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Gender moderates the influence of psychosocial factors and drug use on HAART adherence in the context of HIV and childhood sexual abuse

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Abstract

This study aimed to examine gender moderation within a stress and coping model of HIV medication adherence in adults with a history of childhood sexual abuse (CSA). Sequelae of CSA, including negative coping, psychological distress, and drug use, interfere with adherence to highly active antiretroviral treatment (HAART). These obstacles to adherence are likely moderated by gender. Gender may particularly influence the mediational effect of drug use on adherence. Participants included 206 adults living with HIV/AIDS and CSA. Categorical/continuous variable methodology (CVM) in a structural equation modeling (SEM) framework was used to test a multigroup model with women and men. Gender significantly moderated several effects in the model. For women, the effect of psychological distress on HAART adherence was mediated by drug use, and the effect of drug use on viral load was mediated by HAART adherence. Among men, drug use did not significantly impact adherence. Since gender appears to moderate the effect of drug use on medication adherence, it is particularly important to address drug use within the context of HIV disease management in women with a history of CSA. Further, interventions to increase HAART adherence should take trauma history, gender, and drug abuse into account when assessing efficacy.

Keywords

medication adherence; CSA = childhood sexual abuse; HIV = human immunodeficiency virus; drug abuse; SEM = structural equation modeling; gender difference

Introduction

HIV is a chronic illness that threatens the health of over 1 million individuals living in the United States (CDC, 2012). Among people living with HIV/AIDS, approximately 33% to 53% report a history of childhood sexual abuse (CSA) (Henny, Kidder, Stall, & Wolitski,

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2007; Kalichman, Sikkema, DiFonzo, Luke, & Austin, 2002; Machtinger, Wilson, Haber, & Weiss, 2012; Welles et al., 2009; Whetten et al., 2006). HIV-positive adults with CSA suffer from psychological sequelae that interfere with medication adherence, which in turn affects HIV disease progression (Cohen, Alfonso, Hoffman, Milau, & Carrera, 2001; Markowitz et al., 2011; Meade, Hansen, Kochman, & Sikkema, 2009). For HIV-positive individuals with CSA, unique factors leading to reduced HAART adherence include drug use, poor social support, and traumatic stress symptoms (Liu et al., 2006; Meade et al., 2009). While emerging research has focused on predictors of poor medication adherence in this population, there is a gap in empirical study of mechanisms and moderators of influences on adherence.

Drug use/abuse may represent one mechanism by which a history of CSA results in low HAART adherence. Drug and alcohol use significantly and uniquely predict poorer HAART adherence in a variety of populations (Golin et al., 2002; Hendershot, Stoner, Pantalone, & Simoni, 2009; Kreitchmann et al., 2012; Marks King et al., 2012). Accelerated HIV disease progression in drug users may be mediated by poor health maintenance behaviors, including HAART adherence (Milloy et al., 2012). Given that drug use/abuse is common in those who have experienced CSA, the impact of regular drug use on medication adherence should be examined in this population (Felitti et al., 1998; Molnar, Buka, & Kessler, 2001).

There is evidence to suggest that mediational pathways influencing HAART adherence may differ by gender. Overall, HIV-positive women demonstrate lower HAART adherence compared to their male counterparts (Berg et al., 2004; Tapp et al., 2011). Differences in mediational pathways may explain this gender disparity. For example, in a sample of older adults, depression mediated the relationship between negative coping and adherence for men only (Bianco, Heckman, Sutton, Watakakosol, & Lovejoy, 2011). Additionally, gender moderates the effect of alcohol use on HAART adherence: problematic alcohol use was associated with lower HAART adherence for women only (Berg et al., 2004). Given that CSA history is similarly prevalent in both men and women with HIV (Kalichman et al., 2002), gender effects should be evaluated in the context of CSA sequelae, such as negative coping, psychological distress, and drug use. For individuals with CSA, gender has yet to be examined as a moderating influence on HAART adherence, especially via variables such as depression, PTSD, and drug use.

