

# A Longitudinal Investigation of the Neurodevelopmental Impact of Maternal Immune Activation on Parvalbumin Interneurons in the Prefrontal Cortex in the Rat

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b-neuro  
DEVELOPING TREATMENTS  
FOR MENTAL ILLNESS

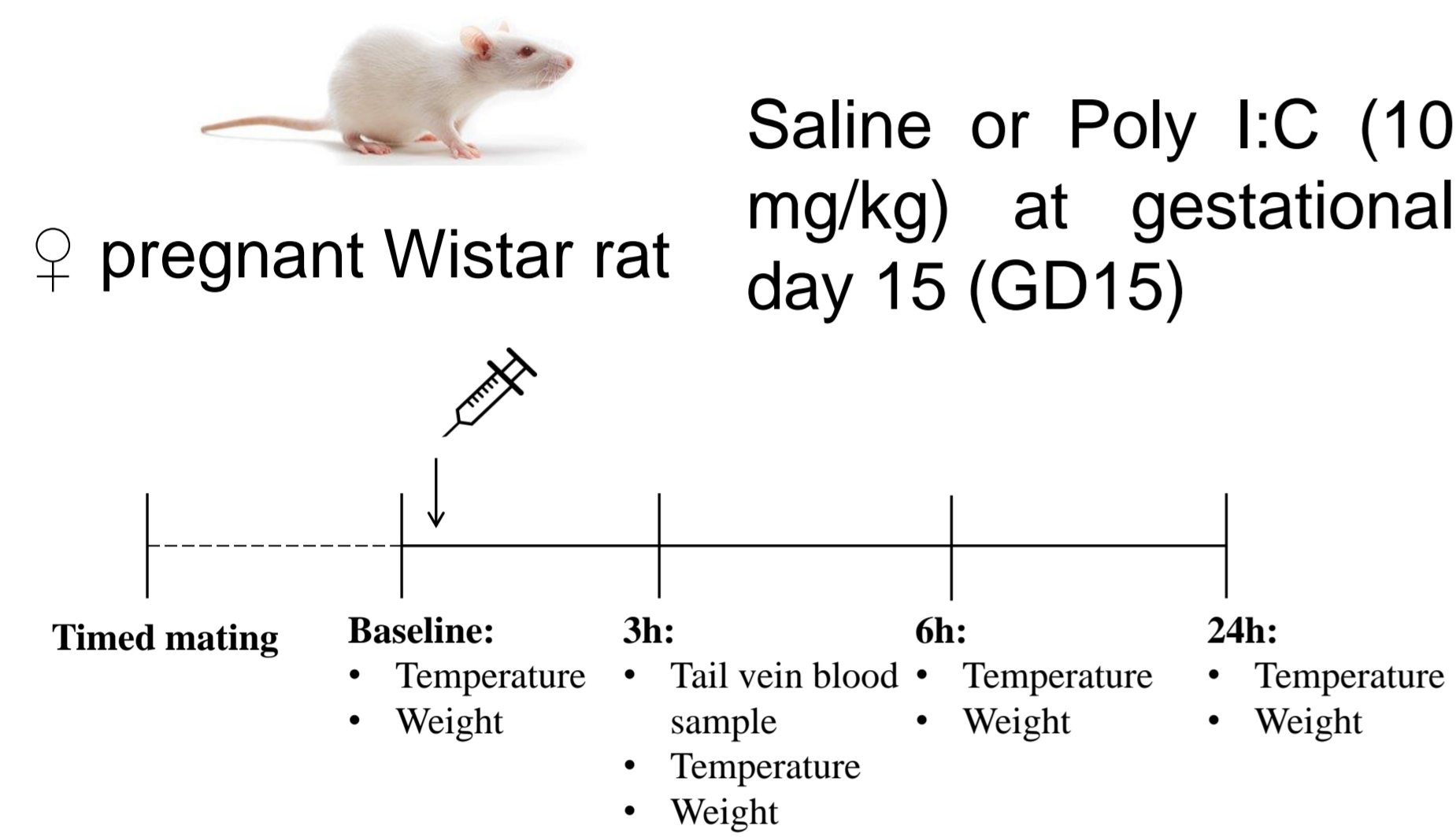
## Introduction

Prenatal environment affects the developing fetus (Knuesel et al, 2014, Nat Rev Neurol, 10:643-660). Maternal immune activation (mIA) in rodents by administration of a viral mimetic polyriboinosonic-polyribocytidylic (poly I:C) is used to study effects of prenatal infection on offspring neurodevelopment (Meyer, 2014, Biol Psych, 75:307-315).

