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Concurrent Treatment for Posttraumatic Stress Disorder and Alcohol Dependence: Predictors and Moderators of Outcome

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Abstract

Objective—The present study examined predictors and moderators of treatment response among 165 adults meeting DSM-IV criteria for comorbid posttraumatic stress disorder (PTSD) and alcohol dependence (AD) who were randomized to 24 weeks of naltrexone (NAL), NAL and prolonged exposure (PE), pill placebo, or pill placebo and PE. All participants received supportive counseling for alcohol use.

Method—Six domains of predictors/moderators (23 variables) were evaluated using measures of PTSD (Posttraumatic Stress Symptom Scale Interview; PSS-I) and AD (percent days drinking from the Timeline Follow-Back Interview) collected every four weeks throughout treatment. Multi-level modeling using the Fournier approach was employed to evaluate predictors and moderators of rates of symptom improvement and post-treatment outcomes.

Results—Combat trauma, sexual assault trauma, and higher baseline anxiety sensitivity predicted slower improvement and poorer PTSD outcome. Combat trauma, white race, and higher baseline drinking severity predicted poorer drinking outcome. PTSD severity moderated the efficacy of PE on PTSD outcomes, such that the benefit of PE over no-PE was greater for participants with higher baseline PTSD severity. Baseline depressive severity moderated the efficacy of PE on drinking outcomes, whereby the benefit of PE over no-PE was greater for participants with higher depressive symptoms. NAL effects were most beneficial for those with the longest duration of alcohol dependence.

Conclusions—These results suggest that concurrent, trauma-focused treatment should be recommended for PTSD-AD patients who present with moderate or severe baseline PTSD and depressive symptoms. Future research should examine the mechanisms underlying poorer outcome among identified sub-groups of PTSD-AD patients.

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Keywords

prolonged exposure; posttraumatic stress disorder; alcohol dependence; naltrexone; predictors; moderators

Posttraumatic stress disorder (PTSD) and alcohol dependence (AD) are highly co-morbid, with nearly half (42%) of individuals with PTSD also meeting criteria for an alcohol use disorder (Pietrzak, Goldstein, Southwick, & Grant, 2011). Despite this co-occurrence, empirical guidelines regarding treatment of this distressed population are woefully limited. Individuals with co-morbid PTSD and AD show greater severity on both PTSD and alcohol measures (Blanco et al., 2013; Brown, Stout, & Mueller, 1999; Kessler, 2000; Ouimette, Brown, & Najavits, 1998; Ouimette, Goodwin, & Brown, 2006) and relapse sooner following alcohol use treatment than patients with other psychiatry comorbidities (Ouimette, Ahrens, Moos, & Finney, 1997). These findings underscore the importance of identifying effective interventions that address PTSD and alcohol dependence (AD) concurrently.

Exposure-based cognitive behavioral therapies (CBT) are recommended as a front-line treatment for PTSD (Institute of Medicine, 2007), with prolonged exposure (PE) gaining the most empirical evidence for its efficacy (see for review: Cahill, Rothbaum, Resick & Follette, 2009). A growing number of studies support the use of exposure-based CBT for co-morbid substance dependence and PTSD, either in addition to traditional alcohol treatments or as an integrated component (Mills et al., 2012; Najavits, Schmitz, Gotthardt, & Weiss, 2005; Triffleman, 2000). Only two randomized controlled trials (RCTs) have looked specifically at PTSD and AD. Sannibale et al. (2013) compared an integrated PTSD-AD treatment that included in-vivo and imaginal exposure to address PTSD symptoms (n = 33) to an AD-only treatment that did not address PTSD symptoms (n = 29). At follow-up, participants who received exposure sessions were twice as likely to achieve clinically significant change in PTSD symptoms. Participants who received AD-only treatment showed superior drinking outcomes; however, the authors note that this finding was confounded by significantly greater use of additional alcohol-related treatment services during follow-up in the AD-only group. In a larger RCT (n = 165), Foa et al. (2013) examined the efficacy of the opioid antagonist naltrexone (NAL) for alcohol dependence and prolonged exposure therapy (PE) for PTSD. Participants received supportive counseling focusing on alcohol use and were randomized to NAL, NAL and PE, pill placebo, or pill placebo and PE. All four groups showed large reductions in both alcohol use and PTSD symptoms. NAL was associated with a lower percentage of days drinking than placebo, and PE was associated with lower rates of relapse over the follow-up period, especially when combined with NAL. The results of this study suggest that concurrent treatment is not only safe, but also may be of particular benefit to individuals with both disorders to promote long-term maintenance of treatment gains.

Research is needed to determine what factors best predict response to concurrent PTSD-AD treatment and whether moderators can be used to inform treatment selection. Indeed, the examination of predictors and moderators is central to the goal of individualizing treatment (Kazdin, 2007). Non-specific *predictors* refer to baseline characteristics that are associated

with symptom change, irrespective of the treatment used (i.e., not specific to one treatment or another; Kraemer, Wilson, Fairburn, & Agras, 2002). Non-specific predictors can thus be used to identify treatment refractory patients that may require refined or augmented interventions. In the context of clinical trials, *moderators* refer to characteristics that predict differential response to one treatment over another. Thus, as noted by Kraemer, Frank, and Kupfer (2006), moderator research helps us understand which treatments work best for which patients, and has important implications for clinical decision-making.

Studies that have investigated the relationship between PTSD treatment response and demographic and psychological baseline characteristics have produced inconsistent results. Several studies have linked lower income and education to drop out in CBT for PTSD (Difede et al., 2007; Rizvi, Vogt, & Resick, 2009). Isolated studies show poorer outcomes among men (Karatzias et al., 2007) and those who live alone (Tarrier, Sommerfield, Pilgrim, & Faragher, 2000). No studies to our knowledge have shown an effect of race or ethnicity on PTSD treatment outcome, although black racial membership has been associated with higher risk of drop out in CBT for anxiety disorders (Chambless & Williams, 1995). Among clinical characteristics, initial PTSD severity has predicted poorer outcome in some studies (Karatzias et al., 2007; Taylor et al., 2001; Van Minnen, Arntz, & Keijsers, 2002) but not in others (Foa, Riggs, Massie, & Yarczower, 1995; Forbes, Creamer, Hawthorne, Allen, & McHugh, 2003). Likewise, some studies have identified comorbid depression as a predictor of poorer outcome (Forbes et al., 2003; Taylor et al., 2001) while others have found no relationship between depressive symptoms and outcome (Hagenaars, van Minnen, & Hoogduin, 2010; Karatzias et al., 2007), and one study found higher depressive symptoms to predict better outcome (Rizvi et al., 2009). Research on moderators of PTSD outcome among different treatment options is scarce, in part because traditional moderator analyses require large sample sizes to ensure adequate power.

The most consistent predictors of alcohol treatment outcome are baseline alcohol consumption and dependence severity (see for review: Adamson, Sellman, & Frampton, 2009). With respect to NAL efficacy, high levels of baseline alcohol craving have been found to moderate the effects of NAL versus placebo in some studies (Jaffe et al, 1996; Monterosso et al., 2001; Volpicelli, Clay, Watson, & O'Brien, 1995). In contrast to craving, high risk alcohol consumption and regular drinking patterns at baseline have been associated with poorer NAL response when provided in combination with cognitive behavioral therapy (Vuoristo-Myllys, Lipsanen, Lahti, Kalska, & Alho, 2014). Some studies have found high baseline depression to predict better response to NAL (Kiefer et al., 2005), while others have reported the inverse (Morley et al., 2006; Morley, Teesson, Sannibale, Baillie, & Haber, 2010). Finally, among demographic predictors, NAL has been found to be more effective than placebo for men but not women in some studies (Garbutt et al., 2005; Hernandez-avila et al., 2006), but not others (Baros, Latham, & Anton, 2008; Morley et al., 2010). The very mixed picture that emerges regarding predictors of AD and PTSD outcome may be due to variable methodologies and trauma samples across studies, as well as limitations in the statistic approaches employed – which have typically been hierarchical regressions co-varying for a small number of putative confounding variables (e.g., baseline severity).

