Effects of ionizing radiation on learning and spatial memory after postnatal mouse brain exposure at low to moderate doses

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Introduction

Computed tomography scan is a medical imaging technique using low doses of X-rays. It is commonly used for head and neck exploration of children. Repeated use of computed tomography scan can lead to a relatively high cumulative dose. Long-term effects of brain exposure, at low to moderate doses (≤ 2 Gy) of ionizing radiation on cognitive functions, such as learning and memory processes, are not well established and is a important scientific issue.

Among brain structures potentially impacted by irradiation, hippocampus is a structure of interest because of its involvement in spatial learning and memory processes. In the hippocampus, new neurons are continuously generated in the subgranular zone of the dentate gyrus during postnatal and adult life which makes it a potentially sensitive structure to X-rays.

Objectives

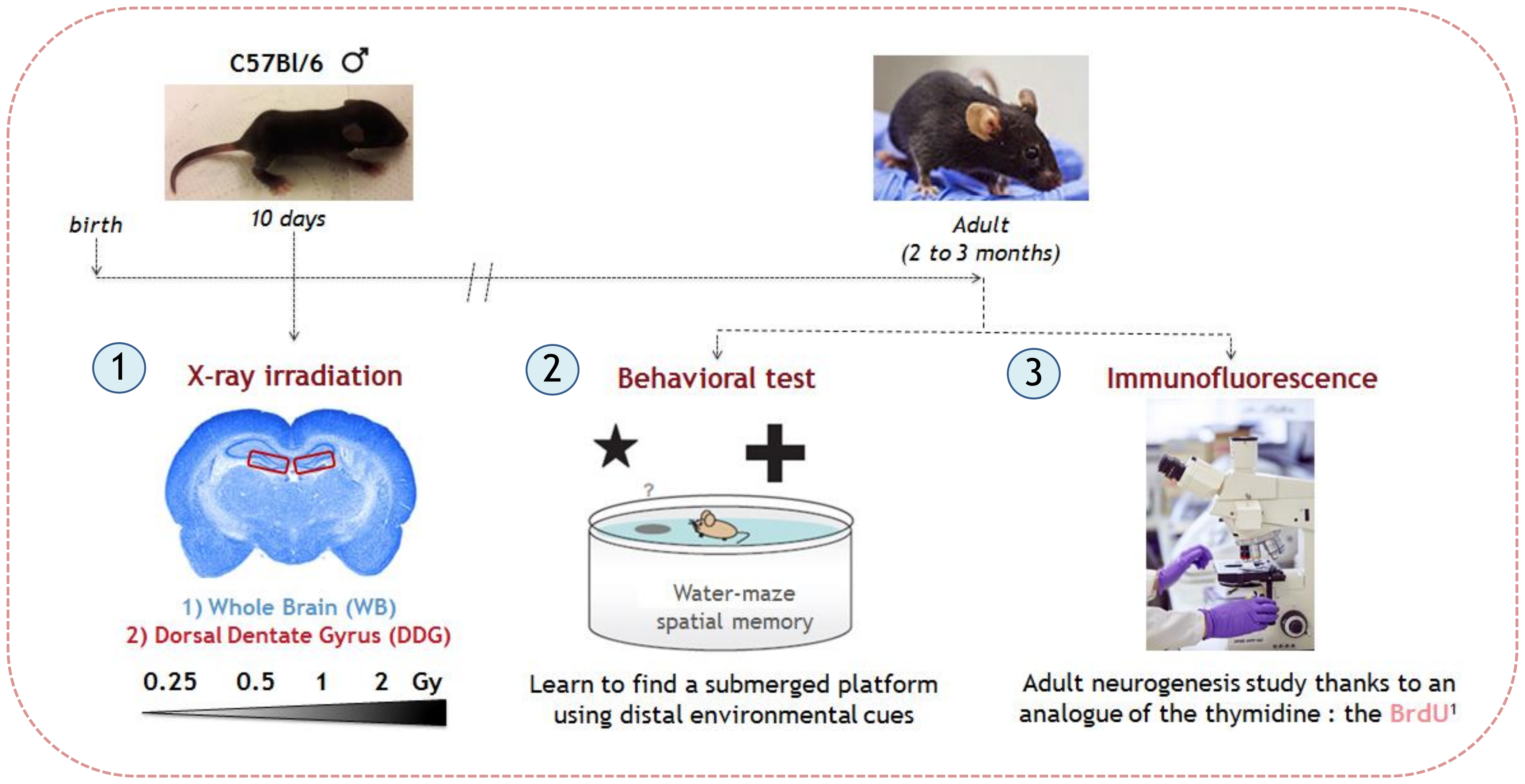
To study the impact of postnatal irradiation **at low-to-moderate doses** thanks to two models of exposure

