Association between PM2.5 exposure by inhalation and brain damages of Alzheimer’s disease in transgenic mice

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\textbf{Title}

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\textbf{ABSTRACT}

\textbf{Background}: Fine particulate matter (PM\textsubscript{2.5}) exposure increases the risk of neurological disorders. However, the relevance between PM\textsubscript{2.5} and Alzheimer’s disease (AD) needs to be identified and the effect of PM\textsubscript{2.5} exposure on the brain in AD mice remains unclear.

\textbf{Objective}: To assess the effects of PM\textsubscript{2.5} exposure on AD and investigate the brain damage in AD transgenic mice exposed to PM\textsubscript{2.5}.

\textbf{Methods}: We searched articles from the database of PubMed for meta-analyses on the association between PM\textsubscript{2.5} exposure and AD. Further, using a novel real-world whole-body inhalation exposure system, wild type (WT) and APP/PS1 transgenic mice (AD mice) were respectively exposed to filtered air (FA) or ambient PM\textsubscript{2.5} for 8 weeks in Taiyuan, China. The pathological and ultrastructural changes and levels of Aβ-42, TNF-α, and IL-6 in brains in FA-WT mice, FA-AD mice, FA-PM\textsubscript{2.5} mice, and PM\textsubscript{2.5}-AD mice were measured.

\textbf{Results}: Long-term PM\textsubscript{2.5} exposure had the association with increased risks of dementia and AD by OR of 1.16 (95% CI 1.07–1.26) and 3.26 (95% CI 0.84–12.74) via meta-analysis. Both lightly- and heavily polluted countries showed such increased risks. In the open field test, the PM\textsubscript{2.5}-AD mice
showed more significant degenerative symptoms of AD by the behavioral change in movement. Hematoxylin-eosin staining results showed that noticeable histopathological injury such as structural disorder, hyperemia, and sporadic inflammatory cell infiltration in the brain of PM$_{2.5}$-AD mice, and transmission electron microscope results displayed that serious damage in the brain in PM$_{2.5}$-AD mice, which maintained disorder of cristae and vacuolation of mitochondria, synaptic abnormalities, and loose myelin sheaths. Aβ-42, TNF-α and IL-6 levels in brains of PM$_{2.5}$-AD mice had raised more strongly than that of FA-WT or FA-AD mice.

**Conclusion:** This study indicated a strong association between PM$_{2.5}$ exposure and AD risks. PM$_{2.5}$ significantly aggravated the severity of neuronal pathomorphological changes and inflammation in AD mice when Aβ-42 levels in the brain were visibly increased.

**Acknowledgment:**

Car-SCs Treatment Technology and Study the Application of Inorganic Nanomatrices on MSC T-cells Proliferation (Project Ref: RMGS-2019-1-03).