Psychological Trauma: Theory, Research, Practice, and Policy

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Machine Learning Models Predict PTSD Severity and Functional Impairment: A Personalized Medicine Approach for Uncovering Complex Associations Among Heterogeneous Symptom Profiles

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Objective: Posttraumatic stress disorder (PTSD) is a debilitating psychiatric illness, experienced by approximately 10% of the population. Heterogeneous presentations that include heightened dissociation, comorbid anxiety and depression, and emotion dysregulation contribute to the severity of PTSD, in turn, creating barriers to recovery. There is an urgent need to use data-driven approaches to better characterize complex psychiatric presentations with the aim of improving treatment outcomes. We sought to determine if machine learning models could predict PTSD-related illness in a real-world treatment-seeking population using self-report clinical data. ***Method:*** Secondary clinical data from 2017 to 2019 included pretreatment measures such as trauma-related

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symptoms, other mental health symptoms, functional impairment, and demographic information from adults admitted to an inpatient unit for PTSD in Canada ($n = 393$). We trained two nonlinear machine learning models (extremely randomized trees) to identify predictors of (a) PTSD symptom severity and (b) functional impairment. We assessed model performance based on predictions in novel subsets of patients. ***Results:*** Approximately 43% of the variance in PTSD symptom severity ($R^2_{\text{avg}} = .43$, $R^2_{\text{median}} = .44$, $p = .001$) was predicted by symptoms of anxiety, dissociation, depression, negative trauma-related beliefs about others, and emotion dysregulation. In addition, 32% of the variance in functional impairment scores ($R^2_{\text{avg}} = .32$, $R^2_{\text{median}} = .33$, $p = .001$) was predicted by anxiety, PTSD symptom severity, cognitive dysfunction, dissociation, and depressive symptoms. ***Conclusions:*** Our results reinforce that dissociation, cooccurring anxiety and depressive symptoms, maladaptive trauma appraisals, cognitive dysfunction, and emotion dysregulation are critical targets for trauma-related interventions. Machine learning models can inform personalized medicine approaches to maximize trauma recovery in real-world inpatient populations.

Clinical Impact Statement

Machine learning models accurately predicted self-reported trauma symptom severity and functional impairment scores in a masked subset of data, consisting of a sample of adults seeking inpatient treatment for posttraumatic stress disorder (PTSD). In order of decreasing importance, anxiety, dissociation, depression, negative trauma-related beliefs about the world, and emotion dysregulation were the greatest contributors of PTSD symptom severity; whereas anxiety, PTSD symptom severity, cognitive dysfunction, dissociation, and depression best accounted for functional impairment. Evidence-based interventions that specifically target these symptoms may be important for reducing the severity and burden of trauma-related illness.

Keywords: trauma, posttraumatic stress disorder, machine learning, dissociation, functional impairment

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Posttraumatic stress disorder (PTSD) is a heterogeneous disorder, where it is estimated that there are approximately 636,120 possible combinations of *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition; *DSM-5*) PTSD presentations (Galatzer-Levy & Bryant, 2013; Neria, 2021; Newson et al., 2021). Given its complex associations with a wide range of symptoms, it is no surprise that PTSD is a debilitating disorder (Harper et al., 2022; Sareen et al., 2007). Individuals with PTSD experience significant functional impairments in well-being, distress, and disability, including greater suicide attempts and long-term reduction of activities (Sareen et al., 2007). Notably, up to 30% of individuals with PTSD exhibit the dissociative subtype, which is characterized by heightened symptoms of depersonalization and derealization (American Psychiatric Association [APA], 2013; Armour et al., 2014; McKinnon et al., 2016; Lanius, 2015; Stein et al., 2013; White et al., 2022; Wolf, Lunney, et al., 2012; Wolf, Miller, et al., 2012). This can present as emotion overmodulation with a constellation of altered psychosomatic perceptions, including out-of-body experiences, feeling disconnected from one's body, and feeling that one's surroundings are dream-like or unreal (Lanius et al., 2010, 2012). Dissociation has been correlated with greater PTSD symptom severity, emotion dysregulation, functional impairment, and neuropsychological impairment, as well as aberrant bodily self-consciousness, and sensorimotor integration (Boyd et al., 2018; Harricharan et al., 2020; Ozer et al., 2003; Park et al., 2021; Stein et al., 2013; Tanner et al., 2019; Warner et al., 2014), with unique neurobiological correlates (Lebois et al., 2021) that differentiate it from the nondissociative subtype of PTSD (Daniels et al., 2016; Lanius et al., 2010, 2012; Nicholson et al., 2015, 2020; Tursich et al., 2015).

In addition to dissociative symptomatology, factors that increase the risk and severity of PTSD include emotion dysregulation, preexisting mental health conditions, childhood adversity, and comorbid mood and anxiety disorders, among others (Able & Benedek, 2019; Brady et al., 2019; Brady & Back, 2012; Greene et al., 2016; Knowles et al., 2019; Norman et al., 2012; Obuobi-Donkor et al., 2022; Stein et al., 2013). Importantly, psychiatric comorbidity in PTSD is the norm, where up to 68.4% of individuals with PTSD have one or more comorbid mental health condition(s) (Greene et al., 2016). Comorbid mood and anxiety disorders have been associated with greater PTSD symptom severity (Knowles et al., 2019), and comorbid major depressive disorder significantly contributes to increasing the risk of suicidality among individuals with PTSD (Panagioti et al., 2012, 2015). Further complicating its presentation, PTSD is associated with impairments in attention, concentration, memory, and executive functioning (El Khoury-Malhame et al., 2011; Hayes et al., 2012; Scott et al., 2015; Vasterling & Brewin, 2005).

Several evidence-based treatments for PTSD exist, including trauma-focused psychotherapies (e.g., cognitive processing therapy, prolonged exposure, and eye-movement desensitization and reprocessing), which outperform pharmacotherapies on relevant PTSD outcome measures, even at 3–9 months posttreatment (Foa et al., 2007; Lee et al., 2016; Merz et al., 2019; Resick et al., 2008). However, approximately 33% of individuals will still meet the criteria for PTSD after completing psychotherapy for PTSD, and 22%–30% of patients with PTSD will drop out of trauma-focused psychotherapies (Bradley et al., 2005; Eftekhari et al., 2020). Indeed, Bae et al. (2016) found that in a specialized trauma clinic, treatment nonresponders displayed significantly higher levels of dissociation symptoms and psychiatric comorbidities, suggesting that more complex or severe symptom profiles respond poorly to existing first-line treatments for PTSD.

