

The role of manganese oxide nanoparticles in the formation of stress granules in the mouse olfactory system

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Key words: nanoparticles, stress granules, nose2brain transport

Motivation and Aim: In recent years, air pollution has increased significantly, and humans, like other terrestrial animals, are constantly exposed to solid aerosols, which may contain various xenobiotics, including nanoparticles (NPs) that can enter the brain from the nasal cavity [1]. Moreover, it was shown that the addition of nanoparticles to the cellular environment induces the formation of stress granules (SG), which are the cellular response to stress [2]. However, whether nanoparticles cause the formation of SG in brain structures is unknown. The aim of this study was to investigate the ability of intranasally administered Mn₃O₄-NPs to induce SG formation in neurons of the mouse olfactory system.

Methods and Algorithms: The work was performed on mice of SPF-status strain C57Bl/6 at the age of 8 weeks. The accumulation of NPs in the olfactory bulbs was assessed using T1-weighted images obtained on a BioSpec 17/16USR ultrahigh-field magnetic resonance tomograph (Bruker, Germany) with a magnetic field strength of 11.7 T. The amount of SG was determined on paraffin sections stained with a mixture of antibodies anti-eIF3 η +anti-G3BP1. The intracellular localization of nanoparticles was studied using transmission electron microscopy (TEM). Paramagnetic Mn₃O₄-NPs were used as nanoparticles.

Results: Using T1-weighted MRI, we were able to demonstrate that the accumulation of Mn₃O₄-NPs in the main olfactory bulb (MOB) of the mouse reaches a maximum 24 hours after their intranasal application. To estimate the role of manganese ions in the formation of the observed MRI signal, we determined the concentration of Mn in the MOB tissue before and after dialysis in mice that were injected with either Mn₃O₄-NPs or MnCl₂ into the nasal cavity 24 hours before the isolation of MOB. As the analysis showed, in animals that were injected with Mn₃O₄-NPs, as a result of dialysis, there is practically no decrease in the concentration of manganese in the tissue. Whereas in mice injected with MnCl₂, dialysis effectively reduces Mn concentrations in the MOB homogenate. This suggests that one day after the intranasal application of Mn₃O₄-NPs, manganese in the MOB is mainly in an insoluble form. Using TEM, we demonstrated that nanoparticles can be transported along the axons of olfactory neurons both intra- and extra-vesicularly, which indicates the possibility of contact between Mn₃O₄-NPs and the contents of the neuron cytoplasm. Finally, using immunohistochemistry, we were able to show that the accumulation of Mn₃O₄-NPs in the MOB can induce the formation of SG in mitral neurons.

Conclusion: Intranasal application of NPs leads to the formation of SG in the olfactory bulbs. Apparently, the role of the dissolution of Mn_3O_4 -NPs in the formation of SG in the mitral cells of the MOB is not significant.

Acknowledgements: The study was supported by Russian Science Foundation grant No. 20-14-00055.

References

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