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Environmental pollution and mental health: a narrative review of literature

Antonio Ventriglio[1], Antonello Bellomo[1], Ilaria di Gioia[1], Dario Di Sabatino[1], Donato Favale[1], Domenico De Berardis[2,3] and Paolo Cianconi[4]

[1]Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy, [2]Department of Mental Health, Teramo, Italy, [3]University of Chieti, Chieti, Italy, and [4]Catholic University, Rome, Italy

Review

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Author for correspondence:
Antonio Ventriglio,
Email: a.ventriglio@libero.it

Abstract

Pollutant agents are exponentially increasing in modern society since industrialization processes and technology are being developed worldwide. Impact of pollution on public health is well known but little has been described on the association between environmental pollutants and mental health. A literature search on PubMed and EMBASE has been conducted and 134 articles published on the issue of pollution and mental health have been included, cited, reviewed, and summarized. Emerging evidences have been collected on association between major environmental pollutants (*air pollutants*, *heavy metals*, *ionizing radiation [IR]*, *organophosphate pesticides*, *light pollution*, *noise pollution*, *environmental catastrophes*) and various mental health disorders including anxiety, mood, and psychotic syndromes. Underlying pathogenesis includes *direct* and *indirect* effects of these agents on brain, respectively, due to their biological effect on human Central Nervous System or related to some levels of stress generated by the exposure to the pollutant agents over the time. Most of emerging evidences are still nonconclusive. Further studies should clarify how industrial production, the exploitation of certain resources, the proximity to waste and energy residues, noise, and the change in lifestyles are connected with psychological distress and mental health problems for the affected populations.

Setting the Scene

Pollutant agents are exponentially increasing in modern society since industrialization processes and technology are being developed worldwide. It is well known that there are various environmental pollutants that may have multiple effects on health of living species. In particular, it is suggested that some pollutants may impact on mental health of humans even if psychological and psychopathological consequences are poorly studied and described. In fact, these aspects are still underestimated even if there is so much interest on the physical consequences of the exposure to various environmental pollutants.

From the industrial age, the pollution related to the work of man has been inserted into the balance of our planet's natural forces. Human industrialization has been also named *Anthropocene.*[1] The negative impact of some global changes and the noxious action of new elements on the ecosystem and human life may be summarized by the term "*pollution.*"

Introduction

Polluting agents are widespread in a complex way on the planet and it may be difficult to estimate the benefits and costs of pollution for the humans. Pollution and its related outcomes should be compared, in an experimental manner, with those from healthy environments like medically or recreationally structured living conditions.[2,3] Environmental pollution is part of the "*flux*" of global events which are leading to the transformation of postmodern societies.[4] The polluting elements can also affect the human nervous system with remarkable consequences on population's mental health.[2,3] Mental health problems may be divided into three main categories according to their causes: *psychogenic* disorders, *endogenous* disorders, and *exogenous* disturbances.[5] In fact, pollution can impact on the expression of genes and the structure of neural tissues (*gene* × *environment interaction*), but also generating a social stress related to unhealthy and poor living conditions in degraded environments.[2,3] In this case, pollution can act as a psychogenic agent since psychogenic disorders are the result of stress, shock, or any kind of psychological traumas in childhood, adolescence, or adulthood.[5]

Also, Anakwenze and Zuberi, in 2014,[2] pointed out that the impact of pollution on human health can be due to an immediate cause–effect relationship but more significantly to long-term effects, often only hypothesized and poorly described or demonstrated. According to this, the damage of a pollutant can be achieved through "*direct*" biochemical mechanisms of the polluting agents on the nervous tissue, or *indirectly*, through the production of a stressful prolonged

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condition impacting on the mental health status. "Direct" impact can be differentiated into "*genetic interference*," "*gestational interference*," and "*post-gestational interference.*"[2,3] "*Genetic interference*" is related to the biochemical modification of human DNA and the consequent transmission of genetic mutations to the following generations with an increased risk of developing mental illness. In the "*gestational interference*" model of action, the embryonic or fetal tissues are directly affected, involving the physiological processes of neurodevelopment, triggering the etiopathogenesis of a mental illness, or generating a condition of vulnerability that may favor the onset of it. In the "*post-gestational interference*" model, additionally, the pollutant interferes with the psychosexual processes occurring from the birth and during the childhood/adolescent stage, or even in the adulthood, favoring a condition of mental illness or distress.[2,3]

The so-called "*indirect*" agents, as stated, may be involved in the etiopathogenesis of a mental disorder by generating a condition of a prolonged stressful condition possibly related to other multiple factors (cultural, psychological, technological, economic and urban, etc.). It is important to highlight that there are several polluting agents that can be defined as "*direct*" and "*indirect*" since they may act with two different models of action.[2,3]

In this narrative review of literature, we intend to focus on the available evidences about the possible relationships between various environmental pollutants and mental health.

