Investigating Minocycline as a Modulator of Perceived Stress Among Chronically Stress Adults

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Melinda Somers

Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill

Introduction

- Chronic stress leads to an exaggerated proinflammatory response in the brain, perturbing healthy brain function (Calcia et al., 2016)
- Minocycline is an anti-neuroinflammatory agent that has been found to reverse anxiety-like and depressive-like behaviors in rodents undergoing chronic stress paradigms (Liu et al., 2018; Wang et al., 2018)
  - It is suggested that microglial activation mediates these behavioral changes.
- Clinically, minocycline has been found to ameliorate symptoms of depression in some studies with treatment-resistant depression patients (Miyaoka et al., 2012; Nettis et al., 2021)
  - Conflicting results show no improvement in depression (Hellman-Regen et al., 2022)

How does minocycline alter perceived stress when looking beyond psychiatric diagnosis?

Methods

Enrollment Visit **(N = 18)**
- unemployed adults aged 25-60
- stressed about employment status and actively seeking work

Medication Period 1
- 5 days (minocycline or placebo)
- daily stress questionnaire (generalized stress + job stress)

Study Visit 1
- PSS-10

2-week washout

~ 1 month

Double-blinded, crossover, placebo-controlled design

Medication Period 2
- 5 days (minocycline or placebo)
- daily stress questionnaire (generalized stress + job stress)

Study Visit 2
- PSS-10

Results

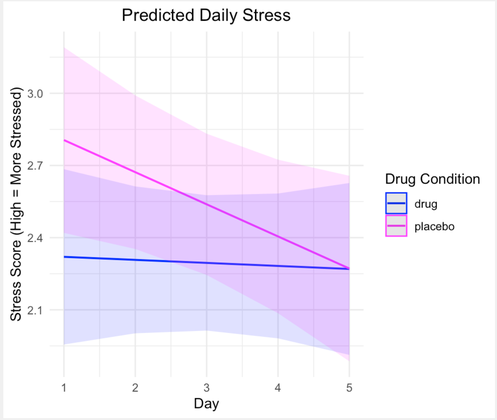

Figure 1. A multilevel model was run to understand the effects of drug condition (minocycline vs. placebo), medication day (out of a five-day medication period), and drug condition x medication day interaction on a single-item generalized stress question. Analyses control for sex, gender, and socioeconomic status. A significant main effect of drug condition on stress score was detected (β = .036, *SE* = .286, *p* = .04). No significant main effect of medication day nor drug condition x medication day interaction were found.

Minocycline had a **significant main effect** on the single-item generalized stress score as compared to placebo.

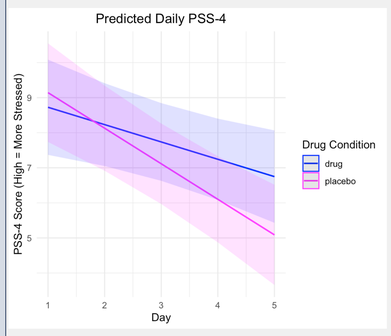

Figure 2. A multilevel model was run to understand the effects of drug condition, medication day, and drug condition x medication day interaction on the 4-item Perceived Stress Scale adapted to ask about job-related stress. Analyses control for sex, gender, and socioeconomic status. A significant main effect of medication day on PSS-4 score was found (β = -.494, *SE* = .189, *p* = .01). No significant main effects of drug condition nor drug condition x medication day interaction were found.

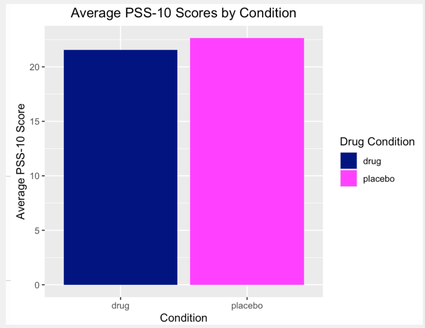

Figure 3. A paired samples t-test indicated no significant differences between the medication conditions on the PSS-10 at Day 6 following the 5-day medication period (*t*(1,29) = -.532, *p* = .60). Descriptively, the average stress score was lower in the minocycline condition (*M* = 21.56) as compared to the placebo condition (*M* = 22.64).

Minocycline had **no significant effect** as compared to placebo on job-related stress or stress on Day 6 following the medication period.

Conclusions

- A 5-day course of minocycline attenuated symptoms of stress among chronically stressed, healthy adults.
- The mechanism by which minocycline has been found to improve depression may lie in its ability to mitigate certain symptoms, such as perceived stress.
- Interventions targeting stress-induced neuroinflammation may be useful in developing therapeutics to enhance overall health

Future Work

- Capture neural correlates of stress
- Collect biomarkers of inflammation (e.g. IL-6, CRP, etc.)
- Collect self-report + physiological stress (e.g. heart rate variability)
- Structured clinical interviews to verify diagnostic status
- Control for time of drug implementation + stress measurement

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