Role Of Extra Cellular Matrix In Brain Plasticity In Context Of Pain Chronification

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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

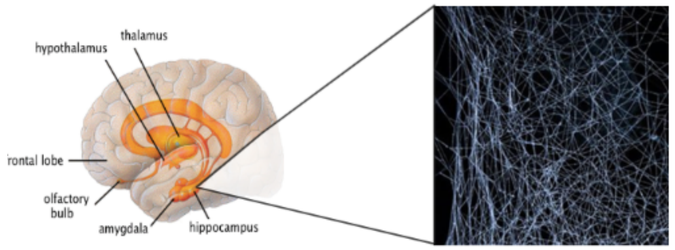

Figure 1: Hippocampus location in the brain and its Extracellular matrix component

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 focuses 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

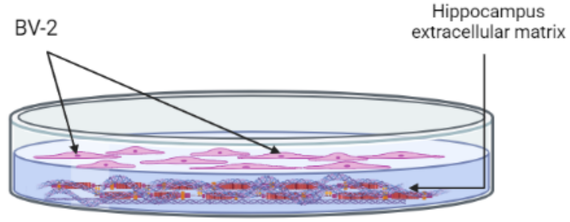

Figure 2: Schematic of culturing BV-2 cells on decellularized hippocampus collected from injured and uninjured mice

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.

Decellularized hippocampus

+

BV-2

↓

Observing microglia morphology by using florescence microscope

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

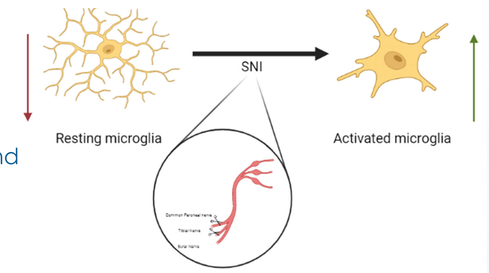

Figure 3: change in morphology of microglia from resting to active as a result of SNI

The importance of extracellular matrix in brain plasticity and pain chronification by using De-cellularized hippocampal sections from injured and uninjured mice

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