THE SOCIAL ENVIRONMENT, GENETICS, AND OBESITY: EVALUATION OF DIATHESIS-STRESS AND DIFFERENTIAL SUSCEPTIBILITY FRAMEWORKS

by

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"Don't worry about the horse being blind,
Just load the wagon.
Sometimes the road to Easy Street
Goes through the sewer."

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While this document may currently exist as the culmination of my work as an academic, my success up to this point would not be possible with the help and support of the people that surround me. Thank you to my friends and family for their unconditional support and understanding. A very special thank you to the faculty and staff in the Department of Sociology at the University of Wisconsin-La Crosse, past and present, whom plucked me from their classes and pushed me to dream bigger – your timing could not have been any more impeccable.

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ABSTRACT

The National Longitudinal Study of Adolescent Health (Add Health) dataset was used to explore how newly-available genetic information can aid social scientists in conducting studies concerned with social outcomes. A key goal of this study is to evaluate two prominent theoretical frameworks in the area of gene-by-environment (GxE) interaction: diathesis-stress and differential susceptibility. The diathesis-stress model has informed nearly all behavioral gene-by-environment studies and is the prevailing theoretical orientation among GxE scholars. Within the last decade, the differential susceptibility framework has been advanced as a viable alternative. Using genetic data collected during Wave IV of the Add Health study, the current study explores how the MAOA and 5-HTTLPR gene alleles interact with known predictors of obesity to compare and contrast the different frameworks. Results reveal that MAOA and 5-HTT do not have the same effect on obesity, especially when socioeconomic status and gender are considered. Results also support both differential susceptibility and diathesis-stress frameworks. Individuals with the low activity 5-HTT allele had higher rates of obesity across all incomes. Individuals with the low activity MAOA allele had higher rates of obesity at low incomes, but lower rates of obesity at higher incomes. These relationships are additionally nuanced by gender. The 5-HTT finding is only significant for females and MAOA is only significant for males. The implications for future gene-environment studies that may wish to use MAOA and 5-HTT alleles in conjunction are discussed.

CHAPTER I

Introduction

Widespread obesity is a new development in the United States, with the emergence of the "obesity epidemic" only in the past 25 years (Burke and Heiland 2007). The prevalence of obesity has slowly increased over time in the United States, but has more dramatically increased since the 1980s, with current figures indicating that more than 30 percent of Americans are now considered obese (Flegal 2005). At its most basic level, obesity is simply excess weight individuals carry. The Centers for Disease Control and the World Health Organization often classify obese individuals using a body mass index (BMI) calculation, where the threshold for being overweight is 25 kg/m^2 and the threshold for obesity is 30 kg/m^2 or higher.

Obesity is of particular sociological relevance because of its broad impact on human life and interaction. Demographically, obesity and weight-related health issues contribute to high levels of morbidity and mortality, including physical ailments such as heart disease, hypertension, stroke, diabetes, and some forms of cancer (Black and Macinko 2008; Flegal 2005). Culturally, obesity rates have challenged notions of acceptable or desirable body image (Schwartz and Brownell 2004). In terms of individual differences in social and environmental context, obesity has been linked to poverty and food availability, access, and security (Black and Macinko 2008; Cummins and MacIntyre 2006; Ulijaszek and Lofink 2006). Obesity rates also differ significantly between genders and racial/ethnic groups (Belcher et al. 2010; Heitmann 2010). The relationships between obesity and the environmental or contextual factors are of particular interest for this study.

While many social factors and influences that contribute to obesity are studied by social researchers, obesity itself is rooted in the human body and it is highly malleable. It is vitally important amidst the obesity discussion to consider two factors that directly contribute to differences in individual weight: physical activity and diet. Obesity itself is simply the product of an imbalance between energy intake and energy output, so naturally many researchers in the social and other sciences focus their studies on eating and exercise behaviors, as well as the co-factors that affect both of these activities (Cummins and Macintyre 2005). Food choice and eating behavior studies have found that obesity can be the result of low-priced, energy-dense foods (Drewnowski 2004), the high cost and/or low availability of fresh produce (Turrell et al. 2002), or the satiability derived from eating sweets and fats (Drewnowski and Specter 2004). In terms of physical activity, studies have linked obesity to increases in contemporary sedentary lifestyles (Martin 2008) and limited access to recreational facilities or space to use for recreation (Morland and Evenson 2009; Booth, Pinkston, and Poston 2005).

