Sex-related response of mice to silver nanoparticles after sub-acute exposure

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Introduction

The extensive use of silver nanoparticles (AgNPs) represents a public concern in regards to safety and health risk (1). Their adverse effects include induction of oxidative stress and may be dependent on AgNPs biological fate and interaction with biomolecules (2 - 8).

This study aimed to investigate the sex-related differences in the biodistribution and oxidative stress response of adult mice after sub-acute exposure to low-dose of AgNPs. Intact and gonadectomised male and female mice were treated intraperitoneally with polyvinylpyrrolidone (PVP)-coated and transferrin (TRF)-coated AgNPs in a dose of 1 mg Ag/kg b.w. during 21 day.

Materials and methods

The total Ag concentrations in the freeze-dried tissue samples were measured with ICPMS after microwave-assisted acid digestion using an Agilent Technologies 7500cx ICPMS system (Agilent, Waldbronn, Germany).

Oxidative stress biomarkers in liver, kidneys, brain and lungs was measured by 2',7'-dichlorofluorescin diacetate (DCFH-DA), dihydroethidium (DHE) and monochlorobimane (MBCl) staining.

Statistical analysis of results was carried out using Dell Statistica 13.2 software (StatSoft, Tulsa, USA). Each group was composed of 5 animals. Normality of distribution was tested with the Kolmogorov-Smirnov test. The comparisons between the control and treated groups for the different measured variables were conducted using one-way ANOVA, followed by Tukey's HSD post hoc test when significant differences were found ($p < 0.05$).

Results

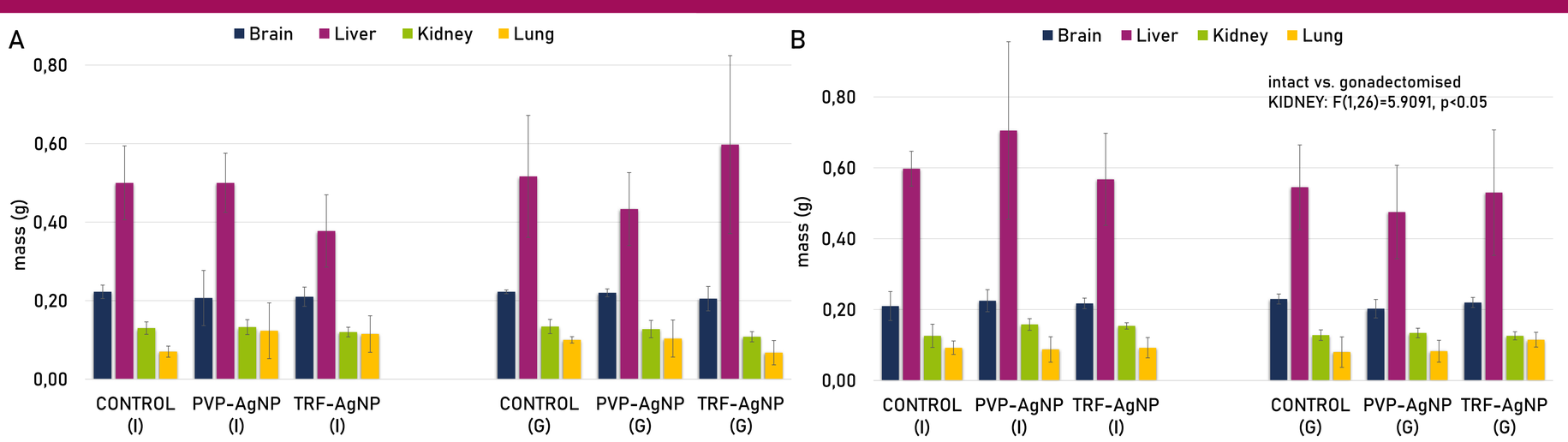

Figure 1. Weights of brain, liver, kidney and lung in female (A) and male (B) mice (intact (I) and gonadectomised (G)) after 21 day exposure to PVP-AgNP and TRF-AgNP. Values represent mean and standard deviation of five rats per group (Main effects ANOVA ($p<0.05$)).

