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Examining Associations Between Cognitive-Affective Vulnerability and HIV Symptom Severity, Perceived Barriers to Treatment Adherence, and Viral Load Among HIV-Positive Adults

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Abstract
Background Little research on symptom impairment and quality of life among HIV-positive (HIV+) individuals has attended to the potential role of cognitive-affective vulnerabilities. Emerging research indicates that emotion regulation (ER), anxiety sensitivity (AS), and distress tolerance (DT) are associated with a range of mental health outcomes and demonstrate meaningful relations to clinical outcomes in HIV+ individuals.
Purpose In this investigation, we sought to concurrently examine these factors in relation HIV symptom severity, barriers to medication adherence, and disease viral load.
Method Participants were 139 HIV+ individuals (34 female; age M=48.2 years, SD=8.1, 42 % Black) receiving outpatient HIV care and prescribed at least one antiretroviral medication. We used hierarchical regression analyses to concurrently examine ER, AS, and DT in relation to severity of HIV symptoms, barriers to medication adherence, and disease viral load.
Results After accounting for alcohol use problems, cannabis dependence, gender, and education, AS was significantly associated with HIV symptom severity (β=.35, p<.01) whereas ER evidenced a trend relation (β=.19, p=.07). ER (β=.45, p<.01), but not AS or DT, was significantly related to barriers to medication adherence, above and beyond variance accounted for by covariates. Finally, ER evidenced a trend level relation to viral load (β=.21, p=.07), above and beyond variance accounted for by cannabis use.
Conclusion Findings provide an extension of previous research, suggesting unique roles of cognitive-affective vulnerabilities in terms of HIV symptom severity, medication use barriers, and infection symptomatology, and inform the refinement of current treatments for HIV+ individuals so as to improve functioning.

Keywords HIV/AIDS · Distress tolerance · Anxiety sensitivity · Emotion regulation · Symptom severity · Antiretroviral therapy adherence · Viral load · Behavioral intervention

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Introduction

An abundance of recent research relevant to HIV-positive (HIV+) populations has focused on the development of interventions to decrease HIV symptom severity [1–3] and increase adherence to antiretroval treatment (ART) [4–7]. Numerous investigations have sought to target specific risk factors that may lead to low ART adherence, such as improving social support, decreasing depression and risk of substance use, and decreasing ART side effects [1–7]. However, ART

adherence interventions have demonstrated only moderate success in preventing ART resistance, increasing CD4 t-cell count, and preventing disease progression [8, 9]. Research within this area is clinically significant given the individual and public health importance of decreasing HIV symptom severity (e.g., pain, lack of energy, insomnia) and increasing treatment adherence. Exploring malleable (i.e., changeable via intervention) cognitive-affective vulnerability factors that have demonstrated both strong theoretical and empirical relations to a range of health risk behaviors (i.e., distress tolerance [10]; anxiety sensitivity, [11]; emotion regulation, [12]), may provide a novel and relevant avenue by which to develop more effective, specialized interventions for individuals with HIV. More specifically, interventions targeting behavioral, cognitive, and physical sequelae associated with HIV, including HIV symptom severity, perceived barriers to ART adherence, and disease presence, progression, and symptomatology, have the potential to result in numerous improvements in overall quality of life (e.g., [13]).

Emerging research suggests that emotion regulation (ER), defined as an individual's ability to understand and accept his or her emotional experience, to engage in healthy strategies to manage uncomfortable emotions when necessary, and to engage in appropriate behavior (e.g., go to work, engage in relationships) when distressed [14], is a particularly promising factor in this domain. Indeed, empirical research within this context posits that negative affect stems from difficulties in self-regulating affective states and/or affect-driven behaviors, while heightened positive affectivity is thought to extend from adaptive self-regulation and self-control in the affective domain [12]. For example, Carrico and colleagues found that HIV+ individuals with greater ER, as characterized by less severe depressive symptoms and positive state of mind, are more adherent to ART and less likely to use substances [15]. Providing theoretical relevance for the role of ER in treatment for HIV+ individuals, work by Kraaij et al. [16] found that HIV+ individuals who report greater use of cognitive coping strategies and higher self-efficacy (e.g., thinking about pleasant activities, attaching a positive meaning to their HIV status) report greater personal growth, an index of the ability to engender positive psychological changes when faced with an adverse life event. Also, among HIV+ individuals, greater cognitive coping (e.g., positive refocusing and less catastrophizing) is related to lower levels of depression and anxiety among HIV+ individuals, after accounting for time since diagnosis, CD4 level, and viral load [17]. In addition, Gonzalez and colleagues [18] found that lower levels of mindfulness (i.e., individual's ability to pay attention to and maintain awareness of the present moment) [19] and greater levels of disengagement coping (i.e., psychological or behavioral withdrawal from a goal due to interference caused by stress) [20] were independently and interactively associated with greater anxiety symptoms among HIV+ individuals. Together, though the research on ER and HIV is only emerging, extant findings suggest its clinical relevance to global impairment in this population.

Two additional promising—though less studied—cognitive-affective vulnerabilities recently investigated in the context of ER processes among HIV+ individuals are anxiety sensitivity (AS) and distress tolerance (DT). AS is characterized by the fear of anxiety and its related health, social, and mental consequences [21], while poor distress tolerance (DT) is characterized by the inability to withstand uncomfortable somatic or emotional perturbation [22]. Both AS [23–27] (e.g., pain, panic disorder, posttraumatic stress disorder, alcohol, and drug use) and DT [22, 26, 28, 29] (e.g., posttraumatic stress, borderline personality disorder, cigarette smoking) have demonstrated empirical relations with negative affect, broadly, as well as a range of psychiatric disorders and substance use disorders.

AS and DT could theoretically be conceptualized as lower-order components of a higher-order emotion regulatory construct but not identical to it. To the best of our knowledge, no empirical models have attempted to document that DT or AS are in fact aspects of emotion regulation, although clinical models have contextualized it as such [30]. Indeed, AS and DT have been shown to be related lower-order facets of a higher order affect tolerance and sensitivity factor [31]. Notably, DT is not empirically or conceptually equivalent to AS. Although correlated, individual differences in AS do not reflect cognitive or behavioral capacities to behaviorally tolerate and persistent in the experience of unwanted distressing states [31].