- Whole Brain *vs* Dorsal Dentate Gyrus -

→ on spatial learning and memory

→ on hippocampal adult neurogenesis

Experimental strategy

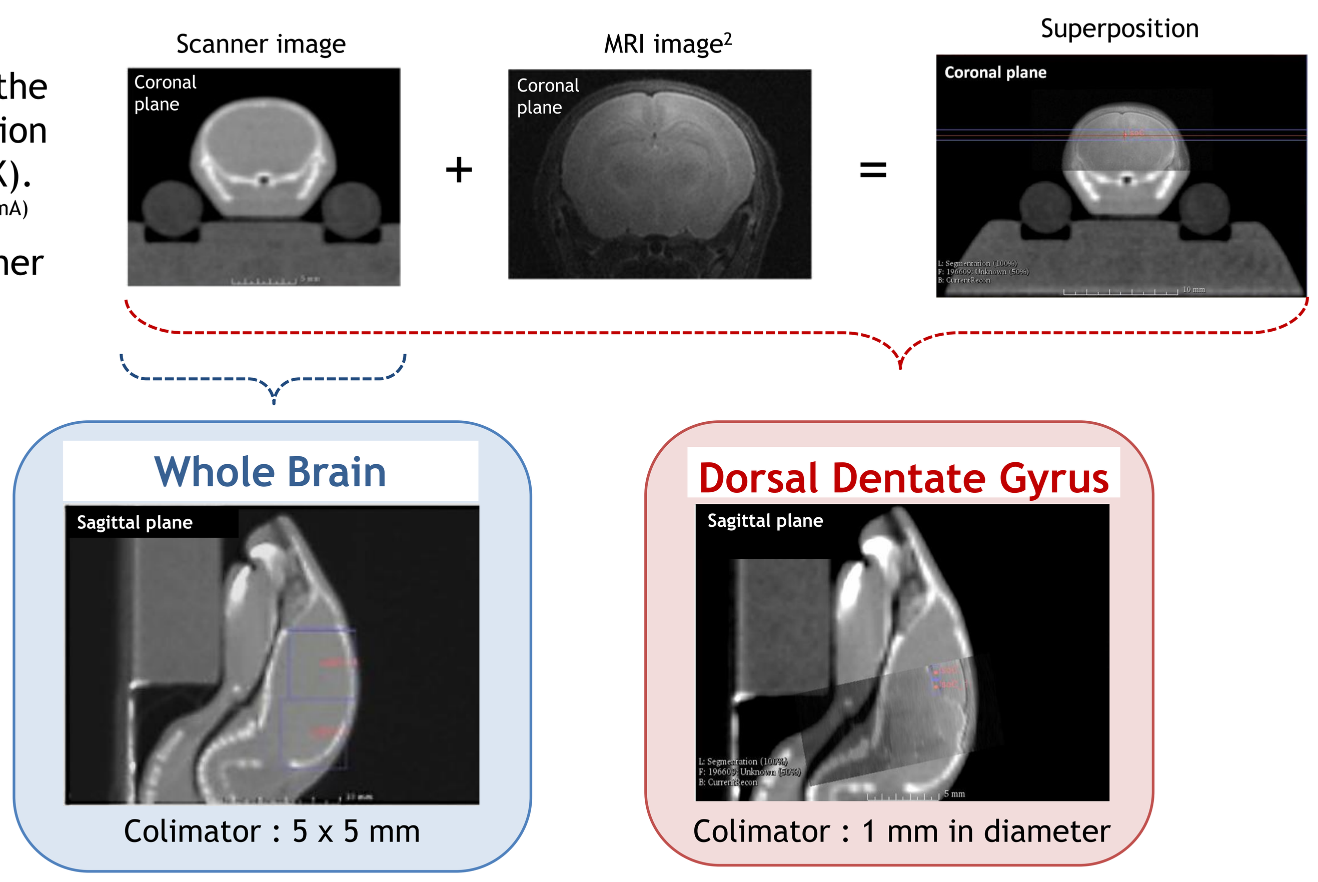


1 Irradiation procedure : Two models of exposure

M. Dos Santos et al., 2018

The irradiations are performed on the SARRP (Small Animal Radiation Research Platform, Xstrahl, Ltd., UK).
