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Association Between MAOA u VNTR genetic polymorphism and Aggression, Gender, and Race in Adolescents

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2020

Abstract

Association Between *MAOA* u-VNTR genetic polymorphism and Aggression, Gender, and Race in Adolescents

by

Almaz Adair Johnson

MA, Bowie State University, 2005

BS, Howard University, 1991

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

A genetic polymorphism found in the upstream region of the monoamine oxidase A (MAOA) gene upstream variable number tandem repeat (u-VNTR) has been shown to have an influence on aggression with mixed results. The purpose of this quantitative study was to examine the association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression in an adolescent population 13–18 years of age. The conceptual framework was based on the biosocial model of antisocial behavior that indicates genes can influence aggressive behaviors with or without environmental influences. Data (N = 2506) from the National Longitudinal Adolescents and Adult Study (Add Health) 2008-2012 were used to calculate descriptive (mean, median, and standard deviation) statistics. Inferential statistics were calculated using independent variables of u-VNTR genetic polymorphism of the *MAOA* gene, gender, and ethnicity; the potential confounder of abuse; and the dependent variable of aggression. Results showed that the presence of low variants of the *MAOA* gene and being male were associated with higher aggression scores. Abuse was not an impactful confounder. The social change implications from these findings include that they may enhance understanding of the role genetics plays in aggression and may increase knowledge of the importance of including genetic research in public health interventions.

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Dedication

This is dedicated to my family. May your hands touch the world.

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Chapter 1: Introduction to the Study

Aggression among adolescents has been labeled a profound public health concern (Abram et al., 2015; Newcorn, Ivanov, Chacko, & Shabnam, 2015; UN World Health Organization [WHO], 2014). This is mainly due to high-risk behaviors among adolescents including aggression and violence. Youth aggression is the most prevalent reason for child and adolescent psychiatric referrals, often in association with emergent symptoms (Newcorn et al., 2015). Youth violence is the third leading cause of death in adolescence, and approximately 600,000 people ages 10–24 are treated for physical assaults in emergency rooms (Centers for Disease Control and Prevention [CDC], 2017). Although not all aggression leads to violence, all violent acts contain aggression. Researchers have examined social, environmental, and other factors that lead to aggression and violence. Genetics is becoming a factor of emerging influence in behavioral outcomes including aggression. The upstream variable number tandem repeat (u-VNTR) genetic polymorphism of the monoamine oxidase A (*MAOA*) gene has been explored as a genetic influence in gambling, ADHD (Karmakar et al., 2017), suicidal depression, weapon carrying, and involvement with gangs (Beaver, Delisi, Vaughn, & Barnes, 2010; Beaver, Barnett & Boutwell, 2013; Ibanez et al., 2000). This genetic polymorphism has been associated with aggressive behaviors with varying results (Buckholtz & Meyer-Linderberg, 2008; Ferguson et al., 2012; Mason & Frick, 1994; Reti et al., 2011). Obtaining a comprehensive understanding of the relationship between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression may support efforts to mitigate violence with early interventions using genetic information. The

current study addressed the gap in the literature on the relationship between this genetic polymorphism and aggression.

Another purpose of this study was to investigate this association through the lens of gender and race. Studies indicated that males are considered to be the more aggressive gender (Bjorkqvist, 2017; Connor, Steingard, Anderson, & Melioni, 2003); however, female carriers with this polymorphism exhibit greater aggression and related aggressive behaviors including suicidal depression (Ducci et al., 2008) and weapon-carrying behaviors (Beaver et al., 2010). Studies have also demonstrated that certain races are considered more aggressive. This genetic polymorphism has been found in greater prevalence among Asian and African Americans (Hernandez & Blazer, 2006). The current study addressed these associations with gender and ethnicity in an adolescent population.

This chapter includes the background of the study, the problem statement, the purpose of the study, and the research questions. The conceptual background is introduced, and the definitions of key terms are presented. Additionally, delimitations, limitations, and assumptions are explained. The significance of the study is described, and the chapter concludes with a summary and transition.

Background

Human aggression is an issue among societies around the world. Governmental interventions and policies that focus on mitigating violence have contributed to decreased violence rates in many countries, although this still remains a significant issue (Anderson & Huesmann, 2003; Cook & Cook, 2011; Federal Bureau of Investigation [FBI], 2015).

Historical accounts of medieval life indicated that aggression and violence were common occurrences. Today, people are less prone to violence than in previous centuries (Anderson & Huesman, 2003; Cook & Cook, 2011). In more recent U.S. history, the highest violence rates were seen during the Great Depression and in the 1980s and 1990s (Anderson & Huesmann, 2003). There were 1,197,967 (375.7/100,000) incidents of violent crimes in the United States in 2014 (Langton & Truman, 2015). Violent crimes include assault, rapes, murder, and robberies (Langton & Truman, 2015). Victimization surveys indicated that there are 4.2 violent crimes per each 100 persons older than 12 years of age (Volavka, 1999). Violence and aggression are public health concerns due to injuries and associated psychological health problems.

Aggression can be assessed on a continuum and as a possible antecedent for violence. Violence is physical aggression at its extreme (Anderson & Huesmann, 2003). Not all acts of aggression are violent. Many violent events are not compartmentalized, and often these acts are a cumulative result of historical aggression (Tremblay et al., 2004). All acts of violence include aggression, and this makes this behavior an attractive focus to mitigate violence (Anderson & Huesmann, 2003). Multidisciplinary approaches have been used to evaluate aggression and to develop theories about why aggression occurs. Public health officials, criminologists, and social scientists have attempted to identify the process underlying violence. Often these explanations have minimized or ignored the aggressive basis of violence (Anderson & Huesmann, 2003). Aggression and the aggression-violence continuum offer a solid basis in mitigating violence in society

and warrant further investigation (U.S. Surgeon General, 2001). Although most acts of aggression will not turn violent, violence has its basis in aggression.

There has been a paradigm shift to the prevention of disease as opposed to its treatment (U.S. Surgeon General, 2001). Prevention as an intervention in early aggression is regarded as a good model for violence prevention (U.S Surgeon General, 2001). The Center for Aggression Management (CAM, 2012) has developed a violence intervention program that focuses on the aggression continuum. The program evaluates and intervenes during the early stages of aggression. The Center for Aggression Management has developed a Critical Access Pathway program that can be used in workplaces, schools, and homes. Academic settings are considered prime locations for interpersonal aggression among children (Wilson & Lipsey, 2007). The necessity of these types of interventions underscores the importance of public health interventions that focus on aggression as a mitigating factor in violence and other antisocial behaviors.

Aggression is also a component in antisocial behaviors. The definition of *antisocial behavior* is any behavior that violates cultural standards (American Psychological Association [APA], 2015; DeWall, Anderson, & Bushman, 2011). Aggression and violence are often characteristics of antisocial behavior, yet these behaviors may be absent in some antisocial behavioral acts. Cultural norms often frame antisocial behaviors (DeWall et al., 2011). For example, some societal norms would prohibit physical violence toward a domestic partner, whereas other cultures would condone or at minimize these actions. Individuals with antisocial personality disorder may display aggression and violence and may also transgress standards of appropriate

behaviors by breaking other laws (APA, 2013; DeWall et al., 2011; Hare, 1991). Aggressive acts and violence may not imply antisocial behaviors. However, these behaviors are seen in antisocial behaviors.

There is a developmental continuum that frames the presentation of aggression. Aggressive facial expressions are seen as early as 4–7 months (Anderson & Huesmann, 2003). Aggressive behaviors are developmentally more prevalent in infant and toddler years; however, the peak of aggression emerges in early childhood and in adolescence (Dodge & Coie, 1997). There are forms of human aggression, including physical, verbal, and indirect aggression (David-Ferdon et al., 2016). Physical aggression may manifest in incidents of pushing, hitting, biting, kicking, and hair pulling. Physical aggression may also include more serious offenses of stabbing, shooting, and rape (David-Ferdon et al., 2016). Verbal aggression may include verbal threats, intimidation, and malicious taunting (Gladden, Vivolo-Kantor, Hamburger, & Lumpkin, 2014). Indirect aggression would include encouraging others to reject or tease another person (Gladden, Vivolo-Kantor, Hamburger, & Lumpkin, 2014). There is also electronic aggression, which is a relatively new phenomenon in which others are teased or malicious verbal expression is posted online (Gladden, Vivolo-Kantor, Hamburger, & Lumpkin, 2014).

There are economic implications of youth aggression. Romeo, Knapp, and Scott (2006) argued that persistent antisocial behavior during childhood and adolescence, which includes aggression, increases the likelihood of problems in adulthood. The financial burden of adolescent criminal behavior on society is estimated to be from $80,000 to $325,000 per juvenile delinquents per year (Waters, Hyder, Rajkotia, Basu, &

Butchart, 2005). Youth aggression and violence in the United States has resulted in more than $158 billion each year. An economic approach has not adequately addressed this public health epidemic despite spending 3.3% of the gross domestic product on mitigating youth violence (Waters, Hyder, Rajkotia, Basu, & Butchart, 2005). In the United States, intrapersonal violence results in $12.6 billion yearly, which is 0.1 % of the gross domestic product (WHO, 2017). Future estimates of these behaviors can increase to over $1.2 million in adults (Pepler & Ferguson, 2013; Scott, Knapp, Henderson, & Maughan, 2001). Aggression is ubiquitous in the human experience, exacting a financial toll for society and for public health.

Adolescence is a prime period for aggression and related behaviors. These occurrences present a particular public health concern. The incidence of youth aggression has been called an epidemic over the past 50 years (Bastiaens, 2006; U.S. Surgeon General, 2001). Longitudinal studies have shown that aggressive school-age adolescents are at increased risk of acting violently in adolescence and into adulthood (Tremblay et al., 2004). Physical aggression, which is thought to decrease as a person transitions from childhood to adolescence, is prevalent among teens (Tremblay et al., 2004). One in three high school students reported that they had been a physical fight in the past year, and the highest occurrence of violence happens between 15 and 35 years of age (CDC, 2016; National Center of Juvenile Justice, 2016). In addition, 40% of male teens and 32% of female teens reported that they had committed serious offenses such as aggravated assault, robbery, or rape by the age of 17 years (Office of the Surgeon General (US), National Center for Injury Prevention and Control (US), National Institute

of Mental Health (US), & Center for Mental Health Services (US), 2001). Male teens are more physically and verbally aggressive and are more likely to be violent at any age (Anderson & Huesmann, 2003). Indirect aggression, however, such as spreading rumors, occurs more often among females. It is clear that aggression has social, environmental, and molecular underpinnings (Anderson & Huesmann, 2003).The social causes of aggression and violence have been well studied. However, the relationship between genetics and aggression warrants further study.

Although research demonstrated that aggression can be influenced by social and environmental factors, limited attention has been given to the genetic influences in human aggression. Genetic polymorphisms have been shown to increase the risk of aggressive behaviors in animals and humans. Specific alleles of the u-VNTR of the monoamine oxidase A (*MAOA*) gene have been shown to impact affective behaviors (Taylor, 2012; McDermott et al., 2009). The low-expressing alleles of the u-VNTR of the *MAOA* gene have been associated with stabbing behaviors (Guo et al., 2008), gang membership (Beaver et al., 2010), shooting and stabbing behavior (Beaver et al., 2013) and aggression (Frazzetto et al., 2007; Kinnally et al., 2009; Sjorberg et al., 2007; Weder et al., 2009). This link has been well established in the literature; however, many of these studies have focused on the behavioral outcomes among males (Beaver et al., 2010; Capsi, McClay, Moffitt, & Craig, 2002; Kim-Cohen et al., n.d.; Saito et al., 2002). Researchers have investigated polymorphism in females in relationship to some psychiatric disorders, including obsessive-compulsive disorder (Camarena, Cruz, De la Fuente, & Nicolini, 2001), trait impulsivity and aggression (Kinnally et al., 2009), panic

disorder (Deckert et al., 1999), conduct disorder (Prom-Wormley et al., 2009), and depression and antisocial personality disorder (Ducci et al., 2008). However, there has been limited research on the association between the u-VNTR polymorphism of the *MAOA* gene and aggression among adolescents.

The *MAOA* gene has an affinity for the neurotransmitter serotonin and dopamine (Shih &Thompson, 1999). *MAOA* is a candidate locus for a functional genetic polymorphism located in the promotion region of the gene. The promoter region is located upstream from the area of translation and directs rRNA translation. There is a u-VNTR polymorphism located on this gene that has been shown to influence the transcription of the gene and results in high or low activity phenotypes (Kinnally et al., 2009; Haberstick et al., 2014). Because the MAOA protein is an enzyme responsible for the degradation of amine neurotransmitters, low-activity alleles produce a low functioning oxidase enzyme and result in greater levels of these transmitters in the central nervous system (D'souza, & Craig, 2005). Greater levels of serotonin and dopamine have been implicated in greater levels of aggression in animals and humans (D'souza, & Craig, 2005). The u-VNTR genetic polymorphism of the *MAOA* gene has been implicated in many behavioral outcomes including taking long-shot risks (Zhong, Israel, Xue, Ebstein, & Chew, 2009), alcoholism and impulsive behaviors (Saito et al., 2002), suicide (Hung et al., 2012), and schizophrenia (Jonsson et al., 2003). This u-VNTR polymorphism has also been studied for its influence on other aspects of behaviors such as suicidal depression (Lung, Tzeng, Huang, & Lee, 2011) and in behavior inhibition in

children (Enoch, Steer, Newman, Gibson, & Goldman, 2010). There is supporting evidence of this association in the literature.

In most developed countries, there is a small subset of persons who commit most violent and aggressive-related behaviors (Tiihonen et al., 2014). The adolescent period is a time of high-risk behavior, and over 15% of high school students report carrying a weapon over the last month and 25,000 cases of aggravated assaukt (Kann et al., 2018; CDC, 2016; National Center of Juvenile Justice, 2016). In addition, 32% of adolescent females reported committing a serious offense such as aggravated assault (U.S. Department of Health and Human Services, 2001). The present study addressed the gap in the literature regarding the relationship between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression, gender, and race in a nationally representative sample of adolescents ages 13–18 years. This study was needed to understand why there is a high incidence of aggression among adolescents who carry the low-expressing form of the u-VNTR genetic polymorphism of the *MAOA* gene. The study was important because adolescents have a disproportionate involvement as perpetrators and victims of aggression and aggressive-related behaviors. Researchers have explored the link between this genetic polymorphism and aggression (Beaver et al., 2014; Guo et al., 2008; Plomin, DeFries, Knopik, & Neiderhiser, 2013); however, there has not been a focus on female carriers of this polymorphism. The current study addressed this relationship among females and races. At the time of this study, there had been no other studies that addressed the relationship between this genetic polymorphism and aggression in adolescents ages 13–18 years in a nationally representative sample. Findings may inform

public health interventions regarding possible genetic propensities and aggression among adolescents.

Problem Statement

Aggression is a public health concern. This behavior serves as a component in violence and antisocial behaviors. Aggression is observed in animals and humans. Some aggression serves as an evolutionary advantage in animals. However, there is support for focusing on aggression as an important societal problem. Both genders experience aggression. Males are generally the more aggressive gender. However, literature indicated that aggression may manifest differently, not so much less, in females (Prom-Wormely, 2007). Researching the association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression in adolescents may reveal important insights through the lens of gender and ethnicity.

The relationship between the low and high-expressing genotypes of the genetic polymorphism of the u-VNTR of the *MAOA* gene and aggression and antisocial behaviors has been investigated with mixed results. Many studies had males as the focus with females being excluded because of the issue with heterogeneity of the u-VNTR genetic polymorphism (Nilsson et al., 2018). These studies have not addressed the low and high-expressing genetic polymorphism of the *MAOA* gene through the lens of gender and race.

Abuse in the presence of the low-activity alleles of the u-VNTR genetic polymorphism of the *MAOA* gene has been considered an essential factor in adverse behavioral outcomes such as violence and antisocial personality disorder (Taylor, 2012;

McDermott et al., 2009). However, studies have also indicated that this genetic polymorphism can directly impact behaviors in the absence of reported abuse (Reti et al., 2011). I sought to examine the modifying presence of abuse in the relationship between the genetic polymorphism and aggression.

Purpose of the Study

The purpose of this quantitative correlational study was to investigate the relationship between u-VNTR genetic polymorphism of the *MAOA* gene and aggression, gender, and race in adolescents. Most studies on the u-VNTR polymorphism of the *MAOA* gene and aggression have focused on males. Investigating this polymorphism from a wider scope using the variables of gender, age, and race may increase the depth of knowledge and inform interventions with implications for personalized health treatments. Data were collected from the National Longitudinal Adolescent and Adult Study (Add Health). This is a nationally representative longitudinal study that began in 1994–1995 and continues to the present (Harris & Udry, 2009). The current study contributed to the body of knowledge related to the u-VNTR genetic polymorphism of the *MAOA* gene and self-reported aggression in this age group. The results may provide the basis for further research on how genetic testing can inform treatment for aggression among adolescents and into adulthood.

This study involved secondary analysis of data from the Add Health study of a nationally representative sample of adolescents in Grades 7–12 that started during the 1994–1995 school year. There are four completed waves (Waves I-IV) of the Add Health Study with one wave (Wave 5) currently in progress. The initial study included a cohort

of adolescents 13–18 years of age obtained from schools in the United States. This cohort from Wave I was followed over several years and is still being studied to date. A major advantage of the study is that biometric (weight, blood pressure, BMI, metabolic screenings) and genetic samples were collected from the participants (Harris & Udry, 2009). The Add Health study was a robust investigation of adolescents beginning from ages 13–18 into young adulthood.

The goal of this current study was to examine the association between the u-VNTR polymorphism of the *MAOA* gene and aggression, gender, and race. The independent variables in this study were *MAOA* u-VNTR polymorphism, gender, and race. The dependent variable was aggression. Previous abuse was considered as a potential confounding variable. The statistical analysis for this study included independent sample *t* tests and linear regression analysis to answer the research questions. Descriptive statistics were also assessed.

The participants in the Add Health study were asked questions related to aggressive behaviors during the first wave. Genetic sampling was obtained through informed consent from sibling and twin pairs (Harris & Udry, 2009). This research included individuals who submitted to the genetic testing and answered all survey questions related to aggression and aggressive-related behaviors. All participants in the sample ($N = 2,747$) were in the seventh to 12th grade (13–18 years) and had submitted genetic samples. Cases included individuals who possess the low-expressing or high-expressing *MAOA* u-VNTR polymorphism. The high-expressing genetic polymorphism group was considered the control group because of the high efficiency transcription of the

monoamine oxidase A enzyme. Excluded from the sample were those who did not answer questions related to aggression or did not have genetic testing for this allele. An existing tool by Cleveland (2003) was used to assess aggression in the Add Health study. Additional information about questions used from the Add Health study can be found in Chapter 3.

Research Questions and Hypotheses

The research questions and associated hypotheses that were addressed in this study were the following:

Research Question 1: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years?

H_o1: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years.

H_a1: There is an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years.

Research Question 2: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene and gender (predictor variables) and aggression (outcome variable), while controlling for abuse, in an adolescent population aged 13–18 years?

H_o2: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene and gender (predictor variables) and aggression (outcome variable), while controlling for abuse, in an adolescent population aged 13–18 years.

H_a2: There is an association between the u-VNTR genetic polymorphism of *MAOA* gene and gender (predictor variables) and aggression (outcome variable), while controlling for abuse, in an adolescent population aged 13–18 years.

Research Question 3: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene and race (African American, Asian, White; predictor variables) and aggression (outcome variable), while controlling for abuse, in an adolescent population aged 13–18 years?

H_o3: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene and race (African American, Asian, White; predictor variables) and aggression (outcome variable), while controlling for abuse, in an adolescent population aged 13–18 years.

H_a3: There is an association between the u-VNTR genetic polymorphism of the *MAOA* gene and race (African American, Asian, White; predictor variables) and aggression (outcome variable), while controlling for abuse, in an adolescent population aged 13–18 years.

Research Question 4: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, and race (African American, Asian, White; predictor variables) and aggression (outcome variable), while controlling for abuse (confounding variable), in an adolescent population aged 13–18 years?

