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Latent typologies of posttraumatic stress disorder in World Trade Center responders

Sarah R. Horn [a, *], Robert H. Pietrzak [b, c], Clyde Schechter [d], Evelyn J. Bromet [e], Craig L. Katz [a], Dori B. Reissman [f], Roman Kotov [e], Michael Crane [g], Denise J. Harrison [h, i], Robin Herbert [g], Benjamin J. Luft [j], Jacqueline M. Moline [k], Jeanne M. Stellman [l], Iris G. Udasin [m], Philip J. Landrigan [g], Michael J. Zvolensky [n], Steven M. Southwick [b, c], Adriana Feder [a]

[a] Department of Psychiatry, Icahn School of Medicine, New York, NY, USA
[b] U.S. Department of Veterans Affairs National Center for Posttraumatic Stress Disorder, VA Connecticut Healthcare System, West Haven, CT, USA
[c] Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA
[d] Department of Family and Social Medicine, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, USA
[e] Department of Psychiatry, Stony Brook University, Stony Brook, NY, USA
[f] National Institute for Occupational Safety and Health, Washington, DC, USA
[g] Department of Preventive Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[h] Department of Environmental Medicine, New York University School of Medicine, New York, NY, USA
[i] Department of Population Health, New York University School of Medicine, New York, NY, USA
[j] Department of Medicine, Division of Infection Diseases, Stony Brook University, Stony Book, NY, USA
[k] Department of Occupational Medicine, Epidemiology and Prevention, Hofstra North Shore-Long Island Jewish School of Medicine, Great Neck, NY, USA
[l] Department of Health Policy and Management, Mailman School of Public Health, Columbia University, NY, USA
[m] Department of Environmental and Occupational Medicine, UMDNJ – Robert Wood Johnson Medical School, Piscataway, NJ, USA
[n] Department of Psychology, University of Houston, USA

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ABSTRACT

Posttraumatic stress disorder (PTSD) is a debilitating and often chronic psychiatric disorder. Following the 9/11/2001 World Trade Center (WTC) attacks, thousands of individuals were involved in rescue, recovery and clean-up efforts. While a growing body of literature has documented the prevalence and correlates of PTSD in WTC responders, no study has evaluated predominant typologies of PTSD in this population. Participants were 4352 WTC responders with probable WTC-related DSM-IV PTSD. Latent class analyses were conducted to identify predominant typologies of PTSD symptoms and associated correlates. A 3-class solution provided the optimal representation of latent PTSD symptom typologies. The first class, labeled "High-Symptom (n = 1,973, 45.3%)," was characterized by high probabilities of all PTSD symptoms. The second class, "Dysphoric (n = 1,371, 31.5%)," exhibited relatively high probabilities of emotional numbing and dysphoric arousal (e.g., sleep disturbance). The third class, "Threat (n = 1,008, 23.2%)," was characterized by high probabilities of re-experiencing, avoidance and anxious arousal (e.g., hypervigilance). Compared to the Threat class, the Dysphoric class reported a greater number of life stressors after 9/11/2001 (OR = 1.06). The High-Symptom class was more likely than the Threat class to have a positive psychiatric history before 9/11/2001 (OR = 1.7) and reported a greater number of life stressors after 9/11/2001 (OR = 1.1). The High-Symptom class was more likely than the Dysphoric class, which was more likely than the Threat class, to screen positive for depression (83% > 74% > 53%, respectively), and to report greater functional impairment (High-Symptom > Dysphoric [Cohen d = 0.19], Dysphoric > Threat [Cohen d = 0.24]). These results may help inform assessment, risk stratification, and treatment approaches for PTSD in WTC and disaster responders.

* Corresponding author. Department of Psychiatry, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1230, New York, NY 10029, USA.

E-mail address: shorn@uoregon.edu (S.R. Horn).

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1. Introduction

Posttraumatic stress disorder (PTSD) is a prevalent, often chronic, and debilitating psychiatric disorders worldwide (Karam et al., 2014). Following the September 11, 2001 terrorist attacks on the World Trade Center (WTC), tens of thousands of individuals were involved in rescue, recovery and clean-up efforts. This diverse group of responders included traditional first responders (police officers) as well as non-traditional responders without prior disaster training (e.g., construction workers and volunteers) (Herbert et al., 2006; Pietrzak et al., 2014a). While the prevalence, correlates and longitudinal course of PTSD symptomatology have been well-documented in WTC responders (Bowler et al., 2012; Bromet et al., 2015, Cone et al., 2015; Luft et al., 2012; Perrin et al., 2007; Pietrzak et al., 2012a, 2014a; Stellman et al., 2008; Wisnivesky et al., 2011; Zvolensky et al., 2015b), no study of which we are aware has evaluated predominant typologies of PTSD symptomatology in this population. Such information is important, as it can inform assessment, risk stratification, and treatment approaches for symptomatic WTC and other disaster responders.