Traditionally academics have explored obesity using niche theories and discipline-specific philosophy (e.g. geneticists study the impact of genes on obesity, social researchers focus on social-environmental contributors). Obesity has been studied extensively at the individual level, but also within families (Martin 2008), neighborhoods (Black and Macinko 2007; Burdette and Whitaker 2003), and between countries (Cummins and Macintyre 2005). Researcher's choice in a particular unit of analysis is often embedded in specific disciplines as well. While disciplinary boundaries still exist, many of the most recent obesity related studies have found common interest in areas of

physiology and eating behavior, occasionally including genetics as well (Ulijaszek and Lofink 2006).

Many of the most recent obesity studies in sociology converge at an interdisciplinary crossroads linking obesity to the combined influence of genetic factors (G) and environmental context (E) (Fuemmeler et al. 2009; Fuemmeler et al. 2008; Hjelmborg et al. 2008; Martin 2008; Ulijaszek and Lofink 2006). Studies in this area focus on the phenomenon known as gene-environment interactions (GxE). The relationship between obesity and both its direct and indirect factors, especially when genetic components are considered, varies greatly by the conceptualization of the relationships between the variables.

Genetics in Sociology

After a long period of exclusion, the use of genetic factors in social research is garnering support, and in some of the most acclaimed sociology journals. Using genetics alongside social research is in no way a novel concept. Sociology has kept genetic research at a distance for important reasons. Many of sociological concerns with genetics are simply philosophical differences, but the discipline has also harbored a pervasive and long-lasting contempt for genetics research based on a past history of gross misuse and abuse of information, and the negligent, destructive, and faulty application of genetics as the explanation for social differences.

Philosophically, social and biological arguments over the general understanding of human life have been at odds for much of human history. The debate is commonly referred to as the "nature versus nurture" argument: whether social forces or biology have greater effect on an individual's life course. While the debate is no longer as volatile as it

once was, rigid disciplinary boundaries still exist (Bearman 2008; Diez Roux 2006; Freese 2008).

The most significant reason social scientists remain averse to biological and genetic arguments concerning human nature. Early geneticists used newfound genetic information as justification for additional research that resulted in heinous violations of human rights, including the use of forced sterilizations and barbaric medical experiments. Paired with interpretations and implications of early "social" research and theory, like Social Darwinism, this specific school of scientific thought also birthed the eugenics movement the Nazi's would embrace. Despite the global reaction to eugenics, American scientists continued egregious human experimentation for decades, notably the infamous Tuskegee syphilis experiments. Revulsion at this and other similar studies, once again justified in the name of scientific progress, spurred ethical reform among scientists regarding human research methods and practice. The practical implications of this reform resulted in much more rigorous standards and guidelines for conducting research with human subjects, but the reform's most significant impact was a change in the perception of medical research.

The atrocities carried out by early medical researchers and biologists have left a lasting impression among social scientists. Yet many of the ideas that fueled these movements have been appropriately retired. Genetic determinism for instance, the notion that genetic makeup is the sole contributing factor to individual differences and outcomes, heavily influenced scientific research for beginning in the late 19th and early 20th centuries (Simons et al. 2011; Martin 2008). This framework has been entirely discredited, and researchers are beginning to understand how important the

environmental context is to an individual *and* their genes. As Simons et al. (2011) explain: "Evidence is overwhelming that human beings are never simply instructed by their genes to show a particular trait or behavior…genes are turned on (i.e., expressed) and messages they transcribe vary depending on environmental circumstances (883)."

Interest in genetics has increased over time among researchers and the public at large. The completion of the Human Genome Project and the launch of a number of new genome sequencing and decoding projects, like the 1000 Genomes Project, have brought genetics to the forefront of sociological conversations (Via, Gignoux and Burchard 2010; Freese 2008). Sociologists are once again confronted with genetics and their purpose and place within social research.

In the last decade, many social researchers have proposed ways to assimilate this new information. Social science research serves to benefit from the inclusion of genetic information in research studies in a variety of ways. It's important to understand that the context of the gene-environment discussion has dramatically changed. Genetic determinism has been abolished and the genetic discussion has instead turned into an exploration and evaluation of genetic-environmental effects arguments (Freese and Shostak 2009). Research that places genes into social context is a rapidly developing area of multidisciplinary study, where different studies explore this interplay with regard to outcomes such as aggression (Simons et al. 2011), depression (Fuemmeler et al. 2009), sexuality (Guo, Tong and Cai 2008), and obesity (Fuemmeler et al. 2009; Fuemmeler et al. 2008; Hjelmborg et al. 2008; Martin 2008; Ulijaszek and Lofink 2006).

