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Snehaa Krishnan Date

Relationship Between Early Trauma and Obstructive Sleep Apnea in Veterans

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Relationship Between Early Trauma and Obstructive Sleep Apnea in Veterans

By

Snehaa Krishnan

Bachelor of Science
Biological Sciences
Drexel University
2015

Thesis Committee Chair: Amit J. Shah, MD, MSCR

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
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2021

Abstract

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By: Snehaa Krishnan

Obstructive sleep apnea (OSA) is a condition which has many downstream health effects. Several studies show a significant association between early trauma and poor sleep health in adulthood. Early trauma is associated with obesity, which is one of the strongest risk factors for OSA. To test the hypothesis that early trauma is associated with OSA through obesity, patients from the Emory Twins Follow-Up study were surveyed about traumatic experiences from their childhood using the Early Trauma Inventory Short Form. OSA was measured using the apnea-hypopnea index and oxygen saturation during sleep. No significant association was found between early trauma and OSA. The model was also analyzed using sociodemographic confounders and mediating variables, which also did not yield any association. This study raised some questions about other potential mediators which could have led to the unique characteristics of this cohort.

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Introduction:

Obstructive OSA (OSA) is a condition where the upper airway closes during sleep, inducing repetitive episodes of complete stoppages of breathing (apnea) and hypoventilation (hypopnea). These episodes lead to frequent awakenings throughout the night, causing daytime sleepiness.[1] Over time, OSA causes maladaptive effects on the heart, brain, circulation, and metabolism. Individuals who suffer from OSA are at higher risk for sudden cardiac death in their sleep. It also increases inflammation, causing vasodilation, stiffening and calcification of arteries and carotid artery atherosclerosis.[2] Prevalence rates of OSA have increased by about 14% to 55% based on age group, sex, and severity level between 1988 to 2010.[3] Since OSA is associated with many negative health consequences, it is crucial to understand the risk factors to work towards prevention.

One factor that has been shown to affect sleep is early trauma, or trauma during childhood. Early trauma has been linked to many chronic health issues in adulthood. The American Academy of Pediatrics asserts that traumatic events in childhood have consequences not only for individuals, but also enormous costs socially and economically. It advocates for investments and policies for community-based interventions to identify and address early trauma.[4] By better understanding the downstream effects of early trauma, public health stakeholders can direct resources towards prevention.

Several studies show a significant association between early trauma and poor sleep health in adulthood.[5,6] In these studies, sleep health was measured both quantitatively and qualitatively. Sleep time and efficiency were measured using actigraphy technology and participants were asked about sleep quality and diagnosis or sleep disorders, such as OSA or sleep paralysis. It is important to note that in this study OSA was measured with a questionnaire rather than a formal sleep study.[7] Several hypotheses have been made about the mechanism by which early trauma impacts sleep health. One of these is obesity.

Studies show that individuals exposed to traumatic events in their childhood are at a higher risk for obesity in adulthood, and this in turn may increase the risk of OSA. These traumas not only include physical and sexual trauma, but also marital conflict between parents and separation from one or both parents. One reason for this association that was explored was diagnosis of a psychiatric disorder as a result of early trauma. In a study comparing non-obese healthy volunteers with no psychiatric diagnoses, obese participants with no psychiatric diagnoses and obese participants with psychiatric diagnoses, there was a significant association between early trauma and obesity. When obese participants with a psychiatric disorder were removed from the analysis, early trauma was still a significant predictor of obesity. [8] Obesity is one of the strongest risk factors for OSA. Fat in tissues of the upper airway could increase the risk of obstruction during sleep, while fat over the chest wall and abdomen reduces lung volumes by lowering chest wall compliance. Weight loss has been shown to significantly decrease the severity of sleep-disordered breathing, although this could also be because of exercise, which seems to influence OSA independent of weight loss.[9]

The links between early trauma and obesity, and obesity and OSA have been well documented. There is also some evidence of the association between early trauma and sleep disturbances, but the mechanism by which this happens is unclear. The aim of this study is to evaluate early trauma is a predictor of OSA, and to study the extent to which this relationship may be mediated by obesity.

Methods:

We are studying patients from the Emory Twins Follow-up Study, which consists of 241 male twin pairs from the Vietnam War Era Twin (VET) Registry (one of the largest twin registries in the United States) who were born between 1946-1956.

