HHS Public Access

Author manuscript

*J Psychosom Res*. Author manuscript; available in PMC 2017 April 01.

Published in final edited form as:

*J Psychosom Res*. 2016 April ; 83: 33–39. doi:10.1016/j.jpsychores.2016.02.008.

# An investigation of vago-regulatory and health-behavior accounts for increased inflammation in posttraumatic stress disorder

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## Abstract

**Objective—**Posttraumatic stress disorder (PTSD) has been linked to chronic inflammation, a condition that poses a risk for cardiovascular disease. Attenuated vagal activity has been proposed as a potential mediator of PTSD and inflammation, although associated behavioral health risks—namely cigarette smoking and alcohol dependence—might also account for that link.

**Methods—**Inflammation was quantified by fasting serum concentrations of C-reactive protein (CRP), tumor necrosis factor (TNF)-α, interleukin (IL)-10, and thymus- and activation-regulated chemokine (TARC)/CCL17 collected from 85 participants with PTSD and 82 without PTSD. Latent variable modeling was used to assess the relationship between PTSD symptom severity and inflammation along with potential mediators vagal activity (respiratory sinus arrhythmia; RSA), smoking status, and lifetime alcohol dependence.

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**Declaration of Interests**

The authors have no competing interests to report.

**Statement of Ethics**

All procedures followed were in accordance with the ethical standards of the Duke University Medical Center and Durham Veterans Affairs Institutional Review Boards and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for their inclusion in the study.

**Results—**PTSD symptom severity was associated with increased inflammation (β = .18, *p* = .02). However, this association was reduced in models that adjusted for RSA, smoking status, and lifetime alcohol dependence. Independent mediation effects were deemed significant via bootstrapping analyses. Together, RSA, smoking status, and lifetime alcohol dependence accounted for 95% of the effect of PTSD symptom severity on inflammation.

**Conclusion—**Although RSA accounted for a modest proportion of the association between posttraumatic stress and pro-inflammatory responses, behavioral factors – specifically cigarette smoking and alcohol dependence – proved to be larger mediators. The benefits of PTSD treatment may be enhanced by additional interventions aimed at modifying these health behaviors.

### Keywords

posttraumatic stress disorder; inflammation; cytokines; cigarette smoking; alcohol dependence; vagal tone

## Introduction

Posttraumatic stress disorder (PTSD) is a chronic condition precipitated by exposure to a traumatic event. It is characterized by intrusive re-experiencing of the traumatic event, avoidance of stimuli evocative of that event, negative alterations in cognitions and mood, and hyperarousal (1). PTSD also frequently conveys physical health symptoms, perhaps most notably cardiovascular disease (2). For instance, PTSD has been prospectively associated with coronary heart disease (3) and cardiovascular mortality (4). Although the pathway from posttraumatic stress to cardiovascular risk is not well understood, emerging evidence suggests that inflammation may play a key role (5).

Under conditions of heightened threat or stress, the sympathetic nervous system activates a “fight or flight” response, characterized by increased cardiovascular and metabolic activity. The immune system also responds in kind, presumably to stave off infections resulting from injuries sustained during such fight or flight. The initial immune response is fast and generalized, during which numbers of phagocytes, including neutrophils and macrophages, are mobilized. Macrophages in turn release pro-inflammatory communication factors (cytokines), including interleukin (IL)-1, IL-6, C-reactive protein (CRP), and tumor necrosis factor alpha (TNF-α), which cause fever and inflammation while contributing to healing. A second, more specific immune response is also initiated in which lymphocytes become activated upon attaching to chemically matched pathogens, thereby initiating lymphocyte expansion and cytokine release. These cytokines include the pro-inflammatory IL-2 and interferon gamma (IFN-γ) as well as the anti-inflammatory IL-4, IL-10, and thymus- and activation-regulated chemokine (TARC/CLL17), which regulate lymphocyte activity.

Over the past two decades, a number of studies have found that psychological stress is associated with elevated cytokine levels, reflecting heightened inflammation (6). For instance, several studies have found that exposure to trauma in childhood (7–9) and in adulthood (10) is subsequently predictive of increased inflammation. One study even found that increased cytokine levels post-trauma were predictive of later development of PTSD (11). In fact, with the exception of a few studies (12–15), PTSD is generally associated with

increased cytokine levels (16–22), even above and beyond the effect of trauma exposure (23, 24).

The link between PTSD and inflammation is complex but may be partially explained by behavioral risk factors associated with PTSD (22). For instance, individuals with PTSD are more likely than those without PTSD to smoke and do so heavily (25), be obese (26), and abuse alcohol (27). Each of these risk factors is independently associated with inflammation (28–30). Autonomic dysfunction may also partially account for the association between PTSD and inflammation. Individuals with PTSD exhibit suppressed heart-rate variability (HRV) (31–33), which is likely due to attenuated vagal regulation of sympathetic arousal (34). Given the central role of the vagus nerve in inhibiting generalized immune response (35–37), vagal dysregulation has been proposed as a pathway by which PTSD is associated with chronic inflammation (38).

