Depression and anxiety symptoms are positively related to mitochondrial reactive oxygen species in CD8+ T-cells among young adults with Adverse Childhood Experiences

IOWA

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Introduction

- Adverse Childhood Experiences (ACEs) are psychosocial stressors occurring prior to the age of 18 and includes physical & sexual abuse, household dysfunction, and community adversity.
- There exists a dose response between ACE, and increased depression & anxiety symptomology.
- We hypothesize immune mediated oxidative stress, marked by increased mitochondrial reactive oxygen species (mtROS) production may contribute to depression and anxiety symptomology in individuals with a history of ACEs.
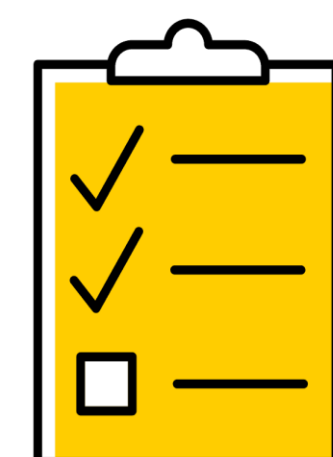
We aimed to investigate associations between ACE exposure, anxiety and depression symptoms, and T-cell mtROS expression

Methods

Questionnaires

ACEs Questionnaire – 10 item
- no ACEs (ACE-)
- high ACES (≥4; ACE+)

Center for Epidemiologic Studies Depression Scale (CES-D) – 20 item
- Assess depression symptomology over the past week
- 4-point likert scale

Zung Self-Rating Anxiety Scale (ZSRA) – 20 item
- Assess anxiety symptomology over the past week
- 4-point likert scale

Physiological Measures

mtROS Fluorescence
- PBMCs isolated from whole blood
- CD8+ T-cells stained and identified
- Flow cytometry using fluorogenic staining (MitoSOX Green) (median fluorescence intensity [MFI; arbitrary units (AU)]).
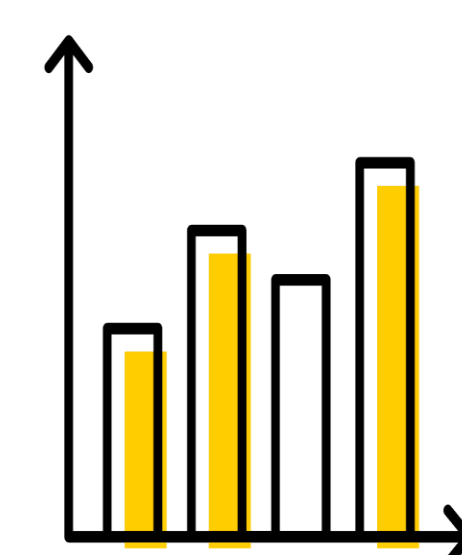
Statistical Analysis

