Mediation and Moderation of Religion-Substance Abuse Relationships By Genotype

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Abstract

Background
The negative correlation between substance abuse and religiosity is well-established, and often cited as a mechanism through which religiosity affects general health. However, little research has examined the mechanism underlying the addiction/religiosity relationship itself. Previous literature on substance abuse documents significant relationships of substance abuse disorders with dopamine and serotonin transporters genes. Other studies demonstrate genetic underpinnings to religiosity. The current study sought to evaluate how religiosity, substance abuse, and genetics may interact.

Methods
Data were drawn from the National Longitudinal Study of Adolescent Health (Add Health), which surveyed over 15000 subjects in four waves, from age 12 to 38. Genotyping was performed for candidate genes previously correlated with mental health: the serotonin transporter promoter (5HTTLPR), dopamine transporter (DAT1), dopamine receptor subtype 4 (DRD4), and monoamine oxidase A (MAOA). For this analysis genotypes were dichotomized by activity levels, per previous literature. Religious variables (attendance, importance of religion, and prayer) were modeled across Waves I-IV using growth mixture modeling. To these models, genotypes were added to assess mediation relationships. Stratified analyses were performed to test for moderation of religion/addiction relationships by genotype.

Results
Evidence of mediation of the religion/substance abuse relationship was apparent for 5HT and DAT. DAT appeared to mediate the relationship of baseline binge drinking to later religious attendance. Multiple relationships of religious importance and frequency of prayer to future substance abuse became non-significant when controlled for 5HTTPLR. Moderation analysis found substantial variation in religion/substance use relationships according to genotype.

Conclusions
This analysis indicates that religiosity may relate to addiction partially through correlation with genes, and that religion/substance use relationships may vary by genotype. Further research on the relationship of 5HTLLPR to religious phenomena, particularly personal prayer, is warranted. Improved understanding of how religion reduces substance abuse will inform prevention and treatment efforts.

Keywords: religion; substance abuse; genetics

1. Introduction

A large body of literature documents correlations between various aspects of religiosity and several positive health outcomes. Religiousness has been found to predict improved surgical outcomes (1), lower incidence of coronary heart disease, hypertension and cerebrovascular disease (2), as well as general longevity (3). In attempting to understand these findings, researchers frequently cite the persistent finding that those who are more religious tend to use fewer substances, including cigarettes, alcohol, and illicit drugs (4).

This phenomenon – that religiousness correlates inversely with substance abuse – has been observed in more than 270 studies (3). This effect is more commonly observed than are negative correlations of religiosity with delinquent behavior. Furthermore, many studies of delinquency and religiosity use substance abuse as part of their measures of delinquency (5). Most religions that proscribe substance use also proscribe antisocial behaviors, but the correlations of religiosity to the former are stronger. Therefore, this may be a specific effect; religion and spirituality may in some specific way protect against addiction. Previous research attempting to explain this connection has largely explored social theories and postulated such mediators as moral beliefs, social support, parenting style, social network closure, and desire for approval from the peer group (6).

However, genetic research indicates there is reason to suspect biological underpinnings to this relationship. Several studies have explored the hypothesis that religiosity may be related to the same genotypes that affect addiction diathesis. Such a relationship would imply statistical mediation, in which the relationship of religiosity to reduced substance use could be accounted for by a shared genotype. In a longitudinal study of 1,796 male twins, Kendler and Myers found that while shared environmental factors mediated the relationship of church attendance to alcohol and nicotine use in the cohort as adolescents, genetic factors appeared to be the main mediator of the attendance to substance use relationship when they became adults (7).

Another hypothesis is that religiosity interacts with genetic diathesis such that heritable risk for substance abuse is attenuated by religious participation. Statistically, this is termed moderation. Timberlake and colleagues analyzed data from the third wave of the National Longitudinal Study of Adolescent Health (Add Health) to examine interactions between religiosity and genetic predictors of smoking in twins and other sibling pairs. Self-rated religiousness appeared to attenuate genetic predisposition to smoking initiation (8). A more recent study found that religiosity moderated the effect of genetics on problem drinking in adolescents but not adults (9).

