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Anxiety sensitivity as a transdiagnostic risk factor for trajectories of adverse posttraumatic neuropsychiatric sequelae in the AURORA study

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ABSTRACT

Anxiety sensitivity, or fear of anxious arousal, is cross-sectionally associated with a wide array of adverse posttraumatic neuropsychiatric sequelae, including symptoms of posttraumatic stress disorder, depression, anxiety, sleep disturbance, pain, and somatization. The current study utilizes a large-scale, multi-site, prospective study of trauma survivors presenting to emergency departments. Hypotheses tested whether elevated anxiety sensitivity in the immediate posttrauma period is associated with more severe and persistent trajectories of common adverse posttraumatic neuropsychiatric sequelae in the eight weeks posttrauma. Participants from the AURORA study ($n = 2,269$ recruited from 23 emergency departments) completed self-report assessments over eight weeks posttrauma. Associations between heightened anxiety sensitivity and more severe and/or persistent trajectories of trauma-related symptoms identified by growth mixture modeling were analyzed. Anxiety sensitivity assessed two weeks posttrauma was associated with severe and/or persistent posttraumatic stress, depression, anxiety, sleep disturbance, pain, and somatic symptoms in the eight weeks posttrauma. Effect sizes were in the small to medium range in multivariate models accounting for various demographic, trauma-related, pre-trauma mental health-related, and personality-related factors. Anxiety sensitivity may be a useful transdiagnostic risk factor in the immediate posttraumatic period identifying individuals at risk for the development of adverse posttraumatic neuropsychiatric sequelae. Further, considering anxiety sensitivity is malleable via brief intervention, it could be a useful secondary prevention target. Future research should continue to evaluate associations between anxiety sensitivity and trauma-related pathology.

Traumatic event exposure is common in the United States (US), with up to 90% of the population reporting lifetime exposure to a traumatic event (Kilpatrick et al., 2013). Of these, approximately 40 million present annually to emergency departments (EDs) for care following traumatic event exposure such as motor vehicle collision (MVC; Roberts et al., 2011). Unfortunately, adverse posttraumatic neuropsychiatric sequelae (APNS) are common and incur substantial burden on the health of an individual following trauma exposure. Specifically, posttraumatic stress disorder (PTSD) is the mental health condition most closely linked to trauma exposure, symptoms of which include re-experiencing the event, avoidance of reminders of the event, negative alterations in cognition and mood, as well as alterations in arousal and reactivity (American Psychiatric Association, 2013). Clinically significant PTSD symptoms occur in approximately 10% of trauma survivors, though this proportion varies depending on trauma type (Kilpatrick et al., 2013). Related symptoms are also common: many trauma survivors report clinically significant anxiety and/or depression (Kenardy et al., 2018), insomnia (Milanek et al., 2019), as well as pain and somatic symptoms, including headaches, dizziness, and nausea (Ulirsch et al., 2014), following trauma exposure. Although these symptoms are discrete and diverse, they are often comorbid, rather than presenting separately. For example, PTSD symptoms often co-occur with sleep disturbance (Short

et al., 2018), pain (Asmundson et al., 2002), and depression (Momartin et al., 2004). These posttrauma symptoms can become chronic and pose a significant burden to society as well as the individual (Kessler, 2000). Although trauma survivors receive care for physical injuries during their ED visits (Grega et al., 2017), there are no widely available interventions to prevent or reduce the burden of APNS. This raises the need to identify and evaluate potential malleable risk factors for these symptoms.

Anxiety sensitivity (AS) is defined as fear of anxious arousal (e.g., fears a racing heart indicates a heart attack; Reiss et al., 1986). AS is a transdiagnostic risk factor for the development of APNS that is considered to be trait-like but malleable via brief, cognitive behavioral interventions (Schmidt et al., 2014). Although initially linked with panic disorder (McNally, 2002), AS is now widely considered to be a transdiagnostic risk factor across anxiety-related and other mental health conditions (Smits et al., 2019). Specifically, cross-sectional research in various samples links AS with PTSD (Lang et al., 2002; Taylor, 2003), depression and anxiety (Allan et al., 2016; Paulus et al., 2018), insomnia and nightmares (Levin et al., 2009; Rogers et al., 2016; Short et al., 2015), pain (Ocañez et al., 2010; Zvolensky et al., 2020), and somatic symptoms (Hensley and Varela, 2008). Meta-analytic studies indicate that although AS is elevated across various conditions, it may be most

closely linked with fear and arousal-based disorders, including PTSD (Naragon-Gainey, 2010).

