiety, and depression ([Rogers et al., 2020](#page-13-0)). The first crosssectional studies on COVID-19 confirmed similar symptoms in COVID-19 patients [\(Romero-Sánchez et al., 2020\)](#page-13-0). Different reports highlighted that COVID-19 patients could suffer from different neuropsychiatric conditions including acute cerebrovascular events (especially ischaemic stroke, intracerebral haemorrhage, and CNS vasculitis) ([Varatharaj et al.,](#page-15-0) [2020;](#page-15-0) [Avula et al., 2020;](#page-9-0) [Mao et al., 2020](#page-12-0); [Liu et al., 2020b](#page-12-0); [Helms et al.,](#page-11-0) [2020\)](#page-11-0), neurological symptoms (i.e. dysgeusia, dizziness, headache, and corticospinal tract signs) [\(Rogers et al., 2020;](#page-13-0) [Varatharaj et al., 2020](#page-15-0); [Mao et al., 2020;](#page-12-0) [Helms et al., 2020\)](#page-11-0), and acute changes in behavior, cognition, and consciousness [\(Varatharaj et al., 2020](#page-15-0); [Mao et al., 2020;](#page-12-0) [Liu](#page-12-0) [et al., 2020b](#page-12-0); [Helms et al., 2020](#page-11-0)). Many patients with altered mental status showed unspecified encephalopathy and encephalitis, while others fulfilled psychiatric diagnoses, including new-onset psychosis, affective disorders, and dementia-like syndromes [\(Rogers et al., 2020\)](#page-13-0). A UK surveillance study concluded that altered mental status was the second most common presentation of COVID-19 infection, associated with encephalopathy, encephalitis or primary psychiatric diagnoses ([Varatharaj et al., 2020\)](#page-15-0). Mao et al. (2020) retrospectively analyzed 214 COVID-19 patients from three different hospitals in China, showing that 36.4% had neuropsychiatric symptoms. The most common neurological symptoms were dizziness and headache, dysgeusia, and anosmia. Anxiety, depression, and delirium were the most common psychiatric manifestations [\(Mao et al., 2020](#page-12-0)). A recent systematic review and meta-analysis of psychiatric and neuropsychiatric presentations of severe coronavirus infections revealed that many patients with COVID-19 exhibited delirium, with confusion, agitation and altered consciousness ([Rogers et al., 2020\)](#page-13-0). The neuropsychiatric manifestations of COVID-19 were directly related to the increase in peripheral immunological markers, the severity of the infection and the death rate ([Banerjee and Viswanath, 2020;](#page-9-0) [Chen et al., 2020b;](#page-10-0) [Yang et al., 2020\)](#page-15-0), and could be explained by a specific neurotrophism of the virus ([Banerjee and Viswanath, 2020\)](#page-9-0), or by a unspecific encephalopathy secondary to the massive systemic inflammatory response ([Filatov et al.,](#page-11-0) [2020](#page-11-0); [Robinson and Busl, 2020](#page-13-0)). The neurotrophism of SARS-CoV-2 is still under discussion. However, in animal studies, the virus nasal inoculation was followed by its spread to the brain and its proliferation in oligodendrocytes and endothelial cells. In post mortem sections, viral particles were present in the piriform cortex, basal ganglia and hypothalamus [\(Chan et al., 2020\)](#page-10-0). Animal and human studies on SARS-CoV-2 suggested different pathways of virus spreading to the CNS: hematogenous diffusion, olfactory bulb crossing, infection of the endothelial cells lining the cerebral vascular system, by using the perivascular spaces of the glymphatic system, or through the nerves, as the trigeminus or the vagus, by a retrograde axonal transport, ([Paniz-Mondol](#page-13-0)fi et al., 2020; [Banerjee and Viswanath, 2020](#page-9-0); Bostancıklıoğ[lu, 2020;](#page-10-0) [Lochhead and Thorne, 2012](#page-12-0); [Driessen et al.,](#page-10-0) [2016;](#page-10-0) [Perlman et al., 1989;](#page-13-0) [Wu et al., 2020b;](#page-15-0) [Desforges et al., 2014;](#page-10-0) [de](#page-15-0) [Wit et al., 2016;](#page-15-0) [Fodoulian et al., 2020](#page-11-0)). Probably, the main SNC targets of the SARS-CoV-2 are represented by regions rich in angiotensinconverting enzyme 2 (ACE2) receptor [\(Steardo et al., 2020a](#page-14-0); [Gowrisankar and Clark, 2016;](#page-11-0) [Xia and Lazartigues, 2010\)](#page-15-0), currently recognized as the principal cellular access site of the virus ([Liu et al., 2020c](#page-12-0); [Lu et al., 2020\)](#page-12-0), that include, in particular, the circumventricular organs (i.e. the subfornical organ, paraventricular nucleus, solitary and ventrolateral rostral medulla) [\(Xia and Lazartigues, 2010\)](#page-15-0), areas with poor protection from the blood brain barrier (BBB) and involved in cardiovascular and respiratory system regulation [\(Kristensson et al., 2013](#page-12-0); [Sisó et al., 2010](#page-14-0); [Takagi et al., 2019\)](#page-14-0). Systemic inflammation is accompanied by a massive release of circulating cytokines ([Filatov et al., 2020](#page-11-0); [Robinson and Busl, 2020](#page-13-0)), that can reach the CNS, damage the microcirculation, inducing edema and thrombosis [\(Klok et al., 2020\)](#page-12-0), and cause neuroglial reactivity, altered neurochemical pathways, neuroinflammation and pathological remodelling of neuronal networks ([Steardo et al., 2020b](#page-14-0); [Sankowski et al., 2015](#page-14-0); [Schwartz and](#page-14-0) [Deczkowska, 2016](#page-14-0); [Klein et al., 2019;](#page-12-0) [Daniels et al., 2017](#page-10-0); [Manglani](#page-12-0) [and McGavern, 2018;](#page-12-0) [Pedersen and Ho, 2020](#page-13-0); [Taylor et al., 2016](#page-14-0); [Verkhratsky et al., 2017\)](#page-15-0). Furthermore, inflammatory cytokines can activate the hypothalamic-pituitary-adrenal axis that might contribute to alterations of cerebral hemodynamics ([Lippi et al., 2020;](#page-12-0) [Alenina and](#page-9-0) [Bader, 2019](#page-9-0); [Diz et al., 2008](#page-10-0)). Emerging evidence demonstrated the pathophysiological role that neuro-inflammation might play in different neuropsychiatric and neuro-cognitive diseases ([Bright et al., 2019](#page-10-0); [Heppner et al., 2015;](#page-11-0) [Rocha et al., 2018\)](#page-13-0), depression ([Bakunina et al.,](#page-9-0) [2015\)](#page-9-0), psychosis [\(Marques et al., 2019\)](#page-12-0), drug abuse [\(Kohno et al.,](#page-12-0) [2019](#page-12-0)), and sleep disorders [\(Nadjar et al., 2017](#page-13-0)). In this context, COVID infection represents an important risk factor that, together with environmental stress related to the fear of getting sick, hospitalization and social restrictions, could contribute to the onset and exacerbation of even greater neuropsychiatric disorders, especially depressive disorder, BD, psychosis, obsessive-compulsive disorder (OCD), and PTSD [\(Steardo](#page-14-0) [et al., 2020b](#page-14-0)). The increase in IL-6 levels could represent the main inflammatory factor that links COVID-19 infection to the onset of many psychiatric disorders. In fact, numerous data reported that severe cases of COVID-19 displayed invariably an excessive immune response characterized by a massive increase of plasma IL-6 levels ([Aziz et al.,](#page-9-0) [2020\)](#page-9-0). Likewise, it is known that high concentrations of IL-6 were found in different psychiatric disorders. Depression was associated with elevated IL-6 concentrations in both plasma and brain [\(Lindqvist](#page-12-0) [et al., 2009;](#page-12-0) [Sasayama et al., 2013](#page-14-0); [Kern et al., 2014;](#page-11-0) [Enache et al.,](#page-11-0) [2019;](#page-11-0) Boufi[dou et al., 2009](#page-10-0); [Hodes et al., 2016\)](#page-11-0). An imbalance between pro-inflammatory and anti-inflammatory cytokines was observed in DB ([Pinto et al., 2018](#page-13-0); [Felger, 2018](#page-11-0)), but still with unclear results. Some studies reported an increase in pro-inflammatory molecules, including IL-6, in the acute phases of the disease with a parallel reduction in anti-inflammatory factors ([Sayana et al., 2017](#page-14-0); [Munkholm et al.,](#page-13-0) [2013\)](#page-13-0). However, these results were not confirmed in a subsequent study [\(Wang and Miller, 2018](#page-15-0)). Increased IL-6 levels were also revealed in subjects with schizophrenia [\(Sasayama et al., 2013](#page-14-0); [Corsi-Zuelli et al.,](#page-10-0) [2020\)](#page-10-0), and in a study on a group of adolescents, high Il-6 concentrations were positively correlated with the onset of psychosis later in life ([Metcalf et al., 2017](#page-13-0)). Positive correlation with pro-inflammatory factors was also demonstrated in OCD [\(Murphy et al., 2006;](#page-13-0) [Gray and](#page-11-0) [Bloch, 2012\)](#page-11-0). Indeed, OCD patients showed higher levels of proinflammatory cytokines, including IL-6, when compared with controls ([Gray and Bloch, 2012](#page-11-0); [Karagüzel et al., 2019](#page-11-0)). Several studies indicated an association between inflammation and PTSD [\(Furtado and Katzman,](#page-11-0) [2015;](#page-11-0) [Schelling et al., 2004](#page-14-0)). PTSD was often accompanied by low-grade inflammation [\(Spitzer et al., 2010\)](#page-14-0), and patients with this disorder showed increased plasma and brain concentrations of proinflammatory factors, especially of IL-6 [\(Lindqvist et al., 2017;](#page-12-0) [Bersani](#page-9-0) [et al., 2016;](#page-9-0) [Tursich et al., 2014](#page-14-0)).