Genetic data has been integrated into a variety of datasets that are popular among social researchers, including the National Longitudinal Study of Adolescent Health (Add

Health) and the National Health and Nutrition Examination Survey (NHANES). Social researchers no longer have the excuse that genotype information is not available. Use of genetic variables has the potential to increase our accuracy in explaining relationships and would allow sociologists to enter into the broad, interdisciplinary discussion of genetics. We have been given another tool to aid in the process of developing a more thorough understanding of social relationships and the opportunity to produce findings that are acknowledged and reputable across disciplines.

CHAPTER II

Literature Review

Genes represent specific parts of the human genome that contribute to the physiological creation of the human body and control bodily functions. Genes can be polymorphic, or have structures that differ slightly between individuals. Each of the possible variations of a gene is known as an "allele" and the alleles are caused by differences in the genetic code sequence within genes (Simons et al. 2011). The genetic code is comprised of nucleotide base pairs (bps), where the four possible bases are adenine (A), cytosine (C), guanine (G), and thymine (T), although uracil (U) takes the place of thymine in RNA sequences. In the typical double helix DNA structure, guanine pairs with cytosine and adenine pairs with thymine.

These pairs appear in a variety of forms, or are organized in a variety of ways, within genes. One particular genetic variation occurs when a set of base pairs is repeated, known as a Variable Number Tandem Repeat (VNTR). The different gene variations based on VNTRs are referred to in the literature as insertion/deletions, where a gene may have additional base pairs (insertion) or may be missing pairs (deletion) when compared between different people. VNTRs can alter various aspects of gene function depending on where the VNTR is located in the code sequence, particularly if the VNTR is located within the promoter region of the code (Simons et al. 2011). The promoter regions are important because they control gene transcription, or the expression of the gene. Variability in the promoter region of serotonin-related genes, for example, can affect the magnitude and duration of the serotonin transportation synapse (Sookoian, Gemma and Garcia 2007).

Genetic research has linked a wide variety of genes to obesity, including those responsible for serotonin transportation. The 2005 Human Obesity Gene Map found significant associations with 127 candidate genes, although consistent findings occurred with only 22 of these (Fuemmeler et al. 2008). The vast majority of genetic obesity studies focus on genes that affect the function of serotonin and dopamine systems in the brain. There are specific genes associated with each system: serotonin (SLC6A4, SLC6A14), dopamine (SLC6A3, DRD2, DRD4) and the enzymes that metabolize both serotonin and dopamine (COMT, MAOA, MAOB) (Fuemmeler et al. 2009; Fuemmeler et al. 2008; Need et al. 2006; Camarena et al. 2004). The related hormones regulate metabolic and eating behaviors (as well as others), which in turn affect obesity (Fuemmeler et al. 2008). More specifically, certain alleles allow the gene to transcribe serotonin or dopamine more or less efficiently than others.

Serotonin-Related Genes and Alleles

Serotonin is a neurochemical associated with changes in an individual's mood, especially pleasure. Genes associated with serotonin include SLC6A14, which affects serotonin synthesis, and SLC6A4, which affects the serotonin transporter. Researchers found SLC6A14 to be significantly associated with obesity in two studies (Durand et al. 2003), but these findings have not been replicated. Many other studies instead focus on SLC6A4 alleles (Simons et al. 2011; Fuemmeler et al. 2009; Guo et al. 2008; Sookoian et al. 2008).

The serotonin SLC6A4 gene is of particular interest in this study, especially alleles in the transporter region of the gene known as 5-HTT. The 5-HTT polymorphism is an allele with a 43-base pair (formerly thought to be a 44-base pair) insertion/deletion

on the promoter region of the SLC6A4 gene, meaning that there are short and long variations of the gene based on the number of sequence repeats (Harris et al. 2013). 5-HTT is the key regulator of transmission of serotonin in the brain (Simons et al. 2011). The group of alleles located in the transporter region of this gene are known as 5-HTTLPR.