Methods

A literature search on PubMed and EMBASE has been conducted using the following set of keywords: pollution, pollutants, air pollution, mental health, stress, psychological distress, radiations, heavy metals, neurotoxicity, noise, environment, urbanicity, and industrialization. All articles dealing with the issue of pollution and mental health (N = 806) have been considered. Redundant articles were analyzed and authors included those reporting significant evidences. Finally, a total of 134 documents were cited, analyzed in this narrative review, and grouped in specific topics of discussion as following.

Findings

Air pollution

Air pollution, based on chemical emissions essentially derived from various urban and industrial activities, can have significant consequences on human neuro-developmental processes and on the Central Nervous System (CNS).[6] Heavy metals are the most studied components of air pollution that have been associated with neurotoxicity; they include polycyclic aromatic hydrocarbons, volatile organic compounds, black coal, environmental tobacco smoke, carbon dioxide, ozone, nitrogen dioxide, and sulfur dioxide, particulate matter (PM) including fine PM < 2.5 μm ($PM_{2.5}$), ultrafine particulates <0.1 μm, and larger particles. It has been demonstrated that air pollutants can have synergistic impact on various human physiological systems such as the neuroendocrine system, the pro-inflammatory immune pathways, and on the redox balance.[7] Several epidemiological and experimental studies describe the association between atmospheric pollutants and chronic inflammation of brain tissues with an activation of microglia and alterations of the brain white matter.[8] Also, it has been described that children, elderly subjects, those with pre-existing health problems, socially excluded or economically disadvantaged subjects, and racial or cultural minorities report greater vulnerability to air pollution impact (probably due to an additive effect to their pre-existing vulnerability).[9,10] In particular, exposure to urban pollution is greater if close to major roads, landfills, and factories, it can seriously harm children's health especially when associated with socio-economic poor conditions.[11] Outdoor air pollution may lead to an immunological activation with systemic inflammation, neuroinflammation, oxidative stress, and immunodisregulation.[12] Also, children may present greater vulnerability to environmental pollutants due to differences in absorption, metabolism, and excretion of chemical agents if compared to adults. In fact, environmental contaminants may have longer half-lives in young children due to the immaturity of metabolic enzyme systems. Cell immaturity and brain susceptibility represent a high risk for children exposed to pollutants, particularly PM, so that they can be considered the most vulnerable subjects of the general population.[12,13] Recently, a comprehensive review confirmed the association between various fossil fuel combustion pollutants and multiple health effects in children.[14]

Exposure to air pollutants during fetal life may be an important risk factor for neurodevelopmental disorders such as autism and major psychoses like schizophrenia.[15] It is generally recognized that the developing brain is much more vulnerable than the mature nervous system.[16] This is due to the phase of synaptogenesis which is considerably susceptible to neurotoxicity.[17,18] A recent review conducted by Annavarapu and Kathi[6] explores recent advances in scientific research about the possible association between the exposure of children to vehicular emissions mainly from 2005 to 2015 and oxidative stress, neurodegeneration, neurodysfunction, attention-deficit/hyperactivity disorder (ADHD), and autism.[6] This study also highlights an important influence of some additional association factors such as younger age, gender, proximity to the source of contamination, and socio-economic conditions of children.[6] Sunyer et al[19] described a correlation between exposure to air pollution and an inflammatory reaction of some specific brain structures such as the prefrontal cortex and the striatum. It has been suggested this may lead to deficits in cognitive development among children. These evidences were confirmed in a study conducted in Mexico City on children reporting neuroinflammation, neurodegeneration, and cognitive deficit after a prolonged exposition to air pollution.[20–24] Authors documented volumetric alterations at magnetic resonance imaging (MRI) involving bilateral temporal and right parietal areas of the brain. According to the same authors, the presence of heavy metals was found in frontal lobes of lifelong exposed children with consequent neuroinflammation and up-regulation of the frontal interleukin-1b and of the cyclooxygenase-2.[25] Recently, de Prado Bert et al[26] summarized evidences regarding the effect of traffic-related air pollution (TRAP) on the human brain integrating epidemiological data with neuroimaging findings. They pointed out that long-term exposure to air pollution agents may have impacts on brain structures (especially white matter) and brain functioning which are described with different MRI techniques. It is suggestive that brain changes may mediate the impact of TRAP on human cognition and to be causally associated to cognitive disorders.