The current study was undertaken to test the hypotheses that 1) the relationship of religiosity to substance abuse is mediated by genotype (mediation; see Figure 1) and 2) religiosity relates differently to substance abuse depending on individual genotype (moderation; see Figure 2). Rather than use traditional twin studies to analyze shared environmental versus genetic determinants of variance in outcomes, the authors used data from the National Longitudinal Study

of Adolescent Health (Add Health) to analyze relationships of religiosity and substance use directly with candidate genes measured in the fourth wave of this large study, which involved over 15,000 participants over fourteen years.

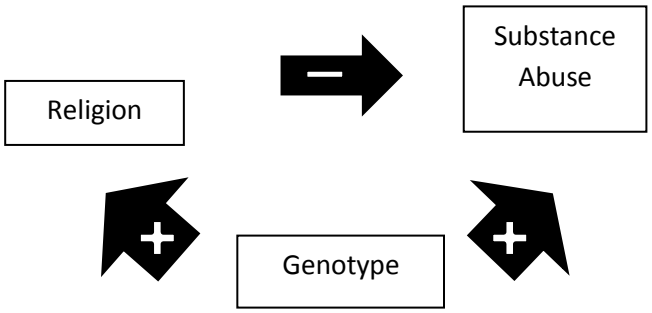

Figure 1. Mediation relationship. Religion to substance abuse relationship explained by common genetic basis.

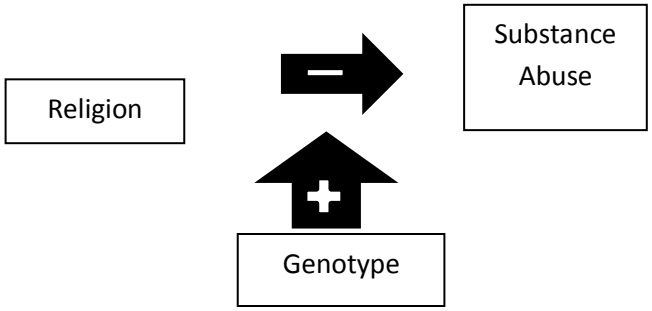

Figure 2. Moderation relationship. Genotype changes relationship of religiosity to substance abuse.

2. Methods

2.1. Sample

The National Longitudinal Study of Adolescent Health (Add Health) included 15,701 respondents who completed in-home surveys in 1995 and underwent follow-up evaluations three additional times; 1996, 2001–2002, and 2008–2009 (Waves I–IV, respectfully; Harris, K.M., C.T. Halpern, E. Whitsel, J. Hussey, J. Tabor, P. Entzel, and J.R. Udry. 2009. The National Longitudinal Study of Adolescent Health: Research Design URL: http://www.cpc.unc.edu/ projects/addhealth/design.) Participating schools were selected and data weighted to ensure a nationally-representative sample. Information was gathered both from adolescents and their parents, as well as data concerning informants' communities and schools. A variety of demographic, social and health variables were also collected, including a comprehensive assessment of

use and abuse of tobacco, alcohol, marijuana, other illicit drugs, and misuse of prescription medication. Religious variables measured at all four waves included attendance at religious services, self-ranked importance of religion, and frequency of prayer. At Wave IV, genetic information was obtained from all respondents.

2.2. Measures

2.2.1. Religious Variables

Three individual-level religious indicators were measured at all four waves of data collection. *Religious attendance* was assessed by the question, "In the past 12 months, how often did you attend religious services?" at Waves I and II. Respondents who had previously indicated no religion were not asked the question. Attendance was measured at Waves III and IV by a similar question, "How often have you attended church, synagogue, temple, mosque, or religious services in the past 12 months?" For this study, responses were recoded where necessary to ensure uniformity across waves so that they ranged from never (1) to more than once per week (4).

Personal importance of religion was measured by the question "How important is religion to you?" at Waves I and II. As with religious attendance, respondents who had previously indicated no religion were not asked the question. Responses ranged from "not important" to "very important". At Waves III and IV, respondents were asked "How important (if at all) is your religious faith to you?" with responses ranging from "not important" to "more important than anything else." To ensure comparability across waves, the variable was recoded into three categories: "not important" (1), "somewhat important" (2), and "very important" (3).