Individuals inherit two copies of this gene, one from each parent, and can have a combination of two long alleles (L/L), two short alleles (S/S), or one of each (L/S). The vast majority of individuals have either a 14-repeat (14R) or 16-repeat (16R) sequence, where 14R is considered the short allele and 16R is the long allele. There are rare cases where individuals have extra-long sequences, comprised of 18, 20, or 22 repeats, but this information is relatively new and the effects of these gene variations has not been thoroughly studied.

Research on 5-HTTLPR alleles focus on a variety of behaviors and disorders as a result of serotonergic function, including mood disorders like depression and anxiety (Fuemmeler et al. 2009; Caspi et al. 2003), antisocial behavior (Lyons-Ruth et al. 2007), aggression (Simons et al. 2011), as well as physiological functions such as sleep and memory (Lucki 1998). The serotonergic alleles, including 5HTTLPR, also affect satiety to some extent, although the genes that regulate dopamine largely control those feelings.

Studies have shown that presence of the short allele in any variety (either in a S/S homozygous or a L/S heterozygous pair) transcribes serotonin less efficiently than homozygous L/L alleles, and the short variations of the gene are significantly associated with risk of overweight or obesity (Fuemmeler et al. 2008; Sookoian et al. 2008; Sookoian et al. 2007). Sookoian et al. (2008) and Sookoian et al. (2007) compared

individuals with any short alleles to individuals with homozygous long alleles and found that the presence of a short allele significantly increased the odds of being obese between from 36% to 85%. Fuemmeler et al. (2008) found that the effects of a short allele varied by sex, where the odds of being obese for males was significantly higher than females. The shorter variations of the serotonin transporter are linked to higher rates of obesity, although nuances based on gender in particular exist. In general, the effects of the 5-HTTLPR short allele on obesity were consistent across cultures, with study populations derived from both the United States and Argentina. In addition, studies using different obesity measurement (both BMI raw scores and BMI *z*-scores) produced similar results.

Dopamine-Related Genes, Alleles, and Enzymes

While serotonin affects mood and can, in turn, alter eating behaviors, dopamine regulates the eating behavior itself. Researchers have analyzed various alleles associated with dopamine regulation, including those that affect dopamine-related enzymes (COMT, MAOA, MAOB), the dopamine transporter (SLC6A3), and the dopamine receptor D2 (DRD2, DRD4) (Fuemmeler et al. 2008; Need et al. 2005). Each gene has a substantial impact on the amount of dopamine available in the brain, altering feelings of hunger and satiety.

Dopamine-related studies of obesity and genetics have produced mixed results. While studies including the transporter SLC64A, receptors DRD2 and DRD4, and the enzyme COMT have not consistently substantiated a relationship with obesity, the MAO alleles, specifically MAOA, continue to be significantly associated with overweight and obesity (Fuemmeler et al. 2009; Fuemmeler et al. 2008; Need et al. 2005; Camarena et al. 2004). The differences between MAOA and MAOB are slight. Monoamine oxidase A

(MAOA) is a gene that produces an enzyme that metabolizes a variety of neurochemicals, including dopamine, serotonin, and noradrenaline (Fuemmeler et al. 2008). MAOB only metabolizes the dopamine neurotransmitter. Only MAOA alleles have been consistently associated with obesity, potentially due to their role in metabolizing serotonin (Need et al. 2005).

MAOA gene alleles are also described by insertion/deletions. The 30-base pair sequence is commonly seen in 3, 3.5, or 4 repeat varieties, where the long alleles (3.5 and 4 repeat) transcribe up to 10 times more efficiently than the short (3 repeat) alleles (Need et al. 2005; Sabol, Hu, and Hamer 1998). Less common are 2 or 5 repeat alleles, and studies analyzing these variants have so far been inconclusive (Need et al. 2005). Similar to 5-HTT short alleles, MAOA short alleles are also associated with higher rates of obesity.

While genes that produce and regulate serotonin and dopamine are most widely used in obesity studies, only those alleles related to serotonin have consistently predicted risk for obesity in past research – not dopamine. This suggests that obesity is potentially linked to the pleasure derived from eating as opposed to feelings of hunger satiety. The SLC6A4 gene and its alleles control the transportation of serotonin. While both MAOA and MAOB produce enzymes that metabolize a variety of neurochemicals, only MAOA produces those which metabolize serotonin. In both cases, gene alleles with low efficiency (slow transportation and slow metabolism of serotonin) are both linked to an increased risk of obesity. Slow metabolism and transportation of serotonin would extend or prolong the pleasurable feelings derived from eating