Relevant work indicates that, among HIV+ individuals, higher levels of AS are correlated with greater somatization symptoms, as well as elevated symptoms of anxiety, depression, and suicidality [32–34]. With regard to DT, a recent longitudinal study of HIV+ individuals indicated that both lower DT and greater past 6-month life events (excluding health-related events) independently and interactively predicted elevations in symptoms of depression, cocaine use, and medication adherence, suggesting that vulnerability to distress exacerbates the impact of life events on these outcomes [35]. In addition, low DT independently predicted greater HIV-related symptoms and use of substances in order to cope [35]. A recent multimethod study of DT among individuals with HIV found that lower self-reported DT was associated with lower objectively measured medication adherence (i.e., pill count), while lower behavioral distress tolerance (mirror tracing) was found to be associated with greater likelihood of detectable viral load [36]. Related, Brandt et al. [37] found that lower levels of DT were significantly associated with depression, social anxiety, and panic symptoms among HIV+ individuals, above and beyond other demographic and HIV-specific characteristics. Interestingly, results indicated that ER fully mediated this relation, suggesting that deficits in

ER may explain the link between low DT and greater psychological distress.

The extant, albeit only emergent, literature has several limitations. First, there is a paucity of research on the role of cognitive-affective vulnerability factors in terms of objective physical and subjective psychological symptoms as well as treatment adherence factors among HIV+ adults. Second, extant work is somewhat limited in its generalizability to treatment-enrolled HIV+ individuals, a growing group whose symptoms and clinical impairment may be distinct from those not regularly engaged in treatment. Finally, to date, only one published study has conducted an investigation of the concurrent associations of ER, AS, and DT in a sample of HIV+ individuals in relation to psychological outcomes. Here, Brandt et al. [38] found that greater deficits in ER were significantly and positively predictive of general anxiety and depressive symptoms, as well as pain-related anxiety, and HIV symptom distress, above and beyond variance accounted for by AS and DT [38]. Though this study is an important first step in understanding the role of ER, AS, and DT among individuals with HIV, it is important to extend this work to factors more directly relevant to HIV treatment adherence and symptom severity, including objective measures.

In the present investigation, we seek to both replicate and extend work by Brandt and colleagues [38] by simultaneously examining ER, AS, and DT in terms of subjective and objective HIV-relevant outcomes. Importantly, by extending previous work by Brandt et al. [38] on a non-treatment seeking group of HIV+ individuals to a group regularly receiving treatment, the current investigation is arguably more generalizable to the current chronic disease model, where far fewer individuals go on to develop AIDS. First, we hypothesized that HIV+ individuals with greater deficits in ER (i.e., greater difficulties in emotion regulation), higher AS, and lower DT, would report significantly greater HIV symptom severity. Second, we also extend this model to the examination of self-reported barriers to ART, which may place an additional burden on these individuals and impact quality of life, for example, via poor ART adherence and subsequent infection symptomatology. Here, we hypothesized that HIV+ individuals with greater deficits in ER, higher AS, and lower DT would report significantly greater perceived barriers to ART adherence. Finally, we sought to examine these vulnerabilities in terms of log-transformed viral load, an objective index of HIV symptom expression; given a dearth of research linking cognitive-affective vulnerabilities to objective indices of physical symptoms in HIV+ individuals, these analyses were exploratory in nature. Hypothesized associations were expected above and beyond the effects of substance use and demographic factors that have not only been shown to be associated with the studied outcomes in prior work [39], but that also demonstrated associations in the present sample.

Method

The current investigation is a secondary analysis of a larger study [39] examining the relation between cannabis use and HIV medication adherence. For inclusion in the study, participants had to be (1) at least 18 years old; (2) HIV+; (3) currently prescribed at least one antiretroviral medication, and (4) undergoing treatment at an outpatient HIV treatment clinic. In addition, approximately one-third of the sample (n=45) met DSM-IV criteria for current cannabis dependence (CD), one-third of the sample (n=46) were non-dependent cannabis users (use in the past 30 days; ND), and one-third of the sample (n=48) reported no cannabis use within the past 6 months (NC). Participants were excluded based on (1) limited mental competency; (2) inability to provide informed, voluntary, written consent; (3) inability to speak and read English; or (4) suicidal ideation as determined by structured clinical interview.

Measures

We obtained participants' viral load (copies/mL), as determined by the most recent blood test, via a review of participants' medical records on file at their HIV clinic. Viral load was used in the present investigation as a reflection of participants' HIV status, burden of infection, and response to ART [40, 41]. Consistent with prior work [40], viral load was log-transformed prior to analysis. Log-transformed viral loads of most HIV+ individuals receiving treatment are less than 50 copies/mL, or 1.7 logs, whereas those experiencing early infection evidence loads of 10 million copies/mL or 7.0 logs [40].

Structured Clinical Interview for DSM-IV Axis I Disorders-non-Participant Edition The *Structured Clinical Interview for DSM-IV Axis I Disorders-non-Participant Edition* (SCID-NP) [42] is a well-established diagnostic interview for psychological problems. In the current investigation, the interview was administered by trained research assistants to determine whether participants had current or past psychotic-spectrum symptoms and other Axis I psychopathology. As part of their training, each research assistant was required to (1) view 3–4 videotaped or live SCID-I-N/P administrations by senior interviewers at the National Center for PTSD, whereby trainee ratings were compared with that of the senior interviewers, and (2) administer 6–10 SCID-I-N/P interviews while under the supervision of senior interviewers until ratings matched those of the senior interviewer on at least 4–5 consecutive administrations. In addition, all interviews were audio-recorded for subsequent review by the last author, a clinical psychologist, with no instances of disagreement.

Alcohol Use Disorders Identification Test The *Alcohol Use Disorders Identification Test* (AUDIT) [43] is a 10-item self-report screening measure developed by the World Health Organization to identify individuals with alcohol problems [43]. There is a large body of literature attesting to the reliability and validity of the AUDIT [44]. In the present study, the AUDIT total score was used to assess hazardous or harmful drinking (scores >8; Cronbach's α=.91).