Although behavioral risk factors and depressed vagal activity have been suggested as potential mechanisms linking PTSD and inflammation, no research has verified this let alone compared their relative mediation effects. Thus, the purpose of the present study was to determine whether the association between PTSD symptom severity and inflammation is partially mediated by vagal activity, smoking status, and history of alcohol dependence, and, if so, which mediator accounts for the largest portion of that association. As such, fasting serum concentrations of CRP, TNF-α, IL-10, and TARC were assayed from a sample of young (i.e., < 40 years of age), largely trauma-exposed adults. Latent variable modeling was used to model inflammation *via* the four cytokines *en route* to testing three sets of hypotheses: 1) PTSD symptom severity is positively associated with inflammation; 2) PTSD symptom severity is associated with reduced vagal activity, greater smoking, and higher rates of lifetime alcohol dependence; and 3) vagal activity, smoking status, and lifetime alcohol dependence partially mediate the association between PTSD symptom severity and inflammation.

## Material and methods

### Participants

Participants were 167 young adults (18–39 years old; 80 women), including 63 U.S. military veterans, who were recruited *via* fliers displayed in hospital clinics and waiting rooms as well as online ads such as Craigslist to complete a study of the metabolic, cardiovascular, and neuroimmunological risk factors associated with trauma exposure. Criteria for exclusion from the study included presence of a) organic mental disorder, b) schizophrenia, c) bipolar I mixed state or bipolar II, d) lifetime PTSD without current PTSD, e) current substance abuse/dependence, f) current major depressive disorder (MDD) without PTSD, g) pregnancy, h) AIDS or HIV, and i) uncontrolled medical condition (e.g., liver failure). Eleven women using birth control and three participants using statins were additionally omitted from the present analysis in light of the potential effects of these drugs on cytokine levels. The study was approved by both the Durham Veterans Affairs and Duke University Medical Center Institutional Review Boards. All patients gave written informed consent before participation. Data were collected between August 2008 and September 2013.

Previous findings from this sample include linkages between PTSD and orthostatic hypotension (39), decreased HRV (32), and dyslipidemia (40).

## Measures

**Posttraumatic Stress Disorder—**PTSD status was assessed using the Clinician Administered PTSD Scale (CAPS) (41), based on DSM-IV criteria (42). The 17-item structured interview was administered by a licensed clinical psychologist or by a trainee under the direct supervision of a licensed clinical psychologist. Interrater reliability among interviewers was high (Fleiss' $k = .94$) across five training tapes. The CAPS interview has excellent reliability within multiple trauma populations and is widely accepted as the state-of-the-art method for PTSD assessment (43).

The 17-item self-report Davidson Trauma Scale (DTS) (44) was used to quantify PTSD symptom severity based on DSM-IV criteria. Each item measures the frequency (0, —not at all,‖ to 4, "everyday") and intensity (0, "not at all distressing," to 4, "extremely distressing") of corresponding symptoms. Total symptom severity scores were calculated by summing frequency and intensity ratings across all items.

**Vagal Activity—**One commonly used method for measuring vagal cardiac control, or activity, is *via* respiratory sinus arrhythmia (RSA) (45), which refers to the naturally occurring fluctuations in heart rate associated with breathing. To capture RSA, beat-by-beat blood pressure and heart rate data were measured continuously using the Finometer noninvasive blood-pressure monitor (Finapres Medical Systems, Amsterdam) under supine conditions. Following five minutes of calibration, one 5-minute file of continuous blood pressure and heart rate measurements was recorded for assessment of RSA while the participants breathed at their regular rate of breathing. Blood pressure waveforms were reviewed, and artifacts due to movement or abnormal heart beats was removed and replaced by the pulse interval values from the preceding beat(s). The beat-by-beat systolic pressure and heart rate data were linearly interpolated and resampled at a frequency of 4 Hz in order to generate an equally spaced time series for the variables. A fast Fourier transform was then applied to the interpolated data after detrending and application of a Hanning filtering window. Power spectra were derived using the Welch algorithm, which ensemble averages successive periodograms (46). The averaged spectrum was derived from the power spectra estimated from nine 60-second data segments, overlapping by half. For each 60-second segment, 256 points were analyzed, which included 240 sampled points with zero padding. Consistent with prior research (47–49), RSA was estimated from the R-R interval power summed across the high-frequency 0.13- to 0.50-Hz respiratory band. Raw RSA was log-transformed before analysis in order to normalize values.

**Smoking Status—**Smoking status was operationalized based on participants' responses to the Fagerström Test for Nicotine Dependence (50). Non-smokers were assigned a value 0; past— but not present—smokers, 1; current smokers who consume 10 or fewer cigarettes per day, 2; and current smokers who consume more than 10 cigarettes per day, 3.

**Lifetime Alcohol Dependence—**The Structured Clinical Interview for the DSM-IV (SCID) (51) was used to assess Axis I disorders, including lifetime alcohol dependence. Study interviewers completed an extensive training program involving the rating of seven video-recorded interviews. Interviewers additionally participated in biweekly reliability meetings and were supervised by licensed clinical psychologists. Interrater reliability among interviewers for Axis I diagnoses was high (Fleiss' $k = .96$).