The current study sought to test and expand upon an empirically-supported model of HAART adherence. Based on a theoretical foundation in stress and coping, Johnson and colleagues (2009) found that the effects of social support and negative coping on HAART adherence were fully mediated by negative affect. This model, which incorporated psychosocial and behavioral influences of HAART adherence, is similar to other theory-driven models (Gonzalez et al., 2007; Simoni, Frick, & Huang, 2006; Weaver et al., 2005). Utilizing a similar theoretical basis, the hypothesized model incorporated aspects of Lazarus and Folkman's stress and coping theory (1984) within a model of behavioral mediation of HIV disease progression (Gore-Felton & Koopman, 2008). According to the theory of stress and coping, psychological symptoms are impacted by life stressors, coping strategies, and cognitive appraisals of stressors. The theoretical model of HIV disease progression hypothesizes that behavioral mechanisms, such as drug abuse and poor medication

adherence, partially mediate the relationship between psychosocial factors and HIV disease progression (Gore-Felton & Koopman, 2008). In keep with these theoretical bases, we included gender as a moderator to examine how effects on HAART adherence differed for men and women.

In the current study, gender moderation was explored within a structural equation model of HAART adherence for HIV-positive adults with a history of CSA. Research goals were to: 1) explore the statistical fit of the negative affect mediation model for a sample of HIV-positive adults with CSA, 2) test whether drug use mediates the effect of psychological distress on HAART adherence, and 3) test whether model paths were moderated by gender. We hypothesized that gender would significantly moderate multiple mechanisms of HAART adherence. Specifically, we predicted that for women, drug use would have a stronger mediational effect on the relationship between psychological distress and adherence.

Method

Design

HIV-positive adults with CSA histories were recruited between March 2002 and January 2004 in New York City to participate in an intervention study on coping with HIV and sexual abuse, Living in the Face of Trauma (LIFT) (Sikkema et al., 2012).

Participants

All participants were recruited from AIDS service organizations and community health clinics in New York City between March 2002 and January 2004. Inclusion criteria were a) sexual abuse as a child and/or adolescent, defined as any unwanted touching of a sexual nature by an adult or by someone at least 5 years older than the participant when the incident occurred, b) current age 18 years or older, and c) HIV-positive serostatus. Exclusion criteria were a) acute distress attributable to sexual revictimization experienced within the past month, b) presence of impaired mental status, or c) extreme distress evidenced by suicidal intent or severe depressive symptomatology with a score of 30 or greater on the Beck Depression Inventory (Beck & Steer, 1993).

Of 33 individuals screened out for study eligibility, 21 did not meet study inclusion criteria (7 severely depressed, 7 not sexually abused, 6 cognitively impaired, and 1 acute sexual revictimization) and 41 declined or were not available for further participation in the study (23 not located, 13 not interested/unable to continue, 3 incarcerated, and 2 died/hospitalized). Thus, 271 individuals participated in baseline data collection. An additional 64 participants were excluded from the analysis because they were not prescribed HAART and had CD4 count over 350. One participant was also excluded for missing demographic data, leaving a final sample size of 206.

Procedure

Baseline assessment data were used for the current analyses. For further information on methods, see previous published studies (Meade et al., 2009; Meade et al., 2010; Sikkema et al., 2007; Sikkema et al., 2008).

Measures

The model was comprised of latent and observed variables, which were either continuous or dichotomous.

Latent life stress—The latent life stress variable was measured with the Life Problems, Stressors, and Concerns questionnaire (LPSC) (DeMarco, Ostrow, & DiFranceisco, 1999). Two LPSC items that assessed stress related to drug/alcohol use were excluded because the variable was intended to capture stress independent of drug use. Following statistical recommendations for parceling (Little, Cunningham, Shahar, & Widaman, 2002), the 26 remaining items were randomly parceled into four indicators of life stress (standardized factor loadings for the four indicators were .79, .78, .87, and .91).

Avoidant coping—Avoidant coping was measured using the Ways of Coping Questionnaire (Folkman & Lazarus, 1988) and the Coping with Illness scale (Namir, Wolcott, Fawzy, & Alumbaugh, 1987). Prior empirical work has found that when these scales are combined, five coping factors emerge (Sikkema, Hansen, Meade, Kochman, & Fox, 2009; Sikkema et al., 2012). The avoidant coping factor was used ($\alpha = .91$) and self-destructive coping was omitted due to multiple items involving drug use.

Latent psychological distress—The latent psychological distress variable was measured with three indicators. The Impact of Events Scale (IES) (Horowitz, Wilner, & Alvarez, 1979) measures overall posttraumatic stress disorder severity ($\alpha = .92$). The Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977) is designed to measure depression severity in clinical populations ($\alpha = .92$). The Symptom Checklist 90-R Global Severity subscale (SCL 90-R) (Derogatis & Cleary, 1977) is regarded as a measure of general psychological wellbeing ($\alpha = .98$).

Drug use—Participants reported the number of days in the past month they used a variety of illicit drugs (i.e., cocaine, crack, heroin, or methamphetamine). Participants received a score of '1' on drug use if they reported using an illicit drug at least 6 days in the prior month. Otherwise, they received a score of '0' on drug use. This methodology for categorizing drug use was adapted from the National Survey on Drug Use and Health (SAMHSA, 2011) in order to capture habitual drug use.

HAART Adherence—Participants reported the percentage of time in the past month that they took all prescribed HAART. In accordance with guidelines of optimal adherence (Paterson et al., 2000), adherence was categorized as optimal (at least 90%) or suboptimal (below 90%). Individuals were also classified as suboptimally adherent if they fit in the following category: CD4 count < 350 but not taking HIV medication. This was intended to capture individuals whose CD4 count was low enough to necessitate HAART but were not taking medication (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2009).

HIV disease progression—Participants reported last measured viral load and CD4 count. Due to its high skewness and kurtosis (5.99 and 38.02, respectively), high variance, and in keeping with previous empirical work, viral load was natural log transformed with a

constant added to retain zero values (Lucas, Cheever, Chaisson, & Moore, 2001; Quinn et al., 2000). A linear transformation (divided by 100) was performed on CD4 count in order to reduce the range of scores. These variables were intended as a validity check on participants' self-reports of medication adherence.

Statistical Methods

Prior to analyses, data were analyzed for patterns of missingness. Bivariate analysis included tests of gender differences in all predictor and outcome variables, as well as correlations among variables. The structural equation model was tested in Mplus Version 6 with continuous/categorical variable methodology (CVM) (Muthen, 1983), which uses a combination of full information maximum likelihood (FIML) and mean- and variance-adjusted weighted least squares estimation. Overall goodness of model fit was assessed with the χ^2 statistic, the root mean square error of approximation (RMSEA), the comparative fit index (CFI), the standardized root mean square residual (SRMR), and the weighted root mean residual (WRMR). Goodness of fit was assessed with the following cutoffs: χ^2 p-value < .05, RMSEA .05, CFI .95, and either SRMR < .08 or WRMR .95 (Hoyle, 2011; Kline, 2010; Yu, 2002). The measurement model estimated all latent variables using a fully saturated model in which all latent variables were allowed to correlate. Given good fit of the measurement model, goodness of fit was then tested for the preliminary structural model, which included key variables, hypothesized paths, and demographic covariates (gender was not taken into account).

In order to test gender moderation in the adherence model, both the measurement model and structural model were considered successively. In keeping with accepted statistical procedures for testing multigroup models (Hoyle, 2011; Kline, 2010), the DIFFTEST command in Mplus was utilized to employ a chi-square difference test to compare the gender equivalence model (H_0) to a series of gender difference models for each model path. After first establishing that male and female participants were equivalent on factor loadings in the measurement model, the structural model was examined. For paths that exhibited gender moderation, path magnitudes were allowed to be estimated freely by gender. Finally, indirect effects were examined for gender moderation.

Results

Bivariate gender differences

Gender differences emerged in bivariate statistical tests. Women and men differed in their years living with HIV, education level, ethnicity, and sexual orientation. Women had fewer years living with HIV, lower average educational attainment and were more likely to be African American and heterosexual (see Table 1). These variables were added as covariates in the model. See Table 2 for the variable correlation matrix by gender.

Preliminary model

Since preliminary fit of the measurement model was not within cutoff values, modification indices were utilized. A path accounting for correlation between two life stress indicators was added to the model. After this modification, overall fit of the measurement model was

within acceptable parameters ($\chi^2 = 25.57$, $p = .01$; CFI = .99; RMSEA = .07; SRMR = .02). Chi-square difference tests of the measurement model did not yield any significant gender differences on factor loadings. Goodness of fit indices for the preliminary structural model (not taking gender into account) were also within acceptable parameters, $\chi^2 (69) = 81.11$, $p = .15$; CFI = .98; RMSEA = .03; WRMR = .52.

Test of structural gender differences

In testing group invariance in the structural model, gender significantly moderated four paths: 1) the effect of psychological distress on drug use, 2) the effect of drug use on medication adherence, 3) the effect of avoidant coping on psychological distress, and 4) the correlation between stress and avoidant coping (see Figure 1 for final model). The multigroup model accounting for gender demonstrated good fit: $\chi^2 (152) = 159.68$, $p = .32$; CFI = .98; RMSEA = .02; WRMR = .75. In contrast to women, two paths were non-significant in the male sample. For men, psychological distress did not significantly predict drug use, nor did drug use significantly predict HAART adherence. However, for women these paths demonstrated strong effects.

Gender was further explored in the context of mediational paths, and gender differences were found in two indirect effects. For women, two indirect effects were significant: a) the effect of psychological distress on adherence, mediated by drug use, $\beta = -.32$, $p = .018$; and b) the effect of drug use on viral load, mediated by adherence, $\beta = .24$, $p = .048$. Female participants demonstrated a marginal indirect effect of psychological distress on viral load through adherence and drug use, $\beta = .12$, $p = .085$. For male participants, no indirect paths were significant.

Discussion

The purpose of this study was to explore gender moderation and drug use mediation within a model of HAART adherence in a sample of people living with HIV/AIDS and CSA. Study results indicated that gender significantly moderated influences on HAART adherence, most notably the effect of drug use. For women, but not men, drug use mediated the association between psychological symptoms and adherence. Results overall provide strong evidence for gender differences in key psychosocial influences on HAART adherence and HIV disease progression.

Study findings expand upon previous research that demonstrates the importance of gender when examining HAART adherence. For women, the relationship between psychological distress, drug abuse, and HAART adherence is likely stronger than for men, though this gender moderation may be especially evident in individuals with CSA. This finding corroborates prior evidence that gender moderates the influence of alcohol use on HAART adherence. Specifically, women, but not men, report lower levels of HAART adherence when they are problem drinkers (Berg et al., 2004). This is noteworthy because in the general population, substance use coping and negative consequences of substance use are associated more with male gender (Bolton, Robinson, & Sareen, 2009). Taken together, these studies suggest that women with HIV and CSA may be more likely a) to use

substances as a coping strategy and b) to experience a negative impact of substance use on HAART adherence.

For men with a history of CSA, no study variables significantly predicted either HAART adherence or drug use. This suggests two hypotheses for further testing. First, men's adherence may be more strongly affected by medication side effects, beliefs/attitudes about HAART. Past evidence suggests that these relationships may be particularly strong for men, but has not specifically tested gender moderation of the influence of these factors on adherence (Berg et al., 2004; Gonzalez et al., 2007). Secondly, HIV-positive men with a history of CSA may use drugs for different reasons than women. In the current sample, drug use was equally prevalent in men and women; however, the associations with drug use differed significantly between genders. There may be culturally-influenced factors that determine predictors and outcomes of drug use in individuals with HIV and CSA. While drug use increases transmission risk behavior (Morin et al., 2005), it may not necessarily lead to decreased HAART adherence.