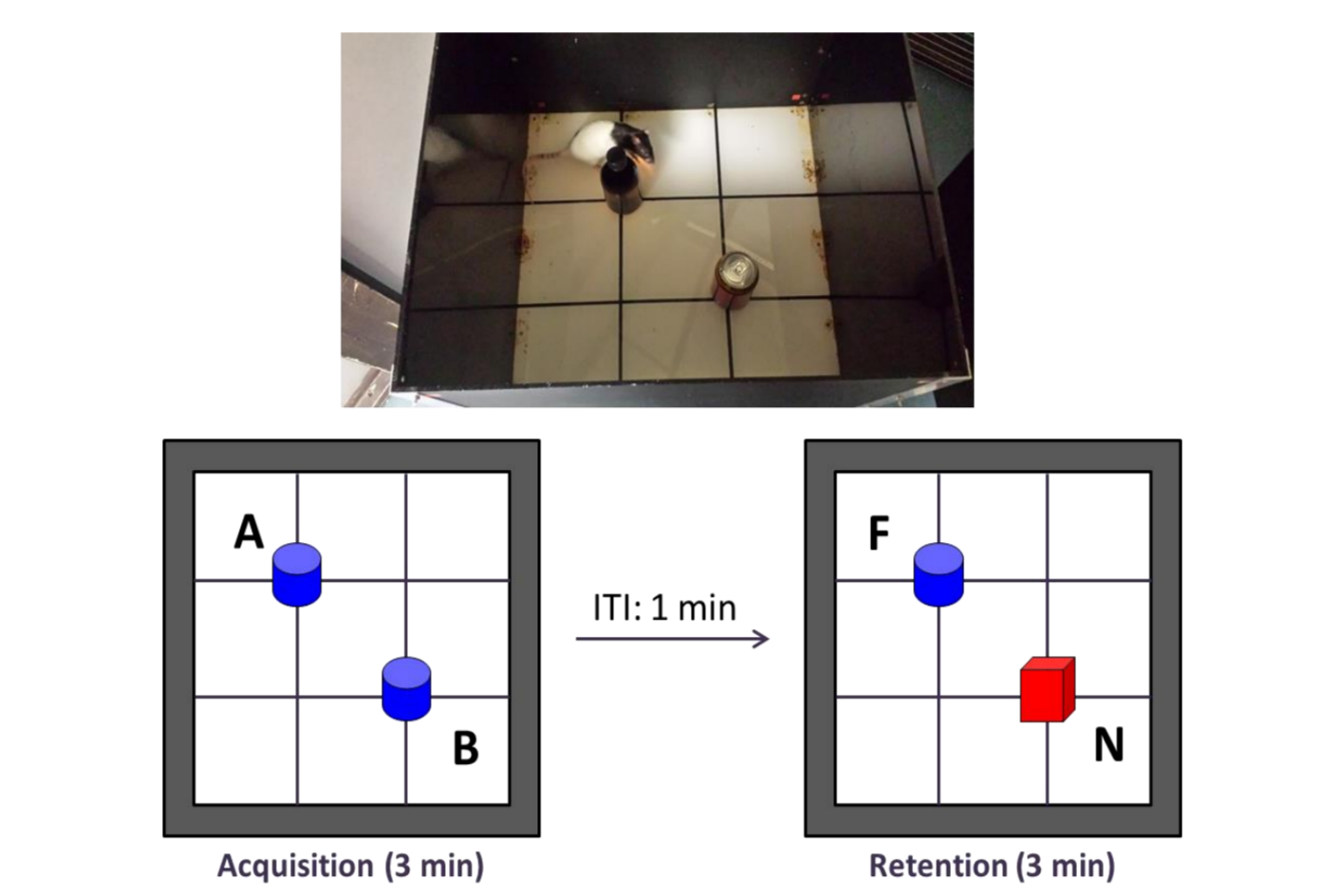
Our aim is to investigate the longitudinal development of PV deficits and to determine whether cognitive deficits and PV reductions in the offspring occur at the same stage of development.

