



The role of modifiable health-related behaviors in the association between PTSD and respiratory illness

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ABSTRACT

Background: Posttraumatic stress disorder (PTSD) increases risk of future respiratory illness. However, mechanisms that underpin the association between these common and debilitating conditions remain unknown. The aim of this study was to identify modifiable, health-related behaviors they may explain the link between PTSD and respiratory problems.

Methods: World Trade Center responders (N = 452, 89% male, mean age = 55 years) completed baseline PTSD and sleep questionnaires, followed by 2-weeks of daily diaries, actigraphy and ambulatory spirometry to monitor lower respiratory symptoms, pulmonary function, activity levels, stressors, and sleep. Lipid levels were obtained from electronic medical records.

Results: Cross-sectional mediation analyses revealed that the association between PTSD and self-reported respiratory symptoms was explained by poor sleep, low activity, and daily stressors. The association between PTSD symptoms and pulmonary function was explained by insomnia and low activity.

Conclusions: A range of health-related daily behaviors and experiences, especially sleep disturbances and inactivity, may explain excess respiratory illness morbidity in PTSD. The findings were generally consistent across daily self-report and spirometry measures of respiratory problems. Targeting these behaviors might enhance prevention of and intervention in respiratory problems in traumatized populations.

1. Introduction

Psychiatric illness has deleterious physical health consequences and the comorbidity between mental and physical disorders is associated with poor treatment adherence, high service utilization, and worse functional outcomes (Cwikel, Zilber, Feinson, & Lerner, 2008; Melek, Norris, & Jordan Paulus, 2014; Mercer, Gunn, Bower, Wyke, & Guthrie, 2012; Weisberg et al., 2002). The current study focuses on posttraumatic stress disorder (PTSD) and respiratory illness, two highly prevalent, recurrent and debilitating conditions that frequently co-occur in trauma-exposed, primary care, and general populations (Scott et al., 2007, 2015; Spitzer et al., 2009; Von Korff, Scott, & Gureje, 2009; Üstün & Sartorius, 1995). PTSD and respiratory illness are also signature disorders in populations exposed to the World Trade Center (WTC) disaster (Aldrich et al., 2010; Bromet et al., 2015; Kotov et al., 2015; Luft et al., 2012; Perrin et al., 2007; Wisnivesky et al., 2011). Importantly, longitudinal studies indicate that PTSD symptoms are a significant risk factor for the onset and chronicity of lower respiratory

symptoms (LRS) in this population, contributing to poorer respiratory health independently of smoking (Kotov et al., 2015; Niles et al., 2011; Waszczuk et al., 2017). This is in line with a large body of evidence demonstrating that PTSD contributes to worse physical illness outcomes (Boscarino, 2004; Coughlin, 2011; Dedert, Calhoun, Watkins, Sherwood, & Beckham, 2010). Despite the prominent comorbidity and the etiologic pathway from PTSD to respiratory symptoms, mechanisms underpinning this association remain unknown.

Existing studies indirectly point to several modifiable behaviors that may explain the connection between PTSD and respiratory illness. However, these potential mechanisms have not been studied jointly in the context of the etiological pathway from PTSD to respiratory symptoms. First, sleep is a fundamental contributor to mental and physical health, regulating diverse functions such as restorative cell processes (Cirelli, 2009; Mackiewicz, Zimmerman, Shockley, Churchill, & Pack, 2009), memory consolidation (Aton et al., 2009; Tononi & Cirelli, 2014) and immunity (Imeri & Opp, 2009). Disturbed sleep is a common consequence of trauma (Krakow et al., 2004; Mellman, David,

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Kulick-Bell, Hebding, & Nolan, 1995; Straus, Drummond, Nappi, Jenkins, & Norman, 2015) and prospective findings point to a bidirectional relationship between PTSD and sleep disturbance, such as insomnia (Germain, 2013; Kleim, Wysokowsky, Schmid, Seifritz, & Rasch, 2016; Koren, Arnon, Lavie, & Klein, 2002; Spoomaker & Montgomery, 2008). In responders, insomnia was found to be associated with greater WTC exposure and psychiatric symptoms (Giosan et al., 2015). Furthermore, insomnia commonly occurs in individuals with respiratory illness (Ohayon, 2002; Sivertsen et al., 2014), perhaps because sleep disturbances increase pro-inflammatory gene expression and heighten systemic inflammation (Irwin et al., 2014; Irwin, Olmstead, & Carroll, 2016; Irwin & Opp, 2017; Morgan, Irwin, Chung, & Wang, 2014), which then contributes to respiratory disease. Taken together, sleep disturbances constitute a plausible path from PTSD to respiratory problems.

