

Prenatal cafeteria diet exposure promotes lymphocyte infiltration into the brain and autism-like behavior in the offspring of C57BL6 mice

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ABSTRACT

BACKGROUND. Autism spectrum disorder (ASD) is a neurodevelopmental disorder with an array of etiological causes, including environmental, genetic, and immunological triggers. High-energy diets activate the immune system during prenatal stages favoring infiltration of peripheral immune cells and cytokines into the brain by the choroid plexus and circumventricular regions and altering microglial activity. Accumulation of immune entities and microglia activation in brain have been reported to disrupt social behavior. However, the interplay between prenatal exposure to high-energy diets, neuroinflammation and defective social behavior has not been reported. **METHODS.** Female C57BL6 mice were exposed to cafeteria diet during pregnancy and lactation. The effect of diet on social, locomotor, repetitive-stereotyped, and anxiety-like behavior was evaluated in the male offspring two-month-old. We quantified the number of infiltrating natural killer (NK1.1⁺), dendritic (CD11c⁺), lymphocytes (CD11b⁻-CD45⁺), macrophages (CD11b⁺-CD45^{high}), and M1 (CD11b⁺-CD45^{low}-CD86⁺) or M2 (CD11b⁺-CD45^{low}-CD206⁺) microglia in the choroid plexus and cerebral cortex, hippocampus, and striatum of the male offspring by flow cytometry. **RESULTS.** Our results demonstrated that exposure to cafeteria diet during prenatal stage primed defective social interaction and repetitive-stereotyped behaviors in male offspring. Flow cytometry analysis showed lymphocyte infiltration in the cerebral cortex and hippocampus compared to the choroid plexus in the offspring exposed to cafeteria diet. No significant changes were observed in the NK, dendritic or macrophage levels in the choroid plexus and the cerebral cortex, hippocampus, and striatum regions of those subjects. The effect of cafeteria diet exposure also did not affect microglial density or M1/M2 phenotypes. **CONCLUSIONS.** Our results indicate that exposure to a cafeteria diet during prenatal development promotes an increase of lymphocytes in brain regions of importance for ASD that could contribute to the behavioral defect in the offspring. Testing the contribution of lymphocyte infiltrates in the development of ASD-like behaviors could better explain the cellular mechanisms related to the disorder.