

Original Article

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Sex-dependent differences in vulnerability to early risk factors for posttraumatic stress disorder: results from the AURORA study

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Abstract

Background. Knowledge of sex differences in risk factors for posttraumatic stress disorder (PTSD) can contribute to the development of refined preventive interventions. Therefore, the aim of this study was to examine if women and men differ in their vulnerability to risk factors for PTSD.

Methods. As part of the longitudinal AURORA study, 2924 patients seeking emergency department (ED) treatment in the acute aftermath of trauma provided self-report assessments of pre- peri- and post-traumatic risk factors, as well as 3-month PTSD severity. We systematically examined sex-dependent effects of 16 risk factors that have previously been hypothesized to show different associations with PTSD severity in women and men.

Results. Women reported higher PTSD severity at 3-months post-trauma. Z-score comparisons indicated that for five of the 16 examined risk factors the association with 3-month PTSD severity was stronger in men than in women. In multivariable models, interaction effects with sex were observed for pre-traumatic anxiety symptoms, and acute dissociative symptoms; both showed stronger associations with PTSD in men than in women. Subgroup analyses suggested trauma type-conditional effects.

Conclusions. Our findings indicate mechanisms to which men might be particularly vulnerable, demonstrating that known PTSD risk factors might behave differently in women and men. Analyses did not identify any risk factors to which women were more vulnerable than men, pointing toward further mechanisms to explain women's higher PTSD risk. Our study illustrates the need for a more systematic examination of sex differences in contributors to PTSD severity after trauma, which may inform refined preventive interventions.

Introduction

Sex differences in posttraumatic stress disorder (PTSD) have been documented widely. Across nations, time, study type, or diagnostic criteria, women have been reported to be at higher risk for PTSD than men (Ben-Ezra *et al.*, 2018; Frans, Rimmo, Aberg, & Fredrikson, 2005; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Otten *et al.*, 2021). Among the general population, women are approximately twice as likely to develop PTSD compared to men (Goldstein *et al.*, 2016; McCall-Hosenfeld, Mukherjee, & Lehman, 2014; Seedat *et al.*, 2009), with the highest reported risk differences ranging up to six-folds greater odds in women (Seedat *et al.*, 2009). In addition, current research suggests women experience more chronic and severe PTSD symptoms than men (Carmassi *et al.*, 2014; Carragher *et al.*, 2016; Haering *et al.*, 2024b; Kessler *et al.*, 1995; Tolin & Foa, 2006). While female sex is sometimes considered a PTSD risk factor itself, settling at this point disregards the underlying mechanisms that drive these risk differences. Rather than oversimplifying this relationship to a maxim in

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which women fundamentally are at higher vulnerability to adverse trauma-related outcomes, a better understanding of which risk factors affect whom, when, and how will allow researchers to design interventions that tackle modifiable constructs such as cognitive, behavioral, or structural processes that are associated with sex.

Several advances have been made in explaining the prominent sex differences in PTSD outcomes. Sexual trauma, for instance, more commonly experienced by women than men (Tolin & Foa, 2006), has been found to be associated with a higher risk for PTSD compared to other trauma types (Kessler et al., 1995; Perkonig, Kessler, Storz, & Wittchen, 2000). Yet, even when controlling for sexual trauma exposure, sex differences in PTSD prevalence and severity remain (Tolin & Foa, 2006), and sex differences in PTSD have also been found in samples of non-sexual trauma survivors, such as victims of motor vehicle accidents (Fullerton et al., 2001). In addition to characteristics of the traumatic event, sex differences in neurobiological processes, such as fear mechanisms (Dark et al., 2022; Ramikie & Ressler, 2018), as well as physiological (Lalonde et al., 2021) and psychosocial risk factors, such as acute stress responses and appraisals (Olf, 2017; Olf, Langeland, Draijer, & Gersons, 2007) have been examined. More recently, researchers also have started to study the impact of gender-related factors such as gender norms or gender role stress (Christiansen & Berke, 2020), and now are slowly beginning to examine the interplay of sex- and gender-related factors (Christiansen, McCarthy, & Seeman, 2022). Tannenbaum, Ellis, Eyssele, Zou, and Schiebinger (2019) define sex as referring to biological attributes, and gender as referring to sociocultural factors, such as gender norms, gender identity, or gender relations. As the analyses included in this study are based on sex assigned at birth, we use the term sex in this text to refer to differences between women and men, while simultaneously acknowledging that both sex and gender are important predictors of health, mutually influence each other, and are often intertwined (Krieger, 2003).

Despite recent progress, reviews on sex and/or gender differences in PTSD risk factors unanimously call for an improved consideration of sex and gender in trauma research, as the full picture of what accounts for the disparities in PTSD outcomes still remains unclear (Christiansen et al., 2022; Olf & Langeland, 2022; Ramikie & Ressler, 2018). This gap in knowledge is not surprising, however, given various methodological challenges in the examination of sex differences in PTSD risk factors: (1) First, risk factors should ideally be examined in a prospective manner. Yet, as it is difficult to foresee traumatic events, designing prospective PTSD studies is challenging. (2) Second, much of the prospective research on PTSD risk factors has been conducted in predominantly male samples, such as soldiers, police officers or firefighters (Eraly et al., 2014; Sopp, Michael, Lass-Hennemann, Haim-Nachum, & Lommen, 2021; Sørensen, Olesen, Midtgaard, & Willert, 2022). However, even in more naturalistic samples, such as prospective emergency department studies, men are studied twice as much as women (Haering et al., 2024b). The lack of female representation becomes even more apparent in psychobiological PTSD research, where only 2% of the research has been conducted in females (Olf, 2017), as it is feared that the 'messy' hormonal variability associated with the female menstrual cycle might confound study results (Bale & Epperson, 2017; Beery & Zucker, 2011). While recent research has shown that this dogma is inaccurate (Levy et al., 2023; Wiseman, 2023), the underrepresentation of females in prospective trauma research

makes it hard to yield optimal conditions for the analysis of sex differences (Rechlin, Splinter, Hodges, Albert, & Galea, 2022). (3) Third, even when males and females are included in studies, sex is infrequently used as a discovery variable to examine potentially different mechanisms in women and men (Haering et al., 2024b; Rechlin et al., 2022). (4) Even if researchers are willing to conduct discovery analyses, they are faced with a lack of best practice examples on how to examine sex differences in risk factors of mental disorders. Other than in pre-clinical studies, studies on PTSD etiology usually have a limited sample size, experimental manipulation and control is not possible, and different statistical approaches come with variable advantages and disadvantages. This situation has, amongst others, led to a substantial proportion of reported sex differences not supported by sufficient statistical evidence (Garcia-Sifuentes & Maney, 2021). (5) Given ongoing controversies on publication bias (Ferguson & Heene, 2012) and hesitancy to publish null results, it is unclear if individual studies that published (statistically supported) sex differences in PTSD risk factors represent replicable insights in underlying mechanisms, or whether they are in fact just statistical artifacts. Given these shortcomings, it is still largely unclear which risk factors do or do not have sex-dependent effects in women and men.