H_o4: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, and race (African American, Asian, White; predictor variables) and

aggression (outcome variable), while controlling for abuse (confounding variable), in an adolescent population aged 13–18 years.

H_a4: There is an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, and race (African American, Asian, White; predictor variables) and aggression (outcome variable), while controlling for abuse (confounding variable), in an adolescent population aged 13–18 years.

Conceptual Framework

The conceptual framework for this study was based on the biosocial model of antisocial behavior. This framework illuminates the relationship between genes on aggressive behaviors. In this framework, genes can influence aggressive behaviors with or without environmental influences (Baker, Raine, & Jacobson, 2008). The biosocial model of antisocial behavioral also depicts the complex interchange of genetics, biological factors, and social factors on aggressive and antisocial behaviors (Baker et al., 2008). The *MAOA* u-VNTR genetic polymorphisms have allelic variations that are subtyped into two categories: low- and high-expressing genotypes. Depending on the allelic variant, the monoamine oxidase A enzymatic activity is impacted and will produce a low activity or high activity. This genetic polymorphism has been shown to affect behavior in the low-expressing variation. The model is an appropriate depiction of the variables in this study including aggression and its subtypes (proactive and reactive). In addition, the biosocial model of antisocial behaviors explains how genetic factors can have a direct impact on antisocial behaviors with or without social risks (Baker, Bezdjian,

& Raine, 2006). Further explanation of the factors and the interactions is provided in Chapter 2.

Nature of the Study

The research questions were addressed using a quantitative design. The goal of quantitative studies is to evaluate the relationship between independent and dependent variables. Quantitative research is considered more reliable and objective, and can incorporate a limited number of variables that can restructure and simplify a scientific problem (University of Southern California, 2016). The relationship between the variables can be investigated and a correlation between variables can be established in tightly controlled study designs. Subjectivity is decreased in quantitative study designs (USC, 2016).

I analyzed secondary data from the National Longitudinal Study of Adolescents and Adults (Add Health). This study began in 1994–1995 and is being continued in the present. There are five waves included in this study. Data from Wave 1 and Wave III were used in this study. The statistical approach included descriptive and inferential statistics that were calculated using the SPSS (Version 22.0) statistical package. This approach included a preliminary screening of the variables to determine validity. An independent samples *t* test was used to test Hypothesis 1. Linear regression was used to test Hypotheses 2, 3 and 4.

Definitions

Aggression: Behavior that is directed toward another individual that is carried out with the immediate intent to cause harm. Actual harm is not necessary (Anderson & Huesmann, 2003; Geen, 2001).

Alleles: One or more alternative versions of a gene at a genetic locus on a chromosome (Pagan et al., 2006).

Base pairs (bp): Two complementary nitrogenous molecules found on the DNA. The bonds between the base pairs are fragile. The pairing of the bases includes adenine with thymine and guanine with cytosine. The base pairings result in accurate DNA replication. The quantification of the base pairs (30 bp) will indicate the physical sequential lengths of nucleotides (U.S. Department of Energy, 2015;Tatton-Brown, 2018).

Concordant pairs: The occurrence of the same genetic traits usually discussed in twin studies where monozygotic twins share 100% of their DNA. Dizygotic twins and siblings share 50% of their DNA (Miller, 2006).

Genetic polymorphism: A natural variation in a gene or chromosome that is proposed to have no adverse effects. These polymorphisms occur frequently in the general population. A genetic polymorphism may have two or more variants at a single base pair (Pagon et al., 2015).

Proactive aggression: Also referred to as instrumental aggression, a planned, calculated behavior with the presence or absence of provocation. This type of aggression

has also been termed predatory or cold-blooded aggression (Card & Little, 2006; Conner, Duberstein, Conwell, & Caine, 2003).

Promoter region: The location on the gene that is upstream and serves as a binding site for transcription. The promoter sequence of DNA is needed to switch a gene on or off. The promoter region has a binding site for an enzyme to make a messenger RNA (National human genome Research Institute (NHGRI), 2017).

Reactive aggression: A retaliatory response that is impulsive behavior to a real or a perceived threat (Renouf et al., 2010; Tuvblad, Raine, Zheng, & Baker, 2009).

Variable number tandem repeat (VNTR): Linear arrangements of several copies of the short-repeated DNA sequences. These repeats vary and are polymorphic. Also, the tandem repeats originated from single genetic locus and the DNA segments repeat and are individualized (Pagon et al., 2015).

Assumptions

I assumed that the sample in the Add Health study was randomized. I also assumed that the sample was representative of adolescents in the U.S. population. The Add Health study's sampling was collected in waves (Harris et al., 2008). The sample included adolescents aged 13–18 years. The assessment of aggression was assumed to be reliable; the aggression tool was assumed to measure aggression and not violence, delinquency, or antisocial behaviors. I also assumed that the genetic testing was appropriate for presence of the u-VNTR genetic polymorphism of the *MAOA* gene.

Scope and Delimitations

The scope of this study was the potential associations between the u-VNTR of the *MAOA* gene and aggression, gender, and race. The study was delimited to participants who possessed the u-VNTR polymorphism of the *MAOA* gene and those who had numerical scores for self-reported aggression. *Aggression* was defined as behaviors that are directed toward others with the intent of causing harm. I did not seek to establish a biological or genetic conceptual framework for the potential associations of the u-VNTR genetic polymorphism of the *MAOA* gene and self-reported aggression, gender, and race. A comparison of specific alleles and their association with aggression was not conducted. Causation was not to be established. Other behavioral outcomes were not studied. The research data and results were only applicable to this study's population. The results cannot be extrapolated to the entire population.

Limitations

This study was a secondary analysis of data from the National Longitudinal Health of Adolescents and Adults study. Secondary data provides information that may be prohibitive in smaller research projects (Boslaugh,2007). Secondary data has often been informed by experts in the field of knowledge and can provide a reliable source of data (Boslaugh, 2007). There are disadvantages to using secondary data such as the lack of control over the selection of the sample. In addition, it is not possible to control the collection methods and the quality of the data when using secondary data from other studies (Boslaugh, 2007; Sorensen, Sabroe, & Olsen, 1996). A survey from a study by

Cleveland (2003) was used to measure aggression. Although this survey tool had been validated, the reliability of the items may be a limitation.

Aggression is a complex construct that overlaps in behavioral presentations of other disorders, which may obscure identification of aggressive behaviors. Aggression is also a component of many other psychiatric disorders, such as attention deficit disorders, and behaviors as serious as rape and murder (Anderson & Huesmann, 2003). Defining the construct of aggression is a limitation and differenting aggression from violence and other antisocial behaviors is a challenge. This limitation is also present in the database used in this study. Aggression can be a component in violence, delinquency, and other antisocial behaviors and may not have been classified accurately during the study.

Another limitation of this study was the use of self-reports to answer survey questions about aggression. However, there is strong evidence that self-reports are a reliable measure of criminal behaviors (Krohn, Thornberry, Gibson, & Baldwin, 2010 ; Fiscella & Fremont, 2006) and that self-reports uncover "middle class crimes or those behaviors that have not resulted in legal charges or reported harm" (Schwendinger & Schwendinger, 2014). There is the risk that the participants may not be truthful in their answers. The fear of punishment for their behavior may have skewed their responses (Lavrakas, 2017). The Add Health study included computerized questions for these responses to lower the response bias. However, the implementation of a confidential setup does not eliminate possible bias.

Significance

I sought to contribute to the body of knowledge pertaining to the association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression, gender, and ethnicity. Findings may lead to further studies to develop a conceptual framework for future research. This project addressed the gap in the literature related to the association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression, gender, and race. Findings may be used to increase awareness regarding youth aggression and how genetic information can inform public health interventions in mitigating violence. Findings may increase the public's understanding of how genes play an important role in behavior.

Summary

Genetic polymorphisms, such as the u-VNTR polymorphism of the *MAOA* gene, have been investigated for their influence on aggression, violence, and other affective disorders. The u-VNTR polymorphism of the *MAOA* gene has been associated with aggression (Beaver et al., 2014; Guo et al., 2008; Plomin, DeFries, Knopik, & Neiderhiser, 2013). This genetic polymorphism is present in males and female and in certain races more than others. The etiology of the genetic influence on behavior is largely unknown. Analysis of the Add Health study data was performed to contribute to the existing body of knowledge on this topic. Chapter 2 presents a review of the literature on the u-VNTR polymorphism of the *MAOA* gene studies, aggression, and related topics through the lens of gender and race.

Chapter 2: Literature Review

Overview

The purpose of this quantitative study was to examine the association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression in an adolescent population 13–18 years of age. Genetic studies of criminal and seriously delinquent behaviors in a nonclinical setting are sparse (Guo et al., 2008). This is especially true as it pertains to the female population. A few studies suggested a plausible interaction between a specific allele (2-repeat) u-VNTR genetic polymorphism of the *MAOA* gene and an increased participation in serious and violent crimes among adolescent females (Beaver, 2008; Guo et al., 2008). However, there is limited research on the association between this polymorphism and aggression among adolescents aged 13 to 18 years. The goal of this study was to address this gap in the literature regarding the u-VNTR genetic polymorphism of the *MAOA* gene, aggression, gender, and ethnicity in an adolescent population.

The upstream variable number tandem repeat (u-VNTR) polymorphism of the monoamine oxidase A (*MAOA*) gene has been associated with several behavioral outcomes including taking long-shot risks (Zhong et al., 2009), alcoholism and impulsive behaviors (Saito et al., 2002), and schizophrenia (Jonsson et al., 2003). The u-VNTR polymorphism has also been studied for its influence on other aspects of behaviors such as suicidal depression (Lung et al., 2011) and behavior inhibition in children (Enoch et al., 2010). This genetic polymorphism continues to serve as a promising focus because of its influence on behavior and psychiatric disorders. The u-VNTR

polymorphism is of particular scientific interest because of its impact on human and animal aggression and violence (Shih &Thompson, 1999). Studies have supported this implication; however, many of these studies have focused on the behavioral outcomes among males (Beaver et al., 2013; Saito et al., 2002). Researchers have investigated this polymorphism in females in relationship to important psychiatric disorders including obsessive-compulsive disorder (Camarena et al., 2001), trait impulsivity and aggression (Kinnally et al., 2009), panic disorder (Deckert et al., 1999), conduct disorder (Prom-Wormley et al., 2009), depression, and antisocial personality disorder (Ducci et al., 2008). Although some researchers have proposed a link between the u-VNTR polymorphism and aggression and criminality, few studies have addressed this association among females.

This chapter includes a review of the research literature about the epidemiology of aggression, its construct, and its subtypes (proactive and reactive). The u-VNTR polymorphism's role and implication in behavioral outcomes are addressed. Connections between aggressive behaviors and this genetic polymorphism are explored in terms of gender, age, and ethnicity. This chapter presents relevant research that has been conducted using the National Longitudinal Adolescent and Adult Health Study (Add Health) and its database.

Literature Search Strategy

Literature was researched using the following terms: *National longitudinal adolescent health survey*, *Add Health*, *aggression*, *antisocial personality*, *antisocial behaviors*, *conduct disorder*, *post-traumatic stress syndrome*, *ethnicity*, *age*, and *gender*.

Articles were reviewed based on the relevance to the research hypotheses and research questions. The literature review was conducted using Academic Complete, ProQuest, Science Direct, and pertinent research journals. Only English-language articles were reviewed. This chapter conclude with a synopsis of the sections and an introduction to Chapter 3.

Aggression Research

Historically, aggression has served ambiguous purposes. On one hand, it has ensured a competitive edge for resources (food, protection). Conversely, it has been an impediment to social harmony (Craig & Halton, 2009). High aggression among animals is used to secure reproductive opportunities and ensure the protection of offspring from outside threats. Such behavior is prevalent among females in the animal kingdom (Craig & Halton, 2009). Aspects of human aggression may have served as an advantageous evolutionary characteristic.

Human developmental aggression research indicated that physical aggressive behavior escalates from 2 to 4 years of age (Provencal et al., 2013; Tremblay et al., 2004). Aggression is most prevalent during the toddler years and during mid-adolescence (Craig & Halton, 2009). For most children, this behavior emerges and then subsides at school entry and into adulthood (Broidy et al., 2003). However, a small cohort of 4–7% of the total population deviates from this trend and maintains a high level of aggression while at high risk for subsequent delinquency (Broidy et al., 2003; Farrington, 2005) and conduct disorders (Loeber & Dishion, 1983). Those with higher levels of aggression during early childhood can become aggressive adults (Tremblay et al., 2004). Those with

sustained high aggression tend to show impulsivity, hyperactivity, and oppositional defiance disorder (Provencal et al., 2013). In addition, this population is at risk for academic difficulties and social maladjustment in adulthood (Nagin & Tremblay, 1999). These patterns of impulsivity and aggression are one of the strongest predictors of adolescent delinquency (Farrington, 2005; Pakiz, Reinherz & Giaconia, 1997). Many aggressive children and adolescents do not progress into violent or criminal adults. Adolescents whose aggressive behaviors remain consistent or progress tend to display antisocial behaviors as a common trait (Vanderstaay, 2006). These adolescents are at risk for aggressive disorders, criminality, family violence, and delinquency (Cummings, Iannotti & Zahn-Waxler, 1989; Farrington, 2005; Loeber & Dishion, 1983; Vanderstaay, 2006). Aggression, as a behavioral trait, may serve as an important focus in deterring the development of aggressive adult behavior.

Pathological aggression and violence have public health implications, yet the etiology and prognosis are understudied (Vitaro et al., 2006). The impact of aggressive behaviors is prevalent in forensic and school settings, yet the etiology and treatment of pathological aggression are poorly understood (Siever, 2008). Aggression is also regarded as a major factor among the modern world's problems (Anderson & Bushman, 2002). Aggression-driven behaviors and crimes have been regarded as so serious that the International Criminal Court has brought these acts under their jurisdiction (Whiting, 2019). There are multifactorial causes of human aggression that include medical reasons to sectarian violence (Dyer, Dorathy, Phill, & Shannon, 2013). The complexity of

aggression is well documented; however, data regarding aggressive behaviors and their neurobiological basis are continuing to emerge.

Researchers have focused on neurobiological and genetic aspects of aggression. The impact of genetics on aggression is an area that researchers are just beginning to research in depth (Siever, 2008). Aggression research is often associated with concurrent aberrant behaviors such as emotional dysregulation, peer rejection, and depression. The effects of aggression are enduring and are manifested in academic failure, adolescent delinquency, antisocial behaviors, and criminality (Card & Little, 2006; Coie, Dodge &, Lynam, 2006; Farrington, 2005). Aggressive behavior has been found to be a foundational factor in psychiatric illnesses including adult antisocial personality disorder, borderline personality disorder, and conduct disorder (Siever, 2008). Other diagnoses that include aggression as a prominent component are antisocial behaviors, delinquency, bipolar disorder, conduct disorder, and post-traumatic stress syndrome.

Epidemiology of Aggression

Aggression and its related disorders are of epidemiological consequence. The lifetime prevalence of adult antisocial behavior is estimated to be as high as 12.3% (Buckholtz & Meyer-Linderberg, 2008). Each antisocial person exacts a financial cost of up to 10 times more than their healthy cohorts in health care and social service expenditures (Buckholtz & Meyer-Linderberg, 2008). There is a hefty financial burden of anti-sociality on public health and on society in general. Targeting the possible etiologies of these behaviors may serve as the foundation for policy-based governmental interventions (Buckholtz & Meyer-Linderberg, 2008). The WHO (2009) reported a 1-

year worldwide estimate of 1.44 million deaths due to self-inflicted or interpersonal violence. Reactive aggression is the impetus of these unplanned episodes of violence (Siever, 2008). Episodic or intermittent impulsive aggression is considered a major characteristic in psychiatric diagnoses such as intermittent explosive disorder per the diagnostic statistical manual IV (Kessler et al., 2006). The lifetime population prevalence of this reactive or impulsive aggressive based diagnosis is 7.3% (Siever, 2008). This is consistent with a reported lifetime prevalence estimate of adult antisocial behavior of 12.2% (Buckholtz & Meyer-Lindenberg, 2008). Aggression is a major component of behaviors that are a public health concern.

One fourth of all men and one half of women report acts of physical aggression against themselves after the age of 18 years (Siever, 2008). Physical and verbal aggression are sometimes linked to personality disorders including antisocial personality disorder (Siever, 2008). The consequences of these disorders can be deleterious. Spousal abuse, job loss, criminal assault, rape, and murder are possible results of those with these aggressive disorders. Aggression is also a major component of other psychiatric disorders such as delinquency, criminality, and conduct disorder (Siever, 2008). Studies have shown that 47% of men and 21% of women who are violent offenders have been diagnosed with antisocial personality disorder (Siever, 2008). These findings indicated that aggression is a public health concern worthy of further investigation.

Aggression Construct

Aggression is a heterogeneous concept. Plomin et al. perationalized antisocial behaviors in three respects (1985). First, antisocial behavior was investigated as a

psychiatric disorder, such as conduct disorder or antisocial personality disorder. Second, antisocial behavior has been examined in terms of violation of social or legal involvement. Third, antisocial behavior has been investigated in terms of aggressive behavior (Plomin et al., 1985).

The classifications of aggression need to be considered in the development of its construct. Aggression can be subtyped using several categories based on the target of the aggression (self-directed or others centered); mode of the aggression (verbal or physical aggression; direct or indirect); or the cause of the aggression such as medical reasons (Siever, 2008). All aggression is not equally maladaptive, and some people may consider certain aggressive attributes as positive (Card & Little, 2006). Although aggression can produce competitive advantages, excess or persistent aggression can be pathological (Nelson & Trainor, 2007). The literature indicated two primary categories in conceptualizing aggression: proactive (premeditated) and reactive (impulsive) aggression (Craig & Halton, 2009; Fite, Rathert, & Stoppelbein, 2012; Siever, 2008). Reactive aggression has been associated with anger. The proactive subtype, or instrumental aggression, is considered to be goal oriented and more purposeful (Nelson & Trainor, 2007). These two types of aggression are often differentiated by the lack (proactive) or excess (reactive) of emotional sensitivity (Craig & Halton, 2009; Wrangham, 2017). Similarly, Fite et al. (2012) supported this categorization and postulated that proactive aggression has premeditated features while reactive aggression is impulsive and often spontaneous.

Historically, the functionality of aggression has been distinguished according to the motives of the actions (Card & Little, 2006; Dodge & Coie, 1987; Chung-Hall & Chen, 2009; Lorenz, 1966). The target of the aggression and the motivation of the behaviors determine categorizing aggression into two subtypes of impulsive and premeditated aggression. There are contrary arguments in the literature against this distinction. Anderson & Bushman (2002) argue that reactive and proactive aggression co-exist, are experienced simultaneously, and that the motives of aggression are mixed when aggression is experienced (Anderson & Bushman, 2002; Baker et al., 2008). An enduring debate regarding the validity of these sub-types still exists.

As with many behavioral phenotypes, aggression's construct has been difficult to define uniformly. This is due to the heterogeneity of aggression and to the instruments that have been used to assess aggression. Aggression subtypes have been delineated in the research with no consensus to date. Some distinctions of aggression in the literature include reactive and proactive aggression, overt and covert aggression, and other forms. Reactive aggression has been customarily defined as affective aggression, and the behavior is usually in response to a stimulus. Proactive aggression is pre-meditative and goal directed (Poulin & Boivin, 2000). There have been attempts to discriminate between the subtypes using factor analysis of aggressive behaviors and by identifying predictors and outcomes. Bjorkqvist et al. (1992) postulated that aggression emerges in early childhood with a more physical manifestation, and this usually changes to more indirect aggression in late childhood to adolescence.

Proactive Aggression

Proactive aggression has also been termed predatory, instrumental, and "cold-blooded" aggression (Card & Little, 2006; Conner et al., 2003). Proactive aggression is not ordinarily accompanied by autonomic arousal and is a strategized behavior towards a specific goal (Card & Little, 2006; Craig & Halton, 2009). In war arenas, premeditated aggression can be socially sanctioned and can serve as a strategic advantage in planning aggression. Proactive aggression is goal oriented, calculated, and can be a learned behavior per social learning theory (Fite et al., 2012). This type of aggression is often associated with psychopathy where the person lacks empathy and remorse (Craig & Halton, 2009). Mass killings and assassinations may be more related to this planned-type aggression (Nelson & Trainor, 2007). Focusing on how to mitigate these actions can strengthen public health interventions related to violence.

