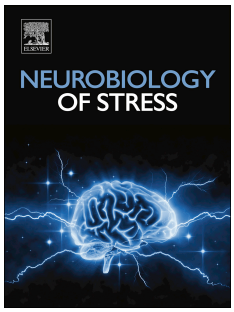
Accepted Manuscript



Evidence for altered brain reactivity to norepinephrine in Veterans with a history of traumatic stress

Rebecca C. Hendrickson, Murray A. Raskind, Steven P. Millard, Carl Sikkema, Garth E. Terry, Kathleen F. Pagulayan, Ge Li, Elaine R. Peskind

PII: S2352-2895(17)30039-5

DOI: 10.1016/j.ynstr.2018.03.001

Reference: YNSTR 103

To appear in: *Neurobiology of Stress*

Received Date: 25 September 2017

Revised Date: 14 March 2018

Accepted Date: 14 March 2018

Please cite this article as: Hendrickson RC, Raskind MA, Millard SP, Sikkema C, Terry GE, Pagulayan KF, Li G, Peskind ER, Evidence for altered brain reactivity to norepinephrine in Veterans with a history of traumatic stress, *Neurobiology of Stress* (2018), doi: 10.1016/j.ynstr.2018.03.001.

Abstract

Background: Increases in the quantity or impact of noradrenergic signaling have been implicated in the pathophysiology of posttraumatic stress disorder (PTSD). This increased signaling may result from increased norepinephrine (NE) release, from altered brain responses to NE, or from a combination of both factors. Here, we tested the hypothesis that Veterans reporting a history of trauma exposure would show an increased association between brain NE and mental health symptoms commonly observed after trauma as compared with Veterans who did not report a history of trauma exposure, consistent with increased the possibility of increased brain reactivity to NE after traumatic stress.

Methods: Using a convenience sample of 69 male Veterans with a history of combat-theater deployment, we examined the relationship between trauma-related mental health symptoms and the concentration of NE in cerebrospinal fluid (CSF). CSF NE levels were measured by HPLC in CSF from morning lumbar puncture. Behavioral symptoms associated with diagnoses of PTSD, depression, insomnia or post-concussive syndrome (PCS), which together cover a wide variety of symptoms associated with alterations in arousal systems, such as sleep, mood, concentration, and anxiety, were assessed via self-report (PTSD Checklist [PCL] for PTSD, Patient Health Questionnaire 9 [PHQ9] for depression, Pittsburgh Sleep Quality Index [PSQI] for sleep problems including insomnia, and Neurobehavioral Symptom Inventory [NSI] for PCS), and structured clinical interview (Clinician Administered PSTD Scale [CAPS]). Individuals meeting criterion A of the DSM-IV diagnostic criteria for PTSD were considered trauma-exposed. Linear regression models were used to quantifythe the association between CSF NE and symptom intensity in participants with and without a history of trauma exposure, as well as in participants with a history of trauma exposure but who were currently taking the noradrenergic receptor antagonist prazosin.