Comparative analysis of microglia morphology in naked mole rat and mouse brains

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Introduction

- **Microglia** are well known as immune cells of the central nervous system but they have also a key role in synaptic dendrite genesis or removal, in synapse formation and pruning, and in brain development.
- Mature microglia can have 2 main shapes: the amoeboid shape (large cell body with few processes) or a ramified shape (small cell body with lots of ramified processes).
- In early life, microglia have an amoeboid shape (until 20 days of life in rodent) and play a significant role in brain development.

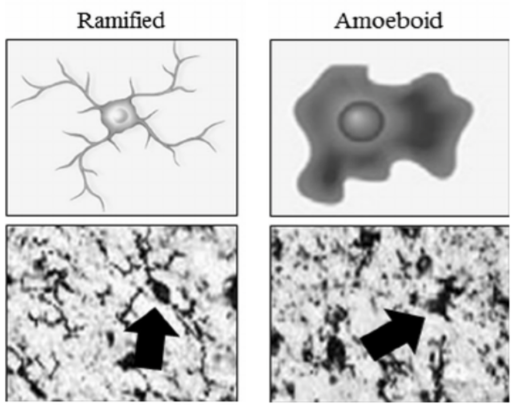

Fig. 1 : Microglia morphology, from Crews et al., 1993

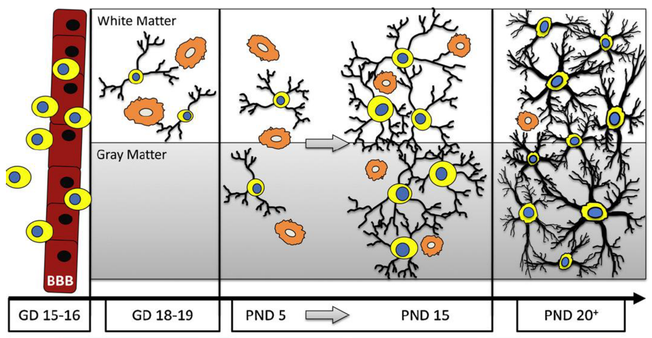

Fig.2 : Microglia development, from Harry and Kraft, 2012

- **Naked mole rats** (NMRs) are remarkable mammals that originate from parts of East Africa. These pink, almost hairless burrowing rodents live underground in low oxygen environments (hypoxic conditions).
- NMRs exhibit remarkable traits such as immunity towards cancer, tolerance towards external noxious stimuli such as ammonia or acid, and an poor ability to regulate their body temperature.
- In addition, NMRs also exhibit a high tolerance towards prolonged hypoxia. Yet the underlying mechanism of this hypoxia tolerance in NMRs is poorly understood.
- Microglia plays a significant role in developmental brain plasticity in other mammals but their role in NMRs is poorly understood.

Hypothesis

Currently, there are no studies that explore microglia development and morphology in NMRs throughout development. Thus, this study will begin by **exploring and describing the morphology during development of NMR microglia** through a comparative study between naked mole rat and murine brain. We hypothesized that NMRs retain juvenile microglia morphology longer than other rodents (mice).

Methodology

Brain Samples:

- Adult mice (2 months, *n* = 2) and adult (1 year), juvenile (5 months) and neonatal (10 days, *n* = 2 each) naked mole rats were euthanized, transcardially perfused with 4% PFA, and brains were extracted.
- 20 µm brain slices were obtained using a cryostat set at ~ -20°C.

Immunohistochemistry:

Immunohistochemistry was performed with anti-Iba-1 antibody on perfused brain slices to label microglia.

Stained microglia are observed through an optical microscope and pictures were taken at 10X and 40X for further analysis to characterize microglia morphology.