Proactive aggression is rooted in Bandura's theory of social-cognitive learning, which suggests that human aggression occurs because favorable outcomes are expected in response to the aggressive behavior (Bandura, 1973, 1996; Card & Little, 2006; Tuvblad et al., 2009). The catalyst for proactive aggression is that the expected success of the behavior outweighs the possible punishment (Tuvblad et al., 2009). Predatory aggression is usually not in response to frustration or in response to a perceived threat (Siever, 2008; Fite et al., 2012). Proactive aggression is not reactionary.

Reactive Aggression

Reactive aggression is defined as a retaliatory response to a real or perceived threat or provocation (Renouf et al., 2010; Tuvblad et al., 2009). This type of aggression

is accompanied by high activity, autonomic arousal and is precipitated by a provocation source that is associated with negative emotions of anger or fear (Siever, 2008; Tuvblad et al., 2009). Reactive aggression may be conceptualized as possessing a lower threshold for the activation of motoric aggressive responses to an external stimulus without explicit, appropriate consideration of the consequences. In this type of aggression, there is little aversion to the possible results of the behavior (Siever, 2008). Of the subtypes, reactive aggression has been associated with negative emotions in a plethora of studies (Card & Little, 2006; Conner et al., 2003; Fite et al., 2009, 2010; Raine et al., 2006). Reactive aggression is a response to a perceived stressor and not necessarily a real experience.

Impulsive aggression, affective aggression, and hostile aggression are other terms used for reactive aggression. This expression of aggressive behaviors becomes pathological when aggressive responses are exaggerated in response to the provocation. This impulsive type of aggression has an affective nature and has been associated with less happiness (Day et al., 1992), depressive symptoms, peer rejection, and social isolation among all ages (Day et al., 1992; Dodge & Cole, 1987; Gilman, Kawachi, Fitzmaurice, & Buka, 2003; Morrow, Hubbard, McAuliffe, Rubin, & Dearing, 2006; Pinstien & Cilessen, 2003; Fite et al., 2012). The line between normal reactive aggression, such as when a threat is imminent, and pathological aggression can often be blurred. The perpetrator may rationalize their acts of pathological aggression or violence as appropriate due to their perception of the threat.

Aggression and Age

There are commonalities in the presentation of aggression in adults and adolescents. The purpose of aggressive behavior is a function of the motivation of the person in both adults and children (Tuvblad et al., 2009). In these two populations, aggression is influenced by the executive function of the brain. Adolescence represents a period when youth are at increased risk for aggressive behavior (Bettencourt & Farrell, 2013). In a nationally representative sample, 21% of students in grades 6–10 were involved in some physical victimization and 54% participated in verbal aggression as either the perpetrator or the victim over their most recent two months (Wang et al., 2009).

Executive dysfunction has been found in those who engage in aggressive behaviors. This increases the risk of engaging in "thrill seeking" activities and criminal behaviors (Holler & Kavanaugh, 2012). Aggressive behaviors and criminality are heterogeneous in nature and have been associated with the externalizing behavior of physical aggression for adults in colleges, prison, and psychiatric inpatient settings (Villemarettepittman, Stanford, & Greve, 2003)

In adolescents, the prefrontal lobe development significantly affects behavioral control. As in adults, executive dysfunction in adolescent males has been closely associated with physical aggression (Holler & Kavanaugh, 2012). However, there have not been consistent findings addressing the association between physical aggression and executive functioning among adolescents as is seen in adults because adolescence can be a time of increased aggression compared to adults (Holler & Kavanaugh, 2012).

As mentioned above, Bjorkqvist et al. (1992) suggested that aggression emerges in early childhood with an increase in physical aggression and that it changes to more indirect aggression in late childhood into adolescence. Also, there tend to be more negative outcomes related to early childhood physical aggression (i.e., peer rejection) (Dodge, 1983) and latent delinquency and externalizing behaviors (Coie & Dodge, 1998). Common to both adults and adolescents, aggressive subtypes have been posited to include impulsive and non-impulsive (Berkowitz, 1974; Linnoila et al., 1983). Impulsive (reactive) aggression has been associated more closely with anger and guilt and remorseful feelings as compared to non-impulsive (proactive) aggression (Vitaro et al., 2006). The dichotomous categories of proactive and reactive aggression are supported in the literature.

Aggression and Gender

Stemming from criminal justice research, many studies have investigated violence prediction models with high-risk males as a sample. Results have led to predictive models and intervention programs tailored toward male offenders (Otto & Douglas, 2010). This has led to the question of whether these interventions can be generalized to a female sample (Logan & Blackburn, 2009). Aggressive-related behaviors and violence committed by females in the public health sector have been poorly understood due to the lack of research into these behaviors among women. Research in this area has also been complicated by the general consideration of females as victims rather than perpetrators of violence (Garcia-Moreno et al., 2006). A literature search using the keywords “female violence” or “women violence” or “woman perpetrators” from 1990–2011 resulted in

sixteen papers and only four of those studies examined women in the community sector rather than in incarceration situations (Yang et al., 2013). This dearth of research on violence among females provides the impetus for this study.

Gender differences in aggression stem from different etiologies based on evolutionary strategies resulting in different behavioral presentations. Several studies have established that males tend to be the more aggressive gender. Males are overwhelmingly involved in aggressive-based crimes in the United States (Craig & Halton, 2009). They are ten times more likely than females to be under correctional supervision and are ten times more likely to commit homicide (Craig & Halton, 2009). A longitudinal study was conducted from a population sample of 1,000 individuals in New Zealand (Moffitt et al., 2001). Over an observation period of 18 years, males were 2.4 times more likely to display antisocial behaviors (Moffitt et al., 2009). Similar findings are congruent with this increased risk, regardless of age (Craig & Halton, 2009).

Campbell et al. (2010) conducted a study that examined the trajectory of physical aggression in both girls and boys. The authors based their study on the findings that proactive aggression results in several adverse behavioral outcomes in adolescence, including adolescent delinquency (Broidy et al., 2003). Adverse behavioral outcomes in adolescence also was a secondary analysis of a National Institute of Child Health and Human Development study of early child care and youth development exploring trajectories of physical aggression as rated by teachers for both girls and boys (Campbell et al., 2010). Part of the motivation for this study is to respond to the lack of attention to aggression trajectories for girls. Campbell et al., (2010) assessed several trajectory

outcomes for a sample of adolescents, including physical aggression and poor school adjustment during the adolescence period. The authors began the study by recruiting children shortly after birth at 10 hospitals in the United States. The mothers were then enrolled in the study and received a home visit when the child was one month old.

Campbell et al. (2010) assessed children from first to sixth grade for physical aggression (N = 1,084). At early adolescence (sixth grade), the sample was assessed for externalizing problems, social skills, mother-child conflict, teacher reports, and child reports of risk behavior (Campbell et al., 2010). Boys who were included in the high stable aggression trajectory group had more externalizing behaviors, conflict in relationships, less social skills, poorer work habits, and more self-reported high-risk behaviors than those in the moderate-decreasing trajectory group (with a difference (Cohen's d) = .35). Similar results were found among the girls in the sample, with the high stable aggression trajectory group members reporting increased high-risk behaviors, relationship conflicts, and poorer work habits compared to girls in the no aggression trajectory group (Campbell et al., 2010). The overall conclusion is that high persistent physical aggression in early childhood results in increased high-risk behaviors in both males and females.

Gender differences in aggression were the focus of a study by Euler et al. (2017). The heterogeneous nature of aggression was considered (proactive and reactive) as a sample of 177 adolescents (Mean (M) = 15.6 years) with mixed genders (33% female) from juvenile institutions were compared to non-institutionalized adolescents (N = 77; 36% female) (Euler et al., 2017). Bivariate correlation examined the covariates of

affective and cognitive empathy and proactive and reactive aggression. Reactive, proactive, and total aggression scores did not differ between the genders. Independent sample *t* tests revealed that girls had significantly lower scores for proactive aggression ($t_{(239)} = 3.27$, $p < .01$), however, there were no significant differences in reactive aggression (females $M = 11.9$, Standard Deviation (SD) = 2.37, males $M = 11.2$, $SD = 2.72$). The total aggression scores were also similar between the genders (females $M = 14.9$, $SD = 3.48$, males $M = 14.6$, $SD = 2.10$) (Euler et al., 2010).

Aggression and Genetics

Aggression has a strong genetic foundation that supports genomic influence. One striking feature of aggression is its dense familial concentration. In any given community, it is estimated that 10% of the families are responsible for greater than 50% of the crimes (Buckholtz, 2008). Given such high concentrations among families, genetic underpinnings must be considered (Craig & Halton, 2009). There has been confirmation of the dense presence of antisocial aggression among families through twins and adoption studies, particularly around psychiatric disorders. Strong evidence exists that psychiatric disorders, including aggression and violence, run in families. Studies have estimated 40–50% of the cases of psychiatric disorders have a familial genetic transmission (Brem et al., 2014; Blazei et al., 2006).

There is a plausible link between aggression and genetics, demonstrated in the research (Brendgen et al., 2006; Truvblad et al., 2009; Yeh et al., 2010; Rowe et al., 2009). Brunner et al. (1993) conducted a seminal study linking the first (and most compelling) candidate gene for aggression and antisocial behavior. The *MAOA* gene was

found during a molecular genetic analysis of a large, multigenerational, and violent Dutch kindred (Brunner et al., 1993). The resultant syndrome appeared to be transmitted by an X-linked mode of inheritance. The syndrome was characterized by mild mental retardation as well as violent, aggressive, and antisocial behaviors. Through molecular analysis, the location of the linkage peak was accompanied by abnormal monoamine metabolism that pointed to the *MAOA* locus on the Xp11.23-11.4. Genetic sequencing exposed a nonsense point mutation in exon 8 of the *MAOA* (C936T) gene that was found among the males in this family.

Brendgen et al. (2006) investigated the association of genetic effects and teacher-rated proactive and reactive aggression. In a study of 6-year-old twins (172 pairs), researchers examined the variance of genetic and environmental factors on proactive and reactive aggression. The sample was followed longitudinally at months 5, 18, 30, 48, and 60 for each study participant. A final wave was conducted when the participants turned 6 years old (Brendgen et al., 2006). The level of proactive and reactive aggression was assessed using the teacher-rated instrument developed by Dodge and Coie (1987). Regarding proactive aggression, items on the scale included use physical force to dominate, getting others to gang up on a peer or threatening and bullying other students (Dodge & Coie, 1987).

The Dodge and Coie teacher rating scale has shown good external validity as evidenced by positive correlations with actual observations (Dodge & Coie, 1987). A three-point scale was provided (0 = Never, 1 = Sometimes, 2 = Often), and then each score was averaged to yield a total reactive and proactive aggression score (M = 0.68,

SD = 1.10) (Brendgen et al., 2006). Internal consistency of the total scale in this sample was in the acceptable range, with Cronbach's alpha of 0.72 for teacher-rated proactive aggression (Brendgen et al., 2006). Researchers have successfully implemented the Dodge and Coie instrument to differentially predict depression and criminal behaviors in adolescents (Brendgen et al., 2001; Vitaro et al., 2002). The statistical analysis included correlation, bivariate, and multivariate analysis to estimate the sources of variability in terms of genetic and environmental factors (Falconer & Mackay, 1996).

Results from Dodge and Coie's (1987) study showed that hereditability accounted for 62% of the proactive aggression in the sample. Also, a strong correlation was observed between latent genetic factors and proactive aggression ($RG_{realpro}$ = .87 (.71–1.00 Confidence Interval (CI)) (Brendgen et al., 2006). Some limitations of the study that were noted include the small sample size and the caution not to generalize the findings to other age groups and other sociocultural arenas (Brendgen et al., 2006). This study does, however, strengthen the argument that there is a genetic component to proactive aggression.

Truvblad et al. (2009) also explored this relationship between genetics and proactive aggression. The goal of the study was to investigate the stability and change in the influence of genetics on proactive, also referred to as instrumental, aggression. Reactive aggression was also explored in the study. Truvblad's research employed a secondary analysis of twins data extracted from a longitudinal study at the University of Southern California (USC). The sample was assessed at age 9–10 years (*N*=51,241) and at age 11–14 years (*N*=5,874) (Truvblad et al., 2009). Aggression was measured using the

Reactive and Proactive Aggression Questionnaire (RPQ) and was completed by the twins' parents. This questionnaire used has been validated in the literature as a 23-item measurement of reactive and proactive aggression in children starting at age 8 and into the adolescent period (Raine et al., 2006). There are 11 reactive aggression items and 12 items to assess proactive aggression including "He/she threatens and bullies other kids" and "He/she damages or breaks things for fun" (Raine et al., 2006l Appendix A). A proactive aggression score was calculated. In Wave I, 32% of the variance was due to genetic factors in reactive and proactive aggression. In Wave 2, the variance due to genetic effects ($p > 0.05$) in proactive aggression increased to 48% (Truvblad et al., 2006). This result supports the genetic influence hypothesis as well as the stability of genetic effects longitudinally. Truvblad et al.'s results also suggest the possible increase in genetic influence over the lifespan. Limitations noted included the bias of parental ratings and high attrition rates (Truvblad et al., 2009).

Yeh et al. (2010) conducted a study of twins (N=7,282) to investigate the genetic influence of aggressive behaviors using the Lifetime History of Aggression Questionnaire: aggression subscale (Coccaro et al., 1997). Both same-sex (N = 5,409) and opposite-sex (N = 1,798) twins were included in the study. The subscale included five items to see if the events had occurred since age 18 years. Questions include, for example, asking whether respondents have "deliberately struck or deliberately broken objects in anger" (indirect aggression, destruction of property), "deliberately hit another person in anger" (physical assault) or "gotten into verbal fights or arguments with other people" (verbal aggression) (Coccaro et al., 1997). This subscale indicated good

concurrent validity, internal consistency (a = .870), and inter-rater reliability, with an intra-class correlation coefficient = .94, and test-retest reliability (r = .80) (Coccaro et al., 1997). Five outcome variables were assessed: temper tantrums, physical assaults, indirect aggression, fighting, and verbal aggression were grouped as General Aggression (GenAg) factors (Coccaro et al., 1997). These were similar indicators of aggression assessed in this study.

The results showed, notably across genders, that genetic influences accounted for 53.9% of the variance in GenAg factors (95% CI = 46.5–60.7%) (Yeh et al., 2010). Genetic influence accounted for 38.3% of the variance in physical aggression (PhysAgg) that included fighting and assault (95% CI = 26.8–49.4%) (Yeh et al., 2010). Hereditability estimates were almost identical for males and females, for example, for physical assaults .23 males and .24 for females (Yeh et al., 2010). The DF regression model provides an estimate of hereditability and environmental variance of aggression. The AGG represents the aggression score for each of the siblings (AGG_1, AGG_2). The R represents the coefficient of the genetic relatedness (1.0 for monozygotic twins, 0.50 for dizygotic twins and full siblings, and .25 for half siblings). The estimated "shared environment effects" is represented with ß as the unstandardized coefficient of relatedness. The DF regression model was employed twice. The heritability measures from the two analyses (Trial 1 and Trial 2) produced similar estimates of $h^{2 =}$ .35, σ = .10, $p < .01$, and h^2 =.32, σ = .12, $p < .05$ which demonstrates that variance in aggression was primarily due to genetic factors (Yeh et al., 2010). The authors concluded that aggression is hereditable.

Aggression and Ethnicity

The relationship between aggression and violence among different ethnicities remains controversial and unresolved. It is well documented that ethnic groups have different involvement in aggression and aggressive-related behaviors. Authors have discussed that African Americans, Native Americans, and Hispanics have more delinquency involvement than whites (Hawkins et al., 2000). However, the Federal Bureau of Investigation (FBI) Uniform Crime reports (2013) show that arrests for aggravated assaults are greater among Whites than African Americans (62.9% vs. 33.5%, respectively). The same trend is seen among arrests for violent crime (Whites 58.4%, African Americans 38.7%) and weapon-carrying (Whites 58.2%, African Americans 39.8%) in the United States (FBI, 2013). Herein lies the discrepancy of results related to ethnicities and aggressive-related outcomes.

The experiences of minorities are usually studied in the context of high-risk environments, or much of what is known about factors related to aggression are gleaned from White adolescents (Henneberger et al., 2016). In a study by Henneberger et al. (2016), the levels of physical aggression were examined through the prism of ethnicities. The sample included African Americans, Whites, and Hispanics. This diverse sample was obtained from 37 schools across the United States. One of the research questions presented asked whether there were ethnic differences in the correlation between family cohesion, parental monitoring, and adolescent aggression for African American, Hispanic, and White adolescents. (Henneberger et al., 2016). The research participants (N = 1,232) were middle school students who were involved in the Multisite Violence

Prevention Project. The aim of this project was to reduce aggression and violence among sixth-grade students (Multisite Violence Prevention Project, 2004). It was found that Hispanic youth had significantly higher levels of physical aggression (M = 1.91, SD = .94) as compared to White adolescents (M = 1.67, SD = 0.82)

A cautionary approach to ascribing risks to certain ethnicities is supported in the literature (Crampton & Parkin, 2007; Perbal, 2012). The complex nature of behavior is important to note. However, this does not eliminate the need to investigate how genetic input influences antisocial behavior and aggression among different ethnicities. The genetic polymorphism of the *MAOA* gene has been well characterized in its association with aggressive-related behaviors. Hook et al. (2009) investigated this association among the Maori people of New Zealand. This is an interesting perspective in that the Maori people are 14.7% of the population, yet they account for more violence than any other group in this country (Statistics New Zealand, 2008). Although the etiology of aggression is multifactorial, it is imperative to consider the genetic underpinnings of the increased violence in certain ethnic populations.

Lea & Chambers (2007) investigated the ethnic differences in the allelic variants of the u-VNTR genetic polymorphism of the *MAOA* gene in New Zealand. The study provided estimates of the allelic variations by genotyping 46 unrelated males (Lea & Chamber, 2007). It was found that the 3-R or the "low" activity allele was found in 56% (95% CI = 42–70%) of the males (Gallardo-Pujol & Buades-Rotger, 2014; Lea & Chambers, 2007). This frequency of the 3-R allele is echoed among African-American males and females worldwide at 59% (95% CI = 46–72%) (Sabol et al., 1998). The

highest frequency of the 3-R allele of the u-VNTR genetic polymorphism of the *MAOA* gene is among Chinese males at 77% (95% CI = 66–88%) (Lu et al., 2002). Pacific Islanders have a 61 % occurrence of the 3-R allelic variation (95% CI = 47–75%) that includes both genders (Sabol et al., 1997). Caucasian males have a 34% frequency of the 3-R (95% CI = 32–36%) (Capsi et al., 2002) and that is one-half of the frequency found in the Maori males (Lea &Chambers, 2007). Historically, the Maori were fearless warriors (Lea & Chambers, 2007) and the dense frequency of the MAOA genetic polymorphism led to the term "warrior gene" which was originally coined by Gibbons (2000) and has been adopted as a cultural term to describe those who possess this polymorphism.

Reti et al. (2011) investigated monoamine oxidase A and antisocial personality in Whites in the absence of physical abuse. The objectives of the study included assessing for aggression. Embedded in the study were other ethnicities such as African Americans, Asians, and Native Americans (Reti et al., 2011). The authors reported that the other ethnicities were grouped with Whites because they are genetically similar to Whites according to a population substructure analysis. Structure 2.2, a population substructure analysis software, was used to cluster the sample according to self-reported race. Among the allelic variations, African Americans showed a 48.70% occurrence of the low activity allele (3-R) compared to Whites at 34.10% (3-R) (Reti et al., 2011). The high-activity alleles; (4-R, 62.80% and 3.5-R, 1.20%) were found in the sample of Whites as opposed to the 45.50% (4-R) and 0.20% (3.5R) in African Americans (Reti et al., 2011). It was found that among Whites with no history of physical abuse, the mean antisocial

personality trait score was 1.38 among the high-activity allele and 1.94 in the low-activity subjects. This represents a 41 % increase between the two types of genetic polymorphisms (Reti et al., 2011). The authors expanded the investigation by removing the other ethnicities and similar findings were elucidated. With this step, the antisocial personality disorder traits score was 1.37 ($p < 0.5$) for the high-activity allele and 1.97 ($p < 0.5$) for the low activity allele, representing a 44% increase in aggressive-related behaviors (Reti et al., 2011).