Frequency of prayer was measured at Waves I and II with the question "How often do you pray?" At Waves III and IV, subjects were asked "How often do you pray privately, that is, when you're alone in places other than a church, synagogue, temple, mosque, or religious assembly?" Responses were recoded to ensure uniformity across waves with choices ranging from never (1) to more than once per day (4).

2.2.2. Demographic Variables

Demographics considered in this analysis include biological sex, race, ethnicity, age and socioeconomic status (SES). SES was operationalized as the highest level of education attained by either of the subject's parents. Age at each wave was accounted for by the use of time scores in all growth models.

2.2.3. Substance Abuse

Substance abuse variables were drawn from Wave IV of Add Health. Outcomes used in the current analysis included 1) tobacco: having tried cigarette smoking and at what age, being a regular smoker and at what age, degree of smoking; 2) alcohol: use of alcohol, degree of alcohol use and binge drinking, qualification for alcohol abuse as defined by DSM-IV (American Psychiatric Association 1994) 3) marijuana: use and age at first use of marijuana, qualification for cannabis abuse 4) other drugs: use of cocaine, steroids, other illicit

drugs, misuse of prescription medications, and qualification for abuse of any drug.

2.2.4. Candidate Genes

Candidate genes tested for association with substance abuse and religiosity included those coding for the promoter region of the serotonin transporter (5HTTLPR), the dopamine transporter (DAT1), dopamine receptor type 4 (DRD4), and monoamine oxidase A (MAOA). Allelic variants were dichotomized in accordance with previous literature (10).

2.4. Analysis

Statistical analyses were conducted using Mplus 7 (Muthen and Muthen, Los Angeles CA). *Growth mixture modeling* was used to identify longitudinal patterns of change in religious variables over the course of adolescence into adulthood. Growth mixture modeling allows for estimation of a parameter's mean level at a specified starting time point, known as the intercept, the rate of increase or decrease over time (the linear trend) as well as the rate of change of the increase or decrease (the quadratic trend). Due to non-convergence, quadratic terms could not be estimated for the current model; as such models estimated the baseline or intercept level of religiosity as well as the linear slope, which represents change over time. Religious attendance, importance of religion, and frequency of prayer from all four waves of Add Health were used to create separate growth models. Subsequent models controlled for demographics. Next, models were created that assessed correlations of these growth parameters (intercept and slope) with substance abuse outcomes drawn from Wave IV.

To test the hypothesis that the relationship of religiosity to substance abuse is mediated by genetic variables, models correlating substance abuse outcomes to religious trajectories were then controlled for genotype, using dichotomized categories in accordance with previous research. Mediation was defined as present if significant correlations of religious trajectories to substance abuse outcomes became non-significant when controlled for genotype.

The hypothesis that the relationship of religiosity to substance abuse was moderated by genotype was assessed using analyses stratified by genotype. Moderation was defined as present where relationships of religious trajectory to substance abuse were significant in the main sample but non-significant in the presence of a specific genotype.

Survey weights were incorporated in analyses to compensate for differences in selection probabilities of cases within sampling units, rates of non-response, and chance fluctuations of the sample from the population as a whole.

3. Results

3.1. Sample Characteristics

Accounting for missing data, the final analyzed sample consisted of 9,422 subjects (60% of the original sample). Participants were 55% female, 65% Caucasian, and 15% Hispanic in ethnicity. Mean level of parental education was some education following high school. Mean age at Wave I

was 15.8 (SD 1.6), at Wave II was 16.8 (SD 1.6), at Wave III was 22.0 (SD 1.7), and at Wave IV was 28.8 (SD 1.6).

3.2. Religion/Substance Abuse Relationships

Controlling for demographics, most substance abuse outcomes correlated with both baseline religiosity and religious change over time. Exceptions to this pattern included relationships of most religious variables to use of anabolic steroids or intravenous drugs, and relationships of frequency of prayer to marijuana abuse, to the age at which one first smoked a cigarette and the degree of smoking among smokers (See table 1).

