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BASIC RESEARCH ARTICLE

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Prospective examination of pre-trauma anhedonia as a risk factor for post-traumatic stress symptoms

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ABSTRACT

Background: Anhedonia, the reduction of pleasure and reward-seeking behaviour, is a transdiagnostic symptom with well-described neural circuit mediators. Although typically observed during disease state, extant hypotheses suggest that anhedonia may also be an early risk factor for development of psychopathology. Understanding the contribution of anhedonia to the trauma-response trajectory may bolster inferences about biological mechanisms contributing to pre-trauma risk versus trauma-related symptom expression, knowledge of which could aid in targeted interventions.

Objective: Using a prospective, longitudinal design in a population at risk for trauma disorders, we tested the hypothesis that anhedonia may be a pre-trauma risk factor for post-traumatic stress disorder (PTSD) symptoms.

Methods: Adult male participants from the Marine Resilience Study (N = 2,593) were assessed across three time-points (pre-deployment, 3-month and 6-month post-deployment). An anhedonia factor was extracted from self-report instruments pre-trauma and tested for its relationship with development of PTSD re-experiencing symptoms after deployment.

Results: Higher pre-deployment anhedonia predicted increased PTSD intrusive re-experiencing symptoms at 3- and 6-months post-deployment when controlling for pre-trauma PTSD and depression symptoms. Depression symptoms were not significant predictors of subsequent PTSD intrusive re-experiencing symptoms. Anhedonia at 3 mo also robustly predicted maintenance of PTSD intrusive re-experiencing symptoms at the 6 mo time point.

Conclusions: Pre-deployment anhedonia may be a pre-trauma risk factor for PTSD, not simply a state-dependent effect of trauma exposure and PTSD symptom expression. Anhedonia may contribute to persistence and/or chronicity of re-experiencing symptoms after the emergence of PTSD symptoms.

Evaluación prospectiva de anhedonia pre-trauma como un factor de riesgo para síntomas de estrés postraumático

Antecedentes: La anhedonia, reducción del placer y del comportamiento de búsqueda de recompensa, es un síntoma transdiagnóstico con circuitos neurales mediadores bien descritos. Aunque es observada típicamente durante estados patológicos, hipótesis existentes sugieren que la anhedonia puede ser también un factor de riesgo temprano para el desarrollo de psicopatología. La comprensión de la contribución de la anhedonia a la trayectoria de la respuesta al trauma puede reforzar las inferencias sobre los mecanismos biológicos que contribuyen al riesgo pre-trauma versus la expresión sintomática relacionada al trauma, conocimiento que puede ayudar en intervenciones dirigidas.

Objetivo: Utilizando un diseño longitudinal prospectivo en una población de riesgo para trastornos traumáticos, probamos la hipótesis de que la anhedonia puede ser un factor de riesgo pre-trauma para síntomas de trastorno de estrés postraumático (TEPT).

Métodos: Participantes masculinos adultos del Estudio de Resiliencia de la Marina (N = 2,593) fueron evaluados a lo largo de 3 puntos temporales (antes del despliegue, a los 3 meses, y a los 6 meses post-despliegue). Se extrajo un factor para anhedonia a partir de instrumentos autoaplicados pre-trauma y fue evaluado por su relación con el desarrollo de síntomas de re-experimentación del TEPT después del despliegue.

Resultados: Una anhedonia más alta pre-despliegue predijo un aumento de síntomas de TEPT a los 3 y 6 meses post-despliegue, al controlar con síntomas de TEPT y de depresión pre-trauma. Los síntomas depresivos no fueron predictores significativos de síntomas de TEPT posteriores. La anhedonia a los 3 meses predijo también de forma robusta la mantención de síntomas de TEPT a los 6 meses.

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关键词
快感缺失; 奖赏; 创伤后应激障碍; 前瞻性; 纵向; 军队

HIGHLIGHTS

- Anhedonia in US Marines significantly increased following combat deployment.
- Anhedonia was associated with re-experiencing symptoms cross-sectionally.
- Anhedonia was associated with re-experiencing symptoms prospectively.
- Anhedonia was associated more strongly with re-experiencing compared to depression.

