Effects of Maternal Separation on Microglia and Immune Marker Expression in the Central Nervous System

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Maternal Separation Model and Its Effects in the Developing Brain?

- Maternal separation is a widely used rodent experimental model to study Adverse Childhood Experiences (ACEs) in humans.
- It includes separation of pups from the mother for a certain period daily during early weeks after birth.
- Research has been linked to neurobiological and behavioral alterations in offspring.

Wikimedia, Seweryn Olkowicz

Hypothesis

- Maternal separation increases neuroinflammation in the offspring's developing brain.
- Offspring's early development plasticity is altered.

Importance of Study

Model for Adverse Childhood Experiences (ACEs) in Humans.

Linked between early life stress and increased risk for depression, substance abuse, and many other factors.

Neuroinflammation has been linked to several neuropsychiatric illnesses.

Microglia contributes to neuroinflammation with an important role in synaptic pruning.

Microglia and Immune Markers

- Microglia are glia cells that provides support and protection to neurons in the Central Nervous System (CNS).
- Iba1 and MerTK are widely used markers for microglia.
- Iba1 has a key role in phagocytosis and is involved in morphological changes of microglia.
- MerTK has a role in phagocytosis and regulating microglia activation state.

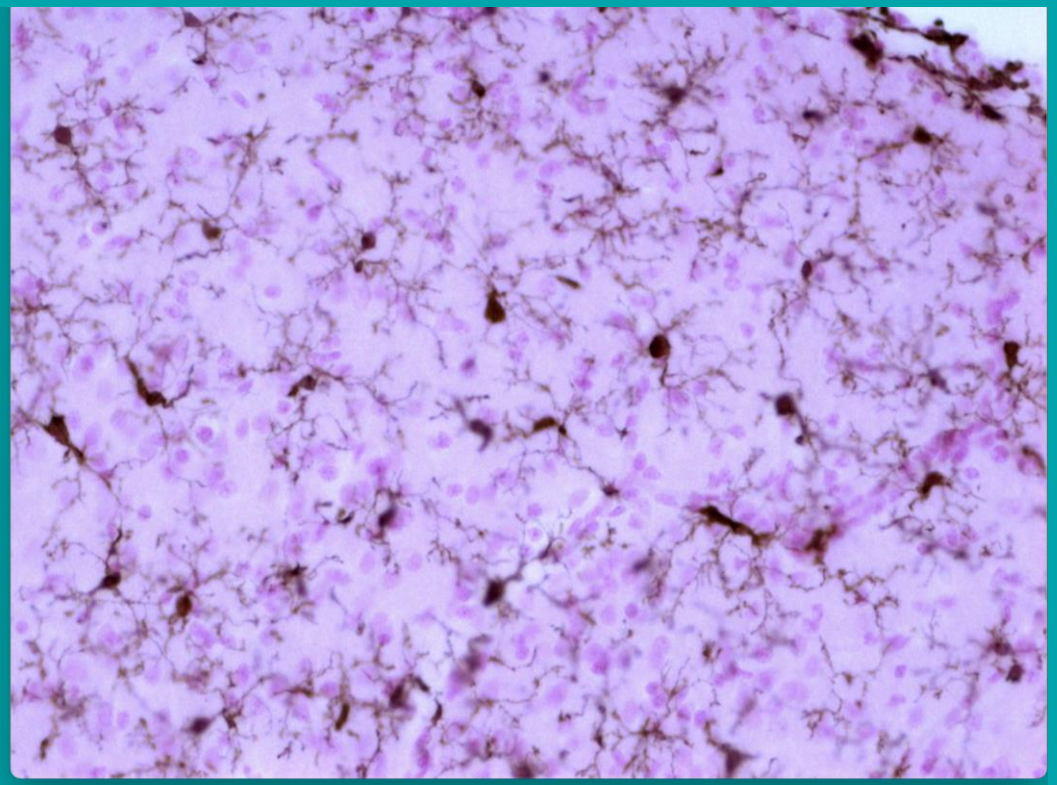
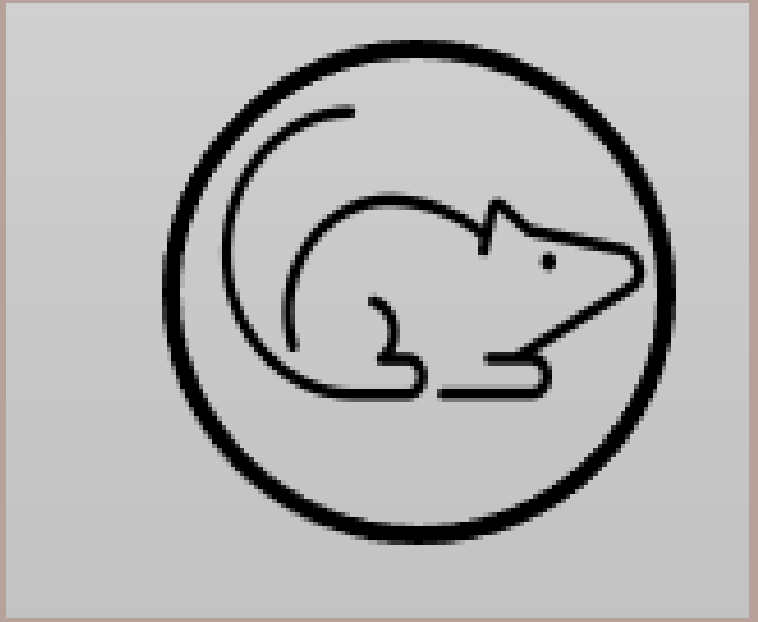


Photo by Marques Jackson, PhD

Mouse Model

- tg-FGFR1-eGFP mouse line
  - Developed in GENSAT project
  - GENSAT modified bacterial artificial chromosome (BAC) BX1215, containing the eGFP protein inserted into the 5’ UTR of the FGFR1 gene
  - SWISS-Webster

All animal procedures are followed according to IACUC policies



https://www.taconic.com/mouse-model/swiss-webster

Experimental Design

01

Mating Pair/ Trio. Set up and track pregnancy.