Early trauma (traumatic experiences before the age of 18) was measured using the Early Trauma Inventory Short Form (ETI-SF). It assesses physical, sexual, emotional abuse and general trauma. Both the number of pre-specified traumas was assessed, as well as their frequency. Summary values (based on number and frequency) from each trauma category were added to form a continuous ETI-SF score. A mean ETI-SF score in healthy individuals was calculated and designated as a cutoff, where those above the cutoff (of 7) were considered to have high levels of early trauma, while those who were below were not considered to have low levels of early trauma.[10]

OSA severity was measured using polysomnography or in-home sleep study (Apnea-Link). Severity was assessed by quantifying the apnea-hypopnea index (AHI). This is measured by the number of apneas (pauses in breathing) plus the number of hypopneas (periods of shallow breathing) occurring per hour, on average, during sleep. OSA was defined AHI values above 15 apneas per hour. Most participants received a polysomnogram in the Emory Sleep Lab. AHI was measured using standard clinical methods for these individuals. For participants who were not able to travel to Emory, a sleep tracker and the ApneaLink software was used to measure AHI. A secondary variable, oxygen saturation (SaO_2) was also measured.

Descriptive analyses and regression models were used for the twin pairs. SAS was used for all analyses. Potential confounders include sociodemographic variables. Other cardiovascular disease risk factors, such as family history and lifestyle factors, will also be adjusted for in other models.

Results:

Table 1 presents the demographic information of the 241 male twin pairs, separated by their scores on the Early Childhood Inventory-Short Form (ETI-SF). They are majority white, with an average age of 68 years old. The average BMI was 29.4 (43.37% of the cohort is obese). Participants with an ETI-SF score greater than 7 also showed more symptoms of PTSD and depression. They were also less likely to be obese or hypertensive and less likely to smoke. However, participants classified as high trauma consumed higher quantities of alcohol on average. In addition, these participants were less likely to be on medications including statins, ACE inhibitors, beta blockers or aspirin. The likelihood of having diabetes was similar in both groups.

There was no clear association between ETI-SF scores and AHI (**Figure 1**). Adjusting for age and education did not improve the association. Adjusting for BMI did not yield a significant association. Adjustment for BMI and alcohol use improved the relationship between early trauma and OSA most noticeably, but it was not significant (0.011, 95% CI [0.07, 0.144]) (**Table 2**). Similar results were seen for the association between ETI-SF scores and SaO_2 (**Figure 2**). This model was also serially adjusted for the same covariates (age, education, BMI, and alcohol use) as the model with AHI and yielded similar results (**Table 3**).

Discussion:

In this cohort of male veteran twins who underwent sleep testing, we did not find that an association between early trauma and OSA. Adjusting for potential sociodemographic confounders, age and education, and potential mediators such as BMI and alcohol use did not change the overall results.

Although this is the first study examining OSA with diagnostic testing, prior studies demonstrate a link between early trauma and sleep time, quality, and efficiency. A large study in U.S. adults aged 25-76 years showed that people who face childhood adversity are more likely to have problems with sleep quality and sleep time.[5] In a smaller study of Canadian university students, those who experienced abuse or trauma (defined as physical abuse, sexual abuse, psychological/emotional abuse and physical/emotional neglect), were more likely to experience a variety of sleep disturbances, including OSA (via questionnaire), than those who did not experience abuse or trauma.[11] An important distinction to make is that this study assessed OSA using a survey, while our study used polysomnography, which is the gold standard. Our study's cohort consisted of a group of only male veterans between the ages of 61-73 years old. Therefore, members of this group were also diagnosed with PTSD from the war, unlike other studies. One possibility is that since these individuals have been diagnosed with PTSD, they may already be paying special attention to their physical and mental health.

Adjustment for obesity reduced the estimate, although the wide confidence interval did not allow for us to make any conclusions beyond chance. Abuse in childhood (which is one source of early trauma) has been shown to have a consistent link with obesity. Follow-up data from the National Longitudinal Survey of Youth 1979, a nationally representative survey of U.S. men and women, showed a relationship between physical abuse and obesity.[12] Data from 5,378 respondents to the 2002 Texas Behavioral Risk Factor Surveillance System survey showed an increase in obesity in individuals who reported household dysfunction and abuse in childhood.[13] Our cohort did not show an increase in obesity with increase in early trauma. There are several possible reasons why this could be the case. First, chronic conditions such as heart failure or cancer can sometimes paradoxically cause weight loss.[14,15] Not all chronic conditions were assessed for in this study. Second, individuals in this cohort who were classified as having experienced high early trauma exhibited higher scores on the depression assessment. Depression can sometimes cause loss of appetite leading to weight loss.[16] Finally, food scarcity can play a role. We did not assess for food insecurity in this cohort.