COVID-19 may adversely affect disabled or more vulnerable individuals, such as patients with preexisting psychiatric disorders. In these subjects, psychiatric disorders may worsen ([Holmes et al., 2020;](#page-11-0) [Costa](#page-10-0) [et al., 2020b](#page-10-0)), also due to the difficulty of access to routine visits [\(Zhou](#page-15-0) [et al., 2020\)](#page-15-0), with an increased incidence of relapses especially for psychotic and mood disorders. New psychiatric symptoms may also appear, including anxiety, depression, and insomnia, attributed to fear of infection, restrictions and isolation [\(Holmes et al., 2020](#page-11-0); [Costa et al., 2020b](#page-10-0); [Zhou et al., 2020;](#page-15-0) [Kozloff et al., 2020](#page-12-0)). Moreover, psychiatric patients are at increased risk of infection compared with the general population, due to the difficulties in adhering to public health measures, such as frequent hand-washing and physical distancing, as well as to poor understanding of the infection risk ([Zhou et al., 2020;](#page-15-0) [Benson et al., 2020;](#page-9-0) [Yao](#page-15-0) [et al., 2020b](#page-15-0); [Zhu et al., 2020](#page-15-0)).

Finally, based on evidence from previous pandemics, the COVID-19 pandemic may also increase the risk for suicidal ideation and behavior ([Holmes et al., 2020;](#page-11-0) [Gunnell et al., 2020;](#page-11-0) [Barbisch et al., 2015\)](#page-9-0), linked to social isolation [\(Yip et al., 2010](#page-15-0)), economic losses [\(Vandoros et al.,](#page-15-0) [2018](#page-15-0); [Kim and von dem Knesebeck, 2016](#page-12-0)), and psychiatric symptoms, especially depression and trauma-related disorders [\(Pfefferbaum and](#page-13-0) [North, 2020;](#page-13-0) [Reger et al., n.d.;](#page-13-0) [Zhou et al., 2020](#page-15-0); [Gunnell et al., 2020](#page-11-0); [Bo et al., 2020](#page-9-0); [Martín-Carrasco et al., 2016](#page-12-0); [Ornell et al., 2020;](#page-13-0) [Tapia](#page-14-0) [Granados and Diez Roux, 2009](#page-14-0)). According to the report of the Well Being Trust (WBT) and the Robert Graham Center for Political Studies in Family Medicine and Primary Care, additional 75,000 Americans could die from suicide, drugs or alcohol abuse, mainly in connection with the high unemployment rate caused from the pandemic [\(Brooks,](#page-10-0) [2020;](#page-10-0) [Petterson et al., 2020](#page-13-0)).