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Supplemental data for this article can be accessed here.

Conclusiones: La anhedonia pre-despliegue puede ser un factor de riesgo pre-trauma para TEPT, no sólo como un efecto dependiente del estado de la exposición al trauma y la expresión de síntomas de TEPT. La anhedonia puede contribuir a la persistencia y/o cronicidad de síntomas de re-experimentación tras el inicio de los síntomas de TEPT.

创伤前快感缺失作为创伤后应激症状风险因素的前瞻性研究

背景: 快感缺失, 即快感和寻求奖赏行为的减少, 是一种具有良好描述的神经回路中介的跨诊断症状。尽管通常在疾病状态下观察到, 现有假设表明快感缺失也可能是精神病发展的早期风险因素。了解快感缺失对创伤反应轨迹的贡献可能会支持关于导致创伤前风险与创伤相关症状表达的生物学机制推论, 了解这些可能有助于针对性干预。
目的: 我们在有创伤障碍风险的人群中使用前瞻性纵向设计, 检验了快感缺失可能是创伤后应激障碍 (PTSD) 症状的创伤前风险因素的假设。
方法: 在 3个时间点 (部署前, 部署后 3个月和部署后 6个月) 评估了来自海军心理韧性研究的成年男性参与者 (*N* = 2,593)。从创伤前的自我报告工具中提取了一个快感缺失因素, 并检验其与部署后 PTSD 再体验症状发展的关系。
结果: 控制了创伤前 PTSD 和抑郁症状时, 较高的部署前快感缺失预测了部署后 3个月和 6个月的 PTSD 症状增加。抑郁症状不是后续 PTSD 症状的显著预测因素。 3个月的快感缺失也稳健预测了 6个月时间点 PTSD 症状的维持。
结论: 部署前快感缺失可能是 PTSD 的创伤前风险因素, 而不仅仅是创伤暴露和 PTSD 症状表达的状态依赖性效应。在 PTSD 症状出现后, 快感缺失可能会导致症状的持续和/或慢性化。

1. Introduction

Post-traumatic stress disorder (PTSD) is phenotypically and aetiologically heterogeneous, posing a significant challenge to the identification of its underlying mechanisms and development of novel therapeutics. Anhedonia, the reduction of pleasure and reward-seeking behaviour, is a transdiagnostic construct that is an important, albeit relatively understudied symptom following trauma, and is a sub-component of disorders such as PTSD (Risbrough et al., 2018). Anhedonia incorporates a distinct symptom cluster in PTSD that includes numbing, diminished interest or participation in activities, feelings of detachment or estrangement from others, and inability to experience positive emotions (American Psychiatric Association [APA], 2013; Armour et al., 2015; Duek, Spiller, Pietrzak, Fried, & Harpaz-Rotem, 2021; Pietrzak et al., 2015). Endorsement of these symptoms ranges from 18% to 75% across civilians with a diagnosis of PTSD and deployed servicemembers (Carmassi et al., 2014; Franklin & Zimmerman, 2001; Hoge, Riviere, Wilk, Herrell, & Weathers, 2014). Endorsement of significant anhedonia symptoms is associated with a range of poor outcomes in individuals with PTSD, notably greater suicidal ideation (Blais & Geiser, 2019), acquired capability for suicide (Spitzer, Zuromski, Davis, Witte, & Weathers, 2018), and suicide risk (Chou, Ito, & Horikoshi, 2020). Additionally, anhedonia is associated with increased PTSD chronicity (Feeny, Zoellner, Fitzgibbons, & Foa, 2000), as well as comorbid anxiety disorders and psychotic disorders (Kashdan, Elhai, & Frueh, 2006). Across anxiety and mood disorders, anhedonia is a predictor of poor treatment response (Craske, Meuret, Ritz, Treanor, & Dour, 2016; McMakin et al., 2012; Uher et al., 2012). Taken together, this evidence suggests that anhedonia is not only a potential symptom component of PTSD but also that when present, it may be predictive of disease trajectory and treatment outcomes.