Relatively few prospective studies have examined whether AS predicts the development of APNS after trauma. The few studies available suggest AS may prospectively predict PTSD, depression, and anxiety symptoms after sexual assault (Short et al., *in press*), and PTSD symptoms in response to a campus shooting (Boffa et al., 2016) and other stressful life events that may not qualify as a Criterion A trauma such as childbirth (American Psychiatric Association, 2013; Keogh et al., 2002). AS may heighten risk for APNS by exacerbating normative post-traumatic stress, which is interpreted as threatening by those with high AS. For example, an individual with high AS may interpret intrusive memories as signs one is “going crazy,” or that increased heart rate in response to trauma reminders is indicative of impending cardiac arrest (Taylor, 2003). As such, those with high AS may experience increased physiological reactivity and distress in response to trauma reminders (McHugh et al., 2017), motivating avoidance, and maintaining PTSD and related symptoms. Despite this theoretical rationale and early promising empirical research, no studies to our knowledge have examined whether AS predicts symptom trajectories of a diverse set of trauma symptoms (i.e., pain, somatic, and insomnia symptoms) in a large sample of mixed trauma survivors recruited immediately posttrauma.

The current study is the first large-scale, multi-site, prospective study of trauma survivors presenting to EDs to assess whether elevated AS in the immediate posttrauma period is associated with more severe and persistent trajectories of common APNS (PTSD, depression, anxiety, pain, insomnia, and somatic symptoms) in the eight weeks posttrauma. Profiles of APNS based on growth mixture modeling were used as outcomes because of the complex temporal nature of APNS following trauma. Specifically, the vast majority of trauma survivors will experience heightened APNS, particularly PTSD symptoms, in the aftermath of trauma. This is an expected and normal part of the trauma recovery process, and not pathological. However, the majority of survivors' symptoms will recover naturally over time, while a small but significant minority of individuals' symptoms will remain heightened and clinically significant (Santiago et al., 2013). Therefore, utilizing trajectory profiles enables the identification of individuals whose symptoms do *not* resolve naturally over time, and thus are at risk of developing chronic APNS. Indeed, prior prospective research of a smaller sample ($n=330$) of physically injured trauma survivors found four latent classes of APNS (only examining PTSD and depressive symptoms): chronic distress, delayed distress, recovered, and resilience (deRoos-Cassini et al., 2010), indicating the importance of examining trajectories of symptoms over time. In regard to the trajectories of APNS following trauma exposure, we hypothesized that 1) elevated AS measured in the two weeks post-trauma will be associated with increased risk for belonging in classes with severe and persistent trajectories of transdiagnostic APNS (i.e., PTSD, depression, anxiety, sleep disturbance, pain, and somatic symptoms) in the eight weeks posttrauma; 2) the associations between AS and APNS will persist after accounting for a variety of important covariates, including sociodemographic, trauma-related, pre-trauma mental health-related, and personality-related factors (i.e., neuroticism); and 3) based on prior research (Naragon-Gainey, 2010), the strongest associations will be found between AS and anxiety and hypervigilance-related symptoms.

1. Methods

1.1. Participants and procedures

AURORA study recruitment occurred from September 2017 to December 2020. The current sample is drawn from the third data release. Patients presenting for emergency care within 72h of trauma exposure at 23 participating study sites were screened for eligibility. Inclusion criteria included: age of 18–75 years, fluent in spoken and written English, alert and oriented at the time of ED presentation, ability

to follow enrollment protocol and use a smart phone, possessed a smartphone for >1 year. Qualifying traumatic events included motor vehicle collision, physical assault, sexual assault, fall >10 feet, or mass casualty incidents. Exclusion criteria included: solid organ injury, significant hemorrhage, need for a chest tube, or likely to be admitted for >72h. A total of 2,654 individuals were included in the entire sample, with 2,305 completing an AS assessment, 2,269 of whom had trajectory data for at least one class of symptoms and were thus included in the final sample for the current study.¹

Potentially eligible participants were approached by site research assistants who screened participants, obtained written, informed consent, and administered a brief ED assessment. After enrollment, participants received a two-week self-report assessment which was completed online. They also received surveys on their smart phones in the eight weeks after trauma, which included a rotating set of self-report questions on a variety of APNS (detailed below). Participants were compensated for their participation in all assessments. AURORA study protocol is described in greater detail elsewhere (McLean et al., 2019). Prior studies have discussed clinical outcomes for AURORA participants (Kessler et al., 2020), a clinical risk tool for PTSD which includes AS items (Ziobrowski et al., 2021), and the analysis of classes of symptom trajectories (without considering AS as a risk factor of these outcomes; Beaudoin et al., *under review*). However, the current results have not been published previously. All procedures were approved by a central Institutional Review Board (IRB) and local IRBs as relevant.

1.2. Measures

Anxiety Sensitivity (AS). The Anxiety Sensitivity Index (ASI; Reiss et al., 1986) was adapted and used to measure AS two weeks after participants presented to emergency care. To maintain assessment brevity in this large study, only three of 16 items were used, with responses rated on a 5-point Likert scale ranging from 0 (*very little*) to 4 (*very much*). Items included were: Item 2, “When I cannot keep my mind on a task, I worry that I might be going crazy; Item 14, “Unusual body sensations scare me;” and Item 15, “When I am nervous, I worry that I might be mentally ill.” The possible score range for the brief ASI was 0–12, with higher scores indicating higher levels of AS. The ASI has strong psychometric properties (Reiss et al., 1986). This brief ASI was used in a prior study of recent trauma survivors and demonstrated good internal consistency ($\alpha = 0.89$; Short et al., *in press*).