We aimed to systematically explore sex differences in PTSD risk factors in a sample of 2924 participants (62% women) enrolled in the AURORA (Advancing Understanding of Recovery after trauma) study, a prospective multisite longitudinal study of the onset and course of adverse posttraumatic neuropsychiatric sequelae. We pre-registered a sex-sensitive framework to systematically explore sex differences in PTSD risk factors with the AURORA consortium (Haering, Stevens, & Powers, 2022). The focus of the current study was to determine if a sex-dependent vulnerability to PTSD risk factors might contribute to women's higher PTSD severity 3-months post-acute trauma, i.e. to examine whether sex moderates the association between a risk factor and PTSD in a way that the strength, significance and/or direction of the association differs between women and men. We selected our predictors of interest based on a literature review of sex differences in PTSD predictors (Christiansen, 2016). Predictors that are assumed to be associated with PTSD differently for men and women, and were assessed in the AURORA study, were included in this analysis. Specifically, preexisting anxiety symptoms, prior trauma exposure, and peritraumatic distress as well as lower socioeconomic status, being member of a marginalized group, being unmarried or being unemployed have been summarized as risk factors more strongly associated with PTSD in men. On the other hand, preexisting depression symptoms, anxiety sensitivity, neuroticism, peritraumatic life threat and dissociation, as well as lack of social support and acute stress disorder have been summarized as risk factors more strongly associated with PTSD in women. Finally, mixed findings have been reported regarding the interaction of sex and age (Christiansen, 2016). In addition to these factors, we further included lifetime sexual assault exposure into our investigation of sex-dependent vulnerabilities. Although sex differences in sexual assault exposure are well-established, the impact of lifetime sexual assault exposure as a risk factor for posttraumatic dysfunction following a *new* trauma exposure has been less explored. Yet, recent evidence has highlighted the role of prior sexual assault exposure on subsequent trauma exposure (Rowland et al., 2023). Thus, we determined, whether the vulnerability to the aforementioned 16 pre-, peri-, and post-traumatic PTSD predictors differed between acutely traumatized women and men.

Methods

Participants and procedure

Data from the $n = 2924$ AURORA participants ($n = 1124$ men and $n = 1818$ women) were collected from September 2017 through June 2021. Detailed information on participant characteristics is given in Table 1. An overview of risk factors by sex and by trauma type (mvc *v.* non-mvc trauma) is presented in eTable 1 and eTable 2 in the Supplement.

The AURORA study procedures are described in detail elsewhere (McLean et al., 2020). In brief, AURORA participants were adults who had experienced a traumatic event within the past 72 h and were evaluated in one of 29 emergency departments (ED) across the United States. Participants were 18–75 years old, able to speak and read English, able to comprehend the enrollment protocol, and possessed a smartphone and e-mail address. Participants were excluded from data collection if they were or became pregnant or incarcerated. In addition, we excluded one participant with missing information on sex assigned at birth. Participants completed assessments in the ED (baseline), and at scheduled follow-ups, during which information on psychological symptoms, physical health, and functioning was assessed. Data for the analyses in this report were collected via self-report at baseline, 2 weeks, 8 weeks, and 3 months post-trauma. All participants provided written informed consent and were compensated for their study participation at each follow-up. The project was approved by each participating institutional review board. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Measures

We assessed 16 PTSD risk factors spanning pre-, peri-, and acute posttraumatic predictors. Pre-traumatic predictors included age, race-ethnicity, marital status, education, income, employment status, pre-trauma depression symptoms, pre-trauma anxiety symptoms, neuroticism and trauma load and lifetime exposure to sexual assault. Peri-traumatic risk factors included peritraumatic distress and perceived life threat; and acute post-traumatic predictors included social support, acute stress disorder, and acute dissociative symptoms. Sex assigned at birth was used as stratification variable. Detailed information on all measures is presented in Supplement 1.

Outcome

The outcome evaluated was self-reported PTSD severity at the 3-month follow-up, as assessed by the PTSD Symptom Checklist for DSM-5 (PCL-5). The PCL-5 is a 20 item self-report questionnaire that assesses the presence and severity of various posttraumatic stress symptoms (Weathers et al., 2013). Participants rated the severity of each symptom on a scale of 0 (*not at all*) to 4 (*extremely*), and items were summed to create a total severity score.

Statistical analysis

All analyses were conducted in R version 4.2.1 (R Core Team, 2022). The code for all analyses can be found in the OSF repository: <https://osf.io/tkncz/>. Missing values for constructs that were assessed longitudinally in the AURORA study (depressive

symptoms, anxiety symptoms, acute dissociative symptoms, and social support) were imputed using multiple imputation with predictive mean matching via the *aregImpute* function of the Hmisc package (Harrell, 2022), including the respective longitudinal assessments of each construct as auxiliary variables. In line with current recommendations for imputing data when moderation analyses are planned, missing values were imputed separately for males and females (Heymans & Eekhout, 2019). Student's *t* tests and χ^2 tests were performed to analyze sex differences in continuous and categorical variables, respectively.

To examine a sex-dependent vulnerability to the selected risk factors, we first calculated sex-disaggregated associations between each predictor and 3-month PTSD severity. As suggested by Christiansen, Olff, and Elklit (2014) the equality of coefficients was tested using Fisher's *z* tests and Zou's confidence intervals, applying the package *cocor* (Diedenhofen & Musch, 2015). Adapted from Jun et al. (2021) we then performed multivariable regression models controlling for participant demographics, baseline mental health, and life-time sexual assault exposure, and conducted subgroup analyses by including an interaction term between sex and the subgroup variable to the multivariable model. This procedure was done for each subgroup variable to identify significant effect differences between women and men. Finally, to assess the robustness of results across trauma types, we performed sensitivity analyses with the motor vehicle collision subgroup only ($n = 2194$, 74.6% of the full sample). Categorical variables were dummy coded, continuous variables were standardized for model estimations. Statistical significance was evaluated using 0.05-level two-sided tests. Most of the risk factors were positively associated with each other (see eTable 3). In spite of this inter-correlation, examination of the variance inflation factors (VIF) provided no indication of multicollinearity of the 16 predictors (all VIF < 3).

Results

Women and men differed significantly in PTSD severity at three months post trauma, with women scoring higher on the PCL-5 than men (M (s.d.)_f = 26.7 (18.9); M (s.d.)_m = 22.3 (19.3); $p < 0.001$). PTSD severity also differed by sex in the subgroup of participants with motor vehicle collisions (MVC; M (s.d.)_{f_mvc} = 26.6 (18.8); M (s.d.)_{m_mvc} = 22.1 (19.4); $p < 0.001$), which accounted for 74.6% of index trauma types in this sample. Sexual assault as index trauma was reported by less than 1% of all participants. As shown in Fig. 1, all 16 risk factors revealed statistically significant univariable associations with 3-month PTSD severity in men. In women, these associations were present for all predictors except for age and minority status. Statistical comparison of the male and female correlations demonstrated significant sex-dependent differences in the association of PTSD severity and five risk factors: acute dissociation (difference *d*, [95% CI] = -0.09 [-0.14 to -0.03], $p = 0.002$), peritraumatic distress ($d = -0.08$ [-0.15 to -0.01], $p = 0.018$), pre-traumatic anxiety symptoms ($d = -0.07$ [-0.13 to -0.01], $p = 0.027$), the participant-reported chance of dying during the index event ($d = -0.07$ [-0.14 to 0.00], $p = 0.044$), and acute stress disorder ($d = -0.05$ [-0.09 to -0.00], $p = 0.039$). As depicted in Fig. 1, the univariable correlations for all these six risk factors with PTSD severity were stronger in men than in women.