Anhedonia can be classified into subcomponent constructs, including reward wanting, liking, and learning (Rømer Thomsen, Whybrow, & Kringelbach, 2015). Within these subcomponents, individuals with PTSD demonstrate decreased reward responsiveness and effortful approach behaviour (aspects of reward wanting) and reduced experience of pleasure (a component of reward liking) compared to individuals without PTSD (Fonzo, 2018; Nawijn et al., 2015). Reductions in reward circuit activation (e.g. ventral striatum BOLD response) are also associated with more severe post-traumatic stress (PTS) symptoms or PTSD diagnosis (Admon et al., 2013; Admon, Milad, & Hendler, 2013; Elman et al., 2009; Sailer et al., 2008). These findings support anhedonia as a robust phenotype associated with reward circuit disruption in individuals with PTSD, similar to its impact in other psychiatric disorders.

What remains less clear is at what point in the trajectory of trauma exposure and symptom development anhedonia is most likely to emerge. Understanding the symptom trajectory of PTSD enables inferences about potential biological mechanisms that contribute to pre-trauma risk versus symptom development after trauma, which in turn could aid in better targeted interventions (Siddiqi et al., 2020). Although anhedonia is usually considered a symptom within a diagnosis, there is evidence that anhedonia or reward processing deficits can presage psychopathology (Kalebasi et al., 2015; Macoveanu et al., 2020; Mallet, Guessoum, Tebeka, Le Strat, & Dubertret, 2020; Pelizza et al., 2020; Rengasamy et al., 2021; Whitton et al., 2016; Williams, Craske, Mineka, & Zinbarg, 2020). However, whether anhedonia and reward dysfunction are precursors to clinical dysfunction precipitated by

other risk factors such as early life stress or lifetime trauma burden or develop only after trauma or chronic stress exposure and trauma-related symptom development, is unknown. At present, evidence for anhedonia as a risk factor for PTSD is preliminary, consisting primarily of correlational and cross-sectional findings. Individuals with remitted PTSD demonstrate aberrant reward learning (Kalebasi et al., 2015), suggesting reward abnormalities may be a trait-dependent risk factor, rather than a state-dependent phenotype for PTSD (Risbrough et al., 2018). However, these data also support the interpretation that anhedonia may be a treatment-resistant symptom. Prospective studies with psychosocial and biological assessments collected pre-trauma are critical in informing how and when risk factors interact with trauma exposure to contribute to PTSD symptom development. The current study has sought to fill this gap in the literature by testing the hypothesis that anhedonia may be a risk factor for PTSD symptom development in a large cohort of military service members assessed prior to and following a combat deployment.

To test this hypothesis, we examined the relationship between anhedonia both pre- and post-trauma to predict PTSD symptom change in a cohort of Marines and accompanying personnel. To operationalize PTSD symptoms and anhedonia, we utilized a factor strategy to derive two factors for re-experiencing symptoms (see Acheson et al., 2019) and self-reported anhedonia based on items from a large battery of standard self-report measures for PTSD, anxiety, and depression. This strategy allowed for the identification of dimensional constructs relevant to psychopathology that may differ in terms of associations relative to traditional diagnostic category measure (CAPS, BDI) which may both contain items measuring the same construct (anhedonia). We also examined what contributions self-reported deployment stress made to the relationship between anhedonia and the pre- to post-trauma change in re-experiencing symptoms, as well as determined the unique contribution of anhedonia as a predictor of re-experiencing symptoms, when controlling for symptoms of depression.