Health Status Questionnaire The *Health Status Questionnaire* [45] is a 43-item measure that was developed by the AIDS Clinical Trials Group to assess HIV symptom severity, including general health, energy, and social, physical, and cognitive functioning in HIV and AIDS patients. For the present investigation, the 20-item portion of the HSQ focused on past 4-week symptom severity was used. Participants were asked to first indicate whether or not each listed symptom was experienced (e.g., fatigue or loss of energy, fever, chills, or sweats) and then indicate the extent to which the symptom bothered them on a 4-point scale (1 = "It doesn't bother me at all" to 4 = "It bothers me a lot"; current sample, Cronbach's α=.94).

Barriers to HAART Adherence Questionnaire The *Barriers to HAART Adherence Questionnaire* (BHAQ) [46] is a 32-item self-report measure used to assess perceived barriers of highly active antiretroviral therapy (HAART) medication adherence among HIV+ individuals. Items are rated on a 4-point Likert-type scale (1 = "strongly agree" to 4 = "strongly disagree") in terms of barriers relevant to social support (e.g., "I am satisfied with the amount of support I get from friends and family"), beliefs about HIV/AIDS severity and utility of medication (e.g., "If I don't take my HIV meds, I will likely develop AIDS"), routine and organization (e.g., "I generally wake up and go to sleep around the same time every day"), and relationship with providers (e.g., "I trust my primary providers at this clinic"). A total score was calculated with higher scores suggesting greater perceived barriers to HAART medication adherence (Cronbach's α=.91).

Anxiety Sensitivity Index The 18-item *Anxiety Sensitivity Index-3* (ASI-3) [48] is a measure of fear or concern about anxiety and its consequences. Items are rated on a 4-point Likert-type scale (0 = "very little" to 4 = "very much"; e.g., "It is important for me not to appear nervous."), with higher scores indicating greater sensitivity and concern about anxiety. The ASI-3 was developed in order to improve upon the psychometric properties of the previously identified factors (physical, cognitive, and social) of the original index [49], and demonstrates good internal consistency, construct validity, and test-retest reliability. The current investigation employed the total score in order to capture all three of its dimensions (current sample, Cronbach's α=.95).

Distress Tolerance Scale The *Distress Tolerance Scale* [50] is a 15-item self-report measure of perceived ability to withstand psychological distress. Items are rated on a 5-point Likert scale (1 = "strongly agree" to 5 = "strongly disagree"; e.g., "Feeling distressed or upset is unbearable to me."). It is comprised of a single higher order distress tolerance factor and four subscales (tolerance, appraisal, absorption, and regulation), such that higher scores indicate a greater ability to cope with psychological distress. Research has indicated good internal consistency, construct validity, and test-retest reliability (current sample, Cronbach's α=.88).

Difficulties in Emotion Regulation Scale The *Difficulties in Emotion Regulation Scale* (DERS) [47] is a 36-item self-report measure of difficulties in emotion regulation, with items rated on a Likert-type scale (1 = "almost never" to 5 = "almost always"). In the current investigation, the total DERS score was used to index general ability to explicitly and implicitly employ emotion regulation strategies. Here, higher scores indicate less access to emotion regulation strategies (i.e., greater emotion regulation difficulty; e.g., "I experience my emotions as overwhelming and out of control."). This scale has demonstrated strong internal consistency, retest reliability, and construct validity [47]. Consistent with past work, the present sample demonstrated good internal consistency (Cronbach's α=.92).

Procedure

The present investigation is a secondary analysis of a study investigating the impact of cannabis use on medication adherence [37]. Interested participants contacted the lab for completion of a phone screen, which assessed for inclusionary and exclusionary criteria. If participants were deemed eligible and still interested, they were scheduled for an in-person session. During this session, participants completed a diagnostic assessment [42] and self-report questionnaires. In addition, with participants' permission, viral load was gathered from recent medical records. The study session duration was approximately 2 h and participants were compensated US$50 upon completion.

Results

Descriptive Data and Correlations Among Theoretically Relevant Variables

Participants were 139 HIV+ individuals (23.0 % female; M_{age}=48.15 years, SD=8.15) recruited from four San Francisco Bay Area HIV clinics between 2010 and 2012. The sample average log-transformed viral load was 1.89 (SD=.79), with an average CD4 count of 525.5 cells/uL

(SD=285.0), which is consistent with that found among individuals undergoing treatment for HIV (Department of Health and Human Services, Center for Disease Control, 2012). In terms of race, 40.3 % of participants identified as Black/Non-Hispanic, 29.5 % as White/Caucasian, 10.8 % as Black/Hispanic, 10.8 % as Hispanic, 1.4 % as Asian, and 7.2 %"Other." In terms of education, the majority of participants reported graduating from high school or completing part of college (56.1 %), with 16.5 % acquiring 12 or fewer years of education, 20.1 % graduating from a two- or four-year college, and 7.3 % completing professional or graduate school. The majority of the sample reported never being married (46.7 %), with 27.1 % separated, divorced, or annulled, 20.4 % of participants married or living with a partner, and 5.8 % widowed. On average, participants met criteria for 1.58 (SD=1.73) DSM-IV Axis-I disorders with 46.0 % meeting criteria for an anxiety disorder, and 21.6 % for a mood disorder. The most common diagnoses in the sample were cannabis dependence (31.7 %), posttraumatic stress disorder (15.1 %), alcohol dependence (12.9 %), major depressive disorder (13.0 %), dysthymia (10.1 %), and specific phobia (9.4 %).

In terms of alcohol use, 40.3 % reported no current alcohol use, 22.3 % reported drinking monthly or less, 17.3 % reported drinking two to four times a month, 8.6 % two to three times a week, and 11.5 % four or more times a week. Of those who reported current alcohol use, most reported just one or two drinks per occasion (60.2 %). On average, participants scored an 8.40 (SD= 9.35) on the Alcohol Use Disorders Identification Test [44], with 39.6 % of participants scoring an 8 or higher, consistent with hazardous or harmful use.

