Title: Air Pollution Nanoparticulate Matter Causes White Matter Damage and Microglial Activation in a Mouse Model.

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Introduction: Ambient air pollution (AAP) exposure is neurotoxic in association with white matter degeneration in young and older populations (1,2,3). AAP models in which mice are exposed to nPM (nano-scale subfraction of AAP) suggest a role of activated microglia in white matter damage of the corpus callosum (4) and subregions of the hippocampus (5). This study characterized regional responses to nPM for myelin damage in relation to microglial responses. **Methods**: nPM was collected in Los Angeles and re-aerosolized for exposure of 3 month C57BL/6J male mice, 15 hours/week for ten weeks (4). White matter damage was characterized as immunofluorescent density of myelin associated glycoprotein (MAG) and degraded myelin basic protein (dMBP). MAG indicates myelin integrity, while dMBP is specific for myelin degradation. Iba-1 immunohistochemistry resolved reactive vs resting microglia by the ratio of cell body to dendritic process size. **Results:** After nPM exposure, the corpus callosum had 35% decreased MAG immunofluorescent density over filtered air [$p<0.001$] and 60% increased dMBP immunofluorescent density [$p<0.001$]. Reactive Iba-1 positive microglia increased 30% [$p<0.05$] with 84% enlargement of the cell body to dendritic process size ratio [$p<0.001$]. In mice exposed to nPM, there was a positive correlation between Iba-1 positive microglia and dMBP immunofluorescence in the corpus callosum ($R=0.83$, $p<0.05$). The hippocampus and other myelinated regions are being analyzed. **Conclusions:** nPM exposure caused myelin degradation in corpus callosum in association with microglial activation. These results expand findings on nPM exposed female C57BL/6J mice that did not find MBP loss in corpus callosum but did show loss in subregions of the hippocampus, using a different antibody (5). Combined, these results suggest sex and regional differences in responses to nPM. Ongoing studies with multiple reagents for MBP and MAG will include other cortical and subcortical regions that are vulnerable to AAP in humans (3).

References: 1, Peterson et al., 2015, PMID: 25807066; 2, Calderon-Garciduenas et al., 2016, PMID: 26829765 ; 3, Casanova et al., 2016 PMID: 27790103; 4, Babadjouni et al., 2018, PMID: 30395590; 5, Woodward et al., 2017 PMID: 28212893

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