## Methods

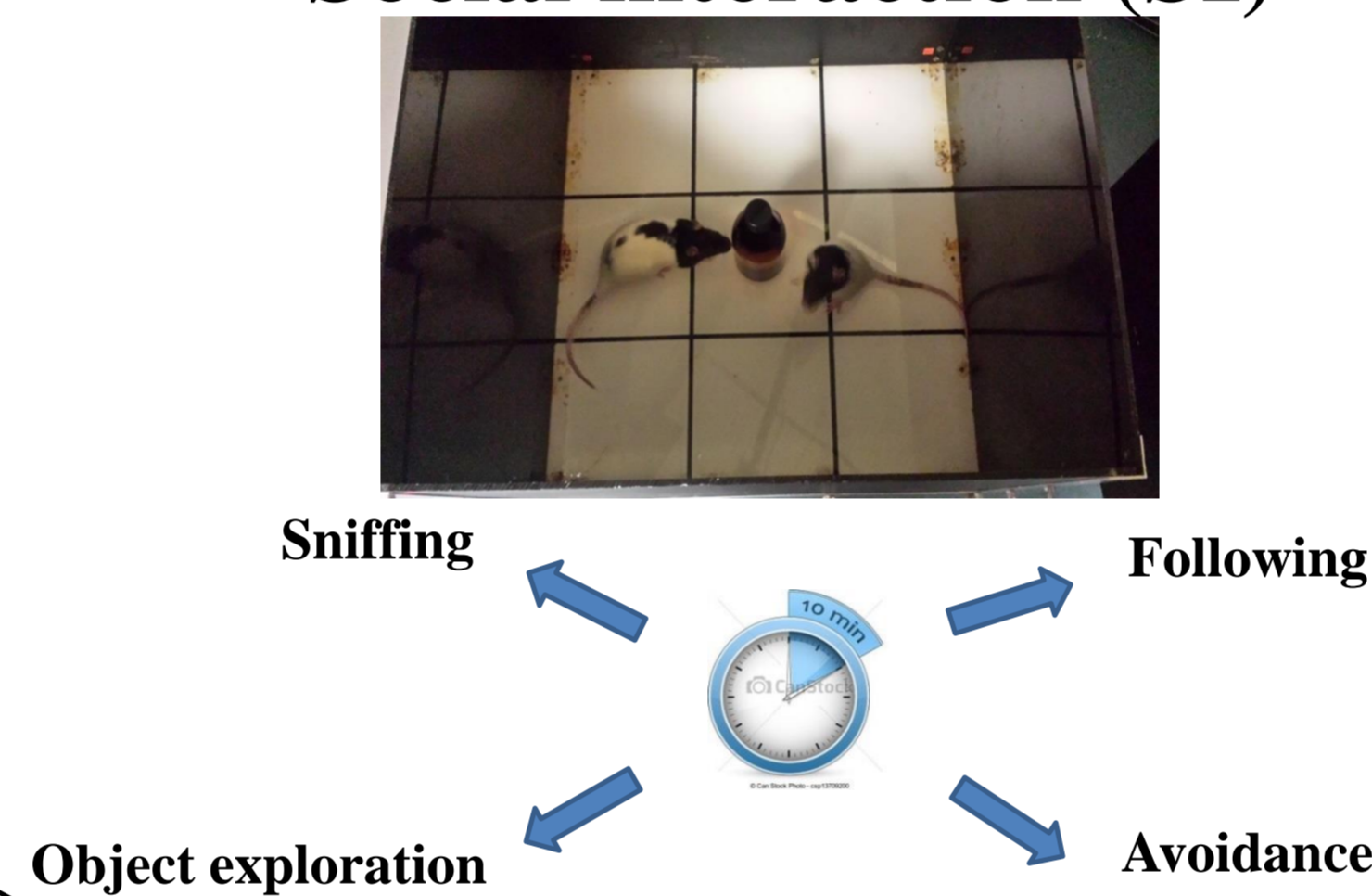
### Maternal Immune Activation (mIA)



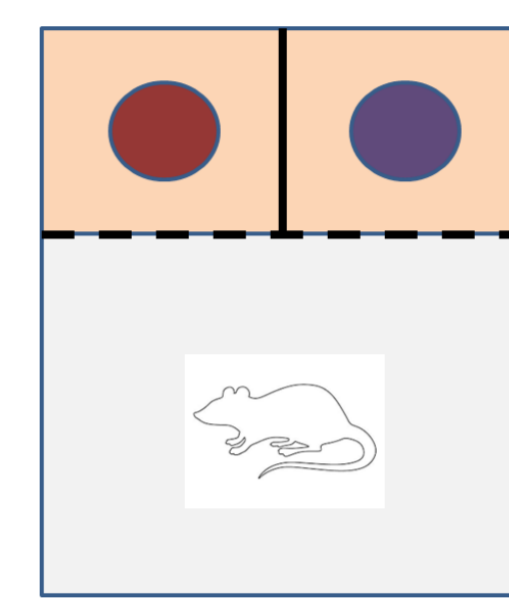
### Novel object recognition (NOR)