First, zero-order correlations between theoretically relevant variables and our dependent variables (i.e., HIV symptom severity, BHAQ, and viral load (VL)) were examined in order to determine model covariates. Pearson's correlations were used for continuous variables, whereas ANOVA was used for rank order and dichotomous variables (e.g., education, cannabis diagnosis). HIV symptom severity was significantly positively correlated with AUDIT total score, and evidenced a significant relation to gender ($p<.05$), cannabis diagnosis ($p<.05$), and education ($p<.05$). Post hoc tests indicated significantly greater self-report of HIV symptoms among participants with marijuana dependence versus those with no use ($p<.05$), as well as those who completed less than high school versus those who completed graduate or professional school ($p=.01$). No significant relations were observed between self-reported HIV symptom severity and age, race, or marital status. BHAQ was significantly positively correlated with AUDIT total score, while ANOVA revealed significant differences in BHAQ based on race ($p<.01$) and education ($p<.05$). Post hoc tests indicated trend level relations. Here, Caucasian/White participants reported lower BHAQ scores than both Black/Hispanic ($p=.06$) and Black/Non-Hispanic ($p=.07$) participants. Also, participants with less than a high school education reported greater BHAQ scores than those who completed graduate or professional school ($p=.06$). Trend level differences for VL were observed based on cannabis group status with post hoc tests indicating higher values among those with those with cannabis dependence versus non-users ($p=.08$). A trend level relation also was observed between VL and race ($p=.07$), but post hoc tests did not reveal significant or trend level differences between groups (please see Tables 1 and 2).

With regard to our main predictors, AS was significantly negatively correlated with DT, and positively correlated with ER, while DT and ER were significantly negatively correlated with each other. This indicates that individuals, who are sensitive to anxiety, are also likely to report greater difficulty in regulating their emotions and a low ability to tolerate distress. HIV symptom severity was significantly positively correlated with ER and AS, and significantly negatively correlated with DT. BHAQ total score was similarly significantly positively correlated with ER and AS and negatively correlated with DT. However, VL was not significantly related to either ER, AS, or DT.

AS, DT, and ER in the Prediction of HIV Symptom Severity

All main predictors were mean-centered for regression analyses to eliminate the potential for multicollinearity. A multiple regression was conducted to test the hypothesis that ER, AS, and DT, evaluated concurrently and above and beyond the variance explained by alcohol use problems, cannabis group status, gender, and education, would predict self-reported HIV symptom severity. Given that race did not demonstrate significant correlations with HIV symptom severity, it was not included as a covariate. Step one of the model accounted for 16.6 % of the variance ($F(4, 134)=6.68$, $p<.01$), with alcohol and education level significantly predicting HIV symptom severity, indicating those with more hazardous alcohol use and less educational achievement reported greater symptom severity. In addition, a trend level relation was observed for gender, indicating that women reported greater HIV symptom severity than men. Cannabis group membership did not significantly predict any model variance in HIV symptom severity (please see Table 3).

With regard to the main predictors examined concurrently at step two, together they accounted for 16.3 % additional model variance ($F(7, 131)=9.19$, $p<.01$). Specifically, greater AS was associated with heightened HIV symptom severity. In addition, a trend level

Table 1 Descriptive data and zero-order Pearson's correlations

	1	2	3	4	5	6	7	8	*M* (SD)
1. HIV_Sx_Sev[a]	1	.31**	.00	−.08	.31**	.49**	−.24**	.43**	32.27 (17.54)
2. BHAQ[b]		1	.17*	.02	.23**	.23**	−.20*	.44**	53.11 (13.95)
3. VL[c]			1	−.06	.08	.02	−.03	.15	1.89 (.79)
5. AUDIT[d]					1	.24*	−.20*	.25**	8.40 (9.34)
6. AS[e]						1	−.48**	.59**	22.05 (17.17)
7. DT[f]							1	−.57**	2.95 (.88)
8. ER[g]								1	84.05 (22.58)

*N= 139. *p<.05; **p<.01*

[a] HIV symptom severity [39]

[b] Barriers to HAART Adherence Questionnaire [40]

[c] Log-transformed viral load [34]

[d] Alcohol Use Disorders Identification Test [37]

[e] Anxiety sensitivity [42]

[f] Distress tolerance [44]

[g] Emotion regulation [41]

relation was observed for ER, indicating that those with greater difficulty in emotion regulation also reported greater HIV symptom severity. DT did not predict any additional model variance in HIV symptom severity.

Table 2 One-way ANOVAs between theoretically relevant variables

	HIV symptom severity[a]
Cannabis group[b]	$F(2, 136)=3.71$, $p=.03$
Gender[c]	$F(1, 137)=5.81$, $p=.02$
Education[d]	$F(3, 135)=3.45$, $p=.02$
Race[e]	$F(5, 133)=.78$, $p=.57$
	Barriers to HAART adherence[f]
Cannabis group[b]	$F(2, 136)=.73$, $p=.49$
Gender[c]	$F(1, 137)=2.43$, $p=.12$
Education[d]	$F(3, 135)=2.76$, $p<.05$
Race[e]	$F(5, 133)=3.08$, $p=.01$
	Viral load[g]
Cannabis group[b]	Welch's $F(2, 76.40)=2.78$, $p=.07$
Gender[c]	$F(1, 137)=.04$, $p=.84$
Education[d]	$F(3, 135)=1.29$, $p=.56$
Race[e]	Welch's $F(5, 9.87)=4.40$, $p=.07$

N=139

[a] HIV symptom severity [39]

[b] Cannabis group (1 = "No use"; 2 = "Non-dependent"; 3="Dependent")

[c] Gender (1 = "male"; 2 = "female")

[d] Education (1 = "Less than high school"; 2 = "High school or part college"; 3 = "Graduated from 2- or 4-year college"; 4 = "Completed graduate or professional school")

[e] Race (1 = "White/Caucasian"; 2 = "Black/Non-Hispanic"; 3 = "Black/Hispanic"; 4 = "Hispanic"; 5 = "Asian"; 6 = "Other")

[f] Barriers to HAART Adherence Questionnaire [40]

[g] Log-transformed viral load [34]

AS, DT, and ER in the Prediction of Barriers to HAART Medication Adherence

A linear multiple regression was conducted to test the hypothesis that ER, AS, and DT, when evaluated concurrently, and above and beyond the variance explained by alcohol use problems, cannabis group status, gender, education, and race, would predict self-report of barriers to HAART medication adherence among HIV-infected individuals. Cannabis group was included in the model based on the study design, as were gender and education. Step one of the model accounted for 9.6 % of the variance ($F(5, 133)=2.81$, $p<.05$), with alcohol and education demonstrating significant associations with BHAQ, indicating that those with more hazardous alcohol use problems and less educational achievement reported greater barriers to adherence. Cannabis group membership, gender, and race did not significantly predict any model variance in BHAQ (please see Table 3).