Another incongruity with prior literature relates to the moderating effect of gender on the relationship between psychological distress and HAART adherence. In the current study, only women exhibited an association between psychological distress and HAART adherence. This finding contradicts results from a study of older adults with HIV, in which depression was associated with lower HAART adherence for men only (Bianco et al., 2011). This difference in findings could be explained by divergent study populations – the current study's sample had experienced significant trauma, were younger, and included a higher percentage of African American participants. This discrepancy in study results advocates for the inclusion of Gender X Age interaction when investigating adherence in a wide age range.

There are some limitations to the study. First, the cross-sectional design limits conclusions regarding directionality of relationships. In order to address this limitation, both theoretical foundations and prior empirical evidence were considered to provide justification for directionality in the model. Additionally, HAART adherence, CD4 count and viral load were assessed by self-report, which could result in decreased reliability. However, self-reported HAART adherence does demonstrate validity when assessed against pill count and viral load (Simoni et al., 2006); further, self-report measures of CD4 count and viral load are comparable to electronic medical records (Kinsler, Cunningham, Mohanty, & Wong, 2008). Given the effect sizes of the relationships between CD4 count, viral load, and self-reported HAART adherence, it is likely that the self-reported variables demonstrate an adequate level of validity. Finally, data for this study were collected 10 years ago, which could adversely affect generalizability to current HIV-positive populations. This is a concern particularly with regard to study of adherence, since simplified HAART medication regimens have the potential to improve adherence overall (Langebeek et al., 2013). However, the effects of CSA on HIV disease trajectory have continued throughout the past decade (Pellowski, Kalichman, Matthews, & Adler, 2013). Thus, it is likely that these findings exhibit current relevance.

Despite these limitations, the study is strengthened by a number of methodological elements. Study hypotheses had a firm basis in theory and previous empirical work, expanding on a previously validated model of negative affect mediation of HAART adherence (Johnson et al., 2009). Additionally, analysis utilized robust statistical methods to assess gender moderation. Finally, the sample included a high ratio of female participants, as well as individuals at multiple phases of disease progression.

Several implications arise for clinical practice and future research. First, gender may moderate multiple influences on HAART adherence, such as medication side effects, food instability, social support, housing status, and trust of health care providers (Cooper, Gellaitry, Hankins, Fisher, & Horne, 2009; Gonzalez et al., 2007; Kalichman & Grebler, 2010; Milloy et al., 2012; Simoni et al., 2006). Future research should consistently test gender moderation of HAART adherence. Secondly, it is critical to treat substance abuse as part of HIV management in women, since alcohol and drug use particularly impact adherence for women. Existing interventions address poor adherence in the context of psychological dysfunction and substance use, such as Cognitive Behavioral Therapy for Adherence and Depression and antiretroviral Directly Observed Therapy (Nahvi et al., 2012; Safren et al., 2009; Safren et al., 2012). Our findings suggest that these interventions could potentially be targeted by gender. One such targeted intervention for HIV-positive women with CSA histories reduced sexual risk behavior and increased HAART adherence (Wyatt et al., 2004). Interventions that focus on underlying gender differences, psychological symptoms, as well as behavioral mechanisms may demonstrate improved efficacy in yielding long-term optimal HAART adherence.

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Figure 1.

Final multigroup model illustrating gender moderation

Note. All paths show standardized estimates. Bolded paths reflect significant gender moderation; separate estimates by gender are noted with female estimates first. Circles denote latent variables, while rectangles denote observed variables. Covariates not depicted are ethnicity (African American vs. not), sexual orientation, years of education, and years living with HIV.