Latent class analysis (LCA) is a data analytic approach often used to identify subgroups of individuals within a larger sample that cluster together based on predominant symptom typologies (Curran and Hussong, 2003; Muthén and Muthén, 2012; Nagin and Tremblay, 2001). A growing body of studies has utilized latent class/profile analyses to identify predominant PTSD symptom typologies in a broad range of traumatized populations, including civilian trauma survivors, combat veterans, and sexual assault survivors (Böttche et al., 2015; Breslau et al., 2005; Hebenstreit et al., 2014; Pietrzak et al., 2014b). Several of the preceding studies applied LCA in trauma-exposed populations with the full spectrum of PTSD symptom severity, including very low or no symptoms, resulting in class solutions focused primarily on levels of "disturbance" or symptom severity (Breslau et al., 2005). For example, an LCA in two large community samples of trauma-exposed respondents yielded 3 classes: no disturbance, intermediate disturbance and pervasive disturbance (Breslau et al., 2005).

More recent studies have aimed to identify latent symptom typologies in samples of individuals meeting criteria for PTSD or probable PTSD (Böttche et al., 2015; Hebenstreit et al., 2014; Pietrzak et al., 2014b). One study found a 4-class LCA solution in a sample of 2425 female veterans with a PTSD diagnosis: High Symptom, Intermediate Symptom, Intermediate Symptom with High Emotional Numbing and Low Symptom (Hebenstreit et al., 2014). Another study employing LCA in a sample of 164 treatment-seeking older adults found that a 3-class solution best fit the data (Intermediate Disturbance, Pervasive Disturbance-Low Avoidance and Pervasive Disturbance-High Avoidance) (Böttche et al., 2015). Overall, the aforementioned LCA studies in PTSD resulted in differentiation of classes by severity, and initial differentiation by symptom clusters.

The current study employs LCA to characterize predominant typologies of PTSD symptoms in WTC responders and diverges from previous LCA studies in its approach aimed at characterizing symptom cluster-based typologies. To our knowledge, this is the largest study of its kind to date. A recent study of a nationally representative sample of 2463 U.S. adults with PTSD identified three predominant typologies of PTSD—Anxious Re-experiencing, Dysphoric and High-Symptom typologies—which were differentially associated with trauma characteristics, psychiatric comorbidities, and health-related quality of life (Pietrzak et al., 2014b). Altogether, these studies suggest that PTSD is a heterogeneous disorder characterized by unique symptom profiles that may be differentially linked to trauma and clinical characteristics.

In the current study, we employed LCA in a sample of 4352 WTC responders with a probable diagnosis of WTC-related PTSD. We also examined how sociodemographic characteristics, WTC-related trauma exposures, and psychosocial characteristics related to these typologies of PTSD, and additionally how these typologies related to other clinical characteristics, including comorbid depression, alcohol use problems and functional impairment.

2. Method

2.1. Participants

Participants were 4352 WTC responders with probable DSM-IV PTSD assessed with the PTSD Checklist-Specific Version (PCL-S) (Weathers et al., 1993) (see *Assessments* section for details). These responders were identified from a cohort of over 32,000 WTC responders who presented for an initial monitoring visit (average 4.5 [SD = 2.4, range = 0.8 to 12.8] years after 9/11/01) at the World Trade Center Health Program (WTC-HP), a regional clinical consortium established by the Centers for Disease Control and Prevention in 2002, comprising five medical institutions in the greater New York City area that provide health monitoring and treatment services for police and other WTC responders (Dasaro et al., 2015; Herbert et al., 2006).

2.2. Assessments

WTC-related exposures were assessed via a clinician-administered interview and a self-report questionnaire, and included early arrival (by 9/13/2001); being caught in the dust cloud; working primarily/adjacent to the collapse site (the 'pit' or 'pile') during September 2001; working more than the median number of hours on the WTC site; exposure to human remains; involvement in search and rescue efforts during September to October 2011; sleeping on site; traumatic death of a colleague, family member or friend on 9/11; being treated for an injury or illness while working on the WTC recovery effort; and knowing someone who suffered an injury on 9/11. The total number (range 0–10) of WTC exposures was included in the main analysis.

Probable Posttraumatic Stress Disorder was assessed using the PCL-S (Weathers et al., 1993). The PCL-S is a 17-item screening instrument based on the DSM-IV criteria for PTSD. It was developed by the National Center for PTSD and contains items assessing PTSD symptoms, with total scores ranging from 17 to 85. Responders rated PTSD symptoms related to WTC-related trauma exposures. Probable PTSD was defined as a score $\geq$50 plus endorsement of "moderate" or greater severity of the requisite number of re-experiencing (1 or more symptoms), avoidance (3 or more symptoms), and hyperarousal (2 or more symptoms) symptoms for a DSM-IV diagnosis of PTSD. Cronbach's α for PCL-S items in the current sample = 0.80.

To compare PTSD symptom profiles of latent typologies of PTSD, we computed summary scores using a contemporary 5-factor model of PTSD symptoms, which has received strong support in the confirmatory factor analytic literature on the dimensional structure of DSM-IV PTSD symptoms (Pietrzak et al., 2012b, 2014a). Re-experiencing symptoms were computed by summing PCL-S items 1–5 (sample item: "In relation to 9/11, in the past month, how much have you been bothered by repeated, disturbing memories, thoughts, or images of the disaster"); avoidance symptoms by summing PCL-S items 6–7 (sample item: "Avoiding activities or situations because they reminded you of the disaster"); emotional numbing symptoms by summing PCL-S items 8–12 (sample item: "Feeling emotionally numb or being unable to have loving feelings

for those close to you"); dysphoric arousal symptoms by summing PCL-S items 13–15 (sample item: "Trouble falling or staying asleep"); and anxious arousal symptoms by summing PCL-S items 16–17 (sample item: "Being 'super-alert,' watchful or on guard"). These sum scores were standardized to permit comparisons of symptom clusters on the same scale, with 0 equal to the mean and units expressed as standard deviations from the mean.