The present study used data from a randomized controlled trial (Foa et al., 2013) to evaluate predictors and moderators of treatment improvement during concurrent treatment of AD and PTSD. To this end, we adopted an advanced analytic approach developed by Fournier (Fournier et al., 2009) that has been employed in recent predictor research (e.g., Amir et al., 2011; Powers et al., 2014; Smits et al., 2013). The present analysis differs from much of the previous research in several ways: First, multilevel modeling (MLM) was employed rather than multiple regression. Since MLM retains all subjects regardless of missing data, it is more powerful and does not require imputation of outcome data. Second, the Fournier approach to moderator analyses allows for the simultaneous entry of numerous putative predictors and moderators, thus providing a relatively thorough array of control variables, to ensure that predictors/moderators that are significant are not better accounted for by other correlated constructs. Third, the present study uses monthly assessment time points to test for the impact of baseline predictors/moderators on both post-treatment outcomes and rates of change during treatment. Variables of interest were grouped into six categories: demographics, socio-economic factors, comorbid psychopathology, trauma features, PTSD features, and AD features. In addition to PTSD features common to the literature (e.g., trauma type; PTSD duration), we have included anxiety sensitivity as a PTSD feature, given evidence that anxiety sensitivity is highly correlated with PTSD diagnosis and symptom severity (Federoff, Taylor, Asmundson, & Koch, 2000; Taylor, Koch, & McNally, 1992). No previous investigations, to our knowledge, have assessed moderators and predictors of drinking and PTSD outcomes in a comorbid sample.

Methods

Participants

Table 1 presents participant baseline characteristics. Participants (n = 165) were adults meeting DSM-IV criteria for current AD and PTSD who were enrolled in a randomized, single-blinded clinical trial at the University of Pennsylvania's Center for the Treatment and Study of Anxiety and the Philadelphia Veterans' Affairs Hospital. Exclusion criteria were: 1) current substance dependence other than nicotine or cannabis, 2) current psychotic disorder (e.g., bipolar disorder, schizophrenia), 3) active suicidal or homicidal ideation, 4) opiate use in the month prior to study entry, 5) medical illnesses that could interfere with treatment (e.g., AIDS, active hepatitis), or 6) pregnancy or nursing. At baseline, the average PSS-I score was 28.5 (SD=6.5), indicating moderately severe PTSD, and mean percentage days drinking over the preceding month was 74.8%.

Procedure

Potential participants completed an intake assessment comprised of a psychiatric evaluation, physical examination, and laboratory assessments. All participants meeting study eligibility criteria completed outpatient detoxification (defined as 3 or more consecutive days of alcohol abstinence as measured by self-report and breathalyzer testing) prior to randomization. Oxazepam was administered as needed to patients who presented during detoxification with elevated withdrawal symptoms requiring medical management, and to those deemed to be high risk for poor response based on a history of elevated withdrawal symptoms. Eligible participants were then consented and randomly assigned to 1 of 4

treatment conditions: NAL + PE, placebo + PE, NAL + no PE, or placebo + no PE. Patients in all conditions received concurrent supportive counseling focusing on alcohol use and medication management. During treatment, blind assessments and self-report questionnaires were completed every four weeks (from week 0 to week 24). All study procedures were approved by the University of Pennsylvania institutional review board.

Measures

Structured Clinical Interview for DSM-IV (SCID-IV; First & Gibbon, 2004)—The SCID is a 60-minute, semi-structured interview that yields current and lifetime DSM-IV Axis I diagnoses for the major psychiatric disorders. The SCID was used to confirm diagnosis of AD and PTSD and to evaluate the presence of other Axis I disorders at baseline and post-treatment. This interview is a widely used and reliable measure of psychopathology, with joint inter-rater reliability coefficients ranging from 0.60 to 0.83, depending on the disorder (Lobbestael, Leurgans, & Arntz, 2010).

The Psychiatric Research Interview for Substance and Mental Disorders (PRISM; Hasin et al., 1996) is a semi-structural interview used to assess disorders that are commonly co-morbid with substance use disorders. In the current study, the PRISM was used to assess for the presence of anti-social personality disorder and borderline personality disorder. The PRISM has shown good diagnostic validity for Axis II personality disorders, high concordance with other established diagnostic measures such as the SCID-II, good-excellent internal consistency, and good inter-rater reliability (κ=0.66-0.75) for the disorders assessed in the current study (Hasin et al., 2006; Torrens, Serrano, Astals, Pérez-Domínguez, & Martín-Santos, 2004).

PTSD Symptom Scale Interview (PSS-I; Foa, Riggs, Dancu, & Rothbaum, 1993)—The PSS-I is a 17-item clinician-rated interview that assesses the severity of PTSD symptoms according to DSM-IV criteria over the preceding two weeks. The PSS-I yields a total score with a possible range from 0 to 51, with higher scores indicating more severe PTSD symptoms. A psychometric study of this measure using the current sample (Powers, Gillihan, Rosenfield, Jerud, & Foa, 2012) demonstrated excellent internal consistency (e.g., α=.90 for the full scale), very good one-month test-retest reliability (r=.80), good inter-rater reliability (ICC=0.73 for total severity score), and good convergent validity with SCID-IV PTSD diagnoses (κ=.75).

Timeline Follow-Back Interview (TFBI; Sobell & Sobell, 1992)—The TFBI interview utilizes a calendar method to assess for frequency and degree of alcohol consumed on a daily basis. In the current study, the TFBI provided information about the percentage of days over the past month spent drinking (PDD). The TLFB has demonstrated good test-retest reliability (α=.79-.94) and concurrent validity (r=.84-.95 with collateral reports of drinking) (Maisto, Sobell, & Sobell, 1982; Sobell, Maisto, Sobell, & Cooper, 1979).

The Penn Alcohol Craving Scale (Flannery, Volpicelli, & Pettinati, 1999)—The Penn Alcohol Craving Scale is a 5-item self-report measure that assesses degree of alcohol craving during the preceding week. The total scores on this measure range from 0 to 30,

with higher scores indicative of higher craving. The PACS has excellent reliability (α=.92), high item-total correlations (*r*=.80-.92), and good concurrent validity (*r*=.55) with the Obsessive Compulsive Drinking Scale (Modell, Glaser, Mountz, Schmaltz, & Cyr, 1992), another validated measure of alcohol craving. Cronbach's alpha in the current sample was . 91.

Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986)—The ASI assesses for fear of anxiety-related sensations and beliefs about the negative consequences of anxiety. The scale consists of 16 items rated on a 5-point Likert Scale which yield a total score ranging from 0 to 64. The ASI has strong documented psychometric properties including good discriminant and predictive validity (Taylor, Koch, & Crockett, 1991), adequate test-retest reliability and good internal consistency (Reiss et al., 1986). Cronbach's alpha in the current sample was .92.

Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996)—The BDI-II is a well validated and widely used measure of depressive symptoms. The BDI-II consists of 21 items scored on a 4-point Likert scale (0-3), resulting in a total score ranging from 0 to 63, with higher scores indicating higher levels of depressive symptoms in the past week. Cronbach's alpha in the current sample was .92.

Treatments

Prolonged Exposure (PE)—PE consisted of 18-sessions provided over 24 weeks (12 weekly sessions following by 6 bi-weekly sessions). Each session was 90 minutes long and contained the key components of PE: imaginal exposure (repeated revisiting of traumatic memories), processing (discussing thoughts and feelings arising from the recounting of the trauma memory), and assignment of in-vivo exposure (confronting trauma-reminders in daily life). PE was provided by doctoral-level psychologists. Overall treatment adherence rate, assessed using a random sample (15%) of video-recorded sessions, was 96%. Participants completed a mean of 6.18 (SD = 3.86) exposure sessions in the PE + NAL group and 6.48 (SD = 3.49) sessions in the PE + placebo group (*p*=0.73).