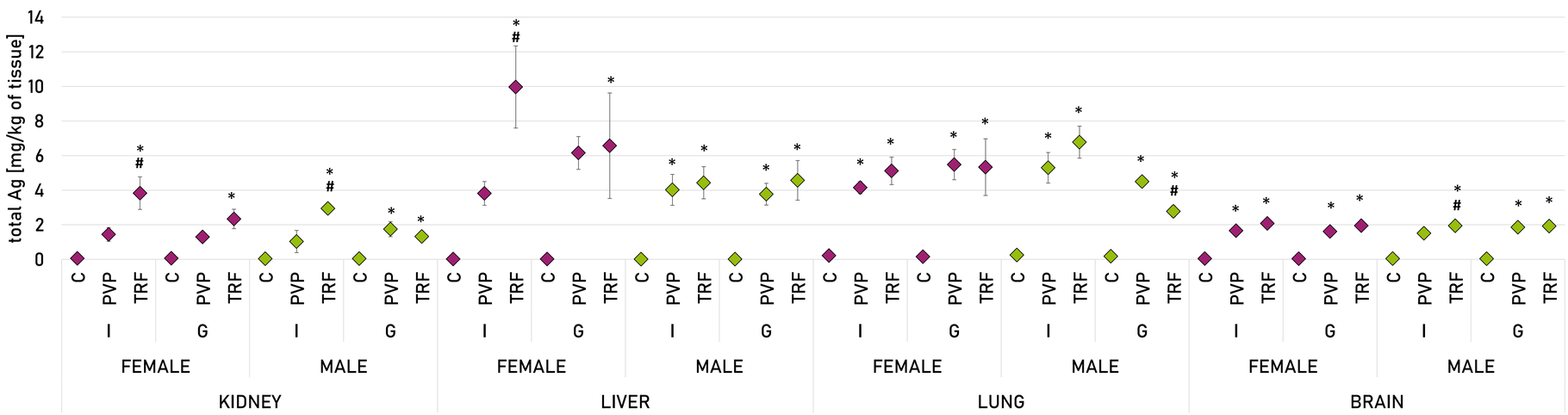

Figure 2. Total Ag levels in kidney, liver, lung and brain of female and male mice (intact (I) and gonadectomised (G)) after 21 day exposure PVP-AgNPs and TRF-AgNPs. Values represent mean (rhombus) and standard error (whisker) of five rats per group. Significant differences ($p<0.05$) between treated and control group are denoted with asterisk (*), and between TRF-coated versus PVP-coated AgNPs of the same sex and gonadectomy status with hashtag (#).

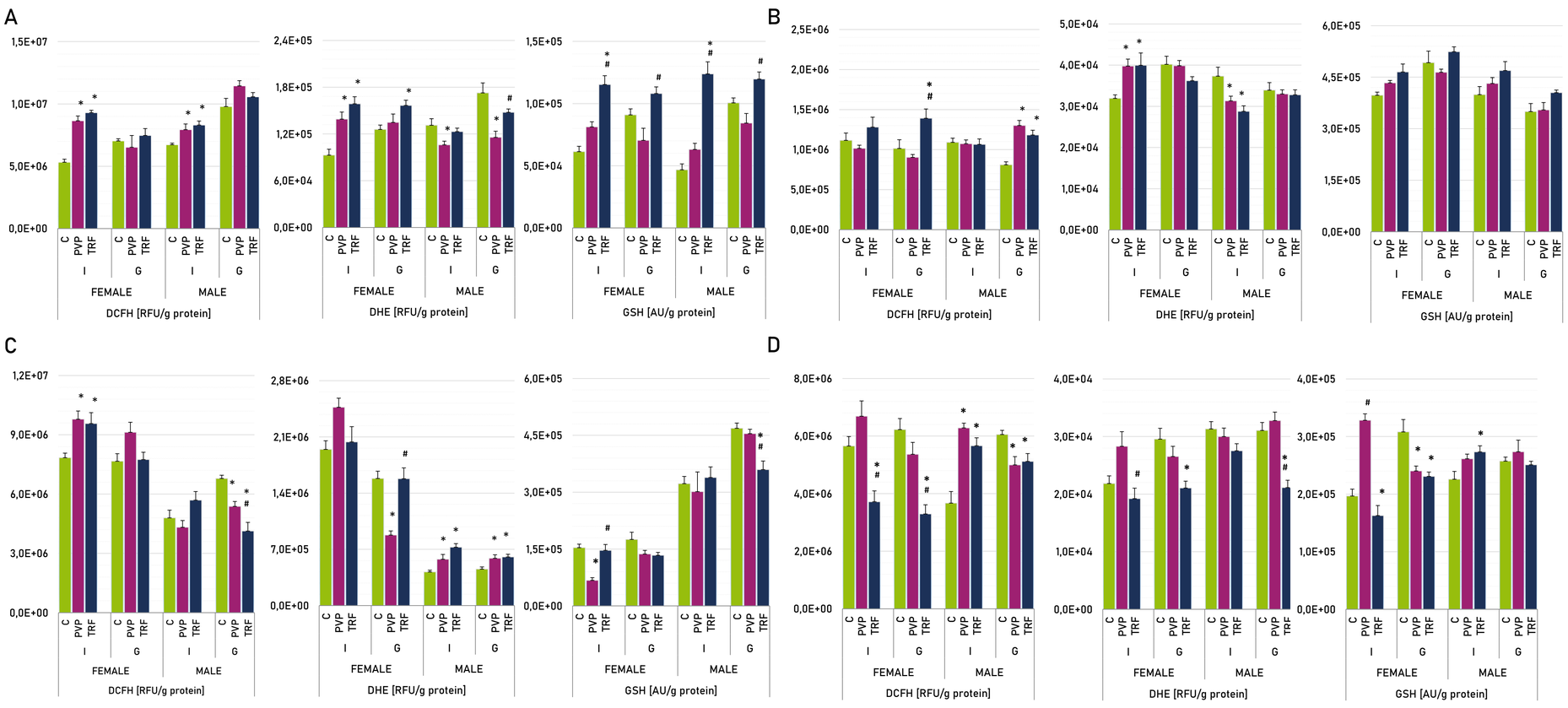

Figure 3. Oxidative stress parameters measured in kidney (A), liver (B), lung (C) and brain (D) of female and male mice (intact (I) and gonadectomised (G)) after 21 day exposure to silver nanoparticles stabilized with PVP-coated (purple) or TRF-coated (dark blue) AgNPs. Values represent mean and standard error of five rats per group. Significant differences ($p<0.05$) between treated and control (green) samples are denoted with asterisk (*) and between TRF-coated versus PVP-coated AgNPs of the same sex and gonadectomy status with hashtag (#).

Conclusion

Accumulation of Ag was significantly higher in the liver of females compared to males, as well as in the lungs of intact males compared to gonadectomised group. The effect of protein corona on AgNP accumulation was the most evident in brain of female mice. Sex-related differences were observed for ROS and GSH levels in almost all tissues. The highest difference was observed in lungs of female mice that responded more intensively to AgNPs exposure than males. AgNP distribution and toxicity are sex-related and dependent on the surface stabilization of AgNPs.

ACKNOWLEDGEMENT
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