Second, metabolic risk factors – such as obesity and abnormal cholesterol and triglyceride levels – frequently co-occur with adverse health outcomes. PTSD in particular has been associated with elevated lipid profiles and obesity (Coughlin, 2011; Dedert et al., 2010; Kagan, Leskin, Haas, Wilkins, & Foy, 1999; Maia et al., 2008; McFarlane, 2010), even when adjusting for lifestyle covariates. Research suggests that PTSD largely drives this association, as it disrupts the HPA-axis and norepinephrine-sympathetic system, consequently contributing to hyperlipidemia and weight gain (Coughlin, 2011; Dedert et al., 2010; McFarlane, 2010). Furthermore, PTSD negatively affects health-related behaviors such as physical activity (Hall, Hoerster, & Yancy Jr, 2015; Zen, Whooley, Zhao, & Cohen, 2012), which in turn can worsen metabolic risk. Obesity and metabolic dysregulation can have deleterious effects on pulmonary physiology (Ali & Ulrik, 2013; Baffi et al., 2016; Beuther, Weiss, & Sutherland, 2006; Brumpton et al., 2013; Lee et al., 2009). Consistently, in WTC responders, elevated lipid profiles predicted future decrease in pulmonary function (Natale et al., 2015). Thus, metabolic changes and lower physical activity might constitute pathways through which PTSD worsens respiratory symptoms.

Third, stress plays an important role in both PTSD and respiratory illness. Trauma exposure leads to an increased reactivity to subsequent stressors, in line with the stress sensitization theories (Post, 1992; Post & Weiss, 1998). Accordingly, stressful experiences in the aftermath of trauma are associated with increased risk, severity and chronicity of PTSD (Brewin, Andrews, & Valentine, 2000; Cerdá et al., 2013; Fukuda, Morimoto, Mure, & Maruyama, 1999; Hammen, Henry, & Daley, 2000; McLaughlin, Conron, Koenen, & Gilman, 2010; Post & Weiss, 1998). In turn, PTSD increases susceptibility to stressful events via the process of stress generation (Conway, Hammen, & Brennan, 2012; Maniates, Stoop, Miller, Halberstadt, & Wolf, 2018). Such reciprocal associations between stress and PTSD, as well as an increased stress sensitivity following trauma exposure, have been reported in WTC responders (Zvolensky, Farris, et al., 2015; Zvolensky, Kotov, et al., 2015). Stress is also known to negatively impact respiratory symptoms, likely by heightening inflammation in the airways (Chen & Miller, 2007; Miller, Chen, & Cole, 2009; Yellowlees & Kalucy, 1990).

Beyond major life events, daily stress from minor events such as hassles and interpersonal conflicts is a significant and independent contributor to mental and physical ill-health (Asselmann, Wittchen, Lieb, & Beesdo-Baum, 2017; DeLongis, Coyne, Dakof, Folkman, & Lazarus, 1982; Kanner, Coyne, Schaefer, & Lazarus, 1981; Miller & Rasmussen, 2010; Monroe, 1983). These minor stressors can constitute unexpected disruptions, as well as reflect ongoing strains that stem from chronic or major stressors, and are much more frequent than major stressful life events. Indeed, effects of daily stress are well documented for PTSD, for example in policemen, job-related organizational stressors were found to be more strongly predictive of future PTSD symptoms than experiencing additional traumatic events (Heron, Bryan, Dougherty, & Chapman, 2013; Huddleston, Stephens, & Paton, 2007; Patterson, 1999). Furthermore, both stress sensitization due to trauma, and stress generation processes, occur at the level of everyday

stressors, for example PTSD symptoms predict poor parental functioning, increased family conflict, and poor overall family adjustment post-deployment (Lester et al., 2010; Milliken, Auchterlonie, & Hoge, 2007). As with major stressful life events, minor daily stress may contribute to inflammatory dysregulation (Eisenberger, Moieni, Inagaki, Muscatell, & Irwin, 2016; Fuligni et al., 2009; Gouin, Glaser, Malarkey, Beversdorf, & Kiecolt-Glaser, 2012), which in turn increase risk for respiratory symptoms (Chen & Miller, 2007; Miller et al., 2009; Yellowlees & Kalucy, 1990). In sum, stressful events of any severity might be another maladaptive process mediating the etiological pathway from PTSD to respiratory illness.

The maladaptive processes outlined above are likely to be inter-related. For example, inadequate sleep predicts lower activity levels (Atkinson & Davenne, 2007; Montgomery, John, & Paxton, 1982; Schmidt, Swang, Hamilton, & Best, 2017; Strine & Chapman, 2005) and future weight gain (Magee & Hale, 2012; Patel & Hu, 2008; Taheri, Lin, Austin, Young, & Mignot, 2004), while sleep itself is negatively affected by stress (Jansson & Linton, 2006; Kim & Dimsdale, 2007; Mezick et al., 2009; Sadeh, Keinan, & Daon, 2004). For this reason, it is crucial to study these mechanisms jointly in an integrated model, which would help to identify the most prominent and non-redundant pathways from PTSD to respiratory illness. Such pathways would be the most promising targets for prevention and intervention.