(technical characteristics : high tension : 220kV ; intensity : 3mA)

Control mice underwent scanner imaging like the other mice.

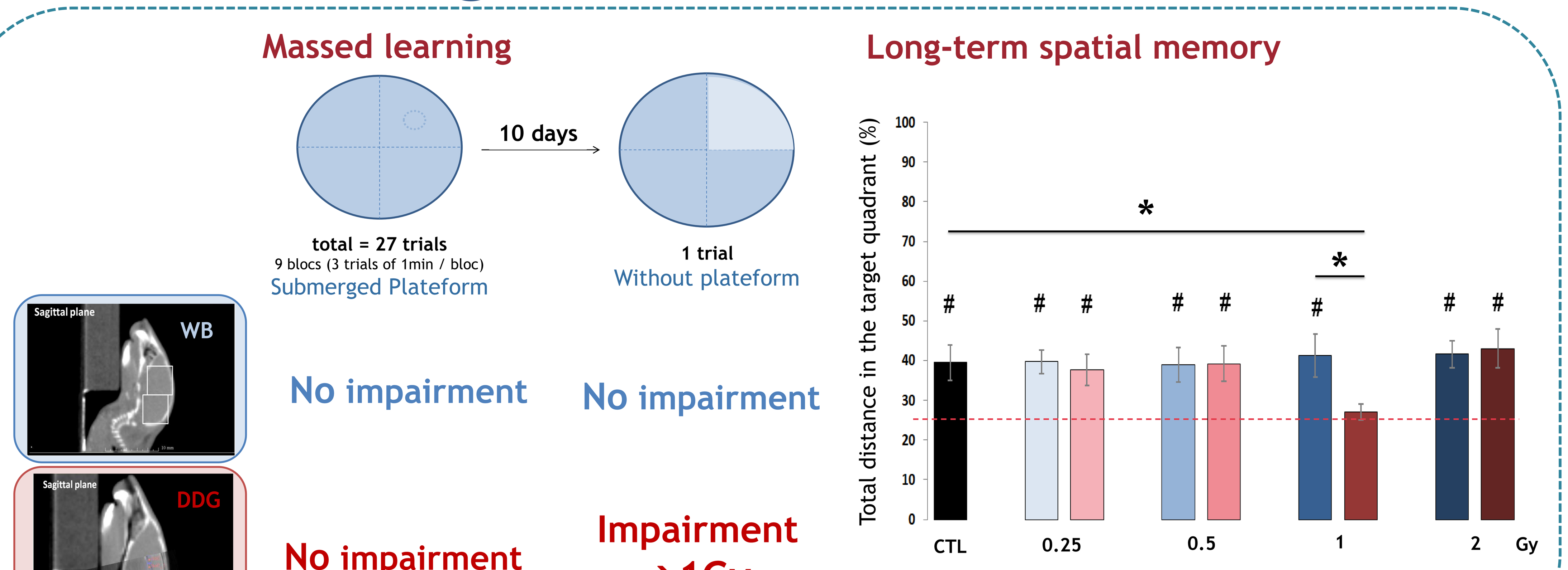


Treatment plan :

Effective energy ≈ 69 keV
Dose rate = 0.5Gy/min
Dose applied : 0.25, 0.5, 1 or 2Gy