2. Methods

2.1. Participants

Full details of the Marine Resiliency Study (MRS) have been reported elsewhere (Baker et al., 2012). Participants (N = 2,593; see Baker et al., 2012 for demographic information) were recruited from U.S. Marine infantry battalions and accompanying Navy personnel preparing to deploy from bases in southern California to Iraq or Afghanistan. All servicemembers were eligible to participate and there were no exclusion criteria. Women were not included in the study as they were not eligible to serve in infantry battalions at the time of testing. Study procedures were approved by the institutional review boards of the Veteran's Administration San Diego Healthcare System, the University of California San Diego, and the Naval Health Research Center. All participants provided voluntary informed consent. Participants were assessed approximately 1 month prior to a 7-month combat deployment and again at 3 months and 6 months following that deployment (i.e. approximately 11 and 14 months following initial assessment). An exception was the deployment stress measure (see below), which was completed at approximately 1-week post-deployment, immediately upon return of the deployed unit to their U.S home base. Sample size varies across time points as not all of the participants assessed at pre-deployment were available for assessment at follow-up (N = 2,052 at the 3-month post-deployment and N = 1,476 at the 6-month post-deployment).

2.2. Measures

2.2.1. Clinician Administered PTSD Scale for DSM-IV (CAPS-IV)

PTSD symptoms were assessed using the Clinician-Administered PTSD Scale for DSM-IV (CAPS-IV; Weathers, Ruscio, & Keane, 1999), a structured diagnostic interview designed to assess DSM-IV PTSD symptoms (Blake et al., 1995). Interrater reliability was high between CAPS interviewers and trained observers (intraclass correlation coefficient = 0.99, n = 261). For purposes of the current analysis, PTSD positive diagnostic status was defined using the partial PTSD criteria articulated by Mylle and Maes (2004). Partial PTSD criteria were chosen due to the relative psychological health of most members of an active duty Marine cohort. Partial PTSD criteria were the presence of at least 1 cluster B symptom, 2 cluster C symptoms, and 2 cluster D symptoms, with minimum CAPS-IV frequency ratings of 1 and minimum intensity ratings of 2. For individual item analyses, a total score for each symptom was calculated with a range from 0 to 8.

2.2.2. Beck Depression Inventory-II (BDI-II)

Depressive symptoms were measured using the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996). The BDI-II measures the presence and severity of depressive symptoms within the past 2 weeks. For purposes of the current analysis, current depression was defined as scoring within the moderate or severe range on the BDI-II (score ≥20). For individual item analyses, scores ranged from 0 to 3.

2.2.3. Beck Anxiety Inventory (BAI)

Anxiety symptoms were measured using the Beck Anxiety Inventory (BAI; Beck & Steer, 1993). The BAI is a reliable measure of general anxiety symptoms present within the past week and discriminates between anxiety vs. depressive symptoms fairly well (Clark,

Steer, & Beck, 1994). For individual item analyses, scores ranged from 0 to 3.

2.2.4. Deployment Risk and Resilience Inventory-2 (DRRI-2)

Stressful experiences during deployment were assessed at approximately 1-week following return from deployment with four scales from the Deployment Risk and Resilience Inventory-2 (DRRI-2; Vogt et al., 2013; Post-Battle Experiences, Combat Experiences, Deployment Concerns, and Difficult Living and Work Environment). A composite score was created from standardized scores on each subscale, with a mean score approximating zero (Glenn et al., 2017).

2.2.5. Composite symptom measure item selection

In order to identify items in our data set, which best differentiated anhedonic, PTSD-related and depressive symptoms, a principal components analysis (PCA) with promax rotation was conducted on all items from the CAPS-IV (total item scores), BDI-II and BAI (Acheson et al., 2019). Full details of the PCA are included in Supplemental Materials. An 8-component solution from the PCA was identified which accounted for 49% of variance in items and provided the most sensible and interpretable results within the context of the planned analysis.