**Trauma Exposure—**Trauma exposure was measured using the Traumatic Life Events Questionnaire (TLEQ) (52), a self-report questionnaire that documents 23 distinct types of traumas including the time of their occurrence. For the purposes of this study, trauma exposure was operationalized as the number of years since one's initial exposure to a traumatic event resulting in feelings of fear, helplessness, and horror. Participants who were never exposed to such a trauma were assigned a trauma-exposure value of 0. We included years of trauma exposure, as opposed to number of types of traumatic experiences or childhood versus adulthood trauma exposure, in the present analysis as a covariate to minimize variance in allostatic load due to varying lengths of trauma exposure.

## Procedure

Participants completed an initial interview and battery of questionnaires in person at intake, including the measures listed above. Health status and current medications were also recorded. Anthropometric measures were taken, including height and weight, from which body-mass index (BMI) was calculated. RSA was measured one week later.

Serum samples were collected at a subsequent session visit between 10am and 1pm to assess overnight fasting cytokine profile. Serum was separated by centrifugation, aliquoted, and stored at −70 F until time of assay. Plasma CRP, TNF-α, IL-10, and TARC were assayed in duplicate using ELISA technology (Meso Scale Discovery, Rockville, MD). The mean lower levels of detection (LLOD) were: CRP = 1.24 pg/ml, IL-10 = 0.23 pg/ml, TARC = 25.42 pg/ml, and TNF-α = 0.21 pg/ml.

A normal human control serum was run on each of the plates to assess plate-to-plate variability. The mean intra-assay coefficients of variation (CV) were: CRP = 1.2%, IL-10 = 4.9%, TARC = 3.2%, and TNF-α = 3.0%. Samples with intra-assay CV > 20% were deemed unreliable and treated as missing. As a result, IL-10 concentration was dropped for one participant with PTSD. Samples falling below the LLOD were replaced with ½ the LLOD. Two samples ($n = 1$ with PTSD) were replaced on account of low IL-10 concentrations. Samples were log-transformed to achieve normality and were similarly analyzed for extreme outliers (i.e., ≥ 5 SD above the mean). One participant with PTSD had an outlying IL-10 concentration that was dropped.

## Analytic Plan

Latent variable modeling was used to test the hypothesis that PTSD symptom severity would be associated with increased inflammation, with subsequent models conducted to the test the mediation hypotheses. Initially, a latent variable representing inflammation was specified using log-transformed concentrations of CRP, IL-10, TARC, and TNF-α. The purpose of

this was to minimize the measurement error in cytokine levels. The adequacy of the inflammation latent variable was determined prior to further modeling using standard fit criteria (53, 54): root mean square error of approximation (RMSEA) ≤ .05, comparative fit index (CFI) ≥ .90, and standardized root mean square residual (SRMR) < .05. The chi-squared test of model fit was also consulted, with non-significance indicative of good model fit.

Initially a direct-effects model was conducted to test the association between PTSD symptom severity and inflammation. In subsequent models, the indirect effect of PTSD symptoms on inflammation via RSA and associated behavioral risk factors was tested. To test the significance of mediation, bootstrapped confidence intervals around the indirect effects of PTSD symptoms on inflammation were generated using resampling. This method offers an advantage over conventional tests, such as Sobel's *z*, because it takes into account the positive skew inherent to indirect effects. As such, bootstrapping methods are more powerful than conventional tests, with mediation deemed significant when the resulting confidence interval does not span 0.

In each of the models, age, BMI, and steroid use (e.g., prednisone) were covaried, given their associations with cytokine levels (28, 55, 56). Note that BMI was not tested as a potential mediator of PTSD symptom severity and inflammation in light of previously published analyses from this sample indicating that PTSD symptom severity was unassociated with obesity (32). Years since initial exposure to a traumatic event resulting in fear, helplessness, and horror was additionally controlled to assess the effect of PTSD status on inflammation independent of trauma exposure. All models were specified with PROC CALIS in SAS v9.2. Full information maximum likelihood estimation was used to handle missing data.

## Results

Participant characteristics and intercorrelations between study variables are presented in Table 1. Eighty-five participants (51%) met criteria for current PTSD. Only 10 participants reported no exposure to a traumatic event resulting in fear, helplessness, and horror. Incidentally, the sample mean on the DTS, 45.72, fell directly between the means from a normative sample (57) for subthreshold PTSD with impairments ($M$ = 20.5) and threshold PTSD ($M$ = 67.1). As hypothesized, PTSD symptom severity was negatively associated with RSA and positively associated with smoking and history of alcohol dependence. However, the bivariate correlations between PTSD symptom severity and unadjusted cytokine levels failed to reach significance.

The initial measurement model of the inflammation latent variable indicated that it was a good fit for the log-transformed cytokine data: RMSEA = 0.004, CFI = 1.000, SRMR = 0.005, and $X^2(1) = 0.07$, $p = .79$. According to a main-effects latent-variable model, inflammation was positively associated with BMI and steroid use (see Figure 1). Inflammation was also positively associated with PTSD symptom severity, thus supporting the first hypothesis. Subsequent modeling further indicated that the associations of RSA, smoking status, and lifetime alcohol dependence with inflammation were significant in the

latent-variable models (see Figures 2–4). Moreover, the direct effect of PTSD symptom severity on inflammation was attenuated in the presence of each, suggesting mediation.