APNS outcomes. Self-report surveys were administered via participants' smart phones using the Mindstrong Discovery™ application at six time points in the eight weeks after trauma (see [Supplementary Table 1](#) for numbers of and a list of items, and precise timing of when administered). Items assessing the a priori-identified constructs of pain, somatic symptoms, sleep, avoidance, re-experiencing, hyperarousal, anxiety, and depression in the past 24 h were administered on a rotating schedule to ensure even assessment of each construct ([Supplementary Table 1](#)). Items were drawn from validated measures including the PTSD Checklist, PROMIS scales, and Insomnia Severity Index (Cella et al., 2010; Morin et al., 2011; National Center for PTSD, 2019), and shortened/adapted as needed to assess state symptoms, as described elsewhere (Beaudoin et al., *under review*; McLean et al., 2019). [Supplementary Table 2](#) provides support for reliability of these measures.

Covariates. Demographics. Sociodemographic data were collected in the ED regarding gender, age, highest grade achieved, income, race/ethnicity, employment, and marital status. **Trauma-related variables.**

¹ Details regarding missing trajectory data were as follows. The class with the most missing data was sleep and nightmares ($n = 27$ of the final sample), followed by depression ($n = 25$), anxiety and arousal ($n = 25$), somatic symptoms and mental fatigue ($n = 19$), re-experiencing and avoidance ($n = 18$), and pain ($n = 10$).

Information regarding the trauma was collected in the ED. Whether or not participants sustained a traumatic brain injury as defined by a diagnosed concussion or if the participant reported their head was hit during the trauma, along with loss of consciousness, amnesia, or disorientation (McLean et al., 2009). Whether or not participants were admitted to the ED was recorded, along with the severity of injury as assessed by the Abbreviated Injury Scale (AIS; Loftis et al., 2018). Participants also self-reported on peritraumatic dissociation using the Michigan Critical Events Perception Scale (MCEPS; Michaels et al., 1999). *Personality.* The Ten Item Personality Index (TIPI; Gosling et al., 2003) was administered at two weeks posttrauma and was used in the current study to index neuroticism. *Pre-trauma mental health symptoms.* Pre-trauma mental health symptoms in the 30 days prior to the event were retroactively assessed at the initial ED visit by altering the instructions to specify this timeframe in each measure. Specific measures were as follows: the Patient Reported Outcome Information System (PROMIS; Cella et al., 2010) evaluated pre-trauma depression and anxiety, the Insomnia Severity Index (ISI; Morin et al., 2011) assessed pre-trauma insomnia symptoms, the PTSD Checklist-5 (PCL-5; Weathers et al., 2013) measured pre-trauma PTSD symptoms (for the PCL-5, individuals who denied disturbing memories; feeling upset when reminded of the trauma; avoiding reminders; feeling cutoff; feeling irritable; and difficulty concentrating were not given the full PCL-5 and their pre-trauma PTSD diagnoses were coded as no pre-trauma PTSD [0]), a pain Numeric Rating Scale (NRS) assessed pre-trauma pain (Farrar et al., 2001), and pre-trauma somatic symptoms were assessed by a 20-item measure adapted from the Pennebaker Inventory of Limbic Languidness (Pennebaker and Watson, 1991) and the Rivermead Post-Concussion Symptoms Questionnaire (Potter et al., 2006) commonly used in studies of trauma survivors recruited from the ED (Ulirsch et al., 2014).

1.3. Data analytic plan

Trajectories for each posttrauma symptom (i.e., re-experiencing, avoidance, hyperarousal, pain, depression, insomnia, nightmares, anxiety, somatic symptoms, mental fatigue) were identified using self-reported state symptoms from the mobile phone-based surveys. Detailed methods and analytic techniques are described in Beaudoin et al. (under review; note the Beaudoin et al. results are related to a smaller initial dataset) and in the supplemental tables. In brief, R (R Core Team, 2022) was used to prepare data for analysis, and MPlus (Muthén and Muthén, 1998–2017) was used for model building. Joint measurement models were developed for each of the ten latent APNS constructs including all six timepoints (see Supplementary Table 2). Latent growth curve models were identified to establish trajectories for each construct, and growth mixture modeling was used to estimate latent trajectory classes. The number of latent classes for each construct was determined by analysis of model fit, BIC, percentage of participants in each latent class, and theoretical expectations/clinical utility. Models with convergence issues or including latent classes with less than 5% participants were excluded first. Afterwards, BIC was used to select the best model. For models with similar BICs, theoretical expectations and clinical utility were used to guide final model selection. Qualitative descriptors of these empirically derived classes were developed by visually inspecting the data. Each participant was assigned to a class based on these analyses, and these class variables were used as dependent variables in the current analyses. Data were treated as missing at random after confirmation that missingness was not associated with the constructs of interest (Beaudoin et al., under review).

