Differentiating Translocated Exogenous vs Bio-generated Endogenous Nanoparticle Types in Olfactory Bulb of Humans with Neurodegeneration

U. M. Graham[1], G. Oberdorster[2]

[1]University of Kentucky, Lexington, KY, [2]University of Rochester, Rochester, NY

An increased risk for Alzheimer's and related dementia has been hypothesized to be causally associated with ambient PM air pollution. Aerosol constituents in polluted air contain redox-active metal- and other nanoparticles (NPs), and mounting evidence supports their role via neuronal nose to brain transport for neurodegeneration at and beyond the rostral (olfactory bulb (OB)) and caudal (brain stem) point of CNS entry. We examined autopsied OBs to determine whether inhaled pollution-derived NPs reach the brain via the olfactory nerve. To understand the accumulation of ambient nanoparticles in the OB requires to differentiate between the sources that are coming either from exogenous (aerosol pollution) or endogenous origins (biomineralization). An example are iron NPs for quantifying the various iron components which is crucial to link exogenous iron to neurodegeneration. Our approach uses analytical high-resolution transmission TEM of OB thin-sections coupled with electron energy loss spectroscopy (EELS) to assess compositions, relative quantities, and redox-activities of distinct NPs and to identify the physiochemical fingerprints of individual iron NPs that either translocated to OB regions (exogenous) or precipitated in vivo (endogenous). We also analyzed particles in OBs that seem to have originated from specific occupational aerosol exposures, for example tungsten particles that were present predominantly in sub-nano scale (0.3-1.5 nm) inside glomeruli and axons. Analyses were performed using a cryo-stage to stabilize the biological sections. We grouped NPs with identical characteristics and used digital imaging and spatial statistics to assess their frequency in the OB. Information on exogenous NPs locations and interactions with axons, mitochondria, amyloid plaques and or Lewy bodies were systematically correlated with Subjects that have well-documented impaired olfaction and dementia. Exogenous silica NPs are typically associated with heavy metal inclusions (Fe, Mn, Zn, Co, Ti, Zr, Cr, As, Se, Pb, among others) which typically occur as ultrafine dispersions and co-translocated (Trojan Horse Mechanism) to OB of select subjects. Exogenous iron NPs included iron oxides and phosphates. The location and frequency of endogenous iron NPs in OB (iron oxyhydroxide; ferritin) are related to the occurrence of amorphous silica, alumina, and carbon NPs as well as heavy metal NPs and may be a marker for inflammation and oxidative stress.