It is important to note that the vast majority of these studies frame gene alleles as inherent individual components that affect susceptibility to, or risk of, obesity, not necessarily causes that determine obesity itself. This highlights the role social and environmental contexts play on the development of obesity within individuals. There is a substantial body of literature outside of obesity studies that focuses on these particular alleles and social-environmental relationships. Caspi et al. (2002) found that MAOA moderates the relationship between children's maltreatment and their tendency to develop violent behaviors. In a similar study, Simons et al (2011) found that presence of the 5-HTTPLR short allele (and its interaction with a long allele DRD4) moderates the relationship between social environments, hostile life orientations, and aggressive behavior. Gene-by-environment studies have shown that genes play an important, although nuanced, role in many of the relationships social researchers study.

Metabolic Modifiers and Phenotypic Obesity

In obesity research, genetic predispositions may increase the odds that an individual is obese, but there are a host of additional factors that have a much more direct influence. Many studies seek to determine obesity risk factors that actually function through differences in eating habits and levels of physical activity as opposed to having a direct influence on obesity (Black and Macinko 2008; Stafford et al. 2007). These studies address the observable, phenotypic expressions of obesity and propose solutions – eating healthier and exercising more – as a way to promote health and change how people look. Diet and physical activity have a relatively direct and immediate impact on individual obesity, making these factors important in obesity research.

In terms of diet, researchers have studied types of food, the quantity of food eaten, and the frequency of meals as indicators of obesity, with the assumption that fresh foods and a balanced eating schedule help to reduce obesity (Stafford et al. 2007). From a physiological standpoint, reducing the amount of calories consumed by substituting lower calorie fresh foods for high carbohydrate, high fat foods is likely to reduce percentage body fat, individual weight, and ultimately rates of obesity.

Researchers have explored how eating and dieting behavior is affected by various individual level factors, including depression (Appelhans et al. 2012), mood/anxiety disorders (Bodenlos et al. 2011), and existing health conditions, such as diabetes (Blazer et al. 2002). While the physiological effects of each of these conditions affect eating behaviors directly, medications prescribed to treat these conditions also alter feelings of hunger and satiety (Bodenlos et al. 2011). The relationship between mental health conditions, obesity, and diet are complicated by the use of medication. Results are mixed, indicating that diet may (Appelhans et al. 2012) or may not (Beydoun and Wang 2009) mediate the relationship between depression and obesity.

Physical activity directly affects obesity by increasing the amount of calories burned. Many studies focus on obesity rates among adolescents because physical activity is often regimented through school and relatively standard among age groups (Harris et al. 2009). Physical activity for adolescents is a requirement for most students (physical education classes) and a wide variety of sports or physically demanding extracurricular activities are generally offered to students through their schools as afterschool programs. Because physical activity is so structured for adolescents, policy changes and implications are relatively straightforward.

Studies that explore the physical activity and obesity relationship among adolescents often incorporate many of the same predictors that are used in diet studies (Appelhans et al. 2012; Beydoun and Wang 2009; Dockray, Susman, and Dorn 2009; Brosnahan et al. 2004). Many of the physical activity studies have been carried out by researchers using large datasets, clinical trials, and experimental/control groups comparisons. Not all studies, however, have found physical activity to be a significant factor in the obesity/depression relationship however (Dockray et al. 2009).

Many of the studies that include diet also include physical activity. Both factors alter caloric intake immediately and directly affect an individual's weight and obesity classification. Statistically, both diet and physical activity are often included as mediators between key independent variables and the obesity outcome (Appelhans et al. 2012; Davis and Cooper 2011; Beydoun and Wang 2009).

Because obesity is a condition that is physically apparent, body image and individual self-concept become important issues and are often the topic of sociological and psychological obesity research (Schwartz and Brownell 2004). Western culture has idealized thinness and stigmatized individuals with excess weight. The effects of body image dissatisfaction are emotional, biological, and physiological changes that can lead to increased eating (Schwartz and Brownell 2004). Schwartz and Brownell (2004) explain that meta-analyses indicate that the first generation of body image studies found a large statistical effect size between obesity and body image, although new body image studies have begun to specify risk factors more clearly.