PTSD symptom heterogeneity presents challenges for effective recovery (Neria, 2021), and yet, the majority of extant literature has focused on the associations across variables in isolation, rendering it difficult to account for the complex relationships among relevant clinical variables. Data-driven analytical techniques, such as machine learning, can allow for a more accurate representation of complex nonlinear relations among PTSD symptoms and the disorder's correlates. For example, machine learning regression models can take input features to predict a continuous target feature, such as the severity score of PTSD symptoms. Here, permutation analyses of feature importance provide an easy-to-interpret way of accurately estimating the amount of variance that each input feature contributes to making correct predictions. Further, the use of multiple training sets provides machine learning regression an advantage over standard regression by mitigating the effects of missing or noisy data. Critically, unlike traditional multivariate statistical analyses using sample inference, machine learning algorithms are evaluated based on their performance in unseen/novel data (i.e., data that were not used to train the model), increasing generalizability of results; are equipped to handle a greater number of input features (i.e., independent variables) with complex, nonlinear associations; and are not constrained or biased by assumptions on variable interactions, variable scales, or model oversimplification (Chekroud et al., 2021; Dwyer et al., 2018). Thus, machine learning regression models are ideally suited to examine outcomes of a highly heterogeneous and complex psychiatric condition such as PTSD.

In the field of psychiatry, the machine learning knowledge base surrounding PTSD is limited, where many studies focus on PTSD diagnosis (i.e., classification) rather than PTSD symptoms on a continuum (i.e., regression; Harricharan et al., 2020; Nicholson et al., 2019; Schultebraucks et al., 2021; Siegel et al., 2021; Wani et al., 2021; Zafari et al., 2021; Ziobrowski et al., 2021). For example, neuroimaging data have been used to classify the dissociative subtype of PTSD, nondissociative subtype of PTSD, and healthy controls with high accuracy (>90% balanced classification accuracy) by our group (Harricharan et al., 2020; Nicholson et al., 2019). However, to our knowledge, no study to date has examined whether PTSD symptom severity and functional impairment can be predicted on a continuum using a naturalistic sample seeking inpatient treatment for this disorder. Given the relative dearth of literature utilizing machine learning regression models, this article seeks to contribute to the field using a novel and versatile statistical method. Critically, most machine learning studies examining PTSD have done so among relatively homogeneous samples of individuals with PTSD, using stringent exclusion criteria (e.g., history of head trauma; neurological disorder; major medical illness; current or past diagnosis of bipolar disorder, schizophrenia, or other psychotic disorders; severe drug use in the past year; severe suicidality in the past 3 months, etc.; Harricharan et al., 2020; Nicholson et al., 2019; Schultebraucks et al., 2021; Siegel et al., 2021). However, this stringent approach may not be representative of the diverse presentations of PTSD in most treatment clinics, thereby limiting the generalizability of these previous results to clinical settings. Although heterogeneous samples may contribute to greater noise in empirical data, they are far more representative of the real-world treatment-seeking population and increase the ecological validity of a study.

Accordingly, the current study employed machine learning models among a sample of adults seeking inpatient treatment for PTSD, with relatively few exclusion criteria. The purpose of this study was to determine if the employed machine learning models could predict: (a) PTSD symptom severity and (b) functional impairment scores in novel samples significantly better than trivial predictors, and at a practically relevant effect size. Ultimately, increasing our knowledge of how relevant variables uniquely predict severity and impairment in PTSD can inform the design of more effective interventions and facilitate a personalized medicine approach (i.e., pair specific clinical profiles with tailored treatment plans). Here, we hypothesized that our models would confirm features that have been identified in the literature as contributing to the severity of PTSD symptoms (e.g., dissociation, emotion dysregulation, depression, and anxiety). We also hypothesized that PTSD symptom severity and cognitive dysfunction would additionally contribute to predicting functional impairment among this sample, where symptom severity is often viewed in the absence of its real-world correlate, functional outcomes.

Method

Participants

This project was approved by the Homewood Health Centre Research Ethics Board (REB 20-04) and the Hamilton Integrated REB (Project Number 8289-C). Secondary clinical data from September 2017 to November 2019 were provided by the Homewood Health Centre, as part of standard clinical practice at admission to the posttraumatic stress recovery (PTSR) unit. The PTSR unit provides specialized inpatient mental health treatment for individuals with PTSD and trauma-related disorders. The data set consisted of treatment-seeking adults in Canada aged 18–80 ($M = 43.7 \pm 9.9$), referred to the program by clinicians for trauma-related distress ($n = 393$, 196 female). Individuals were required to be: (a) 18 years of age or older; (b) able to participate in group therapy in a mixed community milieu; (c) able to tolerate their emotions and manage basic personal safety; and (d) willing to abstain from all substances (e.g., alcohol, tobacco, etc.) throughout the duration of the program. Participants were not eligible for the current study if they had placed exclusions on using their personal health information for research purposes. Demographic characteristics are reported in Table 1.

Procedure

During the first week of their admission to the PTSR program, participants completed a battery of self-report questionnaires, administered electronically using Voxco Survey software (http://www.voxco.com). These questionnaires included assessing demographic variables (i.e., age and biological sex) and mental health symptoms. A subset of these measures was analyzed in the present study and described below.

Measures

All variables of interest were self-reported and included age, biological sex, trauma-related symptoms, other mental health symptoms, and functional measures. Biological sex was self-reported as a binary variable (i.e., male or female). Only data collected at admission to the PTSR program was used for the current study. Unless otherwise specified, sum scores on all the measures were used in our analyses.

