Introduction

- In 2016, CDC estimated that 50M people were suffering from chronic pain, and close to 20M adults had chronic pain which was identified as “high impact chronic pain” [2]
- Chronic pain is a condition in which a longstanding pain can impact someone’s quality of life, such as low back pain, migraine, etc. [3].
- Pain Chronification is often associated with memory deficits and cognitive impairment, which draws attention towards Hippocampus, which plays an essential role in memory formation and storage.

Significance

- The Extracellular matrix component is often overlooked in pain-related studies.
- It can provide evidence to support the pain centralization theory.
- Parallel studies at our lab focus on in vivo and ex vivo effect of ECM on chronic pain.
- Most importantly this study can help to innovate a better and more efficient therapeutic option to manage chronic pain.

Materials and methods

Animals: C57Bl/6J mice aged 12–14 weeks were purchased from a commercial supplier (Jackson Labs, Sacramento, CA, USA) and were housed in groups of 4 on a 12-hr light/dark cycle and an ambient temperature of 22 ± 3 °C, with food and water available ad libitum.

Hippocampus extraction [6]: Mice were euthanized by decapitation method under isoflurane anesthesia. The brain was removed from the skull by using aseptic techniques. After removing the tissue covering medial side of the hippocampus, by using a spatula the hippocampus was isolated and collected in a 15ml centrifuge tube containing cold L-15 conditioned media (Leibowitz L-15 + 0.1% BSA + 1% Penicillin/Streptomycin).

Hippocampus Extracellular Matrix preparation [7]: The process of Decellularization uses series of baths: Water, 0.02% Trypsin/0.05% EDTA, 3.0% Triton X-100, 1.0M sucrose, 4.0% ethanol and PBS in addition to incubation and centrifugation to isolate Extracellular Matrix from hippocampus tissue.

Cell culture: BV-2 cells derived from murine neonatal microglia used substitute for primary microglia. All cells were cultured in growth medium (DMEM) supplemented with 10% FBS, 1% penicillin & streptomycin. Cultures were maintained at 37 °C with 95% humidity and 5% CO2.

Figure 1: Hippocampus location in the brain and its Extracellular matrix component.

Figure 2: Schematic of culturing BV-2 cells on decellularized hippocampus collected from injured and uninjured mice.

Decellularized hippocampus + BV-2

Hippocampus extracellular matrix

Hypothesis

- Upon SNI, the Resting/Activated microglia ratio changes.
- Pro-inflammatory Cytokines will be found in Hippocampus.
- Inflammation causes ECM remodeling.
- This change ultimately correlates with persistent pain.

Acknowledgments

- Members of Tajerian’s lab at Queens College, Dr. Tajerian and Dr. Alvarado.
- Members of the Zakeri ‘Cell Death’ lab (Queens College of CUNY), Dr. Lockshin and Dr. Zakeri.
- This work has been funded by NIH # 2T34GM070387 Grant and MARC-USTAR.

References

8. Tajerian, T., et al., Microglia from resting to active as a ‘Cell Death’ lab (Queens College of CUNY), Dr. Lockshin and Dr. Zakeri.
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Impact Chronic Pain Among Adults


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