Based on the innate preference for novelty  
**Social interaction (SI)**



### Attentional set shifting task (ASST)

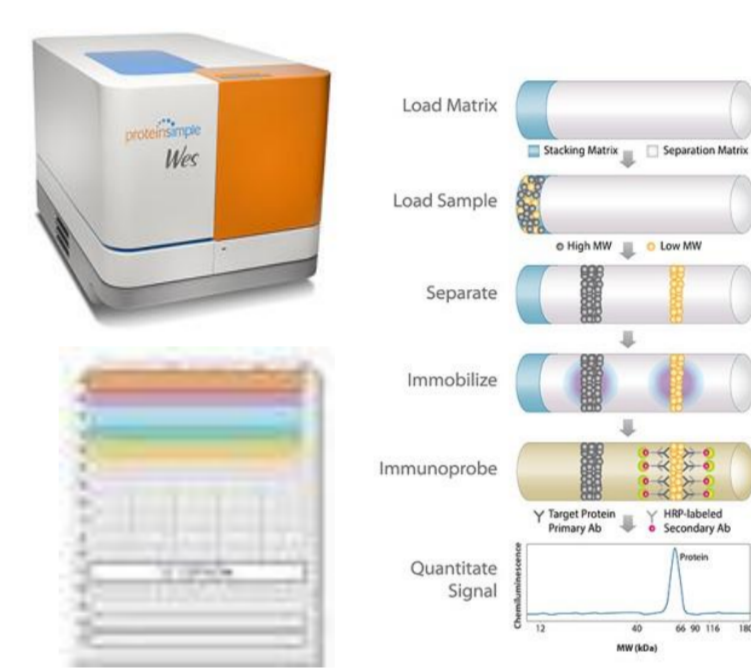


Reasoning and problem solving

Rat analogue of the ID/ED test in CANTAB. Rewarded paradigm – 7 discriminations

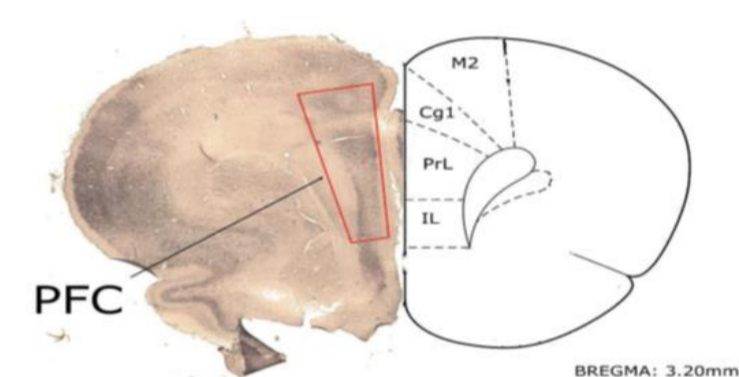
### Protein analysis for Parvalbumin

Westerns (Wes)



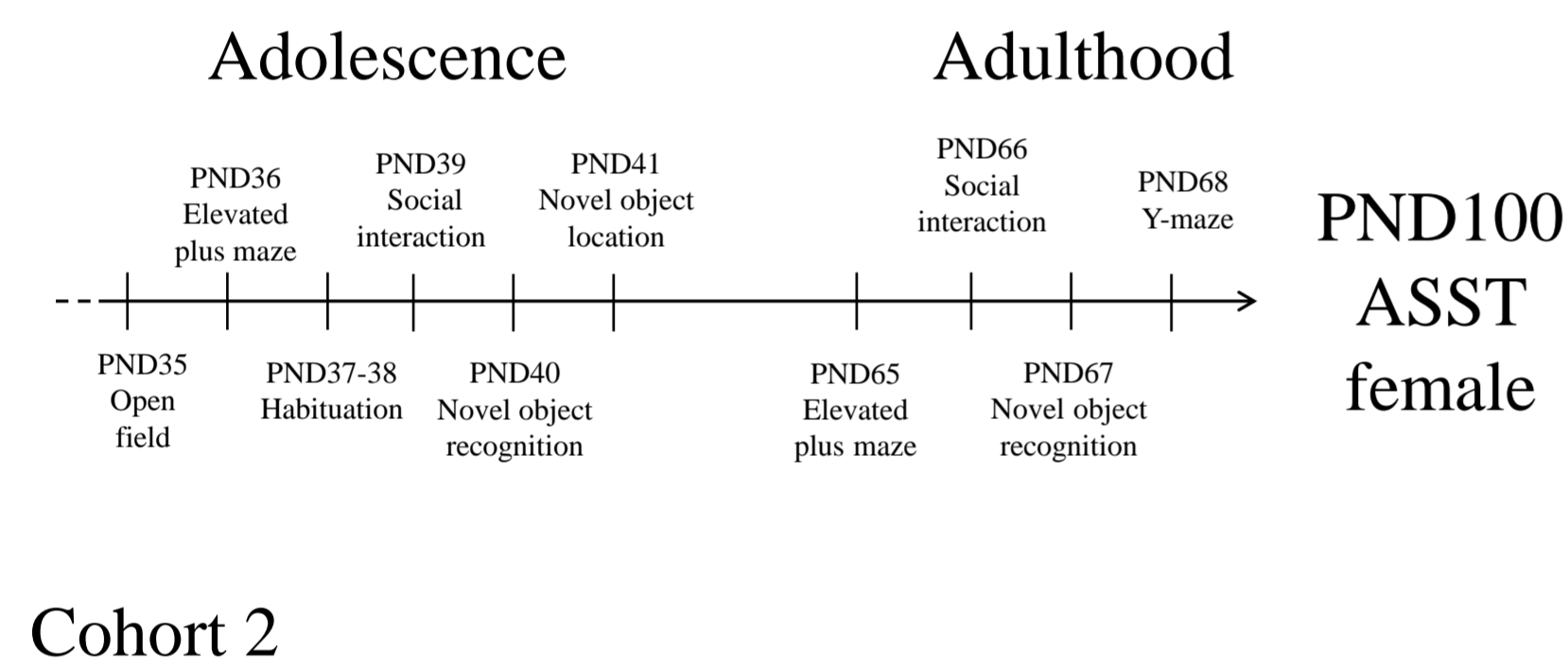
Capillary based automated western blot system. Runs up to 25 samples in 3 hours.  
[www.proteinsimple.com](http://www.proteinsimple.com)