Using these class trajectories, general linear models (GLMs) in SPSS Version 26.0 (IBM Corp, 2019) were used to determine whether self-reported AS assessed two weeks posttrauma predicted class membership in classes with more severe or persistent APNS over eight weeks posttrauma. First, a series of 10 univariate GLMs with AS as a predictor of each construct in separate models were conducted to assess whether

AS predicted these constructs and levels of AS in each class. Simple contrasts were used to evaluate whether AS differed across classes when the omnibus test was significant. Second, the same 10 analyses were estimated using multivariate GLMs with the following covariates: race and ethnicity, employment, and marital status as categorical variables, and gender, age, highest grade achieved, income, peritraumatic dissociation, injury severity, whether the participant was admitted to the ED, whether the participant had a likely concussion, pre-trauma anxiety symptoms, neuroticism, and pre-trauma symptoms for the dependent variable of interest (e.g., for re-experiencing symptoms, pre-trauma PTSD diagnostic status was a covariate; for pain, pre-trauma moderate or severe pain was a covariate) as continuous variables. Effect sizes were evaluated using eta-squared and partial eta-squared. Values of 0.01, 0.06, and 0.14 were considered small, medium, and large effect sizes, respectively (Cohen, 1988; Richardson, 2011). For the current analyses linking AS with APNS trajectories, individuals who were missing class data were dropped from analyses in which their data were missing.¹

2. Results

2.1. Descriptive statistics

Participants were majority women (63.5%), with an average age of about 36 years ($M = 35.82$, $SD = 13.07$). The largest proportion of participants was Black (49.8%), followed by white (34.7%), Hispanic (11.3%), and other (e.g., Asian, Native American; 3.7%). Education levels varied, with a slight majority attaining some college (53.5%). Most participants were employed (73.2%) and reported an income of \$35,000 or less (62.3%). Regarding trauma exposure, the majority experienced MVC (75.6%), were discharged home from the ED (93.9%), and had minimal physical injury (e.g., musculoskeletal strain; AIS $M = 1.19$, $SD = 0.42$). About one third had clinically significant PTSD symptoms prior to the current trauma exposure (31.8%). At eight weeks posttrauma (concurrent to when surveys assessing class trajectories ended), the majority of participants reported clinically significant new or worsening pain (77.1%), while large minorities reported clinically significant insomnia (40.1%), PTSD (38.0%), and depression (27.1%) (see Table 1).

2.2. Class trajectories

A brief summary of results is provided as trajectories are not the main focus of the current manuscript and detailed results are described in elsewhere (Beaudoin et al., under review). First, measurement models for each latent APNS construct demonstrated good fit (CFIs = 0.90–0.99, TLIs = 0.86–0.98, SRMRs = 0.01–0.06, RMSEAs = 0.04–0.11). Most did not have full measurement invariance over time (except Anxiety), likely due to the large sample size (differences over time were <5%). All APNS were best modeled using a piecewise linear trajectory except Anxiety (which was modeled as linear). For each APNS, 2 (sleep; CFI = 0.94, TLI = 0.93, SRMR = 0.04, RMSEA = 0.06), 3 (hyperarousal, depression, nightmares, anxiety, somatic symptoms; CFIs = 0.92–0.95, TLIs = 0.90–0.95, SRMRs = 0.03–0.05, RMSEAs = 0.06–0.09), or 4 (re-experiencing, avoidance, pain, mental fatigue; CFIs = 0.93–0.99, TLIs = 0.93–0.98, SRMRs = 0.03–0.05, RMSEAs = 0.04–0.07) classes of symptom trajectories were identified (see Table 2 for number and percentage of individuals in each class described qualitatively and Fig. 1 for a visual depiction of trajectories).

2.3. Univariate analyses of AS predicting class membership

AS was a significant predictor of trajectories of each trauma-related construct (all $ps < .001$), and AS significantly increased sequentially across each class based on the severity and persistence of symptoms, with the highest levels of AS found among those with the most severe and persistent symptoms (Table 2). AS was associated with higher levels

Table 1
Participant demographic and clinical characteristics (n = 2,269)

| | n (%) |
|--|---------------|
| Age (M [SD]) | 35.82 (13.07) |
| Women | 1440 (63.5) |
| Race/Ethnicity | |
| Hispanic | 257 (11.3) |
| White | 788 (34.7) |
| Black | 1131 (49.8) |
| Other | 85 (3.7) |
| Education | |
| Less than high school | 166 (7.3) |
| High school or equivalent | 84 (3.7) |
| Post-high school training not college/some college | 1210 (53.5) |
| 4-year degree | 175 (7.7) |
| Graduate or professional degree | 626 (27.7) |
| Annual Income | |
| ≤\$19,000 | 721 (31.8) |
| \$19,001–35,000 | 692 (30.5) |
| \$35,001–50,000 | 325 (14.3) |
| \$50,001–75,000 | 198 (8.7) |
| \$75,001+ | 304 (13.4) |
| Work Status | |
| Employed | 1660 (73.2) |
| Retired | 54 (2.4) |
| Homemaker | 52 (2.3) |
| Student | 89 (3.9) |
| Unemployed/disabled/other | 397 (17.5) |
| Trauma Type | |
| Motor vehicle collision | 1715 (75.6) |
| Physical assault | 207 (9.1) |
| Sexual assault | 13 (0.6) |
| Fall <10' | 33 (1.5) |
| Mass trauma event | 10 (0.4) |
| Non-motorized collision | 43 (1.9) |
| Fall >10' or unknown height | 110 (4.8) |
| Poisoning | 2 (0.1) |
| Animal-related | 52 (2.3) |
| Burn | 10 (0.4) |
| Other | 74 (3.3) |
| PTSD prior to current trauma | 722 (31.8) |
| Clinical outcomes at 8 weeks | |
| PTSD | 863 (38.0) |
| Depression | 616 (27.1) |
| Insomnia | 807 (40.1) |
| Clinically significant new or worsening pain | 1481 (77.1) |
| Anxiety (M [SD]) | 7.14 (4.57) |

