THE ENDOCANNABINOID SYSTEM & TRANSITION OF ACUTE TO CHRONIC PAIN IN THE TRAUMATICALLY INJURED

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PAIN AND INJURY

• Acute pain is an inevitable and important part of injury, it protects the individual against further tissue damage.
• Chronic pain is not a protective mechanism\textsuperscript{1} and has a highly negative effect on the quality of life after injury.\textsuperscript{2}
• The prevalence of chronic pain one year after major physical trauma may be as high as 62% and 30% have moderate to severe pain\textsuperscript{3,4}
• The risk for the development of chronic pain can potentially affect 30 million trauma victims each year\textsuperscript{5}
Little is known about the mechanism of this progression in the traumatically injured.

There are few reliable or clinically significant biomarkers.

Clinical and preclinical studies have begun to elucidate the process of this transition.
TRANSITION OF ACUTE TO CHRONIC PAIN

Most of our understanding comes from identification of risk factors at a population level that are associated with the development of chronic pain.

Many studies have identified acute pain intensity as a significant contributor to the development of chronic pain.\(^7,8,9,10,11\)

In agreement, our group found that initial pain predicts the development of chronic pain 4 months post injury and that discharge pain score is highly, positively correlated with 4-month pain score.\(^12\)

Preclinical research suggests a role for the endocannabinoid signaling system (ECSS) in pain.
ENDOCANNABINOID SYSTEM AND PAIN

• Activation of CB1 results in analgesia, it is hypothesized that the mobilization of AEA functions as a feedback mechanism to reduce activation of ascending pain systems, while also protecting against excitotoxicity of the pain system by reducing glutamate release.\textsuperscript{16}

• AEA is catabolized in the nervous system by fatty acid amide hydrolase (FAAH).\textsuperscript{17}

• Several inhibitors of FAAH have been synthesized and demonstrated to produce analgesia in preclinical models through an indirect agonist effect at cannabinoid receptors.\textsuperscript{18}
RESEARCH QUESTION

• What role does the EC system play in the transition of acute to chronic pain in the traumatically injured?

HYPOTHESIS

• Serum EC concentrations correlate with pain scores at baseline and 6 months after traumatic injury.

• Individuals expressing the rare allele (AA) in rs324420 in the gene for fatty acid amide hydrolase (FAAH) are at greater risk to transition to chronic pain.
METHODS

STAR STUDY
RESULTS

- 2-AG at baseline was significantly positively correlated with pain interference at 6 months ($r=0.197, p=0.01$).
- AEA at 6 months was significantly positively correlated with both pain severity ($r=0.164, p=0.04$) and pain interference ($r=0.191, p=0.02$) at 6 months.
- Participants homozygous for the rare genetic allele (AA) at re324420 in FAAH had significantly higher 6 month pain severity compared to the other genotypes (likelihood ratio = 10.431; $p = .034$, Cramer’s V = 0.175).
- Pain scores and PTSD were highly correlated both at baseline and at 6 months ($r=0.3, p<0.001; r=0.4, p<0.001$).
RESULTS
CONCLUSIONS

The ECSS is known to play a role in both the perception of pain and psychological distress.

Similar to previous studies, pain and PTSD was highly comorbid in this population.

These data suggest higher levels of 2AG at baseline and AEA at 6 months may play a role in the development of chronic pain.

Those with genetic FAAH over expression if the rare allele will have higher AEA, and the finding that these individuals have higher pain scores at 6 months is consistent with higher serum AEA also correlating with chronic pain.

These data support the hypothesis that ECSS may play a pivotal role in the development of chronic pain from acute traumatic injury and is potentially a target for intervention, yet more investigation is needed.
NEXT STEPS

Evaluate

- Evaluate the relationships between pain, psychological distress, and the ECCS

Explore

- Further longitudinal exploration of ECSS and the transition to chronic pain
  - Develop a mechanistic model
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QUESTIONS?

References: