Published in final edited form as:
Prev Sci. 2014 June ; 15(3): 257–267. doi:10.1007/s11121-013-0378-6.

Interaction between 5-HTTLPR Polymorphism and Abuse History on Adolescent African-American Females' Condom Use Behavior Following Participation in an HIV Prevention Intervention

Jessica M. Sales, PhD[1,2,3], **Ralph J. DiClemente, PhD**[1,2,3], **Gene H. Brody, PhD**[1,2,3], **Robert A. Philibert, MD, PhD**[3,4], and **Eve Rose, MSPH**[1]

[1]Rollins School of Public Health, Department of Behavioral Sciences and Health Education

[2]Center for AIDS Research, Social & Behavioral Sciences Core

[3]Center for Contextual Genetics and Prevention Science, University of Georgia

[4]University of Iowa, Department of Psychiatry

Abstract

Not everyone exposed to an efficacious HIV intervention will reduce sexual risk behaviors, yet little is known about factors associated with "failure to change" high risk sexual behaviors post-intervention. History of abuse and polymorphisms in the serotonin transporter gene (*5-HTT*) may be associated with non-change. The current study sought to identify genetic, life history, and psychosocial factors associated with adolescents' failure to change condom use behaviors post-participation in an HIV prevention intervention. A sub-set of participants from a clinic-based sample of adolescent African-American females (N = 254) enrolled in a randomized trial of an HIV-prevention was utilized for the current study. 44.1% did not increase their condom use from baseline levels 6 months after participating in the STI/HIV prevention intervention. In multivariable logistic regression analysis, an interaction between abuse and 5-HTTLPR group was significantly associated with non-change status, along with partner communication frequency scores at follow-up. Follow-up tests found that having a history of abuse was significantly associated with greater odds of non-change in condom use post-intervention for only those with the *s* allele. For those with *ll* allele, participants with higher partner communication frequency scores were at decreased odds of non-change in condom use post-intervention. Thus, STI/HIV interventions for adolescent females may consider providing a more in-depth discussion and instruction on how to manage and overcome fear or anxiety related to being assertive in sexual decisions or sexual situations. Doing so may improve the efficacy of STI/HIV prevention programs for adolescent women who have experienced abuse in their lifetime.

Correspondance: Jessica McDermott Sales, PhD, Research Assistant Professor, Rollins School of Public Health at Emory University, Department of Behavioral Sciences and Health Education, 1518 Clifton Rd., NE, Room 570, Atlanta, GA 30322, phone: 404-727-6598; fax: 404-712-9738; jmcderm@emory.edu.

Keywords

adolescent females; condom use; 5-HTTLPR; abuse

INTRODUCTION

Adolescents are disproportionately affected by sexual transmitted infections (STIs) (CDC, 2009). Among adolescents, girls have particularly high rates of STIs. Findings from the Centers for Disease Control and Prevention (CDC) indicate that, overall, one in four girls in the U.S. has an STI; however, the distribution of STIs is not uniform among girls. African-American girls have a markedly higher prevalence of STIs, with nearly half (48%) detected with an STI (Forhan, Gottlieb, Sternberg, Xu, Datta, & Berman, 2008). To contend with the STI epidemic among adolescent females, several efficacious STI/HIV prevention interventions have been developed, including interventions designed to be culturally-congruent for African-American adolescent females (Choi, Hoff, Gregorich, Grinstead, Gomez, & Hussey, 2008; DiClemente, Wingood, Harrington, Lang, Davies, Hook, et al., 2004; DiClemente, Wingood, Rose, Sales, Lang, et al., 2009; Ehrhardt, Exner, Hoffman, Silberman, Leu, Miller, & Levin, 2002; Jemmott, Jemmott, Braverman, & Fong, 2005; Jemmott, Jemmott, & O'Leary, 2007; Sales, Milhausen, & DiClemente, 2006).

Reviews of controlled STI/HIV risk-reduction intervention trials, including tailored interventions for African-American adolescent females, have repeatedly shown positive outcomes (Crepaz et al, 2009; DiClemente, Milhausen, Sales, Salazar, & Crosby, 2005; Sales et al., 2006). Although efficacious interventions to reduce STIs and sexual risk behaviors exist, they are most effective in the short term and are not uniformly effective across participants (Dennis et al., 2001; Kalichman, Cain, Knetch, & Hill, 2005; Wechsberg, Dennis, & Stevens, 1998). Thus, not everyone exposed to an STI/HIV risk-reduction intervention will positively change (i.e., reduce) their STI/HIV-associated sexual risk behavior post-participation in the intervention.

Research conducted with high risk adult samples has recognized the variability of initial and sustained responses to sexual risk reduction interventions (Dennis et al., 2001; Kalichman et al, 2005; Wechsberg et al., 1998). For instance, Kalichman examined patterns of sexual behavior change among adult STI clinic patients who received risk reduction counseling and were subsequently followed for 9 months post-counseling (Kalichman et al., 2005). Cluster analyses identified three subgroups: 1) sustained low risk behaviors over follow-up, 2) significant reduction in risk behaviors over time, and 3) increased risk behavior over follow-up. However, additional analyses to identify potential baseline factors that might differentiate the groups found no significant differences in baseline behaviors between the subgroups' patterns of risk taking post-intervention.

Thus, there is little empirical evidence describing the profile of factors (i.e., genetic, behavioral, and psychosocial factors) associated with "failure to change" high risk behaviors following participation in an efficacious STI/HIV prevention intervention. According to the cognitive-behavioral model of relapse (CBMR) (Marlatt, 1985), a framework used to understand relapse behavior and/or lack of behavior change after exposure to an

intervention, having a history of trauma, among other factors such as substance abuse and relationship status, may influence an individual's response when confronted with high-risk, highly emotional situations post-intervention. Additional, recent findings examining factors associated with adolescents' failure to improve their condom use behaviors after participating in an STI/HIV prevention intervention have observed that adolescents whose condom use did not improve post-intervention were more likely to have a abuse history (Sales, Brown, DiClemente, & Rose, 2012; Sales, DiClemente, Davis, Sullivan & Rose, 2012). Therefore, history of trauma, specifically the experience of abuse, may be an important barrier prohibiting young women from positively changing their sexual behavior following participation in an HIV intervention.

