4-2018 Mexico City air pollution and Alzh's risk

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Hallmarks of Alzheimer disease are evolving relentlessly in Metropolitan Mexico City infants, children and young adults. APOE4 carriers have higher suicide risk and higher odds of reaching NFT stage V at ≤ 40 years of age. Environmental research. 164. 475-487. 10.1016/j.envres.2018.03.023.

Exposures to fine particulate matter (PM2.5) and ozone (O3) above USEPA standards are associated with Alzheimer's disease (AD) risk. Metropolitan Mexico City (MMC) residents have life time exposures to PM2.5and O3above USEPA standards. We investigated AD intra and extracellular protein aggregates and ultrastructural neurovascular pathology in 203 MMC residents age 25.36 ± 9.23 y. Immunohistochemical methods were used to identify AT8 hyperphosphorilated tau (Htau) and 4G8 (amyloid β 17-24).

Primary outcomes: staging of Htau and amyloid, per decade and cumulative PM2.5(CPM2.5) above standard. Apolipoprotein E allele 4 (APOE4), age and cause of death were secondary outcomes. Subcortical pretangle stage b was identified in an 11month old baby. Cortical tau pre-tangles, neurofibrillary tangles (NFT) Stages I-II, amyloid phases 1-2, Htau in substantia nigrae, auditory, oculomotor, trigeminal and autonomic systems were identified by the 2nd decade. Progression to NFT stages III-V was present in 24.8% of 30-40 y old subjects. APOE4 carriers have 4.92 times higher suicide odds ($p = 0.0006$), and 23.6 times higher odds of NFT V ($p < 0.0001$) v APOE4 non-carriers having similar CPM2.5 exposure and age. Age ($p = 0.0062$) and CPM2.5($p = 0.0178$) were significant for developing NFT V.

Combustion-derived nanoparticles were associated with early and progressive damage to the neurovascular unit. Alzheimer's disease starting in the brainstem of young children and affecting 99.5% of young urbanites is a serious health crisis. Air pollution control should be prioritised. Childhood relentless Htau makes a fundamental target for neuroprotective interventions and the first two decades are critical. We recommend the concept of preclinical AD be revised and emphasize the need to define paediatric environmental, nutritional, metabolic and genetic risk factor interactions of paramount importance to prevent AD. AD evolving from childhood is threating the wellbeing of our children and future generations.