In a multi-variable regression model adjusting for participant demographics, baseline mental health, and lifetime sexual assault exposure, female sex remained an independent predictor of PTSD

Table 1. Demographic and trauma characteristics

	Men (N = 1124)	Women (N = 1818)	p value	Overall (N = 2942)
Age mean (s.d.)	36.1 (13.1)	35.8 (13.4)	0.586	35.9 (13.3)
Race/Ethnicity ^a			0.213	
Hispanic	144 (12.8%)	197 (10.8%)		341 (11.6%)
Non-Hispanic Black	533 (47.4%)	925 (50.9%)		1458 (49.6%)
Non-Hispanic White	397 (35.3%)	623 (34.3%)		1020 (34.7%)
Race/Ethnicity not listed	45 (4.0%)	66 (3.6%)		111 (3.8%)
Marriage status			0.106	
Currently married	242 (21.5%)	365 (20.1%)		607 (20.6%)
Previously married	173 (15.4%)	334 (18.4%)		507 (17.2%)
Never married	701 (62.4%)	1110 (61.1%)		1811 (61.6%)
Highest degree ^b			<0.001	
Less than high school	153 (13.6%)	186 (10.2%)		339 (11.5%)
High school	764 (68.0%)	1207 (66.4%)		1971 (67.0%)
College	204 (18.1%)	419 (23.0%)		623 (21.2%)
Currently unemployed ^c	180 (16.0%)	293 (16.1%)	0.676	473 (16.1%)
Family income/year ^d			0.144	
Less than 19 k	304 (27.0%)	546 (30.0%)		850 (28.9%)
Between 19 k and 35 k	283 (25.2%)	511 (28.1%)		794 (27.0%)
More than 35 k	371 (33.0%)	566 (31.1%)		937 (31.8%)
Index trauma			<0.001	
mvc	756 (67.3%)	1438 (79.1%)		2194 (74.6%)
physical assault	143 (12.7%)	128 (7.0%)		271 (9.2%)
fall, <10 feet	52 (4.6%)	109 (6.0%)		161 (5.5%)
animal-related	25 (2.2%)	38 (2.1%)		63 (2.1%)
non-mvc collision	32 (2.8%)	21 (1.2%)		53 (1.8%)
fall, ≥10 feet	34 (3.0%)	17 (0.9%)		51 (1.7%)
sexual assault	0 (0%)	17 (0.9%)		17 (0.6%)
burns	6 (0.5%)	8 (0.4%)		14 (0.5%)
disaster ^f	7 (0.6%)	5 (0.3%)		12 (0.4%)
poisoning	1 (0.1%)	1 (0.1%)		2 (0.1%)
other	68 (6.0%)	36 (2.0%)		104 (3.5%)
Lifetime sexual assault exposure ^e	88 (7.8%)	547 (30.1%)	<0.001	635 (21.6%)

Note: Data available for ^a99.6%, ^b99.7%, ^c88.2%, ^d87.7%, ^e83.3% of the sample, respectively; ^fEvent exposing participant and at least several other individuals to traumatic stress, not covered by other categories (e.g. plane crash, natural disaster).

severity at 3-months (β [s.e.] = 0.13 [0.04], $p < 0.001$, see eTable 4 in the Supplement). Using this model as baseline model, we next performed subgroup analyses to identify significant interactions between sex and each of our predictors of interest (Fig. 2): Analyses identified a statistically significant interaction effect for pre-traumatic anxiety symptoms ($\beta = -0.11$ [0.04], $p = 0.005$) and acute dissociative symptoms ($\beta = -0.10$ [0.04], $p = 0.003$). Figure 3 depicts the sex-by-risk factor interaction effects under the specified model: the graphs show that women and men diverge at the lower end of the risk factor spectrum, with women showing more PTSD symptoms even at lower levels of anxiety and dissociation. Due to men's higher vulnerability to

pre-traumatic anxiety and acute dissociative symptoms, PTSD levels of women and men converge at the upper end of the risk factor spectrum. For the remaining predictors, no significant sex differences in the association with PTSD were detected. Our subgroup analyses identified main effects (but no interaction effects) for acute stress disorder ($\beta = 0.56$ [0.03], $p < 0.001$), anxiety sensitivity ($\beta = 0.44$ [0.03], $p < 0.001$), neuroticism ($\beta = 0.38$, [0.03], $p < 0.001$), lifetime sexual assault ($\beta = 0.29$ [0.10], $p = 0.005$), pre-traumatic depressive symptoms ($\beta = 0.26$ [0.04], $p < 0.001$), peritraumatic distress ($\beta = 0.24$ [0.03], $p < 0.001$), chance of dying ($\beta = 0.20$ [0.04], $p < 0.001$), minority status ($\beta = 0.17$ [0.07], $p = 0.008$), family income < 19 k ($\beta = 0.14$ [0.07], $p = 0.040$), social

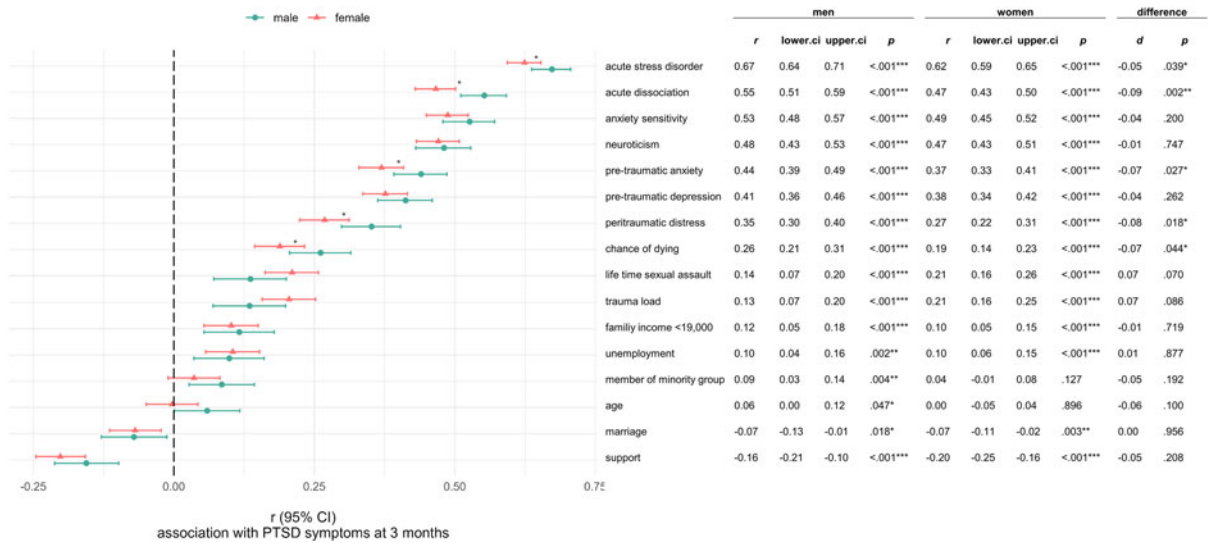


Figure 1. Sex-disaggregated associations with 3-month PTSD severity. The forest plot depicts the univariable associations of each predictor with PTSD severity at 3-months post-trauma disaggregated by sex. The correlations are depicted in blue for men and in red for women. The equality of coefficients was tested using Fisher’s z tests.

support ($\beta = -0.13$, [0.03], $p < 0.001$), age ($\beta = 0.09$ [0.04], $p = 0.006$), and trauma load ($\beta = 0.07$ [0.04], $p = 0.014$).

