Radiation-induced alterations in synaptic transmission of dentate granule neurons depend on the dose and species of charged particles

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We set out to evaluate excitatory and inhibitory neurotransmission in dentate granule (DG) neurons in hippocampal slices from male C57BL/6 mice at 3 months after they were irradiated (whole body) with protons, silicon or iron charged particles. Radiation was delivered at a dose rate of ~2 Gy/min for total doses of 0.1, 0.25, 0.5, and 1 Gy. Whole-cell patch clamp recordings commenced under pharmacological isolation of miniature excitatory (or inhibitory) postsynaptic currents (mEPSCs or mIPSCs) in order to provide a cellular correlate of radiation-induced alterations in excitability of this brain region obtained during extracellular recordings (see R. Vlkolinsky et al poster). Kinetic parameters of rise time, amplitude, charge transfer and decay time constants were obtained for the averaged mEPSCs/mIPSCs. Frequency of miniature synaptic currents was obtained from all events during the recording period. All recordings and analysis were performed by investigators blind to the nature and dose of the charged particle exposure. H^+ irradiation produced dose-dependent decreases in amplitude and charge transfer of mIPSCs. These decrements in inhibitory neurotransmission were consistent with the increased synaptic excitability observed in extracellular recordings in this brain region (see R. Vlkolinsky et al poster). Si^{14+} irradiation had no significant effects on either mEPSCs or mIPSCs of DG neurons. Fe^{26+} irradiation had no effect on frequency or kinetic parameters of mIPSCs, but significantly increased mEPSC frequency at 1 Gy, without changes in mEPSC kinetics. Overall, the data suggest that high-energy particle exposure results in radiation dose- and species-dependent long-lasting alterations in transmitter release and function of ligand-gated ion channels, which mediate excitatory and inhibitory neurotransmission. *Support contributed by: NSCOR grant NNX10AD59G.*