To test significance of RSA, smoking-status, and alcohol-dependence mediation effects, bootstrapped confidence intervals (CI) around the indirect effects of PTSD symptom severity on inflammation were generated from 500 re-samples. In support of the third hypothesis, the indirect effects for RSA (bootstrapped 95% CI of standardized effect: .00 – .09), smoking status (bootstrapped 95% CI of standardized effect: .04 – .17), and lifetime alcohol dependence (bootstrapped 95% CI of standardized effect: .03 – .16) were each significant in separate models, independently accounting for 23%, 57%, and 51% of the effect of PTSD symptom severity on inflammation. In combination, the three mediators accounted for 95% of the effect of PTSD symptom severity on inflammation (bootstrapped 95% CI of combined standardized effects: .06 −.22), with both health risks, but not RSA (bootstrapped 95% CI for standardized effect: −.00 −.07), maintaining significance as independent mediators (bootstrapped 95% CI for standardized effect of smoking status: .02 – .14; bootstrapped 95% CI for standardized effect of lifetime alcohol dependence: .01 – .11).

Given evidence that smoking (58) and drinking (59) are associated with vagal activity, mediation of the association between PTSD symptom severity and RSA by smoking status and lifetime alcohol dependence was further investigated. However, the total effect of PTSD symptom severity on RSA after controlling for age, BMI, steroid use, and trauma exposure was not significant ($\beta = -.14$, $p = .10$), thus ruling out mediation.

## Discussion

The present study examined the association of PTSD symptoms with serum cytokine levels along with potential psychophysiological and behavioral health mediators within a sample of young adults. Consistent with previous work (23, 24), PTSD symptom severity was positively associated with inflammation (i.e., higher cytokine levels) independent of trauma exposure. A novel finding was that this association was partially mediated by attenuated vagal activity as well as smoking status and lifetime alcohol dependence. The behavioral risk variables each explained twice as much of the covariance between PTSD symptom severity and inflammation as vagal activity. Together, the three mediators accounted for the entire effect of PTSD symptom severity on inflammation.

These findings represent an important contribution to the growing literature linking PTSD with inflammation. Although short-term inflammation may be beneficial for staving off infection, long-term inflammation is well-known to increase the risk of chronic medical illness. For one, elevated concentrations of circulating pro-inflammatory cytokines activate inflammatory processes within the cells of blood vessel walls, promoting apoptosis, the adhesion of macrophages to the wall surfaces, and the formation of smooth muscle fibers over the resulting lesions (60). These processes accelerate atherosclerosis and potentiate thrombosis, increasing risk of myocardial infarction and stroke (61). Chronic inflammation has also been implicated in the development of insulin resistance. Elevated levels of circulating proinflammatory cytokines, primarily TNF-α, induce inflammatory signaling

within insulin target cells, thereby disrupting normal insulin-receptor signalizing (62). Thus, inflammation may mark an important pathway by which PTSD conveys cardiovascular and metabolic risk.

In turn, the association between PTSD and inflammation may be largely due to risky health behaviors. Although the hypothesis that attenuated vagal activity partially explains under-regulation of pro-inflammatory processes in PTSD was substantiated, the mediation effect was small, particularly in comparison to those for smoking status and lifetime alcohol dependence. Moreover, the mediation effect for vagal activity was rendered non-significant in a model controlling for smoking status and lifetime alcohol dependence. Considering that smoking (58) and drinking (59) are both known to depress vagal activity, to some extent they may have driven the association between PTSD symptom severity and RSA. In fact, in a recent study based on a subset of the present sample, smoking and drinking accounted for the majority of the association between PTSD symptom severity and HRV, which is influenced by RSA (32). In the present sample, however, there was no support for mediation of PTSD symptom severity and RSA by either behavioral health risk.

It is significant that smoking and drinking accounted for so much of the association between PTSD symptom severity and inflammation. The detection of these effects among young adults reveals just how rapidly PTSD-related health problems may arise due to poor health behaviors. As such, our results emphasize the importance of efforts to reduce nicotine and alcohol consumption among individuals with PTSD. Individuals with PTSD are at least twice as likely as non-affected individuals to smoke (63, 64) and 1.5 times as likely to meet criteria for alcohol abuse or dependence (65). These behaviors pose substantial health risks. As mentioned above, smoking and drinking accounted for a large portion of the covariance between PTSD and HRV in a subset of this sample (32). In two additional sets of analyses from the same sample, smoking and drinking were similarly implicated in linking PTSD with orthostatic hypotension (39) and dyslipidemia (40). Thus, efforts to intervene upon these health risk behaviors could potentially pose a huge impact on the health outlook of trauma-exposed individuals.

Of course, the present findings must be taken into the context of several limitations. For one, the cross-sectional design limits our interpretation of the directionality of the associations. Moreover, mediation detected in cross-sectional data cannot always be generalized to a longitudinal process (66). Despite these limitations, our interpretation is consistent with the conventional view that PTSD engenders excessive use of nicotine and alcohol, and that these health risks are known to convey chronic inflammation (25, 27). Future work testing the prospective effect of PTSD symptom severity on health risks and subsequent inflammation is clearly warranted.

Another limitation was the exclusion of individuals with current alcohol abuse or dependence and the dichotomous nature of the lifetime-alcohol-dependence variable. These likely diminished the sensitivity of that construct. Nevertheless, its influence on inflammation was sufficient in the present study to demonstrate a significant mediation effect. In any case, future research in this area should make use of higher-resolution measures of alcohol consumption and misuse.