A sample if 189 men were used to determine if the u-VNTR genetic polymorphism of the *MAOA* gene alleles created susceptibility for antisocial behavior, including aggressiveness, in the presence of punitive discipline from caregivers. The study population had 44% African Americans and 56% Caucasians (Choe et al., 2014). Once genotyped for the u-VNTR genetic polymorphism of the *MAOA* gene, 35% (N= 83) of the African-American men and 32% (N = 30) of the Caucasian men possessed the low activity allele (3R) that has been associated with increased aggression, antisocial behaviors, and violence (Beaver et al., 2013; Guo et al., 2008). These results are corroborated in other studies (Reti et al., 2011; Sabol et al., 1998; Widom & Brzustowicz, 2006).

Aggression and Abuse

There are several studies that support the confluence of the genetic polymorphism of the MAOA gene and abuse and the impact of these two factors on aggression. Abuse has been characterized as an environmental factor and has been implicated in genetic X environmental influences on aggressive behavior and violence. Capsi et al. (2002)

conducted a study of New Zealanders and found that males who possessed the 3-repeat allele and had experienced child abuse or neglect had a higher prevalence of antisocial behaviors. Fergusson et al. (2011) replicated this result in a 30-year longitudinal study that showed that abused children, who carried the low-activity MAOA variants, developed conduct problems. This gene plus environmental interaction has been supported by multiple studies (Enoch et al. 2010; Fergusson et al., 2011; Frazzetto et al., 2007; Huang et al., 2004; Nilsson et al., 2006; Weder et al., 2009).

Weder et al. (2009) explored this interaction by reviewing a study with 114 children in which 73 were maltreated and 41 were considered the control group. These populations were matched for low socioeconomic status and differed on the exposure to maltreatment or family violence (Weder et al., 2009). In predicting externalizing behaviors, the allele genotypes of the MAOA were statistically evaluated using the Total Trauma Exposure Score (TTES). It was found that that children who had the MAOA-L had a higher rate of inattention in the presence of extreme histories of trauma. It is interesting to note that the children with the MAOA- L alleles had a higher rate of aggression with a moderate trauma history. However, the MAOA genotype had little effect on aggression levels in the presence of extreme abusive trauma experiences (Weder et al., 2009). The study authors indicated a limitation that the sample represented "extreme" cases of traumatic experiences and that more research would be beneficial to explore this genetic polymorphism and different levels of traumatic experiences.

In males who have had adverse childhood experiences and have the low activity MAOA genetic polymorphism, it was found that antisocial outcomes are more prevalent

then among those male cohorts who have not experienced abuse. This interaction is not supported among females. It was found that female cohorts with the low-activity alleles and childhood abuse were not found to exhibit antisocial behaviors (Byrd & Manuck, 2014). Some researchers caution that this gene and environmental interaction should not be considered robust evidence, citing that many of the studies use self-reported life events and are not objective measures of abuse and neglect (Byrd & Manuck, 2014). This was taken in consideration in this research as well. There is a divergence in findings. Among studies that examined violence as an outcome, the authors reported an increase in violent convictions, MAOA-L and childhood physical abuse among males. In contrast, there are studies that have found that the high activity MAOA genetic polymorphism is associated with aggression among boys and men (Beitchman et al., 2004; Manuck et al., 2000).

In examining this genetic X environmental interplay of abuse and the polymorphisms of the *MAOA* gene, several studies have explored the alleles of the *MAOA* gene and aggression or aggressive-related behaviors in the absence of abuse or childhood adverse events (Beaver et al., 2013; Beaver et al., 2010; Campbell et al, 2010; Guo et al. 2008; Reti et al, 2011). This is an important gap in the research. Researching the influence of a genetic polymorphism without abuse would increase the knowledge of a more direct genetic polymorphism influence on behavioral outcomes.

Monoamine Research

Monoamine, a neurotransmitter, transmits neuron signals to receptor cells. There are two types of monoamines: catecholamines and indolamines. The catecholamines are epinephrine, norepinephrine, and dopamine. Monoamines are also neuromodulators that

stimulate distal neurons. This can result in behavioral outcomes such as aggression and depression (Bach & Arango, 2012; Berry et al., 1994). Monoamine oxidases (MAOs) are bioavailable enzymes that process monoamines. These are catabolic enzymes that catalyze the oxidative deamination of biogenic amines and have a primary role in degradation of monoamines. This regulator enzyme metabolizes the neurotransmitters norepinephrine, serotonin, and dopamine at the monoaminergic synapses in several areas of the brain (Buckholz & Meyer-Linderberg, 2008). There are two isoenzymes of the monoamine oxidase gene: monoamine oxidase A (MAOA) and monoamine oxidase B (MAOB). MAOA and MAOB have specific substrates and inhibitor specificities that are encoded by these two genes on the short arm of the X-chromosome at location Xp11-23-11.4 (Beaver et al., 2010; Hook, 2009). These two isoenzymes are involved with the breakdown of neurotransmitters, rendering them inactive. Polymorphisms found on the *MAOA* gene are of particular scientific interest and have been studied for its association with aggression and violent behavior (Pavlov et al., 2011). The variable number tandem repeat (v-NTR) polymorphism found in the promoter region of the *MAOA* gene has behavioral consequences.

The promoter region of a gene is important because it controls genetic transcription and expression. The genetic polymorphism found upstream in the promoter region of the *MAOA* gene is comprised of a variable number of nucleotide tandem repeats (u-VNTR). This results in varying numbers of alleles represented by the nomenclature 2-R, 3-R, 3.5-R, 4-R, and 5-R. Each of these alleles results in varying levels of the oxidase enzyme (Buckholtz & Meyer-Linderberg, 2008). The 2-R, 3-R, and 3.5 R are considered

the “low activity” alleles and will result in an increase in an underperforming enzyme that results in an increase in the bioavailability of neurotransmitters in the system. This excess of neurotransmitters has been associated with increased human aggression (Plomin et al., 1997; Sabol et al., 1999). The 4-R and the 5-R alleles are the “high activity” allele because there is a significantly higher amount of the enzyme present, which results in a decrease in the amount of monoamine oxidase A (MAOA) in the bio system. MAOA is localized to the outer mitochondrial membrane in the presynaptic terminal of the monoamine projections neurons and is also found in the astrocytes. This positions the monoamine oxidase A enzyme to regulate the enzymatic processes that affect the availability of the neurotransmitters for vascular sequestration and their extra synaptic inactivation following release (Buckholtz & Meyer-Linderberg, 2008). The amount of enzymatic activity influences behavior, and a deficiency in this regulation can result in changes in human behavior.

The link between decreased MAOA enzymatic activity and aggressive behavior was cited as early as the 1960s, as observed in rodents that were given *MAOA* inhibitors (Spector et al., 1960). Pintar et al. (1981) documented that there is a point mutation on the *MAOA* gene that was found on the X-chromosome and further studies linked this genetic polymorphism to antisocial behavior in males who possessed an X-chromosome deletion. Cases et al. (1995) reported that knockout mice for the *MAOA* gene possessed higher levels of brain norepinephrine, serotonin, and dopamine and, most notably, an increase in aggression.

Studies have supported the *MAOA* genes' impact on the neural circuitry for affective arousal, emotional regulation, and impulse control, and how this can influence human aggression. Individuals with a genetic risk may display aggressive behaviors and may be vulnerable to the effect of psychosocial adversity. The *MAOA* gene provides encoding of the mitochondrial catabolic enzyme monoamine oxidase A (MAOA). This enzyme catalyzes the oxidative deamination of biogenic amines. The *MAOA* gene maps to adjacent areas on chromosome MAOA Xp11.23 (Grimsby & Chen, 1991). These enzymes are sequestered to the outer mitochondrial membrane within the presynaptic terminal of monoamine projection neurons (Arai et al., 1984; Westlund et al., 1993) and in the astrocytes monoamine A and monoamine B (MAOA and MAOB) (Levitt et al., 1982; Westlund et al., 1988). Both MAOA and MAOB are positioned to regulate the amount of intracellular substrate that is accessible for release. More significantly, these monoamine oxidases control the degree of extra-synaptic monoamine inactivation. The functional genetic polymorphism in the *MAOA* gene is therefore likely to interrupt signaling at monoaminergic synapses throughout the brain (Shih and Thompson, 1999).

Allelic variations of the *MAOA* gene also have an impact on brain structure and function. Newman et al. (2005) researched neurobiological contributions to violence in humans. The research approach was to examine the effect of allelic variations of the functional polymorphism of the *MAOA* gene on the brain structure of healthy volunteers (Newman et al., 2005). The low-expressing variant of the functional polymorphism of the *MAOA* gene resulted in a reduction of the limbic volume and a hyper responsive amygdala when emotionally aroused. There was also a decrease in the activity of the

prefrontal regions of the brain. In addition, the low expression allele was associated with alterations in the orbitofrontal volume and hyperactivity in the hippocampus (Newman, 2005). The research also pointed out that in males with the low-expressing variant led to changes in the orbitofrontal volume and hyperactivity in the hippocampus during the recalling of aversive events. This mimics reactive aggression in behavior (Newman et al., 2005). Differences were noted in the limbic circuitry involved in emotion regulation with those individuals with the low-expressing functional polymorphism of the MAOA gene (Newman et al., 2005). These findings support that there are neural system effects in the human brain and suggests biological underpinnings of aggression and aggressive-related behaviors.

Allelic Variants

The u-VNTR genetic polymorphism allelic variants consists primarily of five repetitive sequences: 2-R, 3-R, 3.5-R, 4-R and 5-R copies, where R stands for "repeats" and the number is how many copies of the repeat. The 3-R and the 4-R are much more common than the 2-R, 3.5-R and 5-R repeats in the human population (Guo et al, 2008). If the alleles are repeated 3.5 or 4 times, it is considered to be the "high expressing" allelic expression of the gene and is transcribed at a rate of 2 to 10 times greater than the "low expressing" alleles (Baker et al., 2006; Baker et al., 2007; Baker et al., 2008; Buckholtz & Meyer-Lindenberg, 2008; Reti et al., 2011; Guo et al., 2008). The resultant low expression will give rise to 10 times less of the *MAOA* enzyme than the 3.5-R or the 4-R repeat allelic variants. (Baker et al., 2006). Decreased production of MAOA results in less serotonin and dopamine degradation such that higher levels of these

neurotransmitters remain bioavailable in the system (Baker et al., 2006). High systemic serotonin and dopamine are known to cause aggressive-based behavioral disorders (Merriman & Cameron, 2007). The following chart presents literature supporting the effects of the low-expressing u-VNTR polymorphism as well as the high-expressing variants of the *MAOA* gene and different behavioral disorders as found in the literature. This supports the variables used in this research, namely, aggression, gender, ethnicity, and other antisocial behaviors as well as the possible association with the low- and high-expressing u-VNTR polymorphism of the *MAOA* gene.

Biochemically, the three genotypes present different levels of MAOA promoter activity. A transient transfection and luciferase assay revealed that the 4-R alleles conduct a higher level of promoter activity than the 3-R sequence (Guo et al., 2008; Sabol et al., 1998). The 3.5-R and 4-R sequences have been shown to transcribe more efficiently than the 3-R and 5-R sequence. Guo et al. (2008) found that the 2-R sequence produced the lowest promoter activity of all the genotypes. The 2-R allele's activity is a fraction of that of the 3-R allele activity and is substantially lower than the 4-R allele (Guo et al., 2008). If the promoter activity is low, as seen in the "low expressing" variant, there is a decrease in enzymatic activity. This results in increased levels of brain neurotransmitters that has been found to increase aggression and antisocial behaviors

The u-VNTR polymorphism found in the promoter region of the *MAOA* gene has been well characterized as having an influence on affective and antisocial behaviors (Capsi et al, 2002). Researchers studied whether antisocial behaviors can be predicted by the confluence of the u-VNTR polymorphism of the *MAOA* gene and maltreatment in a

cohort of males and females that participated in the Dunedin Multidisciplinary Health and Development study (Capsi et al., 2002). The sample was analyzed at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, and 26. The cohort was primarily intact at age 26 years with a 96% follow-up rate (Capsi et al., 2002).

A moderated regression analysis was used to predict scores on a composite antisocial index. The index incorporates four measures of antisocial behaviors: conduct disorder, conviction for violent crimes, z-scores for disposition towards violence, and z-scores for antisocial personality disorder symptoms (Capsi et al., 2002). Maltreated males who possessed the low-expressing u-VNTR genetic polymorphism of the *MAOA* gene had an increased risk to develop conduct disorder with an odds ratio (*OR*) of 2.8 (95% CI) over those with the high-MAOA polymorphism (Capsi et al., 2002). Among males with the high activity genetic polymorphism, having a history of maltreatment did not confer a significant risk of conduct disorder (*OR* 1.54, 95% CI =.89) (Capsi et al., 2002). Similar findings were observed among males with the low-activity alleles in adult violent convictions (*OR* 9.8, 95% CI = .72–3.68%) (Capsi et al., 2002). Overall, carriers of the low activity u-VNTR genetic polymorphism of the *MAOA* gene are more at risk for aggressive-related behaviors. Males with the high-expressing allelic variant of the u-VNTR genetic polymorphism of the *MAOA* gene did not have elevated antisocial scores even when they had experienced maltreatment (Capsi et al., 2002). The high-expressing genetic polymorphism seemed to provide protection against the reaction to maltreatment.

Capsi et al. (2002) reports that the study's focus on males was because of the *MAOA* gene on the X chromosome that yields two genotypes: high activity (63% in this study) and low activity (37% in this study) (Capsi et al., 2002). The genetic polymorphism is also present in females. However, females have two copies of the X chromosome and this produces homozygous genotypes: the high-high group (42%) and the low-low genotype (12%) in this study. There is a third genotype comprised of a heterozygous group of low-high (46% in this study) (Capsi et al., 2002). This complicates the determination of which of the alleles are inactivated in each of the female samples (Capsi et al., 2002). Some of the outcomes could not be analyzed with the female sample due to the small sample size. Females within the low-low activity group were more likely to have a conduct disorder by a strong odds ratio of 5.5 (95% CI = 1.0–32.0%) (Capsi et al., 2002). This study demonstrates the complex nature of examining this functional polymorphism in females.

The rarity of the low-low MAOA genotype (12%) in females and their limited involvement in violent outcomes and convictions (2%) led to negligible results in this study (Capsi et al., 2002). However, outcomes such as adolescent conduct disorder could be analyzed, revealing that females with the low-low-MAOA activity genotype were more likely to develop conduct disorder by a significant odds ratio of 5.5 (95% *Cl* = 1.0–32.0%) if they were maltreated. In contrast, maltreatment did not confer significant risk for conduct disorder (*OR* 1.7, 95% Cl = 0.75–4.2%) among the high *MAOA* genotype. This supports that high MAOA gene enzymatic activity provides a protective aspect

against adverse childhood events among girls (Capsi et al., 2002). Further research was suggested to investigate more X-linked disorders among females.

Samochowiec et al. (1999) investigated the low-expressing variant of the u-VNTR genetic polymorphism found in the promoter region of the X-chromosome of the *MAOA* gene. They explored the polymorphism's influence on an individual's vulnerability to antisocial behavior and liability to alcohol dependence (Samochowiec et al., 1999). The sample included 303 alcohol-dependent males, of which 59 men were diagnosed as having antisocial personality disorder (ASPD). Characteristics of this disorder include diminished social competence, deceitfulness, impulsive-aggressive, and conduct disorder, which includes a juvenile onset (Samochowiec et al., 1999). Statistical analysis was performed using a SAS computer program (SAS Institute Inc., 1988). Odds Ratios (*OR*), Chi-square, and Fisher's exact tests were employed.

Samochowiec et al.'s (1999) authors showed that there was a significant difference in the frequencies of the 3-R alleles in the antisocial alcoholics (f(3) = 0.36, X^2 = 0.035, *df* = 1, *p* = .031) compared to those men with alcoholism without ASPD (f(3) = 0.32, X^2 = 7.037, *df* = 1, *p* = .008). Males who possessed the 3-R allele displayed a 1.9-fold increased risk for antisocial alcoholism compared to those without the 3-R (*OR* 1.91, 95% CI = 1.06–3.46%) (Samochowiec et al., 1999). The results provided evidence that low activity 3-R allele is associated with antisocial behaviors among alcohol-dependent males.

In a sibling sample (*N* =2,534), Guo et al. (2008) investigated the association of the 2-R allele and serious and violent delinquency. The authors constructed a scale to

assess for serious delinquency and violent delinquency by extracting 12 questions used in the National Longitudinal Adolescent and Adult Health Study (Add Health) during Waves I–III (Guo et al., 2008). The goal of the study was to investigate the association between self-reported serious and violent delinquency and the u-VNTR polymorphism of the *MAOA* gene. The hypothesis was that the 2-R polymorphism is associated with higher levels of delinquency. The authors also conducted a functional analysis that examined the promoter activity of the 2-R, 3-R, and 4-R alleles on the 30-bp u-VNTR polymorphism using two human brain-derived cell lines (Guo et al., 2008). A contingency table compared the mean score of serious and violent delinquency across the genotypes (2-R, 3-R, and 4-R). These scores were tabulated over the age continuum.

The results showed that males with the 2-R allele showed much higher mean scores in serious delinquency over Waves I–III (5.63, 3.18, and 1.59, respectively). This increase in the mean for serious delinquency scores was also reflected in the female population (1.16, 1.96, and 1.03, respectively). The means for the violent delinquency scores were also higher for the 2-R allele over the other three alleles among females (0.77, 1.75, 1.46, 3.12, 0.68, and 2.05) (Guo et al., 2008). The males in the sample followed the same trend (3.96, 7.04, 2.45, 5.03, 1.36, and 2.26) (Guo et al., 2008). The regression analysis in this study supported the contingency table results. It was found that for men, the 2-R genotype scored 1.72 times higher ($p = 0.025$) than all the other genotypes combined on the serious delinquency scale. In females, the 2-R allele sample scored 0.48 ($p = 0.025$) points higher than the other alleles. On the violent delinquency scale, those who possessed the 2–R allele scored 1.46 and 0.29 points ($p = 0.025$) higher

than all other alleles combined (Guo et al., 2008). The results show that the people who possess the 2-R allele may have a greater risk of aggressive and delinquent behaviors.

Beaver et al. (2013) also investigated specific alleles and their association with serious delinquent behaviors. The polymorphisms of the *MAOA* gene were divided into two categories of "low" and "high" activity alleles. The low-*MAOA* activity group included the 2-R allele and the 3-R allele (Beaver et al., 2013; Guo et al., 2008). The high activity group consisted of the 3.5R, 4R and 5R alleles (Beaver et al., 2010). This study used secondary data from the Add Health study (2008) and found that 42.3% of males possessed the low-activity alleles versus 57.7% of males having the high-MAOA-activity allele (Beaver et al., 2010). Females who possessed the low-activity allele were 17.4% (homozygous) and 44.7% (heterozygous) for the low-activity MAOA-activity allele. There were 37.9% of females with the homozygous high-activity allele (Beaver et al., 2010). The differentiation between heterozygous and homozygous in females is because this genetic polymorphism is X-linked. Since females have two X-chromosomes, there are two times the effect of the u-VNTR being minimized (Beaver et al., 2010).

