

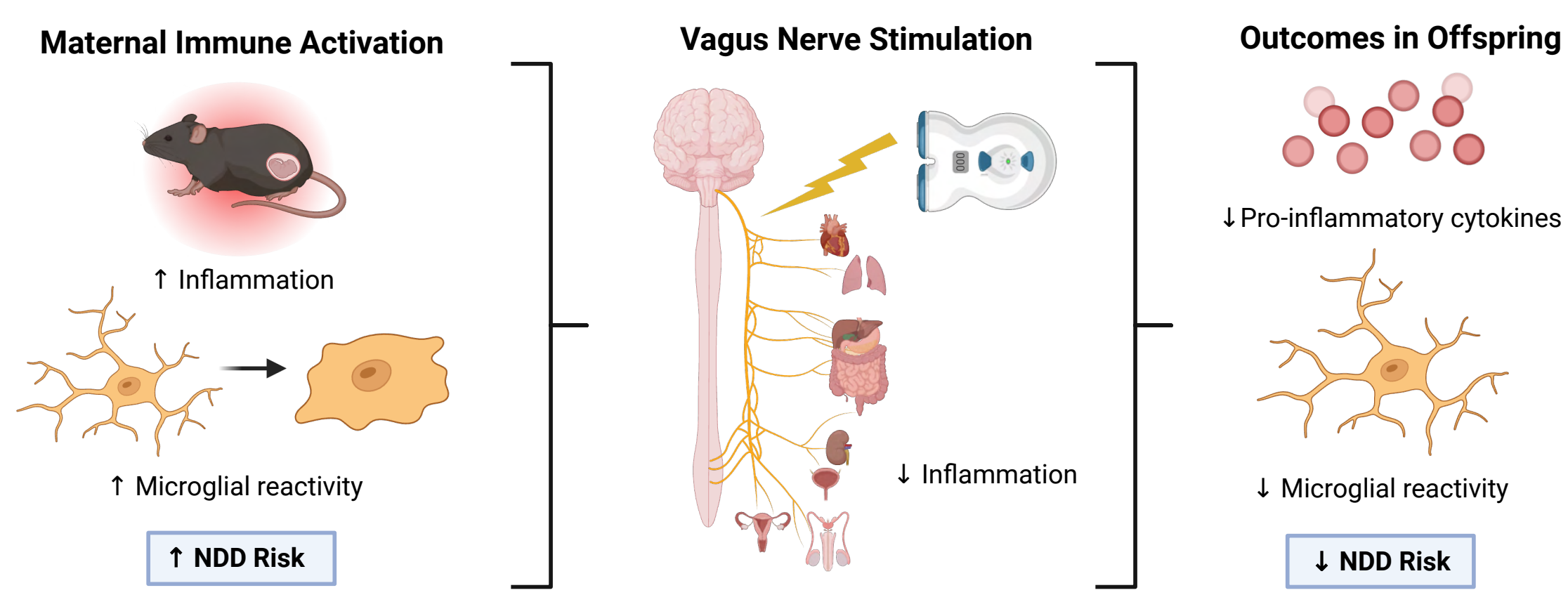
Investigating the effects of non-invasive vagus nerve stimulation on microglia and neurodevelopmental outcomes after maternal infection in mice

Linnea Poyhia¹, Makenna Gargus¹, Benneth Ben-Azu^{1,2}, Antonia Landwehr¹, Joseph P. Errico³, & Marie-Ève Tremblay^{1,4}

¹Division of Medical Sciences, University of Victoria, Victoria, BC, Canada, ²Department of Pharmacology, Faculty of Basic Medical Sciences, Delta State University, Abraka, Nigeria, ³Vagus Nerve Society, Atlanta Beach, Florida, United States of America, ⁴Department of Biochemistry and Molecular Biology, The University of British Columbia, Vancouver, BC, Canada