Sensitivity analyses for the motor vehicle collision (MVC) subgroup showed that sex differences in univariable comparisons remained robust for twelve of the 16 risk factors assessed. Compared to the main analyses, sex differences were no longer found for pre-traumatic anxiety symptoms and participant-reported chance of dying during the index event (see eTable 5). However, among the MVC subgroup significant sex differences

were observed for the associations of 3-month PTSD severity with trauma load ($d = 0.11$ [0.01–0.20], $p = 0.027$) and lifetime sexual assault exposure ($d = 0.14$ [0.04–0.24], $p = 0.005$). In contrast to previous results among the full sample, analyses in the MVC subgroup thus revealed two risk factors for which associations with 3-month PTSD severity were stronger in female than male MVC-exposed individuals, and both reflected exposure to prior stressors, whereas the major risk factors favoring men reflected internal trait-like factors.

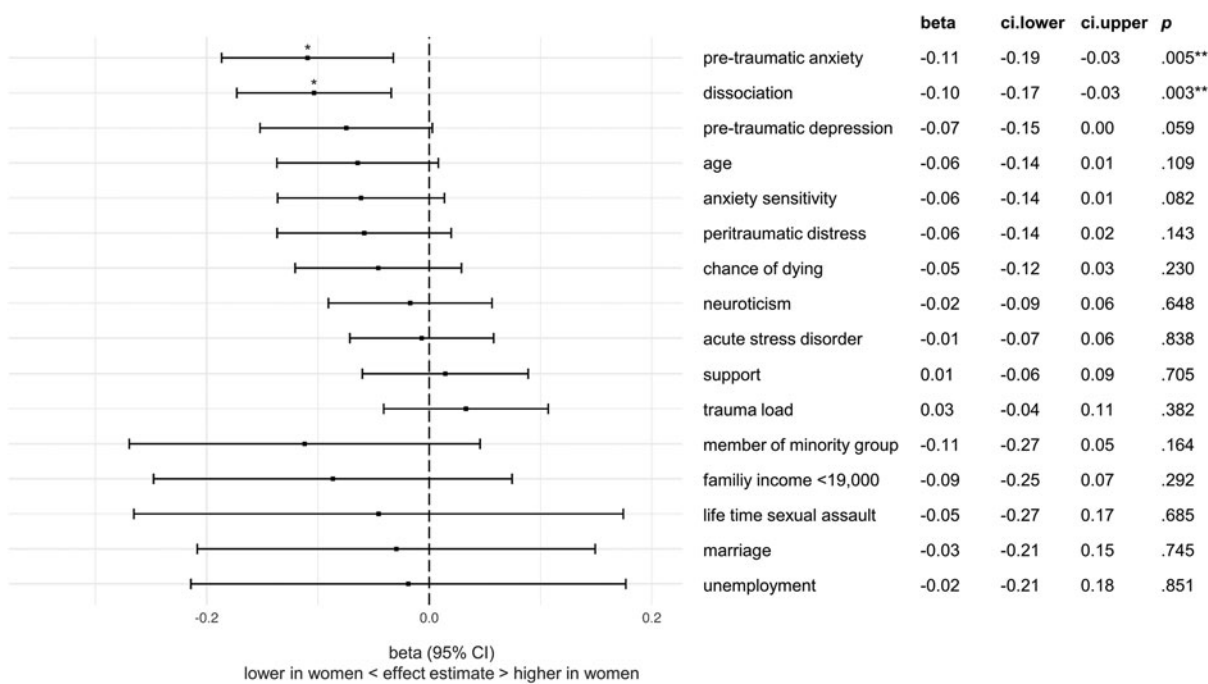


Figure 2. Subgroup analysis for female sex as a predictor of PTSD severity at 3 months. The forest plot depicts the parameter estimate and 95% confidence interval associated with female sex (v. male sex as the reference group) within the subgroup specified in a multivariable regression model, including an interaction term between the subgroup variable and sex, adjusting for demographics, baseline mental health and lifetime sexual assault. Continuous variables were standardized, categorical variables were dummy coded.

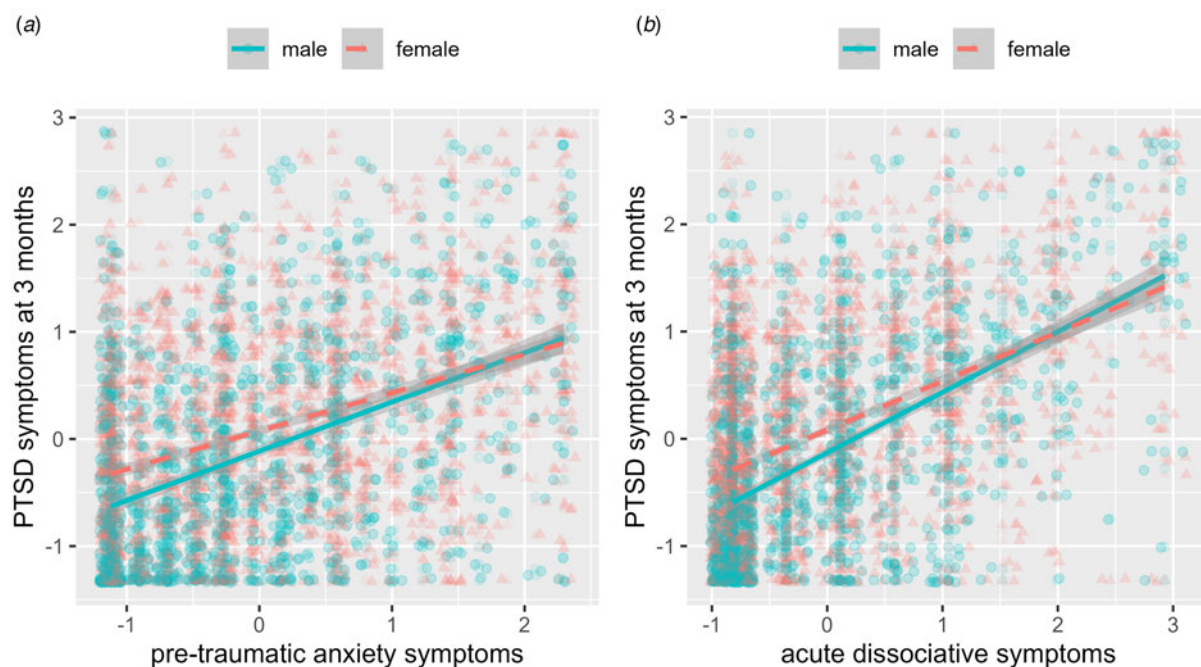


Figure 3. Interaction effects of sex and (a) pre-traumatic anxiety and (b) dissociation at week two post-trauma. The scatter plots depict the interaction effect of sex and (a) pre-traumatic anxiety symptoms as well as (b) dissociative symptoms at two weeks post-trauma, controlling for demographics, baseline mental health, and lifetime sexual assault. All variables were standardized to an overall sample mean of 0 and a standard deviation of 1.