Table 1. Relationship of religious growth parameters across waves to substance abuse at Wave IV, controlled for demographics.

Substance Abuse Outcome	Religious Variable	Intercept			Slope		
		Estimate	S.E.	p value	Estimate	S.E.	p value
Smoked a whole cigarette	Attendance	-0.1110	0.0130	0.0000	-3.1230	0.3380	0.0000
	Importance	-0.1100	0.0170	0.0000	-1.8350	0.3730	0.0000
	Prayer	-0.0310	0.0080	0.0000	-0.5390	0.1630	0.0010
Age when smoked whole cigarette	Attendance	0.6270	0.0840	0.0000	11.8880	2.0890	0.0000
	Importance	0.6360	0.1450	0.0000	7.8510	3.1360	0.0120
	Prayer	0.2030	0.0550	0.0000	1.2720	1.2460	0.3070
Ever regular smoker	Attendance	-0.1460	0.0130	0.0000	-3.8640	0.3170	0.0000
	Importance	-0.1290	0.0160	0.0000	-2.2220	0.3650	0.0000
	Prayer	-0.0450	0.0080	0.0000	-0.6570	0.1640	0.0000
Age of regular smoking	Attendance	0.8320	0.1200	0.0000	15.6010	2.6930	0.0000
	Importance	0.7950	0.1600	0.0000	11.4010	3.7930	0.0030
	Prayer	0.3340	0.0640	0.0000	3.5840	1.3870	0.0100
Number of days smoked in the past month	Attendance	-3.7550	0.3090	0.0000	-104.1450	7.6740	0.0000
	Importance	-2.4350	0.4310	0.0000	-43.0370	9.1690	0.0000
	Prayer	-1.2360	0.2120	0.0000	-18.5720	4.4190	0.0000

Number cigarettes smoked per day	Attendance	-2.0130	0.1840	0.0000	-49.9730	4.7810	0.0000
	Importance	-1.6240	0.2540	0.0000	-26.1110	5.7720	0.0000
	Prayer	-0.7300	0.1180	0.0000	-8.1490	2.6570	0.0020
Number smoked among smokers	Attendance	-1.8040	0.3950	0.0000	-32.4910	9.9260	0.0010
	Importance	-1.8140	0.5360	0.0010	-21.4390	11.8890	0.0710
	Prayer	-0.6130	0.2120	0.0040	-2.8900	4.9580	0.5600
Tried alcohol	Attendance	-0.0610	0.0100	0.0000	-1.9910	0.2940	0.0000
	Importance	-0.0880	0.0120	0.0000	-1.8000	0.2390	0.0000
	Prayer	-0.0220	0.0060	0.0000	-0.6870	0.1250	0.0000
Age when tried alcohol	Attendance	0.7630	0.0830	0.0000	17.6160	2.2440	0.0000
	Importance	0.7660	0.1130	0.0000	10.1270	2.4730	0.0000
	Prayer	0.2400	0.0580	0.0000	3.9030	1.2000	0.0010
Days drank this year	Attendance	-0.4410	0.0490	0.0000	-14.5790	1.3050	0.0000
	Importance	-0.5530	0.0780	0.0000	-14.2550	1.7060	0.0000
	Prayer	-0.2000	0.0960	0.0360	-6.4540	0.1750	0.0000
Number of drinks on each occasion	Attendance	-0.5570	0.0780	0.0000	-16.5020	2.2440	0.0000
	Importance	-0.4240	0.1080	0.0000	-9.5980	2.5410	0.0000
	Prayer	-0.2060	0.0480	0.0000	-3.7600	1.1440	0.0010
Days with binge drinking this year	Attendance	-0.4300	0.0390	0.0000	-13.2240	1.0930	0.0000
	Importance	-0.5000	0.0610	0.0000	-12.5680	1.5210	0.0000
	Prayer	-0.2140	0.0250	0.0000	-5.7290	0.6230	0.0000
Days drunk this year	Attendance	-0.3790	0.0310	0.0000	-12.0920	0.9010	0.0000
	Importance	-0.4420	0.0500	0.0000	-11.3720	1.2240	0.0000
	Prayer	-0.1780	0.0190	0.0000	-4.9020	0.4910	0.0000
Alcohol abuse	Attendance	-0.0370	0.0060	0.0000	-0.9890	0.1760	0.0000
	Importance	-0.0450	0.0090	0.0000	-1.0840	0.2590	0.0000
	Prayer	-0.0150	0.0040	0.0000	-0.4300	0.1000	0.0000
Ever used	Attendance	0.0030	0.0030	0.2810	0.0970	0.0920	0.2910