* $p < .05$. ** $p < .01$

Table 1

Sample characteristics by gender

	Females N = 94 Mean (SD) N (%)	Males N = 112 Mean (SD) N (%)	Difference Test	p value
Age	43.1 (7.2)	41.9 (6.7)	t (204) = 1.24	.22
Years of Education	11.3 (1.9)	13.1 (2.5)	t (201) = -5.71	<.001
Years Living with HIV ^a	8.3 (4.6)	11.2 (5.5)	t (188) = -3.86	<.001
Ethnicity				
Non-Latino White	5 (5.3%)	19 (17.0%)	χ^2 (1) = 6.73	.009
African American	72 (76.6%)	68 (60.7%)	χ^2 (1) = 5.92	.015
Latino/a	14 (14.9%)	21 (18.8%)	χ^2 (1) = 0.54	.46
Multiracial/Other	3 (3.2%)	4 (3.6%)	χ^2 (1) = 0.02	.88
Sexual Orientation				
Heterosexual	76 (80.9%)	11 (9.8%)	χ^2 (1) = 105.69	<.001
Gay/Lesbian	7 (7.4%)	83 (74.1%)	χ^2 (1) = 92.31	<.001
Bisexual	11 (11.7%)	18 (16.1%)	χ^2 (1) = 0.81	.37
Drug Use ^b	9 (9.6%)	15 (13.4%)	χ^2 (1) = 0.72	.40
Cocaine	6 (6.4%)	10 (8.9%)	χ^2 (1) = 0.46	.50
Crack	7 (7.4%)	9 (8.0%)	χ^2 (1) = 0.03	.88
Methamphetamine	0 (0.0%)	4 (3.6%)	χ^2 (1) = 3.43	.064
Heroin	0 (0.0%)	1 (0.9%)	χ^2 (1) = 0.84	.36
Optimal Adherence	63 (67.0%)	78 (69.6%)	χ^2 (1) = 0.16	.69
CD4 Count ^c	462 (361)	375 (257)	t (172) = 1.85	.066
Ln Viral Load ^c	2.52 (5.52)	3.12 (5.79)	t (142) = -0.62	.54

^aData on years living with HIV were missing for 16 participants.^bDrug use was defined as using crack, cocaine, heroin, or methamphetamine at least 6 days in the past month.^cData on self-reported CD4 Count and viral load were incomplete, with missing data points numbering 32 and 62, respectively

Table 2

Correlation matrix by gender

	1	2	3	4	5	6	7	8	9	10	11
1. Life stress ^a	-	.640	.400	.334	-.216	.083	-.108	-.023	.079	-.048	-.091
2. Psychological distress ^a	.530	-	.827	.521	-.337	.129	-.168	.118	-.174	-.102	-.296
3. Avoidant coping ^b	.278	.520	-	.531**	-.309*	.305**	-.211	.013	-.082	.041	-.122
4. Drug use ^c	.099	.186	.068	-	-.324	.283	-.140	.299	.076	-.418*	-.309
5. Optimal adherence ^c	-.019	-.035	.234*	-.164	-	-.426**	.555**	.252	.004	.238	-.153
6. Ln Viral Load ^b	.005	.010	-.083	-.095	-.313*	-	-.384**	.110	-.063	-.017	.073
7. CD4 ^b	-.010	-.019	.216*	-.119	.457**	-.370**	-	.268	-.098	.143	.183
8. African American ^c	-.043	.122	.217	-.333	-.275	.061	-.102	-	.028	.138	-.204
9. Years education ^b	-.140	.065	-.135	.018	.101	.060	-.065	-.174	-	.165	.051
10. Sexual orientation ^d	.151	-.015	-.095	.096	.123	-.043	-.217	.273	-.275*	-	.335*
11. Years with HIV ^b	-.093	-.018	-.098	-.045	-.238	-.060	.099	.096	-.021	-.258*	-

Note. Correlations coefficients are shown for males and females separately; coefficients for females (n = 94) appear above the diagonal, and males (n = 112) appear below the diagonal.

Due to the categorical/continuous variable (CVM) methodology utilized in this analysis, correlations differ in type. Types include: Pearson (for categorical variable pairs), tetrachoric (for dichotomous variable pairs), polychoric (for dichotomous/trichotomous pairs), biserial (for dichotomous/continuous pairs), or polyserial (for trichotomous/continuous pairs). For correlations with latent variables, significance level cannot be calculated in Mplus v6 (L. K. Muthen, 2012).

^a Latent variable.

^b Continuous variable.

^c Dichotomous variable.

^d Trichotomous variable.

* p < .05.

** p < .01