This study has some limitations. First, this cohort seemed to exhibit results unlike similar studies done in other cohorts, such as low obesity among participants with high levels of early trauma. As described earlier, this could have occurred due to a variety of different factors, which were not explored in this study. Second, early trauma was recorded based on self-report, which is subject to recall bias, causing participants to be misclassified. Third, the data was not analyzed using twin modeling, which could have uncovered associations between twin pairs or within twin pairs.

Conclusion & Public Health Implications:

The purpose of this study was to investigate if there was any association between early trauma and OSA. The cohort studied consisted of male twin pairs from the Emory Twins Follow-Up Study. No associations were found between early trauma and OSA both directly, or using certain covariates (age, education, BMI, and alcohol use) as confounders or mediators. This cohort was unique in that the group having high trauma did not have high BMI as previous studies have shown. Future studies should investigate mediating factors that could lead to this, such as other chronic illnesses or food insecurity. Both OSA and early trauma have many downstream effects. Studying these in detail can help determine prevention methods, which can have major social and economic benefits in healthcare.

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Tables & Figures

Table 1. Baseline Characteristics of the Cohort by ETI-SR-SF Score (Frequency, Onset, Emotional Impact of Early Trauma)

	ETI-SR-SF score, No. (%)	
Characteristic	<7	≥7
No.	175	104
Demographic Factors		
Age, mean (SD)	68.26 (2.35)	67.47 (2.64)
White	170 (61.15)	99 (35.61)
Education > 12y	103 (37.05)	70 (25.18)
Psychosocial Factors, median (IQR)		
PTSD Symptom Checklist	3 (8)	10 (16)
Beck Depression Inventory II	3 (5)	6 (8)
Clinical Factors		
Obesity, BMI ≥ 30	76 (27.34)	45 (16.19)
Hypertension	59 (21.15)	39 (13.98)
Diabetes	12 (4.3)	11 (3.94)
Ever Smoker	102 (36.56)	75 (27.24)
Number of alcoholic drinks in 30 days, mean (SD)	1.54 (2.85)	3.07 (10.24)
Medications		
β-Blockers	39 (13.98)	29 (10.39)
Aspirin	82 (29.39)	40 (14.34)
ACE inhibitors	44 (15.77)	29 (10.39)
Statins	92 (32.97)	51 (18.28)

Values are percentages unless indicated. Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ETI-SR-SF, Early Trauma Inventory–Self Report short form; IQR, interquartile range; PTSD, posttraumatic stress disorder.