Sociodemographic characteristics, including age, sex, race/ethnicity, education, marital status and income were assessed.

Psychiatric history prior to 9/11 was assessed by asking respondents if they had ever been diagnosed by a healthcare professional with depression, anxiety disorder or PTSD prior to 9/11. This variable was coded as '0' = no diagnosis or '1' = one or more of these diagnoses.

Stressful life events were assessed with questions from the Disaster Supplement of the Diagnostic Interview Schedule (Robins and Smith, 1983) inquiring about 15 negative life events (e.g., divorce/separation, personal illness, family illness or death) experienced within a year before and since 9/11 (score range 0–15 events the year before and since 9/11).

WTC-related medical conditions were assessed by a comprehensive medical examination. WTC-related medical illness burden was computed as the count of three of the most common WTC-related medical conditions [asthma, gastroesophageal reflux disease (GERD), sinusitis] diagnosed within 3 months of participants' initial visit at the WTC-HP.

Family- and work-related social support were assessed by asking participants to endorse important sources of family and work support while working on the WTC effort For family support, sources were summed to represent a total number (range 0–5, a continuous variable), while for work support, sources (supervisor/co-workers) were used to create a dichotomous variable ('0' vs. 'at least 1').

Alcohol use problems were assessed using the CAGE questionnaire (Mayfield et al., 1974). The CAGE questionnaire is an acronym for the following questions to which participants answer "yes" or "no": (1) Have you ever felt you should *cut* down on your drinking? (2) Have people *annoyed* you by criticizing your drinking? (3) Have you ever felt bad or *guilty* about your drinking? (4) Have you ever had a drink first thing in the morning to steady nerves or to get rid of a hangover (i.e., had an *eye* opener)? A score ≥ 2 is indicative of an alcohol use problem. Cronbach's $\alpha = 0.77$.

Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9) (Kroencke et al., 2001), a 9-item self-report questionnaire that evaluates the presence of depressive symptoms during the prior 2-week period. Scores range from 0 (absence of depressive symptoms) to 27 (severe depressive symptoms), and score ≥ 10 is indicative of a positive screen for depression. Cronbach's $\alpha = 0.88$.

Functional impairment due to emotional problems was assessed using the Sheehan Disability Scale (SDS) (Sheehan, 2000), a participant-rated, discretized analog measure of functional disability in work, social and family life. Cronbach's $\alpha = 0.85$.

2.3. Data analysis

Latent class analyses were conducted to identify predominant typologies of WTC responders who screened positive for WTC-related PTSD using Mplus version 7.11 (Muthén and Muthén, 2012). We compared 1- to 6- class unconditional LCAs on PTSD symptom-level data (dichotomized on the basis of symptom endorsement at "moderate" or greater severity), and assessed their relative fit using conventional fit indices. We considered theory, parsimony, interpretability, and average latent class probabilities of the solutions (Muthén, 2004; Nylund et al., 2007) and aimed to select a final model that contained at least 20% of the sample in the smallest class to increase generalizability of the final solution. The smallest class counts/percentages for each model were 1-class (n = 4,352, 100%), 2-class (n = 1,932, 44.4%), 3-class (n = 1,008, 23.2%), 4-class (n = 379, 8.7%), 5-class (n = 211, 4.8%), and 6-class (n = 212, 4.8%). Following convention, the best-fitting model was assessed on the basis of smaller Bayesian Information Criterion (BIC), sample size-adjusted BIC, and Akaike Information Criterion values; higher entropy values; and on results of likelihood ratio tests (LRTs). Each WTC responder was assigned to the class having the greatest posterior probability. Once the optimal solution was identified, we compared the different PTSD classes with respect to sociodemographic and trauma-related characteristics, psychiatric diagnoses, and other psychosocial factors using a multinomial logistic regression analysis. Finally, we conducted multivariable binary logistic regressions and analyses of covariance (ANCOVAs) to examine associations between the PTSD classes, and positive screens for alcohol use problem and depression, and work, social and family functional impairment, controlling for sociodemographic, psychosocial, clinical and trauma-related variables.

3. Results

Fit statistics for the LCAs are shown in the top panel of Table 1. Based on theory, parsimony, and fit statistics, a 3-class solution was determined to provide the optimal representation of latent classes of PTSD symptoms in WTC responders. Fig. 1 shows plots of symptom endorsement probabilities by latent class. The first class, labeled "Threat" (n = 1,008, 23.2%), was characterized by high probabilities of re-experiencing, avoidance and anxious arousal symptoms, with an average PCL score of 57.56 (SE = 0.21). The second class, labeled "Dysphoric" (n = 1,371, 31.5%) exhibited high probabilities of emotional numbing and dysphoric arousal symptoms, with an average PCL score of 56.69 (SE = 0.18). The third class, labeled "High-Symptom" (n = 1,973, 45.3%), was characterized by high probabilities of all symptoms, with an average PCL score of 68.87 (SE = 0.15). Fig. 2 shows plots of standardized 5-factor PTSD symptom scores by latent class.