Current knowledge about the relationship between PTSD, respiratory symptoms and health-related behaviors largely comes from studies based in labs or clinics. Ambulatory assessments are needed to test these pathways as they occur naturally, free of recall bias and with high ecological validity and reliability (Myin-Germeys et al., 2009; Shiffman, Stone, & Hufford, 2008; Torous, Onnela, & Keshavan, 2017; Trull & Ebner-Priemer, 2013). Ambulatory approach is particularly important for studying respiratory symptoms, as they vary from day to day (Smyth, Soefer, Hurewitz, Kliment, & Stone, 1999). Another important consideration when studying respiratory illness is that self-reported symptoms and objectively-assessed pulmonary function are only modestly related (Curtis & Patrick, 2003; Tsigianni, Kocks, Tzanakis, Sifakakis, & van der Molen, 2011), a finding replicated in the WTC population (Kotov et al., 2015; Luft et al., 2012). This low agreement might be due to different strengths of each approach: while the spirometry assessment is objective and unaffected by potential reporting biases, self-report might be more sensitive to capturing a wider range of respiratory symptoms (e.g. cough frequency) and to rare respiratory events that monitoring is likely to miss, as well as symptoms that have not yet resulted in chronic restriction or obstruction (Skloot et al., 2004). For this reason, to fully understand the association between PTSD and respiratory illness, a multimethod approach should be used.

The aim of the current study was to test modifiable health-related mechanisms that underpin the association between PTSD and respiratory symptoms. Specifically, the current study focuses on four domains of health-related mechanisms: sleep, metabolic processes, physical activity, and stress. We sought to apply multimethod approach to investigate these relationships, including the assessment of respiratory problems both by self-report and ambulatory spirometry, and evaluating symptoms and health behaviors with questionnaires, daily diaries, actigraphy, and blood tests. The current study examined these associations cross-sectionally in order to identify a set of non-redundant potential mediators of the path between PTSD and respiratory illness. The identified paths would be promising targets for longitudinal and treatment studies. Based on previous literature, we hypothesized that each health-related mechanism under consideration – sleep, metabolism, physical activity, and stress – will mediate the association between PTSD and respiratory illness. However, since these mechanisms were never studied together in a joint model, we did not have an a priori hypothesis about independent contribution of each mechanism.

2. Methods

2.1. Participants

Data were collected during first wave assessment of the WTC Health and Personality study, a longitudinal project with two yearly follow up waves currently undergoing data collection. A sample of 452 WTC responders was recruited from a consecutive group of patients seeking treatment from Stony Brook University WTC Health Program, which monitors over 8000 WTC responders from Long Island, NY (Dasaro et al., 2015). Mean age was 55.22 years (SD = 8.73, range = 32–82 years), 89% male, 90% Caucasian, and 91% non-Hispanic. Also, 64% participants were employed in law enforcement on 9/11, with the remaining responders having miscellaneous occupations, including construction workers, electricians, and paramedics. Ten percent of the sample during baseline assessment self-reported regularly smoking cigarettes or e-cigarettes, or chewing tobacco. Exclusion criteria included linguistic, cognitive or physical limitations that would prevent completion of study procedures, such as inability to understand survey questions, attend a baseline appointment, or complete surveys on a mobile device at home. Participants completed a baseline visit, which included questionnaires and device training in how to access the survey application on the mobile phone, as well as correctly use home spirometer and accelerometer. The baseline visit was followed by 2-weeks of daily monitoring of respiratory symptoms, pulmonary function, stressors, and health-related behaviors. Specifically, daily monitoring consisted of a morning survey regarding the prior night's sleep, and an evening survey about symptoms and experiences from the given day, as well as an ambulatory spirometry. Participants wore an accelerometer each day of the monitoring period, removing it only to sleep or shower. The study was approved by the Institutional Reviewer Board of Stony Brook University and all participants provided informed consent.

3. Measures

3.1. PTSD symptoms

PTSD symptoms were measured during the baseline visit using the PTSD Checklist for DSM-5 (PCL-5) (Weathers et al., 2013). It is a 20-item self-report questionnaire assessing, on a five-point scale (1 = not at all to 5 = extremely), the severity of PTSD symptoms in the past month in response to a very stressful experience. The scale demonstrates excellent psychometric properties (Blevins, Weathers, Davis, Witte, & Domino, 2015; Bovin et al., 2016) and had excellent internal consistency in the current sample ($\alpha = 0.95$).

3.2. Respiratory symptoms

Respiratory symptoms were assessed daily across 2-weeks of monitoring in two ways. First, *self-reported lower respiratory symptoms* (LRS) were indexed by the composite of five symptoms in the given day: shortness of breath, chest tightness, wheezing, coughing, and overall difficulty breathing. Questions were derived from standard assessments and adapted to daily format (Waszczuk et al., 2017). Participants rated the severity of each symptom from 1 (none) to 5 (extreme). Scores were averaged across 14 days. Internal consistency of the final measure was excellent ($\alpha = 0.92$).