Naltrexone—Naltrexone is an opiate antagonist treatment for AD approved by the U.S. Food and Drug Administration. Participants were started on 50 mg/d for a minimum of three days and titrated within one week to the target dose of 100 mg/d. Compliance was assessed via weekly pill counts in the first 3 months and biweekly counts for the next 3 months. Most participants tolerated this dosing regimen; a small number (N=3) were titrated back down to 50 mg/d due to side effects.

Supportive Counseling—All participants received 18, 30-40 minute sessions of supportive counseling using the BRENDA model (Starosta, Leeman, & Volpicelli, 2006), which consisted of medication management combined with techniques aimed at enhancing compliance through motivational interviewing (Miller & Rollnick, 1991). Specifically, these sessions entailed the dispensation of medication, compliance monitoring, education regarding AD, and support/advice around drinking. BRENDA sessions were conducted by the study nurse and were provided on the same schedule as PE sessions. Eighty five percent

of the sample met criteria for adherence to medication and supportive counseling (i.e., ≥80% adherence and attendance).

Treatment Retention—Fifty three (32.1%) participants dropped out of the study. Dropout rates did not significantly differ across treatment groups (χ^2_3=1.55; *P* =.67).

Data Analysis

The Fournier approach (see Amir et al., 2011; Fournier et al., 2009; Smits et al., 2013) was employed to identify significant predictors and moderators of change in PTSD symptoms (PSS-I) and percentage days drinking (PDD) across treatment. In this approach, potential predictors/moderators are grouped into domains of related variables (e.g., a demographics domain, a comorbid disorders domain, etc.). Significant predictors/moderators are identified within each domain, and then the significant predictors/moderators from each domain are all entered into a final model. Grouping predictors into domains from which significant predictors are identified and entered into a final model allows the investigation of a large number of predictors without substantially increasing either Type I or Type II error. Type I error is minimized because variables are identified that are predictive over and above others in their domain, and over and above significant predictors from the other domains. Type II error is minimized because the moderation analysis does not include all potential predictors/ moderators in a single, very large model. Multilevel modeling (MLM), an intent-to-treat analysis, was used to analyze PSS-I scores and PDD, which were collected every 4 weeks from baseline to post-treatment (week 24).

Putative predictors and moderators were grouped in six domains: 1) demographics (age, gender, white vs. minority race), 2) socio-economic factors (co-habitation status, employment status, education level, income),3) comorbid disorders (number of comorbid Axis I disorders, presence vs. absence of additional substance use disorders, presence vs. absence of a personality disorder, depressive symptom severity), 4) trauma features (index trauma type [sexual assault, combat, physical assault, other trauma], number of other traumatic events), 5) PTSD features (baseline PSS-I, age of trauma onset, PTSD duration, anxiety sensitivity), and 6) alcohol features (baseline percentage days drinking, craving, age of AD onset, duration of AD). Post-hoc power analyses were performed for the final model using the program PinT 2.12 (Power in Two-Level Models; Snijders & Bosker, 1993). This model included 27 predictors, but had 1003 data points from 165 participants. PintT indicated greater than a .95 power to detect a medium effect size for a moderator or predictor.

The stepwise Fournier procedure for each domain was conducted as follows: In Step 1, all potential moderator variables *within* the domain are included in the analysis. In Step 2, only the variables with a significance level $p<.20$ in Step 1 are included in a second MLM analysis. Step 3 includes all terms from Step 2 that were $p<.10$. The analysis in Step 4 is then comprised of the terms from Step 3 that were significant at $p<.05$. This stepwise procedure using these a priori criteria is performed for each domain of predictors, and identifies significant predictors/moderators from each domain. Then, each term that is significant at $p<.05$ in Step 4 from each domain is included in the final MLM model,

allowing the testing of the effects of each variable while controlling for the effects of the other variables. Variables coding treatment condition and the interactions of treatment condition and Time were included in all MLM models regardless of their significance level. Since treatment condition was comprised of a PE main effect (PE), NAL main effect (NAL), and their interaction, the treatment condition variables that were included in all models were: PE, NAL, PE × NAL, Time, PE × Time, NAL × Time, and PE × NAL × Time. Subcomponents of interactions that were included in Step 4 were also necessarily included in the final model. For example, if the combat trauma × PE × Time interaction was significant in Step 4 of the trauma features domain, its subcomponents (Combat, Combat × Time, and Combat × PE) were also included in the final model (the other subcomponents, PE, Time, and PE × Time, were included in all analyses).

To investigate moderators, we added each potential moderator and its interactions with the treatment condition and Time variables. To understand the nature of the moderator interactions that were found to be significant, we followed the approach developed by Aiken and West (1991), calculating the effect of the treatments at high and low levels of the moderator (usually defined as 1 SD above and 1 SD below the mean, respectively). This technique, which uses all the data in the MLM model to calculate model predicted parameters for different levels of the moderator, allows one to understand how the relationship between treatment and outcome varies for high and low values of the moderator.

As reported previously (Foa et al., 2013), PSS-I and PDD decreased rapidly over time and then leveled off in this study sample. Foa et al. found that, for PSS-I, the change over time was modeled most accurately by using the log of time. Thus, our Time variable for the analysis of PSS-I was ln (week+1). For PDD, the change over time was most accurately modeled by a hyperbolic function. Thus, our Time variable in the PDD analysis was coded as: (1-1/[week+1]). We then centered the Time variable at post-treatment. All variables in the models were converted to z-scores to facilitate comparison among them and to center them at their means for the interactions.

Five of our variables of interest were missing greater than 5% of their data: income (7%), alcohol craving (13%), depressive symptoms (15%), anxiety sensitivity (18%), and presence of a personality disorder (28%). To avoid dropping cases, multiple imputation was employed to impute the missing moderators. Twenty datasets were imputed using the multiple imputation routine in SPSS 21.0. All MLM analyses were then performed on all 20 datasets. The results from these analyses were “pooled” statistically across the 20 datasets according to the appropriate algorithm in SPSS 21.0.

Results

Missing Data

Because MLM assumes that data is missing at random, we examined whether participants who had missing outcome data at some assessments differed from those for whom we had complete data. A MANOVA examining differences on our continuous measures at baseline (e.g., anxiety sensitivity, depressive symptoms, PTSD symptoms, age, etc.) showed no

differences between those with and without missing data (p=.89). Similarly, Fisher Exact Tests showed that there were no differences between the groups on any of the baseline dichotomous measures (e.g., gender, ethnicity, cohabitation, etc.), ps>.21. Thus, there was no evidence that those with no missing data differed from those with missing data at baseline.

Predictor and Moderator Analyses for PTSD Outcome (PSS-I)

Below we report the statistics for all significant predictors identified in Step 4 of each domain, followed by statistics for the variables that remained significant in Step 4 of the final model. A number of complex interactions were significant in the analyses of separate domains but were no longer significant when combined with other variables in the final model. Since these interactions were non-significant when fully controlling for all other variables of interest, we present these interactions in Step 4 of each domain but do not discuss the direction of effects in detail until they are verified as significant in the final model.

Stepwise Analyses within each Domain

Demographics: The only variable from the Demographic domain that was significant in Step 4 was age. There was a significant PE × NAL × age interaction, b=-1.60, t(171)=2.44, p=.015 (as stated above, the form of interactions are only discussed if they are significant in the final model, and are only discussed under the “Final Model”). No other Demographic variables were significantly related to PSS-I.

Socio-economic Factors: Step 4 of the Socio-economic Factors domain showed that participants who were employed had lower PSS-I scores at post-treatment than those who were not employed, b=-2.20, t(157)= -3.96, p<.001. No other socio-economic variable was significantly related to PSS-I.