Demographic, WTC exposure and psychosocial characteristics of each class are presented in the left panel of Table 2. Psychiatric and functional correlates for each class are presented in Table 3. Results of a multinomial logistic regression analysis examining correlates of PTSD latent class are summarized in the bottom panel of Table 2. Compared to the Dysphoric class, the Threat class was more likely to report a higher number of WTC-related exposures. Post-hoc analyses revealed that the Threat class was more likely to report having handled human remains (OR = 0.80), having worked greater than the median number of hours (OR = 0.78), and having been caught in the dust cloud (OR = 0.77) compared to the Dysphoric class. The High-Symptom class was more likely than the Threat class to report knowing someone injured on 9/11 (OR = 1.24).

Compared to those in the Dysphoric class, the Threat class was more likely to have a lower education level. In contrast, the Dysphoric class was more likely to report a greater number of life stressors after 9/11, and fewer sources of work and family support while working for the WTC recovery effort than those in the Threat class. Membership in the High-Symptom class was associated with higher likelihood of a psychiatric diagnosis prior to 9/11, a greater number of life stressors post-9/11 and fewer sources of work support during the WTC recovery effort, when compared to the Threat class. Regarding clinical correlates, the High-Symptom class was more likely than the Dysphoric class, which was in turn more likely than the Threat class, to screen positive for depression (83% > 74% > 53%, respectively), and to report greater functional impairment (High-Symptom > Dysphoric (d = 0.19),

Table 1
Fit statistics of latent class analyses evaluating 1 to 6 class solutions of PTSD latent classes.

Fit statistics for latent class analyses of PTSD symptoms							
Number of classes	Log likelihood	AIC	BIC	SSA-BIC	Entropy	LMR adjusted LRT p value	% Sample in smallest class
1	−29,822.63	59,679.27	59,787.70	59,733.68	–	–	100%
2	−28,274.10	56,618.20	56,841.45	56,730.23	0.71	<0.0001	44.4%
3	−27,686.39	55,478.78	55,816.83	55,648.42	0.68	<0.0001	25.0%
4	−27,489.45	55,120.90	55,573.77	55,348.16	0.71	0.0053	10.3%
5	−27,399.34	54,976.69	55,544.37	55,261.56	0.73	0.3126	5.6%
6	−27,315.98	54,845.96	55,528.45	55,188.44	0.70	0.3081	5.5%

Note. AIC = Akaike Information Criterion; BIC=Bayesian Information Criterion; SSA-BIC=Sample size adjusted Bayesian Information Criterion; LMR adjusted LRT = Lo-Mendell-Rubin adjusted likelihood ratio test.

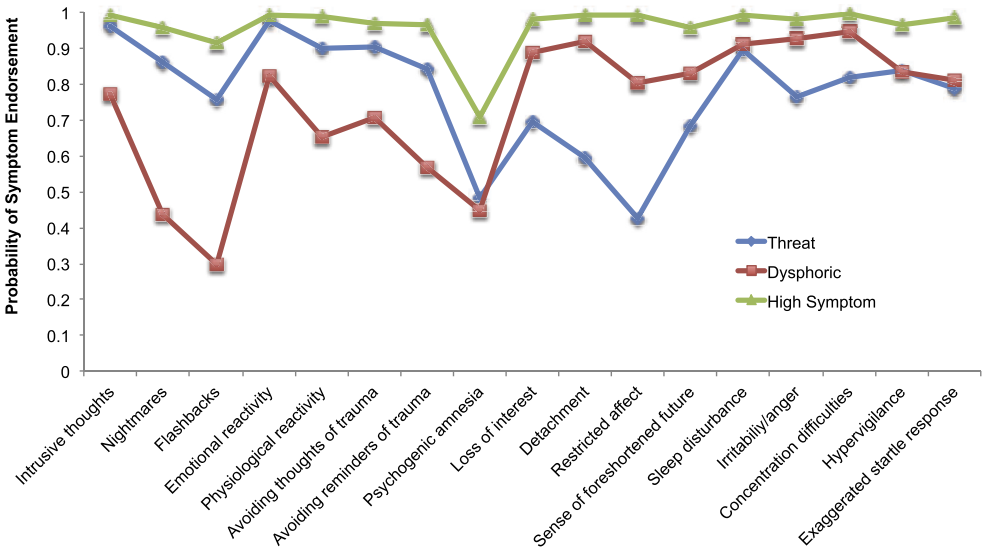
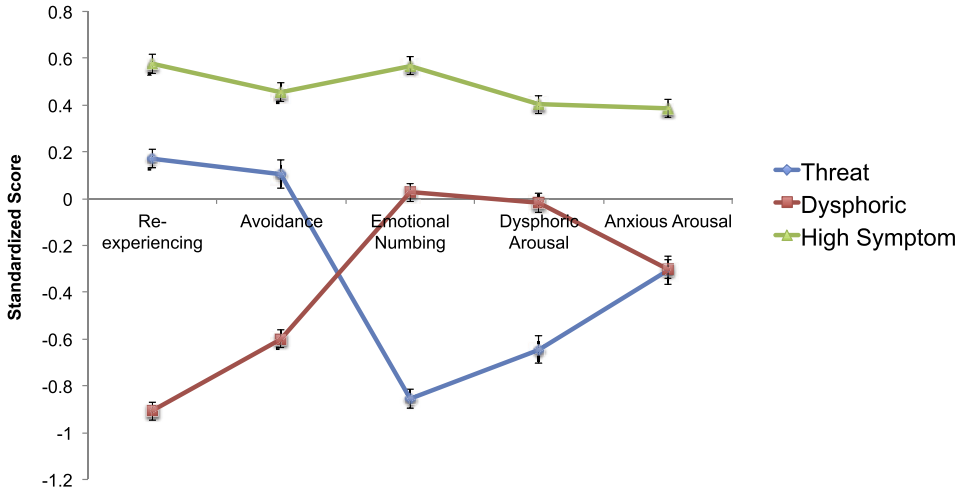