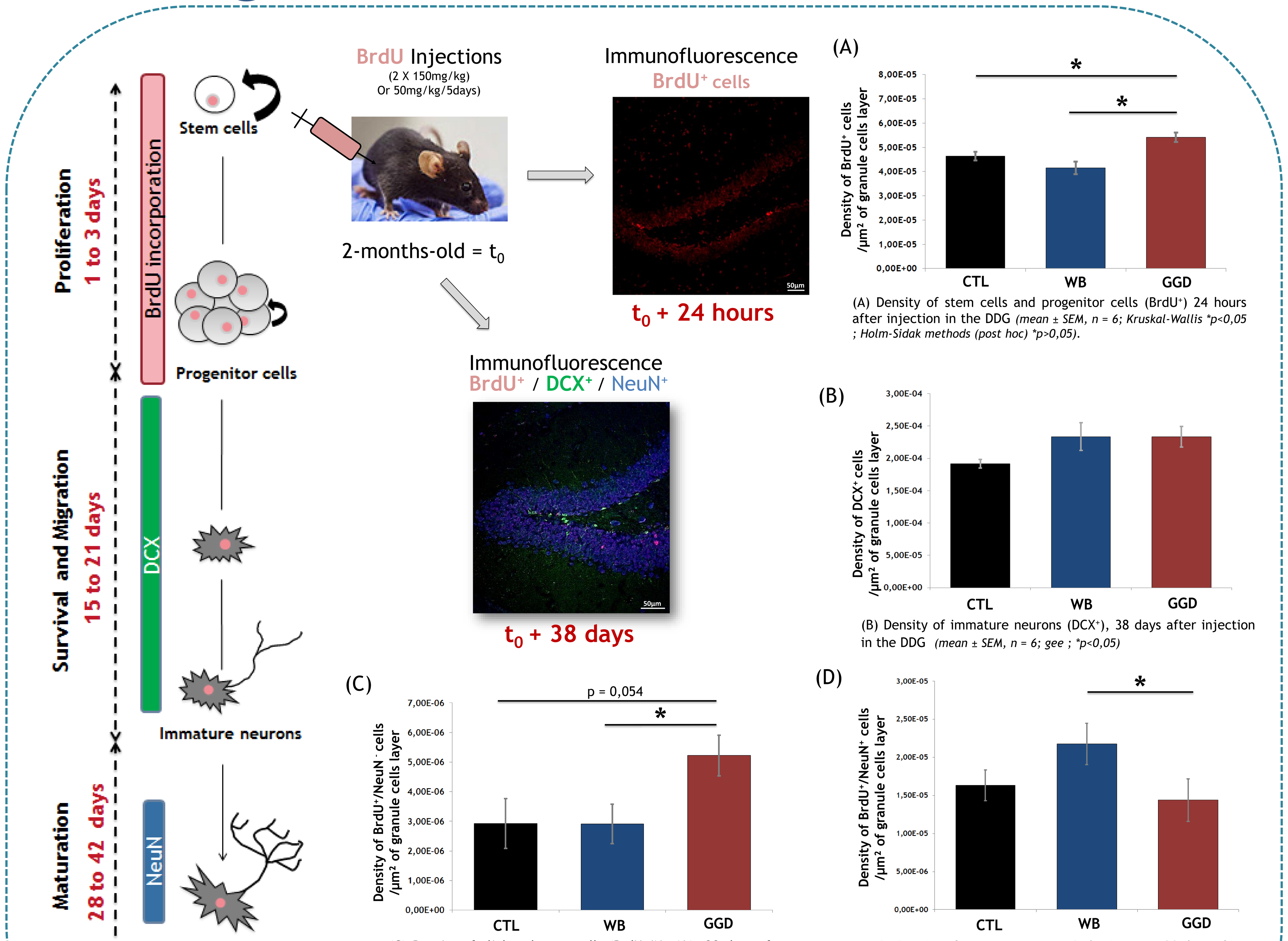
Results

2 Spatial learning and memory



Long term spatial memory. Percentage of distance in the correct quadrant *(mean ± SEM ; CTL n = 15, WB n = 8 to 11, DDG n = 7 to 11 ; One simple t-test (25%) : materialized by red line), # p<0.05 ; One way Anova, *p<0,05).*