Trauma-Related Symptoms

The PTSD checklist for *DSM-5* (PCL-5) assessed PTSD symptom severity on a list of 20 items with a total score ranging between 0 and

Table 1
Demographic and Clinical Characteristics of the Sample

Variable	Total ($n = 337$)	Female ($n = 169$)	Male ($n = 168$)
	M (*SD*)		
Age	44.3 (9.8)	43.1 (10.7)	45.5 (8.6)
PCL-5	57.9 (11.1)	58.3 (10.5)	57.5 (11.7)
WHODAS 2.0	34.6 (8.1)	34.7 (7.3)	34.6 (8.9)
DERS	124.0 (23.6)	125.7 (23.6)	122.4 (23.7)
MDI (DP + DR)	23.4 (9.2)	24.5 (9.5)	22.3 (8.9)
DASS anxiety	21.2 (10.1)	21.6 (10.3)	20.7 (10.0)
DASS depression	23.1 (10.7)	22.9 (10.4)	23.3 (11.0)
TRGI	65.3 (20.5)	69.5 (20.1)	61.0 (20.1)
TRSI	39.6 (20.5)	42.0 (21.0)	37.3 (19.8)
PTCI (World)	5.8 (1.2)	5.8 (1.1)	5.8 (1.2)
CFQ	66.3 (17.4)	68.6 (16.9)	64.0 (17.6)
	n (percentage of sample)		
Education			
Eighth grade or less	2 (0.6)	0 (0)	2 (1.2)
Grades 9–11	13 (3.9)	7 (4.1)	6 (3.6)
High school	42 (12.5)	17 (10.1)	25 (14.9)
Technical or trade school	22 (6.5)	3 (1.8)	19 (11.3)
Some college/University	89 (26.4)	45 (26.3)	44 (26.2)
Diploma/bachelor's degree	131 (38.9)	74 (43.8)	57 (33.9)
Graduate degree	29 (8.6)	19 (11.2)	10 (6.0)
Unknown	9 (2.7)	4 (2.4)	5 (3.0)
Occupation			
Military member	158 (46.9)	118 (69.8)	40 (23.8)
Veteran	42 (12.5)	8 (4.7)	34 (20.2)
PSP	2 (0.6)	1 (0.6)	1 (0.6)
PSP and military/Veteran	130 (38.6)	39 (23.1)	91 (54.2)
Other	5 (1.5)	3 (1.8)	2 (1.2)

Note. PCL-5 = PTSD checklist for *DSM-5*; PTSD = posttraumatic stress disorder; *DSM-5* = *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition); WHODAS 2.0 = World Health Organization disability assessment schedule 2.0; DERS = difficulties in emotion regulation scale; MDI (DP + DR) = sum of the depersonalization and derealization subscales of the multiscale dissociation inventory; DASS-21 anxiety = anxiety subscale of the depression, anxiety, and stress scale-21; DASS-21 depression = depression subscale of the DASS-21; TRGI = trauma-related guilt inventory; TRSI = trauma-related shame inventory; PTCI (World) = negative cognitions about the world subscale of the posttraumatic cognitions inventory; CFQ = cognitive failures questionnaire. "Military member" = current military member; "PSP" = current or former public safety personnel (e.g., paramedics, police officers, firefighters, emergency personnel, etc.).

80 (Weathers et al., 2013). The trauma-related guilt inventory (TRGI) captured experiences of guilt related to traumatic events or their consequences on a list of 32 items with a total score ranging between 0 and 128 (Kubany et al., 1996). Relatedly, the trauma-related shame inventory (TRSI) assessed experiences of shame related to traumatic events such as feelings of personal failure or concerns about how others will evaluate them on a list of 24 items with a total score ranging between 0 and 72 (Øktedalen et al., 2014). Due to the potential for overlap between guilt and shame (Bannister et al., 2019) and to circumvent potential problems of dissociating the unique roles of two highly correlated features in machine learning analyses, the TRGI and TRSI were combined into one variable using a composite score. In addition, the posttraumatic cognitions inventory (PTCI) evaluated trauma-related thoughts and beliefs about the self and others on a list of 33 items with a total score ranging between 33 and 231 (Foa et al., 1999). The PTCI has three subscales assessing negative cognitions about the world (seven items), negative cognitions about the self (21 items), and self-blame (five items). We extracted the "World" subscale to be included as a feature in the machine learning analyses only. Due to the conceptual overlap with the TRGI (e.g., "I blame myself for what happened") and TRSI (i.e., "Because of my traumatic experience, I feel inferior to others"), the PTCI "Blame" (e.g., "The event happened because of the way I acted") and "Self" (e.g., "I am inadequate") subscales were not included as features.

Other Mental Health Symptoms

Symptoms of depression and anxiety were assessed using the two corresponding subscales of the depression, anxiety, and stress scale (DASS-21; seven items per subscale) with a total score ranging between 0 and 21 for each (Parkitny & McAuley, 2010). The multiscale dissociation inventory (MDI) assessed symptoms of dissociation on a list of 30 items with a total score ranging between 30 and 150 (Briere et al., 2005). The MDI subscales of depersonalization and derealization were summed to create a single, PTSD-related measure of dissociation as defined by the *DSM-5* (APA, 2013). In addition, the difficulties in emotion regulation scale (DERS) measured emotion regulation skills on a list of 36 items with a total score ranging between 36 and 180 (Gratz & Roemer, 2004).

Adverse childhood events such as neglect and physical or sexual abuse were assessed using the adverse childhood experiences (ACEs) measured on a list of 10 items with a total score ranging between 0 and 10 (Felitti et al., 1998). The alcohol use disorders identification test (AUDIT) assessed problematic alcohol use over the past year, on a list of 10 items with a total score ranging between 0 and 40 (Babor et al., 2001).

Functioning and Impairment

Functional impairment was assessed using the World Health Organization disability assessment schedule 2.0 (WHODAS 2.0), measured on a list of 12 items with a total score ranging between 12 and 60 (Üstün et al., 2010). Finally, the cognitive failures questionnaire (CFQ) assessed cognitive dysfunction on the list of 25 items with a total score ranging between 0 and 100 (Broadbent et al., 1982).

Data Analytic Plan

These data were stored and analyzed using the secure research environment (SRE) service provided by the Canadian Primary Care Sentinel Surveillance Network (CPCSSN, n.d.). The SRE is based on a data safe haven developed at Queen's University, Canada, and hosted at the Queen's Centre for Advanced Computing in Ontario (Martin et al., 2021). This platform provides researchers with a secure environment for the storage and analysis of health data. The current project acted as a test case of the use of the SRE and in a separate study, will be used to assess its potential to enhance research in military and veteran health by providing a secure platform for advanced analytics.