02

From P1 experimental pups removed from the home cage

03

Away cage from 7 P.M to 10 P.M (3 hours) a day up to P14

04

Weight recorded and returned to home cage.

Research Findings

- An upregulation of Interleukin 6 (IL-6) was observed after maternal separation.
- An ongoing investigation is being conducted to determine the correlation between microglia cell number and activation.
- Immunohistochemistry for IBA1 and MerTK will be used to visualize proteins associated with microglia.

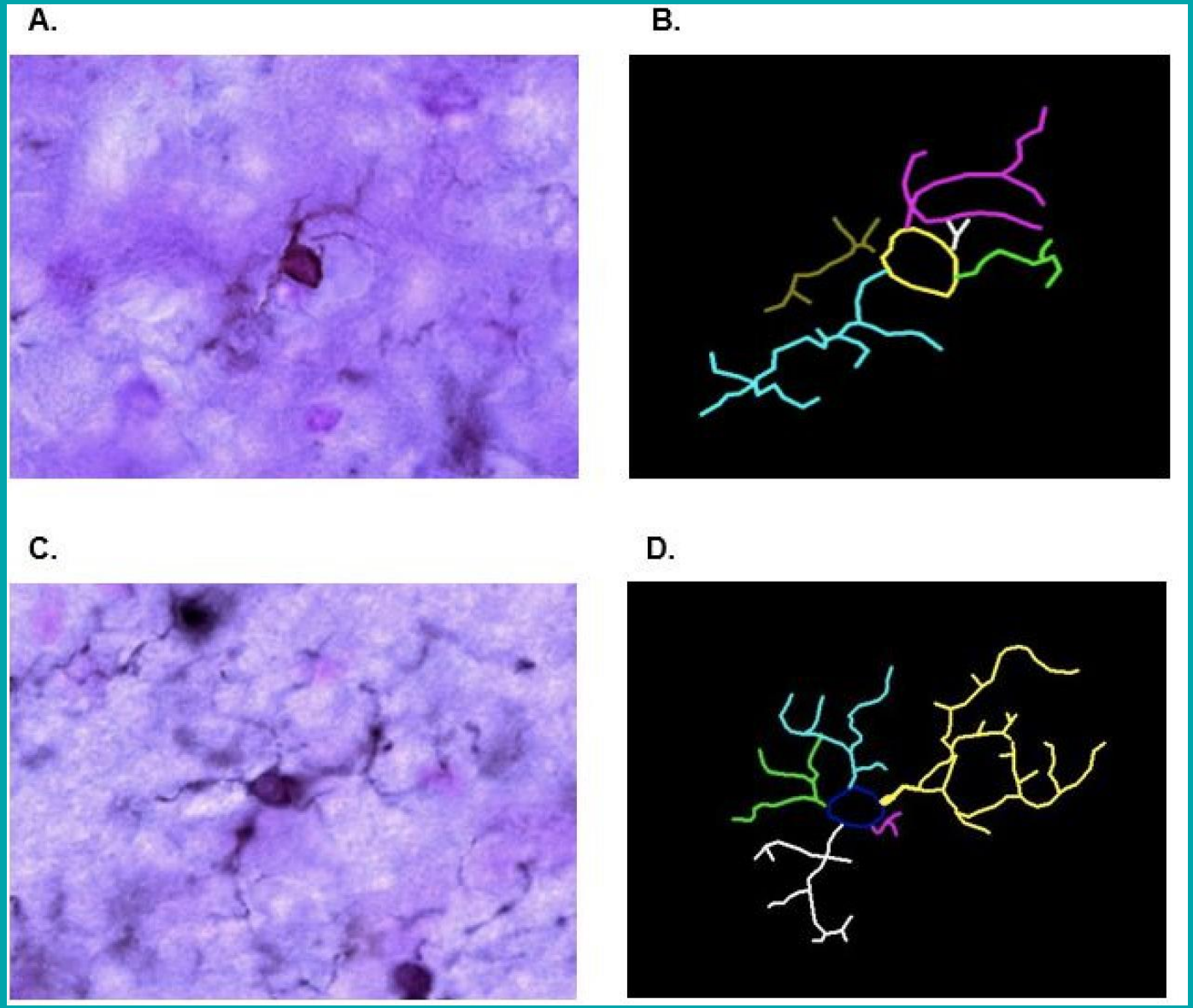


Photo by Marques Jackson, PhD

Significance of Results

- Studying the impact of maternal separation is crucial for understanding how early life stresses affect long-term neurodevelopment.
- Also, it enhances our understanding of the molecular and cellular mechanisms behind neurological and behavioral changes.
- Our findings can pave the way for targeted interventions to mitigate potential negative effects on early life stress on the developing brain.

Future Directions

1. Findings from this research can serve as pathophysiological connection between ACEs and various ACE-driven neurological disorders.
2. Discovering elevated reactive and phagocytic microglia can guide further potential therapeutic strategies to address the enduring impacts of early life stress on brain development.
3. Apart from the uncovering molecular basis to many neuropsychiatric disabilities, exploring resilience factors could inform preventive strategies for individuals exposed to ACEs


Questions?