Evaluating social development in a nonhuman primate model of maternal immune activation

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Introduction

Evidence from human epidemiological studies indicates that maternal infection during pregnancy may increase the risk of neurodevelopmental disorders such as autism and schizophrenia in children (1-4). Animal models of maternal immune activation (MIA) have found that maternal cytokines impact fetal brain development and that animals exposed to MIA in utero have altered brain and behavioral development (5). In the rhesus macaque (*Macaca mulatta*) MIA model, we have evidence of atypical social behavior between 1 - 3 years of age: MIA-exposed animals exhibit atypical interactions with novel social partners early in development and a decrease in affiliative interactions with familiar partners in late adolescence (unpublished data). Here, we assess social attention in the rhesus macaque MIA model in two ways: (1) presenting data from eye tracking studies in MIA-exposed offspring as young adults and (2) describing a new social valuation test.

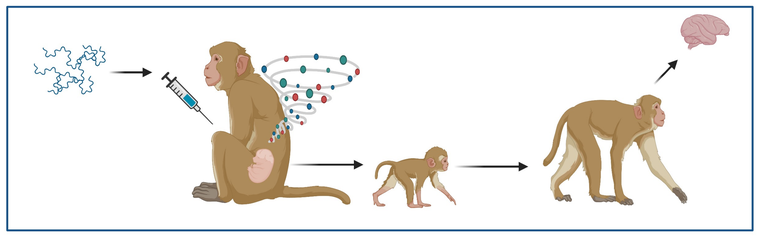

Figure 1. MIA Model Overview. The rhesus macaque MIA model: pregnant animals receive injections of the viral mimic poly I:C during late first trimester of pregnancy. Control dams received saline injections or were untreated. Behavioral and physiological measurements are acquired from offspring from infancy through young adulthood. Figure created with BioRender.com

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Methods

Eye Tracking

28 rhesus male rhesus macaques (N=14 control, N=14 MIA-exposed) were maternally reared until weaning at 6 months of age. After weaning, animals were pair-housed with a familiar peer. Animals were socialized in larger groups for 3 hours each day. (5) Animals participated in non-invasive cooperative eye tracking data collection at 2 years, 3 years, and 4 years of age. At each timepoint, animals were presented with four different facial expressions: neutral, fear grimace (submissive), lipsmack (affiliative), and open mouth threat. Each image was displayed for 15 seconds and each expression was seen 3 different times.

Figure 2. Eye-tracking Data Collection. Animals were placed in a modified transport box and positioned in front of a Tobii Pro TX300 eye tracker (Tobii Technology, Stockholm, Sweden). Gaze data was collected any time the animal looked at the screen. (6)

Social Valuation

Two rhesus macaques (1 male, 1 female; approximately 1 year of age) were presented with two different video conditions: nature and social. Latency to take a food reward was measured under each condition.

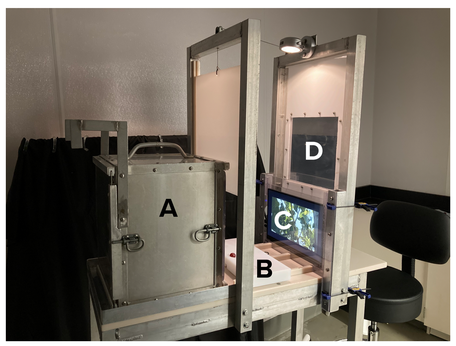

Figure 3. Social Valuation Task. Animals were placed in a modified transport box (A) with a clear plexiglass front and openings so that they could reach out of the box to retrieve food positioned on the treat presentation tray (B). Videos were displayed on a monitor (C) positioned behind the tray. The experimenter was positioned behind a one-way mirror (D).

Results

Eye Tracking

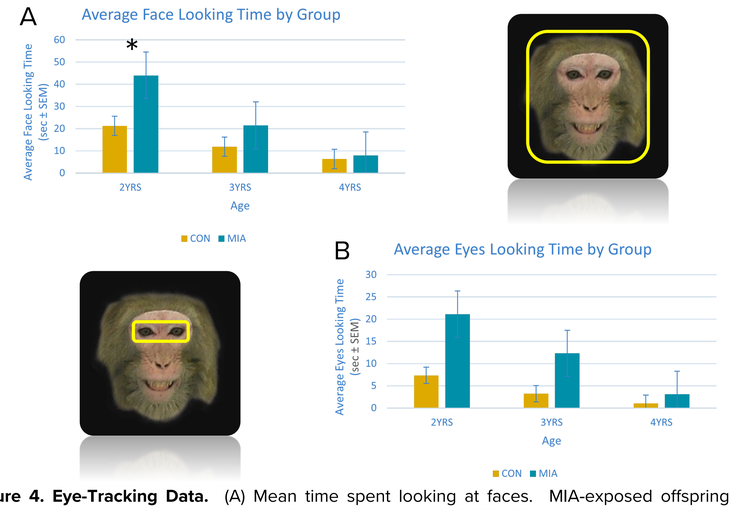

Figure 4. Eye-Tracking Data. (A) Mean time spent looking at faces. MIA-exposed offspring spent more time looking at faces at the 2-year time point ($p < 0.05$). The groups did not differ at the 3-year or 4-year timepoints. (B) Mean time spent looking at eye-regions. Trend level differences at the 2-year time point suggest that MIA-exposed offspring may also spend more time looking at the eye region ($p = 0.07$). The groups did not differ at the 3-year or 4-year timepoints. Bars represent mean looking time (sec) +/- SEM.

Social Valuation

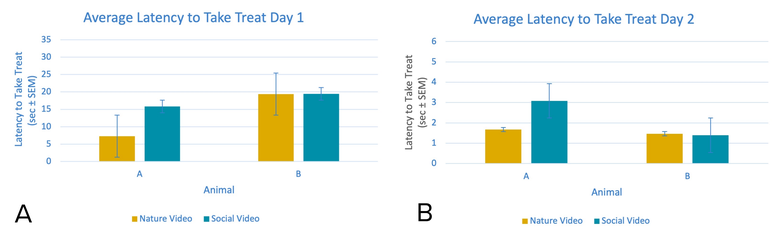

Figure 5. Preliminary Social Valuation Data. Mean latency to retrieve the food reward when viewing nature or social videos on Day 1 (A) or Day 2 (B). Bars represent mean latency (sec) +/- SEM.

Discussion

Rhesus monkey offspring born to MIA-treated dams show increased times looking at the faces and eyes of facial expressions. These differences in gaze patterns occur at a similar time in development when we also see subtle differences in social behavior.

In the future, we plan to implement a social valuation test to further probe differences in social attention in developing rhesus macaques.