Before conducting machine learning analyses, with the aim of balancing theory- and data-driven science, we also calculated intercorrelations of all clinical variables (features; Table 2). Here, we found that neither the ACE nor AUDIT correlated with other features as expected, such as PTSD symptom severity, emotion dysregulation, dissociation, depression, anxiety, and functional impairment, among others ($-.07 \leq r \leq .17$). The lack of, or weak correlations found in our sample were inconsistent with the current research consensus (see Messman-Moore & Bhuptani, 2017, for a review), suggesting that in our study, the ACE and AUDIT scales may not be accurately capturing ACE and alcohol use. Notably, the ACE contains 10 items that assess the presence or absence of an ACE (ranging from one's caregivers going through a divorce to experiencing sexual abuse) but it does not assess the frequency, severity, or psychological impact of such experiences. In this context, the ACE scale may not be ideally suited to accurately capture the direct impact of childhood adversity on our outcome measures of interest. Critically, however, our models included other influential variables that are significantly impacted by childhood adversity, such as emotion dysregulation, dissociation, and anxiety symptoms (Dvir et al., 2014; Messman-Moore & Bhuptani, 2017). Furthermore, a histogram plot revealed that the AUDIT scores were positively skewed ($M = 6.17$, $Mdn = 3$), indicating that most individuals reported low levels of problematic alcohol use. This was not surprising, given that reporting low levels of problematic alcohol use was required for entry into the PTSR program. As such, with the aim of using only features with high construct/convergent validity, the ACE and AUDIT were excluded from our main analyses. This ensured that we avoided potential harm to the field by inaccurately inferring the lack of importance of childhood adversity and alcohol use in relation to PTSD (Brady & Back, 2012). Please refer to File A in the online supplemental materials where we conducted supplemental analyses that included ACE scores as an input feature. Here, prediction accuracy was not significantly affected.

On the other hand, very high correlations ($r > .50$) indicate 25% or more shared variance between features, making it difficult to dissociate unique feature contributions. As such, we also reported model-based feature importance to account for potential inaccuracy in the interpretation of unique contributions of highly intercorrelated features. After removing participants with missing data, the final sample consisted of 337 participants (169 female).

All machine learning analyses were conducted using Python 3.7.9 (Van Rossum & Drake, 2009; scikit-learn 1.0.1, Pedregosa et al., 2011). Given that we wanted to make predictions about the severity of symptoms (continuous target features), we used supervised machine learning regression analyses. Specifically, two nonlinear, decision tree-based machine learning models were trained (extremely randomized trees [ERT]; Geurts et al., 2006). The first model was trained to predict

Table 2

Zero-Order Correlations Between All Variables of Interest, n = *337*

Variable	1	2	3	4	5	6	7	8	9	10	11
1. Biological sex	—										
2. Age	−.074	—									
3. PTSD symptoms	.015	−.044	—								
4. Functional impairment	.012	−.070	.527	—							
5. Anxiety	.049	−.136	.577	.500	—						
6. Depression	−.023	−.136	.532	.435	.600	—					
7. Dissociation	.116	−.109	.517	.435	.515	.417	—				
8. Emotion dysregulation	.082	−.211	.518	.416	.433	.495	.452	—			
9. Negative trauma-related cognitons (world)	−.002	−.104	.508	.311	.392	.392	.377	.404	—		
10. Cognitive dysfunction	.130	−.088	.471	.476	.404	.268	.510	.483	.369	—	
11. Trauma-related guilt and shame	.174	−.210	.459	.325	.419	.435	.445	.475	.385	.333	—

Note. PTSD symptoms = posttraumatic stress disorder checklist for *DSM-5*; *DSM-5* = *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition); functional impairment = World Health Organization disability assessment schedule 2.0; anxiety = anxiety subscale of the DASS-21; Depression = depression subscale of the DASS-21; dissociation = sum of the depersonalization and derealization subscales of the multiscale dissociation inventory; emotion dysregulation = difficulties in emotion regulation scale; negative trauma-related cognitions (world) = negative cognitions about the world subscale of the post-traumatic cognitions inventory; cognitive dysfunction = cognitive failures questionnaire; trauma-related guilt and shame = trauma-related guilt inventory and trauma-related shame inventory; DASS-21 = depression, anxiety, and stress scale-21.

PTSD symptom severity (PCL-5 sum score) and the second model to predict functional impairment (WHODAS 2.0 sum score). ERT was selected for its computational efficiency and strong randomization method, the details of which are outlined by Geurts et al. (2006). This method has also been shown to account for complex nonlinear relations that exist between features, as demonstrated by Eder et al. (2021). Briefly, ERT randomly shuffles out features after training the model, and measures the resulting reduction in model performance (Breiman, 2001; Louppe et al., 2013). Each feature is then rank-ordered based on average contributions to model performance over all iterations of the algorithm. This method highlights the intricacies of features underlying the target variable. Although a fulsome description of ERT is beyond the scope of this article, Geurts et al. (2006) describe the methodology used in this study. To ensure generalizability, we assessed model performance based on predictions in a novel subset of patients by employing a nested cross-validation procedure (80/20 split with 100 iterations each). Cross-validation ensures that the predictions of the model are tested only in the patients (data points) that are not used for training the models, while simultaneously maximizing the amount of data available for training and testing. Nesting this cross-validation (inner and outer loops) allows for hyperparameter tuning in the inner loops. In the case of ERT, these hyperparameters were the number of samples per leaf and the number of features per node. Model performance was compared to that of a model employing trivial predictions (i.e., always predicts a mean value of the target feature). The contribution of each input feature was assessed using permutation feature importance, which measures the relative reduction in the explained variance of the model if a given input feature cannot be used meaningfully by the models (i.e., the relation between this input and target feature is made meaningless by randomly shuffling values of this input). Given that the permutation feature importance is sensitive to high intercorrelations among input features, the model-based feature importance was also calculated. The model-based feature importance is a similar indicator of feature importance but measures the relative reduction in the mean squared error at a given branch when using that input. All features of the model are then rank-ordered based on contributions to variance in the case of permutation feature importance, and on mean squared error in the case of model-based feature importance. Both of our models included eight input features: biological sex, age, DERS, MDI (sum of subscales depersonalization and derealization), DASS anxiety, DASS depression, a composite TRGI and TRSI score, and PTCI negative cognitions about the world. For the second model predicting functional impairment, there were ten input features with the addition of PCL-5 and CFQ (Table 3).

Results

Predicting PTSD Symptom Severity

Our model predicted an average of 43% of the variance in PTSD symptom severity in novel subsets of patients ($R^2_{\text{avg}} = .43$ [$SD = 0.084$], $R^2_{\text{median}} = .44$, $p = .001$). When predicting PTSD symptom severity scores, a scale ranging from 0 to 80, our models were off by an average of 6.5 ± 0.55 points (mean absolute error [MAE]). As measured by the permutation feature importance, the predictors contributing to the most variance of the target feature were symptoms of anxiety (12.6%), dissociation (7.2%), negative trauma-related beliefs about others (6.0%), depression (4.7%), and emotion dysregulation (4.1%; Figure 1). Consistent with the permutation feature importance, the model-based feature importance indicated that the features enhancing accuracy the most were symptoms of anxiety (13.1), dissociation (7.7), negative trauma-related beliefs about others (6.4), depression (6.0), and emotion dysregulation (4.3). Information contained in the variables of trauma-related guilt and shame, biological sex, and age did not significantly aid in the prediction in these models in this context.