Introduction

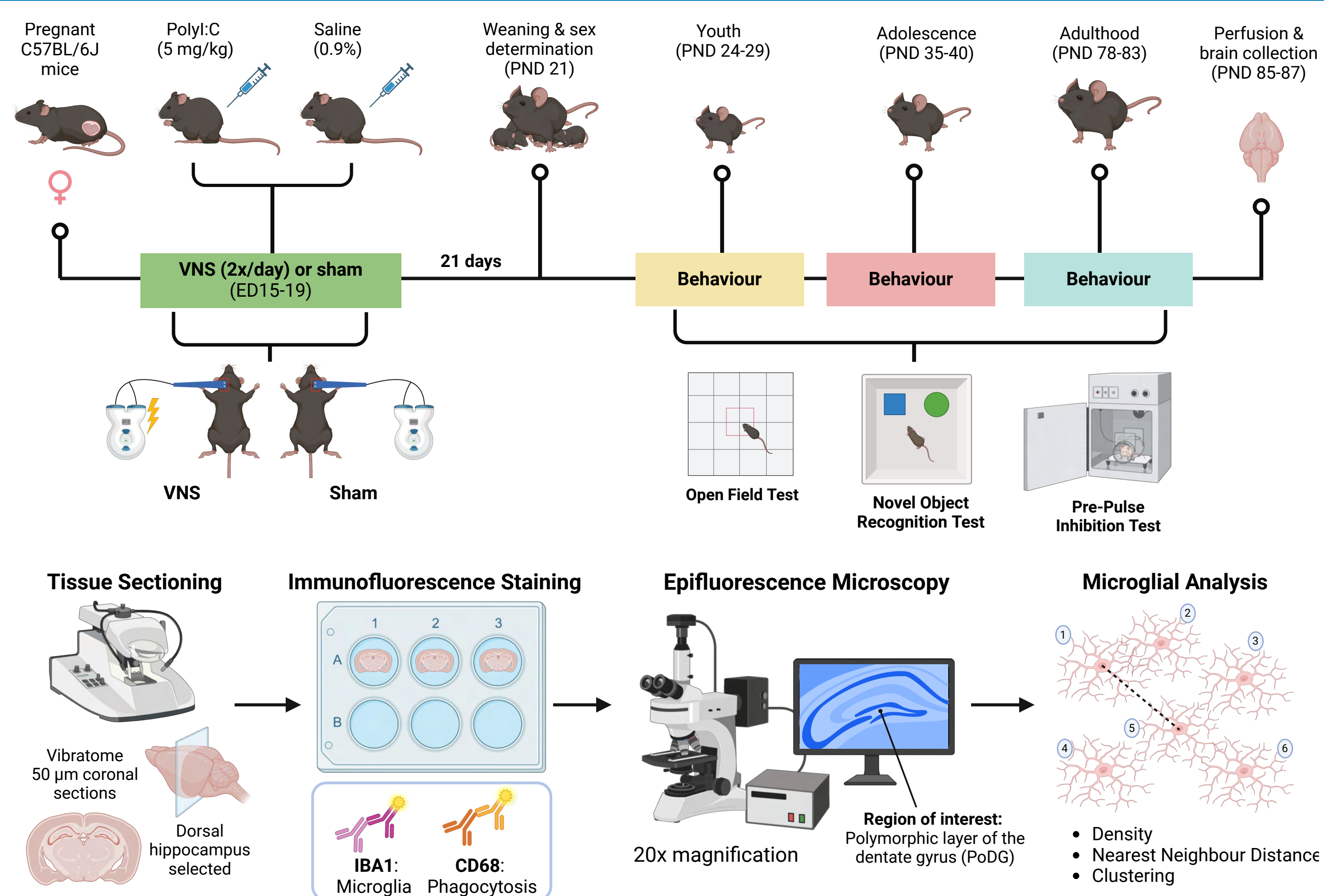
- Microglia:** resident immune cell of the brain, maintain homeostasis throughout the lifespan^{1,6}
 - Prune synapses by phagocytosis to refine neural circuits during postnatal (PND) development⁶
- Maternal immune activation (MIA):** state of increased inflammation and microglial reactivity during pregnancy^{1,2}
 - Risk factor for neurodevelopmental disorders (NDDs), such as autism spectrum disorder and schizophrenia^{1,3}
- Vagus nerve stimulation (VNS):** reduces peripheral inflammation by targeting the cholinergic anti-inflammatory pathway^{4,5}



