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Maternal immune activation: A viable candidate for modelling neurodevelopmental disorders in rats?

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Introduction: Epidemiological evidence supports an association between maternal infection and the risk of neurodevelopmental disorders in offspring (e.g. autism spectrum disorder (ASD), schizophrenia). The aim of this study was to validate this model in rats at an early gestational time point gestational day (GD)12.5 and explore the relevance of a behavioural phenotype to ASD.

Methods: Female Wistar rats were injected (i.p) with poly(I:C) (10mg/kg, *n*=12 dams) or saline (*n*=14 dams) at GD12.5. Offspring from these mothers were monitored throughout early development and into adolescence. Social communication was monitored by ultrasonic vocalisations (USVs) at PD9. A dyadic social interaction test (SIT) was performed at adolescence. For monitoring risk-taking behaviour the open field test (OFT) and elevated plus maze (EPM) tasks were also performed. Time spent grooming in the OFT arena was measured as a read-out of repetitive behaviours relevant to an ASD-like phenotype. The following data represents poly(I:C) M/F *n*=24; vehicle M/F *n*=32. For comparisons between offspring of poly(I:C) and saline-treated pups, a nested-ANOVA was performed with litter treated as a random variable. Homoscedasticity and normality (Shapiro-Wilk) test were performed for each data set. (Data presented as mean ± SEM).

Results: A significant reduction in body weight (BW) was shown in pups at PD1 from dams treated with poly(I:C) compared to vehicle in both males and females (p=<0.001) . The significant reduction in BW was maintained at PD9 in males (p=<0.001) but not females. USVs at PD9 and showed no difference between pups from poly(I:C) treated dams vs. saline. Furthermore no significant difference in early social play behaviours was shown by the SIT. In the OFT time spent in the centre was significantly reduced in male poly(I:C) offspring (p=0.027). No significant difference in risk-taking behaviour was found in the EPM. Both male and female offspring from poly(I:C) treated dams showed on average increased grooming in the OFT but this was not significant.

Conclusion: In summary administration of 10mg/kg poly(I:C) in Wistar rats resulted in a reduction in risk-taking behaviour in the OFT but did not induce a significant behavioural phenotype in relevant to ASD in any other test applied. A significant reduction in BW was shown following exposure to mIA. Further validation of this model is required to determine its relevance for neurodevelopmental modelling. Ex vivo brain tissue analysis is underway to explore effects on gene expression relevant for synaptic pruning and other brain markers relevant to neurodevelopmental disorders.