It has been described that air pollutants, in particular PM, promote oxidative stress. In fact, children exposed to emissions also show mutations of the genes involved in redox pathways.[6,27] Oxidative stress is a central mechanism through which exposure to PM can lead to pathological conditions.[28] In particular, some authors described a specific correlation between autism and the

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exposure to urban TRAP during the pregnancy and the first year of life.[29–32] Ehrenstein et al[33] have shown that exposure to air pollutants from urban traffic and industry emissions during the intrauterine life can be considered an important risk factor for autism. Also, Siddique et al[34] studied the association between atmospheric pollution and neurobehavioral disorders in children, concluding that the prevalence of ADHD was significantly higher among Indian children living in urban areas than children of the same age and gender living in nonurbanized areas. In 2019, Burkhardt et al[35] found also an association between the increase of air pollution and violent crime rates across the continental United States.

Carbon monoxide and neurotoxicity

Carbon monoxide (CO) is a common contaminant of both indoor and outdoor environments and it is a product of incomplete combustion of hydrocarbons. CO is a component of vehicle-related pollution, gas stove pollution, and tobacco smoke. CO can cross the placenta and reach the developing brain via the fetal circulation.[18,36,37] Levy[18] proposed the theory according to which CO is responsible for alterations of neurodevelopment especially in case of exposure during the perinatal period. A work conducted by Vrijheid et al[37] showed an association between exposure to CO during fetal life and abnormalities in cognitive development beyond 14 months of age, regardless of socio-economic conditions. A further study showed a reduction of neuropsychological performance among Guatemalan children at 6 to 7 years of age, after being exposed to chronic indoor wood smoke during the third trimester of pregnancy.[38] From all these studies, a correlation emerges between any exposure to CO in both internal and external environments and abnormalities in neurological development especially if exposure occurs during fetal life. Animal studies have shown that perinatal exposure to CO interferes with the physiological stages of neurodevelopment. For example, Cheng et al, in 2012, identified some important biochemical effects on various elements involved in the programmed cell-death pathways of the brain tissues of mice exposed to CO in the postnatal period.[18,39]

$PM_{2.5}$ and neurotoxicity

Fine PM with an aerodynamic diameter of less than or equal to 2.5 μm ($PM_{2.5}$) is now considered an important risk factor for neurodegenerative disorders and neurological development disorders including autism.[40,41] A study conducted by Wei et al demonstrated that $PM_{2.5}$ involves the redox balance leading to a decrease in GSH/GSSG (glutathione/oxidized glutathione) ratio and abnormal DNA methylation patterns which in turn may cause cognitive deficits or behavioral disorders.[41,42] This work has shown that $PM_{2.5}$ and its extracts impair the SAMe (S-adenosylmethionine) synthesis, remembering that SAMe is fundamental for DNA methylation. The impaired capacity of methylation leads to a global hypomethylation of DNA but also to hyper- or hypo-methylation of some candidate genes for autism. Authors have further analyzed the influence of $PM_{2.5}$ on gene-specific DNA methylation and correlative mRNA expression in some autism candidate genes such as NRXN1 and NLGN3 which codify for synaptic-adhesion molecules. NRXN1 and NLGN3 play a fundamental role in the synaptic transmission by connecting presynaptic and postsynaptic neurons. $PM_{2.5}$ exposition seems also associated with the reduction of expression of adhesion proteins such as Synapsin-1 and PSD-95, which are fundamental for the establishment of synapses, neurotransmission, and axonal growth.[43,44] These findings suggest the hypothesis that $PM_{2.5}$ is associated with synaptic homeostasis and activities involved in neurodevelopmental disorders.[41] Wei et al[40] have founded that $PM_{2.5}$ and its extracts promote cell cycle arrest, cell apoptosis and inhibition of cell proliferation in neuronal tissues. Moreover, they highlight that $PM_{2.5}$ and its extracts increase the hydroxymethylation of the global DNA and in particular of neuronal genes, thus interfering with their expression.

Findings from several studies support a correlation between air pollution and depression. Air pollution exposure has been found to lead to depression-like behaviors in animal studies as well as exposure to $PM_{2.5}$ is associated with increased depression-like responses in mice.[45] Mokoena et al[46] reported anxiety and depression-like behavior in rats following chronic ozone inhalation.[45,46] Jones and Thomsen[47] have reported an association between the increase of pro-inflammatory cytokines and behavioral abnormalities in animals and air pollution has been consistently associated with increases of blood proinflammatory markers and systemic oxidative stress, both involved in the pathogenesis of psychiatric disorders such as depression.[48] Some other studies have reported an association between air pollution and suicide.[49–51] In a recent prospective cohort study conducted by Kioumourtzoglou et al,[52] authors investigated the association between long-term exposures to $PM_{2.5}$ and ozone and the onset of depression among a nationwide cohort of mid-life and older women, during a period of 12 years. The findings[52] of this study suggest that both $PM_{2.5}$ and ozone are potential risk factors for depression even if Zijlema et al[53] investigated the association between air pollution and depressed mood in four European general population cohorts and they found no consistent evidence of an association between air pollution and depressed mood.

Environmental ultrafine particles and neurotoxicity

Allen et al[54] showed the effects of exposure to concentrated environmental ultrafine particles (UFPs) on mice during their postnatal day (equivalent to the third human trimester of life) correlating them with the onset of pathological conditions. The morphological and neurobiological changes found in some brain structures suggest that the equivalent of the third human trimester may be a period of potential vulnerability to the toxicity of UFP, particularly in males. Moreover, it has been hypothesized that exposure to UFP during periods of neurogenesis may be a risk factor for schizophrenia, attention deficit disorder and periventricular leukomalacia. A recent study also has shown that short-term exposure to ultrafine particles has been associated with exacerbations of psychiatric conditions in children as suggested by increased access to the Cincinnati Children's emergency department for psychiatric issues.[55]

Heavy metals

Metals are known to impact on early neurodevelopment, but their effects later in life are not well described. Heavy metals are often generated by the electronic waste. In fact, electronic waste is constituted by plastic components and precious materials such as gold, silver, copper, platinum, and palladium but also iron, aluminium, small amounts of heavy metals (like mercury, lead, cadmium).

According to the World Health Organization (2007),[56] risks for our health may derive from direct contact with harmful materials, inhalation of toxic fumes, and accumulation of chemical substances in the soil, water, and food that constitute also a threat for the biodiversity. Grant et al[57] described change in the thyroid function, worsening in the neonatal health, increases in spontaneous

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abortions, premature births, reduction of the lung functionality after exposure to e-waste (e: electronic). Even if there are possible associations between heavy metals exposure and psychosis, only few studies have investigated putative linking mechanisms.[58]

Lead (Pb)

One study investigated the linking mechanism between early exposure to Pb and the gene expression influencing the risk of psychosis. Lead seems to impact dopaminergic and glutamatergic neurotransmission both involved in the pathophysiology of psychosis. In fact, Cory-Slechta et al showed that the exposure to Pb in early life can lead to hyperactivity of the dopaminergic system.[59] The N-methyl-D-aspartate receptor (NMDAR) for glutamate, which is an excitatory aminoacid playing an important role in regulating dopamine activity, seems to be antagonized by Pb. Since the early '90s, Guilarte and Miceli[60] reported evidences that Pb^{2+} is a noncompetitive antagonist of the NMDAR and disrupts neuronal processes depending on NMDAR activation. Authors added that exposure to Pb during early brain development leads to onset of psychotic symptoms as later confirmed by Opler in 2004.[61]

Mercury

Brain pathophysiology of autism seems to show similarities with brain abnormalities found in mercury intoxication.[62] It is of note that mercury and other heavy metals can employ the sulfur-dependent detoxification system, and glutathione reserves in particular.[63] Children from the Western Amazon have been studied after being exposed to acute TCV-EtHg (thimerosal-containing vaccines—ethylmercury) and to chronic MeHg (methylmercury) from fish consumption. The Mental Development Indices (MDI) and Psychomotor Development Indices (PDI) were calculated at 6 and 24 months of age. The combined exposure to MeHg and EtHg was not associated with differences in PDI but some differences were found for the MDI. However, it has been observed a significant decrease in both PDI scores and MDI scores at 24 months. Also, the combined exposure to Hg caused an increase in neurodevelopmental delays.[64] In 1985, a 16-year-old female, while was working at the thermometer manufacturing factory, developed a mental disorder that was probably provoked by an inorganic mercury poisoning as reported by Jeong et al.[65]

Cadmium

Cadmium impacts on brain and increases reactive oxygen species (ROS) damaging antioxidant defence systems.[66] The mechanism of lead- and cadmium-induced neurotoxicity leading to neuropsychiatric disorder is not fully understood. On the other hand, one developmental hypothesis is that cadmium could be another environmental factor inducing early pathological changes in the brain.[67]

Ionizing radiation

IRs certainly act through "direct" biological mechanisms on the CNS with consequent alterations. However, it should be emphasized that the awareness of being exposed to radiations and the consequent perception of risk to own health is already an important source of psychological stress for healthy subjects. This condition, in the long run, can promote a cascade of biological and pathophysiological mechanisms possibly leading to the etiopathogenesis of mental distress such as depressive and anxious disorders. In eukaryotic cells, IR induces damage to DNA, proteins, and lipids, directly or indirectly, increasing the production of highly reactive free radicals. IR-related brain injuries do not occur as a unitary and immediate event, but can be considered as dynamic and multiphase processes over time. In vitro findings have shown that IR pathophysiologically can lead to direct neuronal damage and death. The CNS histological alterations produced by IR mainly concern the process of demyelination. In Western countries, radiodiagnostics and nuclear medicine are the main sources of exposure to IR and most of the data concerning exposure to IR derive from the evaluations of patients exposed to radiotherapy. Little information is available on medium to low dose range exposure. More evidence is needed to explore dangerous effects of low-moderate doses of IR on the brain which is one of the main organs limiting the dose in radiotherapy.[68]