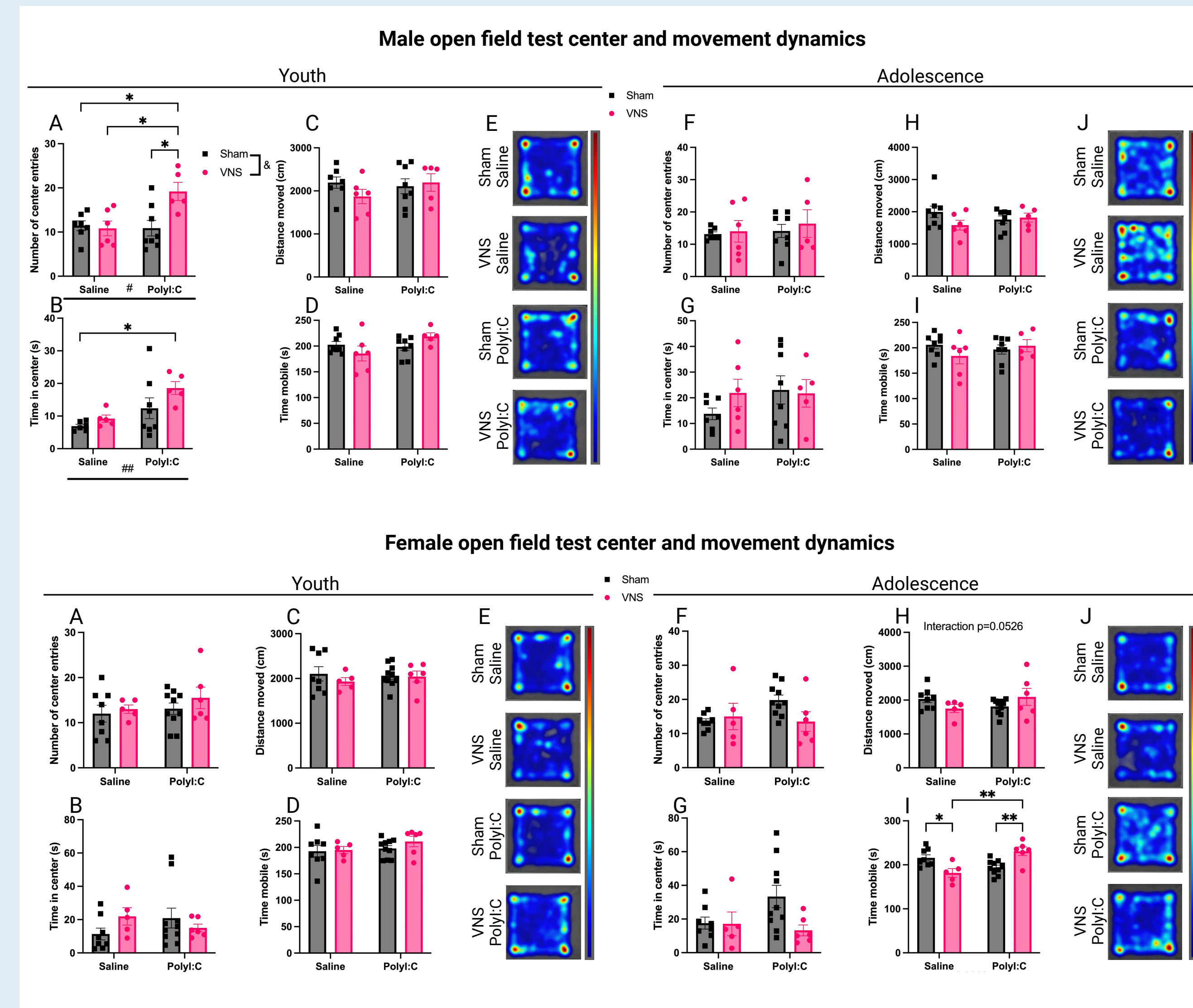
Research Objectives

- Examine the effects of non-invasive VNS on NDD-like behaviour in MIA-exposed offspring.
- Examine the effects of non-invasive VNS on microglial density, morphology, and phagocytic activity in MIA-exposed offspring.

