# ALL THAT GLITTERS IS NOT GOLD

## There are still pitfalls and limitations in the detection of adult neurogenesis in the dentate gyrus of mice.

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## INTRODUCTION

Actually we know that there is neurogenesis in the adult brain of mice. This process is confined to two regions; the subventricular zone of the lateral ventricle and the dentate gyrus.

There's a tangential migration through the subgranular layer and a differentiation into neuroblasts. Then a radial migration into the inner granule cell layer occurs, and these cells will differentiate into dentate granule cells. Finally a synaptic integration into the existing circuitry is needed for complete the process for generating new neurons (fig. 1).

Adult neurogenesis is dynamically regulated by both intrinsic and extrinsic mechanisms.

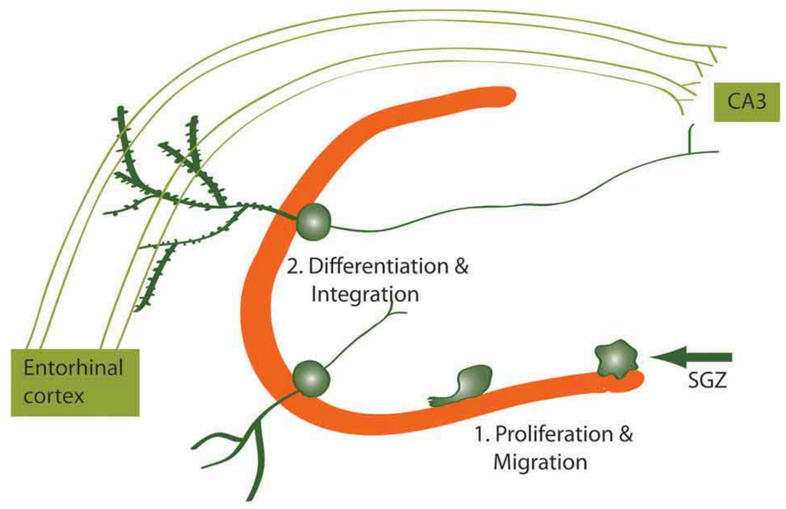


**Fig 1. Neurogenesis in the denate gyrus**. Migration and maturation of new neurons in the dentate gyrus[1].

## OBJECTIVES

Give light about the problems that have the detection of adult neurogenesis.

1. **According to the method used**
2. **According to the strain**
3. **According to the antibodies used**
4. **According to the laboratory conditions**

## RESULTS

### 1

BrdU compromise cell migration and may influence cell fate. The incorporation of BrdU can lead to deleterious effects in gene expression needed for postmitotic migration (fig. 2).

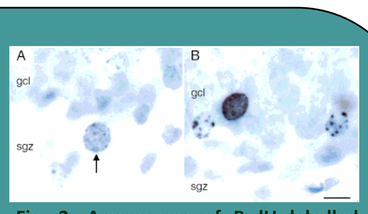


**Fig. 2. Appearance of BrdU labelled cells at different BrdU doses[2].**

The number of BrdU positive cells doesn't reflect the size of cell proliferative population.

There's also reduction of cerebellar cortex size, defects in the foliation pattern, size and weight affection and the mortality of the progeny (fig. 3).

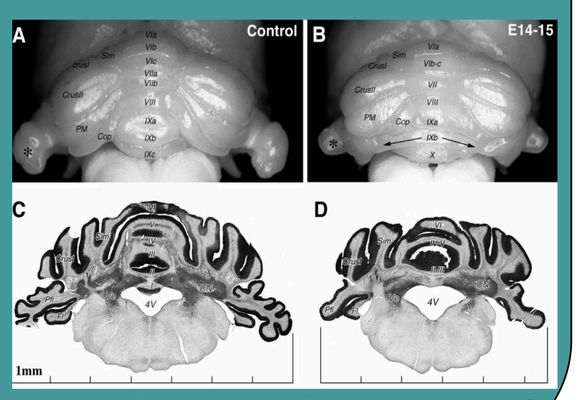


**Fig 3. Malformations derived from BrdU administration[3].**

### 2

The number of cells labelled by exposure to BrdU changes with time as a function of the number of proliferating cells in the population, the length of the S-phase, cell division, the length of the cell cycle and cell death.