Experience of abuse has been consistently associated with increased sexual risk-taking and adverse sexual health outcomes (i.e., STIs and HIV) among young women (Koenig, Doll, O'Leary, & Pequengnat, 2004). To explain the frequently observed association between abuse and sexual risk-taking among women, the Theory of Gender and Power posits that the experience of abuse may disempower women to negotiate safer sexual practices because of the fear of possible ramifications by male sex partners if they are assertive during sexual situations (Silverman, Raj, Mucci, & Hathaway, 2001; Wingood & DiClemente, 1997; Wingood et al., 2001). A recent study of adolescent African-American girls found that those with a history of sexual violence had greater fear of negotiating condom use with their sexual partners resulting in increased sexual risk-behaviors (Sales et al, 2008). Together, these findings suggest girls with abuse histories may be more reticent to engage in sexual risk-reduction decision making and use of preventive strategies, such as condom use negotiation, thus reducing their likelihood of using condoms during sex, even after participating in an efficacious STI/HIV prevention intervention.

Neuroscientists have identified a subgroup that appears to be particularly reactive to threatening environmental stimuli. Functional magnetic resonance imaging (fMRI) studies suggest the amygdala, a region of the brain critical for emotional processing and especially important for detection and processing of fear-related information, is affected by genetic variability in the promoter of the *5-HTT* gene (Nordquist & Oreland, 2010). The *5-HTT* gene is a key regulator of serotonergic neurotransmission, localized to 17p13 and consisting of 14 exons and a single promoter. The common polymorphism in the promoter region results in two variants, a short and a long allele, with the short allele resulting in lower serotonin transporter availability. Individuals with at least one copy of the short (*s*) allele of the *5-HTTLPR* who have also experienced stressful life events have been suggested to have higher rates of depression or depressive symptoms, although there has been debate about the extent to which *5-HTTLPR* moderates the association between stress and depression (see Risch et al., 2009 and Karg, Burmeister, Shedden & Sen 2011 for recent meta-analyses on the topic).

Aside from this conceptualization of the role of 5-HTTLPR in emotion-related processing, other studies have found that individuals with at least one copy of the short (*s*) allele of the *5-HTTLPR* have shown increased amygdale activation to fearful stimuli in facial expression recognition tasks, and enhanced amygdala reactivity to punishment cues in the environment (Battaglia et al., 2005; Hariri et al, 2003; Hariri et al, 2006; Hariri et al, 2002). Further, carriers of at least one copy of the *s* allele also display hyperactive amygdala response to

nonemotional and neutral cues (Heinz et al., 2007; Munafo, Brown & Hariri, 2008), direct preferential attention toward threat-related stimuli, and also have difficulty disengaging from such stimuli (Beevers, Wells, Ellis & McGeary, 2009; Osinsky et al, 2008). The neuroscience research suggests that carrying the *s* allele may prompt emotional arousal to fear-based and threatening environmental events, such as the prospect of negotiating condom use with male sex partners. This could be especially true for individuals with a history of abuse, for whom sexual situations could already be perceived and appraised as threatening. Thus, it may be that adolescent girls in STI/HIV interventions with abuse histories, and who are predisposed toward hypervigilance and emotional reactivity to environmental events (i.e., have at least one copy of the *s* allele of the *5-HTTLPR*), may be reticent to change their condom use behavior post-intervention.

The purpose of the present study was to explore whether history of abuse relates to adolescent female's non-responsiveness to an STI/HIV prevention intervention, as determined by their reporting no increase in condom use from baseline to 6 months post-participation in a demonstrably efficacious STI/HIV intervention. Additionally, the study examined the extent to which abuse history's association with STI/HIV intervention non-responsiveness would vary based on a functional polymorphism (*5-HTTLPR*) of the serotonin transporter gene. We hypothesized a G x E interaction effect in which girls carrying at least one copy of the short (*s*) allele of the *5-HTTLPR* polymorphism would be more likely to be non-responsive to the intervention as evidenced by their lack of increased condom use post-intervention if they reported a lifetime experience of abuse. The AFIYA intervention, guided by Social Cognitive Theory (Bandura, 1994) and the Theory of Gender and Power (Wingood & DiClemente, 2000; 2004) targeted several psychosocial constructs including: fear of condom negotiation, partner communication self-efficacy, partner communication frequency, and parent-adolescent communication. Thus, we also examined the extent to which young women who either increased or did not increase condom-use post-intervention differed in regards to the psychosocial constructs targeted in the intervention at the six month follow-up assessment (post-intervention). Such knowledge would be useful for the creation, revision, or adaptation of sexual risk reduction interventions for this especially vulnerable subgroup of non-responsive adolescents.

METHODS

Description of Parent Study Recruitment

From July 2005 to June 2007 African-American adolescent females were recruited from reproductive health clinics in Atlanta, GA, to participate in an STI/HIV prevention trial. The purpose of the trial was to assess whether a supplemental treatment delivered after intervention workshop participation (via phone calls) enhanced maintenance of a modified efficacious STI/HIV behavioral intervention (HORIZONS) (DiClemente et al., 2009). A young African American woman recruiter approached adolescents in the clinic waiting area, described the study, solicited participation, and assessed eligibility. Eligibility criteria included self-identifying as African American, being 14–20 years of age, and reporting at least one instance in the past 6 months of vaginal intercourse without a condom. Young women were excluded from the study if they were married, pregnant, or attempting to

become pregnant. Those meeting inclusion criteria and interested in participating returned to the clinic to complete informed consent procedures, baseline assessments, and be randomized to trial conditions. Written informed consent was obtained from all adolescents/ young women. Parental consent waived for those younger than 18 due to the confidential nature of clinic services. Of the eligible individuals, 94% (N=701) enrolled in the study, completed baseline assessments and were randomized to study conditions. Participants were compensated $75 for the baseline visit, and $20 for the follow-up assessments. The Emory University Institutional Review Board approved all study protocols.

