Characterization of early maternal immune activation on brain and behavior during adolescence and early adulthood in mice

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Introduction:

- Maternal immune activation (MIA) during pregnancy can alter neurodevelopment in offspring.
- In rodents, changes in brain volume and tissue chemistry can be quantified with magnetic resonance (MR) imaging and spectroscopy, respectively.
- How MIA contributes to changes over time is still an open question in the literature.

Goal: To investigate the relationship between MIA and neurodevelopment with magnetic resonance imaging (MRI), spectroscopy (MRS), and behavior.

1.

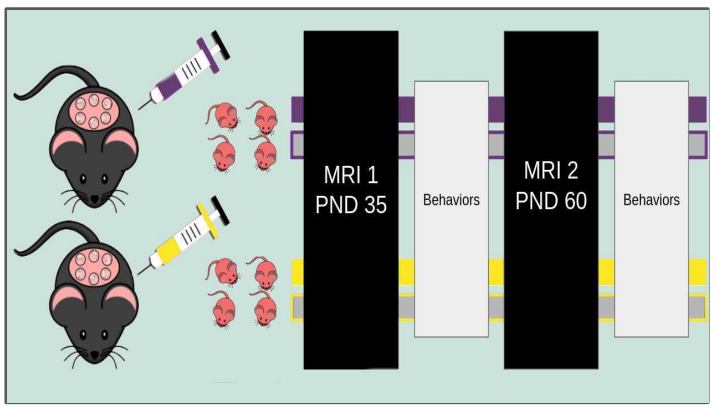


Fig. 1: Experimental Design

Saline Poly I:C both sexes

2.

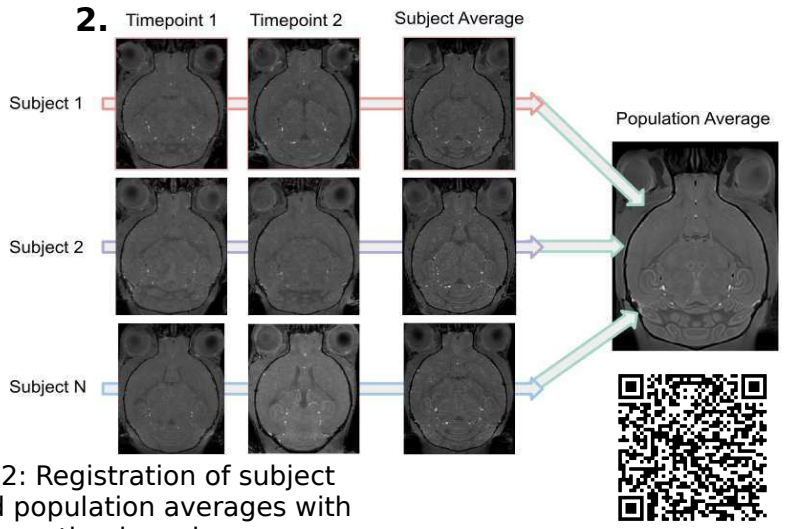


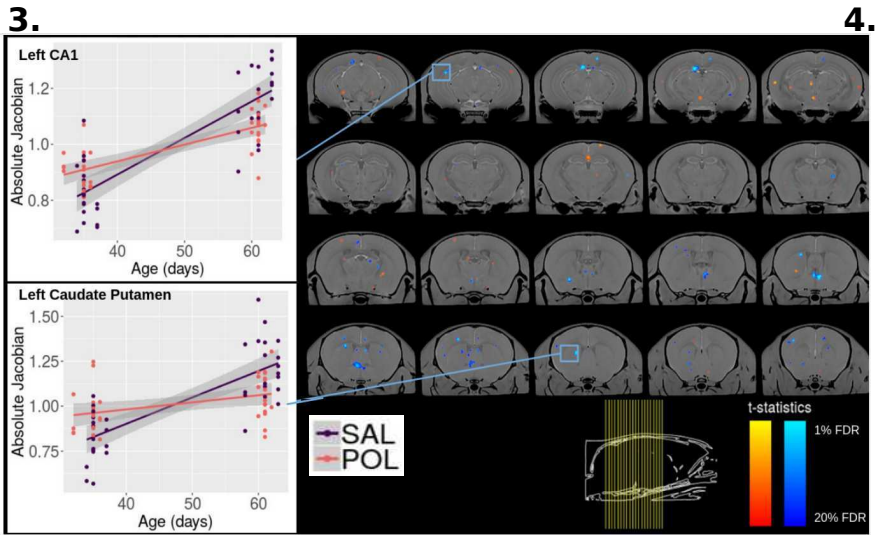
Fig. 2: Registration of subject and population averages with deformation-based morphometry.

Figure viewable at QR code.

Methods:

- MIA induced with 5 mg/kg POLY I:C gestational day 9 (human first trimester)
- T1-w structural MRI & MRS from anterior cingulate area acquired postnatal day (PND) 35 and 60.
- Behaviors (open field test, three-chamber social interaction, prepulse inhibition) acquired 2 days after each scan
- 7T Bruker Biospec with cryogenically-cooled surface coil
- Anaesthetized with isoflurane
- MRI: whole brain, MRS: anterior cingulate cortex

3.



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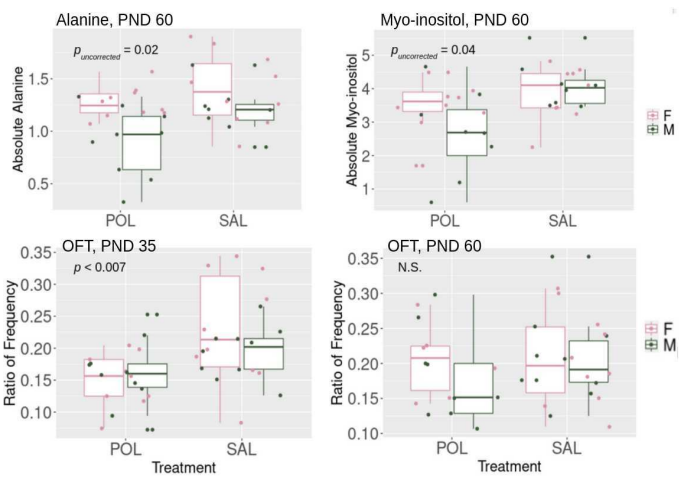

Statistical Methods:

- Linear Mixed Effects Models
  - Fixed effects: Treatment*Age(days) + Sex
  - Random effects: Subject ID and litter
  - False Discovery Rate

Results:

- Altered trajectories associated with first episode psychosis (increased volume in caudate putamen, reduced in hippocampus and anterior commissure (Fig 3, above left).
- At PND 60, trending reduction in concentration of alanine and myo-inositol in anterior cingulate cortex (Fig 4, above right).
- Increased anxiety-like phenotype in open-field task at PND 35, but not 60 (Fig 4, above right).
- No other significant diferences in behaviors

Conclusions:

- MIA induced at GD 9 causes long-lasting changes in neuroanatomy and chemistry.
- Additive risk factors may be necessary to evoke phenotypes reflecting neurodevelopmental \disorders in humans.
- Behavioral effects of MIA are subtle and normalize by adulthood.

References:

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

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