Immunohistochemistry



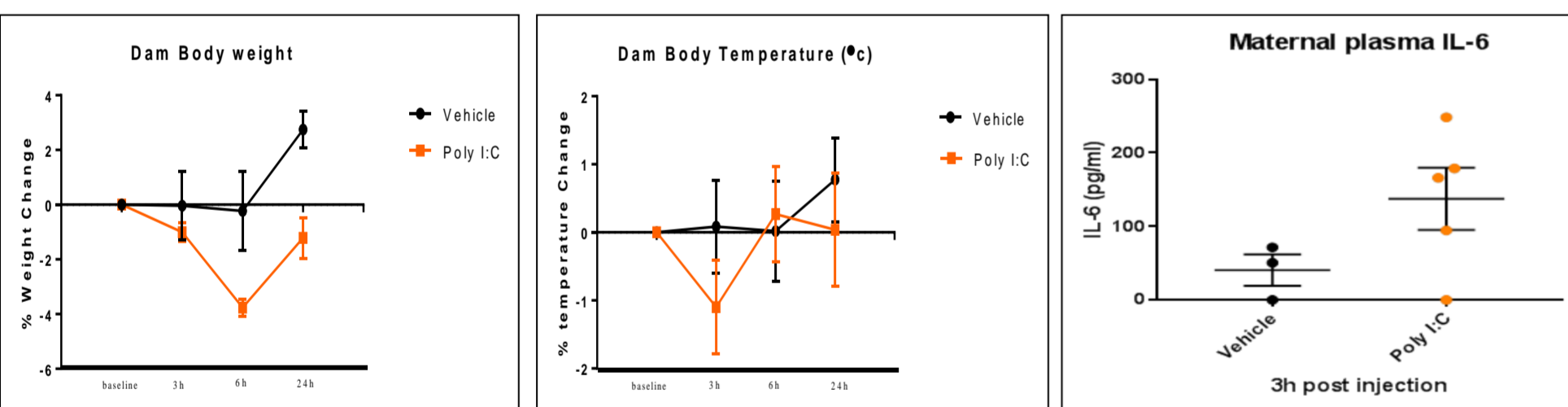
Sections were cut and stained for Parvalbumin with a rabbit polyclonal antibody (1:5000, Swant). The PFC was highlighted and PV positive neurons were counted and analysed live at 20x magnification. Estimations of neuronal density (cells/mm<sup>2</sup>) were carried out in every 6th section, with a minimum of six sections per animal counted.