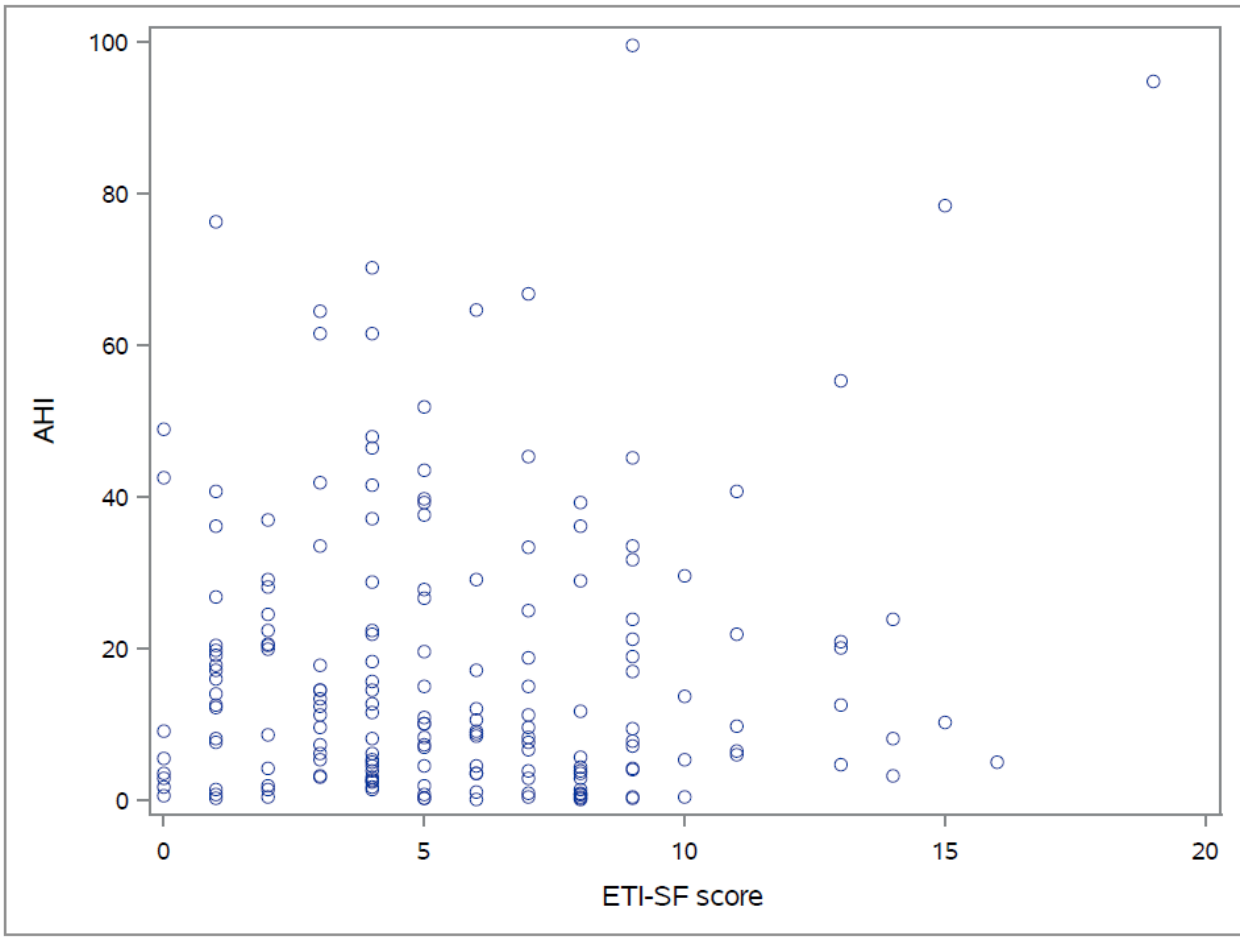

Figure 1. Scatter plot of Apnea-Hypopnea Index (AHI) vs. Early Trauma Inventory-Short Form score (ETI-SF)

Table 2. Cumulative Sequential Models of the Relationship between early trauma and AHI

Model	**Parameter Estimate**	**95% Confidence Interval**
Unadjusted	0.0046	(-0.041, 0.05)
Adjusted for age and education	0.0088	(-0.039, 0.053)
Adjusted for BMI	0.0018	(-0.037, 0.055)
Adjusted for BMI and alcohol use	0.011	(0.07, 0.144)