A last consideration is the reliability of cytokine levels as an indicator of chronic inflammation. The extant literature on PTSD and inflammation is far from definitive, with a number of studies demonstrating at least mixed evidence that PTSD is associated with decreased, rather than increased, levels of pro-inflammatory cytokines (12, 13, 15) or no association at all (14). In the present analysis, PTSD symptom severity was associated with increases in both pro-and anti-inflammatory cytokines, which stands in contrast to other research demonstrating a negative association between PTSD and anti-inflammatory cytokine levels (12, 13, 22). However, a compensatory anti-inflammatory response likely accounts for the present findings of increased pro- and anti-inflammatory cytokine levels associated with PTSD symptom severity (67). Regardless, the temporal reliability of the four cytokines selected for the present study is moderate to high, with 2-year intra-class correlations (ICC) of .76 for CRP, .69 for TNF-α, and .75 for IL-10 (68), and a 3-year ICC of .52 for TARC (69). These suggest that a single measurement of each should provide a fair indication of inflammation. Moreover, our use of latent-variable modeling served to minimize further measurement error by modeling an unobserved, theoretical construct (i.e., inflammation) believed to influence each of the cytokine serum concentrations. These steps likely aided our efforts to gather precise, reliable findings in support of our hypotheses. That the bivariate associations between PTSD symptom severity and cytokine levels failed to reach significance—only the association between symptom severity and IL 10 approached significance—highlights the complexity of these cytokines and the large number of factors that could potentially influence their levels. The amount of noise inherent to their quantification likely underlies the variability in findings associating PTSD with cytokine levels. The use of latent variable modeling to construct an empirically derived composite score based on each of the cytokines represents a potentially useful technique for quantifying inflammation in future research.

In sum, study results further emphasize the deleterious effects of PTSD on health, even among younger adults. In the present study, PTSD symptom severity was significantly associated with inflammation, which is a known cardiovascular and metabolic risk. Moreover, major contributors to this linkage were smoking and alcohol dependence. These findings complement evidence from three additional findings based on the same sample indicating that PTSD is also associated with increased risk of orthostatic hypotension (39), attenuated HRV (32), and dyslipidemia (40). In those analyses, smoking and alcohol dependence were also identified as potential mechanisms for cardiovascular risk. Together, these findings underscore the extent to which interventions for individuals with PTSD aimed at smoking and alcohol cessation could yield meaningful, long-term benefits, both psychiatric and cardiovascular.

## Acknowledgments

Preparation of this work was supported by the National Institute of Mental Health (2R01MH062482), the National Institute on Drug Abuse (5K24DA016388), the Durham, NC Veterans Affairs Medical Center, and the Department of Veterans Affairs office of Research and Development Clinical Science.

The content of this work is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the Department of Veterans Affairs, or the United States Government.

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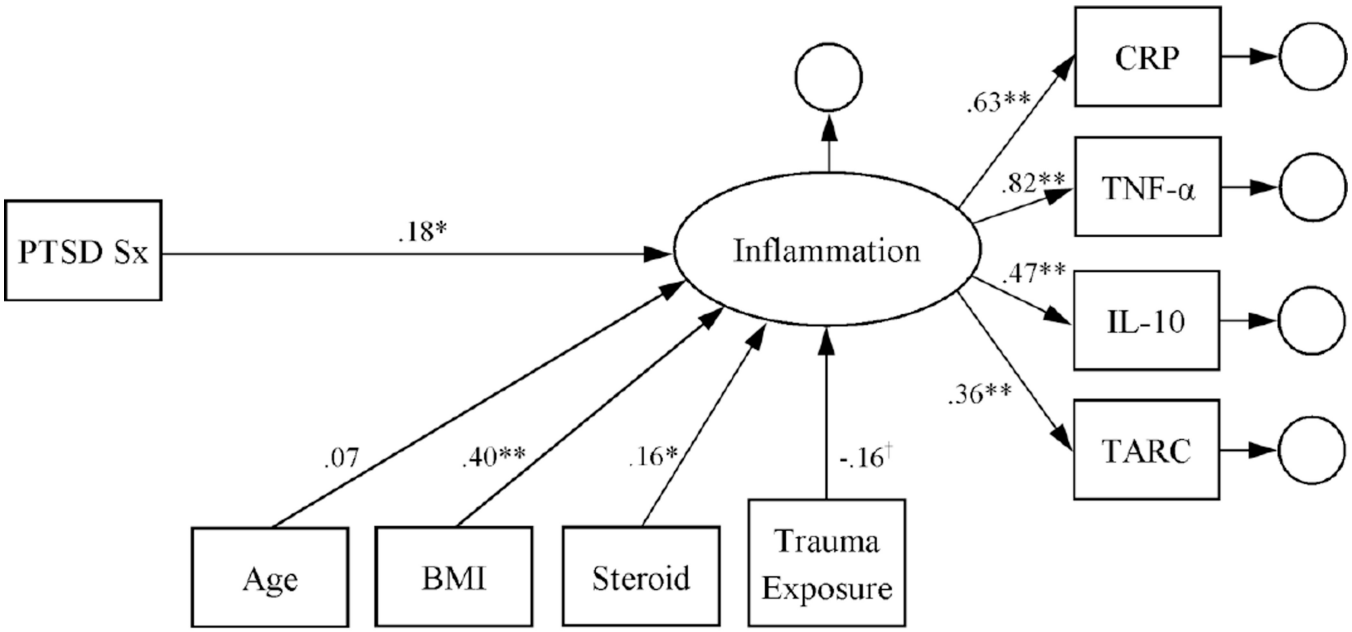
## Highlights

