Silver Nanoparticles and Ionic Silver Have Opposite Effects on Spontaneous Activity and Pharmacological Responses in Neuronal Networks In Vitro

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Silver nanoparticles (Ag NP) are used in a wide range of consumer and medical products because of their antimicrobial properties. Numerous in vivo studies have demonstrated that Ag NPs translocate to distal organs, including the brain, following inhalation and ingestion. Therefore, it is essential to examine neuronal function as part of assessing potential impacts of Ag NPs on human health. In the present study, effects of 3 citrate coated Ag NPs, 3 PVP coated Ag NPs (10, 50, and 75 nm), and $AgNO_3$ on network function in primary cultures of cortical neurons were examined using microelectrode array (MEA) recordings. Non-cytotoxic concentrations for Ag NPs and $AgNO_3$ (0.078-0.63 and 0.08-1.7 μg/ml, respectively) were determined after a 48 hr exposure using Cell Titer Blue and Neutral Red assays. Between days 12 to 19 in vitro, baseline activity (1 hr) was recorded prior to exposure to Ag NPs. Changes in number of total spikes (TS) and number of active electrodes (AE), relative to controls, were assessed 1, 24, and 48 hrs after exposure to FBS pre-coated Ag NP suspensions or $AgNO_3$. After the 48 hr recording, the response to a pharmacological challenge with the $GABA_A$ antagonist, bicuculline (BIC; 25 μM), was assessed. Citrate coated 10 nm Ag NP caused statistically significant concentration-related increases in AEs at 24 hr. After BIC treatment, PVP coated 75 nm Ag NP caused statistically significant increases in AE (0.6 μg/ml) and TS (0.3 μg/ml). $AgNO_3$ had opposite effects on TS and AEs, causing statistically significant decreases in AEs (0.9 and 1.7 μg/ml), negative concentration-related trends in AEs at 24 and 48 hrs, and a significant concentration-related decrease in TS following BIC challenge. These results indicate that the Ag NP size and coating affect their ability disrupt either spontaneous or $GABA_A$ receptor mediated neuronal activity in vitro. In addition, the direction of the effect on neuronal activity for Ag NP was opposite that of $AgNO_3$, indicating ionic silver does not mediate these effects. (This abstract does not reflect Agency Policy.)