anabolic steroids							
	Importance	0.0080	0.0050	0.0820	0.2810	0.1160	0.0150
	Prayer	0.0040	0.0020	0.0760	0.1120	0.0520	0.0310
Ever used marijuana	Attendance	-0.1460	0.0130	0.0000	-3.7850	0.3550	0.0000
	Importance	-0.1870	0.0180	0.0000	-3.8530	0.4790	0.0000
	Prayer	-0.0620	0.0080	0.0000	-1.4400	0.1860	0.0000
Ever used cocaine	Attendance	-0.0910	0.0090	0.0000	-2.4180	0.2490	0.0000
	Importance	-0.1110	0.0150	0.0000	-2.2770	0.3450	0.0000
	Prayer	-0.0350	0.0070	0.0000	-0.7440	0.1510	0.0000
Ever used IV drugs	Attendance	-0.0020	0.0020	0.3520	-0.0200	0.0480	0.6770
	Importance	0.0030	0.0020	0.2330	0.0680	0.0660	0.3060
	Prayer	0.0000	0.0010	0.8280	-0.0140	0.0300	0.6370
Ever misuse prescription drugs	Attendance	-0.0740	0.0090	0.0000	-1.9710	0.2510	0.0000
	Importance	-0.0960	0.0150	0.0000	-1.8540	0.3600	0.0000
	Prayer	-0.0310	0.0060	0.0000	-0.7580	0.1520	0.0000
Age when used marijuana	Attendance	0.7240	0.0990	0.0000	14.1100	2.5640	0.0000
	Importance	0.8200	0.1360	0.0000	9.4010	3.1070	0.0020
	Prayer	0.2580	0.0640	0.0000	2.9660	1.4740	0.0440
Marijuana abuse	Attendance	-0.0270	0.0050	0.0000	-0.5560	0.1330	0.0000
	Importance	-0.0250	0.0090	0.0070	-0.4470	0.2160	0.0390
	Prayer	-0.0050	0.0030	0.1630	-0.0330	0.0830	0.6920
Any drug abuse	Attendance	-0.0270	0.0050	0.0000	-0.5310	0.1340	0.0000
	Importance	-0.0350	0.0090	0.0000	-0.5620	0.2160	0.0090
	Prayer	-0.0090	0.0040	0.0070	-0.1710	0.0800	0.0330

3.3. Mediation Analyses

Mediation was tested for by controlling models of religious growth parameters and substance abuse outcomes for pre-specified categorizations of allele frequencies of 5HTTLPR, DAT1, DRD4, and MAOA. Significant relationships of religious attendance to Wave IV substance use outcomes maintained significance controlling for all genotypes, with one exception. When controlled for genotype at DAT1, baseline attendance no longer significantly predicted frequency of binge drinking (Intercept Est=-0.4320, S.E.=0.2390, p=0.0710). No evidence of mediation by the studied genotypes was evident for the relationship of religious importance to substance use outcomes. More evidence of mediation appeared in

analyses of the frequency of prayer. When controlled for 5HTTLPR genotype (long-long versus any short allele), the relationship of change in prayer over time to age at which subjects first tried smoking became non-significant (Slope Est=2.9990, S.E.=2.3330, p=0.1990). Although change in prayer over time significantly correlated with steroid use, this relationship was non-significant when controlled for 5HTTLPR genotype (Slope Est= -0.0400, S.E.=0.0840, p=0.6290). Likewise, drug abuse no longer related to prayer when controlled for 5HTTLPR (Slope Est= -0.0090, S.E.= 0.0050, p= 0.0690).