Methods

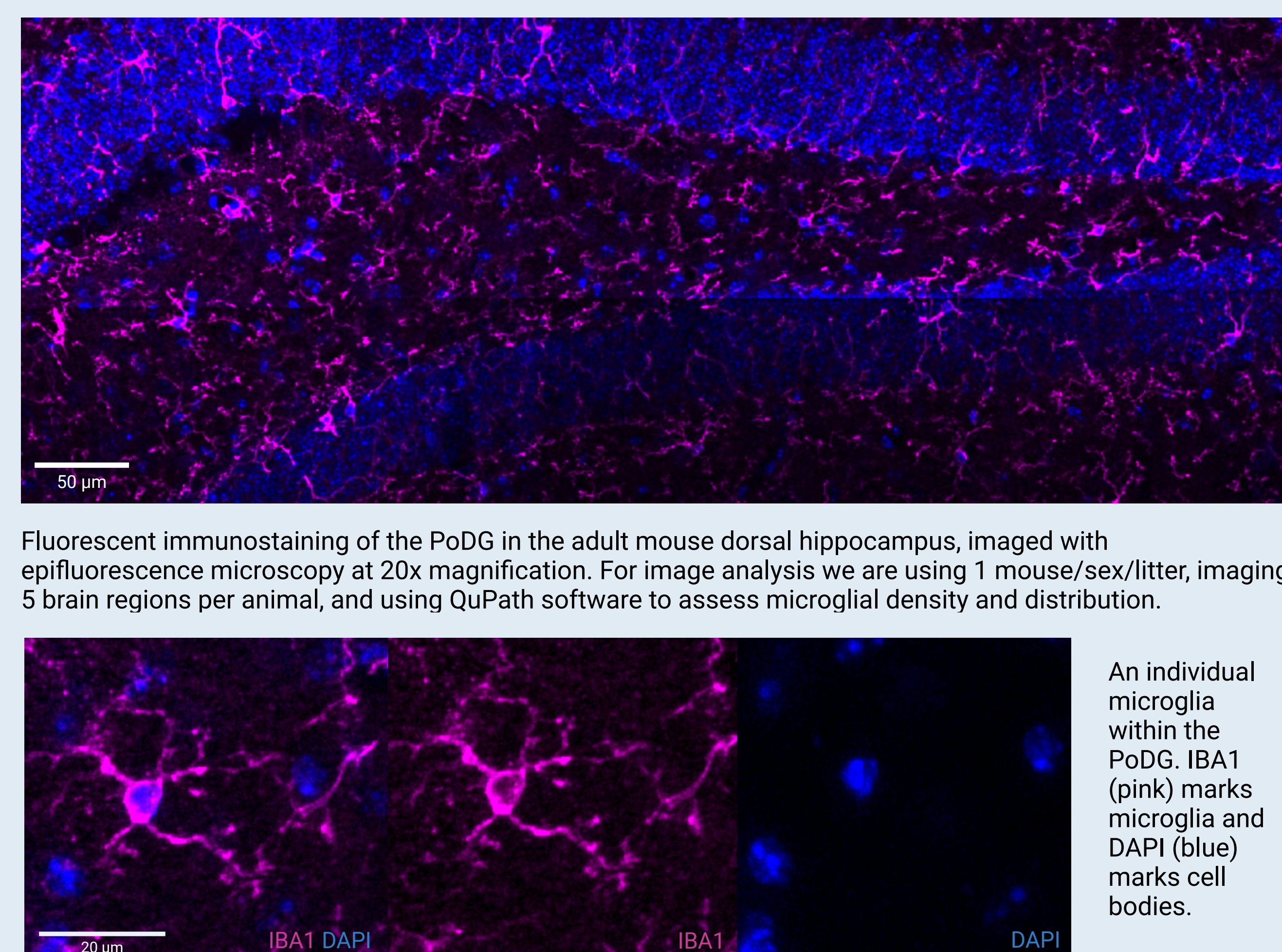


Outcomes on Behaviour



Open field test center entry and movement behaviours in offspring (n = 5-8) across ages and sex. Main effects of treatment are represented by (&) and main effects of condition are represented by (#). Ordinary two-way ANOVA was used to assess the interaction between treatment (sham vs VNS) and condition (saline vs PolyI:C), followed by Tukey's *post-hoc* tests for multiple comparisons in cases of significance. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ and **** $p < 0.0001$. Heat maps represent a subsample of 2-4 mice for each group.

