

Douglas Maternal immune activation early in gestation alters brain volume in mice

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Introduction

- Maternal immune activation [MIA] during pregnancy can increase the risk of neurodevelopmental disorders in offspring [1].
- Experimentally-induced MIA in rodents alters behavior and neuroanatomy across the lifespan [2].

Goal: to investigate this relationship between behavior and neuroanatomy using magnetic resonance imaging [MRI] and behavioral assays.

Conclusions

- •MIA induced with Poly I:C at gestational day 9 in mice alters brain anatomy in offspring during adolescence and early adulthood.
- Prepulse inhibition not statistically impacted, but trending sex-effects.
- Future directions:

Methods

Population Average

 Investigate brain connectivity through functional MRI and chemistry through MR spectroscopy

Behaviors

All Figure Links, Click Here

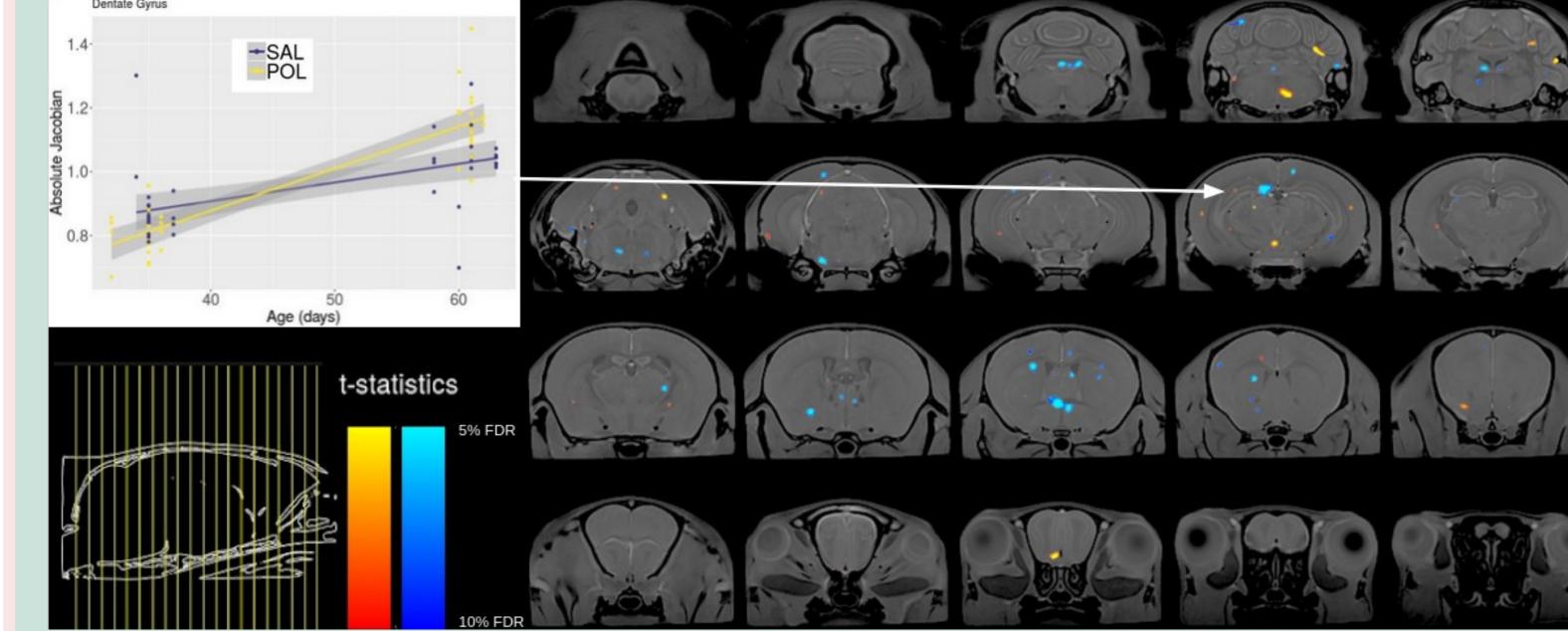
MRI 2

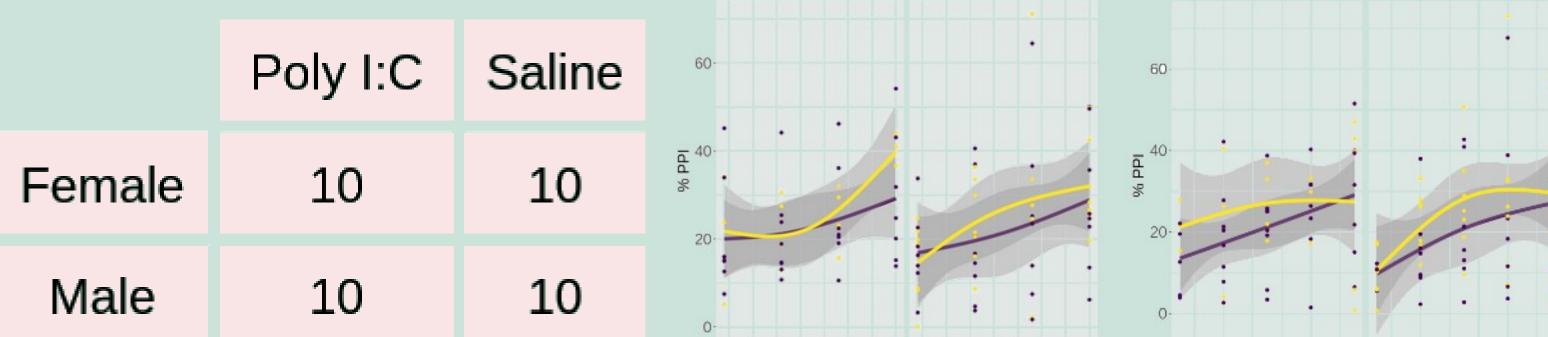
PND 60

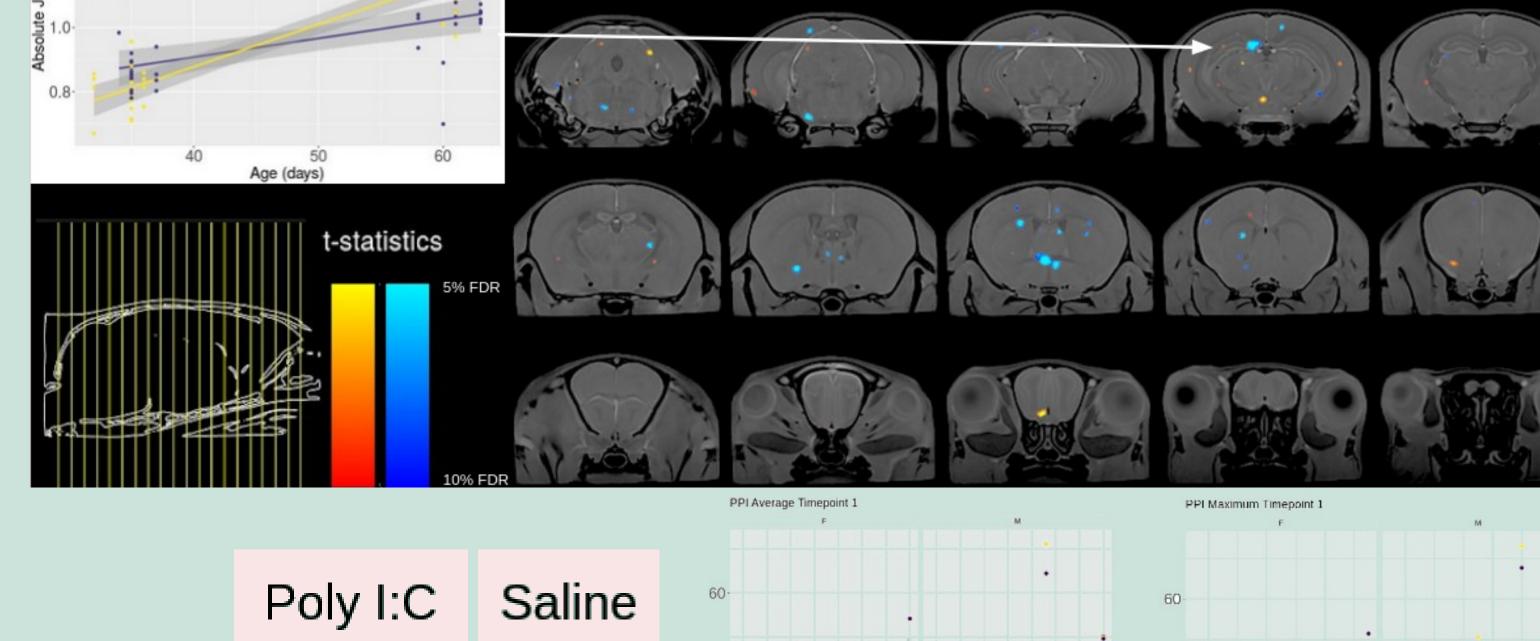
 Integrate modalities with multivariate approaches

