Investigating Sociodemographic Differences in Endocannabinoid Responses to Chronic Pain and Stress in Pediatric Populations

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Background

- Chronic pain is defined as persistent pain lasting longer than 3 months (Chambers et al., 2024)
  - Primary chronic pain is not better defined by another condition
- Overall, chronic pain prevalence among children and adolescents aged 0-19 worldwide is approximately 20.8% (Chambers et al., 2024)
- Primary chronic pain can often be attributed to central sensitization of the nervous system, creating a heightened hyper-responsiveness to pain due to the wear and tear affecting stress and pain pathways
- Endocannabinoids mitigate stress and nociceptive processes within the eCB system
- Sociodemographic inequalities including systemic racism, discrimination, & oppressive lived experiences can cause added stress overwhelming developing nervous systems

Exposure to psychosocial stressors may alter biological stress regulatory systems in developing youth, yet little research has examined whether sociodemographic differences in stress exposures are associated with eCB expression among youth with chronic pain

Aims

- Examine whether endocannabinoid expression moderates the association between stress exposure and pain-related outcomes within pediatric populations
- Determine associations between trauma exposure and biological stress response activity in youth with chronic pain
- Examine sociodemographic differences within endocannabinoid levels among youth with chronic pain

Methods & Materials

Sample Size:
42 youth (ages 11-17); **CWP: n = 21, HC: n = 21**

Study Measures

- Psychosocial functioning was assessed using self-reported questionnaires (PROMIS) of anxiety, depressive symptoms, stress, adversity exposure, and sleep disturbances
- Pain intensity was assessed and a composite pain score was created using self-reported numeric rating scale (NRS) of "worst" and "usual" responses of pain.
- Salivary concentrations of endocannabinoids were collected via passive drool upon waking and summarized into combined factors of AG_factor and EA_factor which reflect arachidonoyl glycerol-like (2-AG) and anandamide-like (AEA) cannabinoids.
  - Including PEA, OEA, SEA, AEA, AG1, and AG2
- Statistical analysis for pain measures, psychological functioning, sociodemographic, and endocannabinoid differences were analyzed using SPSS using ANOVA, along with Hayes' PROCESS macro to examine moderation regressions

Results

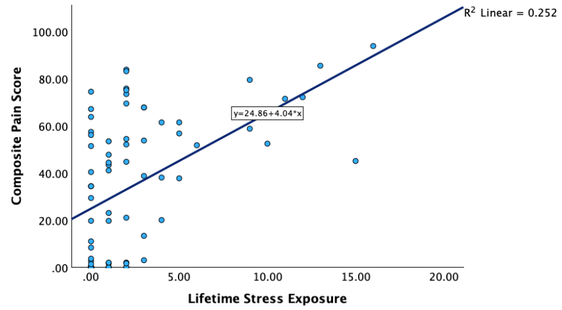

Figure 1. Stress Exposure Predicts Chronic Pain Intensity
Scatterplot examining total childhood traumatic events compared to composite pain data.
Greater lifetime stress exposure predicted increased pain intensity (R^2 = .252, p < .001)

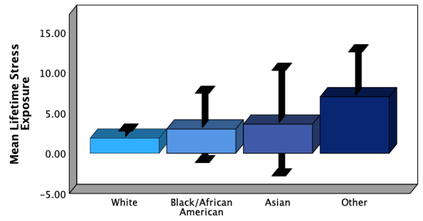

Figure 2. Lifetime Stress Exposure by Race
Bar graph examining total childhood traumatic events compared to Race. Minoritized youth reported significantly greater lifetime stress exposure (p = .003)

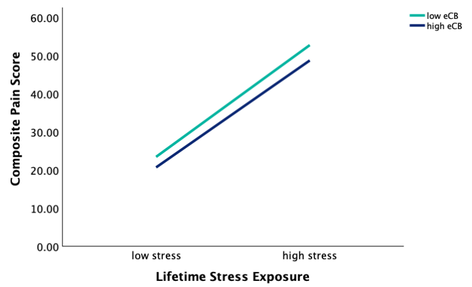

Figure 3. eCB Expression Moderates the Stress-Pain Relationship.
Multiple-line graph examining eCB expression, which significantly moderates the association between lifetime stress exposure and pain intensity. Youth with lower eCB expression demonstrated a stronger stress-pain relationship

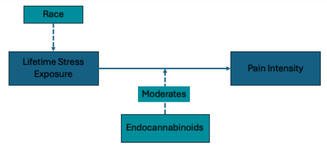

Figure 4. Conceptual Neurobiological Moderation Model
Lifetime traumatic stress contributes to pain intensity, with eCB expression moderating this relationship

Results Summary

- Greater lifetime stress exposure was significantly associated with increased pain intensity, with higher traumatic event exposure predicting increased composite pain scores.
- Lifetime stress exposure differed significantly by Race, where racial/ethnically minoritized youth reported more traumatic events compared to White pediatric patients
- Pain intensity is strongly associated with psychological distress of self-reported stress, anxiety, depression, and sleep disturbance (all ps < .001).
- Importantly, endocannabinoid expression significantly moderated the association between lifetime stress and pain intensity with the full moderation regression model explaining 33% of variance (R^2 = .33, p < .001).
  - Youth with lower eCB expression reported higher overall pain intensity levels and exhibited a steeper increase in pain as chronic stress exposure increased.
  - Youth with higher eCB expression demonstrated comparatively lower pain intensity levels and a weaker lifetime stress exposure to composite pain association.
- Attenuated eCB expression may indicate vulnerability to poorer pain outcomes, whereas higher eCB expression may attenuate the association between stress and pain, suggesting a protective effect.

Overall Takeaway

These findings support a biopsychosocial model in which increased traumatic stress within minority populations contributes to pediatric chronic pain, with endocannabinoid functioning shaping neurobiological vulnerability within youths developing nervous systems.

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The authors report no conflict of interest.

References

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