



## Review article

## Is there a link between air pollution and mental disorders?

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## ABSTRACT

Several studies have demonstrated the association between air pollution and different medical conditions including respiratory and cardiovascular diseases. Air pollutants might have a role also in the etiology of mental disorders in the light of their toxicity on central nervous system. Purpose of the present manuscript was to review and summarize available data about an association between psychiatric disorders and air pollution.

A research in the main database sources has been conducted to identify relevant papers about the topic.

Different air pollutants and in particular PM and nitric oxides have been associated with poor mental health; long exposition to PM<sub>2.5</sub> has been associated with an increased risk of new onset of depressive symptoms (Cohen's effect size *d*: 0.05–0.81), while increased concentration of nitric dioxide in summer with worsening of existing depressive conditions (Cohen's effect size *d*: 0.05–1.77). However, the interpretation of these finding should take into account the retrospective design of most of studies, different periods of observations, confounding factors such as advanced age or medical comorbidity. Further studies with rigorous methodology are needed to confirm the results of available literature about this topic.

## 1. Introduction

Air pollution has devastating effects on public health and it is responsible for high health costs linked to the development of chronic diseases, and their associated disability and mortality (Segalowitz, 2008). A consistent literature has demonstrated a clear association between air pollution and respiratory (Kim et al., 2013) and cardiovascular diseases (Fiordelisi et al., 2017), while the effects of air pollutants on central nervous system (CNS) are starting to be widely recognized. Some research studies have pointed out that highly air polluted environments are responsible for an increased risk of cognitive decline (Power et al., 2011; Tallon et al., 2017) and stroke (Genc et al., 2012). Different agents have been evoked to be toxic for CNS including fine airborne particulate matter (PM<sub>2.5</sub>, PM<sub>5</sub>, PM<sub>10</sub>), nitrogen, sulfur oxides, carbon monoxide (CO), benzene and ozone (O<sub>3</sub>) (Lam et al., 2016). The mechanisms of neurotoxicity of air particulate are not totally clarified, but systemic inflammation and the related brain oxidative stress seem to play an important role in CNS structural and functional changes associated with mental disorders (Calderón-Garcidueñas et al., 2015; Buoli et al., 2017a). Of note, increased inflammation in some brain areas such as hippocampus has been demonstrated in animals exposed to air pollution (Fonken et al., 2011); neuroinflammation due to air particulate is thought to be mediated by epigenetic regulations of genes which have a role in oxidative responses

(e.g. decreased methylation of the inducible nitric oxide synthase gene) (Madrigano et al., 2012). An animal study demonstrated that chronic exposure to sulfur oxides is associated with repression of glutamate receptor gene expression and consequently with impairment in neuron function (Yao et al., 2015).

Till now researchers have given less focus on a probable association between air pollution and mental disorders. This is surprising as a number of authors have reported a higher risk of psychotic disorders in urban areas of different countries (supposed to have a worse quality of air) than in rural ones (Lundberg et al., 2009; Kelly et al., 2010; Padhy et al., 2014). The traditional explanation for a difference on rates of psychotic disorders between cities and country consisted of a major social stress associated with urban life (Lederbogen et al., 2013) and a higher social fragmentation in urban than in rural areas (Kelly et al., 2010); however a role of air pollution in the urban susceptibility to psychiatric disorders cannot be excluded (Kelly et al., 2010; Padhy et al., 2014). The association between air pollution and mental health is also supported by the rapid increase of psychiatry burden in countries like China with an accelerated rural to urban migration (Gong et al., 2012). In light of these considerations, similarly to what happens for respiratory and cardiovascular diseases, it is conceivable that a reduction in levels of pollution can reduce the costs of mental health (Kheirbek et al., 2014).

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Updated systematic reviews about the association of all different psychiatric disorders with air pollution are currently lacking. For this reason, purpose of the present article is to provide a complete and updated review about the risk or worsening of mental disorders in subject over-exposed to air pollution. Specifically we will try to summarize and comment data about the role of pollution on new onset of mental disorders or on aggravating symptoms of subjects suffering from mental conditions.

## 2. Material and methods

A careful search of articles on Pubmed, PsycINFO, Isi Web of Knowledge was performed in order to obtain a comprehensive review about the effects of air pollution on the risk to develop mental disorders.

The term “pollution” has been associated with the words “mental health”, “schizophrenia”, “bipolar disorder”, “depression”, “suicide”, “anxiety”, “obsessive-compulsive disorder”, “Attention Deficit Hyperactive Disorder-ADHD”, “autism”, “eating disorder”, “personality disorder”. Only headings were used to obtain initial search. A manual selection of papers was then performed in order to consider only relevant articles for the topic of the present article. No restriction criteria were established for study design. Exclusion criteria consisted of: 1) animal studies; 2) psychological studies (e.g. assessing the role of air pollution on cognition); 3) review or opinion articles about the risk of single mental disorders as a result of over-exposition to air pollution (they were used for discussion); 4) studies about the relation of pollen with mental disorders; 5) studies about the exposition to insecticides and fertilizers; 6) data on individuals largely or totally overlapping to samples whose results had been already published (e.g. Volk et al., 2014 or Gong et al., 2017); 7) papers not in English. This search covered findings from 1982 and 2017, with last check on 15th February 2018.