Parent Study Intervention Description

All 701 participants received a modified version of a CDC-defined evidence-based HIV prevention intervention designed to be culturally and gender appropriate for African American female adolescents (HORIZONS) (DiClemente et al, 2009). The five-hour group session was facilitated by trained African-American women health educators, and presented to, on average, seven to nine participants attending the session. The intervention was based on Social Cognitive Theory, the Theory of Gender and Power, and previously published interventions for adolescent females seeking clinical services (DiClemente et al, 2004; DiClemente et al., 2009). Intervention sessions were interactive, fostered a sense of cultural and gender pride, and emphasized diverse factors contributing to young peoples' STI/HIV risk; including individual factors (STI/HIV risk-reduction knowledge, perceived peer norms supportive of condom use, condom use skills), relational factors (persuasive communication techniques to enhance male partner responsibility for condom use), and social factors (encouraged participants to reduce douching). Participants also role-played informing STI status to male sex partners and encouraging partners to seek STI screening/treatment.

Summary of Main Intervention Findings

Utilizing generalized estimating equation regression models (with exchangeable correlation), the intervention arm, relative to the comparison group, showed statistically significant differences over 18-months post-intervention: the intervention condition had lower Chlamydia incidence (7% vs. 13.6%; p=.007), lower mean frequency of sex while high on drugs/ alcohol (1.43 vs. 2.67; p=.02), and higher mean percent condom-protected sex acts (56.5% vs. 49.7%; p=.007). Further, no differences between conditions were observed for sociodemographic characteristics at 6-month assessment. Also, for each study condition, no differences were observed on baseline variables for participants retained in the trial compared with those unavailable for follow-up. (For a detailed description of the intervention results, see DiClemente et al., 2010).

Procedures and measures relevant for the current study

As part of the main study's procedures participants completed audio computer assisted self-interviews (ACASI) at baseline prior to randomization, and again at 6-month follow-up assessment. The ACASI data allowed for assessment of all variables included in this study such as the sociodemographics, sexual history, abuse history, attitudes, and psychosocial constructs associated with STD/HIV-preventive behaviors and targeted in the intervention. In addition to the ACASI survey completed as part of the main study, this analysis reports on data from only the 254 participants who, in addition to the baseline assessment,

consented and provided a saliva sample for DNA analysis[1] and completed the 6-month follow-up assessment post-intervention participation (from the 546 who completed the 6-month assessment as part of the main trial). The Emory University Institutional Review Board approved all study protocols.

Primary Outcome Measure of Interest

Change in condom use post-intervention: As part of the main trial's assessments, participants completed computerized interviews assessing their sexual behaviors, condom use, and other variables at baseline and then again at their subsequent 6-month follow-up assessment. Change in condom use was assessed by comparing reported percentage condom use in the 6 months prior to baseline (prior to intervention participation) to reported percentage of condom use in the 6 months between baseline and the 6-month follow-up assessment (post-intervention). If a participant reported any increase in condom use from their baseline level this was considered as "change"; no increase or a decrease in condom use from their baseline level was considered as "non-change". Condom use at the first 6-month follow-up interval post-intervention was selected because most HIV risk-reduction programs see the strongest impact on condom use closer to intervention participation, with effects tending to wane over time (Kalichman, Carey, & Johnson, 1996). The change group and non-change group did not significantly differ in their baseline rates of condom use.

Possible Correlates of Non-Change

Sociodemographic Measures: Age was assessed by asking, "How old are you (in years)?" Receiving federal assistance for living expenses was assessed by 4 binary response format questions (Yes/No). Responses were summed to create an index of family aid.

History of Abuse: Abuse was measured at the 6-month follow-up assessment and was conceptualized as an index comprising four forms of abuse; emotional, physical, forced vaginal sex or forced anal sex. Abuse history was assessed by asking four questions, "Have you ever been emotionally abused (threatened or called names)", Have you ever been physically abused (hit, kicked, slapped, punched)?", "Has anyone ever forced you to have vaginal sex when you didn't want to?", and "Has anyone ever forced you to have anal sex when you didn't want to?". Response choices were yes (1) and no (0). Consistent with the definition used in national surveillance studies (Leeb et al., 2008), a dichotomous composite variable was created in which participants who indicated yes on any of the four items were determined to have a history of abuse, and those who answered no on all items were determined to have no history of abuse. Further support for utilizing a composite variable of abuse to examine associations sexual risk-taking among young women comes from a study by Younge and colleagues (2010) which found that experiencing any form of abuse (physical, sexual, and/or emotional) was associated with increased sexual risk behaviors among adolescent African American females relative to those who had never been abused. Additionally, young women who had experienced either physical or sexual abuse in

[1]The DNA sample collection was an addition to the main trail's data collection, thus not every participant was invited to provide a sample if they: 1) had already completed the trial, or 2.) did not return for the 24 month follow-up assessment when the sample collection occurred. 363 were asked to provide a sample, and only 31 declined.

combination with emotional victimization engaged in more HIV risk behaviors relative to individuals who had experienced only physical or sexual abuse (Younge, Salazar, Sales, DiClemente, Wingood & Rose, 2010).

Depressives Symptoms: Depressive symptoms were assessed with a very brief, 8-item version of the Center for Epidemiological Studies-Depression scale (Melchior, Huba, Brown & Reback, 1993). The CES-D assesses the presence of depressive symptoms in the past 7 days and has been shown to be a valid measure of depressive symptoms in African-Americans (Radloff, 1991). Cronbach's alpha, a measure of the scale's internal consistency, was 0.91.

Fear of consequences of condom negotiation: Fear of consequences of condom negotiation with a sexual partner was assessed by a 7-item scale (DiClemente & Wingood, 1997). Sample consequences were "ignore my request," "hit, push or kick me," "leave me," and "go out with other girls." Cronbach's alpha was 0.87.

Partner communication self-efficacy: A 6-item scale assessed partner sexual communication self-efficacy (Wingood & DiClemente, 1998). Sample items included "With a sex partner, how hard is it for you to ask how many sex partners he has had?" and "With a sex partner, how hard is it for you to ask if he would use a condom?" Cronbach's alpha was 0.82.

Partner communication frequency: Partner communication frequency was assessed by a 5-item scale that assess adolescents' frequency of communicating with male sex partners (Milhausen et al., 2007). Each item required a response based on a four-point Likert-type scale (never to a lot/seven or more times). Higher values indicate more frequent sexual communication. Cronbach's alpha was 0.85.