Anhedonia-related items loaded into a separate factor ('anhedonia') which included the three items from the BDI-II anhedonia subscale (Loss of interest, Loss of interest in sex, Loss of pleasure) and three items from the CAPS-IV (Markedly diminished interest or participation in significant activities, Feeling of detachment or estrangement from others, Restricted range of affect (e.g. unable to have loving feelings)). A 7-item component was identified that we label 're-experiencing symptoms' as this component contained all five items of the CAPS-IV representing the re-experiencing cluster of symptoms as well as two items indexing efforts to avoid trauma reminders. No items indexing anhedonia loaded onto this component. An additional component representing the majority (11) of items from the BDI-II was identified and labelled 'depression symptoms' (Feelings of sadness, Pessimism, Perceived failure, Guilt, Feeling of being punished, Self-dislike, Self-criticism, Suicidality, Crying spells, Indecisiveness, and Feelings of worthlessness). No items from the BAI loaded onto our components of interest. A further component that we labelled 'hypervigilance' emerged from the PCA, though this component was less conceptually coherent relative to 're-experiencing' and the internal consistency of the composite score was low (alpha = .5). Thus, we chose to focus our analyses on the re-experiencing symptom dimen-sion.

Thus, we reduced our data set to 6 items serving as indicators of the construct 'anhedonia,' seven items serving as indicators of the construct 're-experiencing symptoms,' and 11 items serving as indicators of the construct 'depression symptoms.' All individual items selected for each composite measure were z-score standardized to allow combination of items from measures with differing scales (i.e. CAPS-IV and BDI-II). Items were then summed to create composite measures of anhedonia, re-experiencing symptoms, and depression symptoms.

2.3. Data analytic approach

Longitudinal change in anhedonia composite scores across the study was assessed using a linear mixed model with unstructured covariance structure and assessment time point as a repeated effect. Deployment stress was also included as a covariate to control for differences in combat-related experiences across the deployment.

The association of pre-deployment anhedonia and depression symptom composite scores with re-experiencing symptom composite scores at all time points was tested using standard multiple regression analysis at each time point. Standard multiple regression analysis was also used to examine the association between anhedonia and change in PTSD re-experiencing symptoms over time. To control for regression to the mean in analyses involving change scores as a dependent variable, time 1 scores were regressed out using a standard linear regression procedure with the residuals used as the dependent variable in subsequent analyses. For analysis of post-deployment time points (3- and 6-month post-deployment), participants who met criteria for either pre-deployment partial PTSD or moderate-severe depression were excluded from the analysis to allow for assessment of anhedonia's association with symptoms in those who were psychiatrically 'healthy' at pre-deployment (resulting N = 1,974 at the 3-month and N = 1,288 6-month time points).

To examine deployment stress as a moderator of the relationship between anhedonia and re-experiencing symptoms at both follow-up time points, an interaction term represented by the product of both mean-centred variables was entered into the regression equation along with both predictors.

3. Results

3.1. Anhedonia increases from pre-deployment to post-deployment

We first examined overall effects of deployment on anhedonia across the cohort. Anhedonia increased at 3- and 6-months post-deployment compared to pre-deployment levels [$F(2,1540.04) = 16.73$, $p < .0001$; post-hoc tests (pre-deployment to 3-month: $p < .04$; pre-deployment to 6-month: $p < .02$; 3-month to

6-month: ns); pre-deployment = −.98(.06), 3-months post-deployment = −.47(.09) and 6-months post-deployment = −.45(.1)]. As expected, greater deployment stress was associated with greater post-deployment increases in anhedonia (change scores between pre-deployment and 3-months post-deployment, r = .28, $p < .0001$).

3.2. Pre-deployment anhedonia symptoms are associated with pre- and post-deployment re-experiencing symptoms

To test whether anhedonia is associated with current, and more importantly, future re-experiencing symptoms, multiple regression analyses were performed with the re-experiencing symptom composite scores at pre-deployment, 3-months and 6-months post-deployment as the dependent variables and composite scores for pre-deployment re-experiencing symptoms and pre-deployment anhedonia (for the post-deployment time points) as independent variables. To clarify interpretation of the contribution of anhedonia to re-experiencing symptoms, we also added pre-deployment depression symptoms to the models to determine relative strength of anhedonia vs. depression as predictors of current and future re-experiencing symptoms (see Table 1). All overall models were statistically significant [pre-deployment: F(2,2590) = 226.6, $p < .0001$; 3-months post-deployment: F(3,1790) = 20.68, $p < .0001$; 6-months post-deployment F(3,1284) = 16.7, $p < .0001$]. In the cross-sectional pre-deployment analysis, both depression symptoms and anhedonia were significantly associated with re-experiencing symptoms, although the association with anhedonia was notably stronger (standardized beta .31 versus .11). As expected, pre-deployment re-experiencing symptoms were significantly associated with post-deployment re-experiencing symptoms at both follow-up time points. Finally, while pre-deployment depression no longer contributed significantly to the longitudinal regression model, pre-deployment anhedonia retained significant associations with re-experiencing symptoms at both the 3- and 6-month time points.