Second, participants completed daily ambulatory *spirometry* assessments using a hand-held, expiratory flow meter PIKO-6 (nSpire Health, Inc.). Participants received device training, were required to inhale maximally, and then exhale as hard as possible into the mouthpiece for at least 6 s until an end-of-blow beep was heard. They were also trained to verify trial validity (e.g. the signal "I" indicated that a trial was invalid) and repeat the trial if needed. Two trials were done each evening, and the higher score, indicative of higher lung volume and hence better respiratory health, was automatically recorded by the device. Scores

above and below 3 SD from the sample mean were removed, and the data was standardized as proportion of value expected given participant's demographics and height (Hankinson, Odencrantz, & Fedan, 1999). The current analyses focus on the expiratory volume in the first second (FEV 1), a marker of asthmatic airway obstruction, averaged across 14 days.

3.3. Sleep

Sleep was assessed both during the baseline visit and with daily monitoring. In the lab, participants completed the modified *Insomnia Severity Index* (ISI) (Bastien, Vallières, & Morin, 2001; Morin, 1993), a 7-item self-report instrument measuring patients' perception of the severity of sleep-onset and sleep maintenance difficulties, and the degree of distress caused by them. The item on whether sleep problems were noticed by others was dropped due to a clerical error, resulting in a 6-item composite. Each item was rated on a 5-point Likert severity scale. The ISI has excellent psychometric properties and has been validated with respect to daily sleep diaries and polysomnography (Bastien et al., 2001; Morin, Belleville, Bédar, & Ivers, 2011). Internal consistency in the current sample was excellent ($\alpha = 0.90$).

Naturalistic sleep pattern was assessed every morning using the morning survey, based on the Pittsburgh Assessment Conference consensus sleep diary (Carney et al., 2012; Natale et al., 2015). Participants were asked to report the time they fell asleep last night, middle of night awakenings, and the time of their final awakening, which were used to calculate sleep duration. Values outside 3 SD from the mean were removed. We observed a U-shaped association between the number of sleep hours and PTSD and respiratory symptoms, therefore a quadratic variable, centered on the mean of the sample, was created to account for the non-linearity. Participants were also asked to rate the *quality of their sleep* last night on a scale from 1 (very poor) to 5 (very good).

3.4. Metabolic indices

Lipid profile - low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides - was obtained from participants' medical records. Lab tests for a lipid panel in fasting plasma is part of the regular monitoring assessment of the WTC cohort. The nearest available assessment was used (mean number of days between the blood draw for the lipid panel and the baseline visit of 53 days, SD = 21). Outliers outside 3 SD deviation from the mean were removed.

Body mass index (BMI) was calculated using height and weight measurements collected during the baseline visit.

3.5. Activity

Activity was measured using ActiGraph™ WGT3X-BT monitor device (ActiGraph, LLC). It is a triaxial *accelerometer* (Dimensions: 4.6 cm × 3.3 cm × 1.5 cm; weight: 19 g) worn on the waist using an elastic belt to secure above the right hip bone for quantifying the amount and frequency of human movements. The monitor was initialized at a sample rate of 30 Hz to record activities for free-living conditions. Participants were instructed to wear the ActiGraph continuously throughout the daily monitoring period, except for bathing, immersing in water, and sleep. ActiGraph data were downloaded using ActiLife 6 software (ActiGraph, LLC) upon collection of the devices. Downloaded data were integrated into 60-sec epochs. Valid wear time was determined by the timings of the morning and evening surveys, periods when the accelerometer was not worn were excluded. Mean number of steps per day across the whole daily monitoring period was calculated.

3.6. Stress

Stress exposure was assessed daily across 2-weeks of monitoring. Participants completed a checklist of 9 stressors for the monitoring day, which included items about troubles with work and home, problems with transportation, financial issues and interpersonal conflicts. The items were selected from the Daily Stress Checklist (DSC) (Almeida, Wethington, & Kessler, 2002), a brief checklist of common daily stressors, supplemented with non-redundant stem items from the Daily Inventory of Stressful Events (DISE) (Bolger, DeLongis, Kessler, & Schilling, 1989).

4. Analytic approach

First, all variables assessed via daily monitoring were aggregated to create average daily scores. Second, age, sex, race, smoking status, severity of WTC disaster exposure, as indexed by the degree to which participants were directly in the cloud of dust from the collapse of the WTC buildings (Wisnivesky et al., 2011), and employment in the law enforcement on 9/11 were regressed from all study variables prior to analyses, to control for known confounds. Third, bivariate correlations among the study variables were obtained. All variables that significantly correlated with PCL and at least one respiratory measure (LRS and FEV 1) were taken forward to mediation analyses. Specifically, eleven individual cross-sectional mediation analyses were conducted to assess whether each variable significantly explained the association between PCL and respiratory measures. Finally, all variables that emerged as significant mediators were simultaneously entered into two joint cross-sectional mediation analyses for the corresponding model (PCL and LRS or PCL and FEV 1). Mediation analyses were conducted in MPlus and bootstrapping was used to obtain confidence intervals, a method with improved power over the Sobel test (Preacher & Hayes, 2004, 2008).

