Radiation-Induced Suppression of LTP is Associated with Altered Intrinsic Membrane Properties in Hippocampal CA1 Neurons.

I. Sokolova, A. Obenaus, G. Nelson, R. Vikolinsky

A mouse model was used to study long-term effects of low doses of proton radiation (H^+, 150 MeV) on hippocampal-dependent functions of learning and memory. Proton radiation at a dose 1 Gy mimics a Solar Particle Event, which astronauts may experience during the course of deep space missions. It has been reported that radiation at similar doses is associated with acute and chronic elevation of reactive oxygen species (ROS), resulting in a changed neuronal redox state and lasting oxidative stress. Further, loss of hippocampal neural progenitors has been proposed to play contributory, if not causal, role in radiation-induced cognitive impairments. To verify whether radiation-induced cognitive impairments are also associated with changes in the long-term potentiation (LTP) and the basal membrane and synaptic properties of hippocampal neurons, we performed electrophysiological recordings in the CA1 area of the mouse hippocampus in irradiated and control mice 3 months after irradiation. Extracellular recordings of field potentials revealed that radiation reduced neuronal excitability as evidenced by a 19% decrease of the input-output characteristics of the CA3-CA1 synaptic connections (n=5-7). Radiation also suppressed CA1 LTP from 132 ± 6 % to 113 ± 17 % of baseline (n=4-6). Intracellular recordings in CA1 pyramidal neurons using patch-clamp techniques revealed that radiation hyperpolarized CA1 resting membrane potentials from -63.3 ± 0.8 to -67.4 ± 0.6 mV (n=18) and decreased the membrane resistance from 151 ± 7.2 to 131 ± 6.2 MΩ (n=14-15). These changes may underlie radiation-induced changes of neuronal excitability and LTP. Radiation exposure also significantly increased the persistent Na^+ current from -79.8 ± 12.5 to -148.6 ± 25 pA (at -25 mV membrane voltage, n=8). We speculate that the effects evoked by 1 Gy proton radiation result, in part, from the direct effects of oxidative stress on various cellular structures leading to a change in basal neuronal activity. Compensatory mechanisms of homeostatic plasticity also contribute to our observations reported here.