Social-Environmental Influences of Obesity

Underlying the issues of diet and physical activity are the social-structural issues that inform these specific behaviors. Much of the obesity literature focuses on the "built environment" that an individual is placed within and how aspects of that environment influence obesity rates between populations (Black and Macinko 2008; Booth et al. 2005). The social-structural factors that influence individual diet and eating habits include parental eating habits (Martin 2008), peer group eating habits (Cohen-Cole and Fletcher 2008), availability of food (Morland and Evenson 2009; Black and Macinko 2008), and a wide variety of additional environmental factors (Booth et al. 2005). Socioeconomic status (SES) plays an important role in these studies because there is a clear link between individual income, neighborhood poverty rates, and obesity (Beydoun and Wang 2010; Chang and Lauderdale 2005). Even after controlling for individual SES, studies have consistently found a relationship between living in poor neighborhoods and higher rates of obesity (Morland and Evenson 2009).

Studies that seek to establish a relationship between environmental contexts and obesity often use neighborhoods as the unit of analysis instead the individual, and conduct analyses using Census data in conjunction with additional aggregated data (Booth et al. 2005). Neighborhoods affect both eating and exercise habits in a variety of ways. Availability of food, especially fresh food from grocery stores, has a significant association with obesity rates. Studies show healthy foods in poor neighborhoods are less readily available and more expensive than in wealthier communities (Cummins and Macintyre 2006). Some researchers have found that poor neighborhoods in urban settings, where large supermarkets are rare and instead replaced by small family-owned

groceries, generally have a limited selection of food that is also more expensive (Morland, Diez-Roux, and Wing 2006). Places with limited access to healthy food are known as "food deserts." Food deserts are present in both extremely urban and extremely rural settings, although the term is primarily associated with urban settings (Morton and Blanchard 2007).

Type and quality of neighborhood can also directly impact physical activity rates. Neighborhood factors associated with physical activity include perceived safety (Burdette and Whitaker 2003), presence of sidewalks (Giles-Corti et al. 2003), perceived walkability (Saelens et al. 2003), and population density (Ewing et al. 2003). The physical structures that make up the built environment innately promote or inhibit physical activity based on the city's design, appearance, and layout (Black and Macinko 2008). Densely populated areas often require an efficient land use strategy, where physical space for leisure activities is scarce. These areas often have limited amenities and green space, which also serve as deterrents to physical activity (Black and Macinko 2008).

Socioeconomic status (SES) is particularly important because of its direct and indirect effect on individual physical activity and diet. While some studies find significant relationships between obesity and neighborhood structures independent of individual SES (Morland and Evenson 2009), most researchers agree that there is a significant link between neighborhood type and individual income level, occupation, and educational attainment (Beydoun and Wang 2010; Black and Macinko 2009; Chang and Lauderdale 2005). With healthier food sometimes available only at higher prices in urban

settings, SES directly affects obesity rates by limiting residents to inexpensive but high-calorie, high-fat foods (Bowman and Vinyard 2003).

While eating habits and physical activity directly affect obesity through caloric intake and expenditure, an individual's tendency to be physically active or eat healthy are often guided by much less apparent social forces. The physical environment and neighborhood an individual lives in limits the scope of available activities and food choice, all of which is also attributed to socioeconomic status. Among adolescents, the role the parents serve in creating the immediate environment for their children is an additional component to the built environment (Martin 2008). Adolescent obesity researchers have found strong connections between parents' and children's food choices, eating frequency, leisure time activities, and rates of physical activity (Martin 2008).

Socioeconomic status is a critically important predictor when studying obesity because of the breadth of its influence on individual obesity rates. It can be used to approximate a variety of differences between individuals that affect physical activity and eating habits, two factors that have the most direct and immediate effect on obesity. This study will explore obesity using socioeconomic status as a focal point, but it seeks also to determine the extent to which genetic predispositions influence obesity.

CHAPTER III

Theoretical Framework

The vast majority of gene-by-environment studies seek to explain the extent to which particular gene variants magnify the relationships between environmental factors and various outcomes (Freese 2008). These gene variants have been predominantly conceptualized as "risk alleles," genetic variations that increase an individual's *vulnerability* to environmental influence (Simons et al. 2011). Recent research, however, has sought to reshape the theoretical relationship between genes (as risk alleles) and various outcomes by instead conceptualizing genes as "plasticity alleles," gene variations that increase an individual's *susceptibility* to environmental influence (Belsky et al. 2009). The difference is subtle, but important.