Fig. 1. Plot of symptom endorsement probabilities by latent class of PTSD.



Note. Values represent standardized scores with 0 equal to the mean and units expressed as standard deviation units in the full sample. Error bars represent 95% confidence intervals.

Fig. 2. Plot of standardized 5-factor PTSD symptom scores by latent class of PTSD.

Dysphoric > Threat (d = 0.24)). Finally, the High-Symptom and Dysphoric classes were more likely than the Threat class (21% vs. 20% vs. 16%, respectively) to report alcohol use problems.

4. Discussion

In the current study, LCA analyses identified three predominant

Table 2
Sociodemographic, trauma-related, and psychosocial correlates of latent classes.

Variable	Class 1: threat (n = 1008)	Class 2: dysphoric (n = 1371)	Class 3: high symptom (n = 1973)	Dysphoric vs. threat adjusted odds ratio (95% CI)	High symptom vs. threat adjusted odds ratio (95% CI)
Age at visit 1, mean (SE)	45 (0.30)	45 (0.26)	46 (0.21)	0.99 (0.98–1.00)	1.005 (1.00–1.01)
Sex, n (%)					
Male (reference)	813 (80.7)	1121 (81.8)	1602 (81.2)	–	–
Female	195 (19.3)	250 (18.2)	371 (18.8)	0.80 (0.64–1.01)	0.84 (0.68–1.04)
Race/ethnicity, n (%)					
White, non-Hispanic (reference)	478 (47.4)	710 (51.8)	913 (46.3)	–	–
Black, non-Hispanic	118 (11.7)	115 (8.4)	188 (9.5)	**0.64 (0.48–0.85)***	0.82 (0.63–1.08)
Hispanic	345 (34.2)	459 (33.5)	754 (38.2)	0.86 (0.70–1.06)	1.13 (0.93–1.37)
Other	67 (6.6)	87 (6.3)	118 (6.0)	0.89 (0.63–1.26)	0.99 (0.71–1.37)
Education, n (%)					
Less than high school (reference)	177 (17.6)	195 (14.2)	364 (18.4)	–	–
High school or greater education	831 (82.4)	1176 (85.8)	1609 (81.6)	**1.31 (1.03–1.67)***	1.03 (0.83–1.28)
Responder category, n (%)					
Non-traditional responder (reference)	796 (79.0)	1083 (79.0)	1636 (82.9)	–	–
Police	212 (21.0)	288 (21.0)	337 (17.1)	1.20 (0.96–1.51)	0.86 (0.70–1.07)
Marital status, n (%)					
Married or partnered (reference)	579 (57.4)	713 (52.0)	1070 (54.2)	–	–
Never married	151 (15.0)	233 (17.0)	282 (14.3)	1.17 (0.91–1.50)	0.89 (0.70–1.13)
Widowed, separated or divorced	278 (27.6)	425 (31.0)	621 (31.5)	1.15 (0.94–1.41)	0.97 (0.81–1.18)
Income, n (%)					
<US$80 k/year (reference)	790 (78.4)	1082 (78.9)	1606 (81.4)	–	–
>US$80 k/year	218 (21.6)	289 (21.1)	367 (18.6)	0.98 (0.79–1.21)	1.12 (0.92–1.38)
Psychiatric history prior to 9/11, n (%)					
No diagnosis (reference)	741 (73.5)	934 (68.1)	1229 (62.3)	–	–
Diagnosis of depression, anxiety disorder and/or PTSD[a]	267 (26.5)	437 (31.9)	744 (37.7)	1.20 (0.98–1.45)	**1.69 (1.41–2.03)*****
No. of life stressors in year before 9/11, mean (SE)	2.1 (0.09)	2.2 (0.08)	2.2 (0.07)	0.97 (0.94–1.07)	**0.96 (0.93–1.00)****
WTC exposure severity (range: 0–10), mean (SE)	4.5 (0.07)	4.2 (0.06)	4.4 (0.05)	**0.91 (0.87–0.95)*****	0.98 (0.95–1.02)
No. of important sources of family support while working at WTC site, mean (SE)	1.5 (0.04)	1.3 (0.04)	1.3 (0.03)	**0.92 (0.86-0.99)***	0.97 (0.91–1.03)
No. of important sources of work support while working at WTC site, mean (SE)	0.55 (0.02)	0.44 (0.02)	0.42 (0.02)	**0.87 (0.77–0.99)***	**0.84 (0.74–0.94)****
No. of WTC-related medical conditions, mean (SE)	0.63 (0.03)	0.70 (0.02)	0.61 (0.02)	1.09 (0.98–1.21)	**0.89 (0.81–0.99)***
No. of life stressors since 9/11, mean (SE)	4.6 (0.11)	5.2 (0.09)	5.6 (0.08)	**1.06 (1.03–1.09)*****	**1.09 (1.06–1.12)*****

