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Participation in a Family-Centered Prevention Program Decreases Genetic Risk for Adolescents' Risky Behaviors

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Abstract

OBJECTIVE—The present research addressed the following important question in pediatric medicine: can participation in an efficacious preventive intervention ameliorate the risk that a genetic vulnerability factor is hypothesized to confer on increases in risk behaviors across preadolescence?

METHODS—As part of the Strong African American Families preventive intervention study, data were collected from 641 black families in rural Georgia, assigned randomly to the prevention or control condition. The prevention condition consisted of 7 consecutive meetings at community facilities, with separate parent and youth skill-building curricula and a family curriculum. Each meeting included separate, concurrent sessions for parents and youths, followed by a joint parent-youth session in which families practiced skills they learned in the separate sessions. Involvement in risk behaviors was assessed when youths were 11 (pretest), 12 (posttest), and 14 (long-term follow-up) years of age. A genetic vulnerability factor, that is, a variable-nucleotide repeat polymorphism in the promoter region of the *SLC6A4* gene (*5HTT*), was assessed 2 years after the long-term follow-up assessment.

RESULTS—Youths at genetic risk who were assigned to the control condition displayed larger increases in risk behaviors across the 29 months that separated the pretest and long-term follow-up assessments, compared with youths at genetic risk assigned to the Strong African American Families condition and youths without genetic risk who were assigned to either condition.

CONCLUSION—This is the first study to demonstrate that participation in an efficacious preventive intervention can ameliorate a genetic risk for increasing involvement in health-compromising risk behaviors across preadolescence.

Keywords

African American; family interventions; genetic predisposition; prevention; risk-taking behavior

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Historically, residing in rural communities has protected African American adolescents from the high-risk behaviors prevalent in urban areas. Recent epidemiological data, however, indicate that African American youth in rural areas use alcohol and other substances and engage in sexual activity at rates equal to or exceeding those of youth in densely populated inner cities (1, 2). Prevention programs designed to deter substance use and the onset of sexual activity are scarce in most of the rural South (3). In response to this situation, the Strong African American Families (SAAF) program was developed, implemented, and tested in a longitudinal, randomized efficacy trial (4, 5). This family-centered prevention program for 11-year-olds was designed to prevent risk behaviors by enhancing protective caregiving practices and youth self-regulatory competence. Evaluations of SAAF confirmed its efficacy in preventing the initiation of risk behaviors across several years (4, 6, 7), enhancing protective parenting practices (5), and increasing youth self-regulatory capabilities (4, 5). Additional analyses revealed that SAAF is efficacious when the primary caregiver presents clinical levels of depressive symptoms (8) and when families report economic hardship (9).

Randomized prevention trials present a unique opportunity to test hypotheses about gene $\times$ environment (G $\times$ E) interactions (10), the combination of genetic predispositions with environmental processes to create variations in youths' phenotypes over time. The present study was designed to address an important question in pediatric medicine: *Can participation in an efficacious preventive intervention ameliorate the risk that a genetic vulnerability factor is hypothesized to confer on increases in risk behaviors across preadolescence?* The G $\times$ E hypothesis tested concerned a moderation effect in the association of a genetic vulnerability factor, a variable nucleotide repeat polymorphism in the promoter region of the SLC6A4 gene (5HTT), 5HTTLPR, with use of alcohol and marijuana and engagement in sexual intercourse among African American youth during early adolescence. We predicted that participation in SAAF would ameliorate the link between the 5HTTLPR polymorphism and increases in risk behaviors across preadolescence.

A key regulator of serotonergic neurotransmission, 5HTT, is localized to 17p13 and consists of 14 exons and a single promoter. A well-characterized 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. The short variant contains 12 copies of a 22bp repeat element and the long variant has 14 copies of that element. Youth with one or two copies of the short variant are hypothesized to be more involved in risk behaviors than are youth with two copies of the long variant. Genetic association studies indicate that the 5HTTLPR short allele is a risk factor for alcohol dependence and the use of other drugs among adults (11), increases in the use of alcohol and marijuana across early adolescence (12), and alcohol consumption among college students (13). These data converge to support consideration of variation in 5HTT as a vulnerability factor for young adolescents' involvement with risk behaviors.