3.3. Three month post-deployment anhedonia symptoms are associated with change in re-experiencing symptoms from 3 to 6 months post-deployment

A change score was calculated for re-experiencing symptoms across the 3- to 6-month post-deployment time period. A standard multiple regression analysis was performed with the change in re-experiencing symptoms composite score as the dependent variable and 3-month re-experiencing symptoms, depression symptoms, and anhedonia as independent variables. Results are shown in Table 2. The overall model was significant [F(3,1287) = 122.29, $p < .0001$]. Three-month re-experiencing symptoms were negatively associated with change in re-experiencing symptoms at 6-months post-deployment such that those with higher 3-month scores were more likely to show improvement at 6-months post-deployment (standardized beta = −.52). However, 3-month anhedonia scores were positively associated with change in re-experiencing symptoms such that those with higher anhedonia scores at 3-months were more likely to see an increase in re-experiencing symptoms between the 3- and 6-month time points (standardized beta = .24).

3.4. Deployment stress moderates the relationship between pre-deployment anhedonia and 6-months post-deployment re-experiencing symptoms

We next tested the hypothesis that deployment stress moderates the relationship between pre-deployment anhedonia and increased re-experiencing symptoms at 3- and 6-months post-deployment (Table 3). Both overall models were significant [F(4,1743) = 78.98, $p < .0001$; F(4,1257) = 33.73, $p < .0001$, respectively]. At 3-months post-deployment, deployment stress did not significantly moderate the relationship between pre-deployment anhedonia and re-experiencing symptoms. How-ever, a weak moderator effect did emerge at 6-months post-deployment, indicating a stronger pre-deployment anhedonia to post-deployment re-experiencing relationship

Table 1. Pre-deployment anhedonia symptoms are associated with re-experiencing symptoms at pre-deployment and 3-months and 6-months post-deployment independent of depressive symptoms.

Composite Score	Est. (SD)	Standardized Beta	t	*p*-value	95% CI	R^2
Pre-deployment						
Constant	.00 (.09)	-	.006	.995	−.17–.17	.15
Depression	.08 (.02)	.11	4.85	<.0001	.04–.11	
Anhedonia	.35 (.03)	.31	13.12	<.0001	.3–.41	
3-month						
Constant	−.06 (.12)	-	−.54	.59	−.29–.17	.03
Re-experiencing	.24 (.04)	.16	6.66	<.0001	.17–.31	
Depression	.02 (.03)	.02	.69	.49	−.04–.07	
Anhedonia	.1 (.04)	.06	2.52	.01	.02–.18	
6-month						
Constant	.04 (.14)	-	.26	.8	−.23–.3	.04
Re-experiencing	.24 (.04)	.16	5.83	<.0001	.16–.32	
Depression	.03 (.03)	.03	1.06	.29	−.03–.1	
Anhedonia	.1 (.05)	.07	2.17	.03	.01–.2	

Table 2. Three-month post-deployment anhedonia symptoms are associated with change in re-experiencing symptoms from 3- to -month post-deployment.

Composite Score	Est. (SD)	Standardized Beta	t	*p*-value	95% CI	R^2
Constant	−.19 (.11)	-	−1.77	.08	−.4–.02	.22
3-mo Re-experiencing	−.52 (.03)	−.52	−18.62	<.0001	−.58–−.47	
3-mo Depression	−.03 (.02)	−.05	−1.47	.14	−.07–.01	
3-mo Anhedonia	.24 (.04)	.21	6.71	<.0001	.17–.31	

Table 3. Combat exposure moderates the relationship between pre-deployment anhedonia symptoms and re-experiencing symptoms at 6-months but not 3-months post-deployment.