Genetic vulnerability means that individuals with risk alleles are prone to succumbing to negative outcomes given a negative social environment. This model has a variety of names, including the diathesis-stress model (by psychiatrists) and the transactional or dual-risk model (by developmentalists) (Belsky and Pluess 2009). The diathesis-stress model has informed virtually all psychiatric research and been the predominant orientation of genetic researchers working in gene-by-environment studies (Belsky et al., 2009). To some extent the diathesis-stress model had not been thoroughly explored simply due to the tendencies of researchers to focus on negative outcomes. In other words, "vulnerability" adequately explained research findings and lent itself well to policy discussions about individuals experiencing negative outcomes.

In 1997, Jay Belsky proposed the notion of differential susceptibility, an expansion of the vulnerability framework. Differential susceptibility is the notion that

some individuals have inherent predispositions either to amplify or buffer the effects of environmental influences on outcomes depending on the characteristics of an individual's environment (Belsky and Pluess 2009). Both vulnerability and susceptibility theories agree that individuals with risk alleles in negative environments have negative social outcomes, but differential susceptibility would also suggest that those in positive environments also have more positive social outcomes as well. Applying differential susceptibility in the case of the obesity, individuals with specific serotonin and dopamine transporter gene alleles may be either at a greater risk of obesity if the social-environmental conditions that promote obesity are present or at a further decreased risk if the conditions are favorable for deterring obesity.

Belsky et al. (2009) have cited numerous studies that validate differential susceptibility theory in opposition to the prevailing diathesis-stress model, one of which is particularly relevant to this study. Simons et al. (2011) used the DRD4 and 5-HTT gene alleles to explain how differential susceptibility informs individual differences in feelings of aggression. Here the low-activity serotonin transporter allele (short allele 5-HTT) is linked to changes in psychological function, including increased antisocial behavior leading to a propensity to engage in aggressive behavior in an adverse environment and decreased aggression in favorable social environments.

One goal of the current study is evaluate both differential susceptibility and diathesis-stress models using obesity as an outcome variable and various gene alleles as risk/plasticity factors. Socioeconomic status, measured using educational levels, is anticipated to be an important predictor of obesity. Exploring the interaction between socioeconomic status and serotonin-related gene alleles and their effects on obesity will

help to further distinguish the nature of genetic predispositions and contribute to the growing theoretical discussion.

CHAPTER IV

Research Questions

The research questions to be addressed in this study are:

1. *How can genetics be incorporated in social research and tested statistically?*
2. *Does the incorporation of MAOA and 5-HTT plasticity/risk alleles into models significantly aid in the understanding of obesity and its predictors?*
3. *Do MAOA and 5-HTT gene alleles relate to obesity in the same way?*
4. *Does the relationship between obesity, socioeconomic status, and either gene allele lend itself to differential susceptibility and/or diathesis-stress frameworks?*

The overarching goal of this study is creating a more parsimonious model of obesity for future social research. Sociological research predominantly focuses on the effects of social and environmental stressors on outcome. The goal at present is to develop a better model by including genetic variables that are already studied outside of sociology. The relationship between obesity and both the genetic and social-environment variables have been previously established in a broad field of interdisciplinary literature, but they are not often combined and analyzed together.

The sociological focus on the built environment is vitally important to obesity literature. Neighborhoods can promote or inhibit physical activities and control access to food type and quality based on land use, city design, urban sprawl, degradation, wealth, and safety. Wealth, denoted by individual socioeconomic status in this case, is often the key characteristic that distinguishes neighborhoods from one another, because it serves as a proxy for many of the additional factors.

