Examination of the Moderation Effect of Childhood Trauma on Glutamatergic Modulation for Treatment of PTSD symptoms in OEF/OIF Service Members and Veterans

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INTRODUCTION

- Available pharmacological treatments of posttraumatic stress disorder (PTSD), such as selective serotonin reuptake inhibitors (SSRIs), are limited in their effectiveness
- There is a need to examine other mechanisms, such as glutamatergic agents, in treating PTSD symptoms
- Riluzole, a glutamatergic modulator did not show efficacy in reducing PTSD symptoms
- However, a history of childhood trauma (CT) in combat-exposed veterans is associated with worse PTSD and depressive symptoms; little is known about the influence of CT on pharmacologic treatment of PTSD
- Ketamine, a glutamatergic modulator, drug trials for depression have found that history of CT prompted a greater reduction in depressive symptoms.
- The current study aimed to determine if history of CT influences the relationship between use of the glutamatergic modulator riluzole and PTSD symptoms over time

METHODS

- This study is a secondary analysis of an RCT for riluzole augmentation treatment for PTSD
- Participants were 18-65 years old, with a history of combat deployment, a diagnosis of PTSD, and on a stable SSRI/SNRI dose without remission of PTSD symptoms
- Participants were randomized to placebo or riluzole treatment at 50-100mg 2x/day for 8 weeks
- Outcomes were assessed at baseline, week 4, and week 8 via the Clinician-Administered PTSD Scale – IV(CAPS-IV) for PTSD
- CT was defined at baseline of a score of ≥ 8 on any trauma subtype of ≥ 15 for emotional neglect using the Childhood Trauma Questionnaire-Short Form

Individuals with history of high CT had a significantly greater reduction in PTSD symptoms with riluzole augmentation than those with no/low CT history

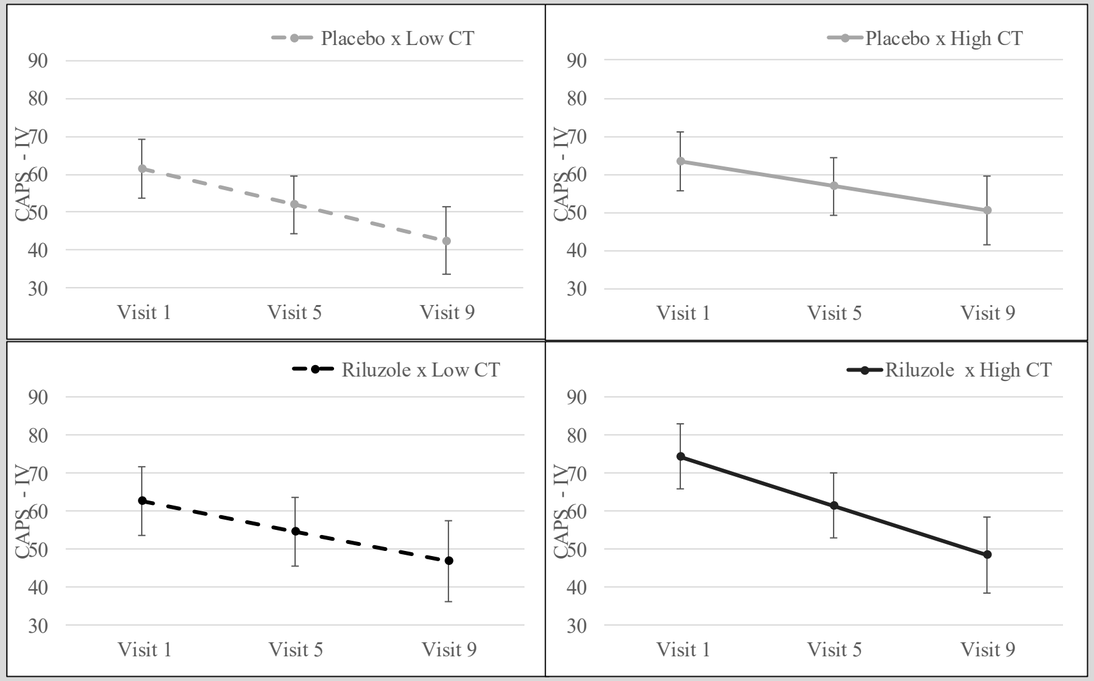

Figure 1. Estimated CAPS symptom trajectories by treatment group and CT designation

RESULTS

The three-way interaction between treatment group (riluzole versus placebo), CT designation (high CT versus no/low CT), and study visit (time) was significant for the CAPS-IV (B = -2.027, SE = 0.983, t = -2.062, p = 0.042).

Simple slopes analyses revealed that while CAPS scores decreased significantly over time for all participants, among those with high CT, those who received riluzole augmentation had a significantly steeper reduction in CAPS scores over time (B = -3.23, 95% CI [-4.20, -2.27]) compared to those receiving placebo (B = -1.60, 95% CI [-2.72, -0.47]).

DISCUSSION

- A three-way interaction for CAPS was observed
- However, the study was underpowered to robustly detect three-way interactions, and confidence intervals are wide
- This finding should be interpreted cautiously as exploratory
- Despite these limitations, these findings highlight the potential benefits of PTSD treatment for individuals with history of CT
- These findings might offer insight into stress sensitization that may happen in childhood that could interact with glutamate modulation to perpetuate PTSD symptoms following later life trauma exposure
- Future research is needed to further elucidate this relationship in a larger sample size

REFERENCES

For references, please follow the CR code

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