Between group t-tests
- CESD
- ZSRA
- mtROS

Spearman Rank Correlation
- CESD & mtROS
- ZSRA & mtROS

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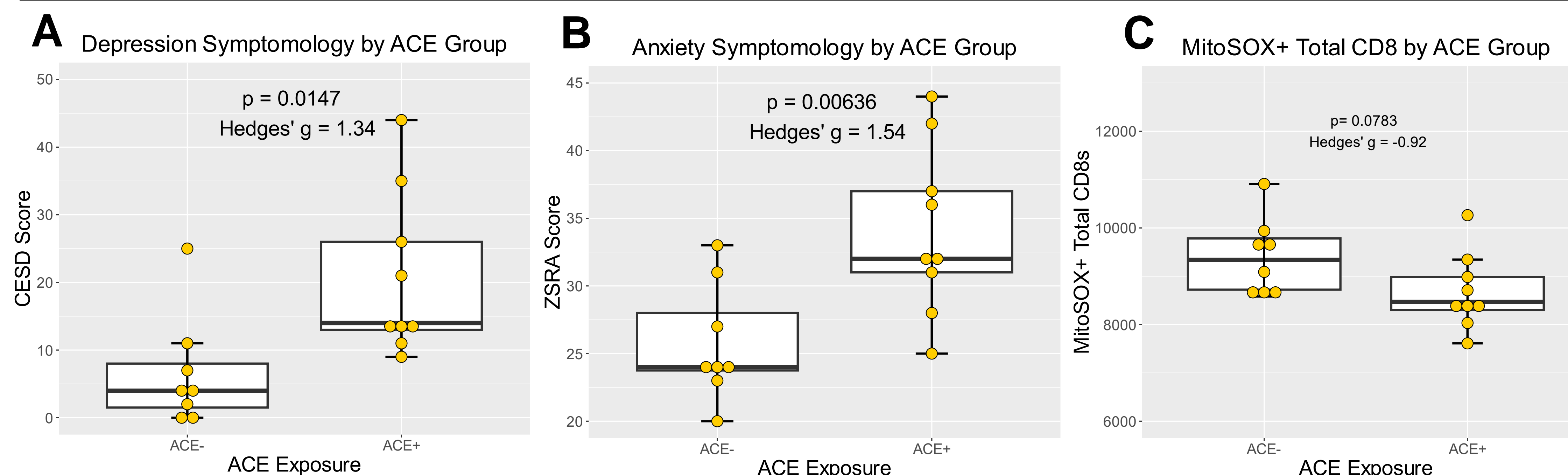
Results

Between Group t-tests

Figure 1. Between group t-test analysis of comparing **(A)** CES-D ($p = 0.015$, Hedges' $g = 1.34$) and **(B)** ZSRA ($p = 0.006$, Hedges' $g = 1.54$) scores found **depression and anxiety symptomology to be significantly higher in ACE+ vs ACE-. (C) mtROS was a higher in ACE-**, but non-significant ($p = 0.078$, Hedges' $g = -0.92$).
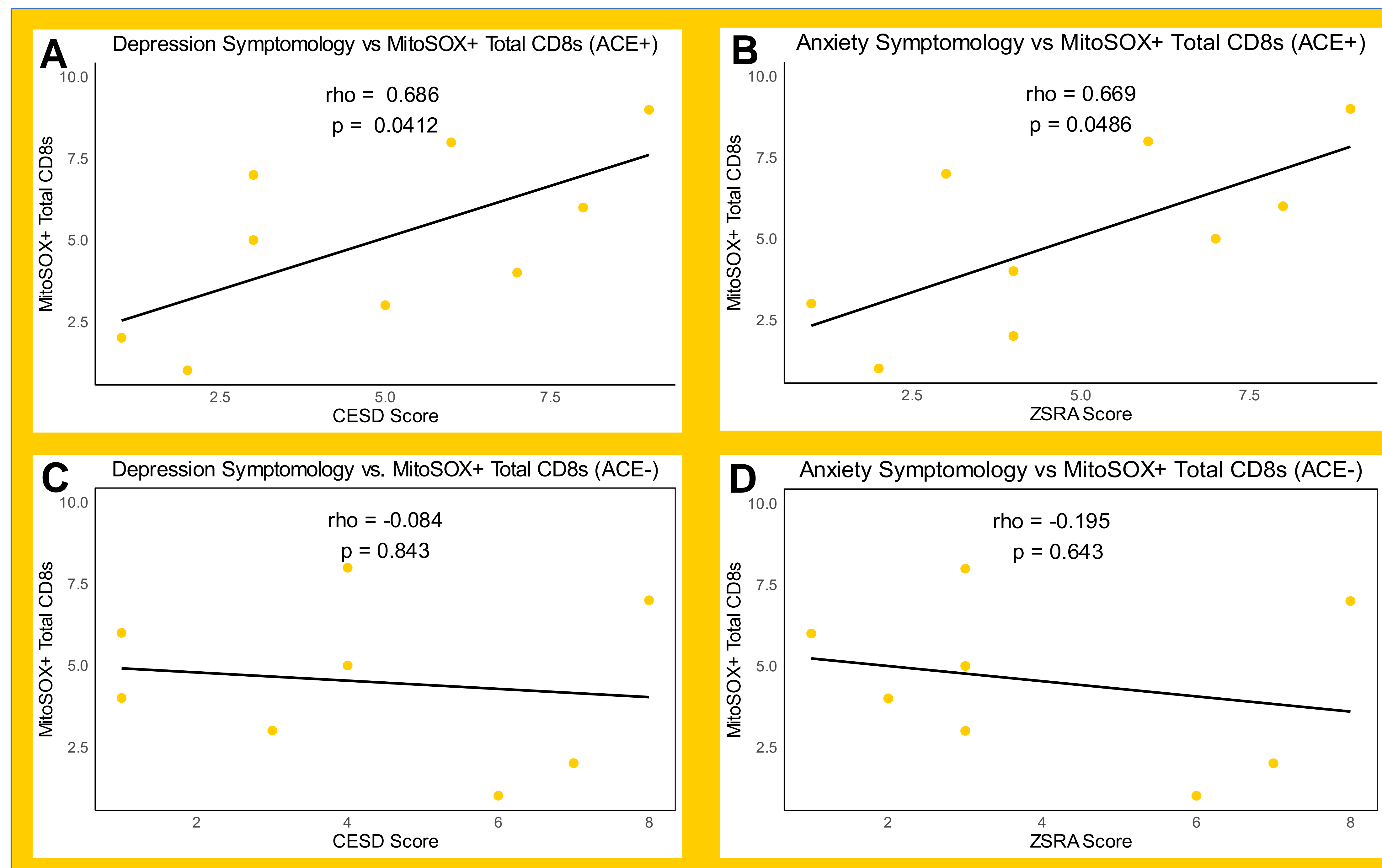
Spearman Rank Correlations