Note. WTC=World Trade Center; PTSD, = posttraumatic stress disorder; SE = standard error; CI, confidence interval.
Reference group = Threat class (Class 1).
AOR = Adjusted odds ratio are adjusted for all demographic variables, pre-9/11 psychiatric history, pre- and post-9/11 number of life stressors, number of sources of work and family support while working at WTC site, and number of WTC-related medical conditions.
Bolded AORs (95% CI) indicate a significant difference compared to the Threat class, *p < 0.05; **p < 0.01; ***p < 0.001.
[a] n (%) of PTSD diagnosis *without* depression/anxiety disorder diagnoses prior to 9/11, by class: Threat: 47 (4.7%), Dysphoric: 64 (4.7%), High-Symptom: 73 (3.7%).

Table 3
Psychiatric and functional variables by PTSD latent class.

	Class 1: threat (n = 1008)	Class 2: dysphoric (n = 1371)	Class 3: high symptom (n = 1973)	Class 1 (threat) reference	Dysphoric vs. threat adjusted odds ratio (95% CI)	High symptom vs. threat adjusted odds ratio (95% CI)
Alcohol use problem, n (%)	162 (16.1)	274 (20.0)	408 (20.7)	1.00 (ref)	**1.27 (1.02–1.58)***	**1.35 (1.10–1.66)****
Positive screen for depression, n (%)	532 (52.8)	1016 (74.1)	1643 (83.3)	1.00 (ref)	**2.43 (2.03–2.91)*****	**3.97 (3.33–4.74)*****
Functional Impairment, mean (SE)				F	p	Pairwise Contrasts
Family	4.44 (0.12)	5.34 (0.11)	6.07 (0.10)	122.55	<0.001	High-Symptom > Dysphoric > Threat
Social	4.66 (0.12)	5.65 (0.11)	6.37 (0.10)	137.95	<0.001	High-Symptom > Dysphoric > Threat
Work[a]	4.12 (0.16)	4.62 (0.15)	5.52 (0.14)	58.43	<0.001	High-Symptom > Dysphoric > Threat

Note. CI, confidence interval; SE = standard error.
Alcohol use problem: Positive score of ≥2 on CAGE.
Positive screen for depression: Score on ≥10 on PHQ-9.
Functional Impairment: Measured using the Sheehan Disability Scale (SDS).
AOR = Adjusted odds ratios and means are adjusted for all demographic variables, pre-9/11 psychiatric history, pre- and post-9/11 number of life stressors, number of sources of work and family support while working at WTC site, and number of WTC-related medical conditions.
Bolded AORs (95% CI) indicate a significant difference compared to the Threat class, *p < 0.05; **p < 0.01; ***p < 0.001.
[a] SDS work scores were assessed only in WTC responders who were currently working (n = 2965).

classes of PTSD in WTC responders —Threat (23.2%), Dysphoric (31.5%) and High Symptom (45.3%). The Threat class exhibited a PTSD symptom profile characterized by high probabilities of trauma-related fear/anxiety symptoms (e.g., re-experiencing, avoidance and anxious arousal symptoms), while the Dysphoric class exhibited a PTSD symptom profile characterized by high probabilities of anhedonic/depressive symptoms (e.g., emotional numbing and dysphoric arousal). The High-Symptom class was characterized by high probabilities of symptoms across all PTSD clusters. This 3-class solution in WTC responders is similar to that observed in the aforementioned study of 2463 U.S. adults with PTSD (Pietrzak et al., 2014b), suggesting that the manifestation of PTSD symptoms in individuals with PTSD may potentially be comparable across trauma-exposed populations.

Previous LCA analyses of PTSD symptoms in trauma-exposed populations have found solutions primarily differentiated by PTSD symptom severity level (Böttche et al., 2015; Breslau et al., 2005; Hebenstreit et al., 2014); however, the current study suggests that PTSD may be represented by typologies differentiated both by symptom severity levels and symptom clusters. Prior LCA analyses identified specific PTSD symptoms, such as emotional numbing and avoidance, which may signal subgroups with higher PTSD severity (Böttche et al., 2015; Hebenstreit et al., 2014). For example, in a sample of female veterans, intermediate and high-symptom classes had higher levels of emotional numbing compared to a low-symptom class (Hebenstreit et al., 2014). Similarly, in the current study, the Dysphoric and High-Symptom classes had higher probabilities of emotional numbing symptoms in comparison to the Threat class, were more likely to screen positive for depression and alcohol use problems, and scored higher on a measure of functional impairment. A severity gradient emerged, in that the likelihood of screening positive for alcohol use problem and depression, and of reporting functional impairment, was lowest for the Threat class, intermediate for the Dysphoric class, and highest for the High-Symptom class, paralleling past findings suggesting that PTSD may be in part a severity-based psychiatric disorder (Böttche et al., 2015; Breslau et al., 2005; Hebenstreit et al., 2014; Pietrzak et al., 2014b).