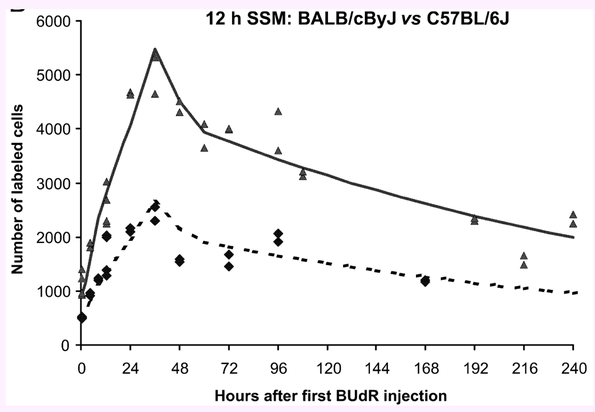


**Fig. 4. Different level of neurogenesis between BALB/cByJ and C57BL/6J[4].**

Some strains have major levels of neurogenesis (fig. 4).

The cell phenotype of the survival cells may differ between strains, 129/SvJ produce more astrocytes.

The differences can be seen either in the sensitivity level of glutamate effects and cell death regulation.

### 3

The number of BrdU labelled cells in the dentate gyrus was dependent to the BrdU antibody used but was unrelated to differences in antibody penetration (fig. 5).

Denaturation steps may compromise the results according that there are different denaturation technics.

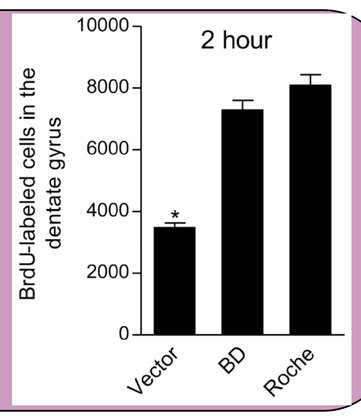


**Fig 5. BD and Roche antibodies detected significantly more BrdU-labelled cells in the dentate gyrus compared to Vector.[5]**

### 4

Stress inhibits adult neurogenesis by decreasing cell proliferation rate, neuronal differentiation and cell survival.

Laboratory animals lose more neurons than the ones that live in a complex environment.

Glucocorticoids inhibits adult neurogenesis in the dentate gyrus, levels of glucocorticoids into the blood can regulate proliferation rate and adult neurogenesis in rodents.

## CONCLUSIONS

- BrdU is a non-specific marker that will label all DNA synthesis. It will cause alterations in the DNA and it might cause abnormalities and malformation of fetus when it is administrated to pregnant animals. The dose that is administreted may cause problems as well, high doses are toxic and low doses won't label the cells. The dose enters inefficiently in the brain.
- The varied genetic background lead to differences on the level of neurogenesis, in the majority of cell type produces and on cell survival.
- There are differences in antibody sensitivity between the ones that are in the market, they don't label an equivalent number of cells.
- Laboratory conditions may due to underestimate the number of new neurons because stress inhibits adult neurogenesis by decreasing cell proliferation rate, neuronal differentiation and cell survival.

## REFERENCES

[1]S. Konefal, M. Elliot, and B. Crespi, "The adaptive significance of adult neurogenesis: an integrative approach.," *Front. Neuroanat.*, vol. 7, July 2013.
[2]C. Heather and R. D. G. McKay, "Adult neurogenesis produces a large pool of new granule cells in the dentate gyrus," *The journal of comparative neurology*, vol. 435, pp. 406-417, 2001.
[3]G. Sekerková, E. Ilijic and E. Mugnaini, "Bromodeoxyuridine administered during neurogenesis of the projection neurons causes cerebellar defects in rat," *The journal of comparative neurology,* vol. 470, pp. 221-239, 2004.
[4]N. L. Hayes and R. S. Nowakowski, "Dynamics of cell proliferation in the adult dentate gyrus of two inbred strains of mice," *Developmental Brain Research,* vol. 134, pp. 77-85, 2002.
[5]B. Leuner, E. R. Glasper and E. Gould, "Tymidine analog methods for studies of adult neurogenesis are not equally sensitive," *J. Comp. Neurol.,* vol. 517, no. 2, pp. 123-133, 2009.