Determining the percentage of the allelic variants is significant when it comes to studying serious and violent behaviors. Guo et al. (2008) used the National Longitudinal Study of Adolescent Health (Add Health) to investigate the association of the 2-R allele and serious or violent delinquency in both males and females. A sibling subsample of 2,524 participants was analyzed while focusing on the allelic representations of 2-R, 3-R and 4-R. A contingency table was used to compare the mean score of serious and violent delinquency across the specified genotypes within the genders in the three waves of the

Add Health study. There were higher mean scores for serious or violent delinquency in both males and females with the 2-R allelic variant (5.63; n=11, SD = 9.05) and (1.16; n = 31, SD = 2.18). This compared with the 3-R allelic variant in males (Guo et al., 2008). Females with the 2-R alleles demonstrated a larger association with serious and violent delinquency at Waves II and Waves III of the Add Health study. Regression analysis compared serious and violent delinquency scores between the 2-R genotype and all the other genotypes within each gender. Similar results were found among the female sample, with a mean score 0.47 higher in serious delinquency and 0.29 points higher on the violent delinquency scale (Guo et al, 2008). This research supports the hypothesis that the low-expressing alleles increase the risk of delinquency.

There is also emerging research that particular genetic polymorphisms can confer criminal or aggressive behavior in the absence of maltreatment (Beaver et al., 2014). The researchers presented the frequency of the 2-R in Caucasians (0.1%) and African Americans (5.2%). The researchers chose only African Americans to analyze due to the negligible number of Caucasians with the 2-R allele (Beaver et al., 2014). The predicted probability of shooting or stabbing of those without the 2-R allele (N = 133) was 0.07, which is substantially lower than the predicted probability of 0.50 that was found in those individuals who did not possess the 2-R allele (Beaver et al., 2014). The 2-R carriers demonstrated a statistically significant effect (OR 12.89, $p < .05$) on the odds of shooting or stabbing someone (Beaver et al., 2014). These findings demonstrate a strong association between the low activity (2R) u-VNTR and aggressive and criminal behavior. A limitation to these studies is that the 2-R allele is often the focus of studies with limited

attention given to the other alleles and their association with aggressive behaviors. In addition, males are often the representative sample, even though females may also be carriers of the low-activity alleles.

The ethnic distributions of the allelic variations of the MAOA polymorphism have been published by Sabol et al. (1998). This was the first publication to discuss this novel polymorphism and its location and prevalence in the population. The allelic frequency in 2,156 chromosomes from four ethnic groups was grouped according to the number of alleles. The authors defined the polymorphism as the MAOA-uVNTR (upstream variable number of tandem repeats) (Sabol et al., 1998), which was first time the polymorphism was discussed in the literature. Both males and females were sampled. Out of a sample of 2,156 chromosomes, the high-expressing 4-R allelic presentation was highest in the Hispanic/Latino population at 70% (*n*=65), and in 64.8% (*n* =1,056) of the White sample in the population (Sabol et al., 1998). The 3-R and the 5-R alleles, both of which have been implicated in aberrant mood disturbances and aggression (Beaver et al., 2010; Brunner et al., 1993; Cases et al., 2002; Manuck et al., 1999; Manuck et al., 2000) was predominantly in the Asian and Pacific Islander population at 61.0% and among African American population at (59.1%) (Sabol et al., 1998). This contrasted with Hispanic/Latinos and Whites (29.3%, *n* = 539; 33.1%, *n* = 539), respectively (Sabol et al., 1998). This quantifies the occurrence of this genetic polymorphism in this population.

Lea & Chambers (2007) documented allelic frequencies among different worldwide ethnic groups. This limited sample (*n*=46; 95% CI = 42–70%) quantified the percent of the population that possessed the “low-expressing” allelic variation. Both

genders were included. The authors found that Chinese males (77%) and Maori/Pacific Islanders (61%) had the highest frequency of the 3-R allelic formation (Lea & Chambers, 2007). The authors echo findings of Sabol et al. (1998) and found that the 3-R allele (low expressing) was found in 59% of the African (male and female) population (Lea & Chambers, 2007). The lowest frequency of the 3-R allele was found among Hispanics (male and female) at 29% (Caspi et al., 2002; Lea & Chambers, 2007).

Conceptual Framework

The genetic underpinnings of human disorders are a complex matter. The challenge is even more so when investigating the link between genetics and behavior. This is a consequence of the difficulty in creating inclusive and uniform constructs related to psychiatric disorders (e.g., antisocial behavior, aggression, and conduct disorder) as well as a lack of consensus regarding the role and impact of genetics and environment in shaping antisocial behavior. Vaughn et al. (2009) posited that antisocial behavior is influenced by genetic, psychological, and environmental factors. A conceptual framework would need to reflect the complex nature of human behavior. There has been a swing of the pendulum of thought from purely nurturing factors in determining behavior that surrounded schizophrenia in the 1940s and 1950s to serious consideration of the impact of genetics on behavior. With Fromm-Reichman's (1948) term of "schizophrenogenic" mother, many studies investigated the dyadic paradigms between pathological (psychiatric) schizophrenic mothers and their children. During this decade, everything from common behavioral problems to schizophrenia was attributed primarily to the mother (Caplan & Hall-McCorquodale, 1985). Subsequently, in the

1980s, with a focus on genetics in physical conditions, the nature conversation prevailed. During this time, genetics were implicated in an array of physical conditions, and environmental influences were minimized. Contemporary thought has since shifted toward a more balanced approach in which both genetics and environment are appreciated for shaping human behavior. There is emerging evidence that genetic disposition may be a greater driving force in antisocial behaviors. In some cases, environmental factors are responsible for turning genes on or off.

The Biosocial Model of Antisocial Behavior underpins the current research because it illustrates the relationship between genes and environment on antisocial behavior. More importantly, this model allows for the possibility of certain genes and gene loci being responsible for antisocial behaviors including or excluding environmental factors (Baker et al., 2006, 2007, 2008). This conceptual model depicts biological and social factors as well as different forms of antisocial behavior. The Biosocial Model of Antisocial Behavior addresses behaviors that are often used interchangeably with aggression, namely antisocial behaviors, criminality, and delinquency. It includes the antisocial subtypes of proactive and reactive aggression that are variables used in this study. This conceptual model includes biological inputs including genes and environment as determinants of risk and protective factors. Both forces are foundational blocks for later processes, and each may directly influence outcomes. The solid straight lines from genetics and environment to biological risks and social risks depict the possible direct influence of these basic processes. Some biological factors include genetics, psychophysiology obstetrics, neuropsychology, and neurotransmitters. The model does

also allow for the confluence of these factors. For example, genetic and environmental factors have direct pathways to antisocial behaviors. The biological and social risk factors may have a reciprocal relationship, as depicted by broken lines connecting "biological risks" and "social risks."

Biological and social risk factors may have direct pathways to antisocial behavior independently of the other factors (Baker et al., 2006). This would assert that genetic factors may be directly responsible for antisocial behaviors independently of the environmental influences. This is a notable aspect of this model in that most studies are premised on environmental + genetic factors contributing to antisocial behaviors. The biosocial model of antisocial behaviors allows for the conception that genetic factors may solely contribute to antisocial behaviors (Baker et al., 2006). There are protective and preventive factors shown in the model. The protective factors, both biological and social, can be employed to reverse these interactions and theoretically mitigate the development of antisocial behaviors (Baker et al., 2006). This concept will be explored further in the social implications of this study. One of the most impactful processes in the model is that biological, social, protective factors, and prevention are able to disrupt all three pathways leading to antisocial behaviors (Baker et al., 2006). Lastly, antisocial subtypes are included in the model. The subtypes of aggression, criminality, and violence are included as outputs (Baker et al., 2006). The biosocial model of antisocial behaviors includes the variables and outcomes applicable to this study.

Summary and Transition

Aggression is a public health concern, particularly among the adolescent population in both genders. However, it seems that female adolescents are experiencing a spike in aggression and criminality as evidenced by an 83% increase in female delinquency (American Bar Association, 2001). Genetic predisposition has provided some insight into how genetics determines behavior, including aggression and criminality. The *MAOA* gene has emerged as a worthy locus, and its role in behavior has started to emerge in the literature. The u-VNTR genetic polymorphism of the *MAOA* gene has been implicated in several behavioral outcomes including aggression and criminality (Ali-Klein et al., 2008; Brunner et al., 1993; Cleveland, 2003; Kinnally et al., 2009; Reti et al., 2011). Literature has shown that both males and females are carriers of this genetic polymorphism, and both genders exhibit behavioral changes when this polymorphism is present. The biosocial model of antisocial behaviors will provide the framework for this study as the relationships between biological (genetic polymorphism) and antisocial aggression are investigated. In chapter 3, I will present the research methods used in this study. The variables will be explained along with the corresponding measures. The statistical analysis will also be presented.

Chapter 3: Research Method

The purpose this quantitative study was to examine the statistical associations between the u-VNTR genetic polymorphism of the *MAOA* gene, race (African American, Asian, or White), gender (male or female), parental abuse (present or absent), and the level of aggression among an adolescent population aged 13–18 years. This study involved an analysis of secondary data from the Add Health study. Chapter 3 presents a description of the background, sample, and setting of the Add Health study. Chapter 3 also presents the research design and methodology, including a description of the population, sample, and sampling procedures. The recruitment procedure, participation guidelines, laboratory procedures, and data collection process are described. The operationalization of the variables is also discussed. The statistical analysis plan included multiple regression. Threats to internal and external validity are addressed. Finally, the protection of the study's participants and the dissemination of findings are addressed.

Research Questions and Hypotheses

The research questions (RQs) and associated hypotheses that were addressed in this study were the following:

Research Question 1: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years?

H_o1: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years.

H_a1: There is an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years.

Research Question 2: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender (predictor variables) and aggression (outcome variable), while controlling for abuse, in an adolescent population aged 13–18 years?

H_o2: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

H_a2: There is an association between the u-VNTR genetic polymorphism of *MAOA* gene, gender and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

Research Question 3: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, race (African-American, Asian, White) (predictor variables), and aggression (outcome variables), while controlling for abuse, in an adolescent population aged 13–18 years?

H_o3: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene, race (African-American, Asian, White) and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

H_a3: There is an association between the u-VNTR genetic polymorphism of the *MAOA* gene, race (African-American, Asian, White), and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

Research Question 4: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race (African-American, Asian, White)

(predictor variables) and aggression (outcome variables), while controlling for abuse (confounding variable), in an adolescent population aged 13–18 years?

H_o4: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race (African-American, Asian, White) and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

H_a4: There is an association between the u-VNTR genetic polymorphism of the MAOA gene, gender, race (African-American, Asian, White) and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

Research Design and Approach

The research design and approach involved an analysis of secondary data collected in Wave III of the National Longitudinal Study of Adolescent and Adult Health (Add Health) from 2008–2012. Data from these time periods were used because they were the most current and included all variables required to address the research questions and test the associated hypotheses. In the original study, a longitudinal approach was advantageous because it was used to assess the population starting in high school and continuing into adulthood (Harris & Udry, 2008). Health and social behaviors were observed over time and therefore may be instrumental in developing trajectories of certain behaviors.

Methodology

Population

The Add Health study is a longitudinal study on adolescents starting in middle school and into young adulthood (Harris & Udry, 2008). There are five Waves that assess

behavioral, social, and biological factors. Waves I (April 1995-December 1995) and Wave III were used in the current study. These waves were pertinent because descriptive data and behavioral outcomes (aggression) and genetic findings (u-VNTR genetic polymorphism of the *MAOA* gene) were assessed during these stages in the data collection.

Sample and Sampling Procedure

The Add Health study is a longitudinal study of seventh to 12th grade adolescents in the United States that focuses on health-related behaviors and social contexts in which they live (Harris & Udry, 2009). All high schools in the United States that had an 11th grade and a minimum of 30 enrollees in the school were included in the primary sampling frame (N = 26,666). There was random sampling of 80 high schools, and the sample was selected proportional to enrollment size stratified by school type, urbanicity, region, and percentage of White adolescents (Harris & Udry, 2009). For each of these high schools, the primary feeder school that included a seventh grade was also included in the recruitment. The final sample was 134 schools. The name of the study was changed in 2015 to the National Longitudinal Study of Adolescents and Adult Health. The new title reflected the continuing study of this sample from adolescence to adulthood (Harris & Udry, 2009). Following this sample longitudinally provided the opportunity to study changes and trajectories of certain behaviors including delinquent involvement.

Wave 1

Of the 119,233 eligible students in Grades 7–12, 90,118 respondents completed an in-school survey between September 1994 and April 1995 (Harris & Udry, 2009).

This sample comprised the first wave (Wave I) of the study. School administrators also completed a survey describing the school policies and climate, student body characteristics, and accessibility of health services within the school (Harris & Udry, 2009). From the list of in-school survey participants and from school rosters, a core random sample stratified by grade and gender with special oversamples of adolescents (African American youth with one or both parents who had a college degree) were selected for in-home interviews.

The first wave (Wave I) of the in-home interviews was conducted from April to December 1995 (Harris & Udry, 2009). The 90-minute computer-assisted interview was completed by 20,745 students and included a wide range of questions on health, risky behaviors, protective factors, family dynamics, adolescents' attitudes, and delinquent and criminal behaviors. Sensitive components of the interview were delivered through earphones with responses entered directly into a laptop computer. Such an approach has been shown to maximize validity of responses among adolescents (Harris & Udry, 2009). Confidentiality was protected through strict protocols at each step of the process (Harris & Udry, 2009). Due to the sensitive nature of the questionnaires and the specimen collection, the participants' results were secured.

From this in-home sample, 14,738 teens completed the second wave of interviews (Wave II) conducted between April and August 1996. The mean interval between Time 1 and Time 2 data collection was 11.0 months (Harris & Udry, 2009). All study protocols received institutional review board approval. Extensive arrangements, including signed contractual agreements by investigators with access to the data, were taken to protect

confidentiality and to conceal the students' identities through deductive means (Harris & Udry, 2009).

Wave III and IV

There are four waves in the Add Health study, with each wave focusing on certain social, behavioral, and biomedical facets. Many of the waves' focuses overlapped. Biospecimens were collected during Wave III and included sexually transmitted infections, HIV status, and genetic data. The participants' DNA was genotyped for certain genetic markers including the u-VNTR genetic polymorphism of the *MAOA* gene (Harris & Udry, 2009). During Wave IV (2008–2009), a fourth of the in-home interview was conducted. These interviews served as a continuation of the nationally representative sample of adolescents who were initially interviewed in 1994–1995 (Harris & Udry, 2009). The purpose of Wave IV was to investigate the trajectories of the adolescents as they transitioned into adulthood.

A study's sample depends on four factors: an acceptable level of significance, the expected effect size, the power of the study, and the foundational event rate in the population (Bhalerao & Kadam, 2010). The Add Health study was a cohort study of adolescents from middle and high schools from all 50 states. Alpha (type I) is the probability of falsely rejecting the null (H_0) hypothesis and detecting a statistically significant difference between the groups when there is no difference (Bhalerao & Kadam, 2010). In other words, type I errors will yield an erroneous rejection of a true null hypotheses or a false positive (Bhalerao & Kadam, 2010). A beta (type II) error is the probability of falsely accepting the H_o and failing to detect a significant difference

between the groups when there is a difference (Bhalerao & Kadam, 2010). A type II error is the failure to reject a false null hypothesis.

Power (1-beta) is the probability of correctly rejecting the H_o and detecting a significant difference between the groups. Power is defined by determining what rate of false negatives is acceptable to adequately power the study to accept or reject the null precisely (Bhalerao & Kadam, 2010). Most researchers accept a power of 80%. This means that 20% of the time a real difference between the groups will not be detected. For the current study, the significance level, or *p* value, was established as $p < 0.05$. This meant that there was a 5% probability that the observed result was due to chance (see Bhalerao & Kadam, 2010).

Effect size is also used to calculate the sample size. Estimation of the effect size is based on preclinical studies or on previous studies. Effect sizes are defined as small, medium, and large (d = .2, .5 and .8, respectively) (Bhalerao & Kadam, 2010). Plomin et al. (2013) reported an effect size of .42 in a study addressing a genetic link of self-reported aggression among siblings. This was a medium effect size. If the effect size is large between the study groups then the sample size required is small (Bhalerao & Kadam, 2010). A medium to large effect size will call for a small to medium sample size. Initially, the Add Health study had 15,197 participants (Harris et al., 2009), however during Wave III, the participants (N = 3,737) provided a genetic specimen (and so are considered potential members of this study). With a 95% confidence level, a level of margin of 5%, and a response distribution of 50%, the sample size should be equal or

greater than 375 (Raosoft, 2004). The sample size for this study will be N =3,737 adolescents.

Instrumentation and Operationalization of Variables

MAOA-uVNTR. During Wave III in the Add Health study (Harris et al., 2009; Smolen et al., 2013), saliva samples were collected from full siblings or twins to genotype for five candidate polymorphisms that included the u-VNTR genetic polymorphism of the *MAOA* gene. This gene has been associated with individual differences in behavior related to mental health (Smolen et al., 2013). The u-VNTR genetic polymorphism of the *MAOA* gene is reported to be functional, exonic, and found in the promoter regions which can influence gene expression. It is expressed in the brain and has an apparent involvement in neurotransmission (Smolen & Hewitt, 2009). The u-VNTR genetic polymorphism of the *MAOA* gene is involved in behavioral differences in individuals.

The u-VNTR genetic polymorphism alleles are grouped into two groups based on their impact on transcription proficiency (Sabol et al., 1998). The 2-R, 3-R, and 5-R alleles have been considered the low-expressing alleles and produce low enzymatic activity. This results in higher levels of neurotransmitters. The literature supports that low-expressing alleles are associated with increases in aggression and criminality (Beaver et al., 2008; Guo et al., 2008). The high-expressing alleles (3.5-R and 4-R) have been shown to produce normal enzymes and have had inconclusive results in their relationship to aggression and criminal behavior. The high-expressing alleles appear to demonstrate a protective attribute in the presence of abuse (Caspi et al., 2002). However,

the high-expressing alleles have been associated with suicidal depression (Du et al., 2002) and suicidal behaviors among female bipolar patients (Ho et al., 2000). This exemplifies the complex nature of genetic and behavioral associations.

The *MAOA* gene, which maps to Chromosome 11 at location Xp11.3-11.4, contains a variable number of alleles in the 5′ regulatory region of the gene (Samochowiec et al., 1999) that may consist of two to five repeats. This u-VNTR genetic polymorphism of the *MAOA* gene has been shown to affect the expression, and likely the enzymatic activity of the MAOA protein (Sabol et al. 1998). In vitro experimental evidence indicates that *MAOA* alleles can be pooled into two groups based on their effects on transcriptional efficiency (Denney et al. 1999; Sabol et al. 1998). The first group (low expressing) consists of the 2-R, 3-R, and 5-R alleles. The second group (high expressing) combines the 3.5-R and 4-R allelic variants. The u-VNTR genetic polymorphism of the *MAOA* gene was assayed by a modification (Haberstick et al. 2005) of a published methodology (Sabol et al. 1998). The primer sequences were forward: 6FAM-ACA GCC TGA CCG TGG AGA AG (fluorescently highlighted); and reverse: GAA CGG ACG CTC CAT TCG GA (Applied Science, Indianapolis, IN) substituted for one-half of the dGTP, 200 nM forward and reverse primers (IDT, Coralville, IA) and one unit of AmpliTaq polymerase (PE-Biosystems, Foster City, CA). Amplification was performed using a version of touchdown PCR and analyzed in an ABI Prism 3100 Genetic Analyzer using protocols supplied by the company (Add Health Biomarkers, 2008). The yielded products included five allele fragment numbers: $N = 291$ (2-R), $N = 306$ (2.5-R), $N = 321$ (3-R), $N = 336$ (3.5-R), $N = 351$ (4-R), and $N = 381$ (5-R) base

pairs (Add Health Biomarkers, 2008). Two individuals independently verified these results. This is a genetic representation of the allele genotypes in the u-VNTR location on the *MAOA* gene.

Gender. Participants in the Add Health study were asked to identify their gender. The assigned values for males and females were 1 and 2, respectively (Harris et al., 2009). Individuals with missing values were excluded from this study.

Age. Participants were asked their age. The interviewers asked participants their age in months and years. The age range was 13–18 years. The Add Health study variable for age is HIGIIM (month) and HIGIIY (year). The question asked was "What is your birthdate? month; What is your birthdate? year." Age will be operationalized according to the Add Health Study. Only the variable HIGIIY (year) will be used for this study. Participants in the Add Health Study were between the ages of 13–18 years, and this is the inclusive age range that will be used in this study. This is consistent with other studies that have used this database (Beaver, 2013; Guo et al., 2008).