3. Conclusions

Climate change, pollution, and virus-triggered outbreaks, such as the current COVID-19 pandemic are all naturally occurring, catastrophic events involving the whole world, with different timescales, but similar consequences on individuals and collectivity, in terms of both health and socio-economic aspects. Although far from reaching a clear conclusion, some evidence highlighted the possible connection between climate change, environmental pollution and COVID-19 pandemic. Air pollutants, in particular CO_2 , CH_4 , O_3 , and NO_x , are indeed considered the main cause of the climate change ([Botta et al., 2019\)](#page-10-0). Furthermore, both air pollution, especially from fine PM, and destruction of the environment resulting from climate change have been associated with COVID-19 pandemic. To confirm these hypothesis, in countries like China and India, among the most polluted countries in the world, it has been shown that traffic restrictions and self-quarantine measures to control COVID-19, reduced environmental pollution ([Chen et al.,](#page-10-0)

[2020c;](#page-10-0) [Agarwal et al., 2020](#page-9-0)), especially $NO₂$ and PM2.5 concentrations, the main pollutants related to traffic, and, consequently, decreased non-COVID-19 deaths, especially from cardiovascular disease and chronic respiratory diseases, the diseases most related to the environmental pollution [\(Chen et al., 2020c](#page-10-0); [Agarwal et al., 2020\)](#page-9-0). Public health interventions such as school closures have obviously also reduced the growth of the epidemic [\(Jüni et al., 2020\)](#page-11-0).

Not surprisingly, increasing recent observations authorize to hypothesize that climate change, environmental pollution, COVID-19 pandemic and mental health might be intertwined.

The effects of climate change on mental health range from high rates of negative emotional responses, including guilt, pain, anxiety and demoralization, to full-blown psychiatric disorders, particularly anxiety and depression disorders, stress/trauma-related disorders, substance abuse, and suicidal thoughts and intentions [\(U.S Global Change, R.P.,](#page-15-0) [2016;](#page-15-0) [Salcioglu et al., 2007](#page-14-0); [Kjellstrom, 2009](#page-12-0); [Brugha and Cragg,](#page-10-0) [1990\)](#page-10-0). It should be noted that the health consequences of climate change are highly variable, as they are influenced by many factors ([Hayes et al., 2019\)](#page-11-0). First, there is a physiological vulnerability to climatic factors, so that some people are more sensitive than others to climate changes (i.e., subjects less able to cope with high levels of heat and/or defend against disease) [\(Hayes et al., 2019\)](#page-11-0). Among the most vulnerable groups there are elderly subjects, children, women, people with pre-existing health problems especially mental illnesses, subjects taking some types of medications including psychotropic drugs, individuals with low socio-economic status, immigrants, and natives ([Schwerdtle et al., 2017;](#page-14-0) [Hayes et al., 2019;](#page-11-0) [Cianconi et al., 2019](#page-10-0); [Furberg et al., 2011](#page-11-0)). Moreover, a heterogeneous meteosensitivity is present among the general population [\(Zikic and](#page-15-0) Žikić, 2018; [Mazza](#page-12-0) [et al., 2012\)](#page-12-0). Middle aged people and women seem to be more sensitive than the other groups ([Mazza et al., 2012;](#page-12-0) [Hedge and Collis, 1987](#page-11-0)). Finally, a geographical vulnerability must be also considered: those subjects living on the plains, on the coast, or in areas prone to desertification or fires, seem to the most vulnerable to the environmental problems, as these areas are the most affected by climate disasters ([Cianconi et al., 2020;](#page-10-0) [Torres and Casey, 2017](#page-14-0)).