In terms of the main predictors examined concurrently at step two, together they accounted for 12.7 % additional model variance ($F(8, 130)=4.66$, $p<.01$). Specifically, ER significantly predicted BHAQ total score, such that those with greater difficulties in regulating their emotions reported greater barriers to adherence. Neither AS nor DT significantly predicted any additional model variance in barriers to HAART adherence.

AS, DT, and ER in the Prediction of Log-Transformed Viral Load

A final multiple regression concurrently examined AS, DT and ER in relation to log-transformed viral load (VL), above and beyond variance explained by cannabis group status. Step

Table 3 Summary of hierarchical regression analyses

	ΔR^2	*t*	β	sr^2	*p*
Criterion variable: HIV symptom severity[a]					
Step 1	.17				<.01
AUDIT[b]		3.20	.27	.06	<.01
Cannabis group[c]		.87	.07	.00	ns
Gender[d]		1.75	.14	.02	.08
Education[e]		−1.99	−.17	.03	<.05
Step 2	.16				.001
AS[f]		3.79	.36	.07	.01
DT[g]		1.12	.10	.01	ns
ER[h]		1.81	.19	.02	.07
Criterion variable: Barriers to HAART Adherence Questionnaire[i]					
Step 1	.10				<.05
AUDIT[b]		2.38	.21	.04	<.05
Cannabis group[c]		.12	.01	.00	ns
Gender[d]		.85	.07	.00	ns
Education[e]		−1.98	−.17	.03	.05
Race[j]		.25	.02	.00	ns
Step 2	.13				.001
AS[f]		−.70	−.07	.00	ns
DT[g]		.65	.07	.00	ns
ER[h]		4.09	.46	.10	<.001
Criterion variable: log-transformed viral load[k]					
Step 1	.03				<.05
Cannabis group[d]		2.01	.17	.03	<.05
Step 2	.02				ns
AS[f]		−.71	−.08	.00	ns
DT[g]		.62	.06	.00	ns
ER[h]		1.81	.21	.02	.07

N= 139

[a] HIV symptom severity [39]

[b] Alcohol Use Disorders Identification Test [37]

[c] Cannabis Group (1 = "No use"; 2 = "Non-dependent"; 3 = "Dependent")

[d] Gender (1 = "male"; 2 = "female")

[e] Education (1 = "Less than high school"; 2 = "High school or part college"; 3 = "Graduated from 2- or 4-year college"; 4 = "Completed graduate or professional school")

[f] Anxiety sensitivity [42]

[g] Distress tolerance [44]

[h] Emotion regulation [41]

[i] Barriers to HAART Adherence Questionnaire [40]

[j] Race (1 = "White/Caucasian"; 2 = "Black/Non-Hispanic"; 3 = "Black/Hispanic"; 4 = "Hispanic"; 5 = "Asian"; 6 = "Other")

[k] Log-transformed viral load [34]

one of the model accounted for 2.9 % of the variance ($F(1, 137)=4.03$, $p<.05$), with cannabis group membership significantly relating to VL, such that those with cannabis dependence had greater VL (please see Table 3).

In terms of the main predictors examined concurrently at step two, together they accounted for 2.4 % additional model variance ($F(4, 134)=1.85$, $p=.12$). Though neither AS nor DT significantly predicted any additional model variance, a trend level relation was observed for ER ($p=.07$), indicating that those with greater difficulties in regulating emotion exhibited a higher VL.

Discussion

Despite recent advances in the treatment of HIV, including interventions designed to directly and indirectly (e.g., via social support, and targeting of co-occurring depression and/or substance sue) [1–7] target medication adherence, individuals with HIV continue to suffer from a range of HIV-related symptoms [8, 9]. Interventions designed to target cognitive-affective risk may present a novel approach toward improving quality of life in this population. The current investigation sought to distill the relations between three theoretically and empirically relevant cognitive-affective factors—ER, AS, and DT—in relation to HIV symptom severity, perceived barriers to medication adherence, and log transformed viral load, among HIV+ individuals enrolled in treatment at a community clinic.

Partially consistent with study hypotheses, AS significantly predicted unique variance in relation to HIV symptom severity above and beyond variance accounted for by alcohol use problems, cannabis group status, gender, and education. Contrary to study hypotheses, DT was not associated with HIV symptom severity, and ER evidenced a trend relation. These findings suggest that HIV+ individuals who report greater sensitivity to anxiety and its potential consequences are at heightened risk for more severe HIV symptoms. This finding is consistent with previous work suggesting that HIV+ individuals high in AS report greater somatic distress, which may broadly overlap with HIV symptoms [32, 33].

A different pattern of relations was observed in terms of barriers to medication adherence. Indeed, ER, but not AS or DT, evidenced a significant relation to medication adherence barriers. This finding suggests that individuals with a greater capacity to accept and understand their emotional distress, and engage in adaptive behaviors despite distress, perceive fewer barriers in terms of their ability to adhere to their medication. This finding is broadly consistent with previous research suggesting that HIV+ individuals with positive states of mind [15], who engage in greater cognitive coping [16, 17], mindfulness, and less disengagement coping [18] are more medication adherent, report greater self-efficacy, and less anxiety, depression, and substance use. It is also consistent with findings by Brandt et al. [37], which suggest that ER mediated an observed relation between DT and a range of psychiatric symptoms among HIV+ individuals.

