Neurogenesis in the Marmoset Brain following Stroke

Mary Burke[1], Mitchell de Souza[2] and James A. Bourne[2]

[1]School of Biomedical Science, Newcastle University, Newcastle Upon Tyne, United Kingdom, [2]Australian Regenerative Medicine Institute, Monash University, Clayton, Victoria, Australia

Introduction

The field of Neurogenesis research has identified two neurogenic sites in the adult brain where neural stem cells (NSCs) are found. One of these sites is the subventricular zone (SVZ) which lines the walls of the lateral ventricles in the brain. A particular aspect of neurogenesis that has been explored increasingly has been its contributing role in repairing the brain after suffering an injury such as stroke.

Previous studies that have been conducted have focussed on the neurogenic response in the SVZ following stroke in the rodent[1] and more recently in the macaque[2].

The purpose of this project is to monitor the acute neurogenic response in the SVZ in the marmoset monkey following stroke.

Like a human a marmoset monkey is a primate mammal. Human and marmoset have structurally similar brains which are also very alike in their overall complexities.

Therefore, it is acknowledged that the neurogenic response in a marmoset's brain mirrors that which occurs in a human's after suffering a stroke.

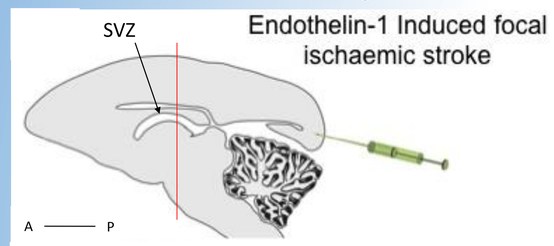


Figure 1: Lateral view of the marmoset left hemisphere *Position of the SVZ in the brain and the posterior cortical site where the stroke is surgically induced. Red line indicates where in the brain images of the SVZ are taken.*

Hypotheses

- A reduction in BrdU positive neural stem cells will be observed in the SVZ of the marmoset's lesioned (left) hemisphere compared to the control (right)
- There will be an observed increase in BrdU positive neural stem cells at the stroke site in the lesioned hemisphere compared to the same site in the control hemisphere

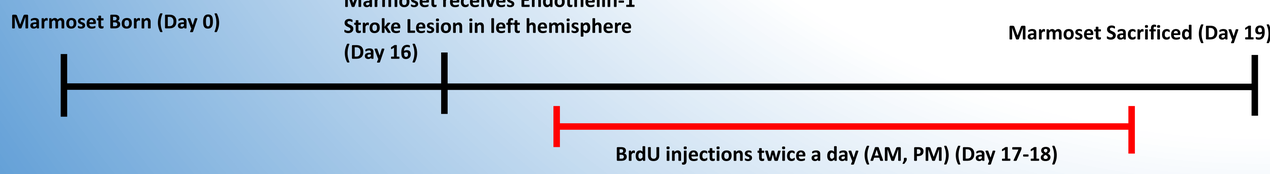
Aims

- To mark proliferating neural stem cells in the marmoset brain using BrdU injections
- To identify these proliferating BrdU positive cells in the SVZ and in the site where stroke has occurred
- Compare the levels of BrdU positive cells between the Left (stroke lesioned) and Right (control) hemisphere in the marmoset brain

Methods

1. Surgically induce stroke using Endothelin-1 in the left cortex (Fig 1) of the marmoset brain and leave the right hemisphere unlesioned as the control
2. Administer BrdU injections on day 17 and 18, twice a day to marmoset after stroke surgery.
3. On day 19 sacrifice and perfuse marmoset.
4. Surgically remove and dehydrate the brain.
5. Cut the brain into sections 40 µm thick using cryostat machine.
6. Perform immunohistochemistry staining to detect BrdU.

Marmoset Experimental Timeline



Results

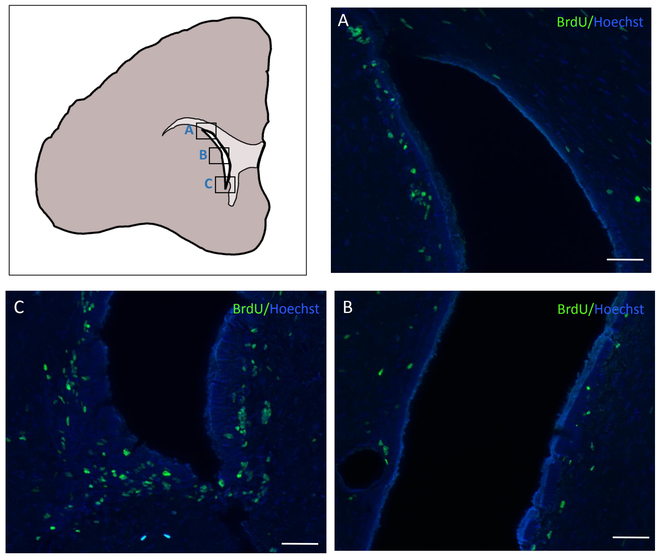


Figure 2: SVZ Control (right) hemisphere schematic and corresponding microscope images. *Scale bar 50µm.*