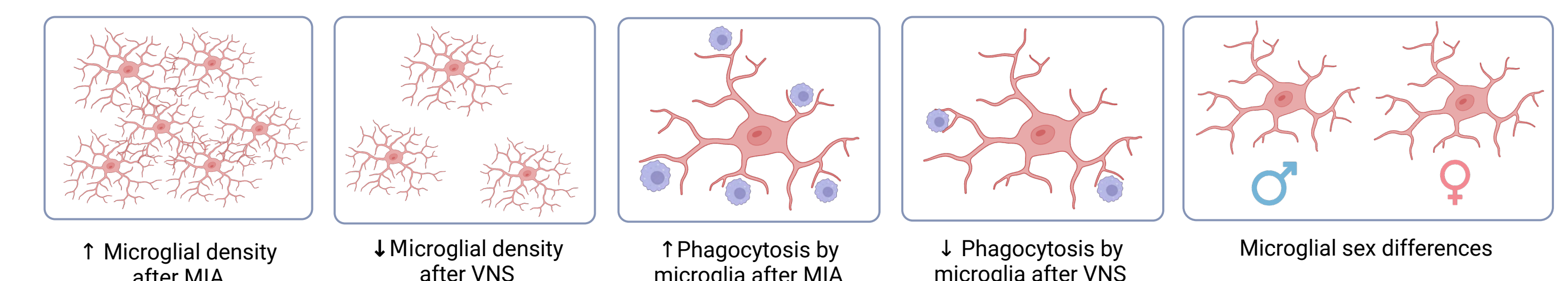
Outcomes on Microglia



Conclusions

- MIA and VNS have differential effects on NDD-like behaviour in male and female offspring during different developmental timepoints.
- We expect to observe differences in microglial density, morphology, and phagocytosis in the brains of affected offspring across sexes and developmental timepoints.

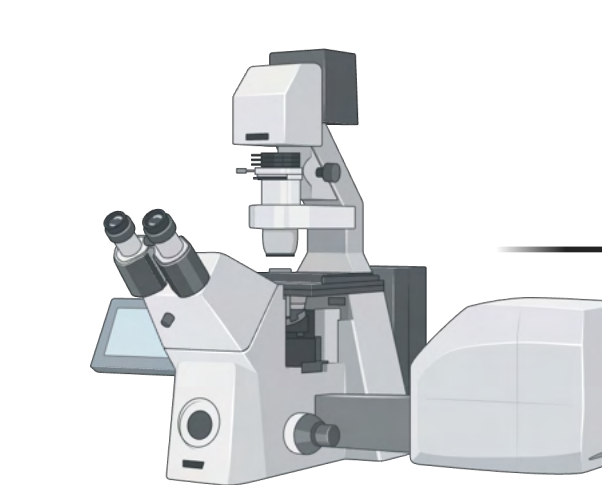
Possible Effects of MIA and VNS on Microglia



Next Steps

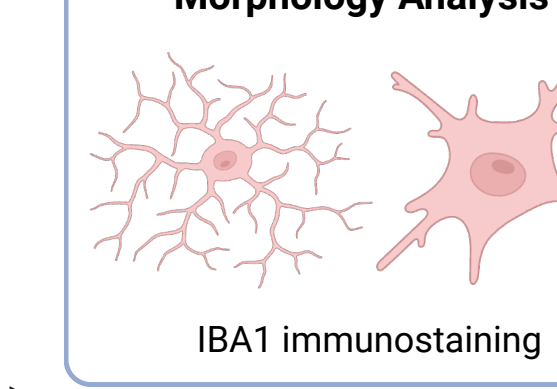
- Analyze data from additional behavioural tests to assess other behaviours associated with NDDs in affected offspring.
- Examine microglial morphology and phagocytic interactions in the PoDG using confocal microscopy.