5. Results

PTSD symptoms were common in the sample (Table 1). The mean standardized spirometry reading (0.84) was near the lower boundary of normal range (0.80), which indicated that objectively-measured respiratory problems were very common in the sample. Blood LDL cholesterol levels were on average elevated in comparison to the recommended healthy limit (< 100), while HDL cholesterol and triglyceride levels were on average near the healthy limit (> 40,

and < 150, respectively). An average BMI fell within the obese range. Sample size was lower for FEV 1 and activity due to compliance with device use during the daily monitoring period. Sample size was lower for the baseline insomnia instrument because the instrument was integrated after the start of data collection.

After adjusting for covariates, PTSD symptoms were strongly associated with LRS ($r = 0.55$) and the association with FEV 1 was also significant ($r = -0.16$) (Table 2). The two respiratory measures were also significantly correlated with each other ($r = -0.24$). Five variables significantly correlated with PTSD symptoms, LRS and FEV 1: insomnia, sleep quality, BMI, activity and stress exposure (absolute $r = .12 - 0.60$). Sleep duration (quadratic term) was associated with both PTSD symptoms and LRS ($r = .10$ and $.11$, respectively), but not with FEV 1. Lipid levels were not associated with PTSD symptoms and LRS, however HDL cholesterol and triglyceride levels were associated with FEV 1 ($r = 0.17$ and -0.16 , respectively).

Health-related behavior variables showed notable associations, but were not redundant with each other. All sleep variables were inter-correlated, with particularly high correlation between baseline insomnia symptoms and sleep quality ($r = -.65$). A relatively small, albeit significant correlation between insomnia and quadratic sleep duration ($r = 0.12$) indicate that these measures capture different aspects of sleep disturbance. There were small to moderate associations between sleep variables and stress exposure (absolute $r = .10-.34$). Insomnia and sleep duration were also associated with lower physical activity ($r = -0.10$ to -0.23) and only the former variable was associated with BMI ($r = 0.11$). Among lipid markers, only HDL cholesterol and triglycerides were significantly correlated with each other ($r = -0.48$). All lipid markers correlated with activity (absolute $r = 0.11-0.22$, respectively). Finally, BMI was correlated with HDL cholesterol and triglycerides ($r = -0.32$ and 0.22 , respectively), daily activity ($r = -0.31$) and higher number of stressful events ($r = 0.12$).

Out of the six variables that were significantly associated with both PTSD symptoms and LRS, four were found to significantly cross-sectionally mediate this relationship (Table 3). Stress exposure accounted for 29% of the association (indirect effect = 0.16, CI: 0.09 - 0.23), and the other three significant cross-sectional mediators were insomnia (indirect effect = 0.07, CI: 0.01 - 0.14), sleep quality (indirect effect = 0.07, CI: 0.03 - 0.11), and activity (indirect effect = 0.02, CI: 0.002 - 0.04), accounting for 14%, 14% and 4% of the total effect respectively. When taken forward to the joint mediation model, all variables, except for insomnia, remained significant independent cross-sectional mediators of the association between PTSD symptoms and

Table 1
Descriptive statistics.

Assessment format	Variable	N	Mean	SD	Minimum	Maximum	Skewness
Baseline	PTSD symptoms	447	34.27	15.32	20.00	96.00	1.48
DM	LRS	436	6.71	2.67	5.00	21.86	2.44
DM	FEV 1	366	.84	.18	.36	1.59	.26
Baseline	Insomnia	355	9.54	6.48	.00	24.00	.37
DM	Sleep hours/night	426	6.92	.96	3.77	9.66	-.16
DM	Sleep quality	435	3.34	.72	1.00	5.00	-.20
ER	LDL Cholesterol	427	108.22	33.79	22.00	228.00	.43
ER	HDL Cholesterol	435	51.71	15.82	21.00	110.00	1.01
ER	Triglycerides	424	125.81	62.88	33.00	368.00	1.30
Baseline	BMI	452	31.41	5.93	19.76	56.57	1.09
DM	Activity (steps/day)	396	6402.00	2972.64	880.08	21331.92	.90
DM	Stressful events/day	436	1.02	1.23	.00	6.40	1.77

Notes.

DM – daily monitoring; ER – electronic medical record; LRS – lower respiratory symptoms; LDL - low-density lipoprotein; HDL - high-density lipoprotein; BMI – body mass index.

Daily monitoring variables were averaged across all available assessment points.

For interpretation purposes, the recommended cut-offs for the variables are: PTSD – a score of 53 or above is suggestive of clinical severity; FEV 1 – a score below 0.80 indicates abnormal respiratory performance; LDL cholesterol above 100 is considered unhealthy; HDL cholesterol below 40 is less than the healthy range; triglycerides score above 150 is considered unhealthy; BMI of 18.5–24.9 is classified as healthy, 25.0–29.9 is classified as overweight and above 30 is classified as obese. The cut-offs for LRS, sleep variables, activity, and stress have not been derived.