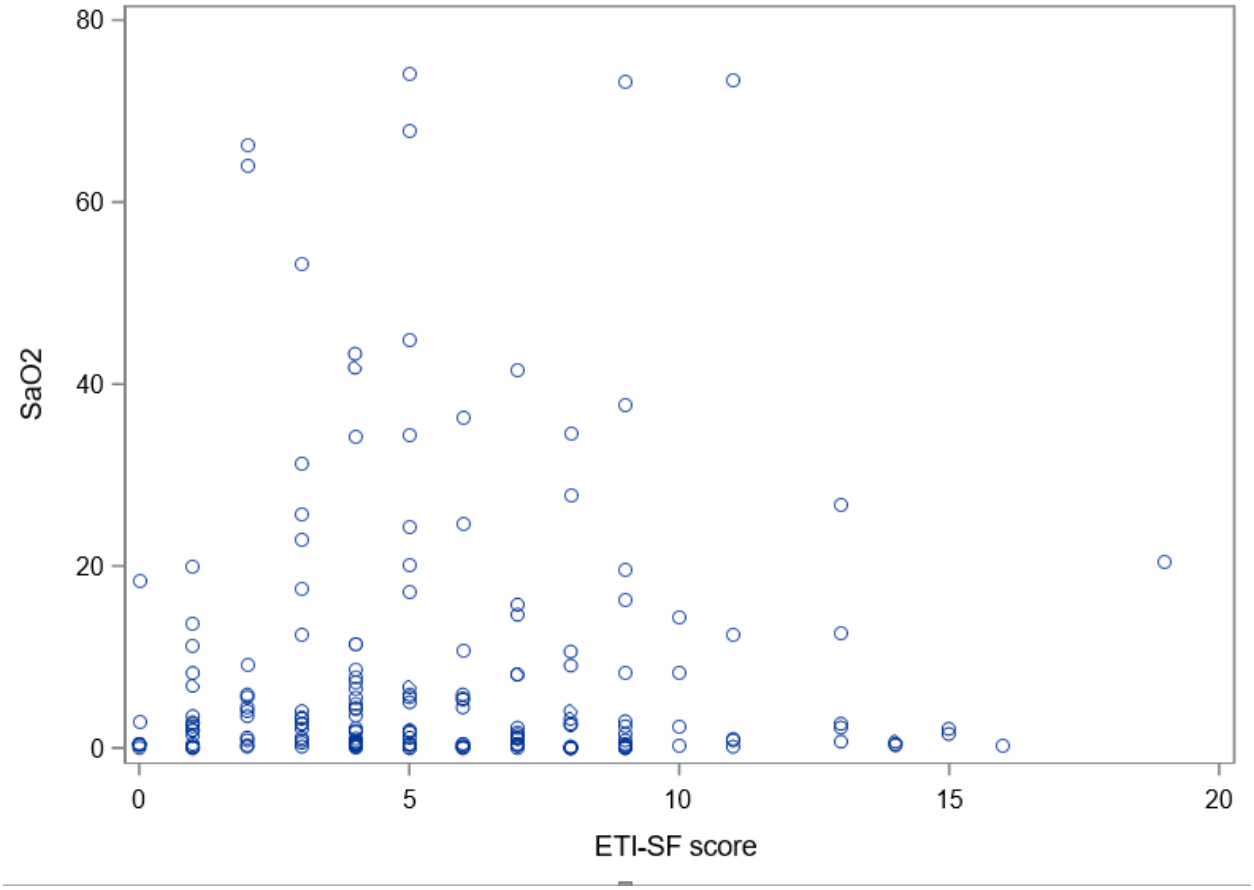

Figure 2. Scatter plot of Oxygen Saturation (SaO_2) vs. Early Trauma Inventory-Short Form score (ETI-SF)

Table 3. Cumulative Sequential Models of the Relationship between early trauma and SaO_2

Model	**Parameter Estimate**	**95% Confidence Interval**
Unadjusted	0.055	(-0.563, 0.673)
Adjusted for age and education	0.114	(-0.516, 0.744)
Adjusted for BMI	0.017	(-0.576, 0.61)
Adjusted for BMI and alcohol use	0.011	(-0.427, 0.711)

Appendix 1: Institutional Review Board Approval Letter

IRB CONTINUING REVIEW APPROVAL

April 14, 2021

Laura Vaccarino, MD, PhD
lvaccar@emory.edu

Title:	PTSD and Ischemic Heart Disease Progression: A Longitudinal Twin Study
Principal Investigator:	Laura Vaccarino, MD, PhD
IRB ID:	CR002-IRB00081004
Funding:	Name: Federal Agency, Emory EPEX ID: 47695, Funding Source ID: NHLBI - National Heart, Lung and Blood Institute; Name: Federal Agency, Emory EPEX ID: 36816, Funding Source ID: NHLBI - National Heart, Lung and Blood Institute; Name: Federal Agency, Emory EPEX ID: 47609, Funding Source ID: NHLBI - National Heart, Lung and Blood Institute; Name: Federal Agency, Emory EPEX ID: 26356, Funding Source ID: NHLBI - National Heart, Lung and Blood Institute
IND, IDE or HDE:	None
Documents Reviewed:	• PTSD and Perfusion protocol 5.7.2019 clean.pdf, Category: IRB Protocol;

Dear Laura Vaccarino:

Thank you for submitting a renewal application for this protocol. The Emory IRB approved it by the expedited process on 4/13/2021, per 45 CFR 46.110, the Federal Register expeditable category F[8c], and/or 21 CFR 56.110.

This reapproval is effective from 4/13/2021 through 4/12/2022. Thereafter, continuation of human subjects research activities requires the submission of another renewal application, which must be reviewed and approved by the IRB prior to the expiration date noted above.

Please note carefully the following items with respect to this approval:

- PTSD and Perfusion protocol 5.7.2019 clean.pdf, Category: IRB Protocol;

In conducting this protocol, you are required to follow the requirements listed in the Emory Policies and Procedures, which can be found at our IRB website.

Sincerely,
Brook Cabrera
IRB Analyst Assistant

Your stamped consent form is available under the "Documents" tab.

Now that your submission has been approved, please take a few moments to complete the Emory IRB Satisfaction Survey. We will use your responses to improve our service to the Emory research community. We appreciate your feedback!