of PTSD symptoms, including re-experiencing, avoidance, and hyperarousal, with large effects. AS was associated with higher levels of pain, with a medium effect size. Those with higher levels of insomnia and nightmares also had higher levels of AS, with medium to large effects. AS was also associated with higher levels of depression and anxiety, with large effects. Finally, AS was associated with higher levels of somatic symptoms and mental fatigue, with medium to large effects.

2.4. Multivariate analyses of AS predicting class membership

In multivariate models including covariates, AS continued to be significantly associated with higher levels of symptoms in each construct (Table 3). Again, AS increased sequentially and significantly across classes, with the groups with the most severe/persistent APNS having the highest levels of AS. Elevated AS continued to be associated with higher PTSD symptoms, including re-experiencing, avoidance, and hyperarousal symptoms, with medium effects. Covariates significantly positively associated with worsened PTSD symptom trajectories (Supplementary Table 3) included identifying as a woman, older age, higher education, higher income level, peritraumatic dissociation, pre-trauma anxiety (for hyperarousal symptoms), neuroticism, and pre-trauma probable PTSD diagnosis (for arousal symptoms). AS was associated with worsened pain trajectories with a small to medium effect. Covariates positively associated with pain trajectories included identifying as

Table 2
Univariate general linear models of anxiety sensitivity levels by class trajectory membership.

| | n (%) | M | SE | df | F | p | η^2 |
|-------------------------|-------------|-------|-----|---------|--------|-------|----------|
| Re-experiencing | | | | 3, 2247 | 178.35 | <.001 | .19 |
| Low | 937 (41.6) | 1.82 | .09 | | | | |
| Moderate recovery | 704 (31.3) | 3.42 | .11 | | | | |
| Moderate | 468 (20.8) | 4.63 | .13 | | | | |
| High* | 142 (6.3) | 6.65 | .24 | | | | |
| Avoidance | | | | 3, 2247 | 143.39 | <.001 | .16 |
| Low | 858 (38.1) | 1.85 | .10 | | | | |
| Moderate Recovery | 453 (20.1) | 2.90 | .14 | | | | |
| Moderate | 703 (31.2) | 4.30 | .11 | | | | |
| High* | 237 (10.5) | 5.52 | .19 | | | | |
| Hyperarousal | | | | 2, 2241 | 301.30 | <.001 | .21 |
| Low | 980 (43.7) | 1.76 | .09 | | | | |
| Moderate | 928 (41.4) | 33.75 | .09 | | | | |
| High* | 336 (14.6) | 5.98 | .16 | | | | |
| Pain | | | | 3, 2255 | 66.43 | <.001 | .08 |
| Low | 288 (12.7) | 1.99 | .18 | | | | |
| Moderate Recovery | 722 (32.0) | 2.57 | .11 | | | | |
| Moderate | 810 (35.9) | 3.35 | .11 | | | | |
| High* | 439 (19.4) | 4.82 | .15 | | | | |
| Depression | | | | 2, 2241 | 399.00 | <.001 | .26 |
| Low | 1072 (46.5) | 1.65 | .07 | | | | |
| Moderate | 847 (37.7) | 4.07 | .11 | | | | |
| High* | 325 (14.1) | 6.17 | .20 | | | | |
| Sleep | | | | 1, 2240 | 286.55 | <.001 | .11 |
| Low | 1159 (51.7) | 2.18 | .09 | | | | |
| High* | 1083 (47.0) | 4.34 | .09 | | | | |
| Nightmares | | | | 2, 2239 | 314.91 | <.001 | .22 |
| Low | 1551 (69.2) | 2.25 | .07 | | | | |
| Moderate | 542 (24.2) | 5.06 | .12 | | | | |
| High* | 149 (6.6) | 6.69 | .23 | | | | |
| Anxiety | | | | 2, 2241 | 318.96 | <.001 | .22 |
| Low | 1178 (52.5) | 1.89 | .08 | | | | |
| Moderate | 814 (36.3) | 4.21 | .10 | | | | |
| High* | 252 (11.2) | 6.21 | .18 | | | | |
| Somatic Symptoms | | | | 2, 2247 | 219.94 | <.001 | .16 |
| Low | 1434 (63.7) | 2.33 | .08 | | | | |

(continued on next page)