Predicting Functional Impairment

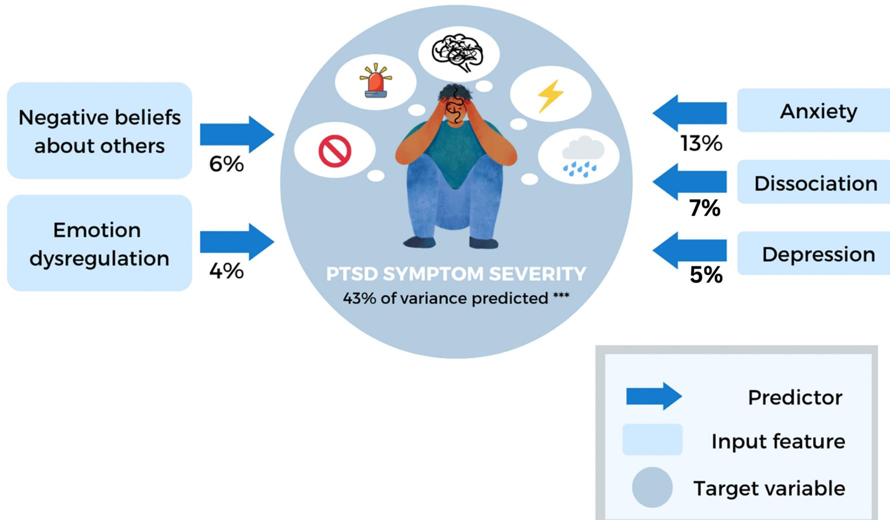
Our model predicted an average of 32% of the variance in functional impairment scores in novel subsets of patients ($R^2_{\text{avg}} = .32$ [$SD = 0.085$], $R^2_{\text{median}} = .33$, $p = .001$). When predicting functional impairment scores, a scale ranging from 12 to 60, our models were off by an average of 5.4 ± 0.39 points (MAE). The predictors contributing to the most variance in functional impairment scores, according to the permutation feature importance, were anxiety (8.1%), PTSD symptom severity (6%), cognitive dysfunction

Table 3
Features Included in Machine Learning Regression Models Predicting PTSD Symptom Severity and Functional Impairment

	PTSD symptom severity	Functional impairment
Input feature	Age	Age
	Biological sex	Biological sex
	Dissociation (depersonalization/derealization)	Dissociation (depersonalization/derealization)
	Emotion dysregulation	Emotion dysregulation
	Anxiety	Anxiety
	Depression	Depression
	Trauma-related guilt and shame	Trauma-related guilt and shame
	Negative beliefs about the world	Negative beliefs about the world
		Cognitive dysfunction
		PTSD symptom severity

Note. Dissociation = sum of the depersonalization and derealization subscales of the multiscale dissociation inventory; emotion dysregulation = difficulties in emotion regulation scale; anxiety = anxiety subscale of the DASS-21; depression = depression subscale of the DASS-21; trauma-related guilt and shame = composite score of the trauma-related guilt inventory and trauma-related shame inventory; negative beliefs about the world = negative cognitions about the world subscale of the posttraumatic cognitions inventory; cognitive dysfunction = cognitive failures questionnaire; PTSD symptom severity = PTSD checklist for *DSM-5*; PTSD = posttraumatic stress disorder; *DSM-5* = *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition); DASS-21 = depression, anxiety, and stress scale-21.

Figure 1
Summary of Most Important Features Predicting PTSD Symptom Severity, According to Permutation-Based Feature Importance



Note. PTSD = posttraumatic stress disorder. See the online article for the color version of this figure.
*** $p = .001$.

(5.8%), dissociation (2.9%), and depression (2.0%; Figure 2). Again, both permutation and model-based feature importance converged, such that the same features contributed most to the accuracy of our target feature: anxiety (5.5), PTSD symptom severity (4.5), cognitive dysfunction (3.2), dissociation (2.3), and depression (1.4). Information contained in the variables of emotion dysregulation, negative trauma-related beliefs about others, trauma-related guilt and shame, biological sex, and age did not significantly aid in the prediction in these models.

Discussion

The purpose of this study was to examine the extent to which clinically relevant variables predicted PTSD symptom severity and functional impairment using machine learning algorithms in a real-world clinical sample of adults seeking inpatient treatment for PTSD in Canada. Our machine learning models predicted PTSD symptom severity and functional impairment (e.g., difficulties with getting dressed, bathing, learning a new task, dealing with unfamiliar people, maintaining friendships, taking care of household responsibilities and self-care, etc.) with high accuracy. Our findings may help to inform personalized medicine approaches for PTSD in such contexts. Below, we expand upon the clinical implications of such findings.

