HelmholtzZentrum münchen
Deutsches Forschungszentrum für Gesundheit und Umwelt

Long-term effects of low-dose irradiation on behavior and hippocampal microglial morphotypes in mice

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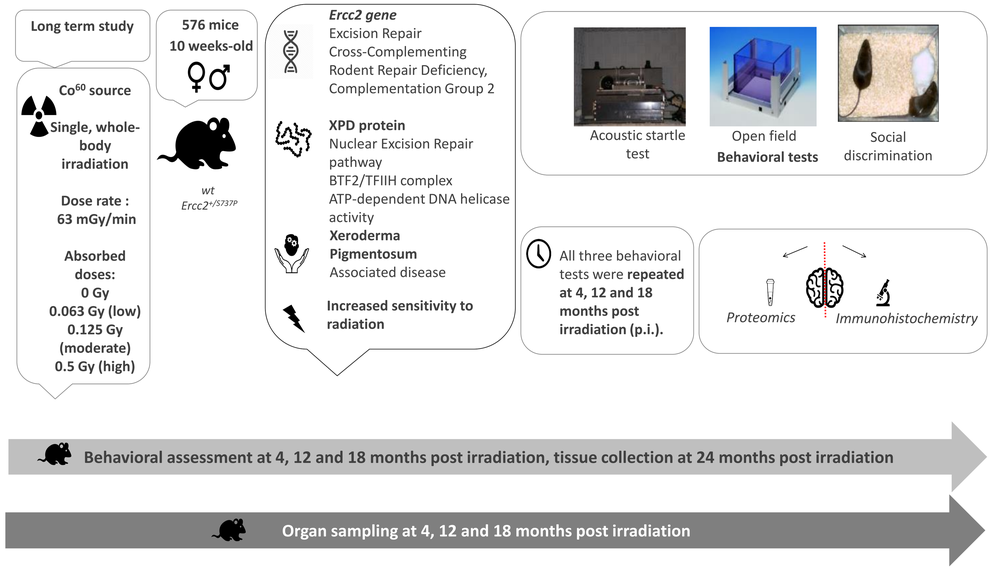
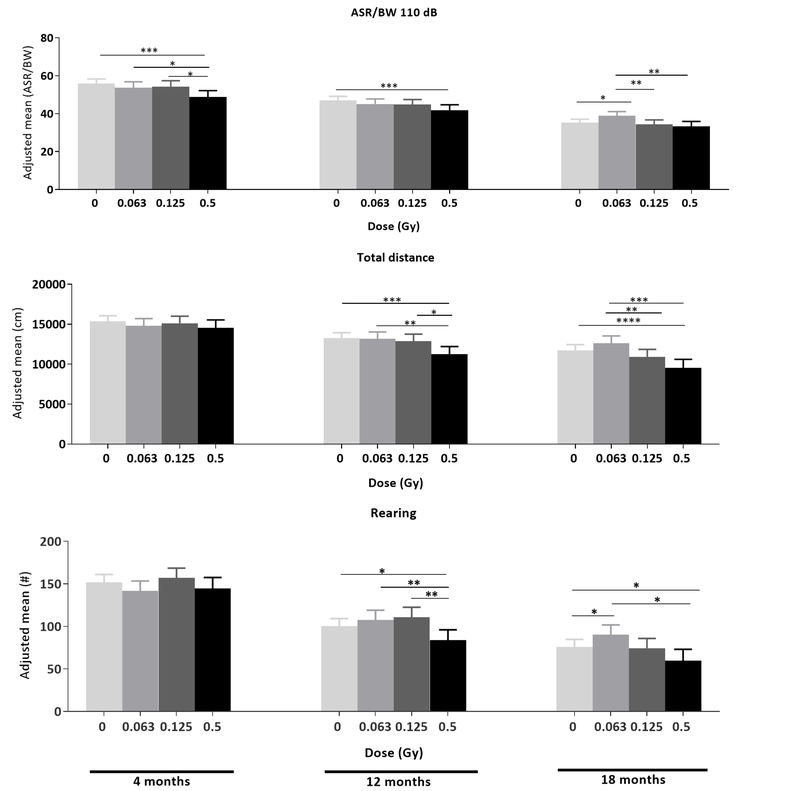
BACKGROUND

- Low-dose ionizing radiation is an **environmental factor** that can contribute to the **development of neurodegenerative diseases.**
- Despite increased use in medicine (e.g. X-ray and CT scans), no studies have yet assessed **long-term effects of low doses (<10 mSv) on brain and cognition**.
- We used the **mouse** to study **long-term effects of low-dose irradiation on behavior and hippocampal glial cell morphology.**
- We observed **early dose effects at 4 months post irradiation** on sensorimotor recruitment and **late dose effects at 12 and 18 months post irradiation** on locomotion and exploration.
- Quantification and morphological characterization of **hippocampal glial cells** revealed that low-dose irradiation induced a long-term **neuroprotective-related microglial morphology**.
- These findings are consonant with hippocampal proteomic analysis from the same mice revealing altered indices of brain-derived neurotophic factor (BDNF) activity