Air pollutants were associated to the pathophysiology of different psychiatric disorders, such as psychotic, depression, anxiety, and neuropsychiatric disorders [\(Attademo and Bernardini, 2020](#page-9-0); [Costa et al.,](#page-10-0) [2020a;](#page-10-0) [Shin et al., 2018;](#page-14-0) [Attademo and Bernardini, 2017;](#page-9-0) [Attademo](#page-9-0) [et al., 2017;](#page-9-0) [Lim et al., 2012;](#page-12-0) [Power et al., 2015](#page-13-0); [Pun et al., 2017](#page-13-0); [Saez](#page-13-0) [et al., 2018](#page-13-0); [Volk et al., 2013](#page-15-0); [Jung et al., 2013](#page-11-0)), as well as with the exacerbation of psychiatric symptoms ([Shin et al., 2018;](#page-14-0) [Bernardini](#page-9-0) [et al., 2020;](#page-9-0) [Szyszkowicz, 2007](#page-14-0); [Yackerson et al., 2014](#page-15-0); [Szyszkowicz](#page-14-0) [et al., 2010;](#page-14-0) [Kim et al., 2010](#page-12-0); [Lin et al., 2016](#page-12-0); [Oudin et al., 2018](#page-13-0); [Lim](#page-12-0) [et al., 2012;](#page-12-0) [Jung et al., 2013\)](#page-11-0). Certainly it should be considered that air pollutants impacts on human health depends on wide range of factors: pollutant type, sources and concentration, time and way of exposure, interaction between different pollutants, as well as biological and socio-cultural factors, such as age, sex, ethnicity, previous illnesses, income, education, and neighbourhood, city, or country in which subject lives [\(Gaddi et al., 2018](#page-11-0); [Stewart et al., 2015\)](#page-14-0). All these variables may in part explain the still inconclusive results of the influence of environmental pollution on mental health.

It is evident that COVID-19 pandemic uncovers all the fragility and weakness of our ecosystem and inability to protect ourselves from biopollutants as part of a broader fight against air pollution. At the same time, it highlights that "every catastrophe has its own origin" [\(Nyerat,](#page-13-0) [2008\)](#page-13-0). Therefore, we must reflect on its meaning in order to prevent similar events in the future. Genetic and molecular analysis supported that Sars-CoV-2 could be originated from bats after passaging in intermediate hosts, highlighting the high zoonotic potential of coronaviruses [\(Salata](#page-14-0) [et al., 2019;](#page-14-0) [Malik et al., 2020\)](#page-12-0). The large animal farms, requiring the destruction of natural habitat of several wild species are considered crucial for the spillover of the virus from animals to humans. It is also suspected that bat species commercialized and used in traditional Chinese medicine

represent the natural reservoirs of the virus are represented by the ([Wassenaar and Zou, 2020](#page-15-0)). As trade in these bats could be a potential risk of spreading zoonoses, it is strongly recommended that these practices be changed [\(Wassenaar and Zou, 2020\)](#page-15-0).

One of the biggest obstacles for the positive interaction between the environment and health is the misperception of climate change, often resulting from psychological barriers of human beings ([Gifford et al.,](#page-11-0) [2011\)](#page-11-0). Gifford identified some main psychological barriers that limit active behaviors against climate change, including limited knowledge about the problem, ideologies that oppose pro-environmental behavior, high cost of solution strategies, discrediting of experts and authorities ([Gifford, 2011\)](#page-11-0). Therefore, it would be essential to promote change of common people's behaviour, through correct information together with an adequate and effective "green" policy worldwide, and not fearing to take effective, albeit unpopular measures to decrease pollutants [\(Gaddi and Capello, 2020\)](#page-11-0), and focused interventions to reduce the effects of dramatic climate change. As already underlined, "Rather than simply attempting to react to crises like COVID-19 after death and destruction are already upon us, we need to address the fundamental underlying causes and act now to prevent the numerous disasters that are literally waiting to happen" ([Wiebers and Feigin, 2020\)](#page-15-0).

In conclusion, the psychological/psychiatric consequences of COVID-19 pandemic, that currently seem unavoidable, represent a sharp cue of our misconception and indifference towards the links between our behaviors and the "health" of our planet and of ourselves, given that, at some point, the sudden emergence of stochastic effects may lead to irreversible disasters [\(Prigogine and Stengers, 1979](#page-13-0)). It is time to move towards a deeper understanding of these relationships, not only for our survival, but also for the maintenance of that balance between man, animals and environment at the basis of life on the earth ([Marazziti, 2020\)](#page-12-0). Without the promotion of a real ecological awareness worldwide, together with appropriate countermeasures to at least reduce, if not revert, climate change, air pollution, and intensive and destructive human activities, there will be no sustainable future.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or nonprofit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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