Schizophrenia and IRs

According to the diathesis-stressor model of schizophrenia, environmental stressors can influence the genetically determined neurobiological vulnerability to schizophrenia. There are comparable reports on the increase of Schizophrenia Spectrum Disorders in persons exposed to IRs as a result of Chernobyl accident, atomic bombings, nuclear weapons tests, environmental contamination by radioactive waste, and finally radiotherapy.[69–71] It has been described that exposure to IR causes brain damage with limbic dysfunctions and affects the processing of information at a molecular level, influencing the development of schizophrenia in exposed subjects.[71] Also, exposure to IR during the early years of life leads to problems in neurodevelopment. This evidence has been reported in an epidemiological study carried out on the Norwegian population with the aim of describing the impact of the Chernobyl nuclear accident in 1989. It has been shown a statistically significant relationship between IR exposure and schizophrenia, epilepsy, cerebral palsy, mental retardation, or hearing or vision problems.[72]

Depression and IR

Depression is one of the most important and long-term effect of nuclear accident (atomic bombings, nuclear testing, and radiation emergences). Chernobyl accident survivors have shown an increased prevalence of depression (18.0% vs 13.1% in controls) and suicide rates.[73] The clinical manifestation of depression would be characterized above all by symptoms of an asthenic type. The etiopathogenesis of depression in these cases is multifactorial, linked to genetic vulnerability, medical comorbidity, psychological factors, environmental conditions, and finally biochemical processes directly derived from the impact of IR with the CNS tissues.[70]

Alzheimer's disease and IR

Significant increase in the incidence of cerebrovascular disease has been demonstrated among nuclear workers employed at the Mayak Production Association (Mayak PA).[74] It has been studied that cerebrovascular dysfunctions are a relevant pathogenetic factor in Alzheimer's disease.[75–77] There would also be other evidences regarding the relationship between cerebrovascular diseases and cortical neurodegenerative diseases affecting the brain, which all are characteristics of Alzheimer's disease such as cerebral β-amyloidosis and cerebral amyloidal angiopathy with amyloid-β plaque production.[78]

Parkinson's disease and IR

CNS exposure to IR would result in inflammatory tissue changes. Histological studies on Parkinson's disease (PD) would confirm the fundamental role of inflammation in the etiopathogenetic

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neurodegenerative pathway.[79] It is demonstrated that oxidative stress is involved in PD progression and increased levels of ROS can damage the target neuronal cells. The dopaminergic neurons of the basal ganglia are particularly vulnerable to oxidative stress and this would be linked to their low intracellular levels of antioxidants and the high rate of metabolic oxygen consumption.[80]

Cognitive deficits and IR

Pediatric patients with brain tumors treated with radiotherapy cycles show a decrease in brain volume during the neurodevelopment process, especially at the frontal and temporal lobes level, which is directly proportional to the dose of IR administered; this condition is related to deficit in cognitive performances as assessed through neuropsychological tests.[81] Therefore, despite the significant therapeutic role of radiotherapy in the brain, it would result in organ damage leading to impairment of acquired cognitive abilities. The neurocognitive domains affected by radiation seem to be executive functions, verbal and nonverbal memory, sustained attention and information processing speed as well as brain structures most affected by radiation damage are the prefrontal cortex and hippocampus.[81] Cognitive processes are mainly determined by a complex network of connections that exists between the frontal cortex and the subcortical level. Radiation injury can affect some or all of these associative pathways through a multifactorial physiopathological mechanism, characterized by inflammation, vascular anomalies, gliosis, demyelination, and necrosis of the white matter in the case of high doses of IR.[82]

