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EFFECTOFAIR POLLUTION ON THE NERVOUS SYSTEM

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ABSTRACT

Pollution and most importantly air pollution is becoming a major problem these days especially concerning with public health sector. From respiratory to cardiovascular, air pollution is now a major factor in central nervous system diseases too. Nano sized particles found in air affect CNS by activating innate immune response, neuro inflammation and oxidative stress are some disorder caused be air pollution. Even with advancement in health sector the underlying molecular mechanisms of susceptibility and disease remain largely elusive. Hence focusing on mechanism how air pollution affect our CNS to dig deeper into the roots of disorders caused by it.

KEYWORDS: Air Pollution, Central Nervous System, Pollutants, Neuro Inflammation, Oxidative Stress, Epigenetic Mechanism

Air pollution is one of the leading causes of mortality and morbidity worldwide. The World Health Organization estimates that 4.6 million people die each year from causes directly attributable to air pollution. World-wide more deaths per year are linked to air pollution than to automobile accidents. We have known its pulmonary and cardiovascular effects but it's effects on our nervous system are still rooted.

Pollution refers to any matter that is "out of place". When toxins, contaminated, and other harmful products are introduced into an environment, disrupting it's normal patterns and functions. Pollution in general refers to introduction of chemicals, particulate, and biological matter that can be harmful to humans, plants and animals, and cause damage to the natural environment.

Earth's atmosphere is made up of nitrogen gas (78%), oxygen gas (21%) and other trace of gases (like argon and carbon dioxide). Air pollution is due to addition of unwanted substance like soot, smoke, dust, asbestos, fibres or gases like CO, NO_2, 3,4 Benzopyrine etc. This unfavourable alteration of air composition due:

Natural occurring phenomena like wildfires releasing smoke and carbon monoxide which increases level of carbon in atmosphere, through volcanic eruptions producing tremendous amount of sulfuric, chlorine, and ash products.

Anthropogenic Causes

Pollution caused by fossil fuels like coal, petroleum and other factory combustibles is major cause of air pollution. Automobiles or other man-made activities like agriculture and animal husbandry. Resulting in acid rain, smog, global warming etc.This imbalance in the quality of air is hazardous to human health. In recent times polluted air's effect apart from cardiovascular and respiratory disorders has been seen on central nervous.

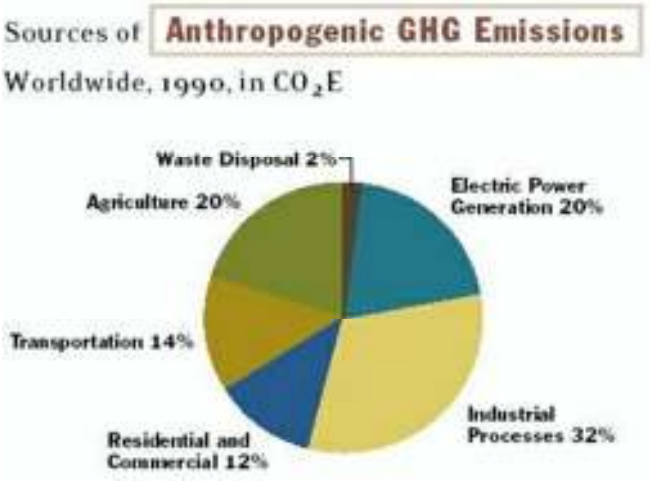

Figure 1: Sources of ANTHROPOGENIC emissions

EFFECT ON NERVOUS SYSTEM

Polluted air has certain particulate matter (PM), characterized by its size, particles less than 10um diameter can be inhaled deep into lungs. Particles from sizes 2.5 to 10 um are denoted as PM_{10}, particles less than 2.5 um as $PM_{2.5}$ and less than 0.1 um as ultra fine (UFPS) or nano-sized (NP) particles (Craig and Brook, 2008). These UFPs are more dangerous than other particles as they are not filtered out during their passage through nose and bronchioles. These

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particles trigger the release of inflammatory agents that could alter the susceptibility of neuroinflammation and neurodegeneration in the CNS (Cunningham, 2009).