Comorbid Disorders: Step 4 of the Comorbid Disorders domain indicated that depressive symptoms moderated the PE × NAL × Time interaction, b=.55, t(115)=2.02, p=.043.

Trauma Features: Step 4 of the Trauma Features domain indicated that those who had trauma due to sexual assault improved more slowly during treatment than those who had other types of trauma, b=.79, t(135)=2.79, p=.005, and they had higher PSS-I at post-treatment, b=2.19, t(144)=2.51, p=.012. Step 4 of this domain also showed a significant combat trauma × PE × Time interaction, b=.62, t(138)=2.18, p=.029.

PTSD Features: Step 4 of the PTSD Features domain showed that higher anxiety sensitivity was related to slower rates of improvement in PSS-I over time, b=.78, t(594)=3.59, p<.001, and to higher post-treatment PSS-I scores, b=2.05, t(188)=3.45, p=.001. In addition, baseline PSS-I was a moderator of the PE × NAL × Time interaction, b=.47, t(603)=2.34, p=.019.

Alcohol Features: Step 4 of the Alcohol Features domain showed that those with higher baseline alcohol craving had higher post-treatment PSS-I scores, b=1.69, t(129)=3.29, p=.001. Also, Step 4 revealed a significant duration of AD × NAL × Time interaction, b=-.62,

t(110)=-2.21, *p*=.027, along with a similar duration of AD × NAL interaction affecting PSS-I scores at post-treatment, *b*=-1.96, *t*(117)=-2.27, *p*=.024.

Final Model for PSS-I—The final model included the simultaneous entry of the predictor and moderator variables found to be significant in Step 4 of the previous sets of analyses (plus the treatment condition and Time variables, and their interactions). Results from the final model are presented in Table 2 and Figures 1 and 2.

Step 4 of the final model showed that participants receiving PE had faster rates of improvement and lower PSS-I at post-treatment than those not receiving PE, *b*=-.98, *t*(498)=-5.00, *p*<.001, and *b*=-2.65, *t*(154)=-4.92, *p*<.001, respectively. There were no significant effects for NAL (*ps*>.10) nor for the PE × NAL interaction (*ps*>.18).

Predictors: Three variables were significant predictors of PSS-I, regardless of treatment condition: sexual assault trauma, combat trauma, and baseline anxiety sensitivity. Sexual assault, combat trauma, and higher anxiety sensitivity were all associated with slower rates of improvement during treatment and with higher levels of PSS-I at post-treatment: for sexual assault trauma, *b*=.75, *t*(488)=3.71, *p*<.001 and *b*=2.53, *t*(146)=4.56, *p*<.001 for the slope and post-treatment effects, respectively; for combat trauma, *b*=.54, *t*(499)=2.68, *p*=.007 and *b*=1.81, *t*(155)=3.24, *p*=.001; and for anxiety sensitivity: *b*=.81, *t*(482)=3.76, *p*<.001 and *b*=2.13, *t*(144)=3.78, *p*<.001.

Moderators: Baseline PSS-I was a significant moderator of the effect of PE on both of the slopes of change over time, *b*=-.54, *t*(493)=-2.76, *p*=.006, and on outcome at post-treatment, *b*=-1.63, *t*(150)=-3.02, *p*=.003 (See Figure 1). Among participants who did not receive PE, participants with high baseline PSS-I (i.e., 1 SD above the mean, PSS-I=35.98) had much higher PSS-I at post-treatment, *b*=4.46, *t*(150)=5.22, *p*<.001, than those with low baseline PSS-I (i.e., 1 SD below the mean, PSS-I=20.3). However, among participants who did receive PE, those with high baseline PSS-I improved much faster than those with low baseline PSS-I, b_{Δ}=2.06, *t*(493)=7.89, *p*<.001, such that they did not have statistically higher PSS-I at post-treatment than those with low baseline PSS-I, *b*=1.22, *t*(150)=1.71, *p*=.087. Another way to look at the moderating effects of baseline PSS-I is that PE did not have a significant effect on post-treatment PSS-I for those with low baseline PSS-I (PSS-I=20.3), *b*=-2.04, *t*(150)=-1.37, *p*=.171 (Figure 1a), but did confer significant benefit for those with high baseline PSS-I (PSS-I=35.98), *b*=-8.52, *t*(150)=-5.49, *p*<.001 (Figure 1b). Calculating the “region of significance” for the effect of PE (i.e., the range of PSS-I values for which PE has a significant effect), PE had a significant benefit on post-treatment outcome for participants with a baseline PSS-I score over 21.

Duration of AD moderated the effect of NAL on PSS-I, *b*=-.71, *t*(493)=-3.55, *p*<.001 for the AD duration × NAL × Time interaction, and *b*=-2.22, *t*(148)=-4.01, *p*<.001 for the AD duration × NAL interaction affecting post-treatment PSS-I (see Figure 2). For those with a shorter duration of AD (i.e., 1 SD below the mean, duration=2.35 years), NAL did not improve post-treatment outcome nor did it lead to faster improvement in PSS-I during treatment (see Figure 2a). But for participants with a longer history of AD (i.e., 1 SD above the mean, duration=24.37; Figure 2b), NAL significantly improved outcome at post-

treatment, *b*=-3.09, *t*(148)=-4.09, *p*<.001 and significantly increased the rate of improvement during treatment, *b*=-1.00, *t*(148)=-3.63, *p*<.001.

Predictors and Moderators of Drinking Outcomes (Percentage Days Drinking; PDD)

The significant results from Step 4 of the Fournier procedure for each domain are presented in Table 3. In the text, we report only the significant results of Step 4 for each domain, and the results from the final model. The nature of the interactions between moderators and treatments are presented in the latter section if the finding retained significance in the final model.

Stepwise Procedure within each Domain

Demographics: Step 4 of the Fournier analyses revealed that white participants reported slower improvement in PDD over time than minority participants, *b*=.33, *t*(870)=3.33, *p*=.001, and higher post-treatment PDD, *b*=.37, *t*(194)=4.47, *p*<.001.

Socio-economic Factors: None of the socioeconomic variables were significantly related to PDD.

Comorbid Disorders: In Step 4 of the Comorbid Disorders domain, depressive symptoms moderated the effect of PE on the rate of PDD reduction over time, *b*=-.33, *t*(740)=-3.32, *p*=.001, and on PDD at post-treatment, *b*=-.26, *t*(155)=-3.07, *p*=.002.

Trauma Features: Step 4 of the Trauma Features domain revealed that those with combat trauma had slower improvement in PDD over time, *b*=.30, *t*(865)=2.87, *p*=.004, and higher PDD at post, *b*=.25, *t*(195)=2.80, *p*=.005. “Other” trauma type was also associated with slower improvement over time, *b*=.23, *t*(862)=2.15, *p*=.031, and higher PDD at post-treatment, *b*=.18, *t*(188)=1.97, *p*=.048. Finally, “other” trauma type moderated the effect of PE on PDD at post-treatment, *b*=.20, *t*(188)=2.30, *p*=.022.

PTSD Features: In Step 4 of the PTSD Features domain, anxiety sensitivity was a significant moderator of the effect of PE on both the slope of PDD over time, *b*=-.29, *t*(672)=-2.84, *p*=.005, and on post-treatment PDD, *b*=-.19, *t*(143)=-2.08, *p*=.040. Step 4 also showed that age at which the trauma occurred and the amount of time since that trauma were both moderators of the effect of NAL on PDD at post-treatment, *b*=-.31, *t*(135)=-2.35, *p*=.019 and *b*=-.27, *t*(135)=-2.01, *p*=.044, respectively.

Alcohol Features: In Step 4, higher baseline PDD was related to faster improvement in PDD over time, *b*=-.22, *t*(730)=-2.25, *p*=.024, but to *higher* post-treatment PDD, *b*=.21, *t*(156)=2.62, *p*=.009. Step 4 also showed that baseline alcohol craving significantly moderated the effect of PE on both the rate of PDD reduction over time, *b*=-.28, *t*(731)=-2.78, *p*=.005, and on post-treatment PDD, *b*=-.20, *t*(157)=-2.53, *p*=.012.