Results

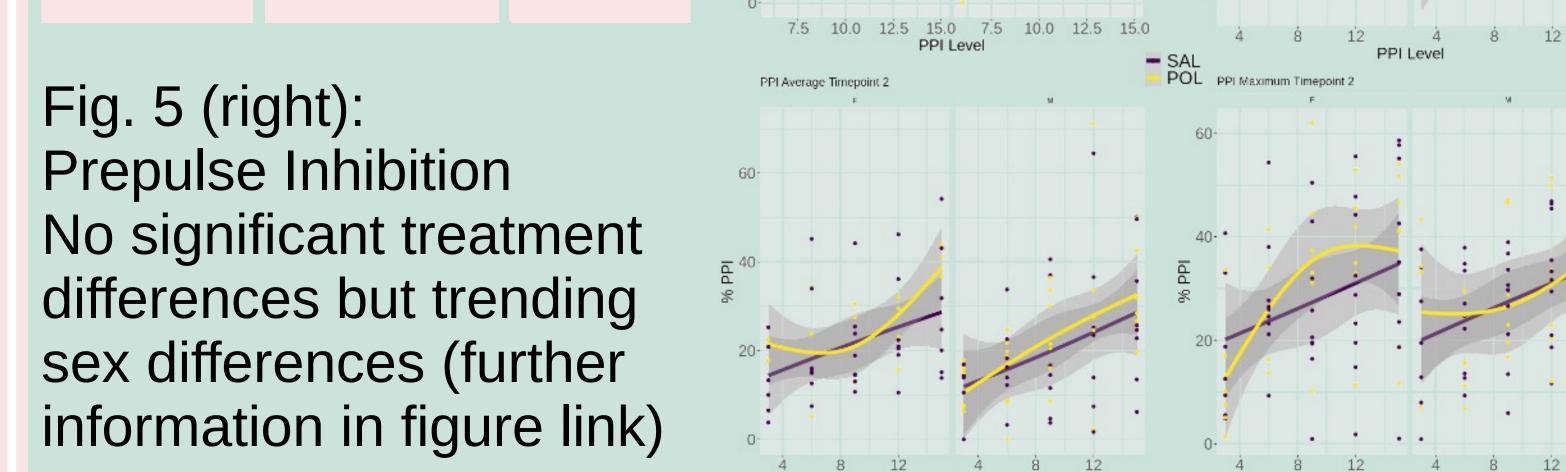
Fig. 3 (above): Volumetric Changes-Left Subiculum Fig. 4 (below): Volumetric Changes-Left Dentate Gyrus