Table 2 (continued)

| | <i>n</i> (%) | <i>M</i> | <i>SE</i> | <i>df</i> | <i>F</i> | <i>p</i> | <i>n</i> ² |
|-----------------------|---------------|----------|-----------|------------|----------|----------|-----------------------|
| Moderate | 601 (26.7) | 4.17 | .12 | | | | |
| High* | 215 (9.6) | 6.35 | .20 | | | | |
| Mental Fatigue | | | | 3, 2246 | 181.72 | <.001 | .20 |
| Low | 841 (37.4) | 1.65 | .10 | | | | |
| Moderate Recovery | 155 (6.9) | 3.25 | .23 | | | | |
| Moderate | 823 (36.6) | 3.56 | .10 | | | | |
| High* | 431 (19.1) | 5.56 | .139 | | | | |

Note: * = *p* < .001 in simple contrasts comparing the high/persistent class with each other class for each respective outcome.

Table 3

Estimates of anxiety sensitivity as a predictor of class membership in multivariate models after covarying for sociodemographic, trauma-related, pre-trauma mental health-related, and personality-related factors.

| | <i>df</i> | <i>F</i> | <i>p</i> | <i>n</i> _p ² |
|------------------|-----------|----------|----------|------------------------------------|
| Re-experiencing | 1, 2004 | 167.95 | <.001 | .08 |
| Avoidance | 1, 2004 | 131.29 | <.001 | .06 |
| Hyperarousal | 1, 2004 | 182.87 | <.001 | .08 |
| Pain | 1, 2010 | 62.93 | <.001 | .03 |
| Depression | 1, 1963 | 213.95 | <.001 | .10 |
| Sleep | 1, 1980 | 74.25 | <.001 | .04 |
| Nightmares | 1, 1980 | 237.77 | <.001 | .11 |
| Anxiety | 1, 1998 | 208.91 | <.001 | .10 |
| Somatic Symptoms | 1, 1969 | 151.69 | <.001 | .07 |
| Mental Fatigue | 1, 1969 | 123.42 | <.001 | .06 |