### Behavioural Batteries

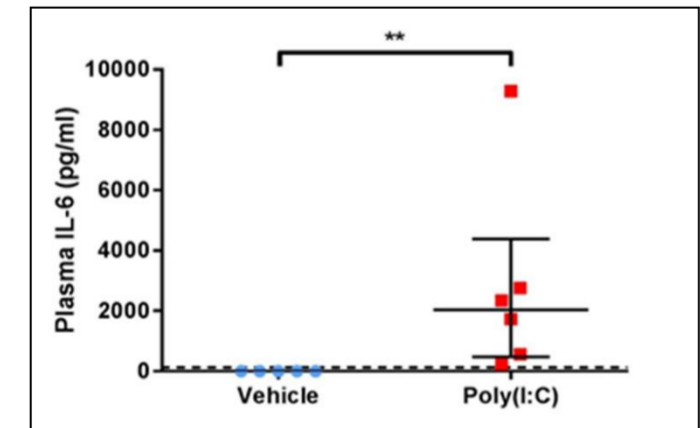


## Results

### Cohort 1 3h post poly IC/saline injection

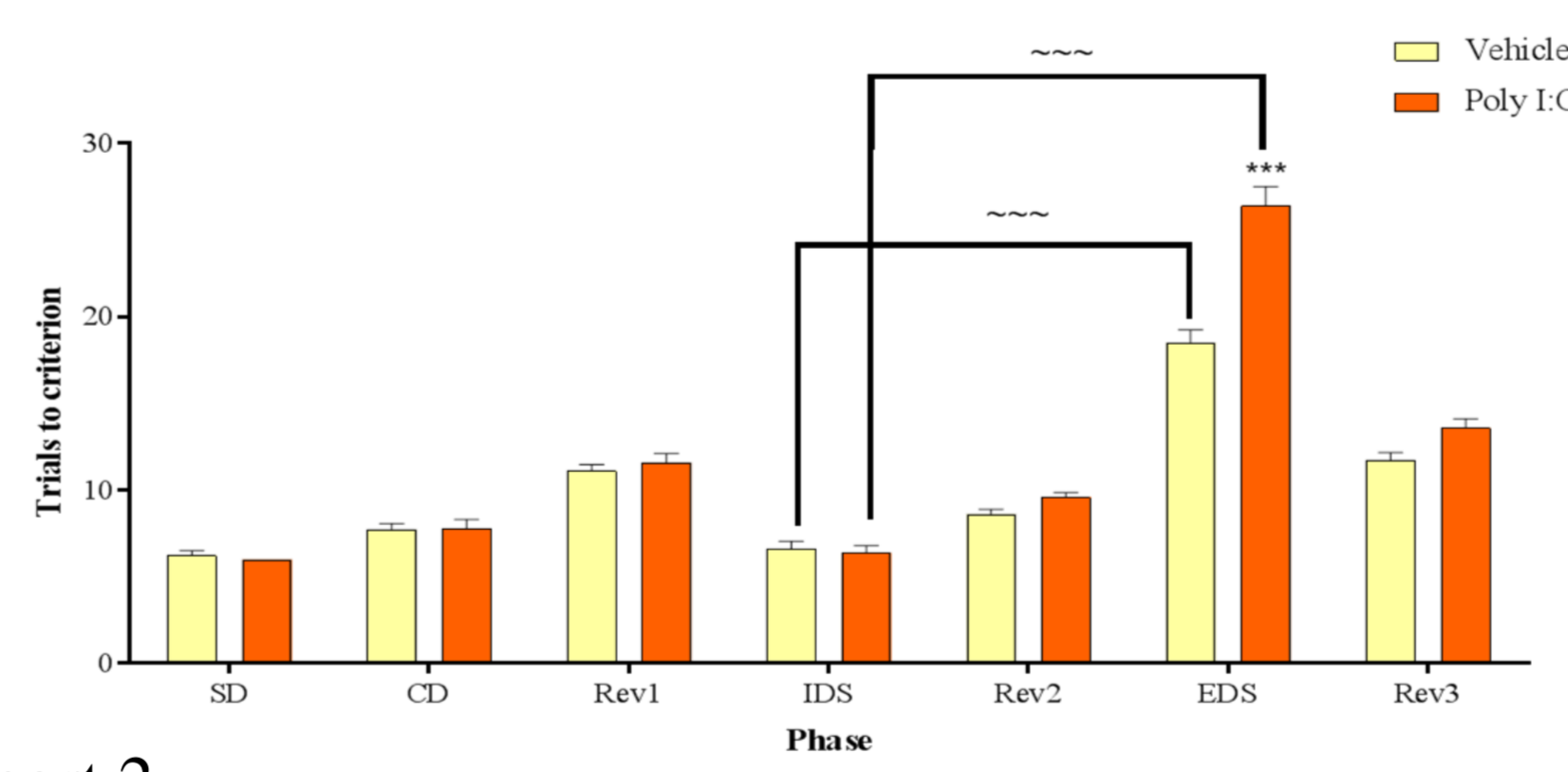


### Cohort 2 3h post poly IC/saline injection



- Reduction in dam body weight and temperature
- A trend in IL-6 in poly IC group (C1)
- Significant increase in IL-6 response 3h post injection (C2)

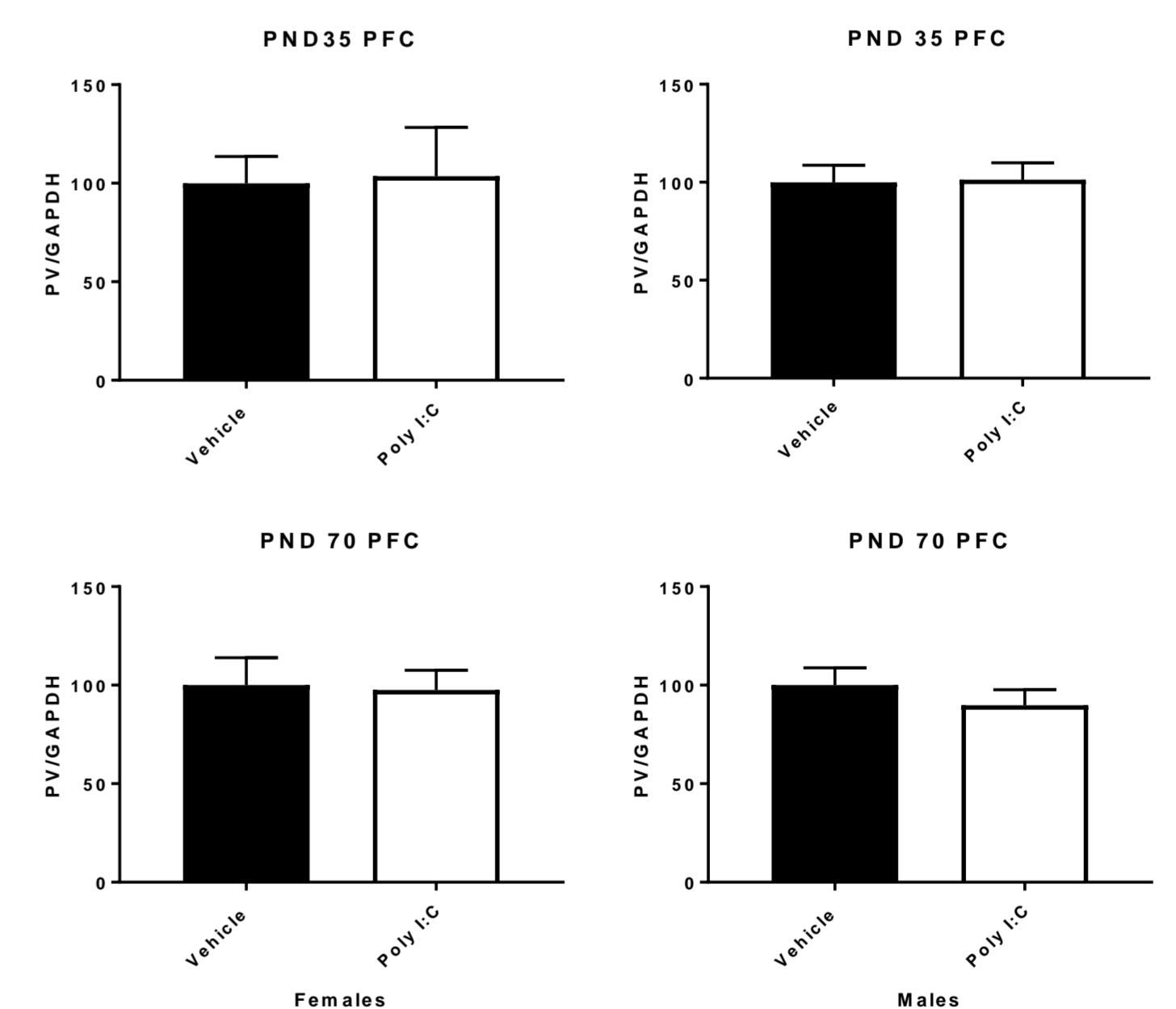
### Attentional Set Shifting Task (ASST)