The systematic inflammation is accompanied by production of pro-inflammatory cytokinesis such as tumor necrosis factor alpha (TNF – ALPHA), interleukin-6 (IL-6) and interleukin-1-beta for which blood vessels in brain exhibit constitutive and induced expression of receptors. The cytokinesis could disrupt the blood-brain barriers (BBB) integrity (Teeling and Perry, 2009). Disruption of BBB could lead to trafficking of mast cells and inflammatory cells expressing CD163, CD68 and HLA-DR to damaged site. Apart from this, the cytokinesis that have been circulating in our blood could lead to stimulate innate immunity, even enter the brain by process of diffusion and active transport which causes much damage synergistically (Dantzer et. al., 2008).

Through inhalation pollutants can reach the olfactory mucosa which could enter cilia of olfactory receptor neurons by pinocytosis or diffusion, they get incorporated into sensory neurons, they could be transported by slow axonal transport along axons to the olfactory bulb.(Figure 2)

Additional direct neuronal entry routes for NPs have been described that involve the retrograde and anterograde transport in axons and dendrites (Oberdorster et. al., elder, rinderknecht, 2009).

Inhaled pollutants also activates sympathetic nervous system and hypothalamus- pituitary- adrenal thereby creating neurohormonal stress.

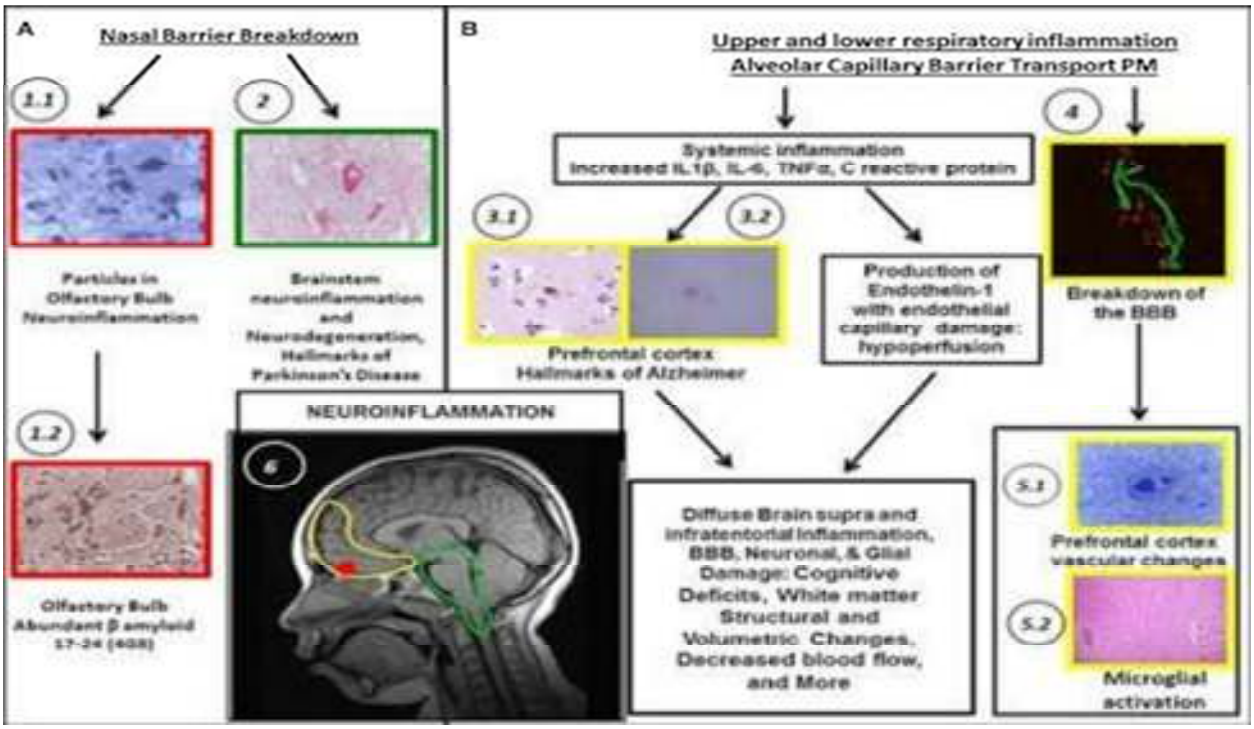

Figure 2: The impact of air pollution on the brain.

The Particulate matter, especially fine particulates (PM2.5), increase the risk of strokes and of death from strokes, especially for women. Data from the Women's Health Initiative show that for each increase of 10µg/m3 in the PM2.5 concentration, women faced a 35% increase in the risk of a cerebrovascular event and an 83% increase in the risk of death from a cerebrovascular event.