Parent-adolescent communication scale (PACS): The PACS is composed of 5-items assessing adolescents' frequency of communicating about sexually related topics with their parents (Sales et al., 2008). Each item required a response based on a 4-point Likert-type scale: 1 (*never*) to 4 (*often*). Higher values indicated more frequent parent-adolescent communication. Cronbach's alpha was 0.91.

Genotyping—DNA was obtained using Oragene™ DNA kits (Genetek; Calgary, Alberta, Canada). Participants rinsed their mouths with tap water, and then deposited 4 ml of saliva in the Oragene sample vial. The vial was sealed, inverted, and shipped via courier to a central laboratory in Iowa City, where samples were prepared according to the manufacturer's specifications. Genotype at *5-HTTLPR* was determined for each sample as previously described (Bradley, Dodelzon, Sandhu & Philibert, 2005). Of the sample, 8.0% were homozygous for the short allele (*ss)*, 32.8% were heterozygous (*sl*), and 53.8% were homozygous for the long allele (*ll*). Consistent with prior research (Hariri, Drabant, Munoz et al., 2005), genotyping results were used to form two groups of participants: those homozygous for the long allele and those with either 1 or 2 copies of the short allele. Among the participants, 5.0% had a "very long" variant of *5-HTTLPR*. Because the activity of this

variant on the hypothesized associations has not been well characterized, these youths were excluded from the data analyses.

Data Analysis Plan—All analyses were limited to the 254 main trial participants who, in addition to the baseline assessment, participated in the STI/HIV intervention workshop, consented and provided a saliva sample for DNA analysis, and completed the 6-month follow-up assessment. Descriptive statistics summarized intervention responsiveness rates. In addition, bivariate analyses examined differences between groups (non-change group versus change group) on sociodemographic variables, *5-HTTLPR* group (i.e., *s* allele group vs. *ll* allele group), psychosocial characteristics, and life history factors (i.e., history of abuse) reported at the 6-month follow-up assessment (prior to intervention participation). Differences were assessed using independent samples *t* tests for continuous variables and Chi-square analyses for categorical variables. Variables significant at the $p \leq .10$ in bivariate analyses were entered into a multivariable hierarchical logistic regression predicting change status at the six month follow-up assessment (Hosmer & Lemeshow, 2000). In the first step, psychosocial factors were entered into the model. In the second step, abuse history and *5-HTTLPR* group were entered into the model. Additionally, to explore whether the association between abuse history and intervention non-responsiveness (i.e., no increase in condom use post-intervention) differed as a function of *5-HTTLPR* group, an interaction between abuse and *5-HTTLPR* group was entered in at the final step into the regression model. Finally, an identical regression analysis was conducted to the one described above utilizing a more conservation measure of abuse. Specifically, women who only experienced emotional abuse (i.e., reported experiencing emotional abuse but no history of physical and/or sexual abuse) were excluded from the abuse composite score.

RESULTS

Sample Description

Mean age of participants in this sample was 18.1 years (SD = 1.4) upon enrollment into the main trial. The majority was still in high-school or had only completed some high-school at enrollment (51.9%). One quarter had a job, and many reported living with their mother only (41.1%) or mother and father (16.1%). The mean number of times having vaginal sex in the 6 months prior to baseline assessment was 33.26 (SD = 58.48), and condoms were used, on average, 48% (SD = .36; range: 0–100%) of the times during vaginal sex in the 6 months prior to baseline assessment and 27% tested positive for one of three STIs (Chlamydia, gonorrhea, or trichomoniasis) at baseline. Additionally, the mean number of times having vaginal sex in the 6 months prior to 6-month assessment was 28.35 (SD = 38.91), and condoms were used, on average, 53% (SD = .40; range: 0–100%) of the times during vaginal sex in the 6 months prior to 6-month assessment.

Of key interest for this study, 44.1% (n = 112) did not increase their condom use from baseline levels 6 months after participating in a culturally and gender tailored STI/HIV prevention intervention that has demonstrated efficacy in reducing sexual risk behaviors (i.e., increasing condom use) and incident STI infections among adolescent African-American girls (i.e., Chlamydia infections) (DiClemente et al., 2009; Lyles et al., 2007).

Pertinent to this study, 50.8% reported a history of abuse based on the composite measure of abuse (any abuse), with 43.3% reporting having experienced emotional abuse in their lifetime, 31.9% reporting physical abuse, and 21.7% reporting sexual abuse. When those experiencing only emotional abuse (in absence of also having experienced physical and/or sexual abuse) are removed from the composite measure of abuse, 39.9% of the sample reported a history of abuse.

Bivariate associations among study variables

A series of chi-squares and t-tests were conducted to explore the association between potential correlates of non-change (Table 1). Compared to the change group (i.e., adolescents who increased their recent condom use from baseline levels at the 6-month follow-up), those in the non-change group had: (a) a greater odds of abuse history; (b) lower levels of parent adolescent communication; (c) lower levels of partner communication frequency; (d) lower levels of partner communication self-efficacy; and (e) higher levels of depressive symptoms (but only at a marginally significant level). Individuals with the *s* allele did not differ in regards to non-change in condom use ($X^2 = 1.89$, p = .17), or history of any abuse ($X^2 = .61$, p = .44) from those with the *ll* allele.[2]

Multivariable hierarchical logistic regression predicting change status post-intervention participation

Factors identified as significant at the $p \leq .10$ level in bivariate analyses (Hosmer & Lemeshow, 2000), were entered into a multivariable hierarchical logistic regression, controlling for group and frequency of sex in the past 6 months, to determine which factors, including an interaction between abuse history and *5-HTTLPR* group, were significantly associated with behavioral change status 6 months after participating in the intervention workshop (See Table 2). Overall, we found that the 3 step model including the interaction term was significant. The interaction between abuse and 5-HTTLPR group was significantly associated with non-change status, along with partner communication frequency scores at follow-up. In order to interpret the interaction effect, separate multivariable logistic regression models predicting behavioral change status were conducted for those possessing one or two copies of the *s* allele and those with the *ll* allele (See Table 3). For those with the *ll* allele, higher partner communication frequency was significantly associated with increases in condom use post-intervention. For those with the *s* allele, having a history of abuse was significantly associated with greater odds of non-change in condom use post-intervention. The same regression analysis shown in Table 2 was conducted utilizing a more conservative abuse measure (i.e., the composite abuse score excludes women who experience emotional abuse only), and the results mirror those presented in Table 2 (see Table 4 for analysis with conservative abuse measure).