We predicted that random assignment to the SAAF prevention group versus a control group would interact with genetic risk to predict increases in youth risk behaviors. Specifically, we predicted that youth at genetic risk from one or two copies of the short allele variant at 5HTTLPR who were assigned randomly to the control condition would display greater increases in risk behaviors compared with (a) youth at genetic risk assigned to the SAAF condition and (b) youth without genetic risk assigned to either the SAAF or the control condition.

PARTICIPANTS AND METHODS

Data reported in this paper were collected from both prevention and control families as part of the evaluation of the SAAF preventive intervention. Risk behaviors were assessed when the youth were 11 (pretest), 12 (posttest), and 14 (long-term follow-up) years old; genetic data were obtained 2 years after the long-term follow-up assessment. Below, we briefly describe subject recruitment and enrollment, intervention implementation and fidelity, and data collection procedures, which are described extensively in earlier reports on SAAF's efficacy (4-7).

Participants

Participants in the SAAF trial included 641 African American families in rural Georgia. From each family, a youth who was 11 years old when recruited (58% girls) and the youth's primary caregiver, typically the biological mother, provided data. At the first data collection session, youths' mean age was 11.21 years ($SD = .41$) and caregivers' mean age was 37.7 years ($SD = 7.62$). Mean household gross monthly income was \$2,109 ($SD = \$1,443$) and mean per capita gross monthly income was \$509 ($SD = \411). Although 74% of the mothers were employed outside the home and worked an average of 39.7 hours per week, 41% of the families lived below federal poverty standards and another 26% lived within 150% of the poverty threshold; they could be described as working poor (14).

Schools in four rural Georgia counties provided lists of 11-year-old students, from which youth participants were selected randomly (see 5). Parents gave written consent to their own and the youths' participation, and youth gave written assent to their own participation. Each family was paid \$100 after each assessment. The sample for the present study included 350 families randomly assigned to receive the SAAF intervention and 291 randomly assigned to the control condition; families assigned to SAAF were oversampled.

Of the families who provided data at the pretest assessment, 91% provided data at the long-term follow-up assessment conducted 29 months after the pretest. Two years after the long-term follow-up (4.5 years after the pretest), we attempted to re-contact the study families to obtain youths' DNA from saliva samples. Of the original sample assessed at pretest, 84% ($n = 539$) of the families were relocated; in the relocated families, 86% ($n = 461$) of the youth agreed to provide DNA. Two equivalence analyses were executed to determine whether any differences existed on demographic characteristics (monthly per capita income; number of children in the household, target gender, and maternal marital status) or the study variables (frequency of past-month alcohol use, marijuana use, and sexual intercourse) between (a) the families with pretest data and the sample with long-term follow-up data and (b) the families of target youth who did ($n = 461$) and did not ($n = 78$) agree to provide DNA (to conserve space, the means and standard deviations for these tests are not presented). For these analyses, *t* tests were used to compare all of the demographic and study measures except gender and maternal marital status, for which chi-square tests were used. No differences emerged on demographic or study variables between the families with pretest data and those with long-term follow-up data. Neither did any differences emerge between families or youth who did or did not agree to provide DNA.

Intervention Implementation

The SAAF prevention program consisted of seven consecutive meetings held at community facilities, with separate parent and youth skill-building curricula and a family curriculum. Each meeting included separate, concurrent training sessions for parents and youth followed by a joint parent-youth session during which the families practiced the skills they learned in the separate sessions. Concurrent and family sessions each lasted 1 hour; thus, parents and

youth received 14 hours of prevention training. During the weeks when the intervention families participated in the prevention sessions, the control families received three leaflets via post mail; one described various aspects of early adolescent development, another dealt with stress management, and the other provided suggestions for encouraging youth to exercise.

Parents in the prevention condition were taught the consistent use of high levels of monitoring and control, adaptive racial socialization approaches that included strategies for dealing with racial discrimination, strategies for communication about sex, and the establishment of clear norms and expectations for the use of alcohol and other substances. Youth learned the importance of having and abiding by household rules, behaviors to use when encountering racism, the importance of forming goals for the future and making plans to attain them, and the characteristics of agemates who use alcohol or are sexually active. Ten three-person teams of African American group leaders, each of whom had received 40 hours of training, conducted 38 intervention groups that ranged in size from 3 to 12 families ($M = 10$). To preserve the random nature of the group assignment, the analyses reported here included all families regardless of the number of prevention sessions that they actually attended (an intent-to-treat analysis).