Final Model for Percentage Days Drinking—Results from the final model are presented in Table 2 and Figures 1 and 2. Step 4 of the final model showed that participants given NAL had faster rates of improvement in PDD over the course of the treatment, *b*=-.07,

t(587)=-2.10, *p*=.035, and lower PDD at post, *b*=-.28, *t*(129)=-3.53, *p*<.001. There were no significant effects for PE (*ps*>.410) nor was there a significant NAL × PE interaction (*ps*>.495).

Predictors: Three significant predictors of PDD were found. White race was associated with slower rates of improvement in PDD over time, *b*=.31, *t*(589)=3.12, *p*=.002, and to higher PDD at post-treatment, *b*=.32, *t*(128)=4.12, *p*<.001. Combat trauma was also related to slower rates of improvement in PDD over time, *b*=.24 *t*(584)=2.27, *p*=.023, and to higher post-treatment PDD, *b*=.24, *t*(126)=2.86, *p*=.004. Higher baseline PDD was related to faster rates of improvement over time, *b*=-.20, *t*(584)=-2.12, *p*<.034, but higher post-treatment PDD, *b*=.23, *t*(123)=3.03, *p*=.002.

Moderators: Baseline depressive symptom severity was a significant moderator of the effect of PE on both the slope of change over time, *b*=-.31, *t*(583)=-3.10, *p*=.002, and on PDD at post-treatment, *b*=-.25, *t*(126)=-3.13, *p*=.002 (Figure 3). To better understand the effect of depressive symptoms on PE, we again used the Aiken and West technique to estimate the predicted effect of PE on PDD at high levels of baseline depressive symptoms (for illustration, we used BDI=40, in the “severe depression” range) and the effect of PE on PDD for those with lower baseline depressive symptoms (for illustration, we used BDI=19, the high end of the range for “mild depression”). Participants with high baseline depressive symptoms (BDI=40) had significantly lower post-treatment PDD when provided PE than when not provided PE, *b*=-.40, *t*(126)=-2.99, *p*=.003. On the other hand, for participants with lower levels of depression (BDI=19), PDD did not differ for those in PE vs. no PE groups (*p*>.12). No other predictor/moderator variables retained significance in the final model.

Post-hoc Analyses

We used pattern mixture modeling (see Hedeker and Gibbons, 2006; Enders, 2011) to determine if the predictor or moderator effects in the final models for PDD or PSS-I differed for dropouts compared to non-dropouts. These analyses found no significant interactions between dropout status and predictor/moderator effects.

Discussion

The present study examined predictors and moderators of symptom improvement during concurrent treatment of PTSD and alcohol dependence (AD), with prolonged exposure (PE) for PTSD and naltrexone (NAL) for alcohol dependence. Our aim was to identify baseline characteristics that can signal patients at risk of poor response regardless of treatment condition (i.e., predictors) and those that might be used guide treatment selection (i.e., moderators). Overall, provision of PE (compared to no-PE) was associated with faster improvement and lower PTSD severity at post-treatment. However, patients who received PE did not achieve better drinking outcomes than patients who received supportive counseling-only. Medication (NAL) was associated with faster reductions in drinking and better post-treatment drinking outcomes, but did not have a significant impact on PTSD

outcomes relative to placebo. These findings support the overall efficacy of PE and NAL on the specific symptoms that they targeted.

Predictors of PTSD Outcome

Two characteristics were associated with slower improvement and poorer PTSD outcomes across treatment groups: trauma type and anxiety sensitivity. Participants with sexual assault and combat trauma showed slower improvement than those with other types of trauma (e.g., physical assaults; natural disasters; accidents) and had higher PTSD severity at post-treatment. This was true when controlling for co-occurring characteristics such as baseline PTSD symptoms, drinking severity, and age of trauma onset. Previous research has generally not found trauma type to impact treatment outcome; however, efficacy studies frequently focus on a single trauma population (e.g., all female assault survivors; all combat veterans) or may have limited variance regarding trauma type. It should be noted that there is a strong evidence supporting PE efficacy with female sexual assault survivors (e.g., Foa et al., 2005; Resick, Nishith, Weaver, Astin, & Feuer, 2002), and rigorous clinical studies have shown excellent response to PTSD treatment among combat veterans, with effect sizes comparable to civilian populations (e.g., Tuerk et al., 2011). Thus, the present results may reflect features specific to our co-morbid and predominantly male sample. Indeed, many studies of PE for sexual assault have included only women; whereas in the current study, 43% of patients reporting sexual assault were male. Future research should examine corresponding therapy processes in PTSD-AD treatment that may account for inferior outcomes among sexual assault and combat trauma survivors compared to other trauma types.

Higher anxiety sensitivity was associated with slower improvement and higher post-treatment PTSD symptoms across all conditions. This finding mirrors previous research showing correlations between anxiety sensitivity reduction and PTSD treatment outcome (Federoff et al. 2000). Anxiety sensitivity is defined as a fear of physical sensations associated with anxiety (Reiss et al., 1986) and thus can amplify the intensity of emotional reactions. To illustrate, a person with PTSD and high anxiety sensitivity may experience fear of trauma reminders compounded by fear of his/her own anxious reactions. In the treatment of PTSD, anxiety sensitivity could influence important treatment processes. For example, individuals with high anxiety sensitivity may be more avoidant and less willing to engage emotionally during exposure exercises. While patients with high ASI showed significant symptom change during treatment, they may benefit from a higher dose of treatment to reach comparable outcomes. In addition, it may be helpful to incorporate interceptive exposures or other treatments for anxiety sensitivity into trauma-focused treatment in order to improve outcomes for patients with high baseline ASI.

Several previously identified predictors of PTSD outcomes were not significant in the current study (e.g., gender, age, education level, depressive symptoms). Of note, age and depressive symptoms were both identified as predictors of PTSD outcomes in the initial model, but neither remained significant in the final model when controlling for co-occurring factors (e.g., anxiety sensitivity; initial PTSD severity). Discrepancies with previous studies could be due to differences in the treatment sample (PTSD-AD) or due to differences in

statistical approach. The present analyses included a wide range of potential predictors, thus providing a relatively thorough array of control variables. Thus, the failure of age and depressive symptoms to be significantly related to PTSD in the final model here may be due to our more thorough control for alternative predictors.

Moderators of PTSD Outcomes

Two moderators of PTSD outcome were identified. First, baseline PTSD severity was found to moderate the efficacy of PE versus no-PE. Specifically, PE was superior to supportive counseling in reducing PTSD symptoms for participants with higher pre-treatment PTSD severity. Indeed, higher initial severity in the non-PE groups was associated with much higher PTSD severity at post-treatment; whereas, in the PE groups, this relationship was not found. Conversely, among those with lower baseline PTSD scores (i.e., PSS-I less than 21), PE was not superior to supportive counseling-only. This finding suggests that non-specific therapy factors (e.g., attention, support, alliance) may be sufficient to reduce PTSD severity in patients with mild PTSD symptoms. On the other hand, patients with moderate-to-severe PTSD symptoms show greater benefit from exposure-based treatments that specifically target trauma symptoms. If replicated, these results have great practical implications for matching patients to therapies. Given that therapists trained in exposure-based treatments with in community settings are often in short supply, the current findings might be used by organizations to most efficiently allocate clinical resources.

