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Letter to the Editor

Influence of Exposure to Particulate Matter on Circulating Levels of Neurotrophic Factors

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Dear Editor-in-Chief

Currently, air pollution attracts critical attention worldwide owing to its health risks. Particulate matter (PM), among various air pollutants, has been proposed as an important contributor to various illnesses, including respiratory and cardiovascular diseases, and is one of the major causes of premature death.

In recent years, large-scale epidemiological studies and animal model experiments conducted on humans have reported that PM could adversely affect the central nervous system and cause dementia and cognitive dysfunction, including Alzheimer's disease (1, 2). The olfactory and secondary systemic routes have been proposed as the main pathways through which PM threatens brain health by inducing structural and functional changes in the brain (2). Specifically, PMs migrate directly to the brain tissue through the olfactory bulb. They are deposited on senile plaques to exacerbate the inflammatory response or stimulate glial cells to stimulate amyloid production (2, 3). In addition, among inhaled PMs, particulates reaching the alveoli without being removed via mucociliary clearance cause inflammation and result in the production of proinflammatory cytokines, which can be delivered to brain tissue through systemic circulation and cause neuroinflammation (2,3). As another route, nanoparticles with small particle sizes in the PM escape the phagocytic cells of the reticuloendothelial system and directly stimulate the blood-brain barrier to increase its permeability. Thus, it has been reported that various pathogens and toxic substances can freely flow into the brain tissue (2,3).

However, neurotrophic factors play a role in regulating the growth and orientation of axons and dendrites, secretion of neurotransmitters, formation and plasticity of new synapses, and regeneration and differentiation of neural stem cells (4,5). Typical examples of such neurotrophic factors are brain-derived neurotrophic factor (BDNF) and vascular endothelial growth factor (VEGF), of which decreases are associated with cognitive dysfunction and the development of neurodegenerative diseases (4,5).

However, although PM is a factor that threatens brain health, studies verifying changes in neurotrophic factors according to PM exposure are limited. Accordingly, the purpose of this study was to verify the effect of PM administration on BDNF and VEGF.

For the experimental animals of this study, 48 4-week-old C57BL/6 male mice were received from Samtako (Osan, Korea). The breeding envi-

ronment was equipped with a high efficiency particulate arrestant with a filter that always supplies sterile clean air, as well as with a positive pressure facility that blocks outside polluted air. Four animals per cage were bread under in an environment of automatically controlled temperature (22 ℃), humidity (55%), and lighting cycle (12:12 h light–dark). During the experiment period, water and food were provided *ad libitum*.

The study protocol was approved by the animal ethics committee of the National Research Foundation of Korea (2019R1F1A1064296).

Twenty-four animals were randomly assigned to each of the saline group and PM groups. For PM treatment, fine dust (PM10-like, ERM-CZ120), certified to be similar to actual PM_{10}, was purchased from Sigma-Aldrich (St. Louis, USA) and injected into the tail vein of mice twice per week with reference to a preceding study (6). Meanwhile, animals in the saline group were injected with 200-µl saline, and the PM group was injected with 200-µl saline mixed with 15 µg of PM. At 4, 6, and 8 weeks after treatment, eight animals in each group were anesthetized with ethyl ether, and blood was collected from the abdominal inferior vena cava. Using the Mouse BDNF DuoSet ELISA kit (DY248, R&D Systems, and Minneapolis, USA) and VEGF Quantikine ELISA Kit (MMV00, R&D Systems, and Minneapolis, USA), serum BDNF and VEGF levels were analyzed from the collected blood.

Statistical analysis was performed using SPSS 26.0 software (IBM Corp., Armonk, NY, USA), and data are presented as the mean ± standard deviation (SD). Differences between groups within a period were verified by an independent *t*-test, and differences between periods within a group were verified by a one-way analysis of variance. All statistical significance levels were set to $\alpha = 0.05$.

Fig. 1 shows the changes in serum BDNF and VEGF according to PM administration. As a result, the PM group showed significantly lower serum BDNF and VEGF levels than the saline group at week 8 ($P<0.05$).

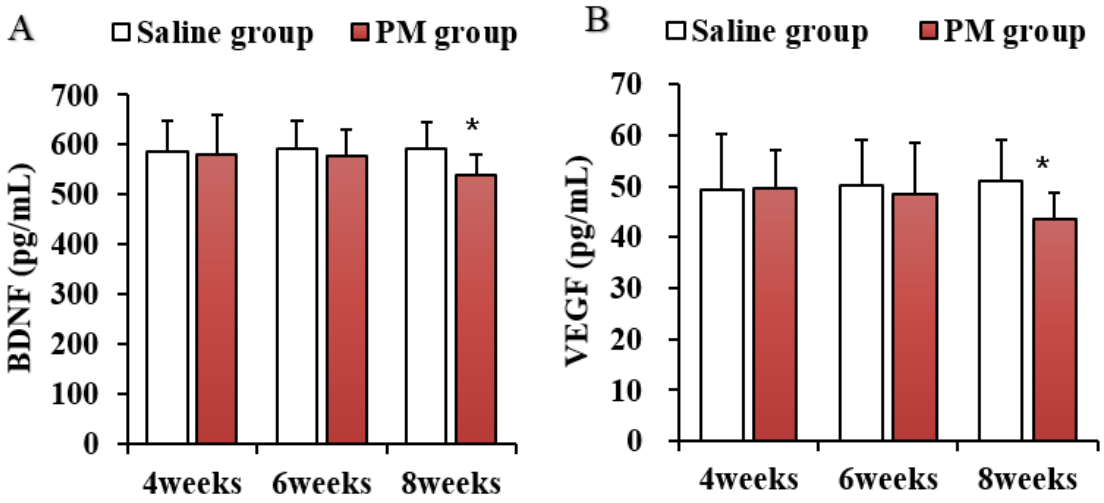

Fig. 1: Changes in serum BDNF (A) and VEGF (B) levels according to PM administration. Data are presented as mean ± SD. *Denotes statistically significant difference compared to saline group ($P<0.05$)

These results suggested that prolonged PM exposure might induce the downregulation of circulating neurotrophic factors. In future studies, it would be necessary to verify the expression of neurotrophic factors in specific regions of the brain, such as the hippocampus.

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Conflict of interest

The authors declare that there is no conflict of interests.

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