3.4. Moderation Analyses

Moderation of the religion/substance abuse relationship by genotype was tested for using stratified analyses for each of the studied genes, dichotomized in accordance with previous literature (10). Several differences were seen in individual relationships of religious variables with substance abuse outcomes as compared with the full sample. Overall, more variation among genotypes was observed for relationships of religious importance and personal prayer to substance abuse than for those involving religious attendance.

3030 subjects had at least one *s* allele at the 5HTTLPR locus, which is associated with reduced serotonergic expression and cellular uptake (11). Associations not observed between religious variables and substance use variables in this subgroup, which were observed in the full sample and in the subgroup with no *s* allele (N=5921) include the following: 1) change in religious attendance over time no longer predicted age of initiation of cigarette use or regular smoking, degree of smoking among smokers 2) change in religious importance over time no longer predicted age of initiation of cigarette use or regular smoking, or age alcohol use initiation 3) baseline religious importance no longer predicted how often and how much subjects reported drinking alcohol 4) change in frequency of prayer no longer predicted smoking experimentation, regular smoking, age at regular smoking, alcohol experimentation, or drug abuse, and 5) baseline prayer frequency no longer predicted meeting criteria for drug abuse.

Subjects with the LL genotype at 5HTTLPR (N=5921) were relatively similar to the full sample. Differences included: 1) baseline attendance and change in this variable over time correlated with use of anabolic steroids 2) change in religious importance no longer predicted abuse of marijuana or other drugs.

The dopamine transporter locus (DAT1) contains a 40 bp VNTR (variable number tandem repeat). Research has associated homozygosity for the 10 repeat alleles with psychopathology (12). Those subjects in the current study with the 10/10 genotype differed from the total sample, and from those not homozygous for the 10 repeat allele, in few analyses. In the DAT 10/10 group (N=5213), change in religious importance was not predictive of the age at which smoking experimentation occurred, and religious importance at baseline or over time was not predictive of marijuana abuse. Rate of change in prayer frequency was not predictive of the number of cigarettes reported per day.

The subgroup not homozygous for the 10 repeat allele of the dopamine transporter (N=3873) differed from the overall group

and for peers homozygous at the domain in several ways. In this group, the trajectory of religious attendance was no longer associated with degree of smoking among smokers, or with drug abuse. Change in religious importance no longer predicted age of smoking experimentation, or meeting criteria for alcohol or drug abuse. Change in frequency of prayer no longer predicted smoking experimentation, age at regular smoking, or age of alcohol experimentation. Baseline prayer was no longer predictive of having used alcohol. Baseline prayer frequency as well as the trajectory of this variable across waves no longer predicted meeting criteria for drug abuse.

The dopamine receptor subtype D4 (DRD4) is coded for by a gene with common allelic variants also depending on a VNTR. Evidence suggests that the presence of a 7 repeat allele results in receptors less sensitive to the agonist activity of dopamine. It has also been associated with a clinical diagnosis of attention deficit hyperactivity disorder (12). Subjects with at least one seven repeat allele at this locus (N=3177) showed differences from those without a seven repeat allele, and from the sample as a whole, as follows: 1) baseline and change in religious attendance no longer predicted degree of smoking among smokers 2) change in both attendance and importance did not significantly correlate with age of marijuana use 3) both baseline and change in attendance predicted use of anabolic steroids in this group 4) change in religious importance did not correlate with marijuana use 5) change in frequency of prayer no longer predicted smoking experimentation, regular smoking, or age at regular smoking 6) baseline frequency of prayer was not associated with alcohol experimentation or drug abuse and 7) this was the only subgroup in which prayer was not predictive of the abuse of prescription medications.

Subjects with no seven repeat allele at the DRD4 locus (N=5927) differed from peers in that change in religious importance did not predict age of smoking experimentation or drug abuse, and baseline attendance did not predict marijuana abuse.