Race. Add Health study participants were asked "What would you describe as your race?" (Harris et al., 2009). The participants were asked if they were Black or African American (H1G16B), American Indian or Native American (H1G16C), or if their race was White (H1G16A). Other options were of Asian background; Chinese (Filipino, H1G17A), Japanese (H1G17B), Asian Indian (H1G17C), Korean (H1G17D), or Vietnamese (H1G17C) (Harris et al., 2009). In this study, the racial groups of African-American (H1G16B), White (H1G16A), and Asian (H1G17B) were included.

Abuse. The participants responded to the question "Did you experience neglect, or physical or sexual abuse while you were in the custody of a biological parent?" The study variable for this question is H3OD38.

Aggression. Aggression was measured using a composite scale previously used by Cleveland (2003). Averages of seven items were combined from the Delinquency, Fighting, and Violence section and the Joint Occurrences section of the Wave I In-Home interview (Cleveland, 2003). The items from the Joint Occurrences section included (A) "You got into a physical fight," and (B) "You pulled a knife or gun on someone." The items of (A) "Have you ever carried a weapon at school," and (B) "Have you ever used a weapon in a fight," were from the Fighting section of the questionnaire (Cleveland, 2003). The response options for both sections spanned from 0 to 2, where 0 represents "never," 1 represents "one time," and 2 represents "two or more times" (Cleveland, 2003). There were three items drawn from the Delinquency section: (1) "How often did you take part in a fight where a group of your friends was against another group?" (2) How often did you get into a serious physical fight?" (3) "How often did you hurt someone badly enough to need bandages or care from a doctor or nurse?" Responses were measured from 0 to 3, representing "never," "one or two times," "three or four times," or "five or more times," respectively (Cleveland, 2003). The respondents were asked if these occurrences happened within the previous 12 months. The lowest possible aggression score is "0," and the highest aggression score is "12". A higher aggression score indicates higher levels of aggression.

Cronbach's alpha is an index of reliability and illuminates the variation accounted by the true score of a foundational construct (Heckler & Hatcher, 1996). It is a measure of reliability of an instrument and is considered an objective measure of reliability (Tavakol & Dennik, 2011). The Cronbach's alpha for this approach was. 79, which indicates appropriate reliability (Tavakol & Dennik, 2011). Responses were recoded into a 0 or 1 format and a square root correction was applied to decrease a positive skew (Cleveland, 2003). To set response patterns equal across items, responses were recoded into a 0 or 1 format. The non-missing responses were summated to create an aggression scale assuming that high scores indicated higher levels of aggression (Cleveland, 2003). By applying these corrections, aggression could be assessed reliably. Table 1 summarizes characteristics of the variables included in this study.

Table 1

Study Variables

Variable	Coding	Function	Level
Polymorphism	High = 1 Low = 2	Independent	Categorical (Ordinal)
Gender	Male =1 Female = 2	Independent	Categorical (Nominal)
Race	Asian =1 African American = 2 White = 3	Independent	Categorical (Nominal)
Aggression	0 to 12 Higher score = higher aggression	Dependent	Continuous (Interval)
Abuse	Present = 1 Absent = 2	Independent	Categorical (Ordinal)

Data Collection

Add Health study respondents who were full siblings or twins were asked to give a saliva sample for DNA analysis (Harris et al, 2009). Consent was secured for participation in the Add Health Wave III study. The respondents agreed to a series of options including (a) to provide a saliva sample for the for genotyping and for DNA archival for future genotyping, (b) saliva for planned genotyping but not for future genotyping, or (c) no saliva (Add Health, 2008).

In-Home Interviews. The interview questions were comprehensive and included several areas of assessment. Questions were asked about general demographic, income, and other socioeconomic questions. There were questions about aggression, serious and

violent delinquency, and legal involvement (Harris et al., 2009). There were also questions on protective and risk factors. The health questions covered biological and health conditions and psychological factors. Health-related questions included acute, chronic, and recurrent health conditions. The questions were presented to participants using an ASCI assistance device on a computer.

Laboratory Components. The genetic measures were collected in collaboration with the Institute for Behavioral Genetics (IBG) in Boulder, Colorado. Trained interviewers collected, extracted, quantified and stored DNA samples per protocol. During Wave III, full siblings and twins were asked to give saliva specimens for DNA analysis. The genetic analyses of these biospecimens allowed for testing specific hypotheses regarding the influence of genes, varying genotypes, and their expression (Smolen & Hewitt, 2008). The Add Health Wave IV candidate gene data included dopamine D4 receptor Exon 3 VNTR, Serotonin transporter-linked polymorphic region, the Monoamine Oxidase A dinucleotide and Monoamine Oxidase A Upstream (VNTR MAOA), which is the variable in this study.

The selected participants were instructed to review and sign a separate informed consent for the DNA collection. No financial incentive was provided. Each subject was instructed to insert a sterile cytology brush into their mouth and rub the buccal and gum areas for 20 seconds. The tip of the brush was placed in a 2-ml screw cap that contained 200 µl of lysis buffer (1% isopropyl alcohol (v/v) in 50 mM Tris-HCL, 1 mM EDTA and 1% sodium dodecyl sulfate, pH 8.0) (Smolen & Hewitt, 2009). After providing the specimen, the participants were asked to swish their mouths with 10 ml of 4% sucrose

vigorously for 30 s, and the contents were discharged into a 30 ml conical test tube that was sealed with parafilm (-wash 11). A second mouthwash was repeated (wash 21) (Smolen & Hewitt, 2009). Each tube was labeled and shipped with ice packs to the University of Colorado for genetic testing. The DNA specimens were prepared in the laboratory of Dr. David Rowe of the University of Arizona. The DNA was isolated from the buccal cell specimen using a modification of previous methods. The mouthwash and brush samples were prepared separately and then combined later in the process (Smolen & Hewitt, 2009). The laboratory component was completed during a three-day process.

Day 1. The lysis buffer (1 ml of 6 M guanidine-HCL, 100 mM Tris-HCL, and 10 mM EDTA, pH 7.5) and 25 µl of proteinase K (10mg/ml) were added to each of the 2 ml tubes containing the swab. The tubes were enclosed on a rotator in a 55°C incubator overnight (Smolen & Hewitt, 2009). The wash 11 and the wash 21 samples were combined and centrifuged at 1,800 rev/min for 10 min at room temperature. The supernatant was discarded and 1 ml of lysis buffer was added to the remaining pellet. The re-suspended pellet was transferred to a fresh 2 ml tube and 25 µl of proteinase K (10mg/ml) was added. These samples were placed in a rotating incubator overnight at 55^0 Celsius overnight (Smolen & Hewitt, 2009).

Day 2. The brush heads were removed from the tubes and 200 µl of binding matrix (10 mM sodium acetate and 0.1ml diatomaceous earth (Sigma) in lysis buffer) was added to each brush and wash tube. The tubes were placed on a rotator for 15 min at room temperature (Smolen & Hewitt, 2009). The tubes were centrifuged at the maximum speed for 2 min. The supernatant fluid was discarded and 1 ml of wash buffer (50%

ethanol in 400 mM sodium chloride, 20 m Tris-HCL and 2 mM EDTA, pH 7.5) was mixed with the pellets. Each of the tubes was placed on the rotator at room temperature for 15 min and centrifuged for 2 min (Smolen & Hewitt, 2009). The sample was vacuumed overnight.

Day 3. Each dried pellet was combined with 200 µl of elution buffer (10 mM Tris-HCL EDTA, pH 8.8). The specimen tubes were centrifuged at a maximum speed for 2 min in a rotating incubator at 55 rpm for 30 min. The individual supernatant fluids (brush and mouth tubes) were mixed and placed in a single 0.5 ml tubes (Smolen & Hewitt, 2009). The DNA yield was quantified by absorbance at 260 nm and an aliquot was diluted to a concentration of 20 µg/µl or less to obtain a working sample. The average yield of DNA was 58 ± 1 µg. The DNA samples were then stored at 4°C and sent to the IBG for genotyping (Smolen & Hewitt, 2003). The results were presented in a written genotype report.

Add Health Quality Assurance. All interviewers were trained and certified to collect data for this study. Quality assurance protocols were developed for the contracting agencies including IBG. Extensive reports regarding the steps used by the contracting agencies were provided to the investigators including written quality control graphs and progress reports. The quality assurance protocols and reporting were applied to all waves of the study: Wave I (1994–1995), Wave II (1996), Wave III (2001–2002), and Wave IV (2008–2009) (Harris et al., 2009).

Secondary Data Access. The data and collection methods are publicly available on the Add Health website in SAS to be exported to SPSS and .XPT files. Data pertinent

to this study includes demographic data (age and ethnicity), behavioral outcomes (aggression), and genetic data (u-VNTR *MAOA*). The data used for demographic and behavioral outcomes are unrestricted-use data sets. The genetic data is considered restrictive-use data and was obtained through a contractual arrangement.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS vs. 22.0 to summarize and examine the relationships between the independent and dependent variables outlined in Table 1. The u-VNTR polymorphism of the *MAOA* gene were classified as either "low" expressing (2-R, 3-R, and 5-R) or "high" expressing (3.5-R, 4-R) alleles. Contingency tables were constructed to examine the associations between the frequencies of these polymorphisms, gender (male or female), and race (White, African American, and Asian).

Research Question 1: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years? was addressed using an independent samples *t*-test. The dependent variable was the aggression score. The independent variable was the polymorphism of the u-VNTR gene, with two levels (high and low allelic variant groups). The associated hypotheses were tested applying the $p < .05$ significance level.

Research Question 2: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, and aggression controlling for abuse, in an adolescent population aged 13–18 years? was addressed using multiple linear regression. The dependent variable was the aggression score. The independent variables were

polymorphism, gender, and abuse, and their interactions. The associated hypotheses were tested applying the $p < .05$ significance level.

Research Question 3: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, race, and aggression, while controlling for abuse, in an adolescent population aged 13–18 years? was addressed using multiple linear regression. The dependent variable was the aggression score. The independent variables were polymorphism, race, and abuse, and their interactions. The associated hypotheses were tested applying the $p < .05$ significance level.

Research Question 4: Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race, and aggression, while controlling for abuse, in an adolescent population aged 13–18 years? was addressed using multiple linear regression. The independent variables were polymorphism, gender, race, and abuse, and their interactions. The associated hypotheses were tested applying the $p < .05$ significance level.

Threats to Validity

There are few threats that impact the external or internal validity of this secondary analysis of archival data from the Add Health study. No experimental strategies were employed for the purpose of this research. Therefore, any threat to the validity of this study was minimized and pertains only to the original methods of data collection. The original study did not use self-reported responses, which can result in biases related to social desirability and recall reliability (Althubaiti, 2016). Other threats to internal validity include instrumentation and mortality (Teson, 2017). Due to the sensitive nature

of some of the questions presented to the sample, underreporting should be assumed and could result in self-reporting errors (Himes et al., 2005). The Add Health study has been regarded as the comprehensive data collection of adolescents into adulthood. This database has been extensively used to investigate variables related to adolescent populations (Add Health, 2008). The findings of this study may be impacted by the underreporting of behaviors and should not be generalized to the general population.

Protection of Human Participants

This study was conducted as a secondary data analysis of the Add Health study data and no original data were collected. Consequently, no informed consents were required beyond that which was procured during the original study. Published steps were taken to protect the human participants in this study. No protected health information was linked with any data from the Add Health Study. All study participants and data were anonymous and protected under the Add Health study protocol. Add Health participants provided written consent in accordance with the University of North Carolina School of Public Health Institutional Review Board guidelines based on the Protection of Human Subjects 45CFR46 (Harris et al., 2009). This study was approved and protected by the Walden Institutional Review Board #11-05-18-0154727.

Dissemination of Findings

The findings of this study will be disseminated in three ways. First, the results will be submitted to peer-reviewed journals for publication. The findings will also be submitted to Walden University's research journal and poster sessions. In addition, the findings will be presented at a yearly conference sponsored by the National Longitudinal

Study of Adolescent and Adult health (Add Health) in Bethesda, Maryland, at the National Institutes of Health.

Summary

The purpose of this study was to examine the statistical associations between the u-VNTR genetic polymorphism of the *MAOA* gene, aggression, gender, race, and parental abuse among an adolescent population. Four research questions were addressed, and associated hypotheses were tested using independent sample *t*-tests and multiple linear regression with SPSS Statistics v22.0. All study participants and data were anonymous and protected under the Add Health Study Protocol as found in the Code of Federal Regulations on the Protection of Human Subjects 45CFR46 and approved and protected by the University of North Carolina Institutional Review Board.

Chapter 4: Results

The purpose of this study was to examine the statistical associations between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race, parental abuse, and aggression among adolescents aged 13–18 years using secondary data extracted from Wave III of the National Longitudinal Study of Adolescent and Adult Health (Add Health) collected from 2008–2012. Table 2 defines the variables used to examine the hypothesized statistical associations.

Table 2

Definitions of Variables Used for Statistical Analysis

Variable	Data extracted from the Wave III Add Health database
Aggression	In the past 12 months: 0 to 2 = Taken part in physical fight 0 to 2 = Often taken part in physical fight; 0 to 2 = Pulled knife or gun on someone; 0 to 2 = Often used weapon to fight; 0 to 2 = Shot or stabbed someone; 0 to 2 = Carried gun to school/work; 0 to 3 = Number of times physically injured in fight; 0 to 3 = Number of times hurt someone badly enough to require healthcare. Total aggression score ranged from 0 to 16 (where 0 = zero aggression: 16 = highest level of aggression).
u-VNTR polymorphism of the upstream region of the *MAOA* gene	1 = Low allelic variant group (2-R, 3-R, 5-R) 0 = High allelic variant group (3.5-R, 4-R)
Gender	1 = Male 0 = Female
Race	1 = White; 0 = Not White 1 = African American; 0 = Not African American 1 = Asian; 0 = Not Asian 1 = Hispanic; 0 = Not Hispanic
Abuse (by biological and foster parents)	1 = Present 0 = Absent

The variables defined in Table 2 are different from those outlined in Table 1 because after downloading and extracting the data from the Wave III Add Health database, I realized that the data were not the same as those outlined in Table 1. Furthermore, the dichotomous variables (u-VNTR polymorphism of the upstream region of the *MAOA* gene, Gender; Race and Parental abuse) had to be re-coded in binary format (i.e., 0 or 1) to comply with the requirements of the statistical analysis. Table 3 presents the characteristics of the sample consisting of $N = 2{,}506$ adolescents aged 13 to 18 years.

Table 3

Characteristics of Sample

Variable	*Category*	*n*	%
Gender	Female	1307	52.2
	Male	1199	47.8
Race	White	1803	71.9
	African American	477	19.0
	Hispanic	344	13.7
	Asian	209	8.3
Parental abuse	Absent	19	0.8
	Present	2487	99.2
Polymorphism (i.e., u-VNTR polymorphism of the upstream region of the *MAOA* gene)	2-R (low)	14	0.6
	3-R (low)	727	29.0
	5-R (low)	45	1.8
	3.5-R (high)	17	0.7
	4-R (high)	1703	68.0

Note. $N = 2506$

The proportion of males and females was approximately equal. The most frequent race was White, followed in order of frequency by African American, Hispanic, and Asian. Less than 1% of the participants reported that they had been abused by a biological parent or a foster parent, of which over half ($n = 10$, 52.6%) were male. The

most frequent u-VNTR polymorphism of the *MAOA* gene were 4-R and 3-R followed in order of frequency by 5-R, 3.5-R, and 2-R. The low-expressing alleles (2-R, 3-R, and 5-R) were found in n = 786 (31.4%) of the sample. The high-expressing alleles (3.5-R and 4-R) were found in n = 1720 (68.6%) of the sample. Table 4 presents a 2 x 2 cross-tabulation of the gender of the participants vs. the frequencies of the u-VNTR polymorphism in the *MAOA* gene, classified as high or low. The low-expressing alleles were more frequent in the males (n = 523, 43.6%) than in the females (n = 263, 20.1%).

Table 4

Cross-Tabulation of the u VNTR Polymorphism in the MAOA Gene vs. Gender

u-VNTR polymorphism of the *MAOA* gene	Gender				Total
	Female		Male		
	n	% within Gender	*n*	% within Gender	
High (3.5-R and 4-R)	1044	79.9	676	56.4	1720
Low (2-R, 3-R, and 5-R)	263	20.1	523	43.6	786

Table 5 presents a 2 x 2 cross-tabulation of the race of the participants vs. the frequencies of the u-VNTR polymorphism in the *MAOA* gene, classified as low or high. The low-expressing alleles were less frequent in the White racial group (n = 501, 27.8%) than in the other racial groups, specifically African American, Hispanic, and Asian (n = 285, 40.5%). Table 6 presents the frequency distribution of the total aggression scores, which ranged from a minimum of zero to a maximum of 16. Table 7 presents the descriptive and reliability statistics for the aggression scores.

Table 5

Cross-Tabulation of the u VNTR Polymorphism in the MAOA Gene vs. Race

u-VNTR polymorphism of the *MAOA* gene	Race				Total
	Other		White		
	n	% within Race	*n*	% within Race	
High (3.5-R and 4-R)	418	59.5	1302	72.2	1720
Low (2-R, 3-R, and 5-R)	285	40.5	501	27.8	786

Table 6

Frequency Distribution of Aggression Scores

Aggression Score	*n*	%
0	2099	83.76
1	173	6.90
2	103	4.11
3	47	1.88
4	30	1.20
5	16	0.64
6	17	0.68
7	5	0.20
8	6	0.24
9	3	0.12
10	1	0.04
12	3	0.12
13	1	0.04
14	1	0.04
16	1	0.04

Note. N = 2506

Table 7

Descriptive and Reliability Statistics of Aggression Scores

Minimum	Maximum	M	SD	Median	Mode	Skewness	Cronbach's
0	16	0.41	1.28	0.18	0	5.11	.69

Note. N = 2506

The frequency distribution of the aggression scores was positively skewed (skewness = 5.11). The distribution was strongly skewed because most (83.67%) of the 2,506 participants self-reported a zero score for aggression. Skewness created a very large mode on the left-hand side of the distribution, while the mean and median scores were not at the center of the distribution. This distribution could not be normalized using a data transformation (i.e., square root, logarithm, or Box-Cox). The internal consistency reliability of the aggression scores (Cronbach's alpha = .69) was relatively low, and less than that (Cronbach's alpha = .79) reported by Cleveland (2003).

Table 8 presents the descriptive statistics of the aggression scores classified by the u-VNTR polymorphism of the *MAOA* gene. The aggression scores for the low allelic variant group (M = 0.49; Mdn = 0.21) appeared to be higher than the aggression scores for the high allelic variant group (M = 0.37; Mdn = 0.21).

Table 8

Descriptive Statistics of Aggression Scores Classified by Polymorphism

u-VNTR polymorphism of the *MAOA* gene	Minimum	Maximum	*M*	*SD*	Median	Mode	Skewness
High (3.5-R and 4-R)	0	16	0.37	1.18	0.17	0	5.34
Low (2-R, 3-R, and 5-R)	0	14	0.49	1.47	0.21	0	4.64

Note. N = 2506

Testing of Hypotheses

Prior to the testing of the hypotheses, the theoretical assumptions of the inferential statistics were checked. It is a misconception to assume that the dependent variable must be normally distributed, or needs to be transformed to normality, before conducting a *t* test (Rasch, Kubinger, & Moder, 2011) or a linear regression analysis (Li, Wong, Lamoureux, & Wong, 2012). So long as the sample size is large enough to provide sufficient statistical power, the statistical inferences of *t* tests and regression analysis are robust even when the dependent variable deviates strongly from normality (Li, Wong, Lamoureux, & Wong, 2012).

It was essential to test for equality of variance because heteroskedasticity (i.e., the inequality in the variance of the dependent variable across the independent variables) severely compromises the statistical inferences of *t* tests and regression (see Salkind, 2010). I also tested for outliers (i.e., extreme cases that were not representative of the sample) and multicollinearity (i.e., strong correlation between the independent variables). The presence of outliers and multicollinearity compromise the statistical inferences of

multiple regression by disproportionally inflating the standard errors of the regression coefficients (Osborne & Overbay, 2004; Yoo et al., 2014).