Figure 2. Spearman rank correlations between **(A)** CES-D & mtROS (rho = 0.686, $p = 0.0412$) and **(B)** ACE+ ZSRA & mtROS (rho = 0.669, $p = 0.0486$) in ACE+ were each significant. **(C)** Spearman rank correlations between CES-D & mtROS (rho = -0.084, $p = 0.826$) and **(D)** ACE- ZSRA & mtROS (rho = -0.195, $p = 0.643$) in ACE- were not significant. **Only ACE+ associations were significant.**

Descriptive Statistics

	ACE+ (n=9)		ACE- (n=8)	
	Mean	SD	Mean	SD
Age	23	3	22	3
Height	165	9.2	171.5	10.6
Weight	58.3	10	65.7	14.2
BMI	21.5	3.9	22.2	3.5
ACE Score	5	1	0	0
	n	%	n	%
Male	3	33	3	37
Female	6	67	5	63
White	4	44	5	63
Black	1	11	1	12
Asian/Pacific	2	22	1	12
Other	2	22	1	12

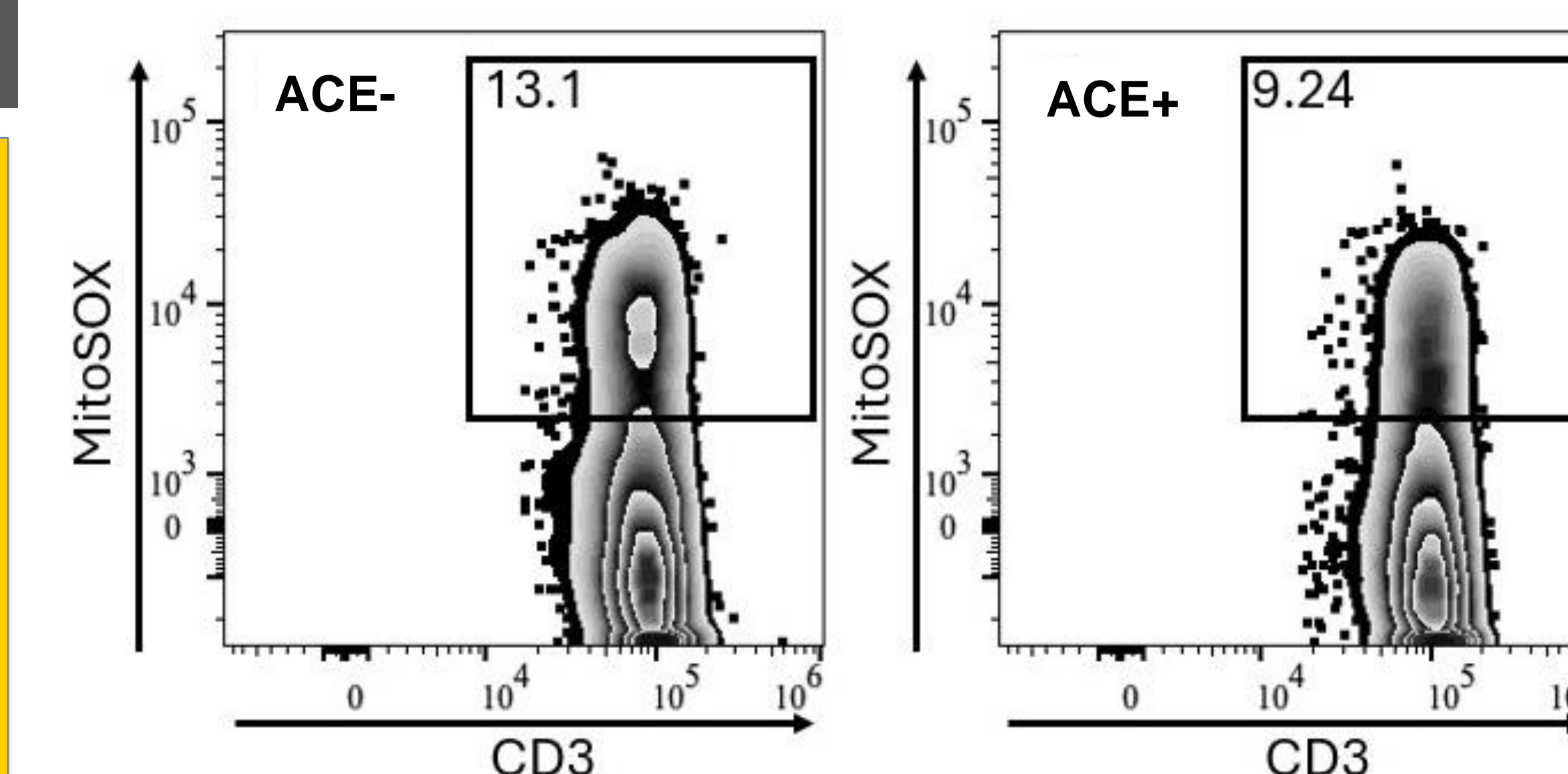**Table 1.** Descriptive variables for ACE- & ACE+.

mtROS Fluorescence

Figure 3. Representative flow cytometry dot plots depicting CD3 and MitoSOX presence in CD8 T-cells in ACE- (left) and ACE+ (right) participants. Fluorescence in cells falling within the defined gate were analyzed. Analysis of cells falling within the selected gate parameters found **ACE- participants displayed higher MitoSOX expression compared to ACE+.** This suggests ACE- participants may display lower mitochondrial oxidative stress.

Conclusions

- Higher depression and anxiety symptomology was observed in ACE+.($p < 0.015$)
- Higher mtROS presence was observed in ACE-
- Expected significant positive associations between CESD, ZSRA and mtROS in ACE+ ($p ≤ 0.0486$) but no significant associations in ACE- ($p ≥ 0.643$).

ACE related depression and anxiety symptomology could play a role in immune mediated oxidative stress.