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Association of Cortisol & Allostatic Load with PTSD Symptoms following mTBI: A NEXUS Study

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Introduction

- Mild traumatic brain injury (mTBI) accounts for most civilian and military TBI.
- Allostatic load (AlloL) represents the cumulative impact of chronic stress and life events, measured through biomarkers and clinical symptoms, that may influence psychological health (PH) and limit mTBI recovery.
- Cortisol (CORT) is a complex biomarker that can reflect an acute trauma response in the context of chronic AlloL.1
- Here, we report how systemic CORT and AlloL affect PH symptom burden in an adult civilian cohort with acute mTBI versus orthopedic injury (OI).

Materials and Methods

We enrolled military-aged civilians within 72 hours of injury (mTBI, N=120; OI, N=84). At enrollment, participants completed multiple PH and AlloL measures:

- PH
  - Generalized Anxiety Disorder (GAD-7)
  - Patient Health Questionnaire (PHQ-9)
  - Post-traumatic Stress Disorder Checklist (PCL-5)
- AlloL
  - Functional and Social Support Questionnaire (FSSQ)
  - UCLA Loneliness Scale (UCLA-LS)
  - Perceived Stress Scale (PSS)
  - Connor-Davidson Resilience Scale (CD-RISC)

Serum CORT was measured using ELISA (Salimetrics) and adjusted for time-of-day.

Statistical Analysis

We used K-means clustering to identify unique groups based on AlloL profiles. Zero-inflated Negative Binomial (ZINB) regression was used to examine time-of-day adjusted CORT, age, sex, and AlloL clusters on PH symptoms.

Table 1. Descriptives (Enrollment Visit)

	Overall N = 204[1]	mTBI N = 120[1]	OI Control N = 84[1]
Time-adjusted Cortisol (ng/mL)	93 (62, 128)	95 (61, 146)	88 (62, 114)
Sex			
Female	123 (60%)	76 (63%)	47 (56%)
Male	80 (39%)	43 (36%)	37 (44%)
Not Reported	1 (0.5%)	1 (0.8%)	0 (0%)
Age	28 (22, 43)	28 (22, 45)	27 (22, 36)
PHQ9	3.0 (0.0, 9.0)	4.0 (1.0, 10.0)	1.0 (0.0, 5.5)
PCL5	5 (0, 20)	9 (0, 23)	1 (0, 16)
GAD7	3.0 (0.0, 9.0)	5.0 (1.0, 9.0)	1.0 (0.0, 6.0)
CDRISC	30 (24, 36)	29 (23, 34)	31 (24, 37)
FSSQ	36 (28, 40)	36 (28, 40)	37 (29, 40)
UCLA	14.0 (13.0, 18.0)	14.5 (13.0, 19.0)	14.0 (13.0, 18.0)
PSS	18 (14, 22)	18 (15, 21)	20 (12, 22)

[1] Median (Q1, Q3); n (%)

Figure 1. AlloB Measure Distribution by Cluster

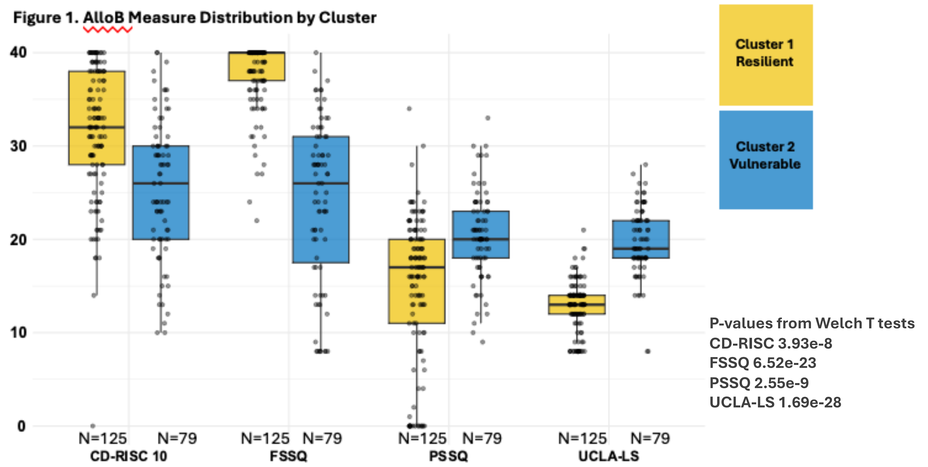


Figure 2. PH Measure Distribution by Cluster

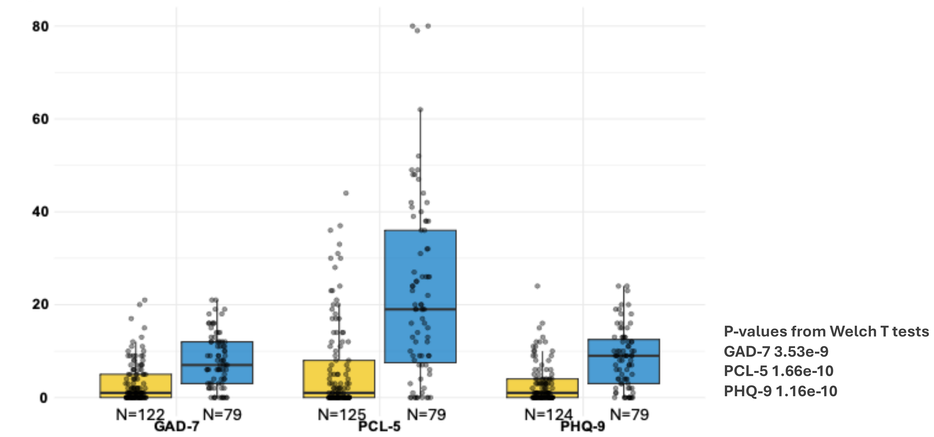
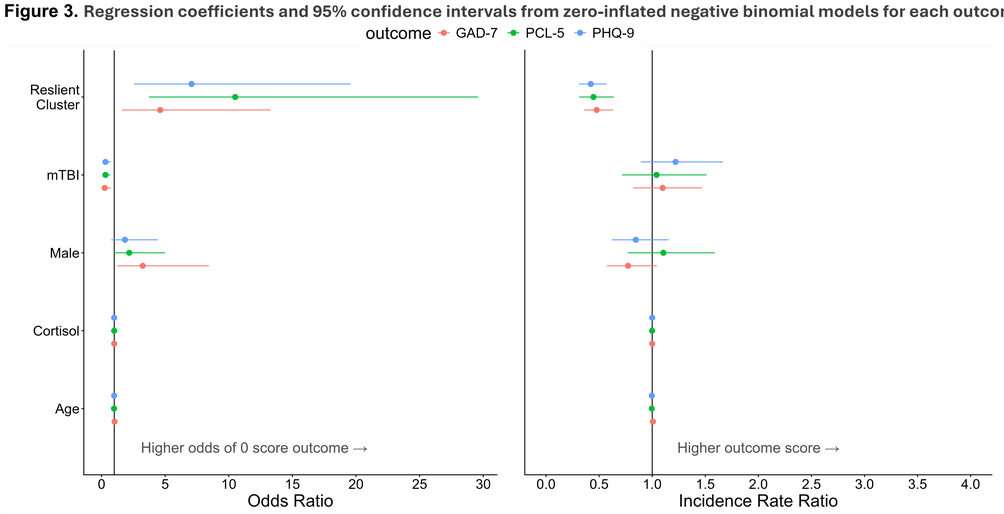


Figure 3. Regression coefficients and 95% confidence intervals from zero-inflated negative binomial models for each outcome



Results

K-means clustering identified 2 primary clusters comprised of both mTBI and OI controls:

- The **resilient** cluster (mTBI: N=69, OI: N=41) had a higher median time-adjusted CORT level (mTBI: 102.3ng/mL; OI Control: 97.87ng/mL) that did not significantly differ by mTBI status (p=0.054).
- The **vulnerable** cluster (mTBI: N=44, OI: N=31) had a lower median adjusted CORT level (mTBI: 87.72ng/mL; OI Control: 78.28ng/mL) that also did not significantly differ by mTBI status (p>0.9).

Bivariate analysis:

- The **resilient** cluster was characterized by a higher mean CD-RISC and FSSQ score and a lower mean UCLA-LS and PSS score compared to the **vulnerable** cluster (p<0.001 all comparisons)

ZINB regression:

- The **resilient** cluster was significantly associated with lower (better) PHQ-9, PCL-5, and GAD-7 scores
- Those with mTBI (vs. OI group) were less likely to be symptom free on the PHQ-9, PCL-5, and GAD-7 (p<0.01, all comparisons)
- Men were more likely to report being symptom-free on these PH measures (p<0.1) compared to women regardless of injury group.
- After adjusting for covariates, mTBI status remained a significant contributor to PH symptom severity.

Discussion

- Impact of chronic stress and life events and can be measured through clinical symptoms and biomarkers.[2]
- Stress-sensitive molecules (CORT) may underlie AlloL and affect mTBI symptoms and/or PH.[3]
- Known sex differences exist with CORT and PTSD symptom development,[4] but were not replicated here.
- mTBI remained an independent risk factor for baseline symptoms severity that suggest the need for vigilance with PH symptom severity and appropriate intervention selection.

Conclusions

- Higher AlloL within 72h of injury was associated with worse baseline PH scores and higher CORT. mTBI (compared to OI) was associated with being symptomatic on PH, whereas male sex was associated with being symptom free on PH when adjusting for other covariates.
- Future work will focus on AlloL relationships to life-time trauma history, early childhood adversity and TBI relevant biomarkers

References

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