Table 2
Bivariate correlations among adjusted study variables.

	PTSD	LRS	FEV 1	Insomnia	Sleep hours	Sleep quality	LDL Cholesterol	HDL Cholesterol	Triglycerides	BMI	Activity
LRS	.55*										
FEV 1	-.16*	-.24*									
Insomnia	.60*	.41*	-.26*								
Sleep hours	.10*	.11*	-.03	.12*							
Sleep quality	-.43*	-.37*	.14*	-.65*	-.17*						
LDL Cholesterol	-.01	-.02	.02	-.05	-.03	-.03					
HDL Cholesterol	-.06	-.01	.17*	-.09	-.01	.02	.02				
Triglycerides	.08	.06	-.16*	.03	.04	-.03	.09	-.48*			
BMI	.12*	.12*	-.18*	.11*	.06	-.07	-.09	-.32*	.22*		
Activity	-.15*	-.21*	.22*	-.23*	-.10*	.10	.11*	.22*	-.20*	-.31*	
Stressful events	.53*	.50*	-.11*	.34*	.10*	-.33*	-.03	-.01	-.01	.12*	-.08

Notes.

*denotes $p < .05$.

LRS – lower respiratory symptoms; LDL – low-density lipoprotein; HDL – high-density lipoprotein; BMI – body mass index.

All analyses control for age, sex, race, smoking status, severity of WTC disaster exposure, and employment in the law enforcement on 9/11. For unadjusted correlations, see Table A1 in the Appendix.

Quadratic sleep hours variable was used to assess non-linear relationship.

LRS, jointly accounting for 43% of the total association (Fig. 1a). Stressful events remained the strongest cross-sectional mediator (indirect effect = 0.15, CI: 0.08 – 0.22), followed by sleep quality (indirect effect = 0.05, CI: 0.001 – 0.10) and activity (indirect effect = 0.02, CI: 0.001 – 0.04).

Out of the five variables that were significantly associated with both PTSD symptoms and FEV 1, only two were found to significantly cross-sectionally mediate this relationship (Table 3). Insomnia symptoms accounted for 75% of the association (indirect effect = –0.12, CI: –0.21 to –0.04). The other significant mediator was activity (indirect effect = –0.03, CI: –0.05 to –0.003), accounting for 18% of the total effect. When taken forward to the joint mediation model, both insomnia (indirect effect = –0.11, CI: –0.19 to –0.02) and activity (indirect effect = –0.03, CI: –0.05 to –0.001) remained significant cross-sectional mediators of the association between PTSD symptoms and FEV 1 (Fig. 1b). The joint model accounted for 81% of the total association between PCL and FEV 1, with the direct effect becoming non-significant.

6. Discussion

The current study is the first to investigate health-related behavioral mechanisms underpinning the connection between PTSD and respiratory problems. We find that sleep disturbances (insomnia and low sleep quality), physical inactivity, and daily stress independently

mediate the association between PTSD and respiratory symptoms in WTC responders. The results are generally consistent across self-report and spirometry measures of respiratory problems. The identified health-related daily behaviors and experiences might explain the connection between PTSD and respiratory illness. Targeting these modifiable mechanisms might enhance prevention and intervention in respiratory problems in patients with PTSD.

First, daily experience of poor sleep quality emerged as a potential mediator of the association between PTSD and self-reported LRS, while insomnia symptoms mediated the association between PTSD and FEV 1. Both sleep measures capture subjective evaluations of sleep quality and are related, albeit sleep quality focuses on everyday satisfaction with sleep, while insomnia indexes a broader sleep disturbance that includes problems such as difficulty falling asleep, waking up at night, and the impact on daily functioning. The results are in line with previous findings that PTSD is associated with and contributes to sleep disturbances (Germain, 2013; Giosan et al., 2015; Kleim et al., 2016; Koren et al., 2002; Spoormaker & Montgomery, 2008). PTSD is frequently characterized by sleep disturbances such as nightmares, and both hyperarousal and numbing symptoms can further worsen sleep quality. In turn, poor sleep is known to result in worse respiratory health (Ohayon, 2002; Sivertsen et al., 2014), likely due to systemic inflammation associated with inadequate sleep (Irwin et al., 2014, 2016; Irwin & Opp, 2017; Morgan et al., 2014).

Second, low physical activity helped to explain the relationship

Table 3
Individual mediation models.