Monoamine oxidase A (MAOA) breaks down monoamine neurotransmitters such as serotonin and dopamine (13). The genetic locus coding for MAOA features a 30-bp VNTR polymorphism which is associated with activity of the enzyme. Subjects with active variants (N=4405) differed from peers in that change in religious importance did not correlate with age of smoking experimentation, age of marijuana use, or drug abuse. Both baseline and change in importance failed to predict degree of alcohol consumption. The trajectory of prayer frequency no longer correlated with smoking experimentation or the age at which this occurred, and also failed to predict the age of marijuana use.

Those with MAOA polymorphisms associated with low expression (N=4699) differed from those with active alleles and with the total sample in the following ways: 1) baseline and change in attendance were not associated with degree of cigarette use among active smokers 2) change in attendance no longer predicted drug abuse 3) change in importance no longer related to frequency of alcohol use 4) baseline importance did not associate with marijuana abuse 5) baseline prayer was not associated with alcohol experimentation 6) change in prayer over time no longer predicted age of

regular smoking, or abuse of marijuana or other drugs.

4. Discussion

The current study sought to further previous literature on genetics, religion and substance abuse, using several candidate genes commonly studied by behavioral geneticists. It furthered the literature in this area by using molecular genetics in a large sample rather than twin data. Several findings bear discussion.

Firstly, the field of religion/health research has been criticized for the heavy reliance on cross-sectional data, which has been prevalent as the field has emerged. The current study documents that religiosity in early adolescence as well as change over time is predictive of multiple substance abuse outcomes in adulthood. These effects were independent of race, age, gender, and socioeconomic class. These consistent findings imply a protective effect that is maintained over time.

Secondly, our results illuminate the relationship between genetic predisposition and experience, specifically the effect of religious beliefs and behaviors. Analyses indicated that, to some degree, relationships between religiosity and substance abuse may be explained by common genetic underpinnings. This was most apparent in analyses of self-reported frequency of prayer versus substance abuse, when controlled for genetic variation at 5HTLLPR. A previous report found correlations of the serotonin transporter gene with several religious variables, but only the relationship of the gene to frequency of prayer could not be accounted for by demographics (14). A small experimental study concluded that the serotonin system may play a role in spiritual experiences (15). Another study found correlation between 5HTTLPR and the character trait of spiritual acceptance (16). Personal prayer as a psychological phenomenon is relatively understudied in comparison to other religious variables, most notably service attendance. The current findings suggest that the serotonergic system may relate somehow to the psychology of prayer and help explain its putative salutary effects. More research in this area is warranted.

Analyses of how genotype influences the relationship of religiosity and substance abuse further imply that heredity is important in our understanding of religion/health relationships. Particularly with regard to religious importance and frequency of prayer, variation in the strength of the religion/substance use relationship was observed when stratified by genotype. Some previous literature has found modification of religion/health relationships by genetic factors. Koopmans and colleagues found that genetic contributions to variance in alcohol use varied in adolescents with and without religious upbringing (17). Similarly, Beaver and colleagues found that polymorphisms in genes coding for dopamine receptor D2 interacted with religiosity in the prediction of adolescent delinquency (18). Much variation was apparent in the current study, which will need to be further explored and replicated in alternate data sets.

5. Limitations

Several factors limit the interpretability of the current study, which

should be considered exploratory. Only three religious constructs were explored, which cannot adequately capture the full range of religious beliefs and experiences. The sample is representative of the U.S. population only, and is predominantly Christian. The specific genes analyzed may relate to religiosity based on theory but may not be the optimal loci for this exploration. Furthermore there was no consideration of interactions between genes, which is likely prevalent and complex. Inferences based on analyses of moderation must be tempered by consideration of smaller sample sizes in each of the genotypic subgroups. Although each subgroup exceeded 3000 participants, it is possible differences in statistical significance may stem from reduced power.

In conclusion, results indicate that relationships of religiosity, substance abuse, and genetics are complex and diverse. Genetic variables appear to variably mediate and moderate religiosity's effect on substance abuse. Further research should seek to replicate and clarify these findings. Ultimately this line of research can enhance our understanding of how religiosity acts to protect health, at which stages of life it is most effective and which aspects of religiosity are most protective, as well as the neurological underpinnings of religion and of substance abuse.

6. Acknowledgements

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