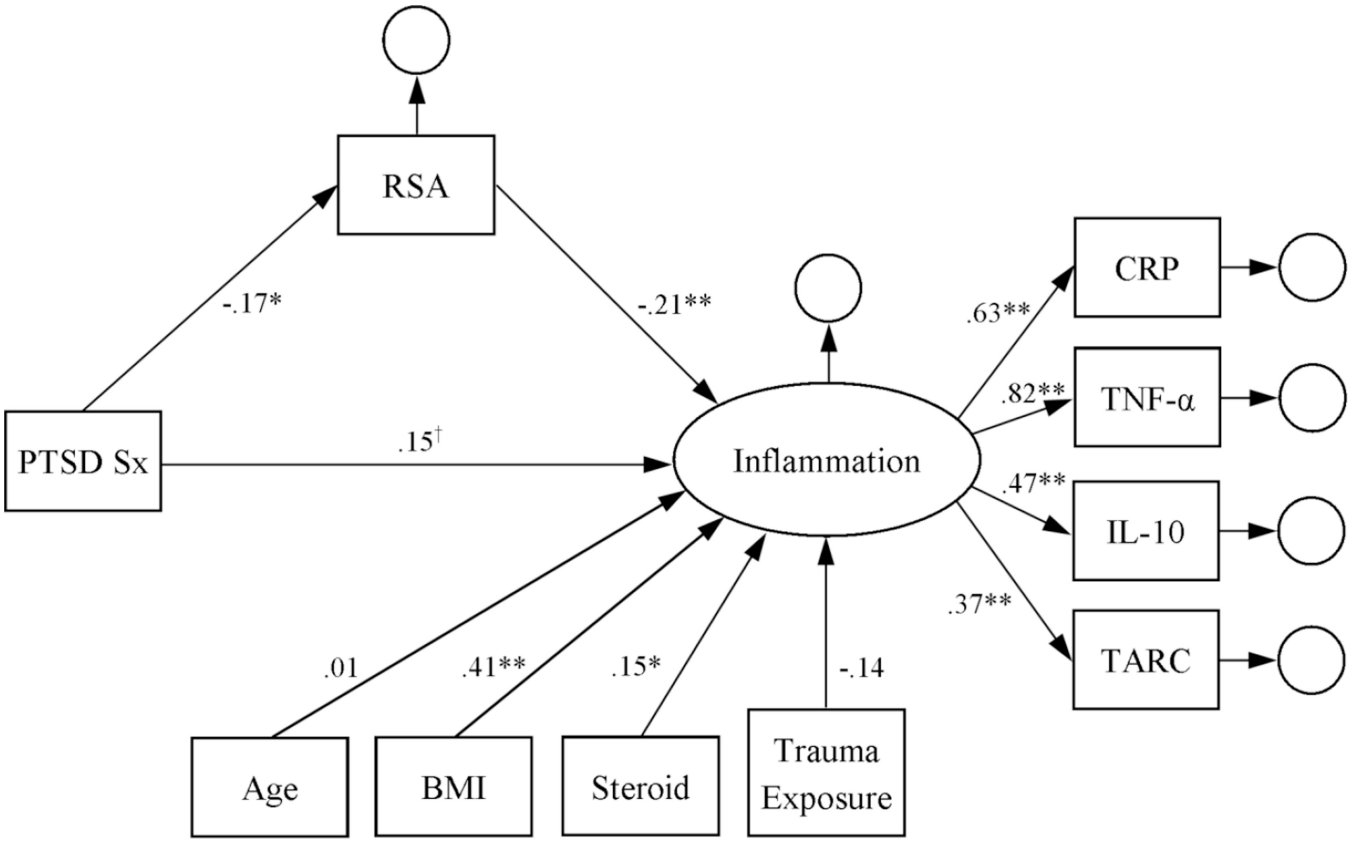
- Fasting serum cytokine levels of young adults with and without PTSD were assessed.
- PTSD symptom severity was positively associated with CRP, TNF-α, IL-10, and TARC.
- Smoking, alcohol dependence, and RSA each independently mediated that association.
- The effects of smoking and alcohol dependence were larger than that of RSA.
- All three mediators accounted for 95% of the link between PTSD and cytokine levels.