Compared to the Dysphoric and High-Symptom classes, the Threat class reported higher levels of social support during the WTC recovery effort. Social support has consistently been found to be a potentially protective factor in studies of trauma-exposed populations (Charuvastra and Cloitre, 2008; Feder et al., 2013; Kaniasty and Norris, 2008; Pietrzak et al., 2010). The association between higher levels of social support and the Threat class may also be related, in part, to lower severity of PTSD symptoms. Prior studies have indicated that individuals with lower symptom severity and higher resilience to stress may be more likely to enlist social support following exposure to traumatic events (King et al., 1998; Pietrzak et al., 2010; Sharkansky et al., 2000). Compared to the Threat class, the Dysphoric and High-Symptom classes reported lower levels of social support as well as higher levels of post-9/11 stressors, lending further support to King's hypothesis that secondary stressors deplete social support resources, which may in turn lead to increased PTSD symptom severity (King et al., 1998).

On the other hand, lower education, a commonly identified risk factor for psychopathology, was also associated with a Threat symptom presentation relative to the Dysphoric class. One interpretation of these results is that lower education may be linked to reduced reappraisal skills and lower emotional regulation ability, therefore increasing the likelihood of threat symptoms (Boden et al., 2012; Ehring and Quack, 2010; Goldin et al., 2008; Rabinak et al., 2014). Alternatively, lower education may be associated with higher exposure to life-threatening traumas, a finding frequently documented in the combat literature, in which younger, less educated soldiers are often exposed to higher "doses" of combat (Macklin et al., 1998; McNally and Shin, 1995; Smid et al., 2013), as well as in trauma-exposed adult populations (Frankenberg et al., 2013; Lunau et al., 2015; Ullman and Brecklin, 2002).

Other risk factors including life stressors experienced before 9/11 and number of WTC-related medical conditions also predicted membership in the Threat class compared to the High-Symptom class. Furthermore, in this study, a higher number of WTC-related exposures predicted membership in the Threat class compared to the Dysphoric class. Conversely, in the aforementioned LCA study of PTSD in the general US population (Pietrzak et al., 2014a), greater trauma burden predicted membership in the High-Symptom class. Differential findings across studies might relate to how trauma exposure was ascertained and greater heterogeneity of trauma exposures in the U.S. general population. Taken together, these findings underscore the importance of understanding both the nature and severity of PTSD symptom typologies. While the Threat class could represent a "less severe" form of PTSD, as it is associated with lower functional impairment and lower likelihood of problematic alcohol use and depression, it appears to be associated with certain risk factors, including lower education, and higher numbers of pre-9/11 stressful life events, WTC-related exposures and WTC-related medical conditions, compared to the Dysphoric and High-Symptom manifestations of PTSD.

Membership in the Dysphoric and High-Symptom classes was associated with other risk factors identified in meta-analyses of risk for PTSD in trauma-exposed populations (Brewin et al., 2000; Ozer et al., 2003) and in WTC responders (Bowler et al., 2010; Cukor et al., 2011; & Perrin et al., 2007), relative to the Threat class. These included a positive psychiatric history prior to trauma exposure and a higher number of stressful life events following trauma exposure (Pietrzak et al., 2014a). Of note, the "kindling hypothesis" postulates that affective disorders may be more easily triggered over time due to progressive lowering of the threshold for the impact of accumulating stressful life events (Hageman et al., 2001; Kendler et al., 2000; Post et al., 1981). The kindling theory might partially explain the greater likelihood of the more severe Dysphoric and High-Symptom PTSD profiles in individuals with a prior psychiatric history, as they may be more likely to have onset or worsening of PTSD following a new stressful life event due to increased stress sensitivity. This finding also aligns with prior work suggesting that secondary stressors (e.g., divorce and job loss) are linked to greater severity and chronicity of PTSD in trauma-exposed samples (Appleyard et al., 2005; Galea et al., 2002; Green et al., 1990; Kessler et al., 2012; Luszczynska et al., 2009; Pietrzak et al., 2013), including WTC responders (Zvolensky et al., 2015a).

Exposures experienced during the WTC recovery effort were also differentially associated with the latent typologies of PTSD, suggesting that specific types of traumatic experiences might be etiologically linked to distinct clinical phenotypes within the broader PTSD syndrome (Pietrzak et al., 2014a). In particular, some of the more emotionally disturbing experiences, i.e., those more likely to activate the hypothalamic-pituitary-adrenal (HPA) axis—handling human remains or being caught in the dust cloud as the towers fell—were associated with the Threat class, characterized by high probabilities of re-experiencing and anxious arousal symptoms. A higher number of WTC-related exposures was also predictive of membership in the Threat compared to the Dysphoric class. On the other hand, knowing someone injured on 9/11 was associated with membership in the High-Symptom class, a PTSD symptom profile characterized by both threat and dysphoric symptoms. These findings are consistent with those of a recent LCA of PTSD typologies in the general US adult population (Pietrzak et al., 2014b), in which assaultive traumas (sexual and physical)

and military combat were more likely to be associated with Anxious-Re-Experiencing and High-Symptom classes, while traumatic losses such as unexpected deaths and serious illnesses/injuries were associated with a more Dysphoric presentation of PTSD symptoms. It is possible that feelings of grief or guilt in trauma survivors may contribute to dysphoric or high-symptom presentations (Beck et al., 2011; Henning and Frueh, 1998; Lee et al., 2001).