Cohort 2

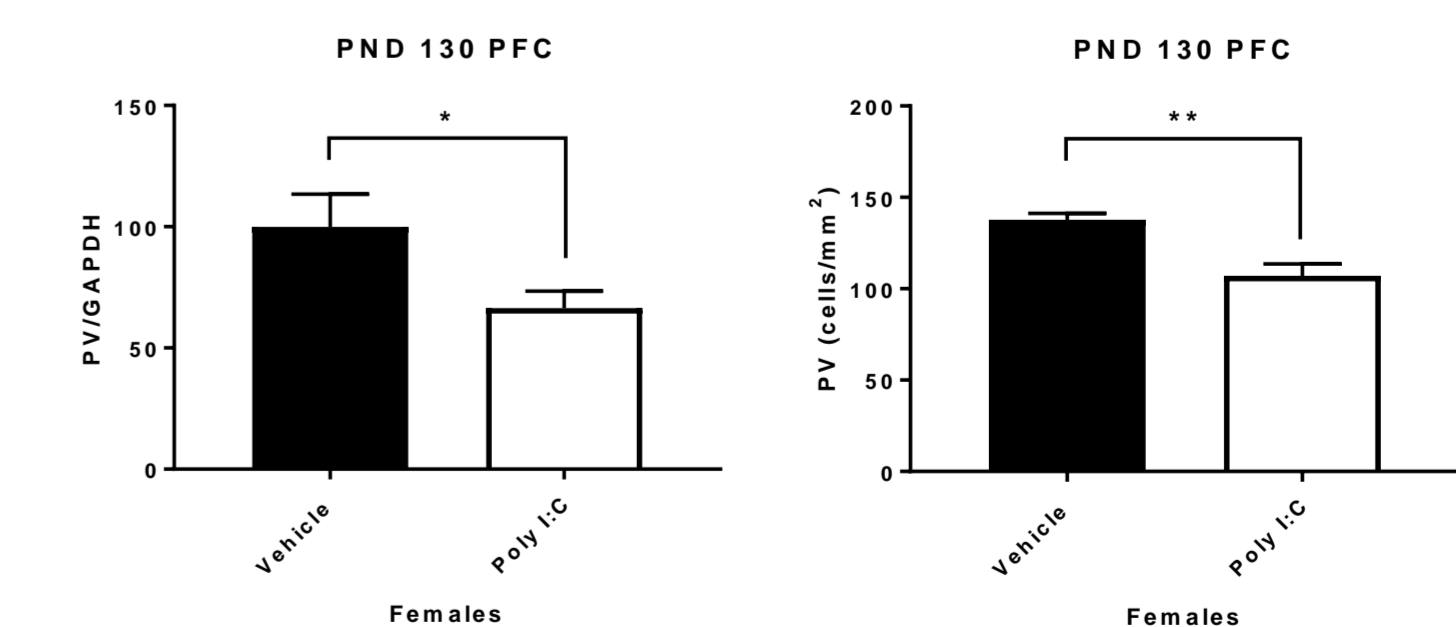
- Poly I:C treatment produces no effect on novel object recognition in adolescent (PND 41) in the male and female offspring.
- Poly I:C treatment impairs novel object recognition in adult (PND 67) female offspring.
- Poly I:C produces a reduction social behaviours in adolescent (PND 39) in the female offspring.
- Enhanced reduction in social behaviours following treatment with Poly I:C in adult (PND 66) in female offspring.
- Poly I:C treatment significantly increases trials to criterion in the EDS phase of the ASST in adult (PND 100) in the female offspring.

### Cohort 1: Parvalbumin levels in PFC at PND 35 and PND 70



- A two-way Anova revealed no significant effect of treatment or sex on PV levels in the Prefrontal Cortex (PFC) at PND35 or PND 70. Data are presented as Mean ± SEM with Vehicle normalised to 100%.