3 Adult neurogenesis processes : Focus on the dose of 1Gy



(A) Density of stem cells and progenitor cells (BrdU+) 24 hours after injection in the DDG *(mean ± SEM, n = 6; Kruskal-Wallis *p<0,05 ; Holm-Sidak methods (post hoc) *p>0,05).*

(B) Density of immature neurons (DCX+), 38 days after injection in the DDG *(mean ± SEM, n = 6; gee ; *p<0,05)*

(C) Density of glial and stem cells (BrdU+/NeuN-), 38 days after injection in the DDG *(mean ± SEM, n = 6; gee ; *p<0,05)*

(D) Density of mature neurons (BrdU+/NeuN+), 38 days after injection in the DDG *(mean ± SEM, n = 6; gee ; *p<0,05)*

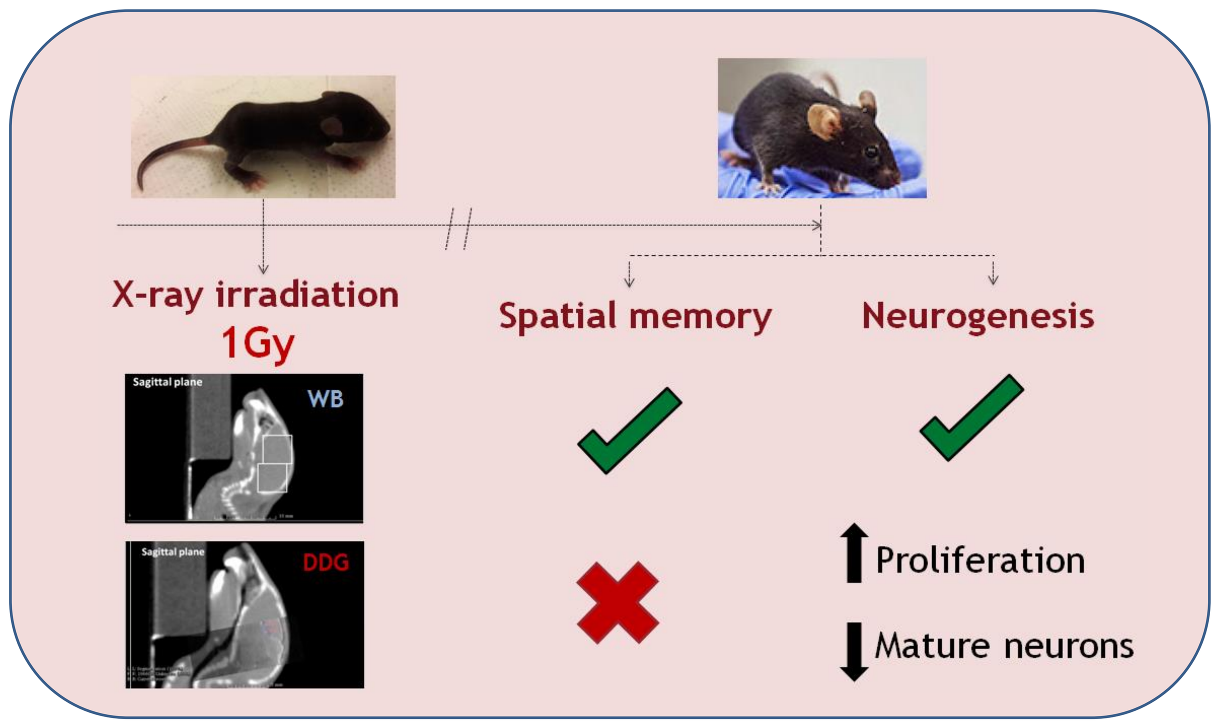
Targeted exposure impacts on the process of hippocampal adult neurogenesis contrary to whole brain exposure

Discussion and perspectives

An exposure at the postnatal stage can induce detrimental consequences 3 months later.

The effects of X-rays at low-to-moderate doses (0.25 to 2Gy) on spatial memory are not linear after targeted exposure.
Spatial memory impairment observed between our two mouse models, exposed at the dose of 1Gy, could partially be explained by selective alterations in hippocampal adult neurogenesis.

However, it will be necessary to explore the different steps of adult neurogenesis more precisely. The inflammatory response will also be evaluated in parallel.



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