Functional Effects of Proton Radiation on Synaptic Transmission and Plasticity in the Hippocampus of APP/PSEN1 Transgenic Mice

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Space radiation consisting of protons and high-LET particles may affect CNS and thus represent significant health risk for astronauts. The hippocampus has been identified as a particularly susceptible structure, with exposure resulting in oxidative stress, synaptic alterations, reduced neurogenesis and neuroinflammation. These changes are also the hallmark in Alzheimer's diseases (AD), hence it has been hypothesized that radiation may affect and/or accelerate the onset of neurodegenerative disease. We previously showed that iron radiation at 2 Gy accelerated synaptic decrements in hippocampal CA1 neurons of APP23 transgenic mice. Here we used APP/PSEN1 double transgenic (tg) mice with an early onset of AD-like neurodegeneration and used conventional electrophysiological recordings in hippocampal slices to compare effects of low doses (0.1-1.0 Gy) of proton radiation (150 MeV/n) on synaptic plasticity. We evaluated changes in excitatory postsynaptic potentials (EPSPs) in all three neuronal fields of the hippocampal slice - dentate gyrus (DG) and *Cornu Ammonis* (CA3 and CA1) - *in vitro* at 6 and 9 months post irradiation. In addition, at 9 months only we performed identical experiments in control (0 Gy) wild-type (wt) mice and wt irradiated with 0.5 Gy. The electrophysiological data has been correlated with behavioral analyses (Morris water maze and Barnes Maze) conducted at 3 and 6 months post irradiation. The electrophysiological data are currently under evaluation. Preliminary data at 6 months indicate subtle, possibly statistically insignificant increases in long-term potentiation (LTP) in irradiated CA1 neurons at 0.1 and 0.5 Gy, while CA3 neurons exhibit slight decreases in LTP with increasing radiation dose, mostly statistically insignificant. No radiation-induced LTP changes were observed in DG. Our electrophysiological data await further detailed evaluation and correlations with behavioral analyses where we did not reveal radiation-induced decrements at either 3 or 6 months post irradiation. The lack of an effect on LTP would suggest that proton radiation at low doses does not impact synaptic plasticity in APP/PSEN1 tg mice.

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