IV	DV	M	IV to M	M to DV	IV to DV	Indirect effect	Minimum CI	Maximum CI	% of IV-DV association due to M
PTSD	LRS	Insomnia	.61*	.12*	.47*	.07*	.01	.14	14%
		Sleep hours	.10	.06	.54*	.01	-.01	.02	02%
		Sleep quality	-.43*	-.17*	.48*	.07*	.03	.11	14%
		BMI	.12*	.06	.54*	.01	.00	.02	02%
		Activity	-.15*	-.14*	.53*	.02*	.002	.04	04%
		Stressful events	.53*	.30*	.39*	.16*	.09	.23	29%
	FEV 1	Insomnia	.60*	-.21*	-.04	-.12*	-.21	-.04	75%
		Sleep quality	-.43*	.10	-.12*	-.04	-.09	.01	24%
		BMI	.12*	-.15*	-.13*	-.02	-.04	.00	16%
		Activity	-.15*	.19*	-.13*	-.03*	-.05	.00	18%
		Stressful events	.53*	-.04	-.14*	-.02	-.09	.05	13%

Notes. *denotes $p < .05$. Significant results are also in bold.

IV – independent variable; DV – dependent variable; M – mediator variable; CI – confidence Intervals; LRS – lower respiratory symptoms; BMI – body mass index. Each model was run with only one mediator at the time.

CIs for indirect effects were obtained by bootstrapping. The IV to DV pathway represents the direct effect, controlling for the mediator.

All analyses control for age, sex, race, smoking status, severity of WTC disaster exposure, and employment in the law enforcement on 9/11.

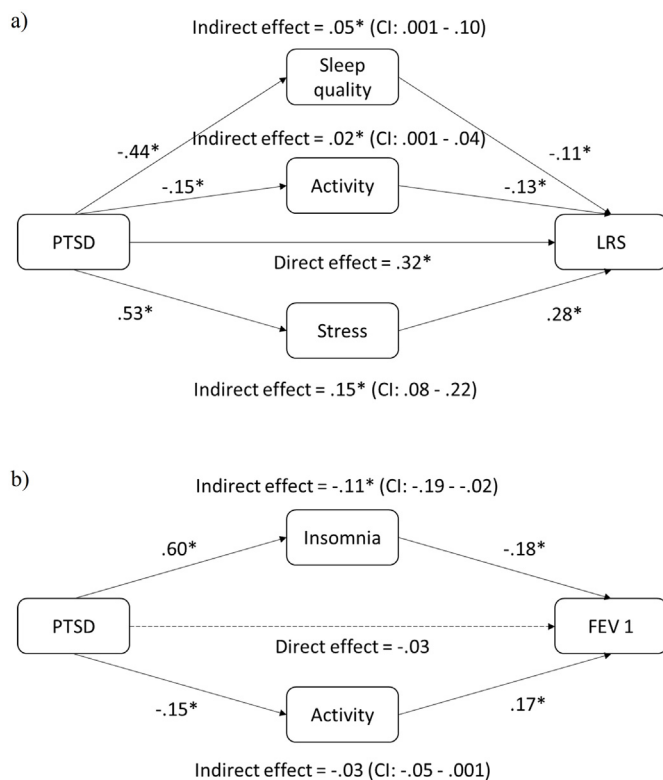


Fig. 1. Final mediation models.

*denotes $p < .05$.

CI - Confidence Intervals; LRS - lower respiratory symptoms.

CIs for indirect effects were obtained by bootstrapping. Direct effect paths control for the mediators. Mediators combined explained 43% of the total association between PTSD symptoms and LRS, and 81% of the association between PTSD symptoms and FEV 1.

All analyses control for age, sex, race, smoking status, severity of WTC disaster exposure, and employment in the law enforcement on 9/11.

between PTSD symptoms and both self-reported and objective respiratory symptoms. This is in agreement with previous studies that demonstrated that PTSD leads to less activity (Hall, Hoerster, & Yancy, 2015; Zen et al., 2012), which might be due to avoidance of bodily arousal symptoms and decreased motivation to be active because of numbing symptoms (Assis et al., 2008). Physical inactivity may in turn lead to worse respiratory health via the allostatic load and systemic inflammation associated with sedative lifestyle (Ali & Ulrik, 2013; Baffi et al., 2016; Beuther et al., 2006; Brumpton et al., 2013; Lee et al., 2009). Furthermore, presence of respiratory illness might prevent responders from being active as it could temporarily aggravate their symptoms.

Third, stressful daily experiences helped to explain the association between PTSD and self-reported respiratory symptoms, but not pulmonary function. The results are in line with findings that PTSD increases stress exposure via stress generation (Conway et al., 2012; Maniates et al., 2018; Zvolensky, Kotov, et al., 2015); for example, angry outbursts are relatively common in PTSD could lead to a higher number of interpersonal conflicts (Galovski & Lyons, 2004). Stressful daily experiences are also known to exacerbate PTSD symptoms (Heron et al., 2013; Huddleston et al., 2007). In turn, daily stressors could lead to poorer respiratory health via systemic inflammation (Chen & Miller, 2007; Miller et al., 2009; Yellowlees & Kalucy, 1990). However, given that the findings emerged only for self-reported LRS, it is also plausible that psychological processes associated with LRS, PTSD and stress reaction, such as anxiety sensitivity, could contribute to higher attention to and endorsement of respiratory symptoms (Dales, Spitzer, Schechter, & Suissa, 1989; Mahaffey et al., 2017; Yellowlees & Kalucy, 1990).