†$p < .10$, *$p < .05$, **$p < .01$

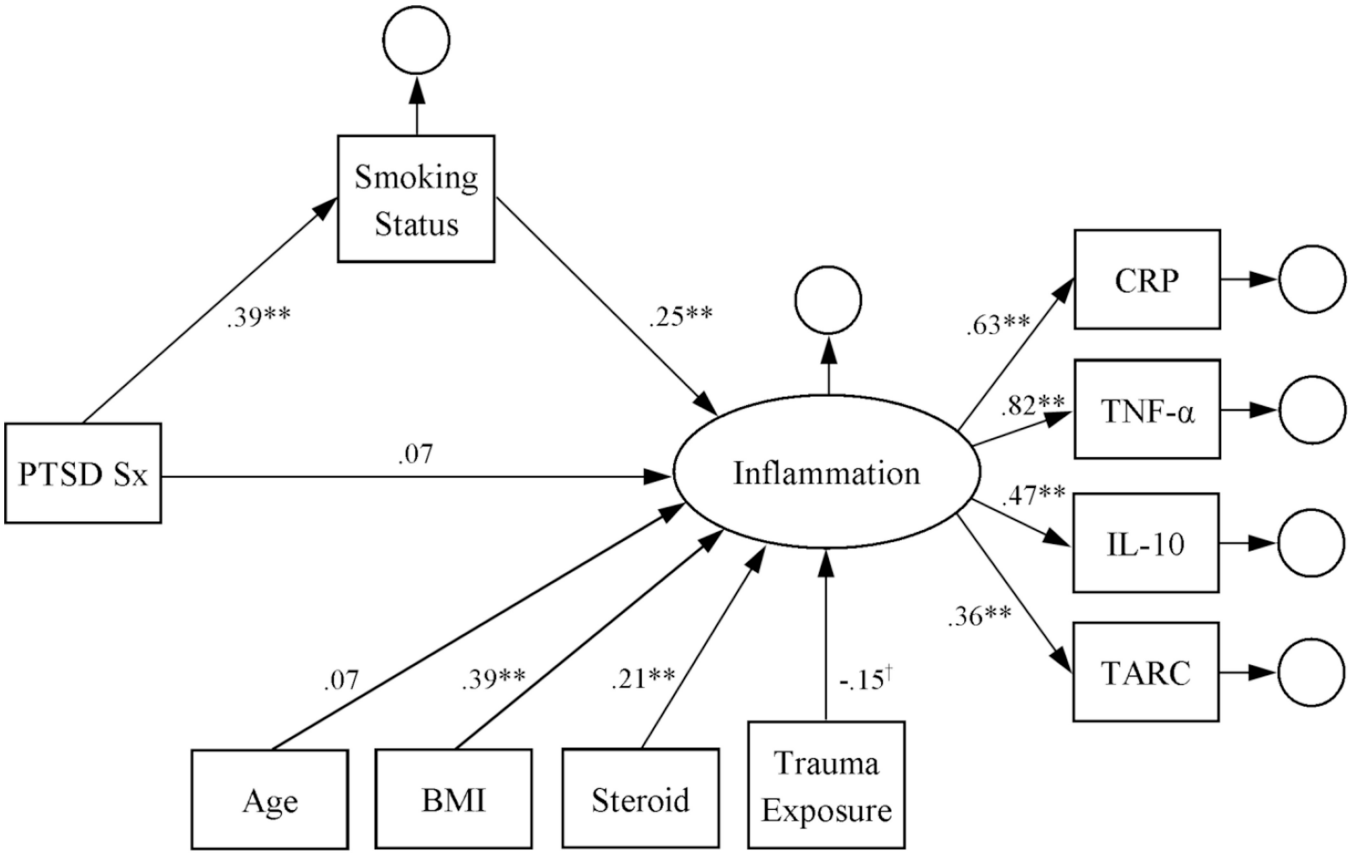
**Figure 1.**

Latent variable model of inflammation as a function of PTSD symptom severity. Estimates represent standardized coefficients. N = 164.