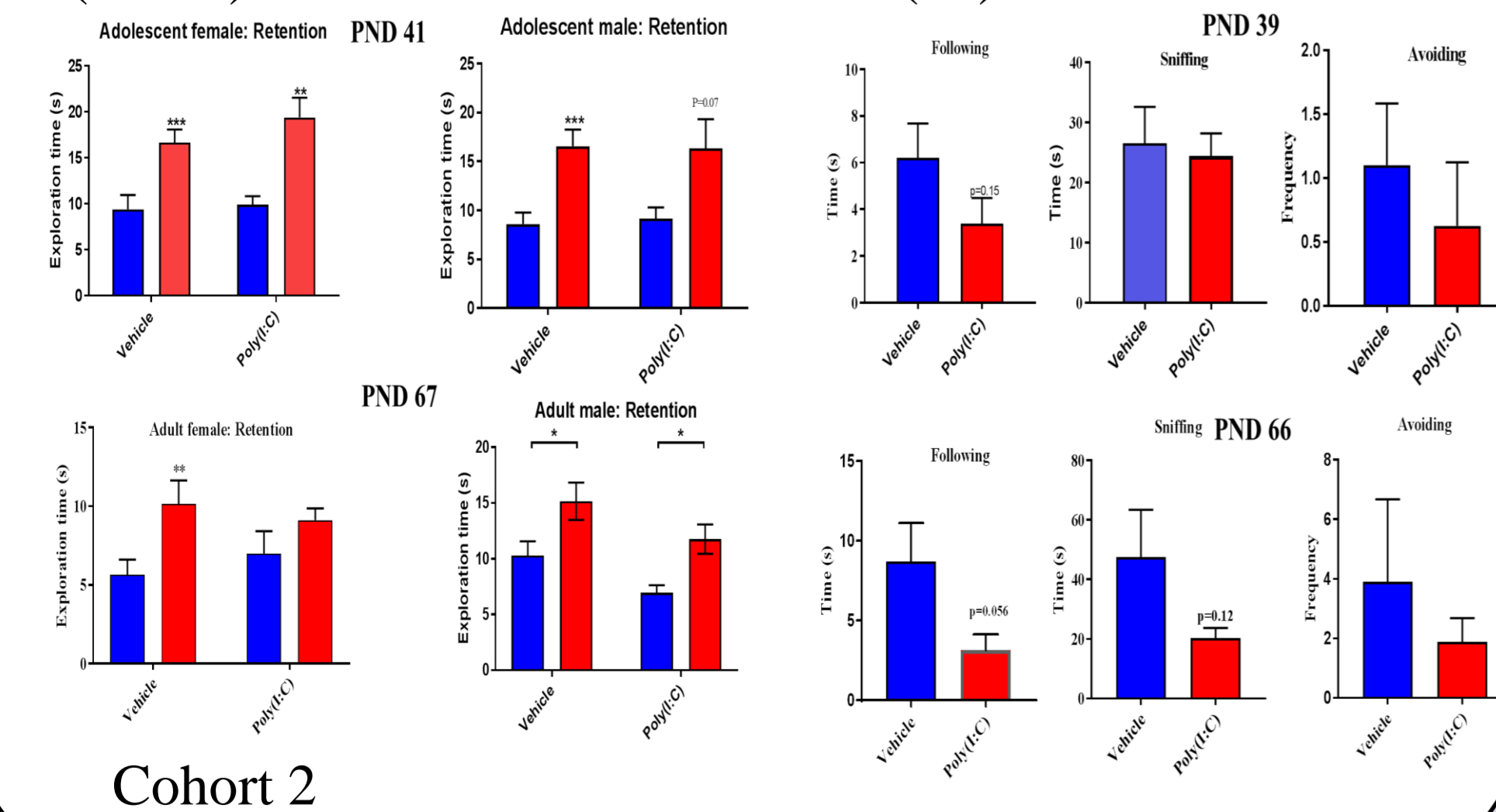
### Cohort 2: Parvalbumin levels in PFC at PND 130



- Univariate General Linear model revealed a significant effect of treatment on PV levels in the Prefrontal Cortex (PFC) at PND130 for both western and immunohistochemistry. Data are presented as Mean ± SEM, \*P<0.05, \*\*P<0.01 vs Vehicle.

### Novel Object Recognition (NOR)

### Social Interaction (SI)



Cohort 2

## Conclusions

- Poly I:C (10mg/kg) produced an inflammatory response in the pregnant dam shown by increases in IL-6 concentration.
- Significant behavioural deficits were not detectable during adolescence.
- Social behaviour deficits seemed to be emerging and a cognitive phenotype was clearly observed in adult females, particularly in the prefrontal cortical mediated ASST at the later stage of PND 100.
- No changes in PFC PV at PND35 or PND70 but a significant decrease in female offspring in adulthood (PND130), suggesting a co-occurrence between the timing of behavioural deficits and reduced PV in the PFC.
- This supports the hypothesis that PV deficits are a mechanism for cognitive dysfunction in this model although further studies are required to understand the origin of the reduced PV.