Organophosphate pesticides

Organophosphorus pesticides (OPs) are commonly used as insecticides and are particularly toxic to humans.[83,84] The OPs are rapidly absorbed through the respiration, through the skin, the mucous membranes, and the gastrointestinal tract. Usually, acute intoxication occurs after inhalation and causes the rapid onset of multiple symptoms caused by inhibition of AChE (acetylcholinesterase), the enzyme that inactivates acetylcholine; this process is responsible for the accumulation of acetylcholine in cholinergic synapses and then for a peculiar syndromic picture.[85,86] Unlike acute exposure to high concentrations of OPs, chronic exposure is associated with sometimes debilitating neuropsychiatric conditions such as anxiety, depression, and suicide.[87–96] A review by Voorhees et al[96] shows the correlation between chronic occupational exposure to OPs and neurotoxicity. Concerning the correlation between OPs exposure and psychiatric disorders, controversial data emerge from scientific studies with some epidemiological studies supporting the close correlation as well as a meta-analysis conducted in 2013 showing results as limited and not very conclusive.[88,91–94] Some other evidences have described alterations in cytoarchitecture or in the morphology of nerve cells among OPs exposure effects[96]: these alterations mainly consist in variation in length, number, or ramifications of axons or dendrites and all have been associated with psychiatric manifestations, including depression, anxiety, Alzheimer Disease (AD), and PD.[96–99] A substantial part of the scientific literature indicates that chronic exposure to OPs is associated with deficits in cognition, impairment of learning, memory, and behavior on the base of neuroinflammation.[96] Paul et al[100] recently published a study that strongly supports a relationship between OP pesticides, cognitive decline and mortality among older Mexican Americans. In fact, exposure to pesticides has been associated with the pathogenesis of various mental disorders, especially in individuals exposed for professional reasons, such as farmers. In a recent Brazilian study conducted on a sample of a rural population resident in a place where tobacco farming is the main economic activity, researchers found an association between pesticides exposure and common mental disorders, including self-reported depression.[101] Harrison and Mackenzie[102] in a study published in 2016, analyzed the relationship between low-level cumulative exposure of OPs in sheep farmers and their mental health. In this study, the researchers used both self-evaluation measures and structured clinical interviews. The exposed cohort reported significantly higher rates of anxiety and depression than the control subjects when self-report questionnaires were used taking into account stressful life events and other factors.

Light pollution

Life on Earth is adapted to the 24-hours solar day allowing the synchronization of behavioral and biological processes to the external environment.[103] The invention of electric light has led to "*round-the-clock*" societies: all persons living in the United States and Europe are exposed to unnatural light and about 20% of the population has a shift work.[104] These changes obviously have biological implications. In mammals, circadian photoentrainment is mediated by intrinsically photosensitive retinal ganglion cells (ipRGCs) that project these information to various brain regions such as the suprachiasmatic nucleus regulating the circadian rhythm. The same projections reach other areas involved in mood regulation, such as the prefrontal cortex, hippocampus, and amygdale, suggesting that artificial light could have a role in influencing mood.[105]

Deregulation of circadian rhythm and mood disorders

Many studies identified a link between the induced deregulation of circadian rhythm and the onset of mood disorders. Any unnatural timing of light exposure can cause a desynchronization between internal biological processes and the external environment, leading to mood alterations. There are in fact several instances associating depression with environmental lighting cues. Seasonal depression is in fact a well-known phenomenon afflicting nearly 10% of the population.[106] In such cases, morning bright light therapy, particularly blue wavelengths, may have a therapeutic role.[107] Another study considered shift workers population. In this population, the prevalence of major depression disorder is higher than in general population.[108] Young student nurses performing night shift work developed depressive symptoms after only 3 months of night work.[109] The involvement of psychiatric disorders is due to the consequences that sleep deprivation has on the monoaminergic system.[110] For example, monoamine oxidase A transcription is regulated by some clock components.[111] Environmental circadian disruption alternating clock-genes expression could modulate neurotransmitters system, potentially leading to depressed mood. Moreover, exposure to unnatural light at night alter neurotrophin and neurotransmitter systems as demonstrated among mice exposed to 4 weeks of dim light at night which showed depressive symptoms and lower brain-derived neurotrophic factor mRNA in the hippocampus than mice exposed to a typical light–dark cycle.[112] Moreover, the disruption of circadian rhythms plays an important role even in generating organic health problems. For example, the WHO recently referred to shift work as a probable carcinogen.[113] In Denmark, for example, it is recognized a reward for those women who developed breast cancer after working night

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shifts.[114] In conclusion, further studies are needed to better know the artificial light effects on human health.

Noise pollution

Noise represents the most frequent stressor and is caused by work environment and house hold appliances, planes, and city traffic.[115] Acoustic pollution could be defined as an indirect pollutant because essentially its consequences on mental health are mediated by generating stress even if there may be some direct biological mechanisms that involve CNS tissues. Children living in noisy areas reported reduction of problem solving, impaired hearing, poor reading, and frustration.[116] In fact, noise affects neurotrasmitters level in different parts of the brain, impairs cognition and memory, increases plasma levels of corticosteroids, decreases dendritic count.[117–122]

About the relationship between environmental noise and schizophrenia Tregellas et al[123] reported that hippocampal hyperactivity, determined by environmental noise, may cause a reduced recruitment of attention networks in schizophrenia. The effects of environmental noise on cognition in schizophrenia have been analyzed by Wright et al in 2016.[124] Cognitive impairment, especially in executive function domains, memory, and attention are frequently present and linked to low functional outcomes in schizophrenia. In healthy adult population, environmental noise damages many cognitive domains, including those compromised in schizophrenia. It has been demonstrated that noise has negative effects on the working memory and verbal domains in psychotic patients as well as healthy participants. This may add more distress and lead to poorer outcome in schizophrenia patients with pre-existing comprised cognition. The role of noise in clinical environments has been studied by Brown et al[125] with particular interest for the mental health. All clinical environments have a "*soundscape*." This includes noises from machines, the rhythms of the day and the activities of other people in the hospital. Distracting sound may have a negative effect especially on those who are more susceptible, yet this does not necessarily mean that silence is better than noise!