Data Collection Procedures

African American students and community members served as home visitors to collect pretest and long-term follow-up data. During the pretest and long-term follow-up data collections, field interviewers who were blind to the families' group assignments made one home visit lasting 2 hours to each family. The time from pretest to long-term follow-up averaged 29 months. Informed consent forms were completed at all data collection points. During the home visits, self-report questionnaires were administered to caregivers and youth in an interview format. Each interview was conducted privately, with no other family members present or able to overhear the conversation.

Measures

Demographics—Youth age and gender, maternal age, maternal employment, and monthly income were recorded. Each caregiver reported the number of children and adults living in the home and her marital/significant relationship status.

Risk behavior—Risk behavior was evaluated with items that are commonly used in the public health literature (15) that we also have used previously with rural African American youth (4, 16, 17). Youth indicated how many times during the past month they had drunk beer, wine, wine coolers, whiskey, gin, or other liquor (alcohol use); used marijuana; or had sexual intercourse. Asking preadolescents about their risk behavior frequencies during the past month yields more valid and reliable recall data than does the use of a longer time frame (2). Past-month frequencies of alcohol use, marijuana use, and sexual intercourse were summed to form a risk behavior index.

Genotyping—Youths' DNA was obtained using Oragene™ DNA kits (Genetek; Calgary, Alberta, Canada). Youth rinsed their mouths with tap water, 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 5HTTLPR was determined for each youth as previously described (18). Of the sample, 6.4% were homozygous for the short allele (*ss*), 35.2% were heterozygous (*sl*), and 58.4% were homozygous for the long allele (*ll*). None of the alleles deviated from Hardy-Weinberg equilibrium ($p = .77$, ns). Consistent with prior research

(19), 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.

RESULTS

Descriptive Statistics

As expected, mean prevalence rates for past-month risk behavior at pretest, when the youth were 11 years old, were low: .09 for alcohol use ($SD = .63$), .01 for marijuana use ($SD = .20$), and .04 for sexual intercourse ($SD = .40$). The mean risk behavior index score at pretest was .14 ($SD = .86$). Frequency of past-month risk behavior rates increased over time. At long-term follow-up, when the youth were 14 years old, mean past-month frequencies were .19 for alcohol use ($SD = .77$), .03 for marijuana use ($SD = .27$), and .21 for sexual intercourse ($SD = 1.25$). The mean risk behavior index score was .37, $SD = 1.56$. These low rates of risk behavior for African American youth during early adolescence are consistent with data from other studies (20).

Genetic Risk, SAAF Participation, and Risk Behavior Increases

A partial correlation was executed between 5HTTLPR risk status (one or two copies of the *s* allele versus two copies of the *l* allele) and the risk behavior index at long-term follow-up to determine whether genetic risk status was associated with increases in risk behavior across the 29 months from pretest to long-term follow-up. The pretest risk behavior index scores and group assignment were controlled when genetic risk status was correlated with the risk behavior index at long-term follow-up. Controlling for pretest levels of risk behaviors allows an analysis to determine whether risk status is associated with increases over time in risk behaviors. Genetic risk status was correlated with increases in youth risk behavior across the 29 months from pretest to long-term follow-up, $r(419) = .11$, $p < .03$.

Four groups were formed to test the hypothesis that participation in SAAF would moderate the association between youths' 5HTTLPR status and increases over time in their risk behavior: (a) youth in the SAAF condition at genetic risk ($n = 98$), (b) youth in the SAAF condition without genetic risk ($n = 146$), (c) youth in the control condition at genetic risk ($n = 73$), and (d) youth in the control condition without genetic risk ($n = 102$). A one-way analysis of variance was used to determine the four groups' pretest equivalence on the demographic and study variables, and chi-square tests were used to determine group equivalence on youth gender and maternal marital status. No equivalence comparison was significant. Pretest levels of the risk behavior index were controlled in the following analyses; this is standard practice because it allows hypothesized group differences in changes across time in outcome variables to be tested.