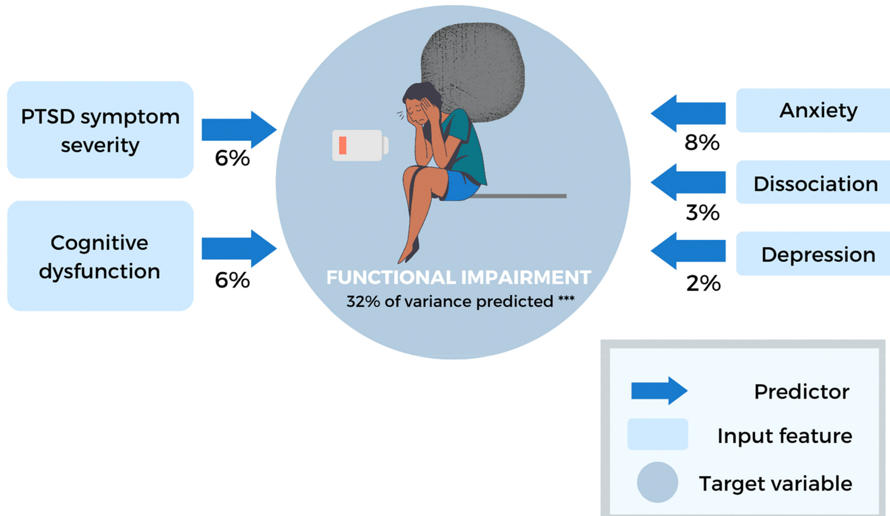
Predicting PTSD Symptom Severity

Symptom-based measures including anxiety, dissociation, depression, negative trauma-related beliefs about others, and emotion dysregulation, were most influential in making accurate predictions about PTSD symptom severity. Specifically, our model accurately predicted PTSD symptom severity scores within approximately 6.5 points on the PCL-5 (a scale ranging from 0 to 80) in a novel subset of patients. Anxiety and depression symptoms collectively predicted approximately 17% of the variance, adding to the literature demonstrating that they are associated with greater PTSD symptom severity (Knowles et al., 2019). This is in line with another machine learning study that classified PTSD cases using clinical symptom measures and blood biomarkers (Siegel et al., 2021). This group found that depression was an important predictor in classifying the clinical severity of PTSD, with 94% of individuals in the severe group experiencing current or lifetime depression, as compared to 64% among the group characterized by less severe PTSD (Siegel et al., 2021). Moreover, our findings point toward the particular importance of anxiety symptoms, relative to depression, in contributing to PTSD symptom severity. Anxiety and PTSD both share fear and avoidance of triggers, which may account, in part, for the greater contribution of anxiety symptoms than depression in predicting PTSD symptom severity. Furthermore, the DASS-21 anxiety subscale assesses physiological arousal and anxiety sensitivity, which is a core component of PTSD symptomatology. The fact that anxiety symptoms emerged as an important predictor in our model highlights how physiological reactivity and fear responses may play a key role in worsening PTSD symptoms.

Importantly, our finding that dissociation was an important predictor of PTSD symptom severity supports a growing body of literature on trauma-related dissociation. Dissociation has been associated with trauma memory fragmentation and disruptions in self-referential processes (Halligan et al., 2003; Huntjens et al., 2013; Kleim et al., 2008; Lanius et al., 2011), thereby significantly impairing the formation of an integrated and cohesive sense-of-self. These alterations may interfere with the contextualization of trauma-related memories and cues (i.e., in person, place, and time; Ehlers & Clark, 2000; Huntjens et al., 2013; Rothschild, 2009) and often disrupt bodily self-consciousness across the domains of time, thought, body, and emotions (Frewen & Lanius, 2015). Interestingly, a study by Halligan et al. (2003) found that dissociative experiences of emotional numbing, confusion and altered sense of time were highly predictive of chronic

Figure 2

Summary of Most Important Features Predicting PTSD Functional Impairment, According to Permutation-Based Feature Importance



Note. PTSD = posttraumatic stress disorder. See the online article for the color version of this figure.
*** $p = .001$.

PTSD. Rothschild (2009) contends that dissociation disrupts the ability to locate oneself in both time and place, which is required for self-awareness and self-reflection. The ability to elaborate on the traumatic event and assimilate it into one's narrative is likely also impeded by dissociation (Ehlers & Clark, 2000; Huntjens et al., 2013). This is clinically relevant, as the elaboration of trauma memories, experience of primary emotions related to the memory, and assimilation into one's narrative are the key goals of cognitive processing therapy (Resick et al., 2008). Currently, essentially all existing trauma-focused psychotherapies require an active approach toward trauma cues (i.e., recalling and examining the trauma memory and its associated triggers, emotions, thoughts, and behaviors). This is in direct opposition to trauma memory and emotion processing barriers facilitated by dissociative symptoms (i.e., involving detachment/derealization, depersonalization, emotional numbing, blunted arousal, and fragmented trauma memories). Taken together, our results further reinforce the notion that addressing dissociative symptoms is a critical step toward optimizing trauma recovery.

Negative trauma-related beliefs about others also predicted PTSD symptom severity. These beliefs are extreme assumptions about the world and other people that became cemented following the traumatic event(s) (e.g., "people can't be trusted," "you never know who will harm you," "the world is a dangerous place," "I can't rely on other people," etc.; Foa et al., 1999). Although these negative appraisals may instill a sense of control, safety, and predictability in the short-term, they are associated with avoidance of potential triggers, which may prevent fear extinction and maintain PTSD symptoms (see Bryant, 2019, for a review). Such beliefs can lead to isolation and an associated reduction in social support, which has been shown not only to be protective against the development of PTSD following trauma exposure but also to be beneficial for posttraumatic growth and recovery (Dai et al., 2016; Prati & Pietrantoni, 2009). Notably, empirically supported trauma-focused psychotherapies such as cognitive processing therapy and prolonged exposure either directly or indirectly target these catastrophic thoughts, with the aim to make them more accurate or adaptive (Foa et al., 2007; Resick et al., 2008).

Another important predictor of PTSD symptom severity was emotion dysregulation, which is characterized by difficulties with impulse control, emotional awareness, emotional clarity, accepting emotional experiences, engaging in goal-directed behavior, and accessing emotion regulation strategies (Gratz & Roemer, 2004). In line with our findings, a meta-analysis by Seligowski et al. (2015) reported that PTSD symptoms had the largest association with general emotion dysregulation, followed by rumination, thought suppression, and experiential avoidance. Powers et al. (2015) also found that difficulties obtaining emotional clarity and negative beliefs about being able to regulate their emotions were associated with greater PTSD severity. Our findings here confirm the notion that emotion dysregulation uniquely contributes to predicting PTSD symptom severity and may be an important target for intervention.

Interestingly, age, biological sex, and trauma-related guilt and shame collectively accounted for only 2% of the variance in our machine-learning models, despite being associated with PTSD symptom severity in statistical models (Badour et al., 2017; Bannister et al., 2019; Konnert & Wong, 2014; Olff, 2017). Dynamic factors (i.e., mental health symptoms), rather than biologically predisposed factors (i.e., sex and age), were most important in predicting the severity of PTSD symptoms in a novel subset of patients. To illustrate, women or older individuals may experience higher rates or severity of PTSD, but variable factors such as the severity of anxiety or dissociation (i.e., rather than by virtue of being a woman or of their age) appear more important in predicting whether they will experience greater mental health burdens in this context. Critically, however, more research is required to confirm whether trauma-related guilt and shame contribute to predictive accuracy of PTSD severity in machine learning models. It is possible that patients are experiencing high emotion dysregulation and thus have impaired awareness and clarity of trauma-related emotions (i.e., identifying or naming the emotion). This may lead to reduced reporting of trauma-related guilt and shame, despite the direct experience of these emotions.