Methodological limitations of this study must be noted. First, analyses were based on the DSM-IV version of the PCL-S, so it remains to be determined whether the predominant typologies of PTSD would differ if DSM-5 criteria were to be employed; nevertheless, as the 5-factor model of DSM-IV PTSD symptoms employed in this study to illustrate between-class differences in PTSD symptom profiles has been replicated using the DSM-5 version of the PCL, results would likely generalize to DSM-5 PTSD symptom assessments (Bovin et al., 2015; Tsai et al., 2015). Given the more nuanced assessment of negative alterations in cognitions and mood in DSM-5, and the addition of externalizing behavior symptoms, additional research is needed to evaluate for whether other distinctive latent profiles exist for the DSM-5 PTSD criterion symptoms in trauma survivors. Further, data was available on 10 WTC-related exposure types, but not for the new DSM-5 A4 criterion: "repeated or extreme exposure to aversive details of traumatic events," which many responders likely experienced. While the DSM-5 definition of PTSD also includes a dissociative subtype, the PCL for DSM-IV does not evaluate dissociative symptoms of PTSD. As prior LCA studies have identified a dissociative subtype of PTSD, future work should evaluate how the classes might differ with respect to dissociative symptoms (Wolf et al., 2012a, 2012b).

Second, the cross-sectional study design precludes knowledge of how these syndromes evolved over time or possibly from one another, as well as inferences of causality between psychosocial characteristics and PTSD class. Third, retrospective recall bias may have influenced responses to the questions about pre-9/11 mental health problems and past stressful life events. Lastly, the current study did not have information on the patient's medical or psychiatric treatment histories and was unable to further explore how therapy or medication usage differentiated between the classes.

Despite these limitations, the study builds upon prior work (Böttche et al., 2015; Pietrzak et al., 2014b) to suggest that there are three predominant latent typologies of PTSD in a large cohort of WTC responders with probable PTSD, which are uniquely related to sociodemographic, trauma-related, and clinical characteristics, thereby highlighting potential implications for assessment, risk stratification, and treatment planning efforts in WTC and other disaster responders. The High-Symptom class requires particular attention in clinical settings, as this group had substantially elevated rates of all symptom clusters, as well as higher likelihood of excessive alcohol use, co-morbid depression and functional impairment. Further, it is likely that groups of patients with contrasting PTSD symptom typologies would benefit from different treatment approaches. For example, responders in the Threat group might benefit from treatments that work to alleviate intrusive trauma-related thoughts and hyperarousal, such as exposure-based therapies (Foa et al., 2007; Krakow et al., 2001; Rothbaum and Mellman, 2001), while the Dysphoric group might benefit from treatment focused on mitigating emotional numbing and dysphoric symptoms, such as behavioral activation approaches (Gros et al., 2012; Jakupcak et al., 2006; Kashdan et al., 2006). Pharmacotherapeutic approaches may similarly be tailored to different PTSD symptom profiles pending additional research (Asnis et al., 2004; Khachatryan et al., 2015; Marshall et al., 2001; Raskind et al., 2003). Additional research is needed to assess the generalizability of these results to other samples of WTC and other disaster responders, explore latent typologies of PTSD symptoms using DSM-5 criteria, and evaluate the development and natural history of different typologies of PTSD symptoms over time using longitudinal study designs.

Conflict of interest

Dr. Feder (co-inventor) and Mount Sinai have been named on a use patent application of ketamine for the treatment of post-traumatic stress disorder; patent is currently pending. Dr. Schechter has received consulting fees from Accolade, Inc., for analysis of claims data in evaluation of the effectiveness of their services and for technical support provided to in-house statistical staff. Dr. Crane has received funding from the CDC/NIOSH WTC Health Program contract # 200-2011-39356. Dr. Southwick has received royalties from two books published by Cambridge University Press: *Resilience: The Science of Mastering Life's Greatest Challenges* and *Resilience and Mental Health: Challenges Across the Lifespan*. Dr. Pietrzak is a scientific consultant to CogState Ltd. Drs. Bromet, Katz, Reissman, Kotov, Harrison, Herbert, Luft, Moline, Stellman, Udasin, Landrigan, Zvolensky and Pietrzak, and Ms. Horn report no competing interests.

Contributors

The following authors contributed to study design: A. Feder, C. Schechter, E. Bromet, C. Katz, M. Crane, D.J. Harrison, R. Herbert, B.J. Luft, J. M. Moline, J.M. Stellman, I.G. Udasin, P.J. Landrigan, S.M. Southwick, and R.H. Pietrzak.

The following authors contributed to study conduct: S.R. Horn, A. Feder, S.M. Southwick, R.H. Pietrzak.

The following authors contributed to manuscript preparation and review: S.R. Horn, A. Feder, C Schechter, E.J. Bromet, C.L. Katz, D.B. Reissman, R. Kotov, J. Moline, M.J. Zvolensky, S.M. Southwick, R.H. Pietrzak.

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