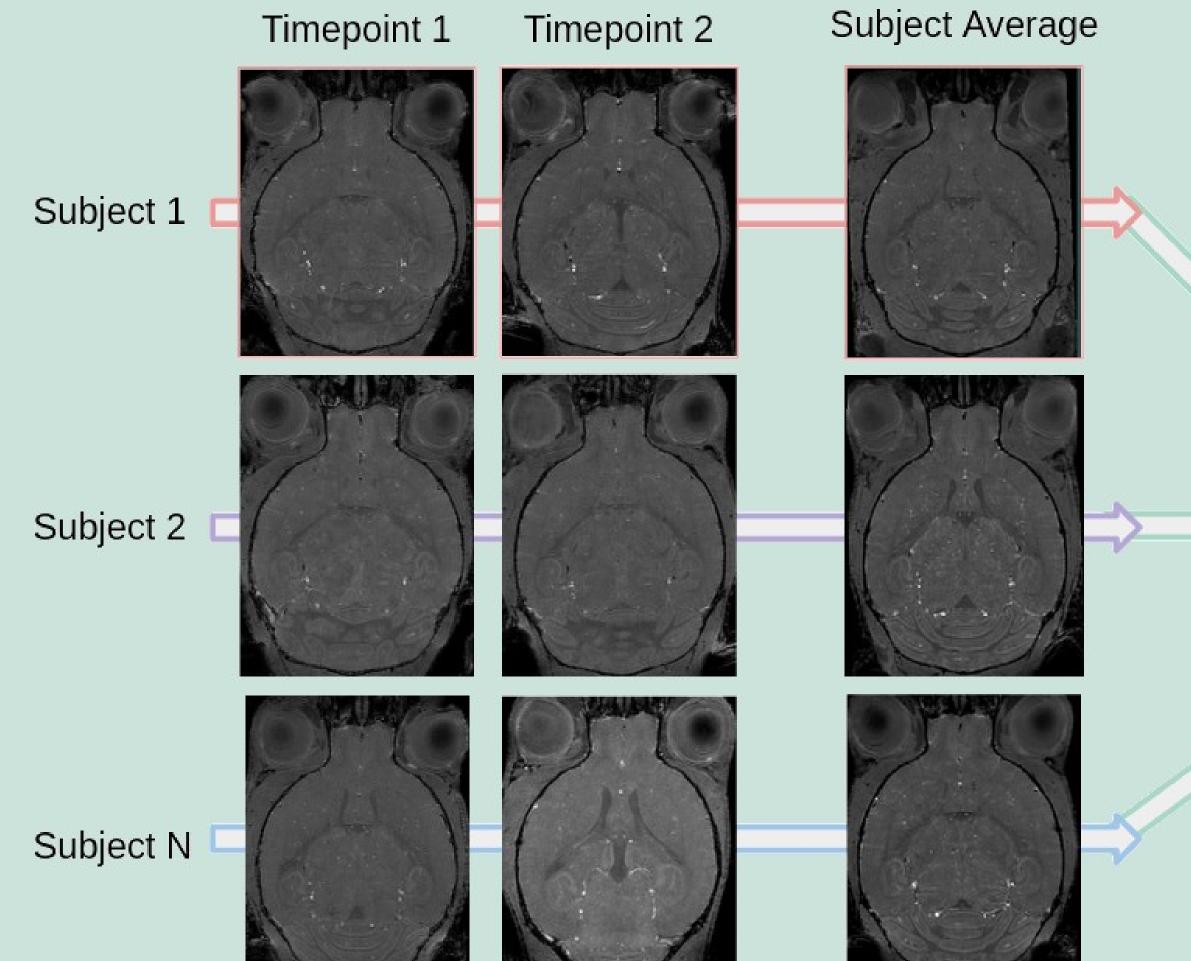


Female	10	10	Id 40 20 20 1	a 40-
Male	10	10	0-	0-
Fig. 5 (right):			7.5 10.0 12.5 15.0 7.5 10.0 PPI Level PPI Average Timepoint 2	12.5 15.0 4 8 12 4 8 12 SAL POL PPI Meximum Timepoint 2 F 4 8 12 POL PPI Meximum Timepoint 2 F 4 8 12 POL PPI Meximum Timepoint 2



Behaviors

- Prepulse inhibition for sensorimotor gating
- MR Acquisitions
- •7T Bruker Biospec, cryogenic surface coil
- Anaesthetized with isoflurane
- •T1-weighted structural MRI (fast low-angle sequence, 70 µm3)
- MIA
- 5mg/kg polyinosinic:polycytidillic acid
- Gestational Day 9



Statistical Methods

Fig. 1 (above): Experimental Design

Linear mixed effects model

MRI 1

PND 35

- Fixed effects: Treatment (Poly I:C/Saline); Sex; Age
- Random effects: Subject ID
- Multiple Comparison Corrections
- False Discovery Rate, 10%-5%

Fig. 2 (above): Formation of subject and population averages with deformation-based morphometry

²⁾ Guma, et al. (2019). The role of maternal immune activation in altering the neurodevelopmental trajectories of offspring... Neuroscience & Biobehavioral Reviews.





¹⁾ Estes, M. L., & McAllister, A. K. (2016). Maternal immune activation: Implications for neuropsychiatric disorders. Science.