Research Question 1

Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among an adolescent population aged 13–18 years?

H_o1: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among an adolescent population aged 13–18 years.

H_a1: There is an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among an adolescent population aged 13–18 years.

RQ 1and its associated hypothesis were addressed using an independent samples *t* test. An independent samples *t* test was conducted assuming unequal variances because Levene's test was statistically significant (F (1, 2504) = 15.42, $p < .001$). The *t* test was statistically significant (t (2504) = 2.31, $p = .033$). The mean aggression score for the low allelic variant group ($M = 0.49$) was significantly greater ($M_D = 0.12$) than the mean aggression score for the high allelic variant group ($M = 0.37$). The effect size indicated by Cohen's *d* was 0.09.

The results supported H_{a1} because a statistically significant association was found between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years. This finding was consistent with the conclusion that the low-expressing alleles (2-R, 3-R, and 5-R) may be associated with increased levels of aggression (see Beaver et al., 2008; Guo et al., 2008). However, the strength of the association was very weak, as indicated by the very small effect size (Cohen's $d = 0.09$).

The interpretation of the effect size was based on Ferguson's (2009) suggestion that Cohen's $d = 0.41$ is the "recommended minimum effect size representing a practically significant effect for social science data" (p. 533). Therefore, the effect of the u-VNTR genetic polymorphism of the *MAOA* gene on the mean aggression scores may have limited practical significance, where practical significance refers to whether a measured effect appears to be large enough to be meaningful in a real-world context (see Frost, 2019).

Research Question 2

Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender and aggression while controlling for abuse, in adolescent population aged 13–18 years?

H_o2: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, and aggression, while controlling for abuse, in adolescent population aged 13–18 years.

H_a2: There is an association between the u-VNTR genetic polymorphism of *MAOA* gene, gender and aggression, while controlling for abuse, in adolescent population aged 13–18 years.

Table 9 presents the results of multiple linear regression to predict the effects of the genetic polymorphism of the u-VNTR of the *MAOA* gene, gender, and abuse (independent variables) on the aggression scores (dependent variable) after exclusion of 97 multivariate outliers (indicated by $p < .001$ for Mahalonobis d^2). Polymorphism of the *MAOA* gene and gender was statistically significant ($p < .05$) predictors of the aggression

scores assuming abuse was constant. The unstandardized coefficients (computed using the original measurement scales) indicated that, assuming abuse was constant, when polymorphism changed from 0 (i.e., high activity) to 1 (i.e., low activity) the aggression score increased by $b = .114$. Also, when gender changed from 0 (i.e., female) to 1 (i.e., male) the aggression score increased by $b = .463$.

Table 9

Multiple Regression Analysis to Predict Aggression vs. Polymorphism, Gender, and Abuse

Independent variables	Unstandardized coefficients *b*	Standardized coefficients β	*t*	*p*	Collinearity *VIF*
(Constant)	.135		3.99	< .001*	
Polymorphism	.114	.045	2.13	.033*	1.08
Gender	.463	.200	9.45	< .001*	1.09
Abuse	−.164	−.013	−0.41	.683	2.37
Gender x Abuse	.331	.019	0.62	.537	2.26
Polymorphism x Abuse	.029	.001	0.02	.981	1.13

Note. * Statistically significant ($p < .05$), *VIF*: variance inflation factor.

The standardized regression coefficients (computed using a common scale, ranging from −1 to +1) indicated that gender (β = .200) was a stronger predictor of the aggression scores than polymorphism (β = .045). There were no significant interactions, implying that abuse did not act as a moderator of the relationship between gender, polymorphism, and aggression. All the variance inflation factor (*VIF*) statistics were < 5 implying that the statistical inferences were not compromised by multicollinearity (i.e., there were no strong correlations between the independent variables). The residual plot in

Figure 1 shows that the residuals were not randomly distributed either side of zero, and did not reflect equality of variance, but the residuals displayed a geometric pattern, reflecting heteroskedasticity.

The effect size (Adjusted R^2 = .046) indicated that the multiple regression model constructed to address Research Question 2 explained 4.6% of the variance in the aggression scores. This effect size was very small based on Ferguson's (2009) suggestion that R^2 = .041 is the "recommended minimum effect size representing a practically significant effect for social science data" (p. 533).

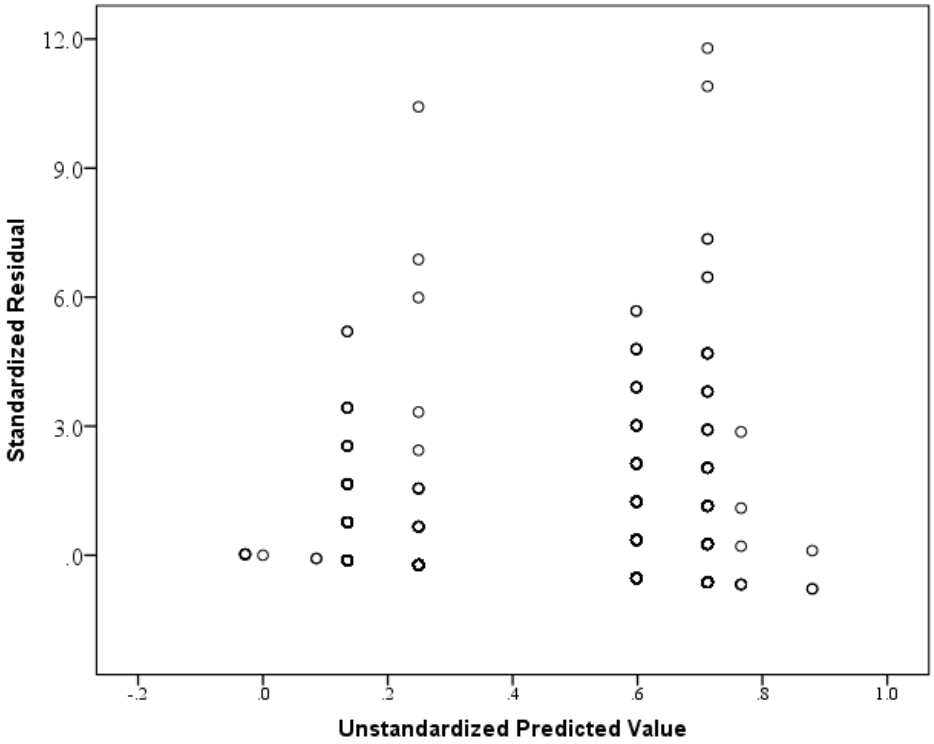

Figure 1. Residual plot for multiple regression analysis to predict aggression using polymorphism, gender, and abuse.

The conclusion is that the results supported the hypothesis H_{a2} because statistically significant associations were found between the u-VNTR genetic

polymorphism of *MAOA* gene, gender, and aggression, while controlling for abuse, in an adolescent population aged 13–18. However, the effect of polymorphism and gender on the mean aggression scores appeared to have limited practical significance, and the results of the regression analysis were compromised by heteroskedasticity.

Research Question 3

Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, race and aggression, while controlling for abuse, in an adolescent population aged 13–18 years?

H_o3: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene, race and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

H_a3: There is an association between the u-VNTR genetic polymorphism of the *MAOA* gene, race (African-American, Asian, White), and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

Research Question 3 and associated hypotheses were addressed. Table 10 presents the results of multiple linear regression to predict the effects of the genetic polymorphism of the u-VNTR of the *MAOA* gene, race, and parental abuse on the aggression scores, excluding outliers. The model satisfied the condition of multiple linear regression that the number of binary-coded dummy variables in a nominal variable with more than two categories must be one less than the total number of categories (Rawlings, Pantula, & Dickey, 2013). For this reason, Hispanic was excluded from the four categories of race, and race was represented by three racial groups: White, African American, and Asian.

Polymorphism of the *MAOA* gene was a statistically significant ($p < .05$) predictor of the aggression scores. The unstandardized coefficients indicated that when polymorphism changed from 0 (i.e., high activity) to 1 (i.e., low activity), the aggression score increased by .249. The three variables representing race (White, African American, and Asian) were not significant predictors; however, the *VIF* statistics for the three racial categories were > 5, implying that the statistical inferences were compromised by multicollinearity.

Table 10

Multiple Regression Analysis to Predict Aggression vs. Polymorphism, Race, and Abuse

Independent variables	Unstandardized coefficients *b*	Standardized coefficients β	*t*	*p*	Collinearity *VIF*
(Constant)	1.104		1.66	.097	
Polymorphism	.249	.098	4.69	< .001*	1.02
White	−.791	−.300	−1.19	.234	148.23
African American	−.760	−.261	−1.14	.254	121.48
Asian	−.856	−.182	−1.29	.199	46.90
Abuse	.264	.021	0.83	.409	1.46
African American x Abuse	−.795	−.032	−1.20	.229	1.65
Asian x Abuse	−.512	−.009	−.043	.669	1.08
Polymorphism x Abuse	.187	.003	0.15	.885	1.25

Note: * Statistically significant ($p < .05$)

There were no significant interactions, implying that abuse did not act as a moderator of the relationship between race, polymorphism, and aggression. The residual plot in Figure 2 shows that the residuals were not randomly distributed either side of zero, and did not reflect equality of variance, but displayed a geometric pattern, reflecting heteroskedasticity. The effect size (Adjusted $R^2 = .008$) indicated that the multiple

regression model constructed to address Research Question 3 explained only 0.8% of the variance in the aggression scores.

The conclusion is that the results did not support the hypothesis H_{a3} because no overall association was found between the u-VNTR genetic polymorphism of *MAOA* gene, race, and aggression, while controlling for abuse, in an adolescent population aged 13–18. Furthermore, the strength of this association, indicated by the effect size, was negligible, and the statistical inferences were compromised by multicollinearity and heteroskedasticity.

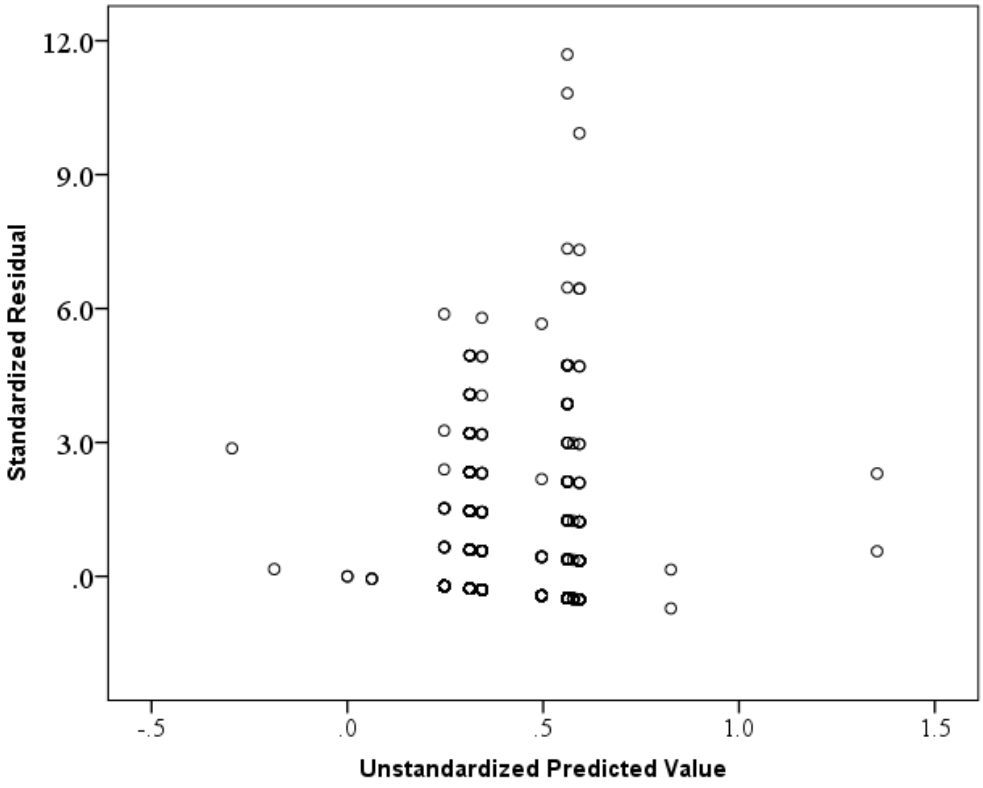

Figure 2. Residual plot for multiple regression analysis to predict aggression using polymorphism, race, and abuse.

Research Question 4

Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race (African American, Asian, White) (predictor variables) and aggression (outcome variables), while controlling for abuse (confounding variable), in an adolescent population aged 13–18 years?

H_o4: There is no association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race (African American, Asian, White) and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

H_a4: There is an association between the u-VNTR genetic polymorphism of the MAOA gene, gender, race (African American, Asian, White) and aggression, while controlling for abuse, in an adolescent population aged 13–18 years.

Table 11 presents the results of multiple linear regression to predict the effects of the genetic polymorphism of the u-VNTR of the *MAOA* gene, gender, and race, and parental abuse on the aggression scores after exclusion of outliers.

Table 11

Multiple Regression Analysis to Predict Aggression vs. Polymorphism, Race, Gender, and Abuse

Independent variables	Unstandardized Coefficients *b*	Standardized Coefficients β	*t*	*p*	*VIF*
(Constant)	.887		1.36	.174	
Polymorphism	.106	.042	1.96	.051	1.11
Gender	.465	.201	9.46	< .001*	1.09
White	−.764	−.290	−1.17	.242	148.23
African American	−.694	−.238	−1.06	.289	121.49
Asian	−.778	−.166	−1.19	.234	46.91
Abuse	.009	.001	.018	.986	4.04
Gender x Abuse	.208	.012	0.35	.730	2.85
White x Abuse	.009	.001	0.03	.986	192
African American x Abuse	−.441	−.018	−0.75	.452	1.35
Asian x Abuse	−.109	−.002	−0.10	.923	1.01
Polymorphism x Abuse	.248	.004	0.20	.845	1.27

Note. * Statistically significant ($p < .05$)

Gender was the only statistically significant ($p < .05$) predictor of the aggression scores. The unstandardized coefficient indicated that when gender changed from 0 (i.e., female) to 1 (i.e., male) the aggression score increased by $b = .465$, assuming that abuse was constant. The three variables representing race (White, African American, and Asian) were not significant predictors; however, the statistical inferences for race were compromised by multicollinearity, indicated by $VIF > 5$. There were no significant interactions, implying that parental abuse did not act as a moderator of the relationship between gender, race, polymorphism, and aggression. The residual plot in Figure 3 shows

that the residuals were not randomly distributed either side of zero, and did not reflect equality of variance, but displayed a geometric pattern, reflecting heteroskedasticity.

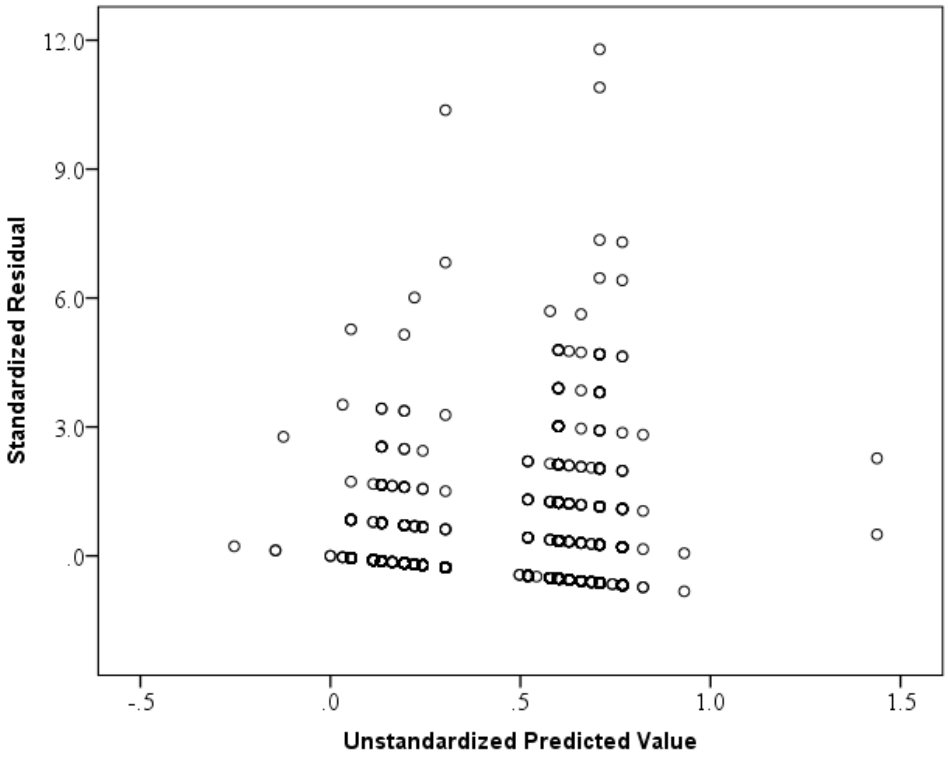

Figure 3. Residual plot for multiple regression model to predict aggression vs. polymorphism, gender, race, and abuse.

The effect size (Adjusted R^2 = .045) indicated that the multiple regression model constructed to address Research Question 4 explained 4.5% of the variance in the aggression scores. The conclusion is that the model did not support the hypothesis H_{a4} because no overall association was found between the u-VNTR genetic polymorphism of *MAOA* gene, gender, race and aggression, while controlling for abuse. The strength of this association, indicated by the effect size, was very small (based on the criteria defined by Ferguson, 2009). Moreover, the statistical inferences (*p*-values) were compromised by heteroskedasticity and multicollinearity.

Summary

The next chapter provides a summary of the results presented above, interprets the findings in the context of the literature, considers the implications and limitations of the findings, and provides recommendations for further research.

Chapter 5: Discussion, Conclusions, and Recommendations

The purpose of this quantitative study was to examine the association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression in an adolescent population 13–18 years of age. There is emerging research indicating that particular genetic polymorphisms can confer criminal and/or aggressive behavior in the absence of maltreatment (Beaver et al., 2014). A genetic polymorphism found in the upstream region of the *MAOA* gene (u-VNTR) has been shown to have an influence on aggression (Beaver et al., 2014; Guo et al., 2008). At the time of this study, however, researchers had not examined the relationship between the u-VNTR genetic polymorphism and aggression in a nationally representative sample of adolescents. Data from the National Longitudinal Adolescents and Adult Study (Add Health) 2008-2012 were analyzed to answer four research questions and test the associated hypotheses positing that the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race, while controlling for parental abuse, were associated with the level of aggression of a sample of adolescents.

The study sample consisted of $N = 2{,}506$ adolescents (age 13 to 18 years). The proportion of males and females was approximately equal. White was the most frequent racial group. Less than 1% of the participants reported parental abuse. The most frequent u-VNTR polymorphism of the *MAOA* gene were 4-R and 3-R followed by 5-R, 3.5-R, and 2-R. The low-expressing alleles were more frequent in males than in females, and less frequent in the White racial group than in other racial groups. The aggression scores that were measured using a tool devised by Cleveland (2003) exhibited relatively low internal consistency reliability. The scores were positively skewed because most of the

participants self-reported a zero score for aggression. Table 12 outlines the main findings based on the results of a *t* test and multiple linear regression to answer the four research questions and test the associated hypotheses.