Second, duration of alcohol dependence moderated the efficacy of NAL versus placebo on PTSD outcomes. NAL enhanced the rate of PTSD improvement in patients with long alcohol dependence history (e.g., 24 years or more), but did not improve PTSD outcomes among those with a shorter duration of alcohol dependence (e.g., 2-3 years or less). This finding may be accounted for by reduction in alcohol use. Lower levels of drinking during treatment would be expected to improve PTSD outcomes, as drinking is hypothesized to be a means of avoiding trauma-related thoughts and, thus, may block emotionally processing of the trauma. Overall, those who received NAL in the current study exhibited faster decreases in drinking behavior and lower post-treatment alcohol use. A post-hoc comparison indicated that, among participants with longer alcohol duration, those receiving placebo had a higher number of drinking days than those on NAL ($p < .05$). While precise investigation of the mediating effect of within-treatment drinking is beyond the scope of the current paper, this an important issue to pursue in future research. For patients whose alcohol dependence is more entrenched, NAL may be particularly beneficial for enhancing PTSD treatment outcomes in concurrent alcohol dependence and PTSD treatment.

Predictors of Drinking Outcome

Three factors emerged as negative predictors of drinking outcomes across treatment conditions: higher baseline severity of drinking, combat trauma, and white race. Participants with higher baseline drinking showed poorer post-treatment drinking outcomes, but *faster* improvement in alcohol use during treatment. This suggests that with additional time, this subset of patients may achieve comparable outcomes, a hypothesis that would be beneficial to examine empirically. Baseline alcohol consumption has been identified as one of the most

consistent predictors of alcohol dependence treatment outcome in previous research (Adamson et al., 2009).

Patients with combat-related trauma showed slower reductions in drinking behavior and poorer post-treatment drinking outcomes. Thus, in the present study, combat trauma emerged as a negative predictor of both PTSD and drinking outcomes. Prevalence of heavy drinking in military personnel is substantial (15-20%; Bray & Hourani, 2007) and significantly higher than that of age-matched civilian samples (Ames & Cunradi, 2004). It is possible that the dominant culture of alcohol use in the military might make this maladaptive coping strategy more resistant to change in combat-trauma survivors. The current results suggest that, compared to other trauma types, individuals with combat-trauma may require additional support or treatment modification to improve the efficacy of concurrent PTSD-AD treatment.

Finally, white race predicted poorer drinking outcomes in the current study. Large-scale epidemiological studies such as the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) show both a higher lifetime prevalence of alcohol dependence in individuals identifying as white compared to black or Hispanic, and a distinctly shorter average time from first drink to dependence trajectory (whites: 8 years; blacks and Hispanics: 16 years) (Lopez-Quintero et al., 2011). The current findings suggest that white patients may also be more resistant to treatment. This mirrors the results of one of the largest clinical trials of alcohol use treatments, Project MATCH (Project Match Research Group, 1997). Secondary analyses from this study found that, among those receiving treatment in an outpatient setting, white participants reported significantly lower rates of monthly abstinence relative to black participants at both six and twelve month follow-up (Tonigan, 2003).

Moderators of Drinking Outcome

Severity of depressive symptoms emerged as the only significant moderator of PE efficacy. Specifically, patients with higher baseline depression (i.e., in the moderate-severe range) had *lower* percentage days drinking at post-treatment if they received PE (versus no-PE). For those with lower depressive severity, receiving PE did not influence drinking at post-treatment. The effects of PE on drinking outcomes among patients with high baseline depression may have been mediated by reduction of depressive symptoms. Standard PE incorporates behavioral activation for patients with depression and has been shown to reduce depressive symptoms, guilt, and general anxiety in addition to PTSD symptoms (e.g., Keane, Marshall, & Taft, 2006; Rauch et al., 2010). Research strongly supports negative affect as a cue for alcohol cravings (e.g., Nosen et al., 2012; Sinha et al., 2009) and relapse (Greenfield et al., 1998; Marlatt & Gordon, 1980). Thus, it is plausible that PE promotes better drinking outcomes for patients with moderate-to-severe depressive symptoms by reducing negative affect. Additional research is required to evaluate this hypothesis.

Limitations

Several limitations should be noted. First, participants in the current study showed lower treatment attendance than is typical in PTSD treatment studies. Thirty two percent of the

sample dropped out of the study, and the average number of sessions attended in PE was six out of a possible 18 sessions. Comparable rates of adherence to therapy have been found in other studies involving comorbid substance dependence and PTSD samples (e.g., Hien et al., 2009; Sannibale et al., 2013), suggesting that poor adherence to treatment is a challenge inherent to this population requiring additional study. Germane to the present results, however, MLM is capable of handling this level of missing data, producing unbiased estimates of regression coefficients in data sets with dropout as high as 90% (Hedeker & Gibbons, 2006). Moreover, no differences were found between dropouts and non-dropouts with respect to baseline characteristics, and pattern-mixture modeling revealed that predictor/moderator effects in the final model did not differ based on dropout status.

Second, due to safety concerns, participants in all four treatment conditions received supportive counseling. As such, it is difficult to isolate the separate contribution of this intervention or to assess the generalizability of the current findings to settings where adjunctive supportive counseling is not provided. This limitation is particularly relevant for moderator findings, as the inclusion of supportive counseling may have obscured potential moderators of the effectiveness of PE or NAL compared to a no-treatment group. Third, regarding NAL adherence, pill counts were used to determine medication compliance in the present study, and use of other methods (e.g., blood samples) in future studies would provide a more reliable measure of adherence. Conclusions regarding NAL effects are thus limited by this feature. Finally, some demographic features in the current sample were restricted. For example, only a small proportion of participants (6%) represented racial memberships other than white/Caucasian or black/African American, and – as such – we were limited in our ability to investigate more nuanced differences among racial or ethnic groups.

Conclusions

This study is the first to evaluate predictors and moderators of outcome in concurrent treatment for AD and PTSD. The non-specific predictors identified here – particularly combat trauma, anxiety sensitivity, and white race – warrant replication and additional research to better understand the mechanisms underlying poorer response to treatment. The present findings suggest that pre-treatment severity of PTSD, depressive symptoms, and duration of alcohol dependence may be useful in determining the most effective combination of therapies for this population. Specifically, concurrent trauma-focused exposure therapy appears to be of additive benefit to PTSD-AD patients who present with moderate or severe PTSD and moderate or severe depressive symptoms; while NAL confers most benefit for those with longer durations of alcohol dependence.

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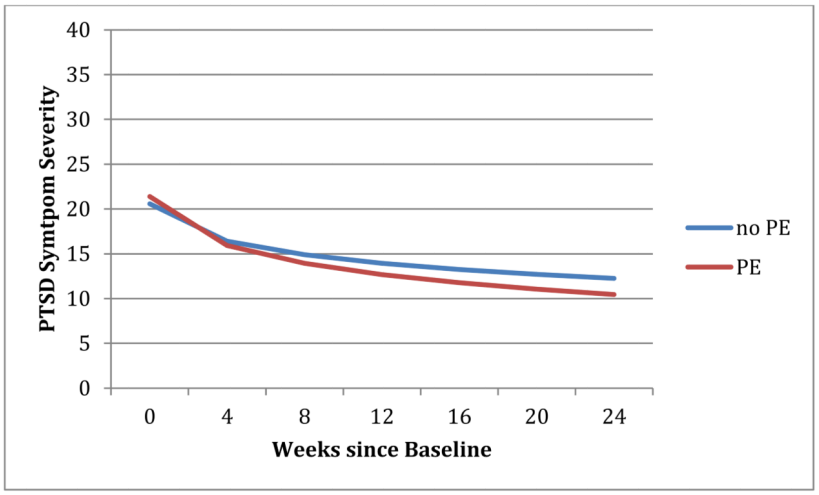
Public Impact

This study suggests that, when treating comorbid PTSD and alcohol dependence, prolonged exposure therapy significantly improves PTSD outcomes for patients with moderate or severe PTSD symptoms.

Individuals with mild PTSD symptoms may not derive additional benefit from prolonged exposure compared to supportive counseling alone.

The opioid antagonist naltrexone showed greatest effects among patients with longer histories of alcohol dependence.

a.