Predicting Functional Impairment

Anxiety, PTSD severity, cognitive dysfunction, dissociation, and depression were most important in predicting functional impairment. Specifically, our model accurately predicted functional impairment scores within approximately 5.5 points on the WHODAS (a scale ranging from 12 to 60) in a novel subset of patients experiencing symptoms of PTSD. Emotion dysregulation, biological sex, trauma-related guilt and shame, age, and negative beliefs about the world did not add predictive value to our model (collectively accounted for less than 1% of variance). Although these variables have been linked to greater functional impairment across studies using statistical models, our results from machine learning analyses, which are better at making more accurate predictions based on such associations, found that other symptom measures were more influential.

As discussed above, it is not surprising that symptoms of anxiety and PTSD severity predicted functional impairment. This link has been extensively studied and supported (Knowles et al., 2019; Sareen et al., 2007). Our findings confirm the associations between anxiety, PTSD severity, and functional impairment, and further add to the literature, showing that symptoms of anxiety and PTSD symptom severity were the most important predictors of functional impairment (collectively predicting 15% of the variance). Again, anxiety emerged as an important predictor suggesting that physiological reactivity and fear responses in PTSD exacerbate day-to-day impairment. Our finding also confirms that cognitive dysfunction symptoms (e.g., forgetting appointments, accidentally throwing away the wrong items, starting one thing and becoming unintentionally distracted into doing something else) contributes to impaired day-to-day functioning among individuals experiencing PTSD. This is in line with previous studies that show self-reported cognitive dysfunction as being associated with psychological and emotional distress, symptoms of depression, as well as poor physical functioning (Donnelly et al., 2018; Stulemeijer et al., 2008).

Dissociation was another important predictor of functional impairment, confirming that dissociation is associated with a more severe illness presentation (Boyd et al., 2018; Lebois et al., 2021; Ozer et al., 2003; Park et al., 2021; Stein et al., 2013; Tanner et al., 2019). The core features of the dissociative subtype of PTSD are depersonalization and derealization, both of which involve a disconnect between the external physical environment and the intrapsychic experience. In this way, PTSD-related dissociation can be understood as a disorder of sensory integration (Scalabrini et al., 2020). Such interruptions in sensorimotor processing are demonstrated by the highly specific neural reorganization seen in dissociation and among those with PTSD and a history of childhood sexual and emotional abuse (Harricharan et al., 2020; Heim et al., 2013; Nicholson et al., 2016; Rabellino et al., 2018; Reinders et al., 2006). For example, patients in a state of dissociation from trauma memories experienced decreased sensorimotor reactivity (e.g., visual, auditory, olfactory, pain, etc.) and reduced regional cerebral blood flow to regions associated with somatosensory awareness (Reinders et al., 2006). Much like dissociation, poor sensory processing has also been hypothesized to impair adaptive behaviors such as cognitive and physiological self-control, self-other processing, cooperation, and well-being (Acevedo et al., 2018). Our finding highlights the importance of paying particular attention to individuals with heightened dissociation, as they not only experience more severe PTSD symptoms, but may also experience significant impairments in activities of daily living.

Symptoms of depression also contributed to functional impairment in our study. In addition to anhedonia, depressive symptoms include fatigue, hopelessness, sense of worthlessness, and lack of future-oriented thinking (APA, 2013). Given that these symptoms can facilitate PTSD-related avoidance and exacerbate existing difficulties in engaging in self-care or previously enjoyed activities among those with PTSD, the consideration of comorbid depression will be important for improving overall life functioning.

Implications and Clinical Applications

Currently, treatment planning for trauma-related disorders typically involves a categorical approach, with standardized intervention protocols assigned to those diagnosed with a trauma- and stressor-related disorder. This approach focuses on the presence or absence of a mental health diagnosis rather than the heterogeneity of symptom patterns among individuals. Critically, however, the consideration of unique symptom profiles at the individual level will be important for maximizing treatment gains. This is illustrated by Cloitre et al.'s (2012) study, where women with childhood abuse-related PTSD were randomly assigned to one of three types of sequential treatment that involved: (a) improving emotion regulation and interpersonal functioning, followed by a modified version of prolonged exposure; (b) improving emotion regulation and interpersonal functioning, followed by supportive counseling; or (c) supportive counseling, followed by a modified version of prolonged exposure. Here, improvements in PTSD symptoms were the greatest among women receiving the first type of treatment, where those with higher baseline levels of dissociation showed faster and greater improvements in both dissociation and PTSD symptoms. These results suggest that the combination of trauma-focused therapy, with sessions targeting emotion regulation and interpersonal functioning, can significantly benefit individuals with PTSD, particularly when they present with severe dissociation (Cloitre et al., 2012). Taken together with the results of the current study, this body of evidence points clearly toward the importance of matching specific clinical symptom profiles with tailored evidence-based interventions.

Our work highlights further how the consideration of heterogeneous symptom presentations can help identify a targeted intervention approach that best suits an individual's needs. Existing trauma-focused therapies target negative appraisals and extinguish fear responses using an active approach toward processing trauma memories, which are beneficial for trauma recovery (Bisson et al., 2007; Lee et al., 2016). However, our findings that anxiety and emotion dysregulation predict greater illness severity highlight the potential importance of scaffolding these existing interventions with skills that improve physiological and emotional regulation. These skills can be found in evidence-based interventions such as dialectical behaviour therapy, acceptance and commitment therapy, and mindfulness-based cognitive therapy, which may provide additional benefit for clients with heightened physiological reactivity and emotion dysregulation (Goldberg et al., 2018; Hayes et al., 1999; Lynch et al., 2007). For example, dialectical behaviour therapy, originally tailored to treat borderline personality disorder, includes specific modules for building emotion regulation, distress tolerance, and mindfulness skills (Lynch et al., 2007). It has since been adapted for PTSD and shown to significantly reduce dissociation symptoms, emotion dysregulation, self-harming behaviors, and improve PTSD symptom remission (Bohus et al., 2013, 2020).