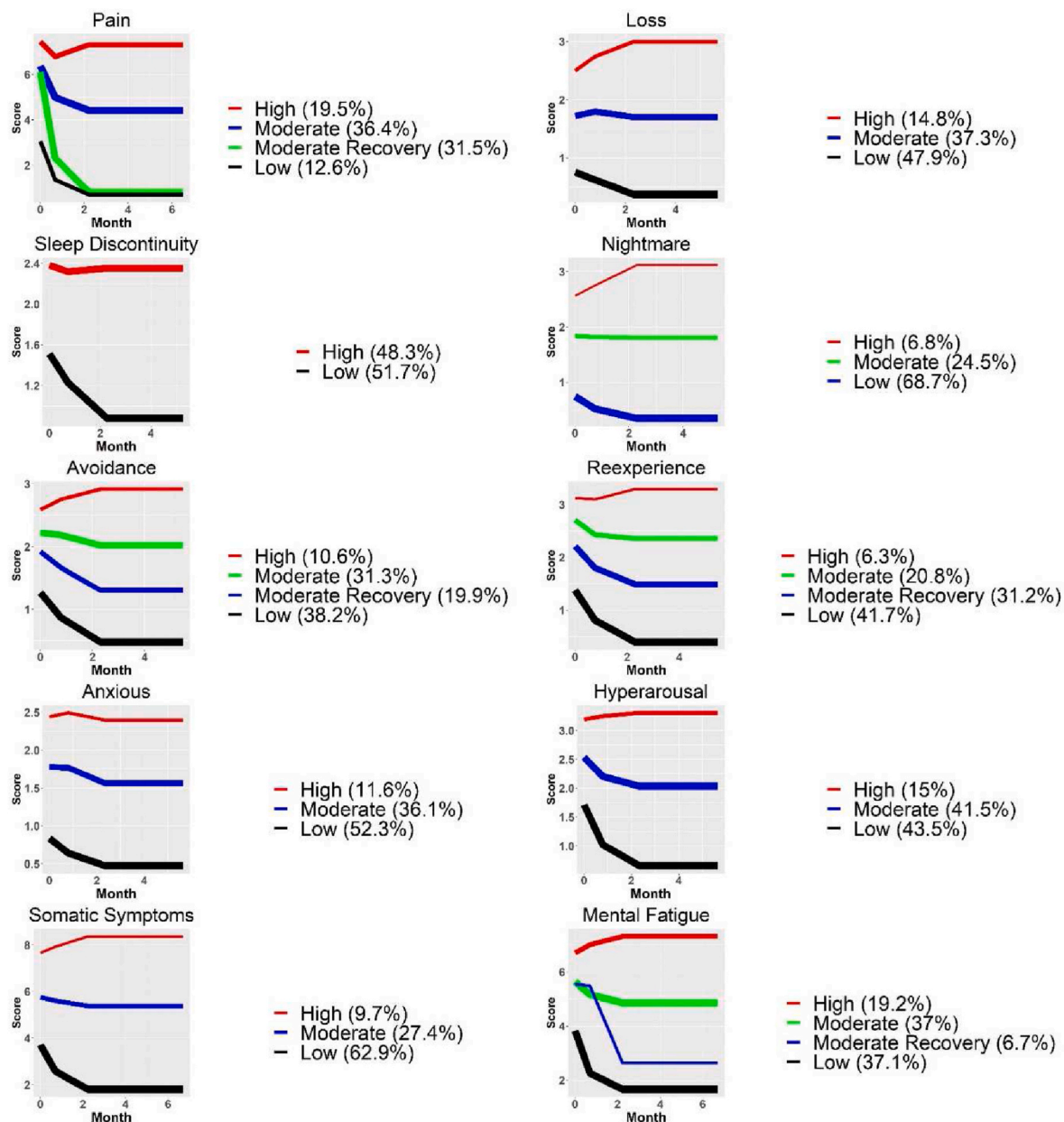


Fig. 1. Visual depictions of latent class trajectories for each construct.

a woman, older age, higher education and income levels, peritraumatic dissociation, pre-trauma anxiety, neuroticism, and pre-trauma clinically significant pain.

Further, AS was associated with increased insomnia and nightmares, with small to medium and medium to large effects, respectively. Covariates associated with more severe sleep disturbance trajectories included older age (for insomnia), higher education and income (for nightmares), peritraumatic dissociation, neuroticism (for insomnia), pre-trauma anxiety (for nightmares), and pre-trauma insomnia symptoms. AS was associated with depression and anxiety with medium to large effects. Covariates predicting worsened depression and anxiety trajectories were: identifying as women (for anxiety), older age, higher levels of education (for depression) and income, peritraumatic dissociation, pre-trauma anxiety, neuroticism, and pre-trauma depression (for depression symptoms). AS was also associated with higher levels of somatic symptoms and mental fatigue with medium effects. Covariates predicting poor somatic and mental fatigue trajectories included identifying as a woman, older age, higher education (for somatic symptoms) and income levels, peritraumatic dissociation, pre-trauma anxiety, neuroticism (for mental fatigue), and pre-trauma somatic symptoms (for somatic symptoms).

3. Discussion

Growth mixture modeling revealed distinct trajectories of APNS, including PTSD, pain, depression, anxiety, sleep disturbance, and somatic symptoms among a large sample of 2,269 trauma survivors presenting to EDs following trauma exposure. Consistent with prior research (deRoos-Cassini et al., 2010), for each APNS construct, trajectories typically indicated at least one class of trauma survivors had more severe and/or persistent symptoms in the eight weeks posttrauma. Findings from the current study support the hypothesis that AS in the aftermath of traumatic event exposure would prospectively predict more severe or persistent trajectories of transdiagnostic APNS including PTSD, depression, anxiety, pain, somatic symptoms, and sleep disturbances in a large sample of individuals with diverse trauma exposures. Indeed, trauma survivors with the most severe and persistent symptoms across APNS reported the highest levels of AS. Results were robust to a variety of important sociodemographic, trauma-related, pre-trauma mental health, and personality-related covariates. These findings are consistent with a large body of previous cross-sectional work linking AS with PTSD symptoms (Lang et al., 2002; Naragon-Gainey, 2010; Taylor, 2003). The current results also build upon limited prospective work of smaller, single trauma-exposed (i.e., sexual assault, campus shooting) samples suggesting AS may prospectively predict PTSD symptoms after trauma (Boffa et al., 2016; Keogh et al., 2002; Short et al., in press) by including a large sample of diverse trauma survivors, and examining transdiagnostic APNS.

In terms of mental health-related APNS, elevated AS in the immediate posttrauma period was associated with higher levels and persistence of re-experiencing, avoidance, and hyperarousal symptoms with medium effects ($\eta_p^2 = .03-.11$) in multivariate models adjusting for important sociodemographic, trauma-related, pre-trauma mental health, and personality-related covariates. Further, extending on prior prospective studies of adolescents (Allan et al., 2016) and cross-sectional studies of trauma-exposed adults (Paulus et al., 2018), AS was associated with increased severity and persistence of depression and anxiety with medium to large effects. To our knowledge, one other study has found that AS prospectively predicts anxiety and depression after trauma (specifically sexual assault; Short et al., in press), but this is the first study to prospectively link AS with increased anxiety and depression among a large, diverse sample of trauma survivors. Based on the results of the current study and others in the literature, AS may be an important predictor of various mental health-related APNS after trauma exposure.