Analyses focused on the association between AS, DT, and ER and log-transformed viral load provided little insight into the clinical utility of these cognitive-affective vulnerabilities in relation to a biomarker of HIV, with just a trend relation observed for ER. That being said, in combination with the finding suggesting ER is relevant to medication adherence, this trend level relation further highlights the potential importance of targeting difficulties in emotion regulation among individuals with HIV.

Only one study to our knowledge has concurrently examined AS, DT, and ER in terms of HIV symptom distress [38]. Whereas the present investigation indicated AS, rather than DT or ER, is the strongest predictor of HIV symptom severity, Brandt et al. [38] found that ER, but not DT and AS, uniquely and significantly predicted HIV symptom distress. These differing findings may be a result of sample characteristics. For example, approximately half of the individuals in the investigation by Brandt and colleagues [38] were diagnosed with AIDS, whereas the individuals in the current investigation were HIV+ individuals maintained on ART and generally characterized as having low viral load and high absolute CD4 t-cell lymphocyte count. Also, given the large body of empirical evidence suggesting the transdiagnostic relevance of AS, current findings may have been impacted by the high prevalence of comorbid mental illness and substance use observed in the current sample, despite the inclusion of cannabis diagnosis and alcohol use as covariates.

The lack of observed significant relations between DT and HIV symptom severity and barriers to ART adherence were somewhat surprising given previous reports of relations between DT and medication adherence, and HIV symptoms [35, 36]. Several explanations may be relevant. First, previous studies examined the role of DT in the absence of other relevant cognitive-affective vulnerabilities; thus, it is possible that previously observe relations may have been better accounted for by seemingly more robust cognitive-affective factors, such as ER. In support of this, two investigations by Brandt and colleagues [37, 38] suggest that both AS and ER evidence greater specificity to poor outcomes among HIV+ individuals, as compared with DT. Alternatively, the method of measurement of DT may have contributed to this null finding [28]. Given the observed differential relations between objective and subjective measures of DT among individuals with HIV [36], it is possible that including a multimethod assessment of DT in the present investigation would have provided more nuanced findings in terms of the importance of DT in the measured outcomes. Further, recent factor analytic work suggests that a higher order DT construct may be indexed by items from the anxiety sensitivity index and the distress tolerance scale [51], providing additional evidence for their overlap. Future work would benefit from a multimethod examination of each predictor. Finally, previous work indicates that DT and ER may exhibit an interactive relation in terms of maladaptive avoidance behavior [52]. Therefore, future work may benefit from the examination of interactive relations between these affective vulnerabilities in terms of avoidant behavior relevant to this population (e.g., poor medication adherence).

Further detailing these findings in light of significant relations observed between covariates and HIV outcomes is additionally informative. In the present investigation, HIV+ individuals with greater alcohol use problems and lower educational attainment reported greater HIV symptom severity and barriers to HAART adherence. This indicates that co-occurring alcohol problems may play an important and unique role in terms of poor HIV outcomes, suggesting assessment for hazardous use and concurrent alcohol treatment may help improve outcomes among individuals with HIV, consistent with prior postulations [53]. Additionally, there is some evidence to suggest that comorbid alcohol use problems and HIV status may result in emotion processing deficits [54]. Therefore, it is possible that individuals in the present sample who were characterized by this comorbidity may be at even greater risk for cognitive-affective vulnerability, particularly deficits in the ability to regulate emotions. Given the significant relation observed between educational attainment and HIV symptom severity, it may be important to tailor interventions to be sensitive to level of educational attainment. Importantly, the directional basis for observed relations cannot be determined in the present findings, so implications for the development of interventions should be informed by additional research elucidating these relations prospectively.

The current investigation has several relevant limitations. First, the sample was primarily male and comprised of older adults; therefore, results may not be generalizable to a diverse set of HIV+ individuals. Similarly, these individuals were recruited from community clinics, receiving ART, and evidenced relatively low viral loads, which may have resulted in fewer HIV symptoms. Third, the present findings are cross-sectional in nature. Although ER, AS, and DT have been characterized as relatively stable, trait-like vulnerabilities, it is possible that such risk factors are activated or exacerbated following an acute or series of unique stressors, such as HIV diagnosis and subsequent health and lifestyle changes. Future work in this domain should seek to better understand the prospective relations between these vulnerabilities and HIV symptom severity across time. This is particularly relevant given symptom expression changes depending on stage of illness [55, 56] and side effects associated with short- [50] and long-term ART [57–59]. Finally, as alluded to previously, it is possible that the relation between AS and HIV symptom severity is moderated by an activating event (e.g., major life stressor), behaviors (e.g., avoidance via substance use or self-harm), or cognitions (e.g., hopelessness). Future prospective investigations should seek to elucidate these relations in order

to build theoretically and empirically relevant treatment adjuncts for individuals with HIV.

Despite these limitations, the current study provides additional support for the clinical significance of increasing our understanding of malleable cognitive-affective vulnerabilities among HIV+ individuals. Specifically, findings indicate that HIV+ individuals high in AS who also report difficulties in emotion regulation may particularly benefit from specialized interventions that specifically target the improvement of these vulnerability factors so as to reduce HIV symptoms, barriers to medication adherence, as well as viral load levels. For example, interoceptive exposure exercises may be useful in reducing anxiety sensitivity [60, 61], while mindfulness and acceptance-based strategies [62, 63] or emotional awareness exercises may aid in the improvement of emotion regulation. These strategies might be incorporated into existing empirically supported cognitive-behavioral treatments or utilized to construct novel, specialized interventions for this population.

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Conflict of Interest Dr. Leyro, Dr. Vujanovic, and Dr. Bonn-Miller declare that they have no conflict of interest.

Statement of Human and Animal Rights Dr. Leyro, Dr. Vujanovic, and Dr. Bonn-Miller conformed to the Helsinki Declaration of 1975, as revised in 2000 and 2008, concerning human rights and informed consent, including following the correct procedures regarding the ethical treatment of humans in research.