Critically, dissociation emerged as a potential target for intervention in reducing both PTSD symptom severity and functional impairment. Dissociation has been shown to interfere with sensory-motor integration and bodily self-consciousness across the domains of time, thought, body, and emotions (Frewen & Lanius, 2015). A sense of disembodiment can also arise, in which an individual experiences a disconnection from their hands and feet or a lack of boundary around one's body (Blanke & Arzy, 2005; Schimmenti & Caretti, 2016; van der Kolk et al., 2016; Warner et al., 2014). As such, those with chronic trauma and symptoms of dissociation may benefit from sensory-based approaches that facilitate bodily awareness and target traumatic memories through bottom-up processing (Kaiser et al., 2010; McGreevy & Boland, 2020). Specifically, approaches that involve improving embodiment, awareness, reflection, and regulation of the self in time and place (such as therapies that target dysregulated brain regions in dissociative PTSD patients) may be helpful (Frewen & Lanius, 2015; McGreevy & Boland, 2020; Warner et al., 2014, 2020). In a safe and controlled environment, this might be done through body scans that build awareness of one's body in the present moment, grounding exercises that engage the five senses, and attending to the present moment (Frewen & Lanius, 2015; McGreevy & Boland, 2020). For instance, sensory motor arousal regulation treatment, which focuses on strengthening bottom-up processing (i.e., awareness, regulation, and integration of somatosensory experiences), has been shown to reduce somatic, depression, and anxiety symptoms, as well as PTSD-related hyperarousal (Warner et al., 2014, 2020). Relatedly, sensory integration treatment among traumatized individuals has been associated with improvements in affect and impulse regulation, as well as negative self-perceptions such as believing oneself as helpless or ineffectual (Kaiser et al., 2010). Given that improved sensory processing is intrinsically tied to emotion processing and adaptive engagement with the environment (Gogolla, 2017; Straube & Miltner, 2011), sensory-based therapies may be a strong candidate for improving symptoms of PTSD with elevated dissociation.

Finally, novel adjunctive treatments tailored to regulate the neural mechanisms associated with specific PTSD symptom profiles may be beneficial for improving treatment outcomes. For example, neurofeedback is a noninvasive method by which individuals can learn to regulate brain signals associated with unique symptom presentations in real time through biofeedback (i.e., with functional magnetic resonance imaging or electroencephalography; Nicholson et al., 2022; Ros et al., 2014; van der Kolk et al., 2016). Randomized controlled trials of novel adjunctive treatments such as neurofeedback also show that polytraumatized adults with chronic PTSD show significant reductions in PTSD symptom severity, emotion dysregulation, and identity impairment following neurofeedback training, as compared to waitlist-controls (Gapen et al., 2016; van der Kolk et al., 2016). Such interventions may be particularly useful among those individuals who may be too anxious, dissociated or emotionally dysregulated to tolerate exposure-based treatments or trauma-focused psychotherapies (van der Kolk et al., 2016). Moreover, given that dissociative versus nondissociative PTSD has been shown to be related to opposing neural substrates of emotion over- and undermodulation (Lanius et al., 2010; Nicholson et al., 2019), treatment interventions such as neurofeedback that can target unique neural mechanisms associated with specific symptom profiles (i.e., dissociation, emotion dysregulation, anxiety, depression) may be beneficial for reducing PTSD symptoms within this highly heterogeneous disorder. Thus, scaffolding trauma-focused therapy with skills that regulate emotional and physiological arousal (i.e., via bottom-up approaches that anchor patients in person, place, and the present moment) may provide a more stable foundation from which patients can begin to effectively engage, examine, process, and integrate their trauma-related memories into a coherent narrative (i.e., via top-down cognitive approaches of trauma memory processing; Kaiser et al., 2010).

Limitations and Future Directions

Our data were cross-sectional such that we could not draw conclusions about any changes in symptoms over time or the outcome of a specific intervention. Leveraging machine learning algorithms to predict symptom-based changes throughout and after the completion of trauma-focused interventions will be a key step toward identifying variables that predict treatment response at the individual level. Patients in our study were also asked to identify their biological sex from a binary category at the time the questionnaires were administered. In future studies, it will be critical to examine the roles of diverse sex and gender, ethnic, and racial identities. They may also consider investigating resiliency factors (i.e., perceived social support, cognitive flexibility, self-efficacy, etc.; Gallagher et al., 2020; Kashdan & Rottenberg, 2010; Lee, 2019; Richardson & Jost, 2019) in predicting PTSD symptom severity and functional impairment. Although it was not possible to examine the effect of problematic alcohol use in our models, it would be fruitful to conduct studies that can disentangle the role that substance use plays in predicting trauma-related outcomes, given that higher rates of alcohol and substance use have been associated with PTSD, depression symptoms, negative emotionality, and childhood trauma (Brady & Back, 2012; Brady et al., 2019; Greene et al., 2016). Additional research will be needed to elucidate how guilt and shame interact with trauma-related variables such as emotion dysregulation and the type of traumatic event exposure (Bannister et al., 2019). It will also be important for future machine learning studies to assess the extent to which childhood abuse and neglect predicts these outcomes. Finally, variables that were not able to be assessed in the current study may be considered in future studies, such as the type and severity of traumatic event(s), medical and psychiatric comorbidities, including sleep problems (Dewar et al., 2020; Miles et al., 2022).

Conclusion

This was the first study to utilize machine learning algorithms to predict PTSD symptom severity and functional impairment in a clinical sample of adults seeking treatment for PTSD. Our machine learning models predicted PTSD symptom severity and functional impairment with high accuracy in a novel subset of patients, accounting for 43% and 32% of their respective variances. Specifically, our models accurately predicted PTSD symptom severity scores within approximately 6.5 points (a scale ranging from 0 to 80), and functional impairment scores within approximately 5.5 points (a scale ranging from 12 to 60). This study highlights the clinical utility of machine learning methods in uncovering unique contributors of mental illness burdens and potential targets for their interventions. Dissociation emerged as an important predictor in both models, indicating that dissociative symptomatology may be a critical target for trauma-based interventions. Moreover, our results point to the importance of targeting maladaptive trauma appraisals, cognitive dysfunction, and emotion dysregulation in order to decrease the severity of trauma-related illness.

Critically, the consideration of unique symptom profiles of individuals with PTSD will help guide tailored treatment plans to maximize trauma recovery. In addition to existing trauma-focused therapies that facilitate top-down processing of traumatic memories, individuals with PTSD may further benefit from bottom-up approaches (i.e., emotional and physiological regulation strategies) as well as novel adjunctive treatments such as neurofeedback training, particularly when they present with high clinical severity. Overall, this research demonstrates that machine learning models are a powerful tool for elucidating the complex associations between trauma-related symptoms, and for informing a personalized medicine approach in a highly heterogenous psychiatric disorder such as PTSD.

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