Table 1 provides an evaluation of the quality of included studies according to Qualitative Assessment Tool for Quantitative Studies (Effective Public Health Practice Project) (Armijo-Olivo et al., 2012) as well as a summary of the results of the included studies and their effect sizes.

The original effect sizes (reported in Table 1) have been converted in Pearson's *r* and Cohen's *d* effect sizes for an easy comparison of the results reported by the different studies.

If not explicitly reported, the outcomes of the manuscripts have been considered as:

- related to the new onset of mental disorders (prescription of psychotropic compounds).
- related to the worsening of existing mental disorders (emergency department visits, hospitalizations).

## 3. Results

One thousand five hundred twenty-nine papers were initially identified, 615 were duplicates and 871 were excluded for above mentioned criteria. Forty-three papers satisfied the inclusion criteria (Fig. 1). Different air pollutants have been studied with regard to mental disorders. Some studies investigated the risk of mental disorders as a consequent of air pollution, while others the worsening of already existing mental conditions. Generally studies about the risk of the new onset of mental disorders considered long-term expositions to air pollutants, while studies about the worsening of existing mental conditions took into account a short time of exposition to pollutants.

### 3.1. General psychiatry

#### 3.1.1. Risk of mental disorders

A first longitudinal study investigated if the air pollution was

associated with an increased risk of prescription of antipsychotics or sedative compounds in children and adolescents (Oudin et al., 2016). The authors found that a  $10 \mu\text{g}/\text{m}^3$  increase of nitric oxide ( $\text{NO}_2$ ), but not of  $\text{PM}_{10}$  or  $\text{PM}_{2.5}$  significantly contributed to a higher frequently prescription of psychotropic drugs in children and adolescents (Oudin et al., 2016). A subsequent recent American study showed a linear correlation between average daily density of  $\text{PM}_{2.5}$  and number of poor mental health days (Ha, 2017).

#### 3.1.2. Worsening of mental disorders

A first study reported that a  $10 \mu\text{g}/\text{m}^3$  increase of air PM was significantly associated with hospitalizations for schizophrenia in female subjects living in Beijing (China) (Gao et al., 2017). Furthermore, increased levels of  $\text{PM}_{10}$  were found to be associated with higher number of visits in the psychiatry emergency unit in Sweden during the warm season, but not during the cold one (Oudin et al., 2018). Finally, a Chinese study investigated the effect of different air pollutants on number of daily hospital admissions for mental disorders: sulfur dioxide ( $\text{SO}_2$ ) air concentrations were significantly associated with an increased number of psychiatry hospitalizations especially in warm season (Chen et al., 2018).

#### 3.1.3. Summary

Taken as a whole, the results of the cited studies show that poor mental health is associated with increased levels of different air pollutants including PM,  $\text{NO}_2$  and  $\text{SO}_2$ . Increased levels of PM may have a role in aggravating symptoms of existing mental disorders. It must be highlighted that the studies described in this section include use rough measures for mental health assessment. The prescription of psychotropic compounds (especially in children and adolescents) is usually associated with new onset mental disorders, while the risk of emergency department visits or hospitalizations usually regard subjects affected by mental disorders.

### 3.2. Schizophrenia

With regard to the risk of developing schizophrenia, a unique first observational research found that the exposition to benzene and CO was significantly associated with the diagnosis of this condition (Pedersen et al., 2004).

With regard to the worsening of the disorder, a study conducted in Israel reported that the concentration of solid air-suspended particles positively correlated with number of psychotic attacks in schizophrenia patients, particularly during the periods with dominant eastern winds (from desert) (Yackerson et al., 2014). However, despite the positive trend, the correlation did not reach a statistical significance in the selected sample of schizophrenia subjects (Yackerson et al., 2014).

Few and contradictory data regard the association between the diagnosis or severity of schizophrenia and air pollution.

### 3.3. Bipolar disorder

Till now no researches have been conducted about the role of air pollution on the onset of bipolar disorder.

### 3.4. Depression

#### 3.4.1. Risk of depression

An American study did not find a positive association between short-term changes in pollutant levels such as  $\text{PM}_{2.5}$  and depressive symptoms in a cohort of geriatric adults (age  $\geq 65$  years) (Wang et al., 2014). In contrast, a European study who integrated the results of different cohorts (Germany, Norway, Netherlands and Finland) found a positive association between increased concentration of  $\text{NO}_2$  and  $\text{PM}_{10}$  and risk of depressed mood in case of the exclusion of the smallest Finnish sample (Zijlema et al., 2016). A further Korean study confirmed

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