Composite Score	Est. (SD)	Standardized Beta	t	*p*-value	95% CI	R^2
3-Month						
Constant	−.04 (.11)	-	−.38	.7	−.25–.17	.15
Re-experiencing	.21 (.03)	.14	6.37	<.0001	.15–.28	
Combat Exposure	1.92 (.13)	.34	14.75	<.0001	1.67–2.18	
Anhedonia	.1 (.04)	.06	2.71	.007	.03–.17	
Anhedonia x Combat Exposure	−.05 (.04)	−.03	−1.07	.29	−.13–.04	
6-Month						
Constant	.13 (.13)	-	.98	.33	−.13–.4	.09
Re-experiencing	.22 (.04)	.15	5.59	<.0001	.14–.3	
Combat Exposure	1.51 (.16)	.26	9.24	<.0001	1.19–1.84	
Anhedonia	.1 (.04)	.06	2.25	.02	.01–.18	
Anhedonia x Combat Exposure	.11 (.05)	.06	2.10	.04	.01–.21	

as deployment stress scores increased (standardized beta = .06).

4. Discussion

The current study sought to examine anhedonia and its role as a correlate and risk factor for PTSD-related symptoms in a deployed military service cohort assessed longitudinally. The principal findings were: (1) Anhedonia significantly increased after deployment across the cohort as a whole, even when controlling for deployment stress intensity, (2) higher pre-deployment anhedonia was associated with greater PTSD re-experiencing both cross-sectionally and prospectively at 3- and 6-month post-deployment timepoints, (3) when comparing anhedonia and depression symptoms cross-sectionally, anhedonia was more strongly associated with re-experiencing than depression symptoms.

Regarding anhedonia symptom increases after deployment across the cohort as a whole, some of this post-deployment increase in anhedonia was explained by the level of deployment stress. But, increased anhedonia was detectable even when controlling for deployment stress intensity suggesting that both deployment stress and other factors contributed to anhedonia increases after deployment. Importantly, we found that higher anhedonia before leaving for a combat deployment was associated with increased pre-deployment and post-deployment PTSD re-experiencing symptoms. These results indicate that pre-deployment anhedonia may be a pre-trauma risk factor for PTSD, not simply a state-dependent effect of trauma exposure and post-trauma PTSD symptoms. Additionally, anhedonia at the 3-month post-deployment timeframe predicted increased re-experiencing at the 6-months post-deployment assessment, suggesting that anhedonia may also contribute to maintenance and/or chronicity of re-experiencing symptoms after PTSD symptom emergence. In our analysis, this association was only weakly moderated by deployment stress at the 6-month time point, suggesting that trauma exposure alone explains only a small part of the contribution of anhedonia to re-experiencing symptoms.

Higher pre-deployment anhedonia was associated with greater PTSD re-experiencing symptoms both cross-sectionally and prospectively at 3-months and 6-months post-deployment. While the observed longitudinal associations between anhedonia and PTSD re-experiencing symptoms were small, it is important to note that these associations span 11 and 14 months time periods, including a combat deployment. In contrast, a pre-deployment depression symptom composite score intensity was associated with re-experiencing symptoms only cross-sectionally, not prospectively. Further, when comparing anhedonia and depression symptoms in the cross-sectional analyses, anhedonia was more strongly associated with re-experiencing symptoms than depression symptoms. Evidence of depression as a risk or vulnerability factor for post-combat PTSD is mixed, and not all significant associations reported controlled for baseline PTSD (Stander, Thomsen, & Highfill-mcroy, 2014). Furthermore, failure to differentiate anhedonia from other symptoms of depression limits inferences about the independent contributions of anhedonia to PTSD risk over time. In the current study, higher anhedonia at 3-months post-deployment was associated with an increase in re-experiencing symptoms from 3- to 6-months post deployment. Taken together, these findings suggest that anhedonia may have important utility as a correlate and prospective risk factor of re-experiencing PTSD symptoms, independent of other

depression symptoms. These findings underscore the importance of examining dimensional constructs relevant to psychopathology, which may differ in their associations as compared to more traditional diagnostic categories.

