Depressed? Anxious? Air pollution may be a factor

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In the 1990s, residents of Mexico City noticed their dogs acting strangely—some didn't recognize their owners, and the animals' sleep patterns had changed.

At the time, the sprawling, mountain-ringed city of more than 15 million people was known as the most polluted in the world, with a thick, constant haze of fossil fuel pollution trapped by thermal inversions.

In 2002, toxicologist and neuropathologist Lilian Calderón-Garcidueñas, who is affiliated with both Universidad del Valle de México in Mexico City and the University of Montana, examined brain tissue from 40 dogs that had lived in the city and 40 others from a nearby rural area with cleaner air. She discovered the brains of the city dogs showed signs of neurodegeneration while the rural dogs had far healthier brains.

Calderón-Garcidueñas went on to study the brains of 203 human residents of Mexico City, only one of which did not show signs of neurodegeneration. That led to the conclusion that chronic exposure to air pollution can negatively affect people's olfactory systems at a young age and may make them more susceptible to neurodegenerative diseases such as Alzheimer's and Parkinson's.

The pollutant that plays the "big role" is particulate matter, said Calderón-Garcidueñas. "Not the big ones, but the tiny ones that can cross barriers. We can detect nanoparticles inside neurons, inside glial cells, inside epithelial cells. We also see things that shouldn't be there at all—titanium, iron and copper."

The work the Mexican scientist is doing is feeding a burgeoning body of evidence that shows breathing polluted air not only causes heart and lung damage but also neurodegeneration and mental health problems.

It's well established that air pollution takes a serious toll on the human body, affecting almost every organ. Asthma, cardiovascular disease, cancer, premature death and stroke are among a long list of problems that can be caused by exposure to air pollution, which, according to the World Health Organization, sits atop the list of health threats globally,

causing 7 million deaths a year. Children and infants are especially susceptible.

Sussing out the impact of air pollution on the brain has been more difficult than for other organs because of its inaccessibility, so it has not been researched as thoroughly, according to researchers. Whether air pollution may cause or contribute to Alzheimer's or Parkinson's is not settled science. But Calderón-Garcidueñas' work is at the leading edge of showing that air pollution goes directly into the brain through the air we breathe, and has serious impacts.

Some psychotherapists report seeing patients with symptoms stemming from air pollution. Not only does the pollution appear to cause symptoms or make them worse; it also takes away forms of relief.

"If we exercise and spend time in nature we become extra resilient," said Kristen Greenwald, an environmental social worker and adjunct professor at the University of Denver. "A lot of folks do that outside. That's their coping mechanism; it's soothing to the nervous system."

On polluted days a lot of her clients "can't go outside without feeling they are making themselves more sick or distressed."

Megan Herting, who researches air pollution's impact on the brain at the University of Southern California, said environmental factors should be incorporated in doctors' assessments these days, especially in places like Southern California and Colorado's Front Range, where high levels of air pollution are a chronic problem.

"When I go into a medical clinic, they rarely ask me where I live and what is my home environment like," she said. "Where are we living, what we are exposed to, is important in thinking about prevention and treatment."

In the last two decades, with new technologies, research on air pollution and its impact on the human nervous system has grown by leaps and bounds.

Research shows tiny particles bypass the body's filtering systems as they are breathed in through the nose and mouth and travel directly into the brain. Fine and ultrafine particles, which come from diesel exhaust, soot, dust and wildfire smoke, among other sources, often contain metals that hitchhike a ride, worsening their impact.

A changing climate is likely to exacerbate the effects of air pollution on the brain and mental health. Warmer temperatures react with tailpipe emissions from cars to create more ozone than is generated when it's cooler. And more and larger forest fires are expected to mean more days of smoky skies.

Ozone has been linked to neurodegeneration, decline in cerebral plasticity, the death of neurons, and learning and memory impairment. Ozone levels are extremely high in Los Angeles and the mountain valleys of the West, including the Front Range of Colorado, Phoenix and Salt Lake City.

Air pollution also causes damage from chronic inflammation. As air pollution particles enter the brain, they are mistaken for germs and attacked by microglia, a component of the brain's immune system, and they stay activated.

"Your body doesn't like to be exposed to air pollution and it produces an inflammatory response," said Patrick Ryan, a researcher at Cincinnati Children's Hospital, in an email. "Your brain doesn't like it either. There's more than 10 years of toxicological science and epidemiologic studies that show air pollution causes neuro-inflammation."

Much of the current research focuses on how pollution causes mental health problems.

Damage to the brain is especially pernicious because it is the master control panel for the body, and pollution damage can cause a range of neuropsychiatric disorders. A primary focus of research these days is how pollution-caused damage affects areas of the brain that regulate emotions—such as the amygdala, prefrontal cortex and hippocampus. The amygdala, for example, governs the processing of fearful experiences, and its impairment can cause anxiety and depression. In one recent review, 95% of studies looking at both physical and functional changes to areas of the brain that regulate emotion showed an impact from air pollution.

A very large study published in February in *JAMA Psychiatry*, by researchers from the universities of Oxford and Peking and Imperial College London, tracked the incidence of anxiety and depression in nearly 400,000 adults in the United Kingdom over a median length of 11 years and found that long-term exposure even to low levels of a combination of air pollutants—particulate matter, nitrogen dioxide and nitric oxide—increased the occurrence of depression and anxiety.

Another recent study, by Erika Manczak at the University of Denver, found adolescents exposed to ozone predicted "for steeper increases in depressive symptoms across adolescent development."

But the epidemiological research has shortcomings because of confounding factors that are difficult to account for. Some people may be genetically predisposed to susceptibility and others not. Some may experience chronic stress or be very young or very old, which can increase their susceptibility. People who reside near a lot of green space, which reduces anxiety, may be less susceptible.

"Folks living in areas where there is greater exposure to pollutants tend to be areas under-resourced in many ways and grappling with a lot of systemic problems. There are bigger reports of stress and depression and anxiety," said Manczak. "Given that those areas have been marginalized for a lot of reasons, it's a little hard to say this is due to air pollution exposure."

The best way to tell for sure would be to conduct clinical trials, but that comes with ethical problems. "We can't randomly expose kids to air pollution," Ryan said.