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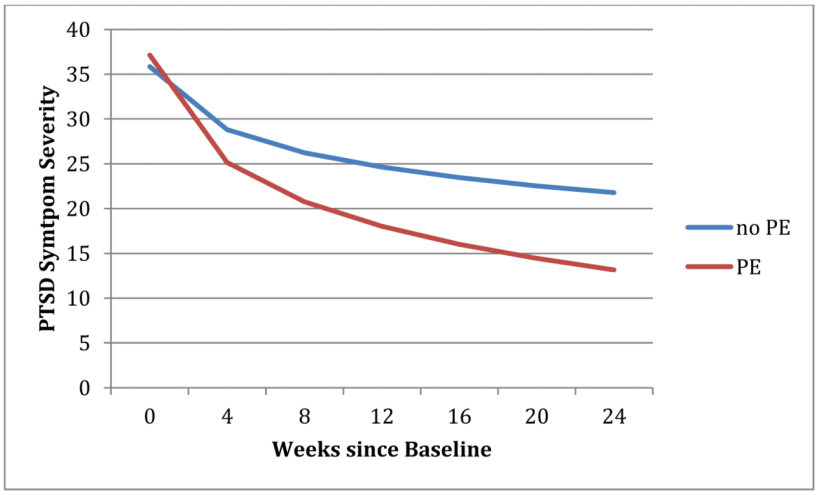
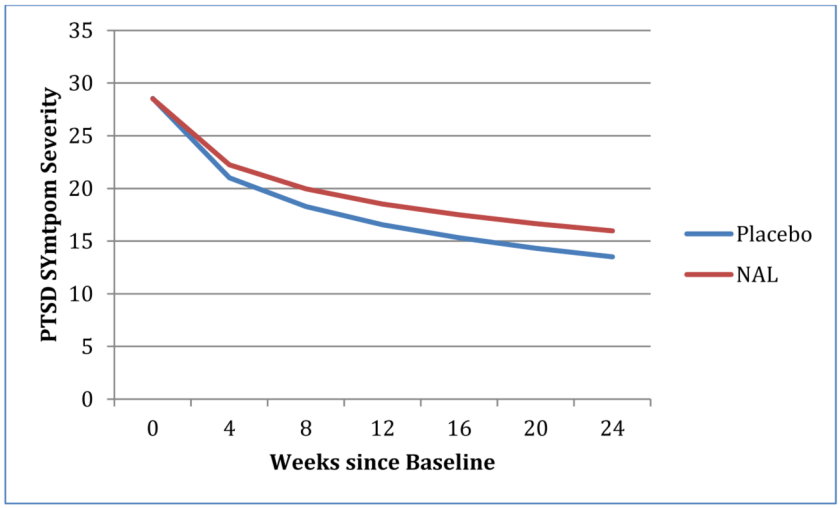


Figure 1. The effect of PE on PTSD outcome moderated by baseline PTSD severity

a. Effect of PE on PSS-I for Low Baseline PSS-I (1 SD below mean)

b. Effect of PE on PSS-I for High Baseline PSS-I (1 SD above mean)

a.



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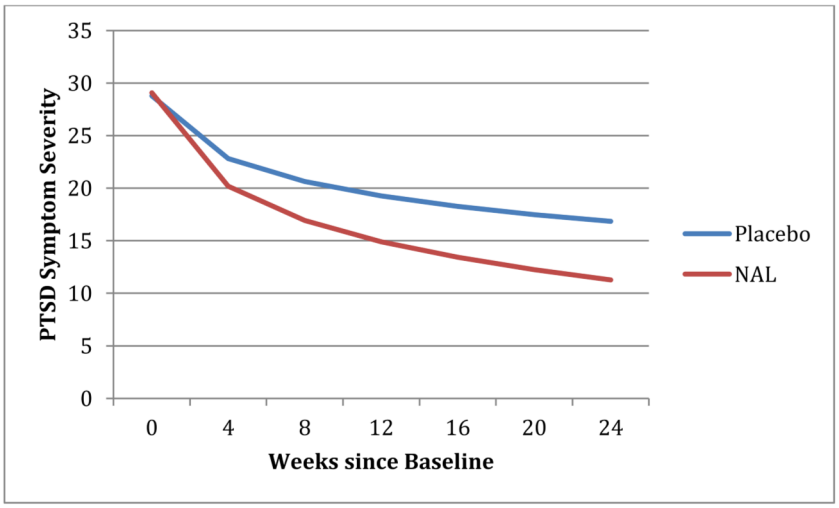
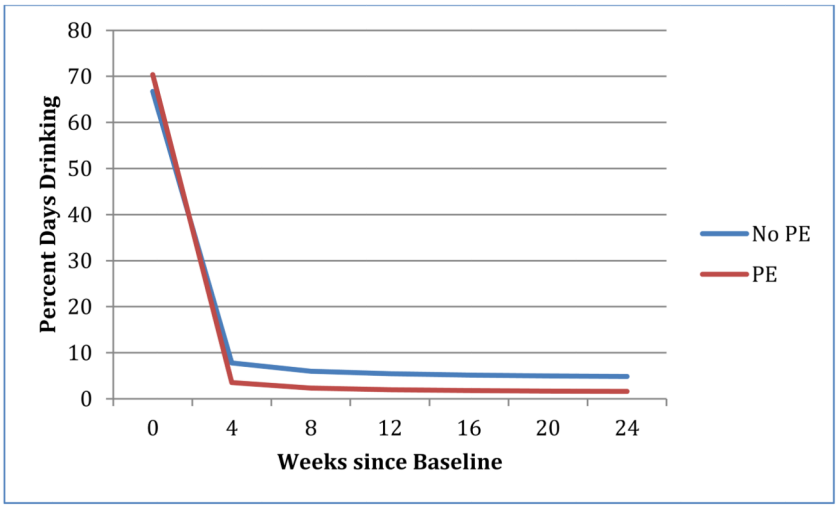


Figure 2. The effect of NAL on PTSD outcome moderated by duration of alcohol dependence

a. The effect of NAL on PSS-I for participants with short duration of alcohol dependence

b. The effect of NAL on PSS-I for participants with long duration of alcohol dependence

a.



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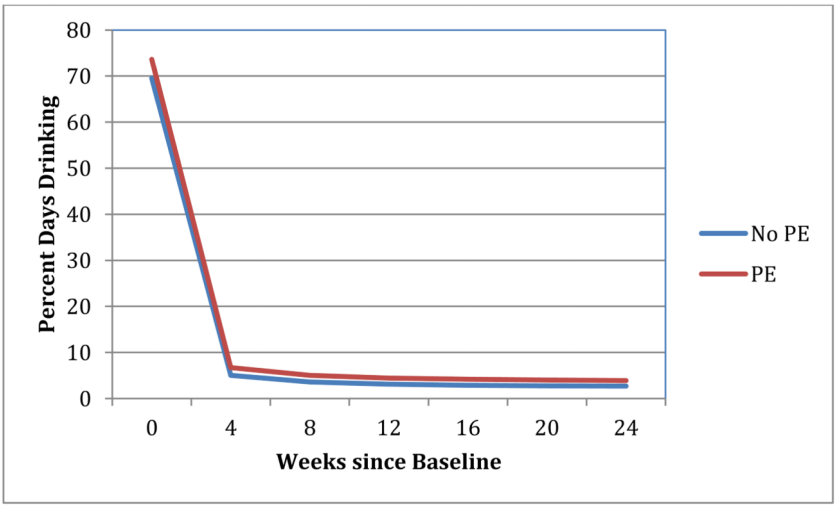

Figure 3. The effect of PE on percent days drinking moderated by baseline depressive symptoms

a. The effect of PE on PDD for participants with severe baseline depression (BDI = 40)

b. The effect of PE on PDD for participants with mild baseline depression (BDI = 19)

Table 1

Baseline Characteristics (*n* = 165)