References

1. Duncan LG, Moskowitz JT, Neilands TB, Dilworth SE, Hecht FM, Johnson MO. Mindfulness-based stress reduction for HIV treatment side effects: a randomized, wait-list controlled trial. J Pain Symptom Manage. 2012;43(2):161–71.
2. Rao D, Nainis N, Williams L, et al. Art therapy for relief of symptoms associated with HIV/AIDS. AIDS Care. 2009;21(1):64–9.
3. Webel AR. Testing a peer-based symptom management intervention for women living with HIV/AIDS. AIDS Care. 2010;22(9):1029–40.
4. Ammassari A, Trotta MP, Shalev N, et al. Timed short messaging service improved adherence and virological outcomes in HIV-1-infected patients with suboptimal adherence to antiretroviral therapy. J Acquir Immune Defic Syndr. 2011;58(4):e113–5.
5. Johnson M, Charlebois E, Morin SF, Remien RH, Chesney MA. Effects of a behavioral intervention on antiretroviral medication adherence among people living with HIV: the healthy living project randomized controlled study. J Acquir Immune Defic Syndr. 2007;46(5):574–80.
6. Safren SA, O'Cleirigh CM, Bullis JR, Otto MW, Stein MD, Pollack MH. Cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected injection drug users: a randomized controlled trial. J Consult Clin Psychol. 2012;80(3):404–15.
7. Galárraga O, Genberg BL, Martin RA, Barton LM, Wilson IB. Conditional economic incentives to improve HIV treatment adherence: Literature review and theoretical considerations. AIDS Behav. 2013;17:2283–92.
8. Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med. 2007;167(6):540.
9. Simoni JM, Pearson CR, Pantalone DW, Marks G, Crepaz N. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load: a meta-analytic review of randomized controlled trials. J Acquir Immune Defic Syndr. 2006;43:S23–35.
10. Leyro T, Zvolensky M, Bernstein A. Distress tolerance and psychopathological symptoms and disorders: a review of the empirical literature among adults. Psych Bull. 2010;136(4):576–600.
11. Keough M, Schmidt N. Refinement of a brief anxiety sensitivity reduction intervention. J Clin Consult Psychol. 2012;80(5):766–72.
12. Aldao A, Nolen-Hoeksema S, Schweizer S. Emotion-regulation strategies across psychopathology: a meta-analytic review. Clin Psychol Rev. 2010;30(2):217–37.
13. Bernstein A, Marshall E, Zvolensky M. Multi-method evaluation of distress tolerance measures and construct(s): concurrent relations to mood and anxiety psychopathology and quality of life. J Exp Psychopathol. 2011;2(3):386–99.
14. Gratz KL, Roemer L. Multidimensional assessment of emotion regulation and dysregulation: development, factor structure, and initial validation of the difficulties in emotion regulation scale. J Psychopathol Behav Assess. 2004;26(1):41–54.
15. Carrico AW, Johnson MO, Moskowitz JT, et al. Affect regulation, stimulant use, and viral load among HIV-positive persons on antiretroviral therapy. Psychosom Med. 2007;69(8):785–92.
16. Kraaij V, van der Veek SM, Garnefski N, Schroevers M, Witlox R, Maes S. Coping, goal adjustment, and psychological well-being in HIV-infected men who have sex with men. AIDS Patient Care STDs. 2008;22(5):395–402.
17. Kraaij V, Garnefski N, Schroevers MJ, van der Veek S, Witlox R, Maes S. Cognitive coping, goal self-efficacy and personal growth in HIV-infected men who have sex with men. Patient Educ Couns. 2008;72(2):301–4.
18. Gonzalez A, Solomon SE, Zvolensky MJ, Miller CT. The interaction of mindful-based attention and awareness and disengagement coping with HIV/AIDS-related stigma in regard to concurrent anxiety and depressive symptoms among adults with HIV/AIDS. J Health Psychol. 2009;14(3):403–13.
19. Brown KW, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol. 2003;84(4):822–48.
20. Carver CS, Scheier MF, Weintraub JK. Assessing coping strategies: a theoretically based approach. J Pers Soc Psychol. 1989;56(2):267–83.
21. Reiss S, McNally RJ. Expectancy model of fear. In: Reiss S, Bootzin RR, editors. Theoretical issues in behavior therapy. San Diego: Academic; 1985. p. 107–21.
22. Leyro TM, Zvolensky MJ, Bernstein A. Distress tolerance and psychopathological symptoms and disorders: a review of the empirical literature among adults. Psychol Bull. 2010;136(4):576–600.
23. DeHaas RA, Calamari JE, Bair JP. Anxiety sensitivity and the situational antecedents to drug and alcohol use: an evaluation of anxiety patients with substance use disorders. Cog Ther Res. 2002;26(3):335–53.
24. Norton GR. Substance use/abuse and anxiety sensitivity: what are the relationships? Addict Behav. 2001;26(6):935–46.
25. Ocañez KL, McHugh KR, Otto MW. A meta-analytic review of the association between anxiety sensitivity and pain. Depress Anxiety. 2010;27(8):760–7.
26. Olatunji BO, Wolitzky-Taylor KB. Anxiety sensitivity and the anxiety disorders: a meta-analytic review and synthesis. Psychol Bull. 2009;135(6):974.