Table 12

Summary of Hypotheses-Testing Findings

Research question	Answer
1. Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene and aggression among adolescents aged 13–18 years?	The association between the u-VNTR genetic polymorphism of the *MAOA* gene on the mean aggression scores was statistically significant ($p < .05$) but the effect size (Cohen's $d = .09$) reflected limited practical significance.
2. Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender and aggression while controlling for abuse, in an adolescent population aged 13–18 years?	Statistically significant associations ($p < .05$) were found between the u-VNTR genetic polymorphism of the *MAOA* gene, gender and aggression, while controlling for abuse. The combined effect of the polymorphism, gender, and abuse on the aggression scores reflected limited practical significance ($R^{2 =} .046$) and the results of the regression analysis were compromised by heteroskedasticity.
3. Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, race, and aggression while controlling for abuse, in an adolescent population aged 13–18 years?	A statistically significant association ($p < .05$) was found between the u-VNTR genetic polymorphism of *MAOA* gene and aggression, but no significant associations were found between the polymorphism, and race (White, African American, and Asian) while controlling for abuse. The combined effect of the polymorphism, gender, race, and abuse on the aggression scores reflected negligible practical significance ($R^{2 =} .008$) and the results of the regression analysis were compromised by heteroskedasticity and multicollinearity.
4. Is there an association between the u-VNTR genetic polymorphism of the *MAOA* gene, gender, and race, and aggression, while controlling for abuse in an adolescent population aged 13–18 years?	A statistically significant association ($p < .05$) was found between the u-VNTR genetic polymorphism of *MAOA* gene and aggression, but there no significant associations were found between the polymorphism, gender, and race (White, African American, and Asian) while controlling for abuse. The combined effect of the polymorphism, gender, race, and abuse on the aggression scores reflected limited practical significance ($R^2 = .045$) and the results of the regression analysis were compromised by heteroskedasticity and multicollinearity.

Interpretation of the Findings

The findings outlined in Table 12 were interpreted by complying with the formal guidelines for the interpretation of *p* values recently issued by the American Statistical Association (Wasserstein & Lazar, 2016, pp.129–133): (a) *p*-values do not measure the probability that the studied hypothesis is true; (b) Scientific conclusions and decisions should not be based only on whether a *p*-value passes a specific threshold; (c) A *p*-value, or statistical significance, does not measure the size of an effect or the importance of a result; and (d) By itself, a *p*-value does not provide a good measure of evidence regarding a model or hypothesis.

Furthermore, my interpretation of the results was influenced by the following recommendations by Wasserstein, Schirm, and Lazar (2019, p. 1): (a) Don't believe that an association or effect is absent just because it was not statistically significant; (b) Don't conclude anything about scientific or practical importance based on statistical significance.

The implications of the American Statistical Association guidelines (Wasserstein & Lazar, 2016; Wasserstein et al., 2019) as well as several other recent articles concerned with the unsuitability of null hypothesis significance testing using the interpretation of *p* values (Goodman, 2019; Halsey, Curran-Everett, Vowler, & Drummond, 2015; McShane & Gal, 2017; Sczucs & Ioannidis, 2017) are that I was not able accept or reject any of the stated hypotheses, draw any scientific conclusions, or make any decisions concerning social change depending on whether the *p* values satisfied an arbitrary, convenient, and obsolete rule of thumb devised nearly 100 years ago (specifically $p < .05$). The findings

were interpreted mainly with reference to the estimated effect sizes (Cohen's *d* and R^2), which reflected the practical and not the statistical significance of the results, as recommended by many statisticians (see Aarts, Van den Akker & Binkens, 2014; Barry et al., 2016; Ferguson, 2009; Frost, 2019; McLeod, Cappelleri, & Hayes et al., 2016). To interpret the findings, I had to determine the extent to which the effects of the u-VNTR genetic polymorphism of the *MAOA* gene, gender, race, and parental abuse on the level of aggression in an adolescent population were large enough to be meaningful in the real world based not only on the results of the current study but also on the results of previous studies in the peer-reviewed literature addressed in Chapter 2.

Studies in which researchers attempt to explain human behavior (e.g., aggression) tend to have small effect sizes because human behavior is difficult to predict and there is usually an inherently large amount of variance in a dependent variable reflecting human behavior that cannot be explained using a limited number of predictor variables (Frost, 2019). In the current study, the only variables that were identified to explain the aggression scores were the u-VNTR genetic polymorphism of the *MAOA* gene and gender; however, the effect sizes indicated by Cohen's *d* and R^2 were less than or very close to the acceptable minimum to reflect practical significance (see Ferguson, 2009). Despite the small effect sizes, some conclusions can be drawn.

Descriptive Statistics

The finding of the current study based on descriptive analysis was that the most frequent u-VNTR polymorphism of the *MAOA* gene were 4-R and 3-R followed in order of frequency by 5-R, 3.5-R, and 2-R. This distribution was consistent with previous

studies that indicated that the 3-R and the 4-R are much more common than the 2-R, 3.5-R and 5-R repeats in the human population (see Guo et al., 2008). The finding of the current study, that the frequencies of the low-expressing u-VNTR polymorphism of the *MAOA* gene (2-R, 3-R, and 5-R) were more frequent in males than in females, was consistent with previous studies (see Beaver et al., 2013; Guo et al., 2008). Furthermore, the finding of the current study, that the frequencies of the low-expressing u-VNTR polymorphism of the *MAOA* gene (2-R, 3-R, and 5-R) were more frequent in Asian, African American, and Asian racial groups than White racial groups, was also consistent with previous studies (see Brunner et al., 1993; Beaver et al., 2010; Cases et al., 2002; Lea & Chambers, 2007; Manuck et al., 1999; Manuck et al., 2000; Sabol et al., 1998).

Research Question 1

The results of the *t* test in the current study were consistent with the results of previous studies indicating that the genetic polymorphism found in the upstream region of the *MAOA* gene (u-VNTR) may be associated with aggressive behavior (see Beaver et al., 2014; Guo et al., 2008) possibly because the low-expressing polymorphisms are implicated in aberrant mood disturbances associated with aggression (see Beaver et al., 2010; Brunner et al., 1993; Cases et al., 2002; Manuck et al., 1999; Manuck et al., 2000). The current study contributed to an improvement in knowledge and understanding by indicating that that the low-expressing polymorphisms (2-R, 3-R, and 5-R) may be associated with increased levels of aggression after environmental influences (specifically parental abuse) have been controlled. However, it is still not clear whether the statistical association between the u-VNTR polymorphism of the *MAOA*

gene and human behavior is strong enough and meaningful enough to reflect a cause and effect relationship in a real-world context. Furthermore, the results of this study did not indicate the extent to which expressing genetic polymorphism may have provided protection against the reaction to maltreatment (see Capsi et al., 2002).

Research Question 2

The results of the multiple linear regression in the current study were consistent with the results of previous studies indicating that the low-expressing polymorphisms (2-R, 3-R, and 5-R) may be associated with increased levels of aggression (see Beaver et al., 2014; Guo et al., 2008). The regression model also predicted that males exhibited more aggressive behavior than females. The current study contributed to an improvement in knowledge and understanding by indicating that the low-expressing polymorphisms (2-R, 3-R, and 5-R) may be associated with increased levels of aggression in males after environmental influences (specifically parental abuse) have been controlled. The differences between the aggressive behaviors of males and females may be due to the genetic polymorphism of the *MAOA* gene being linked to the X chromosome. Because females have two X-chromosomes it is possible that the effects of the u-VNTR are minimized (Beaver et al., 2010). However, the results were compromised by violation of the assumptions of regression, particularly the high level of heteroskedasticity, and it is still not clearly understood whether the statistical association between the u-VNTR polymorphism of the *MAOA* gene, gender, and aggressive behavior is strong enough and meaningful enough to reflect a cause and effect relationship in a real-world context.

Research Question 3

The results of the multiple linear regression conducted in the current study were consistent with the results of previous studies concluding that the low-expressing polymorphisms (2-R, 3-R, and 5-R) may be associated with increased levels of aggression, particularly in males (Beaver et al., 2010, 2014; Guo et al., 2008). However, no definitive conclusions on the effects of the low-expressing polymorphisms (2-R, 3-R, and 5-R) among different racial groups (White, African American, and Asian) could be drawn. The inconclusive results were mainly due to strong violations of the theoretical assumptions of regression analysis, specifically, high levels of heteroskedasticity and multicollinearity. Therefore, the regression analysis failed to determine the extent to which the statistical association between aggressive behavior and the u-VNTR polymorphism of the MAOA gene was related to race and parental abuse.

Research Question 4

No definitive conclusions regarding the combined effects of the u-VNTR polymorphism of the *MAOA* gene, gender, race, and abuse on the aggression scores could be drawn because results of the regression analysis were compromised by heteroskedasticity and multicollinearity. Therefore, the regression analysis failed to determine the extent to which the statistical association between aggressive behavior and the u-VNTR polymorphism of the *MAOA* gene was related to gender, race, and parental abuse. A study by Zhung et al. (2016) investigated the interaction of the u-VNTR genetic polymorphism of the *MAOA* gene, gender, abuse and aggressive behaviors in a population of Asian adolescents. It was found that the presence of abuse had a more

significant impact on aggressive behaviors than the presence of the genetic polymorphism. The results also showed that the sample that reported abuse and possessed the low-variant polymorphism showed increased aggression (Zhung et al., 2016). These findings support the results of this study which indicate that carriers of the low-variant polymorphism that have experienced parental abuse have an increased risk of aggression. This concludes the interpretation of the findings of this study. The limitations of the study will now be explored.

Limitations of the Study

The results of this study were dependent on the accurate measurement of the aggressive behavior of the participants. Aggression was measured as a component of violence, delinquency, and other antisocial behaviors and during the study using a survey tool devised by Cleveland (2003). Although this survey tool was validated in a previous study, the relatively low reliability of the items in the current study, measured using Cronbach's alpha, may be a limitation. Just because the reliability of a survey tool has been established after administration to one sample of participants in one particular survey does not imply that the same tool will also provide reliable data when administered to another sample, in another survey, using a different sample of participants (Brannick, 2005; Thompson, 2003). The low reliability of the aggression scores may be due to aggression being a complex construct that overlaps with the presentations of other behavioral disorders, which vary among different samples (Anderson & Huesmann, 2003). It would be interesting to repeat this research while controlling for other behaviors that are related to aggression with more delineated

diagnostic criteria such as violence or intermittent anger disorder, as found in the Diagnostic and Statistical Manual of Mental Disorders–DSM-5 (APA, 2015).

A second limitation of this study was the use of self-reports to answer the survey questions about aggression and abuse. It is possible that some participants were not truthful in their answers due to social desirability bias, defined as the tendency of some survey respondents to answer sensitive questions in a manner that will be viewed favorably by others. Social desirability bias is often manifested by the participants over-reporting their good or desirable behavior, and under-reporting their bad or undesirable behavior (Lavrakas, 2017). Social desirability bias may explain why the mode of the highly skewed frequency distribution of the aggression scores was zero, and why only a few (19) participants reported abuse by their biological or foster parents. The majority of the respondents may have failed to report any type of aggressive or abusive behavior for many reasons. For example, acts of real or imagined physical violence are often denied by survey respondents due to fear of punishment, even if the survey is anonymous (Krumpal, 2013).

The final limitation of this study was the use of old-fashioned techniques developed over 100 years ago that often produce misleading results, mainly due to violations of statistical assumptions, and the misinterpretation of the statistics. For example, Young (2007), in a review of statistical errors in medical research, argued that simple univariate statistics such as a *t* test are "to statistics what cupping, bloodletting and leaches are to medicine: of historical interest, on rare occasions still useful, but largely superseded by superior methods" (p. 42). In a review of linear regression analysis in

psychological research, Ernst & Albers (2017) concluded that 92% of all articles were unclear about the implications of the violation of theoretical assumptions (e.g., heteroskedasticity and multicollinearity), contradicting the guidelines in the APA publication manual. Syll (2012) asserted that the results of regression analysis should be put in the garbage can where they belong. More modern statistical methods that do not depend on so many restrictive assumptions are considered in the next section.

Recommendations

This study presents several recommendations for further research and can accelerate awareness of the importance of genomics in clinical and public health practice. The first recommendation is that the existing data should be reanalyzed using more modern statistical techniques. The second recommendation is that the research should be repeated using more reliable tools to measure aggression and parental abuse. As personalized medicine is emerging as a standard consideration when treating patients or the public, this study supports the recommendation to consider genetic information in developing treatment interventions. The results of this research can also be used to inform incarceration mitigation and to impact violence in general, which is considered a public concern.

Several statistical techniques have been developed in the 21st century that overcome the limitations of the statistical techniques developed in the 20th century that are still supported, maintained, and taught using traditional software such as SPSS. For example, in a review entitled "Moving to a world beyond $p < 0.05$," Wasserstein et al. (2019, p. 1) recommend several alternative modern statistical techniques that enable

researchers to compute sample statistics with probabilities close to their corresponding population parameters, avoiding the problems associated with the interpretation of *p*-values and the violations of the theoretical assumptions that plague classical null hypothesis significance testing. However, none of these techniques are supported by SPSS.

Alternative modern techniques that have been developed to replace multiple linear regression, not available in SPSS, include multivariate modeling involving the calculation of partial least squares (PLS) rather than ordinary least squares (OLS). Haenlein & Kaplan (2005) suggest that PLS has the advantage that it involves no theoretical assumptions about the population or scales of measurement. PLS operates without distributional assumptions using nominal, ordinal, and continuous variables, and PLS is robust regarding several inadequacies of the data (e.g., skewness, heteroskedasticity, and multicollinearity). Vinzi, Trinchera, and Amato (2010) recommend that PLS is especially applicable when the assumptions of OLS are not tenable. Hair, Anderson, Babin, Tatman, and Black (2010) consider that PLS is particularly useful because its statistical power is higher than OLS even when the sample size is low (e.g., less than 30).

In future surveys, alternative tools could potentially be administered to measure the aggressive behavior of adolescents. How aggression is defined and measured (e.g., whether it is a temporary state or a permanent personality trait) potentially influences the outcomes and conclusions that can be drawn from the analysis of the scores. For example, Suris, Lind, Emmett, Borman, Kashner, & Barratt (2014) reviewed a wide range of tools that can be administered in clinical or research settings to measure

aggression, anger, hostility, and impulsivity as either a state, a trait, or a state and a trait (see Appendix A).

With respect to the measurement of parental abuse, the United Nations International Children's Emergency Fund (UNICEF) has developed a tool to measure multiple indicators of violence against children for application by researchers worldwide (UNICEF, 2005). The violence indicators chosen for the UNICEF tool quantify the levels of child rights violations or violations of international standards for violence against children in different environments, including at home, at school, and elsewhere. Therefore, the UNICEF tool generates more comprehensive and reliable data on violence against children than simple questions concerning the presence or absence of parental abuse that were administered in the current study.

It remains to be seen whether the use of modern statistical techniques or other survey tools to measure aggression and abuse among adolescents will provide new results from which more definitive conclusions can be drawn regarding the associations between the u-VNTR genetic polymorphism of the MAOA gene, gender, race, abuse, and aggressive behavior.

Theoretical and Practical Implications

The theoretical significance of this study is that the results support the Biosocial Model of Antisocial behavior, positing that genes can influence aggressive behaviors with or without environmental influences (Baker et al., 2006, 2007, 2008). This research builds on the study conducted by Reti et al. (2011) that discovered the direct influence on the u-VNTR of the *MAOA* gene and behavior in the absence of physical abuse. Although

there is a reluctance on emphasizing this possibility because of the prevailing belief that there must be some type of abuse to witness an increase in aggression among carriers of the low-expression variant of the u-VNTR, this study presents the exciting possibility of a direct genetic-to-behavior relationship as presented in the Biosocial Model of Antisocial behavior (2008). The results from this study support the use of genomic screenings in patient interactions, especially in psychiatric services. A case can be made that genomics should be included in all health-related interactions, from primary care to public health programs. In addition, since public violence has become ubiquitous, the results of this study provide another tool in mitigating violence. Genetic screenings, including testing, can be used to decrease the public health burden of aggressive-related behaviors, incarceration, and mental health disorders. The practical implications of this study are that new information contributing to a gap in the literature has been presented regarding the extent to which the u-VNTR genetic polymorphism is related to aggression, gender, and parental abuse in an adolescent population.

Conclusion

Adolescent aggression is considered a public health crisis (Abram et al., 2015; Newcorn et al., 2015; World Health Organization, 2014). The adolescent developmental period is a time of high-risk behaviors, including aggression and violence (Newcorn et al., 2015). There are approximately 600,000 youths that are treated for physical assaults in U.S. emergency rooms (CDC, 2015). The proliferation of aggressive acts is obvious, and this study supports the importance of employing research to impact

public health using genomics. This study found that there is a relationship between the low-expressive variant of the u-VNTR of the *MAOA* gene and an increase in aggression.

Human behavior is influenced by many factors; therefore, it would be naïve to identify one component and draw a conclusion related to a behavioral outcome. However, this study did prove that the presence of the low-expressive polymorphism does result in an increase in aggression among this population in the absence of sexual abuse. Although this is not a purely novel association (Reti et al., 2011), to date there has not been a duplication of the results of this study until now. The results of this study cannot be extrapolated to the general public, but it does provide a framework for further research to expand this association in the absence of other adverse childhood events.

This study did follow the results of other studies that found an association between the u-VNTR genetic polymorphism of the *MAOA* gene and increased aggression. The study failed to find an association between the u-VNTR genetic polymorphism of the *MAOA* gene and an increase in aggression among different races among a sample of adolescents aged 13–18 years; however, there was a contribution to knowledge. First, this work clarified the ambiguous results of previous research by strengthening the finding that there is an association between the low-expressive u-VNTR genetic polymorphism of the *MAOA* gene and aggression; second, it has provided the basis for further research in genetics and behavior. Finally, it has presented a methodologic model for investigating behavior and genetics using the Add Health study data.

Although the study did not find the hypothesized relationship to the u-VNTR genetic polymorphism of the MAOA gene, aggression, gender, race, and abuse, the study did confirm that gender and the presence of the low-variant genetic polymorphisms of the *MAOA* gene are significant risk factors in predicting increased aggression. The pressing problem of aggression and violence supports the importance of the results of this study. Research needs to continue to understand other factors in aggression as well as to increase research on clarifying the possibility of a direct relationship between genetics and behavior. The results of this study indicate the importance of considering genetics as an option for preventing aggression among adolescents.

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Appendix: Tools Devised to Measure Aggression, Anger, Hostility, and Impulsivity

Measure type	Measure title	
State	Anger Attacks Questionnaire	Modified Overt Aggression Scale
	Anger Self-Report	Modified Taylor Aggression Task
	Brief Agitation Rating Scale	Overt Aggression Scale
	Brief Psychiatric Rating Scale	Point Subtraction Aggression Paradigm
	Calgary General Hospital-Aggression Scale	Rating Scale for Aggressive Behavior in the Elderly
	Cohen-Mansfield Agitation Inventory	Report Form for Aggressive Episodes
	Continuous Performance Task	Scale for the Assessment of Aggressive and Agitated
	Driving Anger Scale	Behaviors
	Lions Scale	Staff Observation of Aggression Scale
Trait	Abusive Violence Scale	Duke Social Support Index
	Aggression Inventory	Early Experience Questionnaire
	Aggression Questionnaire	Expagg Questionnaire
	Anger Expression Scale	Eysenck's Personality Questionnaire-II
	Anger, Irritability, Assault Questionnaire	Feelings and Acts of Violence
	Anger Questionnaire	Gender Role Conflict Scale
	Attitudes Toward Aggression	Hand Test
	Barratt Impulsivity Scale-11	Hostility and Direction of Hostility Questionnaire
	Brief Anger–Aggression Questionnaire	Intermittent Explosive Disorders Module
	Brown–Goodwin Assessment for Life History of Aggression	Interpersonal Hostility Assessment Technique
	Buss–Durkee Hostility Inventory	Millon Clinical Multiaxial Inventory (MCMI-III)
	Conflict Tactics Scale	Motivation Assessment Scale
	Draw-A-Person Test	Multidimensional Anger Inventory
	Driving Anger Scale	MMPI-Overcontrolled Hostility Scale
	NEO-Personality Inventory	Novaco Anger Inventory
	Past Feelings and Acts of Violence	Suicide and Aggression Scale
	Physical Aggression Scale	Thematic Apperception Test
	Prediction of Aggression and Dangerousness in Psychotic Patients	Tridimensional Personality Questionnaire
	Reaction Inventory	Verbal Aggressiveness Scale
	Risk of Eruptive Violence Scale	Violence Scale
		1.7 Impulsiveness Questionnaire
State and Trait	Aggressive Acts Questionnaire	State–Trait Anger Expression Inventory-2
	Brief Symptom Inventory	State–Trait Anger Scale
	Clinical Anger Scale	Suicide and Aggression Survey
	Novaco's Anger Scale	Violence and Suicide Assessment Form

Source: Suris et al. (2014).