In MVC subgroup analyses of the multivariable models, sex remained a robust moderator of acute dissociative symptoms ($\beta = -0.11$ [0.04], $p = 0.007$). Moreover, an interaction of sex with anxiety sensitivity was observed ($\beta = -0.09$ [0.05], $p = 0.044$), albeit with the 95% confidence interval nearly including zero. Detailed results of the multivariable MVC subgroup analyses are presented in eTable 6.

Discussion

The current study systematically examined sex differences in the vulnerability to PTSD risk factors to better understand which processes drive the prominent sex disparities in PTSD outcomes. In univariable analyses we found sex-dependent associations with 3-month PTSD severity in five of 16 risk factors, which previously had been hypothesized to show different associations with PTSD for women and men: pre-traumatic anxiety symptoms, peritraumatic distress, perceived chance of dying during the trauma, acute dissociative symptoms, and acute stress disorder symptoms showed stronger associations with PTSD severity at 3 months in men than in women. Two of these predictors, pre-traumatic anxiety and acute dissociative symptoms, also showed sex-dependent effects in multivariable models with interaction terms, indicating men might be more vulnerable to these risk factors than women, even when controlling for demographics and baseline mental health. Our main analyses did not indicate any risk factor to which women were more vulnerable, which was surprising given the selection of predictors based on prior research (Christiansen, 2016). Subgroup analyses of an MVC-only sample suggested trauma type-conditional sex vulnerabilities for trauma load and lifetime sexual assault exposure. Finally, a number of known PTSD risk factors showed similar predictive value for females and males, both in the main and subgroup analysis, including age, income below poverty line, racial/ethnic minority

status, social support, trauma severity, and a variety of symptoms and personality factors.

Our study suggests how underlying processes may contribute differentially toward PTSD severity in men and in women. The results of our main analyses highlight two risk factors that consistently showed a stronger impact on men compared to women. First, pre-existing anxiety symptoms were more strongly related to PTSD severity in men than in women. This finding is in line with previous research, suggesting traumatized men are more vulnerable to pre-existing anxiety than women (Bromet, Sonnega, & Kessler, 1998; Christiansen & Elklit, 2008, 2012). Second, acute dissociation also showed stronger associations with PTSD severity in men than in women. Given previous evidence on sex-dependent effects of dissociation (Bryant & Harvey, 2003; Christiansen & Elklit, 2008; Fullerton et al., 2001), which suggested a stronger negative impact in women, this finding is unexpected. However, among prior studies, peritraumatic dissociative experiences rather than acute dissociative responses were examined (Fullerton et al., 2001), and reporting of sex differences was not always supported by sufficient statistical evidence (Bryant & Harvey, 2003; Christiansen & Elklit, 2008; Garcia-Sifuentes & Maney, 2021). Interpreting our results, it might be that men with high levels of dissociative experience are at greater risk for PTSD symptoms than women, as greater mental health stigma among men amplifies the negative impact of maladaptive cognitive beliefs. Previous evidence has shown a link between negative appraisals of initial PTSD symptoms (such as dissociative experiences) with later PTSD outcomes (Brown, Wood, Carter, & Kannis-Dyand, 2022; Kannis-Dyand, Carter, Lane, & Innes, 2019). Such negative appraisals include for instance interpretations of PTSD symptoms as meaning 'I am going crazy' (Steil & Ehlers, 2000). Given that men seem to hold greater stigmatizing beliefs about mental health symptoms (Bradbury, 2020; Chandra & Minkovitz, 2006), it might be that

seemingly ‘abnormal’ experiences like dissociative experiences are more strongly linked to PTSD severity in men than in women, as men might have greater negative interpretations about them, which in turn affects PTSD development and maintenance.

Of note, within our study the majority of risk factors showed tendencies toward stronger negative impacts in men, i.e. a male vulnerability. Despite women’s higher PTSD risk, these findings warrant the need for a closer examination of PTSD risk factors from a men-centered perspective. For men, our results suggest possible mechanisms that might be targeted when designing sex-sensitive preventive interventions, especially since men benefit less from trauma-focused treatment interventions for manifested PTSD. Exploring effective prevention options that integrate our full knowledge on sex-dependent mechanisms is needed.

Although our main analyses did not identify any risk factors to which women were more vulnerable than men, sensitivity analyses point toward trauma type-conditional effects: In sub-group analyses of the MVC sample, trauma load and lifetime sexual assault exposure entered in as sex-dependent risk factors, showing greater univariable associations with 3-month PTSD severity in women than in men. Interestingly, only MVC-specific analyses revealed risk factors to which women were more vulnerable to than men. Our subgroup analyses of the MVC sample thus suggest that for MVC-exposed individuals, men might be more vulnerable to internal factors, whereas women might be more vulnerable to external, exposure-based factors. One reason for the differences in the main *v.* subgroup analyses might be the fact that after an MVC, individuals are generally less likely to develop PTSD symptoms compared to other trauma types (e.g. interpersonal trauma; Kessler *et al.* (2017)). Thus, predisposing factors such as exposure-based predictors for women (i.e. lifetime sexual assault exposure, trauma load), might carry more weight in accidental traumas than in assault-based traumas, where individuals are at a higher risk for PTSD symptom development and variables such as perpetration characteristics may become more salient. Clearly, our findings once more are a testament to the intricate interplay of sex and trauma type which needs to be better understood in order to realize the full potential of targeted interventions.

Importantly, even though women in our main sample were less affected by the negative impacts of pre-existing anxiety or acute dissociation symptoms, they largely still experienced greater PTSD symptoms than men. Our results highlight the need to explore further aspects that contribute to women’s higher PTSD severity, including different constructs, pathways, and mechanisms. For instance, understanding how sex interacts with cognitive factors might provide modifiable targets for early interventions. Furthermore, greater knowledge about hormonal (Ney, Gogos, Ken Hsu, & Felmingham, 2019) or genetic (Yu *et al.*, 2018) factors can increase our knowledge of sex-based contributors to PTSD. Finally, independent of vulnerability differences, i.e. differences in the strength of an association between a risk factor and PTSD severity, differences in risk factor prevalence/severity among women and men can further contribute to sex differences in PTSD severity. Thus, greater exposure to certain risk factors (Christiansen & Hansen, 2015) might help to explain women’s higher PTSD severity in the present sample. A systematic overview of risk pathways between sex and PTSD as well as a complementary analysis is presented in Haering *et al.* (2024c). A clear distinction between various forms of sex-related effects will not only help to better understand sex differences in mental health

outcomes, it will also help to create a more rigorous and replicable mental health science.