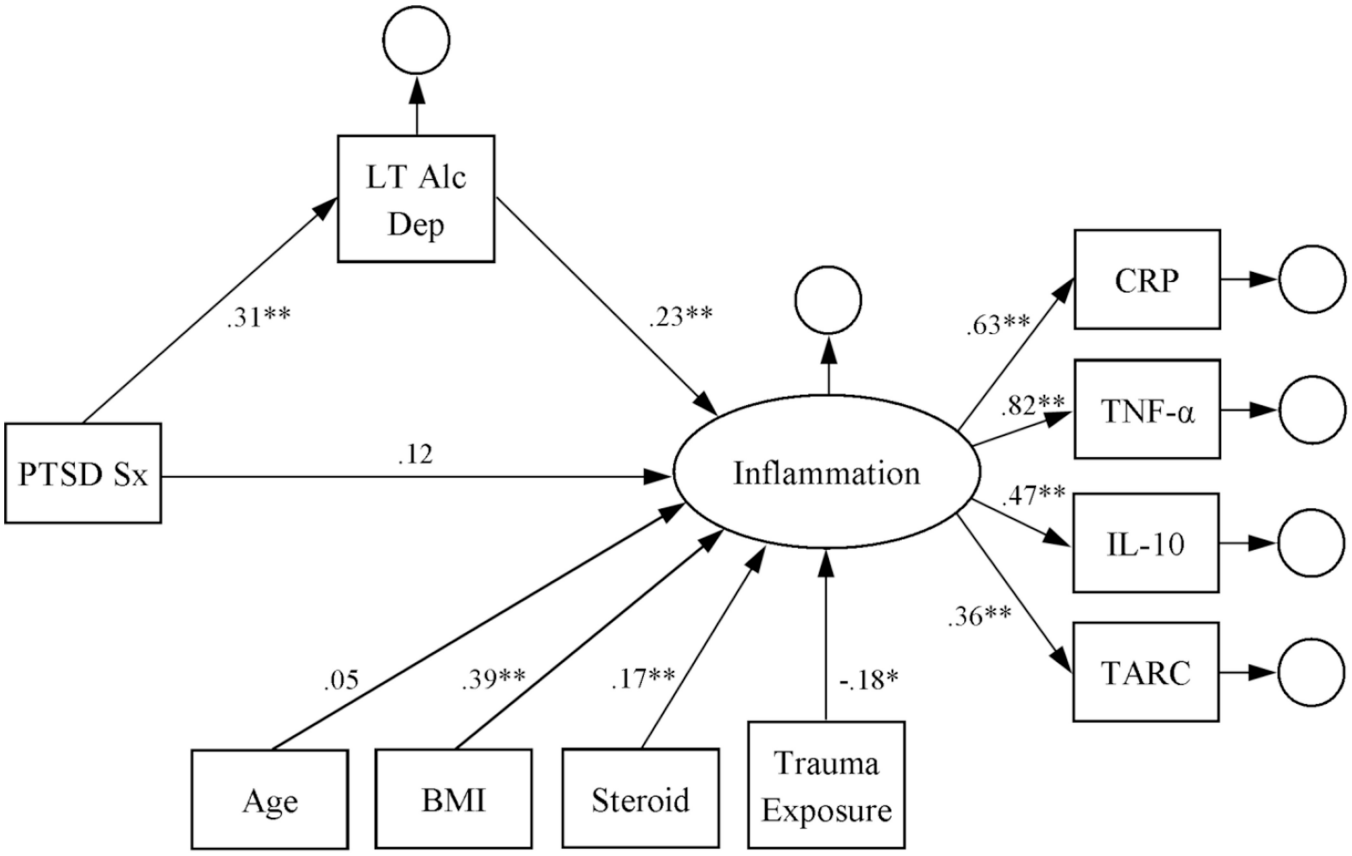

†$p < .10$, *$p < .05$, **$p < .01$

**Figure 2.**
Latent variable model of inflammation as a function of PTSD symptom severity and RSA. Estimates represent standardized coefficients. N = 164.




†$p < .10$, *$p < .05$, **$p < .01$

**Figure 3.**
Latent variable model of inflammation as a function of PTSD symptom severity and smoking status. Estimates represent standardized coefficients. N = 164.




*$p < .05$, **$p < .01$

**Figure 4.**

Latent variable model of inflammation as a function of PTSD symptom severity and lifetime alcohol dependence. Estimates represent standardized coefficients. N = 164.

**Table 1**

Participant Characteristics and Intercorrelations

| Variables | Means (SD)/Freq (%) | Intercorrelations (*r*-values) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | (2) | (3) | (4) | (5) | (6) | (7) | (8) | (9) | (10)[a] | (11)[a] | (12)[a] | (13)[a] |
| Age (1) | 29.78 (5.53) | −.03 | .07 | .09 | .61** | .22** | .05 | .22** | −.28** | .09 | .01 | −.12 | −.10 |
| Sex, female (2) | 80 (48%) | | .10 | .11 | .06 | −.08 | −.18* | −.31** | .14† | .04 | −.16* | −.12 | −.06 |
| BMI (3) | 29.83 (6.69) | | | .11 | .06 | .08 | .05 | .07 | −.01 | .50** | .22** | .04 | .17* |
| Steroid use (4) | 7 (4%) | | | | .07 | .05 | −.16* | −.04 | −.07 | .18** | .01 | −.00 | −.19* |
| Trauma exposure, years (5) | 17.89 (9.65) | | | | | .44** | .15* | .28** | −.17* | .07 | −.09 | −.02 | −.01 |
| DTS total (6) | 45.72 (37.78) | | | | | | .39** | .31** | −.17* | .04 | .06 | .15† | .03 |
| Smoking status (7) | 0.77 (0.83) | | | | | | | .34** | −.15† | .01 | .13 | .06 | .13 |
| LT alcohol dependence (8) | 53 (32%) | | | | | | | | −.22** | .10 | .16* | −.04 | .06 |
| RSA, logged (9) | 6.49 (1.25) | | | | | | | | | −.07 | −.11 | −.11 | −.04 |
| Cytokine levels, pg/ml | | | | | | | | | | | | | |
| CRP (10) | 4628.92 (6919.20) | | | | | | | | | | .27** | .23** | .10 |
| TNF-α (11) | 3.20 (1.17) | | | | | | | | | | | .33** | .15* |
| IL-10 (12) | 1.19 (1.79) | | | | | | | | | | | | .13† |
| TARC (13) | 902.16 (760.15) | | | | | | | | | | | | |

*Note*. Correlations between sex, steroid use, and LT alcohol dependence are tetrachoric. BMI = body-mass index; DTS total = Davidson Trauma Scale total score; LT Alcohol Dependence = lifetime alcohol dependence; RSA, logged = respiratory sinus arrhythmia (logged values); CRP = C-reactive protein; TNF-α = tumor necrosis factor-α; IL-10 = interleukin-10; TARC = thymus activation-regulated chemokine.

[a]Spearman rank-order correlations reported given pronounced positive skew of cytokine levels.