Variable	Number (%)
Gender	
Female	57 (34.5)
Male	108 (65.5)
Race/Ethnicity	
Black/African-American	105 (63.6)
White/Caucasian	50 (30.3)
Hispanic/Latino	7 (4.2)
Other	3 (1.8)
Living Alone	36 (21.8)
Employed	57 (34.5)
Median Income Range	$15,000-20,000
Education	
Some College or More	84 (50.9)
High School or Less	81 (49.1)
Types of Trauma	
Sexual Assault	42 (25.5)
Physical Assault	62 (37.6)
Combat	19 (11.5)
Other	42 (25.5)
Number of additional Axis I diagnoses	
0	95 (57.6)
1	44 (26.7)
2	19 (11.5)
3	3 (1.8)
4	3 (1.8)
5	1 (.6)
Other Substance Use Disorder	35 (21.2)
Current Personality Disorder	41 (24.8)

Variable	M (SD)
Age	42.78 (9.76)
Alcohol Dependence Duration	13.36 (11.04)
PTSD Duration	14.55 (15.26)
Baseline PSS-I	28.14 (7.86)
% Drinking Days	74.82 (25.26)
Alcohol Craving	18.38 (6.91)
ASI	27.44 (13.95)
BDI	26.31 (11.54)

Note: The precise *n* per variable differed due to missing data on some variables. ASI: Anxiety Sensitivity Index, BDI: Beck Depression Inventory, PSS-I: PTSD Symptom Scale Interview

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Table 2

Predictors and moderators of PTSD outcome (PSS-I) in Step 4 and the Final Model

Domain/Predictor	Post-Treatment Main Effects			Slope Effects		
	b	*t*	*p*	*b*	*t*	*p*
Demographic variables						
Gender	1.04	1.65	.098	-	-	-
Age	-.24	-.36	.716	-	-	-
Age × NAL	-1.17	-1.79	.073	-	-	-
Age × PE	.83	1.26	.210	-	-	-
Age × NAL × PE	-1.60	-2.44	.015	-	-	-
Socio-economic factors						
Employment	-2.20	-3.96	<.001	-	-	-
Comorbid disorders						
Depressive Symptoms (BDI)	1.33	1.71	.087	-1.00	-3.73	<.001
Depressive Symptoms (BDI) × NAL	-.19	-.25	.805	-.07	-.26	.798
Depressive Symptoms (BDI) × PE	-.80	-1.00	.323	-.48	-1.75	.080
Depressive Symptoms (BDI) × PE × NAL	1.45	1.80	.073	.55	2.02	.043
Trauma features						
Sexual Assault	2.19	2.51	.012	.79	2.79	.005
Sexual Assault × PE	.75	1.28	.202	-	-	-
Combat	1.71	1.93	.054	.46	1.60	.109
Combat × PE	1.24	1.42	.156	.62	2.18	.029
PTSD features						
Baseline PSS-I	2.77	4.60	<.001	-1.54	-7.20	*p*<.001
Baseline PSS-I × NAL	-.40	-.71	.479	-.19	-.95	.341
Baseline PSS-I × PE	-1.46	-2.61	.009	-.50	-2.52	.012
Baseline PSS-I × NAL × PE	1.40	2.47	.013	.47	2.34	.019

Domain/Predictor	Post-Treatment Main Effects			Slope Effects		
	b	*t*	*p*	*b*	*t*	*p*
Anxiety Sensitivity (ASI)	2.05	3.45	.001	.78	3.59	*p*<.001
Alcohol features						
Craving	1.69	3.29	.001	-	-	-
Duration of AD	.20	.23	.816	-.14	-.48	.633
Duration of AD × NAL	-1.96	-2.27	.024	-.62	-2.21	.027
Final model predictors						
Baseline PSS-I	2.89	5.00	<.001	-1.50	-7.08	<.001
Anxiety Sensitivity (ASI)	2.13	3.78	<.001	.81	3.76	<.001
Duration of AD	-.38	-.70	.487	-.18	-.92	.357
Combat	1.81	3.24	.001	.54	2.68	.007
Sexual Assault	2.53	4.56	<.001	.75	3.71	<.001
Final model moderators						
Baseline PSS-I × PE	-1.63	-3.02	.003	-.54	-2.76	.006
Duration of AD × NAL	-2.22	-4.01	<.001	-.71	-3.55	<.001

Note. All variables were z-scored before computing interactions. Hence, main effects for all predictors/moderators reflected their effects for the mean of the present sample. ASI = Anxiety Sensitivity Index; AD = alcohol dependence; BDI = Beck Depression Inventory; NAL = naltrexone vs. placebo; PE = prolonged exposure therapy vs. supportive counseling; PTSD = post-traumatic stress disorder; PSS-I = PTSD Symptom Scale Interview

Table 3

Predictors and moderators of drinking outcome (percent days drinking) in Step 4 and the Final Model

Domain/Predictor	Post-Treatment Main Effects			Slope Effects		
	b	*t*	*p*	*b*	*t*	*p*
Demographic variables						
Race (white vs. non-white)	.37	4.47	<.001	.33	3.33	.001
Socio-economic factors						
Education	-.12	-1.45	.147	-	-	-
Education × NAL	-1.49	-1.84	.066	-	-	-
Education × PE	.13	1.66	.096	-	-	-
Comorbid disorders						
Depressive Symptoms (BDI)	-.05	-.65	.517	-.06	-.64	.521
Depressive Symptoms (BDI) × PE	-.26	-3.07	.002	-.33	-3.32	.001
Trauma features						
Sexual Assault	.08	.84	.400	.09	.79	.428
Sexual Assault × PE	.03	.36	.720	-	-	-
Combat	.25	2.80	.005	.30	.2.87	.004
Combat × PE	.16	1.87	.061	-	-	-
Other Trauma	.18	1.97	.048	.23	2.15	.031
Other Trauma × PE	.20	2.30	.022	-	-	-
PTSD features						
Anxiety Sensitivity (ASI)	-.02	-.19	.846	.03	.32	.751
Anxiety Sensitivity × PE	-.19	-2.08	.040	-.29	-2.84	.005
Age of Trauma Onset	-.04	-.27	.785	-	-	-
Age of Trauma Onset × NAL	-.31	-2.35	.019	-	-	-
PTSD Duration	-.02	-.18	.861	-	-	-
PTSD Duration × NAL	-.27	-2.01	.044	-	-	-

Domain/Predictor	Post-Treatment Main Effects			Slope Effects		
	b	*t*	*p*	*b*	*t*	*p*
Alcohol features						
Craving	.12	1.50	.136	.19	1.93	.054
Craving × PE	-.20	-2.53	.012	-.28	-2.78	.005
Age of AD Onset	.05	.61	.541	-	-	-
Age of AD Onset × NAL	-.08	-1.05	.296	-	-	-
% Days Drinking at Baseline	.21	2.62	.009	-.22	-2.25	.024
Final model predictors						
% Days Drinking at Baseline	.23	3.03	.002	-.20	-2.12	.034
Depressive Symptoms (BDI)	-.06	-.77	.440	-.05	-.55	.581
Sexual Assault	.08	.93	.351	.10	.93	.353
Combat	.24	2.86	.004	.24	2.27	.023
Other (General Trauma)	.11	1.31	.192	.14	1.28	.202
Race (white vs. non-white)	.32	4.12	<.001	.31	3.12	.002
Final model moderators						
Depressive Symptoms (BDI) × PE	-.25	-3.13	.002	-.31	-3.10	.002

Note. All variables were z-scored before computing interactions. Hence, main effects for all predictors/moderators reflected their effects for the mean of the present sample. ASI = Anxiety Sensitivity Index; AD = alcohol dependence; BDI = Beck Depression Inventory; NAL = naltrexone vs. placebo; PE = prolonged exposure therapy vs. supportive counseling; PTSD = post-traumatic stress disorder.