Several limitations need to be taken into consideration when looking at our findings. Possible selection bias in who gets treated in the ED after trauma may impact generalizability of results. While EDs visits present a unique opportunity for providing traumatized individuals with secondary interventions, it is unclear, to what extent our findings may be transferable to other study contexts. It is furthermore not clear, whether results are generalizable across cultures, as data for this study was collected in the US only. Future research with international (Haering *et al.*, 2024a; Young & Chan, 2015) as well as intersectional (Bryant-Davis, 2019; Crenshaw, 2013; Seng, Lopez, Sperlich, Hamama, & Reed Meldrum, 2012) perspectives can help to further improve our understanding of health disparities in trauma-related health outcomes and beyond. Furthermore, the majority of participants included in this study were individuals who experienced an MVC. Future research should aim to specifically target large and diverse samples beyond MVC-exposed individuals to disentangle how sex and trauma characteristics interact in the case of physical and sexual assault as well as other trauma types. Another limitation includes the assessment of PTSD symptoms via self-report. Clinician-based interviews have been shown to increase diagnostic accuracy through better comprehension of symptoms or increased awareness (Kramer, Whiteman, Petri, Spitzer, & Weathers, 2023). Finally, this study is limited to the analysis of sex differences. To fully disentangle why women are more vulnerable to PTSD development, future studies should take gender-related aspects as well as the interplay of sex and gender into account. These limitations notwithstanding, to the best of our knowledge, this study was the first to examine how the effects of a comprehensive set of risk factors, that have previously been suggested to show sex-differential associations with PTSD development, differs between men and women. The strengths of our study include its prospective design, controlled timing of assessments following trauma, as well as size and diversity of the study sample. Moreover, all statistical code for the analyses is shared open-access, and we encourage researchers to perform replication analyses to examine the generalizability of our findings in further study cohorts.

In summary, our study highlights the need for more sex- and gender-sensitive examinations of PTSD risk factors. Our results point toward the need to consider other pathways and mechanisms to explain women’s higher PTSD risk. Our study also indicates mechanisms to which men might be particularly vulnerable. Continuing our efforts to disentangle sex differences in PTSD risk factors can help to more accurately understand how underlying mechanisms contribute toward an individual’s PTSD risk and may lead to the development of refined targeted preventive interventions.

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Competing interests

- Dr Neylan has received research support from NIH, VA, and Rainwater Charitable Foundation, and consulting income from Jazz Pharmaceuticals.
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- Dr Jones has no competing interests related to this work, though he has been an investigator on studies funded by AstraZeneca, Vapotherm, Abbott, and Ophirex.
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- Dr McLean served as a consultant for Walter Reed Army Institute for Research and for Arbor Medical Innovations.
- In the past 3 years, Dr Kessler was a consultant for Cambridge Health Alliance, Canandaigua VA Medical Center, Holmusk, Partners Healthcare, Inc., RallyPoint Networks, Inc., and Sage Therapeutics. He has stock options in Cerebral Inc., Mirah, PYM, and Roga Sciences.
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References

- Bale, T. L., & Epperson, C. N. (2017). Sex as a biological variable: Who, what, when, why, and how. *Neuropsychopharmacology*, *42*(2), 386–396. <https://doi.org/10.1038/npp.2016.215>
- Beery, A. K., & Zucker, I. (2011). Sex bias in neuroscience and biomedical research. *Neuroscience & Biobehavioral Reviews*, *35*(3), 565–572. <https://doi.org/10.1016/j.neubiorev.2010.07.002>
- Ben-Ezra, M., Karatzias, T., Hyland, P., Brewin, C. R., Cloitre, M., Bisson, J. I., ... Shevlin, M. (2018). Posttraumatic stress disorder (PTSD) and complex PTSD (CPTSD) as per ICD-11 proposals: A population study in Israel. *Depression and Anxiety*, *35*(3), 264–274. <https://doi.org/10.1002/da.22723>
- Bradbury, A. (2020). Mental health stigma: The impact of age and gender on attitudes. *Community Mental Health Journal*, *56*(5), 933–938. <https://doi.org/10.1007/s10597-020-00559-x>
- Bromet, E., Sonnega, A., & Kessler, R. C. (1998). Risk factors for DSM-III-R posttraumatic stress disorder: Findings from the national comorbidity survey. *American Journal of Epidemiology*, *147*(4), 353–361. <https://doi.org/10.1093/oxfordjournals.aje.a009457>
- Brown, R. L., Wood, A., Carter, J. D., & Kannis-Dymand, L. (2022). The meta-cognitive model of post-traumatic stress disorder and metacognitive therapy for post-traumatic stress disorder: A systematic review. *Clinical Psychology & Psychotherapy*, *29*(1), 131–146. <https://doi.org/10.1002/cpp.2633>
- Bryant, R. A., & Harvey, A. G. (2003). Gender differences in the relationship between acute stress disorder and posttraumatic stress disorder following motor vehicle accidents. *Australian & New Zealand Journal of Psychiatry*, *37*(2), 226–229. <https://doi.org/10.1046/j.1440-1614.2003.01130.x>
- Bryant-Davis, T. (2019). The cultural context of trauma recovery: Considering the posttraumatic stress disorder practice guideline and intersectionality. *Psychotherapy*, *56*(3), 400–408. <https://doi.org/10.1037/pst0000241>
- Carmassi, C., Akiskal, H. S., Bessonov, D., Massimetti, G., Calderani, E., Stratta, P., ... Dell'Osso, L. (2014). Gender differences in DSM-5 versus DSM-IV-TR PTSD prevalence and criteria comparison among 512 survivors to the L'Aquila earthquake. *Journal of Affective Disorders*, *160*, 55–61. <https://doi.org/10.1016/j.jad.2014.02.028>
- Carragher, N., Sunderland, M., Batterham, P. J., Calear, A. L., Elhai, J. D., Chapman, C., & Mills, K. (2016). Discriminant validity and gender differences in DSM-5 posttraumatic stress disorder symptoms. *Journal of Affective Disorders*, *190*, 56–67. <https://doi.org/10.1016/j.jad.2015.09.071>
- Chandra, A., & Minkovitz, C. (2006). Stigma starts early: Gender differences in teen willingness to use mental health services. *Journal of Adolescent Health*, *38*(6), 754.e1–754.e8. <https://doi.org/10.1016/j.jadohealth.2005.08.011>
- Christiansen, D. M. (2016). Sex differences in PTSD: Mediation and moderation effects. In C. R. Martin, V. R. Preedy, & V. B. Patel (Eds.), *Comprehensive guide to post-traumatic stress disorders* (pp. 1465–1481). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-08359-9_4
- Christiansen, D. M., & Berke, E. T. (2020). Gender- and sex-based contributors to sex differences in PTSD. *Current Psychiatry Reports*, *22*, 1–9. <https://doi.org/10.1007/s11920-020-1140-y>
- Christiansen, D. M., & Elklit, A. (2008). Risk factors predict post-traumatic stress disorder differently in men and women. *Annals of General Psychiatry*, *7*, 24. <https://doi.org/10.1186/1744-859X-7-24>
- Christiansen, D. M., & Elklit, A. (2012). Sex differences in PTSD. In E. Ovuga (Ed.), *Post traumatic stress disorders in a global context* (pp. 113–142). Rijeka, Croatia: InTech. <https://doi.org/10.5772/28363>
- Christiansen, D. M., & Hansen, M. (2015). Accounting for sex differences in PTSD: A multi-variable mediation model. *European Journal of Psychotraumatology*, *6*(1), 26068. <https://doi.org/10.3402/ejpt.v6.26068>
- Christiansen, D. M., McCarthy, M. M., & Seeman, M. V. (2022). Where sex meets gender: How sex and gender come together to cause sex differences in mental illness. *Frontiers in Psychiatry*, *13*, 856436. <https://doi.org/10.3389/fpsy.2022.856436>
- Christiansen, D. M., Olff, M., & Elklit, A. (2014). Parents bereaved by infant death: Sex differences and moderation in PTSD, attachment, coping and social support. *General Hospital Psychiatry*, *36*(6), 655–661. <https://doi.org/10.1016/j.genhosppsych.2014.07.012>
- Crenshaw, K. W. (2013). Mapping the margins: Intersectionality, identity politics, and violence against women of color. In M. A. Fineman (Ed.), *The public nature of private violence* (pp. 93–118). New York: Routledge.
- Dark, H. E., Harnett, N. G., Hurst, D. R., Wheelock, M. D., Wood, K. H., Goodman, A. M., ... Knight, D. C. (2022). Sex-related differences in violence exposure, neural reactivity to threat, and mental health. *Neuropsychopharmacology*, *47*(13), 2221–2229. <https://doi.org/10.1038/s41386-022-01430-1>
- Diedenhofen, B., & Musch, J. (2015). Cocor: A comprehensive solution for the statistical comparison of correlations. *PLoS ONE*, *10*(4), e0121945. <https://doi.org/10.1371/journal.pone.0121945>
- Eraly, S. A., Nievergelt, C. M., Maihofer, A. X., Barkauskas, D. A., Biswas, N., Agorastos, A., ... Baker, D. G. (2014). Assessment of plasma C-reactive protein as a biomarker of posttraumatic stress disorder risk. *JAMA Psychiatry*, *71*(4), 423. <https://doi.org/10.1001/jamapsychiatry.2013.4374>
- Ferguson, C. J., & Heene, M. (2012). A vast graveyard of undead theories: Publication bias and psychological science's aversion to the null.