Given our findings that anhedonia increases PTSD risk and chronicity, underlying biological mechanisms are important to consider. Whether these biological mechanisms may be related to those for depression, and whether they are heritable and via shared environmental factors is unknown. Recent studies suggest that genetic risk scores for depression are also associated with anhedonia across self-report, behaviour, and neuronal circuit measures (Guffanti et al., 2019); it is not known, however, if genetic risk scores associated with PTSD (Nievergelt et al., 2019; Stein et al., 2019) are also associated with anhedonia phenotypes. Exposure to various forms of early adversity is also consistently associated with anhedonia (Cohen, McNeil, Shorey, & Temple, 2019; Davis et al., 2019; Frewen, Dozois, & Lanius, 2012) and aberrant reward processes (Dennison et al., 2019; Fareri & Tottenham, 2016; Novick et al., 2018) across multiple levels of analysis in humans, as well as in rodent models (Bolton et al., 2018; Glynn & Baram, 2019; Luby, Baram, Rogers, & Barch, 2020). Finally, peripheral inflammation and individual differences in immune signalling are emerging risk factors for increased enduring responses to stress from recent clinical and rodent model studies. Anhedonia is one of the more common neuropsychiatric symptoms associated with both peripheral and central inflammation (Felger et al., 2016; Felger & Miller, 2020). Studies in animals suggest individual responses to severe stress can be predicted by pre-stress immune reactivity patterns (Deslauriers, Powell, & Risbrough, 2017), and pre-trauma inflammation in humans is associated with increased risk for PTSD (Breen et al., 2017; Eraly et al., 2014). With evidence that anhedonia may predict and worsen PTSD symptoms over time, we can utilize this phenotype to probe these and other mechanisms of anhedonia symptom trajectories in PTSD. Finally, anhedonia and reward processing have well-established neural circuits (i.e. cortical striatal network) and signalling mechanisms that are under intense investigation as novel transdiagnostic neuromodulation and pharmacological interventions (Harnett et al., 2020; Pizzagalli et al., 2020; Spano et al., 2019). The current data also support further exploration focused on whether treatment of anhedonia symptoms might potentially mitigate ongoing post-trauma symptom increases or might mitigate risk for negative comorbidities and negative outcomes, such as suicide and substance use (Fani et al., 2020).

This study has some notable limitations. The MRS cohort is composed of young, relatively healthy, military-age males. Thus, caution should be taken when generalizing the results of these analyses to more heterogenous populations. It should be noted, however, that the sample size is quite large (N = 1,974 at 3-month and N = 1,288 6-month time points) and thus is a rigorous examination of the hypothesis overall. Second, the MRS study lacked high-resolution measures of anhedonia, especially those needed to understand specific subcategories of anhedonia (e.g. reward wanting vs. liking) that may most strongly contribute to risk (Rizvi, Pizzagalli, Sproule, & Kennedy, 2016). Despite these limitations, the overall results are consistent with growing evidence for anhedonia as a marker of neuropsychiatric risk across multiple disorders.

In summary, the results of the current study suggest that anhedonia may be a pre-trauma risk factor for developing PTSD, rather than merely a state-dependent effect of trauma exposure and current PTSD symptom expression. Thus, understanding the development of, and neurobiology underlying, anhedonia may be important to developing strategies to mitigate risk for developing PTSD following trauma exposure. Further, the current results suggest that anhedonia may contribute to the maintenance or chronicity of re-experiencing symptoms following PTSD symptom emergence, indicating that anhedonia may be an important focus for effective treatment of PTSD.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data that support the findings of this study are available from the corresponding author, DTA, upon reasonable request. United States Department of Veteran's Affairs privacy regulations do not allow for the public sharing of individual data.

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