Effect of Air Pollution on Alzheimer

Air pollution is also being major cause of Alzheimer's now. According to Jin-Chiuan, studies- there are scientific evidences that indicates that air particles accelerating aging by interacting with Alzheimer's risk gene. There are air pollutants inside the protein deposits called amyloid plaques which shows their presence in alzheimers's

brain; indicating these particles responsible for development of Alzheimer's. Experiments done on s brain have also shown effect of air pollution; increase in the levels of the protein amyloid; one of the hallmark of disease.

Effect of Air Pollution on Epigenetic Mechanism

Air pollution can also change gene expression through a broad array of gene regulatory mechanisms. Epigenetics; a post transcriptional process control the mechanism in gene regulation. There occur change in DNA methylation and histone acetylation which results to imprinting, gene silencing and suppression of gene expression without alteration of sequence of silenced genes.

According to a study, published in PubMed by Campbell A in 2014, human microglia, neurons and astrocytes were grown separately and then exposed to aqueous UFP suspensions. Reactive oxygen species (ROS) formation and the pro-inflammatory cytokine tumor necrosis factor alpha were measured as markers of oxidative stress. Their results revealed that after exposure to 2ug/ml of particles, normal human neurons exhibit a decrease in ROS formation and an increase in TNF- alpha. The observed decrease in ROS formation persisted in the presence of glial cells, which contracts previous studies done in rodent cells reporting that PM- induced microglial activation modulates neuronal responses. Indicating CNS cells responded differently compared to rodent cells.

RESULTS

The effects of air pollutants are thus a high level of interest for scientific**,** governmental**,** and public communities**.** An increasing number of people are exposed to a complex mixture of inhalable NPs and toxic chemical.

Study discusse above highlight the critical effects of UFPs on CNS. Air borne particles causing neuropathological symptoms mediated directly or indirectly causing pro inflammatory and oxidative response. Air pollution cut out white matters in brain having adverse effect in brain aging. The ultrafine particles enter the brain particularly olfactory area. The inflammation they cause is compatible with an increase in attention deficit and hyperactivity symptoms. Epigenetic changes contribute to neurological symptoms caused by air pollution. Time of exposure to the polluted air plays the major role in damage(Dusinska, 2009)

One such study demonstrated the upregulation of inflammatory and innate immunity pathway components in mouse immortalized BV2 cells when exposed to CAPS (Sama, Long, Hester et al., 2007)

Abbreviations concentrated ambient tparticles (CAPs), 2'7'-dichloflurescein-diacetate (DCFH-DA),. dopaminergic (DA), diesel exhaust particles (DEPs), enzyme linked immuno sorbent assay (ELISA), interleukin-6 (IL-6), lactate dehydrogenase (LDH), malodialdehyde (MDA) nitric oxide (NO), reactive oxygen species(ROS), tyrosine hydroxylase (TH), tumor necrosis factor alpha (TNF- alpha), ventral mesencephalic (VM).

The study aboveis indicating about dose-response relationships of in-vitro toxicity .For instance, low concentrations of oxygen-ozone were not toxic to astroglial cells, while high concentrations severely decreases cell viability. (Zhou et. al., 2008). Air pollution in Delhi (Table 1).

Table 1: Air pollution in Delhi data

Source	Contribution in %		
	PM 2.5	SO_2	NO_x
Transport	17	2	53
Gen sets	6	4	25
Brick klins	15	11	2
Industry	14	23	11
Construction	5	-	1
Waste burning	8	1	1
Road dust	6	-	-
Power plants	16	55	7
Domestic	12	6	1

Results from the survey given above indicates that; power plant and transportation are the major cause of air pollution in capital city, Delhi.

Considering above factors we can conclude that air pollution is a global problem. Especially in India, air pollution is becoming serious issue with time and has been affecting masses. Adverse effects of air pollution on CNS have been widely ignored till now. Air pollutants being neurotoxic and killing brain cells; accelerating brain aging, brain volume loss on long exposure, breakdown of blood-brain barrier, reduction in Intelligence Quotient (IQ) is also seen.

Proper steps need to be taken to control air pollution, especially traffic derived pollution causing CNS damage and neurological diseases. Astroglia, cerebral endothelial cells and microglia in respond to components of air pollution with chronic activation, inflammation and oxidative stress.

Reducing exposure to polluted air, control of particulate matter by installing arresters and scrubbers in factory, redesigning engines and fuel technologies are some ways we can control increasing air pollution. Biological studies can strengthen the use of discovery of tools for toxicity screening.

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