- Perspectives on Psychological Science*, 7(6), 555–561. <https://doi.org/10.1177/1745691612459059>
- Frans, O., Rimmo, P.-A., Aberg, L., & Fredrikson, M. (2005). Trauma exposure and post-traumatic stress disorder in the general population. *Acta Psychiatrica Scandinavica*, 111(4), 291–290. <https://doi.org/10.1111/j.1600-0447.2004.00463.x>
- Fullerton, C. S., Ursano, R. J., Epstein, R. S., Crowley, B., Vance, K., Kao, T.-C., ... Baum, A. (2001). Gender differences in posttraumatic stress disorder after motor vehicle accidents. *American Journal of Psychiatry*, 158(9), 1486–1491. <https://doi.org/10.1176/appi.ajp.158.9.1486>
- Garcia-Sifuentes, Y., & Maney, D. L. (2021). Reporting and misreporting of sex differences in the biological sciences. *eLife*, 10, e70817. <https://doi.org/10.7554/eLife.70817>
- Goldstein, R. B., Smith, S. M., Chou, S. P., Saha, T. D., Jung, J., Zhang, H., ... Grant, B. F. (2016). The epidemiology of DSM-5 posttraumatic stress disorder in the United States: Results from the national epidemiologic survey on alcohol and related conditions-III. *Social Psychiatry and Psychiatric Epidemiology*, 51(8), 1137–1148. <https://doi.org/10.1007/s00127-016-1208-5>
- Haering, S., Kooistra, M. J., Bourey, C., Chimed-Ochir, U., Doubková, N., Hoerber, C. M., ... De Haan, A. (2024a). Exploring transdiagnostic stress and trauma-related symptoms across the world: A latent class analysis. *European Journal of Psychotraumatology*, 15(1), 2318190. <https://doi.org/10.1080/20008066.2024.2318190>
- Haering, S., Schulze, L., Geiling, A., Meyer, C., Klusmann, H., Schumacher, S., ... Engel, S. (2024b). Higher risk—less data: A systematic review and meta-analysis on the role of sex and gender in trauma research. *Journal of Psychopathology and Clinical Science*, 133(3), 257–272. <https://doi.org/10.1037/abn0000899>
- Haering, S., Seligowski, A. V., Linnstaedt, S. D., Michopoulos, V., House, S. L., Beaudoin, F., ... Stevens, J. (2024c). Disentangling sex differences in PTSD risk factors. *Nature Mental Health*, 2, 605–615. <https://doi.org/10.1038/s44220-024-00236-y>
- Haering, S., Stevens, J. S., & Powers, A. (2022). Gender-based analysis of PTSD Risk Factors in the AURORA study. *Analysis Proposal Submitted to AURORA Executive Committee, University North Carolina on 2022-09-02*.
- Harrell, F. (2022). *Hmisc: Harrell Miscellaneous. R package version 4.7-0*. <https://CRAN.R-project.org/package=Hmisc>
- Heymans, M., & Eekhout, I. (2019). *Applied missing data analysis with SPSS and R studio*. Amsterdam: R bookdown. <https://bookdown.org/mwheymans/bookmi/>
- Jun, T., Nirenberg, S., Weinberger, T., Sharma, N., Pujadas, E., Cordon-Cardo, C., ... Huang, K. (2021). Analysis of sex-specific risk factors and clinical outcomes in COVID-19. *Communications Medicine*, 1(1), 3. <https://doi.org/10.1038/s43856-021-00006-2>
- Kannis-Dyand, L., Carter, J. D., Lane, B. R., & Innes, P. (2019). The relationship of peritraumatic distress and dissociation with beliefs about memory following natural disasters. *Australian Psychologist*, 54(4), 311–321. <https://doi.org/10.1111/ap.12377>
- Kessler, R. C., Aguilar-Gaxiola, S., Alonso, J., Benjet, C., Bromet, E. J., Cardoso, G., ... Koenen, K. C. (2017). Trauma and PTSD in the WHO world mental health surveys. *European Journal of Psychotraumatology*, 8(sup5), 1353383. <https://doi.org/10.1080/20008198.2017.1353383>
- Kessler, R. C., Sonnega, A., Bromet, E. J., Hughes, M., & Nelson, C. (1995). Posttraumatic stress disorder in the national comorbidity survey. *Archives of General Psychiatry*, 52(12), 1048. <https://doi.org/10.1001/archpsyc.1995.03950240066012>
- Kramer, L. B., Whiteman, S. E., Petri, J. M., Spitzer, E. G., & Weathers, F. W. (2023). Self-rated versus clinician-rated assessment of posttraumatic stress disorder: An evaluation of discrepancies between the PTSD checklist for DSM-5 and the clinician-administered PTSD scale for DSM-5. *Assessment*, 30(5), 1590–1605. <https://doi.org/10.1177/10731911221113571>
- Krieger, N. (2003). Genders, sexes, and health: What are the connections – and why does it matter? *International Journal of Epidemiology*, 32(4), 652–657. <https://doi.org/10.1093/ije/dyg156>
- Lalonde, C. S., Mekawi, Y., Ethun, K. F., Beurel, E., Gould, F., Dhabhar, F. S., ... Michopoulos, V. (2021). Sex differences in peritraumatic inflammatory cytokines and steroid hormones contribute to prospective risk for nonremitting posttraumatic stress disorder. *Chronic Stress*, 5, 247054702110322. <https://doi.org/10.1177/24705470211032208>
- Levy, D. R., Hunter, N., Lin, S., Robinson, E. M., Gillis, W., Conlin, E. B., ... Datta, S. R. (2023). Mouse spontaneous behavior reflects individual variation rather than estrous state. *Current Biology*, 33(7), 1358–1364.e4. <https://doi.org/10.1016/j.cub.2023.02.035>
- McCall-Hosenfeld, J. S., Mukherjee, S., & Lehman, E. B. (2014). The prevalence and correlates of lifetime psychiatric disorders and trauma exposures in urban and rural settings: Results from the national comorbidity survey replication (NCS-R). *PLoS ONE*, 9(11), e112416. <https://doi.org/10.1371/journal.pone.0112416>
- McLean, S. A., Ressler, K., Koenen, K. C., Neylan, T., Germine, L., Jovanovic, T., ... Kessler, R. (2020). The AURORA study: A longitudinal, multimodal library of brain biology and function after traumatic stress exposure. *Molecular Psychiatry*, 25(2), 283–296. <https://doi.org/10.1038/s41380-019-0581-3>
- Ney, L. J., Gogos, A., Ken Hsu, C.-M., & Felmingham, K. L. (2019). An alternative theory for hormone effects on sex differences in PTSD: The role of heightened sex hormones during trauma. *Psychoneuroendocrinology*, 109, 104416. <https://doi.org/10.1016/j.psyneuen.2019.104416>
- Olf, M. (2017). Sex and gender differences in post-traumatic stress disorder: An update. *European Journal of Psychotraumatology*, 8(sup4), 1351204. <https://doi.org/10.1080/20008198.2017.1351204>
- Olf, M., & Langeland, W. (2022). Why men and women may respond differently to psychological trauma. *Psychiatric Times*, 39(4), 11–13.
- Olf, M., Langeland, W., Draijer, N., & Gersons, B. P. R. (2007). Gender differences in posttraumatic stress disorder. *Psychological Bulletin*, 133(2), 183–204. <https://doi.org/10.1037/0033-2909.133.2.183>
- Otten, D., Tibubos, A. N., Schomerus, G., Brähler, E., Binder, H., Kruse, J., ... Beutel, M. E. (2021). Similarities and differences of mental health in women and men: A systematic review of findings in three large German cohorts. *Frontiers in Public Health*, 9, 553071. <https://doi.org/10.3389/fpubh.2021.553071>
- Perkonig, A., Kessler, R. C., Storz, S., & Wittchen, H. U. (2000). Traumatic events and post-traumatic stress disorder in the community: Prevalence, risk factors and comorbidity. *Acta Psychiatrica Scandinavica*, 101(1), 46–59.
- Ramkikie, T. S., & Ressler, K. J. (2018). Mechanisms of sex differences in fear and posttraumatic stress disorder. *Biological Psychiatry*, 83(10), 876–885. <https://doi.org/10.1016/j.biopsych.2017.11.016>
- R Core Team. (2022). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. <https://www.R-project.org>
- Rechlin, R. K., Splinter, T. F. L., Hodges, T. E., Albert, A. Y., & Galea, L. A. M. (2022). An analysis of neuroscience and psychiatry papers published from 2009 and 2019 outlines opportunities for increasing discovery of sex differences. *Nature Communications*, 13(1), 2137. <https://doi.org/10.1038/s41467-022-29903-3>
- Rowland, G. E., Roekner, A., Ely, T. D., Lebois, L. A. M., van Rooij, S. J. H., Bruce, S. E., ... Harnett, N. G. (2023). Prior sexual trauma exposure impacts posttraumatic dysfunction and neural circuitry following a recent traumatic event in the AURORA study. *Biological Psychiatry Global Open Science*, 3(4), 705–715. <https://doi.org/10.1016/j.bpsgos.2023.02.004>
- Seedat, S., Scott, K. M., Angermeyer, M. C., Berglund, P., Bromet, E. J., Brugha, T. S., ... Kessler, R. C. (2009). Cross-national associations between gender and mental disorders in the world health organization world mental health surveys. *Archives of General Psychiatry*, 66(7), 785. <https://doi.org/10.1001/archgenpsychiatry.2009.36>
- Seng, J. S., Lopez, W. D., Sperlich, M., Hamama, L., & Reed Meldrum, C. D. (2012). Marginalized identities, discrimination burden, and mental health: Empirical exploration of an interpersonal-level approach to modeling intersectionality. *Social Science & Medicine*, 75(12), 2437–2445. <https://doi.org/10.1016/j.socscimed.2012.09.023>
- Sopp, M. R., Michael, T., Lass-Hennemann, J., Haim-Nachum, S., & Lommen, M. J. J. (2021). Longitudinal associations between hair cortisol, PTSD symptoms, and sleep disturbances in a sample of firefighters with duty-related trauma exposure. *Psychoneuroendocrinology*, 134, 105449. <https://doi.org/10.1016/j.psyneuen.2021.105449>
- Sørensen, L. N., Olesen, K. H., Midtgaard, C. D., & Willert, M. V. (2022). Risk of post-traumatic stress disorder following major disasters and critical