[2]Because we utilized a two group structure to explore the association between 5-HTTLRP status and the outcome of interest we present this data for those with an s allele versus those with the ll allele. However, by request the outcome by the three groups (ss, sl, ll) can be made available.

DISCUSSION

Similar to the limited findings reported in the adult HIV prevention literature on non-change in preventive behaviors post-intervention (Kalichman et al., 2005), nearly half of adolescents who participated in a demonstrated efficacious STI/HIV risk-reduction program did not increase their condom use post-intervention. As hypothesized, history of abuse was significantly related to not increasing condom use. Further, as predicted, the association between abuse and non-responsiveness to the intervention (i.e., no increase in condom use) was only observed for adolescents identified with the *s* allele of the *5-HTTLPR*.

According to the Theory of Gender and Power (Wingood & DiClemente, 2000; 2002), the experience of abuse disempowers women to negotiate safer sexual practices in their current sexual relationships because they may fear possible ramifications by male partners if they attempted to do so (Silverman et al., 2001; Wingood & DiClemente, 1997; Wingood et al., 2001). The findings of this study provide some support for this position by demonstrating that adolescents who carry the *s* allele of the *5-HTTLPR*, a functional polymorphism found to be related to high reactivity to emotional and/or threatening cues, and who also have a history of abuse, are more likely to be non-responsive to the intervention. Interestingly, the associations between stress or depression were not independently associated with non-responsiveness when the interaction was in the equation indicating. This finding suggests that the addition of genotyping allowed for the identification of this potential link between an emotional processing mechanism and sexual decision making post-intervention that would not have surfaced through the assessment measures employed in the main study. Combined, the findings imply that similar to successful interventions designed to reduce traumatic stress and sexual risk behaviors among people living with HIV who have histories of abuse (Sikkema, Wilson, Hansen et al., 2008; Sikkema, Hansen, Kochman et al., 2007), STI/HIV prevention interventions for adolescent girls may consider providing more in-depth discussion and instruction on specific strategies to manage and overcome fear or anxiety related to past abuse, as well as fear/anxiety about being assertive in current sexual situations. Doing so may improve the efficacy of STI/HIV prevention programs for adolescents who have a history of abuse.

Many HIV prevention programs designed for adolescent females, including HORIZONS (DiClemente et al., 2009), include a small component on unhealthy relationships (i.e., identifying abusive relationships). However, they do not delve into the multitude of other factors stemming from prior abuse (i.e., hyperarousal, fear, and anxiety) that may be hindering young women from living both emotionally and physically healthy lives. Further, most HIV intervention research does not even assess factors related to hyperarousal, fear-reactivitiy or anxiety, therefore are not capturing the degree to which these constructs impact young women's decision-making in arousing contexts like ones involving sex. Thus, interventions should increase awareness of the co-occurrence of abuse, hyperarousal/anxiety/fear, and sexual risk behaviors, focus on developing cognitive and behavioral skills needed to accurately appraise risk, identify triggers associated with negative affect and sexual risk-taking, and developing strategies to avoid situations that trigger engaging in sexual risk-taking. Additionally, assessment instruments may benefit by including measures of hyperarousal, fear, and anxiety.

Although the aforementioned suggestions are offered for additional content to include in STI/HIV intervention programs for adolescents with histories of abuse, especially in the cases of those who may be genetically inclined to be highly reactive to environmental events, it is not clear from this study exactly why they are not responding to the intervention. One possibility is that they may have an inability to process potentially emotion-inducing information presented in the intervention sessions (i.e., practicing condom use negotiation skills; using condom correctly) because the content of the intervention triggers especially strong reactions that could interfere with information processing and learning. Another possibility is that adolescents did attend and acquired the prevention information and were unable to enact the skills learned because they were especially fearful of negative emotional responses by male sex partners. Further research is needed to systematically assess information processing among STI/HIV intervention participants to better understand where in the process barriers occur. Regarding intervention delivery, because these young women may need additional content to address their unmet needs they may require a more intensive intervention (more than one session) to incorporative the additional content required by this sub-group. Additionally, whereas group formats have demonstrated efficacy for the majority of participants in group-based formats, some individuals may benefit from additional individual sessions which are specifically tailored to meet the needs (e.g., anxiety reduction) of this subgroup of participants at particularly high risk.

Limitations

This study is not without limitations. First, the data employed in this study were only from participants who returned for follow-up assessment after the intervention workshop. It is possible that returning participants may have differed in meaningful ways from those who did not return for follow-up, but we have no way to formally exclude this possibility. However, analyses of baseline socioeconomic and behaviors indicate no significant differences between those who returned for follow-up and those who did not. Additionally, participants who provided DNA samples may have differed from participants who did not provide a specimen. However, we experienced a low rate of non-participation for the DNA saliva collection (8%), and a comparison of baseline characteristics indicates no observed differences in sociodemographics, psychosocial variables, or behavioral outcomes.

Conclusion

Several efficacious STI/HIV prevention programs exist for a variety of populations, including African-American adolescent girls (Sales et al., 2006; DiClemente, Crittenden, Rose et al., 2008). Despite the demonstrated efficacy of interventions to reduce STI/HIV-associated sexual risk behaviors, not every individual who participates in such a program will positively change their sexual risk behaviors (i.e., increase condom use). The ability to identify barriers and possible causal factors that differentiate those who increased condom use post-intervention from those who did not may be a critical first step in refining, adapting, or designing new STI/HIV prevention programs to optimize their appropriateness and efficacy for these especially vulnerable youth.

Acknowledgments

FUNDING: This research was supported by a grant, number K01 MH085506, from the National Institute of Mental Health to the first author, and grant number R01 MH070537, from the National Institute of Mental Health to the second author, and number P03 DA027827 to the third author. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Mental Health, the National Institute on Drug Abuse, or National Institute of Health.