Environmental catastrophes

The relationship between environmental catastrophes due to human action and consequences on mental health is a very difficult topic to deal with. Loss of pipelines, damage to oil extraction platforms, contamination of forests and ecosystems may produce enormous psychological distress. Data on these disastrous events are few. The damage is not only due to direct pollution by the polluting agents, but also indirect pollution due to the sense of irreparable catastrophe and injustice. This sense of injustice is due to both the negligence of the control systems and the vastness of the destruction. Mental health assessment after the gulf coast oil spill have been analyzed by Buttke et al.[126] On April 20, 2010, 40 miles south of the coast of Louisiana in the United States, the mobile offshore drilling unit Deepwater Horizon exploded. The oil released by Deepwater Horizon has damaged the tourism industries of the Gulf coast, fishing as well as physical and mental health for those affected or exposed to the oil spill. Following an oil spill, however, longitudinal studies indicate that the subsequent psychiatric effects can be more widespread than physical health outcomes.[127,128] In fact, these studies have demonstrated higher levels of depression, anxiety, and stress in individuals and communities either exposed to oil, or financially impacted by the spill, than in communities not exposed. People interviewed were divided in three groups reporting, respectively, depressive symptoms, symptoms consistent with an anxiety disorder, and other reporting 14 or more mentally unhealthy days within the past 30 days. A cluster sampling methodology was used to evaluate the mental health status of coastal residents in the Gulf Coast counties in Mississippi at fifth month after the oil spill, in three counties in Alabama 4 months following the 2010 Deepwater Horizon Oil Spill (DWHOS). The proportion of respondents reporting negative mental health parameters in the affected Alabama and Mississippi coastal communities is bigger than the proportion reported in the 2008 and 2009 Behavioral Risk Factor Surveillance System state, indicating that the public health response to the DWHOS should concentrate on mental health services in these communities. Rung et al[129] analyzed domestic conflict, mental distress, and depression among Louisiana Women exposed to the DWHOS in the WATCH Study. A part of them reported symptoms of depression, others severe mental distress, others an increase in the number of fights with their partners, and a small part an increase in the intensity of partner fights. Both economic and physical exposure were significantly associated with depressive symptoms, whereas only physical exposure was related to mental distress. Mental health effects of DWHOS on residents in heavily affected areas have been studied also by Osofsky et al.[130] The greatest effects on mental health were related to the extent of disruption to participants' social engagement, family, work, lives with increased symptoms of posttraumatic stress, depression, and anxiety. Given the location of the oil spill hitting communities that had been destroyed by Hurricane Katrina, results also showed that losses from Hurricane Katrina were linked to negative mental health outcomes. The mental health consequences of disasters, including oil spills, have also been analyzed by Rung et al.[131] The social capital and social support were studied and also the effects of exposure to the DWHOS on depression among women. Data for the analysis come from a longitudinal study of the health effects of women exposed to the oil spill in southern Louisiana, United States. Women were interviewed about social support, cognitive social capital (sense of community and informal social control), structural social capital (neighborhood organization participation), depression symptomatology, and their exposure to oil spill. It was demonstrated that structural social capital was linked to increased levels of cognitive social capital, which had as consequence higher levels of social support and then lower levels of depression. Social capital and social support appeared beneficial for depression postoil spill; however, they were themselves negatively damaged by the oil spill. Social capital and social support are coping-resources that are helpful for depression postdisaster. The findings indicate that social resources can be changeable and can be harmed by disasters, conditioning a population's degree of depression. Responses and resilience of people and communities impacted by the DWHOS have been studied by Glenn Morris.[132] Significant social and economic impact in all the four communities, regardless of distance from the site of DWHOS, has been showed. High levels of stress and concern related to the uncertainty of the long-term economic and ecological impacts were commonly noticed by respondents. Mental health problems continue to be present, and in some cases are worsening for residents of northeastern Gulf Coast communities 1 year after the DWHOS. Some of the anxious symptomatology, particularly hyperarousal, may also be linked to media exposure.

All findings of this narrative review are reported and summarized in the following Table 1.