There were also associations between AS levels in the two weeks posttrauma and physical or somatic APNS. Elevated AS was associated

with worsened pain trajectories (i.e., more severe pain that failed to recover over time) with a small to medium effect. This finding is consistent with prior work linking AS with increased pain severity (Ocañez et al., 2010), including in trauma-exposed samples (Zvolensky et al., 2020); however, to our knowledge this is the first study to suggest that AS is associated with escalating pain after traumatic event exposure. Complementing prior cross-sectional and RCT studies among samples of undergraduates, community individuals with high AS, and psychology clinic outpatients (Levin et al., 2009; Rogers et al., 2016; Short et al., 2015), increased AS had small to medium associations with insomnia symptoms (higher levels that did not recover over time) and nightmares (higher levels that worsened over time) in the aftermath of trauma. Finally, heightened AS was associated with increased somatic symptoms and mental fatigue that worsened over time, with medium effect sizes. This is consistent with a relatively small body of research linking AS with somatic symptoms in the aftermath of trauma (Hensley and Varela, 2008), and trouble concentrating among headache sufferers (Smitherman et al., 2015). Taken together, our findings expand upon prior work linking AS with a variety of physical and somatic symptoms (i.e., pain, sleep disturbance, somatic symptoms, mental fatigue) by suggesting AS is prospectively linked with severity and persistence of these symptoms after trauma exposure.

Regarding strength of associations, all effects were in the small to medium range in multivariate models. Most effects were of medium size, including for re-experiencing, avoidance, hyperarousal, depression, nightmares, anxiety, somatic symptoms, and mental fatigue. Associations between AS and pain and sleep were in the small range. Thus, there was no evidence for specificity or a qualitatively stronger relationship between AS and hyperarousal or anxiety-related constructs. This is in contrast with prior meta-analytic work suggesting AS has stronger associations with hyperarousal symptoms of PTSD compared to re-experiencing or avoidance symptoms (Naragon-Gainey, 2010). These discrepant findings may be due to methodological differences as prior studies often included participants with chronic PTSD, while the current study includes recent trauma survivors who vary in the clinical significance of their PTSD symptoms. It is possible that AS plays a broader predictive role in the immediate aftermath of trauma, reinforcing its importance as a clinical target in preventing APNS after trauma exposure.

The current results also have clinical implications. In the context of a large body of prior work linking AS with trauma-related pathology (Allan et al., 2016; Boffa et al., 2016; Paulus et al., 2018; Short et al., in press; Zvolensky et al., 2020), AS may be a transdiagnostic prospective predictor of the development of a variety of APNS among trauma survivors presenting to EDs. Fortunately, AS is a malleable target for treatment, and can be reduced using cognitive behavioral therapy-oriented interventions. These interventions can be delivered via fully computerized treatments as brief as 1 h conducted in a single session (Schmidt et al., 2014). Such AS interventions have been found to reduce symptoms of anxiety, depression, PTSD, and insomnia among individuals with elevated AS (Allan et al., 2015; Schmidt et al., 2014). However, prior work has been conducted among samples of individuals who have established, often chronic, mental health disorders, including experiencing traumas that occurred many years in the past. Future research would benefit from testing whether targeting AS with brief interventions in the immediate aftermath of trauma could mitigate the development of APNS. Considering that AS interventions can be brief and autonomous, they may be feasible for dissemination in the ED setting. If efficacious, this could potentially have a major positive clinical impact in preventing the development of various impairing and distressing APNS ranging from PTSD to depression to pain.

The current findings should be considered in the context of this study's strengths and limitations. Strengths of the current studies include a large sample size of trauma survivors who completed state assessments of their symptoms utilizing validated measures. Regarding limitations, first, future research may benefit from utilizing the full ASI

or ASI-3 (Reiss et al., 1986; Taylor et al., 2007) to assess AS, as the current study used a brief, 3-item measure of AS to accommodate the need to measure many constructs in this large study. In particular, the brief ASI used in the current study only assessed the cognitive and physical components of AS, and did not assess the social component of AS. Therefore, it is unclear how results of the current study apply to the various subfactors of AS. Second, AS was measured in the two weeks posttrauma, rather than prior to trauma exposure. Thus, it remains unclear whether trauma itself may impact the development of AS (for a more detailed discussion, see Short et al., in press). However, regardless of whether AS is impacted by trauma, it may be a malleable risk factor in the immediate aftermath of trauma that could identify those at risk for poor outcomes. Further, even among those with more chronic symptoms, research has indicated that targeting AS is effective in reducing PTSD symptoms (Short et al., 2017). Therefore, although it is important for theoretical reasons to understand whether elevated AS precedes trauma exposure or not, clinically, it remains a useful risk factor to consider using framework developed by Kraemer et al. (1997) as it 1) is correlated with the outcome of interest, 2) occurs prior to the development of the outcome of interest (even if not necessarily prior to trauma exposure itself), and 3) is malleable, with reductions in AS being associated with reductions in PTSD and other APNS. Third, it is important to note that many trauma survivors do not present to emergency care, particularly those who have experienced traumas placing them at high risk for PTSD such as sexual assault (Rennison, 2002). Thus, it is unclear if results would generalize to this population. However, this is a clinically important population with a valuable preventative intervention opportunity in the ED setting.

The current results suggest AS in the two weeks posttrauma is a transdiagnostic predictor of negative outcomes posttrauma, including PTSD, pain, depression, sleep disturbance, anxiety, and somatic symptoms. Future research directions include replicating these findings in diverse samples of trauma survivors, determining mechanisms underlying associations between AS and APNS (particularly considering AS is linked with a diverse array of APNS), and whether targeting AS in the aftermath of trauma would mitigate the development of these symptoms.

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