References

Bandura, A. Social cognitive theory and exercise of control over HIV infection. In: DiClemente, RJ.; Peterson, J., editors. Preventing AIDS: Theories and Methods of Behavioral Interventions. New York: Plenum Publishing; 1994. p. 25-59.

Battaglia M, Ogliari A, Zanoni A, Citterio A, Pozzoli U, Giorda R, Marino C. Influence of the serotonin transporter promoter gene and shyness on children's cerebral responses to facial expressions. Archives of Genenal Psychiatry. 2005; 62:85–94.

Beevers CG, Wells TT, Ellis AJ, McGeary JE. Association of the serotonin transporter gene promoter region (5-HTTLPR) polymorphism with biased attention for emotional stimuli. Journal of Abnormal Psychology. 2009; 118:670–681. [PubMed: 19685963]

Bradley SL, Dodelzon K, Sandhu HK, Philibert RA. Relationship of serotonin transporter gene polymorphisms and haplotypes to mRNA transcription. American Journal of Medical Genetics: Behavioral Neuropsychiatry Genetics. 2005; 136B:58–61.

Centers for Disease Control and Prevention (CDC). Sexually Transmitted Disease Surveillance, 2008. Atlanta, GA: Department of Health and Human Services; 2009.

Choi KH, Hoff C, Gregorich SE, Grinstead O, Gomez C, Hussey W. The efficacy of female condom skills training in HIV risk reduction among women: A randomized controlled trial. American Journal of Public Health. 2008; 98:1841–1848. [PubMed: 18703460]

Crepaz N, Marshall KJ, Aupont LW, Jacobs ED, Mizuno Y, Kay LS, O'Leary A. The efficacy of HIV/STI behavioral interventions for African American females in the United States: A meta-analysis. American Journal of Public Health. 2009; 19:190–203.

Dennis M, Wechsberg W, McDermeit M, Campbell R, Rasch R. The correlates and predictive validity of HIV risk groups among drug users in a community-based sample: Methodological findings from a multi-site cluster analysis. Evaluation and Program Planning. 2001; 24:187–206.

DiClemente RJ, Crittenden CP, Rose E, Sales JM, Wingood GM, Crosby RA, Salazar LF. Psychosocial predictors of HIV-associated sexual behaviors and the efficacy of prevention interventions in adolescents at-risk for HIV infection: What works and what doesn't work. Psychosomatic Medicine. 2008; 70:598–605. [PubMed: 18541908]

DiClemente RJ, Milhausen R, Sales JM, Salazar LF, Crosby RA. A programmatic and methodological review and synthesis of clinic-based sexually transmitted infection risk reduction interventions: Research and practice implications. Seminars in Pediatric Infectious Diseases. 2005; 16:199–216. [PubMed: 16044394]

DiClemente RJ, Wingood GM, Harrington KF, Lang DL, Davies SL, Hook EW 3rd, Robillard A. Efficacy of an HIV prevention intervention for African American adolescent girls: a randomized controlled trial. Journal of the American Medical Association. 2004; 292:171–179. [PubMed: 15249566]

DiClemente RJ, Wingood GM, Rose E, Sales JM, Lang DL, Caliendo A, Crosby RA. Efficacy of STD/HIV sexual risk-reduction intervention for African American adolescent females seeking sexual health services: A randomized controlled trial. Archives of Pediatric and Adolescent Medicine. 2009; 163:1112–1121.

DiClemente, RJ.; Wingood, GM.; Rose, E.; Sales, JM.; Hardin, J.; Latham, TP. Enhancing maintenance of HIV intervention efficacy by brief, telephone-delivered, tailored counseling for young African American women. Paper presented at the biennual meeting of the International AIDS conference; Vienna, Austria. 2010 Jul.

Ehrhardt AA, Exner TM, Hoffman S, Silberman I, Leu CS, Miller S, Levin B. A gender-specific HIV/STD risk reduction intervention for women in a health care setting: Short- and long-term results of a randomized clinical trial. AIDS Care. 2002; 14:147–161. [PubMed: 11940275]

Forhan, S.; Gottlieb, SL.; Sternberg, MR.; Xu, F.; Datta, SD.; Berman, S. Prevalence of Sexually Transmitted Infections and Bacterial Vaginosis among Female Adolescents in the United States: Data from the National Health and Nutritional Examination Survey (NHANES), 2003–2004. Paper presented at the National STD Prevention Conference; Chicago, IL. 2008 Mar.

Hariri AR, Drabant EM, Munoz KE, Kolechana BS, Mattay VS, Egan MF, Weinberger DR. A susceptibility gene for affective disorders and the response of the human amygdala. Archives of General Psychiatry. 2005; 62:146–152. [PubMed: 15699291]

Hariri AR, Drabant EM, Weinberger DR. Imaging genetics: Perspectives from studies of genetically driven variation in serotonin function and corticolimbic affective processing. Biological Psychiatry. 2006; 59:888–897. [PubMed: 16442081]

Hariri AR, Mattay VS, Tessitore A, Fera F, Weinberger DR. Neocortical modulation of the amygdala response to fearful stimuli. Biological Psychiatry. 2003; 53:494–501. [PubMed: 12644354]

Hariri AR, Mattay VS, Tessitore A, Kolachana B, Fere F, Goldman D, Weinberger DR. Serotonin transporter genetic variation and the response of the human amygdala. Science. 2002; 297:400–403. [PubMed: 12130784]

Heinz A, Smolka MN, Braus DF, Wrase J, Beck A, Flor H, Weinberger DR. Serotonin transporter genotype (5-HTTLPR): Effects of neutral and undefined conditions on amygdala activation. Biological Psychiatry. 2007; 61:1011–1014. [PubMed: 17157270]

Hosmer, DW.; Lemeshow, SL. Applied logistic regression. New York: Wiley; 2000.

Jemmott JB, Jemmott LS, Braverman PK, Fong GT. HIV/STD risk reduction interventions for African American and Latino adolescent girls at an adolescent medicine clinic: A randomized control trial. Archives of Pediatric and Adolescent Medicine. 2005; 159:440–449.