A one-way analysis of covariance (ANCOVA) was computed on the four Genetic Risk $\times$ Prevention Condition groups to test the gene $\times$ environment hypothesis. Results of the ANCOVA revealed a significant group effect, $F(1, 411) = 5.05$, $p < .002$, effect size = .19. Tukey post hoc tests indicated, as predicted, that youth at genetic risk in the control condition ($M = 1.13$) evinced greater increases from ages 11 to 14 years in the frequency of past-month risk behaviors than did youth at genetic risk in the SAAF condition ($M = 0.30$) and youth not at genetic risk in either the control ($M = 0.33$) or the SAAF ($M = 0.22$) condition; all $ps < .025$. Figure 1 illustrates these findings, which support the proposition that participation in an efficacious family-centered preventive intervention can ameliorate genetic risk for preadolescents' involvement in risk behaviors.

DISCUSSION

Using a randomized prevention trial, we tested a G×E hypothesis to determine whether participation in SAAF, an efficacious prevention program for African American youth, could ameliorate a genetic vulnerability factor for increases in risk behaviors. We found that youth at genetic risk who were assigned to the control condition evinced larger increases in risk behaviors than did youth at genetic risk assigned to the SAAF condition and youth with no genetic risk assigned to either the SAAF or the control condition. To our knowledge, this is the first study to demonstrate that participation in a preventive intervention can ameliorate a genetic risk for increasing involvement with health-compromising behaviors. This finding adds to results from research with twins, in which protective activities (e.g., sports involvement) helped to shield youth from genetic risk (21).

In SAAF, parents learn caregiving practices that have been found to deter African American youth from engaging in high-risk behaviors. These practices include racial socialization, high levels of vigilance and monitoring along with high levels of emotional support, clearly articulated norms and expectations concerning risk behaviors, and bidirectional family communication (15, 22, 23). Because substance use and early sexual activity share common causes that include ineffectiveness in monitoring, communication, and discipline on the parents' part and low self-regulation on the youth's part (12), we expected enhancement of protective caregiving practices and strengthening of youth self-regulation via SAAF to mitigate the risk that the short allele version of 5HTTLPR confers.

The results also demonstrate that randomized prevention trials present a unique opportunity to test G×E hypotheses, an important emerging area in pediatric research and practice. Use of randomized control trials offer advantages over observational designs for detecting G×E interactions in children and adolescents. Observational designs are limited in their ability to identify a true environmental exposure or effect, particularly if the exposure occurs over an extended period of time. The use of intervention strategies such as randomized prevention trials is one means of determining whether an environmental factor has attained causal status. Through the implementation of trials such as SAAF, a causal relation between an environmental manipulation and the alteration of the course of a targeted outcome can be identified (24).

Several limitations of the present research should be noted. First, only one genetic polymorphism was examined, which does not represent all the genetic variation that conceivably could place youth at risk for health-compromising behaviors. Many genetic variants may alter risk, the expression of which may emerge only in particular environmental contexts. A corollary of this limitation is the perception that genes confer only risk. Genetic effects may also be protective, and that which is conceptualized as a risk-promoting genetic effect may actually be the absence of protective effects. Second, the long-term follow-up assessment described in this paper, conducted 2 years after the intervention ended, included only young adolescents. As we continue to follow the sample, we will be able to determine if the G×E findings carry forward throughout adolescence and early adulthood.

CONCLUSIONS

This study was designed to address the question: Can participation in an efficacious preventive intervention ameliorate the risk that a genetic vulnerability factor is hypothesized to confer for increases in risk behaviors across preadolescence? The results demonstrate the potential of efficacious prevention programs to protect youth, particularly those who are at risk for involvement, from engaging in risk behaviors that undermine their health and

development. The results further demonstrate the importance of enhancing protective parenting and youth self-regulatory processes during a developmental period when some youth initiate and escalate health-compromising behaviors. As protective genes are identified, future research should examine the potential for participation in preventive interventions to compensate for the absence of those genes. Finally, the findings indicate the importance of inoculating youth with culturally and racially specific protective factors. To move this effort forward, a new generation of research is needed that will identify prevention programs that offer youth protection against genetic and environmental risk factors.

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Abbreviations

ANCOVA	analysis of covariance
SAAF	Strong African American Families program

Figure 1.
Changes in mean risk behavior frequency according to group assignment and genetic risk.