Confocal Microscopy

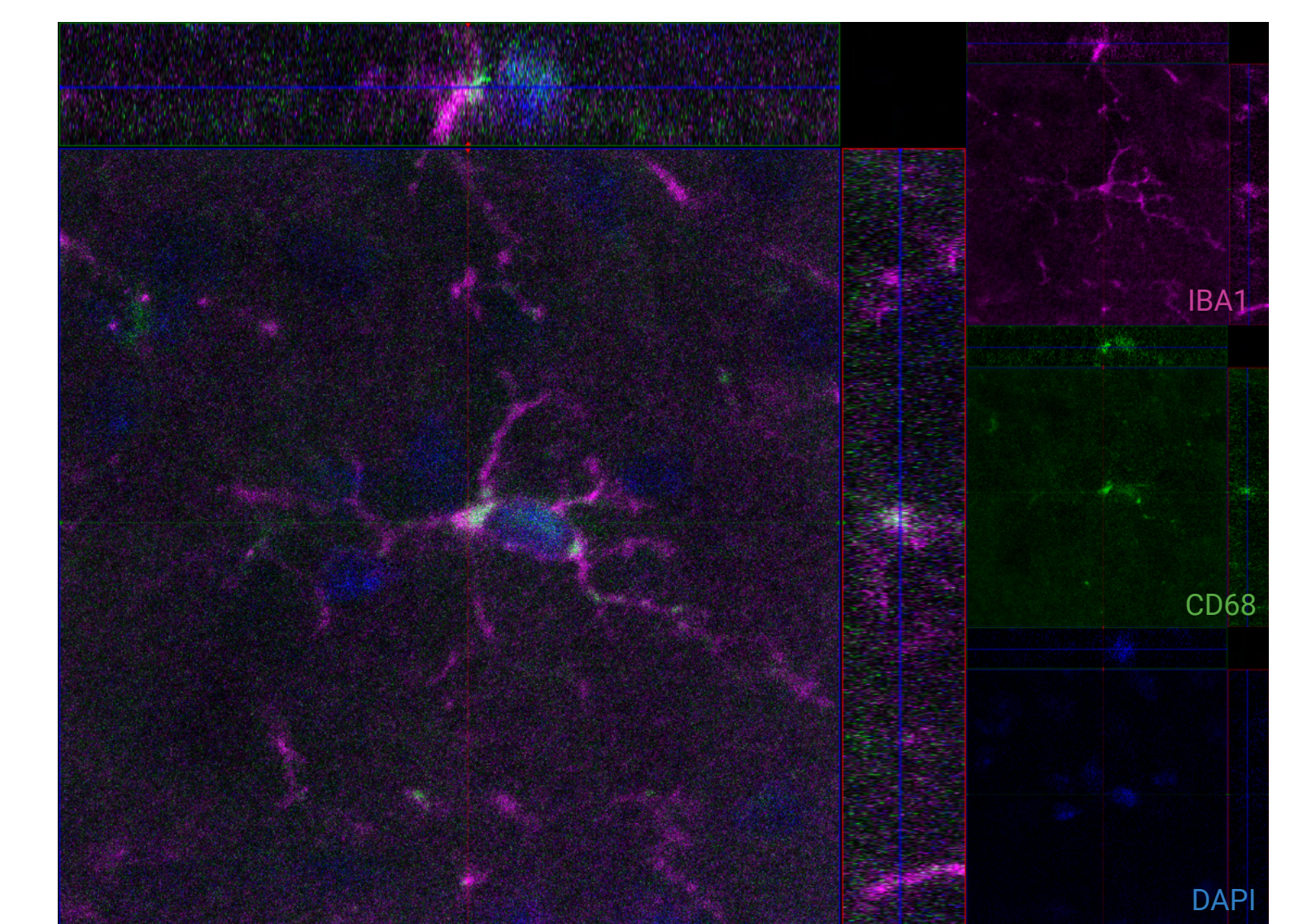
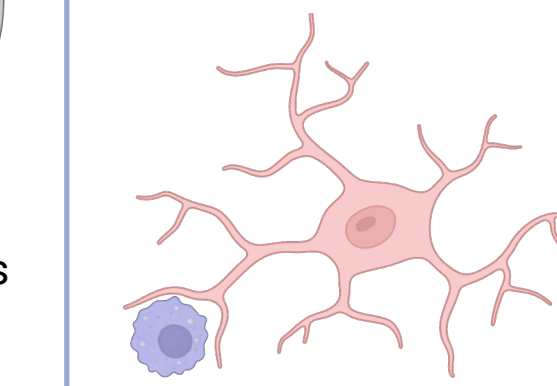


PoDG of the hippocampus

Morphology Analysis



Phagocytosis Analysis



A microglia in the PoDG, captured using confocal microscopy.

Acknowledgements

References

- Paliocelli & Feretti (2017) doi: 10.3389/fnsyn.2017.00009
- Hui *et al.* (2018) doi: 10.3389/fnmol.2018.00013
- Mastenbroek *et al.* (2024) doi: 10.1007/s00281-024-01017-6
- Gargus *et al.* (2024) doi: 10.3389/fnins.2024.1527842
- Corsi-Zuelli *et al.* (2017) doi: 10.3389/fimmu.2017.00618
- Anderson & Vetter (2019) doi:10.1002/dvdy.1

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Poster created on March 8th, 2025.