Jemmott LS, Jemmott JB, O'Leary A. Effects on sexual risk behavior and STD rate of brief HIV/STD prevention interventions for African American women in primary care settings. American Journal of Public Health. 2007; 97:1034–1040. [PubMed: 17463391]

Kalichman SC, Cain D, Knetch J, Hill J. Patterns of sexual risk behavior change among sexually transmitted infection clinic patients. Archives of Sexual Behavior. 2005; 34:307–319. [PubMed: 15971013]

Kalichman SC, Carey MP, Johnson BT. Prevention of sexually transmitted HIV infection: a meta-analytic review of behavioral outcome literature. Annuls of Behavioral Medicine. 1996; 18(1):6–15.

Karg K, Burmeister M, Shedden K, Sen S. The serotonin transporter promoter variant (5-HHTLPR), stress, and depression Meta-analysis revisited. Archives of General Psychiatry. 2011; 68(5):444–454. [PubMed: 21199959]

Koenig, LJ.; Doll, LS.; O'Leary, A.; Pequengnat, W. From Child Sexual Abuse to Adult Sexual Risk: Trauma, Revictimation and Intervention. Washington, DC, US: American Psychological Association; 2004.

Leeb, RT.; Paulozzi, LJ.; Melanson, C.; Simon, TR.; Arias, I. Child maltreatment surveillance: Uniform definitions for public health and recommended data elements, Version 1.0. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2008.

Lyles C, Kay LS, Crepaz N, Herbst JH, Passin WF, Kim AS, Mullins MM. Best-evidence interventions: Findings from a systematic review of HIV behavioral interventions for US populations at high risk, 2000–2004. American Journal of Public Health. 2007; 97:133–143. [PubMed: 17138920]

Marlatt, GA. Relapse prevention: Theoretical rationale and overview of model. In: Marlatt, GA.; Gordon, JR., editors. Relapse prevention. New York: Guilford Press; 1985. p. 250-280.

Melchior LA, Huba GJ, Brown VB, Reback CJ. A short depression index for women. Education and Psychological Measurement. 1993; 53:1117–1125.

Milhausen RR, Sales JM, Wingood GM, DiClemente RJ, Salazar LF, Crosby RA. Validation of a partner communication scale for use in HIV prevention intervention. Journal of HIV/AIDS Prevention in Children and Youth. 2007; 8:11–33.

Munafo MR, Brown SM, Hariri AR. Serotonin transporter (5-HTTLPR) genotype and amygdala activation: A meta-analysis. Biological Psychiatry. 2008; 63:852–857. [PubMed: 17949693]

Nordquist N, Oreland L. Serotonin, genetic variability, behaviour, and psychiatric disorders a review. Upsala Journal of Medical Sciences. 2010; 115:2–10. [PubMed: 20187845]

Osinsky R, Reuter M, Kupper Y, Schmitz A, Kozyra E, Alexander N, Hennig J. Variation in the serotonin transporter gene modulates selective attention to threat. Emotion. 2008; 8:584–588. [PubMed: 18729589]

Radloff LS. The use of the Center for Epidemiologic Studies Depression Scale in adolescents and young adults. Journal of Youth and Adolescence. 1991; 20:149–166. [PubMed: 24265004]

Risch N, Herrell R, Lehner T, Liang K, Eaves L, Hoh J, Merikangas KR. Interaction between the serotonin transporter gene (5-HTTLRP), stressful life events, and risk of depression. Journal of the American Medical Association. 2009; 301(23):2462–2471. [PubMed: 19531786]

Sales JM, Brown JL, DiClemente RJ, Rose E. Exploring factors associated with nonchange in condom use behavior following participation in an STI/HIV prevention intervention for African-American adolescent females. AIDS Research and Treatment. 2012; 2012:9. Article ID 231417. 10.1155/2012/

Sales JM, DiClemente RJ, Davis TL, Sullivan S, Rose E. Exploring why young African-American women do not change condom use behavior following participation in an HIV prevention untervention. Health Education Research. 2012 May 28. [Epub ahead of print].

Sales JM, Milhausen RR, DiClemente RJ. A decade in review: Building on the experiences of past adolescent STI/HIV interventions to optimize future prevention efforts. Sexually Transmitted Infections. 2006; 82:431–436. [PubMed: 17151029]

Sales JM, Milhausen RR, Wingood GM, DiClemente RJ, Salazar LF, Crosby RA. Validation of a parent-adolescent communication scale for use in STD/HIV prevention interventions. Health Education and Behavior. 2008; 35:332–345. [PubMed: 17200099]

Sales JM, Salazar LF, Wingood GM, DiClemente RJ, Rose E, Crosby RA. The mediating role of partner communication skills on HIV/STD-associated risk behaviors in African American female adolescents with a history of gender-based violence. Archives of Pediatric and Adolescent Medicine. 2008; 162:432–438.

Sikkema KJ, Wilson PA, Hansen NB, Kochman A, Neufeld S, Ghebremichael MS, Kershaw T. Effects of a coping intervention on transmission risk behavior among people living with HIV/AIDS and a history of childhood sexual abuse. Journal of Acquired Immune Deficiency Syndrome. 2008; 47:506–513.

Sikkema KJ, Hansen NB, Kochman A, Tarakeshwar N, Neufeld S, Meade CS, Fox AM. Outcomes from a group intervention for coping with HIV/AIDS and childhood sexual abuse: reductions in traumatic stress. AIDS and Behavior. 2007; 11:49–60. [PubMed: 16858634]

Silverman JG, Raj A, Mucci LA, Hathaway JE. Dating violence against adolescent girls and associated substance use, unhealthy weight control, sexual risk behavior, pregnancy and suicidality. Journal of the American Medical Association. 2001; 286:572–579. [PubMed: 11476659]

Wechsberg W, Dennis M, Stevens S. Cluster analysis of HIV intervention outcomes among substance-abusing women. American Journal of Drug and Alcohol Abuse. 1998; 24:239–254. [PubMed: 9643464]

Wingood GM, DiClemente RJ. Child sexual abuse, HIV sexual risk, and gender relations of African-American women. American Journal of Preventive Medicine. 1997; 13:380–384. [PubMed: 9315271]

Wingood GM, DiClemente RJ. Relationship characteristics and gender-related factors associated with noncondom use among young adult African American women. American Journal of Community Psychology. 1998; 26:29–51. [PubMed: 9574497]

Wingood GM, DiClemente RJ. Application of the Theory of Gender and Power to examine HIV related exposures, risk factors and effective interventions for women. Health Education and Behavior. 2000; 27:539–565. [PubMed: 11009126]

Wingood, GM.; DiClemente, RJ. The Theory of Gender and Power: A social structural theory for guiding the design and implementation of public health interventions to reduce women's risk of HIV. In: DiClemente, RJ.; Crosby, RA.; Kegler, M., editors. Emerging theories in Health Promotion Practice and Research: Strategies for Enhancing Public Health. San Fancisco: Jossey-Bass; 2002. p. 313-347.