- incidents in police officers – a systematic review. *Journal of Police and Criminal Psychology*, 37(4), 752–768. <https://doi.org/10.1007/s11896-022-09547-1>
- Steil, R., & Ehlers, A. (2000). Dysfunctional meaning of posttraumatic intrusions in chronic PTSD. *Behaviour Research and Therapy*, 38(6), 537–558. [https://doi.org/10.1016/S0005-7967\(99\)00069-8](https://doi.org/10.1016/S0005-7967(99)00069-8)
- Tannenbaum, C., Ellis, R. P., Eyssel, F., Zou, J., & Schiebinger, L. (2019). Sex and gender analysis improves science and engineering. *Nature*, 575(7781), 137–146. <https://doi.org/10.1038/s41586-019-1657-6>
- Tolin, D. F., & Foa, E. B. (2006). Sex differences in trauma and posttraumatic stress disorder: A quantitative review of 25 years of research. *Psychological Bulletin*, 132(6), 959–992. <https://doi.org/10.1037/0033-2909.132.6.959>
- Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P., & Schnurr, P. P. (2013). *The PTSD checklist for DSM-5*. National Center for Posttraumatic Stress Disorder. <https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp>
- Wiseman, S. (2023). Female mice behave well. *Nature Neuroscience*, 26(4), 534–534. <https://doi.org/10.1038/s41593-023-01303-w>
- Young, M. Y., & Chan, K. J. (2015). The psychological experience of refugees: A gender and cultural analysis. In S. Safdar, & N. Kosakowska-Berezecka (Eds.), *Psychology of gender through the lens of culture* (pp. 17–36). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-14005-6_2
- Yu, S., Chen, C., Pan, Y., Kurz, M. C., Datner, E., Hendry, P. L., ... Linnstaedt, S. D. (2018). Genes known to escape X chromosome inactivation predict co-morbid chronic musculoskeletal pain and posttraumatic stress symptom development in women following trauma exposure. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 180(6), 415–427. <https://doi.org/10.1002/ajmg.b.32706>