The null findings for the lipid panel and BMI are also notable. While previous studies demonstrated the link between these metabolic markers and both PTSD (Coughlin, 2011; Dedert et al., 2010; Kagan et al., 1999; Maia et al., 2008; McFarlane, 2010) and LRS (Natale et al., 2015), we find that the associations become non-significant when accounting for other mechanisms. This highlights the value of studying daily processes jointly in a comprehensive model to identify the non-redundant pathways.

The current results are generally consistent across self-reported respiratory symptoms and spirometry. We achieved a significant convergence between the two measures, likely due to an increased ecological validity and reliability of repeated assessments collected across 14 days. Such approach might be important for improving future studies of respiratory illness, which has an episodic course and might not be captured well with a one-off measure in a laboratory setting. The convergence of findings, as well as the emergence of common correlates and mediators that were assessed objectively (actigraphy, sleep hours, BMI), further support the notion that the association between PTSD and respiratory illness is not an artifact of psychosomatic and other psychological processes, and instead point to the significant role of behavioral and biological mechanisms in this association.

Our findings carry important implications for interventions to preempt the deleterious impact of PTSD on respiratory illness, in particular if replicated in prospective longitudinal studies. Specifically, the results suggest that therapeutic and lifestyle interventions should focus on modifying three domains of health behavior: sleep, physical inactivity, and stress management. For example, sleep disturbances could be treated with cognitive-behavioral therapy for insomnia, a multi-component intervention involving restricting sleep, stimulus control, sleep hygiene, and cognitive restructuring (Smith, Huang, & Manber, 2005). Physical activity could be enhanced via exercise programs, exercise counseling, lifestyle interventions, tai chi, or physical yoga (Rosenbaum, Tiedemann, & Ward, 2014; Stathopoulou, Powers, Berry, Smits, & Otto, 2006). Stress management intervention could consist of relaxation techniques, cognitive behavioral restructuring, and training in problem-solving, assertiveness, goal setting and time management (Barlow, 2007). An additional advantage of modifying these three domains of everyday health behaviors is that they are likely to have a broad impact on other aspects of mental and physical health, and might be more appealing to patients than approaches directly targeting respiratory illness symptoms or mental health. Furthermore, intervention that target sleep, inactivity and stress management have also been shown to significantly lower PTSD symptoms (Bisson et al., 2007; Cox, Tuck, & Olatunji, 2017; Margolies, Rybarczyk, Vrana, Leszczyszyn, & Lynch, 2013; Rosenbaum et al., 2015; Talbot et al., 2014).

6.1. Limitations

The current study has several strengths, such as a large sample exposed to a uniform trauma, and multimethod assessments that include validated questionnaires, daily diaries, ambulatory measures and blood tests, resulting in a high degree of ecological validity and objectivity, and less shared methods variance. Nonetheless, the findings are tempered by a number of limitations. First, despite PTSD being assessed at baseline and respiratory symptoms assessed subsequently over the monitoring period, the current study is essentially cross-sectional. Longitudinal research is required to disentangle the directions of effect in the mediation models. In fact, prospective longitudinal analyses are the next step of the current project, once three waves of data collection are completed. Second, sleep was only assessed using self-report questionnaires and surveys. Although these frequently used measures have demonstrated excellent psychometric properties and have been validated with respect to objective assessments (Bastien et al., 2001; Morin et al., 2011), future studies ought to employ gold standard diagnostic interviews and polysomnography to assess sleep disorders, as well as sleep duration and quality (Chesson et al., 1997, 2000; Morgenthaler

et al., 2007). Third, daily stressors were assessed with a checklist, which covered only a limited number of possible events and responses could be biased by subjective interpretation and distress. Findings should be replicated using gold standard stress interviews (Hammen, 2016). Fourth, there is no available information on substance abuse, medication use, or non-WTC-related medical conditions, thus it is unclear whether these factors play a role in the association between PTSD and respiratory conditions. Finally, the associations between PTSD, respiratory illness and health-related behaviors should be studied in other trauma-exposed populations, and in more diverse populations than the current mostly Caucasian male sample, to test the generalizability of the current findings.

7. Conclusions

The current study is the first to identify modifiable health-related behaviors that may explain the link between PTSD and respiratory symptoms, indicating that sleep disturbances (insomnia symptoms and poor sleep quality), low physical activity, and stressful events all independently mediate this relationship. These identified maladaptive mechanisms could be targeted to intercept the impact of PTSD on future respiratory illness, for example by using therapeutic and lifestyle interventions, such as cognitive behavioral therapies for insomnia symptoms and stress management. The results were generally consistent across daily self-report and spirometry measures of respiratory symptoms, suggesting that repeated, ecologically-valid assessment of respiratory symptoms should be used in future studies.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.brat.2018.10.018>.

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