Wingood GM, DiClemente RJ, Hubbard McCree D, Harrington K, Davies S. Dating violence and African-American adolescent females' sexual health. Pediatrics. 2001; 107:E72–E75. [PubMed: 11331722]

Younge SN, Salazar LF, Sales JM, DiClemente RJ, Wingood GM, Rose E. Emotional victimization and sexual risk-taking behaviors among adolescent African American women. Journal of Child & Adolescent Trauma. 2010; 3(2):79–94.10.1080/19361521003761523

Table 1

Group differences in sociodemographic, life history, genetic, and psychosocial characteristics assessed at follow-up assessment (N = 254).

Study variables	Non-Change Group (n = 114)	Change Group (n = 140)	Test statistic	*p*
Sociodemographic				
Age[b]	18.04 (1.47)	18.06 (1.35)	0.08	.94
Family aid index[b]	.85 (1.01)	.88 (1.04)	0.21	.83
Life history				
History of abuse[a]	69 (60.5)	60 (42.9)	7.85	.005
Psychosocial factors				
Depressive symptoms[b]	14.10 (6.33)	12.71 (5.50)	−1.86	.06
Fear of condom negotiation[b]	8.50 (3.87)	8.02 (2.57)	−1.13	.26
Partner communication self-efficacy[b]	20.84 (3.25)	21.52 (3.27)	1.65	.10
Partner communication frequency[b]	10.10 (4.01)	12.66 (4.91)	4.59	.001
Parent-adolescent communication[b]	11.41 (4.87)	12.86 (4.92)	2.35	.02
Genotyping				
5-HTTLPR s allele group[a]	45 (39.5)	67 (47.9)	1.79	.18

Note:

[a] Chi-square is test statistic and frequency (percent) are reported,

[b] t-test is the test statistic and mean (standard deviation) are reported

Table 2

Multivariable hierarchical logistic regression predicting behavioral change status 6 months after participating in an STI/HIV intervention.

			95% CI			
Predictors	**β**	**SE**	**Odds Ratio**	**Lower**	**Upper**	***p***
STEP 1:						
Psychosocial factors						
Depressive symptoms	.03	.03	1.03	.98	1.08	.26
Partner communication self-efficacy	−.03	.05	.97	.89	1.06	.47
Partner communication frequency	−.11	.03	.90	.84	.96	.001
Parent-adolescent communication	−.01	.03	.99	.93	1.05	.77
STEP 2:						
Genotype						
5-HTTLPR group	−1.02	.44	.36	.15	.85	.02
Life history						
History of Abuse	−.10	.38	.90	.43	1.89	.78
STEP 3:						
Interaction						
Abuse X 5-HTTLPR group	1.35	.58	3.86	1.23	12.12	.02
Step 1 χ^2 =	38.10					.001
Step 2 χ^2 =	3.12					.210
Step 3 χ^2 =	5.52					.019
Overall Model χ^2 =	46.75					.001

Note: Group and frequency of vaginal sex in the past 6 months were controlled for in regression.

Table 3

Multivariable logistic regressions predicting behavioral change status 6 months after participating in an STI/HIV intervention, separately for each 5-*HTTLPR* group.

			95% CI			
Predictor	**β**	**SE**	**Odds Ratio**	**Lower**	**Upper**	***p***
	5-HTTLPRsallele group					
Life history						
History of Abuse	1.31	.51	3.69	1.36	10.03	.01
Psychosocial factors						
Depressive symptoms	.02	.04	1.02	.94	1.10	.71
Partner communication self-efficacy	.02	.08	1.02	.87	1.20	.85
Partner communication frequency	−.10	.06	.90	.81	1.01	.06
Parent-adolescent communication	−.08	.05	.92	.84	1.02	.10
Overall χ^2 =	25.33					.001
	5-HTTLPRl/allele group					
Life history						
History of Abuse	−.10	.43	.90	.39	2.07	.81
Psychosocial factors						
Depressive symptoms	.05	.03	1.05	.98	1.12	.14
Partner communication self-efficacy	−.03	.06	.97	.85	1.10	.60
Partner communication frequency	−.13	.05	.88	.80	.97	.01
Parent-adolescent communication	.03	.04	1.03	.95	1.13	.69
Overall χ^2 =	22.37					.002

Note: Group and frequency of vaginal sex in the past 6 months were controlled for in regressions.

Table 4

Multivariable hierarchical logistic regression predicting behavioral change status 6 months after participating in an STI/HIV intervention utilizing a more conservation abuse measure.

			95% CI			
Predictors	**β**	**SE**	**Odds Ratio**	**Lower**	**Upper**	***p***
STEP 1:						
Psychosocial factors						
Depressive symptoms	.03	.03	1.03	.98	1.08	.24
Partner communication self-efficacy	−.04	.05	.96	.88	1.05	.41
Partner communication frequency	−.11	.03	.90	.84	.96	.001
Parent-adolescent communication	−.01	.03	.99	.94	1.06	.86
STEP 2:						
Genotype						
5-HTTLPR group	−0.76	.38	.47	.23	.98	.04
Life history						
History of Abuse (excludes those with emotional abuse only)	−.10	.39	.91	.43	1.93	.80
STEP 3:						
Interaction						
Abuse X 5-HTTLPR group	1.24	.59	3.45	1.10	10.89	.03
Step 1 χ^2 =	38.10					.001
Step 2 χ^2 =	2.94					.230
Step 3 χ^2 =	4.57					.032
Overall Model χ^2 =	45.61					.001

Note: Group and frequency of vaginal sex in the past 6 months were controlled for in regression.