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Abstract

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Hippocampal Neurogenesis Is Enhanced by Microbeam Hippocampal Transections

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Abstract

Objectives: Hippocampal neurogenesis provides an essential substratum to learning and memory . Disruption of neurogenesis by exposure to whole brain irradiation leads to dementia. Microbeam irradiation delivered to the normal hippocampus of 8 weeks old Wistar rats showed not only preservation but also enhancement of hippocampal neurogenesis . This phenomenon has not been described before and could be of great clinical interest in order to better understand how to prevent and treat dementia.

Methods: 10 rats acted as control and received general anesthesia only but no irradiation,10 rats received bilateral hippocampal conventional broadbeam irradiation delivering 10 Gy , 10 rats bilateral hippocampal microbeam irradiation delivering 300 Gy and 10 rats received bilateral hippocampal microbeam irradiation delivering 600 Gy . Microbeam irradiation was performed by 10 parallel microbeams 75 μm wide, spaced 400 μm center-to-center, delivered perpendicular to the dorsal hippocampus 1 to 5 mm posterior to the bregma.Behavioral testing was performed 7-9 months after irradiation. Sacrifice occurred 11 months after irradiation to perform immunohistochemical analysis and quantification of hippocampal adult neurogenesis. During further experiments , it was assessed wheter neurogenesis appeared early (after 6 weeks) and extensive behavioral testings were performed.

Results: We quantitated neurogenesis by stereological counts of BrdU-positive in the subgranular zone of the hippocampal dentate gyrus at 1.75, 8.25 and 10.75 months after irradiation.300 Gy microbeam irradiation significantly increased the number of BrdU-positive in the dentate gyrus in all 3 protocols tested . To identify the phenotype of these BrdU-positive cells in the subgranular zone of the hippocampal dentate gyrus, we performed a double immunolabelling with BrdU and NeuN, a neuronal cell marker. Colocalization of NeuN and BrdU marks over the same cells indicated that these BrdU-positive cells are mature neurons, originated by neural progenitors proceding toward neuronal phenotype after microbeam irradiation.

Conclusion(s): Microbeam irradiation of both dorsal hippocampal regions with arrays of parallelel 75 μm wide microbeam, delivering peak doses of 300 Gray (Gy) to healthy rats, significantly reduced depressive-like behavior and increased hippocampal neurogenesis at an early and late stage after irradiation while it did not affect spontaneous locomotor activity and hippocampal-mediated cognitive functions.
Histological analysis showed structural integrity of all irradiated brain regions with cell death observed only along the peak dose path and robust evidence of neurogenesis adjacent to the microbeam paths.
Enhanced neurogenesis followìng hippocampal microbeam irradiation is a novel observation of great interest. Hippocampal neurogenesis is a key factor in the genesis of new memories and the maintenance of healthy cognitive functions. This study shows that microbeam irradiation did not only enhance neurogenesis but also lead to improved cognitive function, likely related to proliferation and differentiation of neural progenitors into new functioning neurons. This phenomenon has great interest for the study of ways to prevent and cure and dementia and needs to be studied and characterized further.