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**Particulate matter and the Central Nervous System. Brain inflammation and neurodegeneration in exposed children and young adults**

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Chronic exposures to air pollutants are associated with brain inflammation, and neuronal, endothelial and smooth muscle accumulation of the 42-amino acid form of  $\beta$ -amyloid ( $A\beta_{42}$ ) in cognitively intact adults (average age  $58.1 \pm 13.8$  years)(Calderón-Garcidueñas et al., 2004). Brain inflammation and  $A\beta_{42}$  accumulation precede the appearance of neuritic plaques and neurofibrillary tangles, hallmarks of Alzheimer's disease. Chronic inflammatory processes play an important role in the pathogenesis of AD. The objective of this work was to determine if a younger population chronically exposed to significant concentrations of particulate matter exhibits evidence of brain inflammation and  $A\beta_{42}$  accumulation. We studied subjects from two age- and gender-matched cohorts of clinically cognitively and neurologically intact children, adolescents and young adults, all of whom had sudden deaths. The high exposure cohort (n:28,  $23.6 \pm 8.6$  years) was composed of Mexico City residents, and the control cohort (n:8,  $22.6 \pm 6.5$ y) included subjects from 2 cities with pollution levels that rarely exceed the standards. We compared the expression of mRNAs encoding the inflammatory mediator genes cyclooxygenase-2 (COX2) and interleukin-1b (IL-1 $\beta$ ) and localized  $A\beta_{42}$  in olfactory bulb and frontal cortex. We found a significant upregulation of COX2 and IL1 $\beta$  mRNA expression in the olfactory bulb and frontal cortex of young subjects residing in Mexico City. The highly exposed subjects exhibited significant lung inflammation,  $A\beta_{42}$  deposition in neurons, astrocytes and smooth muscle cells of blood vessels in the olfactory bulb and diffuse amyloid plaques in the frontal cortex. Combustion-associated metals were detected in the frontal cortex and UFPM were seen by EM in brain endothelial cells and RBC. Particulate matter particularly fine and UF particles likely play a crucial role in the brain inflammation and the accumulation of  $A\beta_{42}$  in target brain areas. The nasal pathway is an important portal of entry of pollutants into the brain. Early and sustained exposures to significant concentrations of PM might be an early risk factor for Alzheimer's disease.

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