STUDY DESIGN

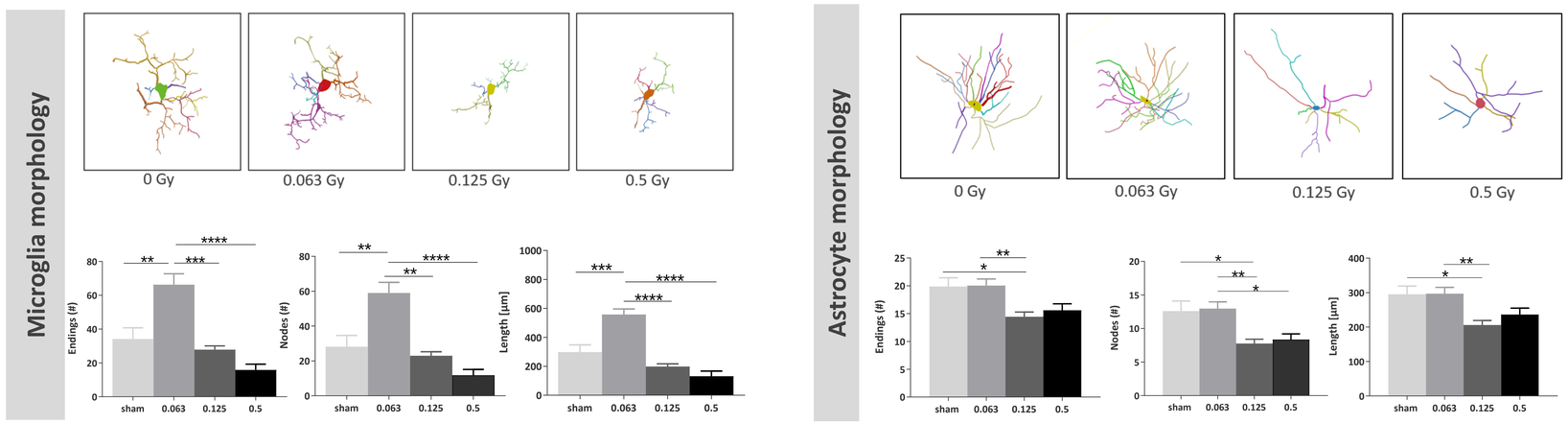


LONG-TERM PROTECTIVE EFFECTS OF LOW-DOSE RADIATION ON BEHAVIOR



- 0.5 Gy radiation decreased acoustic startle reactivity (ASR/BW) at 110 dB 4 months p.i compared to sham controls and lower doses and persisting to 12 p.i. compared to shams. 0.063 Gy radiation caused a late increased ASR compared to shams and the two higher doses.
- 0.5 Gy radiation decreased total distance travelled and rearing in the open field at 12 and 18 months p.i. compared to sham controls and lower doses. 0.063 Gy radiation increased rearing activity in the open field at 18 months post-radiation compared to control mice.
- *p<0.05, ** p<0.01, *** p<0.001 between highlighted groups

LOW-DOSE RADIATION CAUSED LONG-TERM NEUROPROTECTIVE MICROGLIAL MORPHOLOGY ALTERATIONS



Morphometric analysis of total number of endings, nodes and branch length of microglia in the dentate gyrus revealed significant increases in the 0.063 Gy irradiated group compared to sham and other irradiated groups 24 months post-irradiation. Clear hyper-ramification occurs 24 months after 0.063 Gy radiation and the de-ramification after 0.5 Gy radiation (n = 7 sham, n = 13 0.063 Gy, n = 6 0.125 Gy, n = 6 0.5 Gy, *p < 0.05, **p<0.01, ***p < 0.0001). 3D-tracing of representative cells (G) from sham, 0.063 Gy, 0.125 and 0.5 Gy-irradiated animals is depicted. Total number of endings nodes and branch length of astrocytes revealed significant decreases in the 0.125 Gy irradiated group compared to the sham and 0.063 Gy groups 24 months after the irradiation event. A similar pattern of a decrease is evident in the 0.5 Gy irradiated group.

CONCLUSIONS

In mice, low-dose ionizing irradiation exposure induced delayed protective effects on locomotor and exploratory activity and sensorimotor recruitment while high radiation dose inducing long-term and opposing adverse effects. The hyper-ramified hippocampal microglia also evident in the low-dose irradiated mice suggests enhanced surveillance capacity of these cells required to maintain healthy brain and decrease neurodegenerative disease risk. The long-term decreased complexity after the high dose irradiation indicates a more amoeboid, phagocytic function of microglia more predisposed to releasing pro-inflammatory cytokines that can increase neurodegeneration and associated disease risk.

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