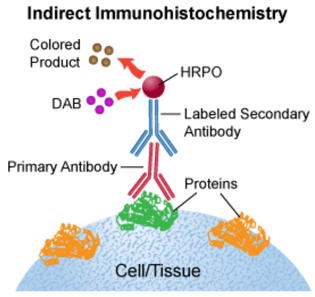

Fig. 3: Immunohistochemistry principles, from leinco.com website

Results

Mature microglia in 2 month old adult mouse

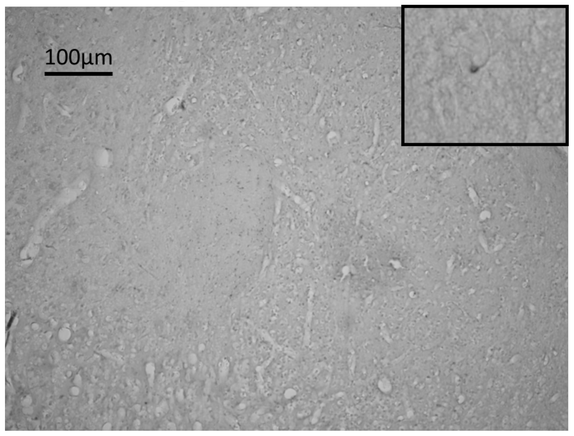

Fig. 4: Microglia in adult mice cortex , 10x and 40x in the square

Immature microglia in 5 month old Naked mole rat

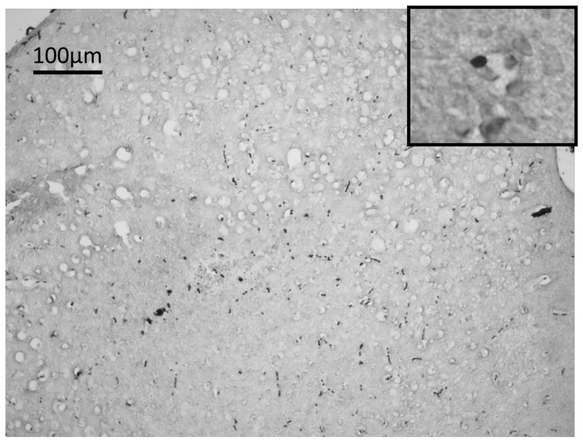

Fig.5: Microglia in 5 month old NMR (10x objective, 40x innset)

Conclusions

- In 5 month old NMRs, microglial maturation is delayed – microglia still have an amoeboid shape.
- The immunohistochemistry protocol needs to be adjusted for adults vs. neonates.

Future Work

- Future studies will focus on the microglia development in NMRs after acute and chronic hypoxia and ischemic insults.
- The goal is to focus on understanding the role of microglia development in NMR brains to help elucidate the relationship and function (with a specific interest in **synaptic pruning** and brain plasticity) between microglia and NMR tolerance to hypoxic conditions.

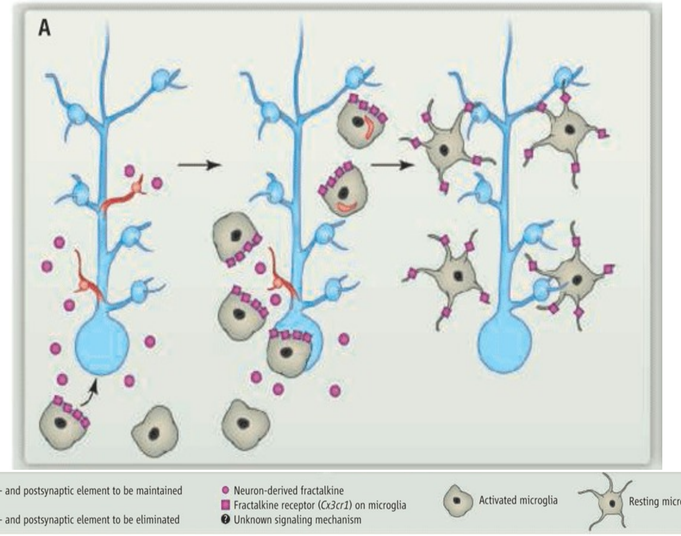

Fig. 6 : Synaptic pruning performed by microglia, from Ransohoff and Stevens, 2011

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