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Table 1. Polluting Agents and their Putative Effects on Human Central Nervous System and Mental Health.

Topic	References	Polluting Agents	Findings
Air pollution	6–37		Reported association between atmospheric pollutants and chronic inflammation of brain tissues with an activation of microglia and alterations of the brain (white matter). Outdoor air pollution may lead to an immunological activation with systemic inflammation, neuroinflammation, oxidative stress, and immunodisregulation. Most involved brain areas are prefrontal cortex and the striatum.
	38–41	Carbon monoxide (CO)	CO is responsible for alterations of neurodevelopment especially in case of exposure during the perinatal period.
	42–55	$PM_{2.5}$ Fine particulate matter	It is recognized a role in neurodegenerative disorders and neurological development disorders including autism or depression. Processes involved are DNA methylation, redox balance, and an increase of pro-inflammatory cytokines.
	56, 57	Environmental ultrafine particles (UFPs)	Exposure to UFP during periods of neurogenesis may be a risk factor for schizophrenia, attention-deficit disorder, and periventricular leukomalacia.
Heavy metals	61–63	Lead (Pb)	Early exposure to Pb impacts on gene expression for dopaminergic and glutamatergic neurotransmission influencing the risk of psychosis.
	64–67	Mercury	Mercury and other heavy metals can employ the sulfur-dependent detoxification system, and glutathione reserves in particular. Mercury is supposed to be related to autism and neurodevelopmental delay.
	68,69	Cadmium	Cadmium impacts on brain and increases reactive oxygen species damaging antioxidant defence systems with resulting neurotoxicity.
Ionizing radiations (IRs)	71–74	Schizophrenia and ionizing radiations	It has been described that exposure to IRs causes brain damage with limbic dysfunctions and affects the processing of information, influencing the development of schizophrenia in exposed subjects.
	72–75	Depression and ionizing radiations	Depression is a long-term effect of nuclear with an increase of suicide rates. The clinical manifestation of depression would be characterized by symptoms of an asthenic type.
	76–80	Alzheimer's disease and ionizing radiations	IRs are associated with a significant increase in the incidence of cerebrovascular disease as well as cerebral β-amyloidosis and cerebral amyloidal angiopathy with amyloid-β plaque production.
	81,82	Parkinson's disease and ionizing radiations	IRs are associated with a documented oxidative stress of dopaminergic neurons of the basal ganglia.
	83,84	Cognitive deficits and ionizing radiation	Prefrontal cortex and hippocampus are affected by radiation damage with possible impairment of executive functions, verbal and nonverbal memory, sustained attention and information processing speed.
Organophosphate (OPs) pesticides	85–104		OPs intoxication may lead to inhibition of AChE (acetylcholinesterase), the enzyme that inactivates acetylcholine; this process is responsible for the accumulation of acetylcholine in cholinergic synapses with neuropsychiatric conditions such as anxiety, depression, and suicide.
Light pollution	108–116		Light pollution may lead to a deregulation of circadian rhythm, reduction of monoamnergic neurotransmission, alteration of clock-genes expression with resulting mood disorders.
Noise pollution	117–127		Noise affects neurotrasmitters level in different parts of the brain, impairs cognition and memory, increases plasma levels of corticosteroids, decreases dendritic count. Effects on mental health are related to hippocampal hyperactivity with risk of stress-related disorders, psychosis, and cognitive disorders.
Environmental catastrophes	127–134		Exposure to environmental catastrophes may lead to acute stress-reactions with fear, anxiety, insomnia, and concerns for psychological and physical health. In the long term, higher levels of depression, anxiety, and stress (post-traumatic stress disorder) have been observed among individuals and communities exposed.

Conclusions

Pollution and mental health is a relevant but poorly described topic. This narrative review aimed to summarize available evidences on sources of pollution and correlation with psychopathology. Polluting elements considered were *air pollutants*, *heavy metals*, *IR*, *organophosphate pesticides*, *light pollution*, *noise pollution*, *and environmental catastrophes.* It has been highlighted how the effects on the individuals and on the collectives can be *direct* on the tissues (eg, on the CNS tissue) or *indirect,* mediated by stress or stigma following the exposure to the known pollutant. This is a relatively

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new field of studies and more research is needed to understand how direct and indirect effects of pollutants may damage groups and can lead to mental health disorders. For most of described pollutants, data are nonconclusive. Limitations of this review may include the fact that most of evidences come from retrospective studies with a lack of longitudinal studies, and there may be a possible role of socioeconomic status as a mediator of some described effects of pollution on mental health in different layers of population. Further studies should clarify how industrial production, the exploitation of certain resources, the proximity to waste and energy residues, noise and the change in lifestyles are connected with psychological distress and mental health problems for the affected populations.

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