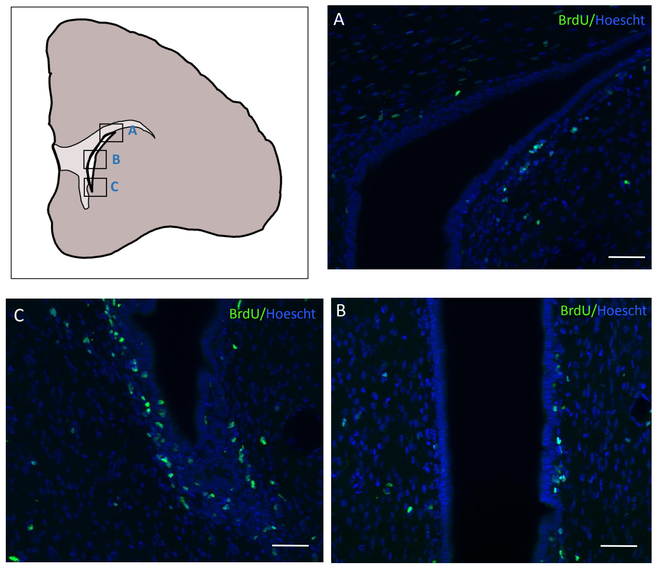


Figure 3: SVZ Lesion (left) hemisphere schematic and corresponding microscope images. *Scale bar 50µm.*

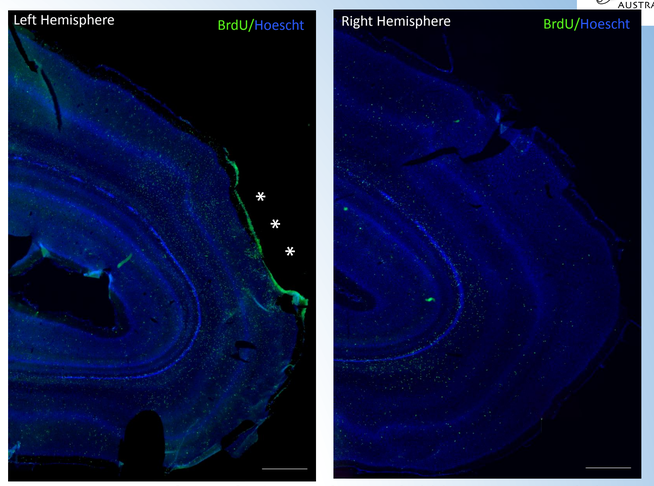


Figure 4: Images of site of injury and control. ****Injury site. Scale bar 200µm*

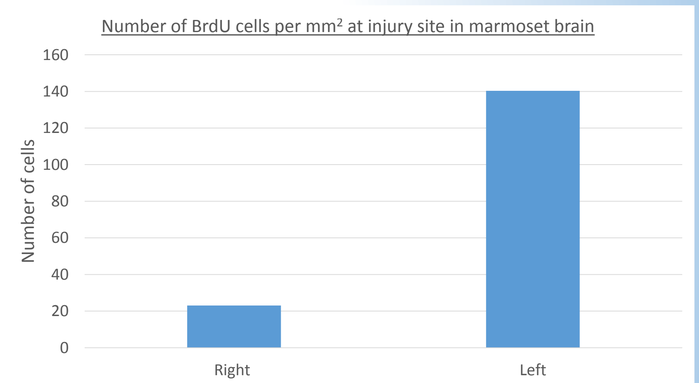


Figure 5: Graph showing the number of BrdU positive cells at the surgical stroke site in the left and right hemisphere. *Six times more BrdU positive cells per mm² in the left hemisphere compared to the right. (n=1)*

Conclusions

- 3 days post injury there is no visible reduction in the amount of proliferative neural stem cells in the SVZ of the injured hemisphere compared with the control SVZ. Quantification is necessary.
- There is an increased amount of proliferative neural stem cells in the injured hemisphere stroke site compared with the control hemisphere, demonstrating neurogenesis as a response to injury
- Further research is necessary in order to establish the origin of the neurogenic cells found at sites in the adult brain where injury is suffered.

Glossary

- **BrdU:** DNA thymidine base analogue which incorporates into the DNA of actively replicating cells
- **Endothelin-1:** Substance which causes constriction of the blood vessels local to its injection site
- **Ischaemia/Ischaemic:** Insufficient oxygen delivery to tissue resulting in cell death

References: 1) Goings, G.E *et al* (2004) 'Migration patterns of subventricular zone cells in adult mice change after cerebral cortex injury', *Brain Research*, 996(2): 213–226.

2) Tonchev, A.B *et al* (2005) 'Enhanced proliferation of progenitor cells in the subventricular zone and limited neuronal production in the striatum and neocortex of adult macaque monkeys after global cerebral ischemia', *Journal of Neuroscience Research*, 81(6): 776–788.

Acknowledgements: With thanks to the Bourne Lab for this placement opportunity and to Newcastle University for the funding throughout.