27. Simpson T, Jakupcak M, Luterek JA. Fear and avoidance of internal experiences among patients with substance use disorders and PTSD: the centrality of anxiety sensitivity. J Trauma Stress. 2006;19(4):481–91.
28. Bernstein A, Marshall EC, Zvolensky MJ. Multi-method evaluation of distress tolerance measures and construct (s): concurrent relations to mood and anxiety psychopathology and quality of life. J Exp Psychopath. 2011;2(3):386–99.
29. Vujanovic AA, Bonn-Miller MO, Potter CM, Marshall EC, Zvolensky MJ. An evaluation of the relation between distress tolerance and posttraumatic stress within a trauma-exposed sample. J Psychopathol Behav Assess. 2011;33(1):129–35.
30. Inserting LM. Skills training manual for treating borderline personality disorder [e-book]. New York: Guilford; 1993.
31. Bernstein A, Zvolensky M, Vujanovic A, Moos R. Integrating anxiety sensitivity, distress tolerance, and discomfort intolerance: a hierarchical model of affect sensitivity and tolerance. Behav Ther. 2009;40(3):291–301.
32. Gonzalez A, Zvolensky MJ, Parent J, Grover KW, Hickey M. HIV symptom distress and anxiety sensitivity in relation to panic, social anxiety, and depression symptoms among HIV-positive adults. AIDS Patient Care STDS. 2012;26(3):156–64.
33. Gonzalez A, Zvolensky MJ, Solomon SE, Miller CT. Exploration of the relevance of anxiety sensitivity among adults living with HIV/AIDS for understanding anxiety vulnerability. J Health Psychol. 2010;15(1):138–46.
34. Capron DW, Gonzalez A, Parent J, Zvolensky MJ, Schmidt NB. Suicidality and anxiety sensitivity in adults with HIV. AIDS Patient Care STDS. 2012;26(5):298–303.
35. O'Cleirigh C, Ironson G, Smits JA. Does distress tolerance moderate the impact of major life events on psychosocial variables and behaviors important in the management of HIV? Behav Ther. 2007;38(3):314–23.
36. Oser ML, Trafton JA, Lejuez CW, Bonn-Miller MO. Differential associations between perceived and objective measurement of distress tolerance in relation to art adherence and response among HIV+ individuals. Behav Ther. 2013;44:432–42.
37. Brandt CP, Zvolensky MJ, Bonn-Miller MO. Distress tolerance, emotion dysregulation, and anxiety and depressive symptoms among HIV+ individuals. Cognit Ther Res. 2013;37:446–55.
38. Brandt CP, Gonzalez A, Grover KW, Zvolensky MJ. The relation between emotional dysregulation and anxiety and depressive symptoms, pain-related anxiety, and HIV-symptom distress among adults with HIV/AIDS. J Psychopathol Behav Assess. 2013;35(2):197–204.
39. Bonn-Miller MO, Oser ML, Bucossi MM, Trafton JA. Cannabis use and HIV antiretroviral therapy adherence and HIV-related symptoms. J Behav Med. 2014;37:1–10.
40. Mellors JW, Munoz A, Giorgi JV, et al. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. Ann of Intern Med. 1997;126(12):946–54.
41. U.S. Health Resources and Services Administration, 2012. http://www.hrsa.gov/index.html. Accessed 10 Feb 2013.
42. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV-TR Axis I disorders, research version, non-patient edition. SCID-I/NP, 11/2002 revision. New York: Biometrics Research, New York State Psychiatric Institute; 2002.
43. Babor TF, de la Fuente JR, Saunders J, Grant M. AUDIT: Alcohol Use Disorders Identification test: guidelines for use in primary health care. Geneva: World Health Organization; 1992.
44. Saunders JB, Aasland OG, Babor TF, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption—II. Addiction. 1993;88(6):791–804.
45. Chesney MA. Factors affecting adherence to antiretroviral therapy. Clin Infect Dis. 2000;30 Suppl 2:S171–6.
46. Murphy DA, Sarr M, Durako SJ, Moscicki AB, Wilson CM, Muenz LR. Barriers to HAART adherence among human immunodeficiency virus-infected adolescents. Arch Pediatr Adolesc Med. 2003;157(3):249–55.
47. Gratz KL, Roemer L. Multidimensional assessment of emotion regulation and dysregulation: development, factor structure, and initial validation of the difficulties in emotion regulation scale. J Psychopathol Behav Assess. 2004;26(1):41–54.
48. Taylor S, Zvolensky MJ, Cox BJ, et al. Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. Psychol Assessment. 2007;19(2):176–88.
49. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. Beh Res Ther. 1986;24(1):1–8.
50. Simons JS, Gaher RM. The Distress Tolerance Scale: development and validation of a self-report measure. Motiv Emotion. 2005;29(2):83–102.
51. McHugh RK, Otto MW. Refining the measurement of distress intolerance. Behav Ther. 2012;43(3):641–51.
52. McHugh RK, Reynolds EK, Leyro TM, Otto MW. An examination of the association of distress intolerance and emotion regulation with avoidance. Cognitive Ther Res. 2013;37(2):363–7.
53. Azar MM, Springer SA, Meyer JP, Altice FL. A systematic review of the impact of alcohol use disorders on HIV treatment outcomes, adherence to antiretroviral therapy and health care utilization. Drug Alcohol Depen. 2010;112(3):178–93.
54. Schulte T, Muller-Oehring EM, Sullivan EV, Pfefferbaum A. White matter fiber compromise contributes differentially to attention and emotion processing impairment in alcoholism, HIV-infection, and their comorbidity. Neuropsychologia. 2012;50(12):2812–22.
55. Cook PF, Sousa KH, Matthews EE, Meek PM, Kwong J. Patterns of change in symptom clusters with HIV disease progression. J Pain Symptom Manag. 2011;42(1):12–23.
56. HIV InSite, UCSF Center for HIV Information, 2013. http://hivinsite.ucsf.edu/ Accessed 25 Mar 2013
57. Foster C, Fidler S. Optimizing antiretroviral therapy in adolescents with perinatally acquired HIV-1 infection. Expert Rev Anti Infect Ther. 2010;8(12):1403–16.
58. Palella Jr FJ, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. J Acquir Immune Defic Syndr. 2006;43(1):27–34.
59. Quinn TC. HIV epidemiology and the effects of antiviral therapy on long-term consequences. AIDS. 2008;22 Suppl 3:S7–S12.
60. Boswell JF, Farchione TJ, Sauer-Zavala S, Murray HW, Fortune MR, Barlow DH. Anxiety sensitivity and interoceptive exposure: a transdiagnostic construct and change strategy. Behav Ther. 2013;44:417–31.
61. Otto MW. Anxiety sensitivity, emotional intolerance, and expansion of the application of interoceptive exposure: commentary on the special issue. J Cognitive Psychother. 2008;22(4):379–84.
62. Keng SL, Smoski MJ, Robins CJ, Ekblad AG, Brantley JG. Mechanisms of change in mindfulness-based stress reduction: self-compassion and mindfulness as mediators of intervention outcomes. J Cognitive Psychother. 2012;26(3):270.
63. Phillippot P, Segal Z. Mindfulness based psychological interventions: developing emotional awareness for better being. J Consciousness Stud. 2009;16:285–306.