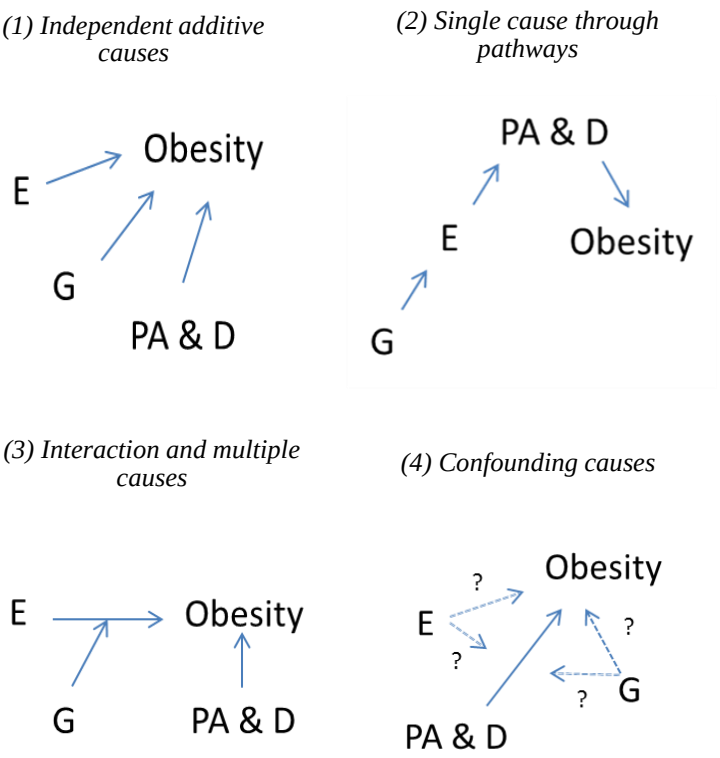

Figure 1. Potential relationships between predictors and obesity outcome (adapted from Freese 2008). "E" indicates environmental factors. "G" indicates genetic traits and characteristics. "PA" and "D" stand for physical activity and diet respectively.

The first research question is an important starting point for gene-by-environment studies. Figure 1 suggests four possible orientations to use for exploring the relationships between factors associated with obesity. Each model has practical implications when it comes to determining the specific type of analysis used to explore obesity. Models 1, 2, and 3 can all be tested using various statistical procedures. Model 4 depicts an important relationship that researchers must also consider after analyses have been performed. Researchers too often focus on their specific predictors of interest and do not adequately acknowledge the potential influence of unobserved variables (Freese 2008). Model 2, depicting obesity as the outcome of a series of intervening factors through a single

pathway, would require a path analysis technique (or more likely structural equation modeling due to latent constructs). The current study will test and evaluate Model 1 and Model 3, which can be done using regression techniques.

The second and third research questions regard the role MAOA and 5-HTT alleles play in the more broad obesity context. It is anticipated that both the MAOA and 5-HTT low-activity (short) alleles will be associated with higher rates (or odds) of obesity and overweightness, but the exact relationship is yet to be determined. Previous research has established significant links between both alleles and obesity, but recent research has provided additional insight into the subtle nature of gene interaction. Harris and colleagues (2013) explain that additive gene models (such as Model 1) are at odds with much of what the most current genetic studies have uncovered. Such designs should hypothetically fail to find a significant relationship between gene alleles and outcome variables outright because the nature of gene-by-environment interactions *should* be nuanced (Harris et al., 2013). Statistically significant associations between genes and outcomes like obesity may actually be attributed to a spurious relationship driven by unobserved variables, (Model 4) an important consideration that researchers must make when working with genetic variables (Freese 2008).

The final research question is an evaluation of both prevailing theories in gene-by-environment studies, diathesis-stress and differential susceptibility. The evaluation will focus on socioeconomic status to see if individuals with low activity plasticity/risk alleles have higher obesity rates among low SES (relative to those without the alleles), lower obesity rates when SES is high (relative to those without the alleles), or both.

CHAPTER V

Methodology

Data

This study employs various statistical techniques to better understand the relationship between social-environmental factors, genetics, and obesity among adults. The research questions will be tested using data from the National Longitudinal Study of Adolescent Health (Add Health). The Add Health study is a longitudinal cohort study conducted by the University of North Carolina at Chapel Hill. The study population is a nationally representative sample of over 20,000 individuals who were in grades 7 to 12 during 1994-95 in the United States.

The longitudinal cohort completed in-home interviews at four different time points (Wave I: 1994-95, Wave II: 1995-96, Wave III: 2001-02, and Wave IV: 2007-08). In addition to the in-home interview portion of the study, a variety of supplemental data were collected at each wave. At Wave III, a saliva sample used for DNA analysis was collected from a sub-sample of individuals identified as twins or full siblings at earlier waves. At Wave IV, the majority of remaining Add Health participants submitted DNA for genotyping. Analysis for this study is based on the Wave IV data (N=15,701).

Variables – Dependent Measure

The dependent variable is obesity, indicated using a BMI score calculation (weight in kilograms divided by height in meters squared). The standard definition and official classification of "obese" according to the Center for Disease Control and the World Health Organization is a raw BMI score of 30 kg/m^2 or above. This study will employ the BMI raw score measurement. The final obesity measure is dichotomous,

coded (0) normal weight (<30 kg/m^2) and (1) obese (≥30 kg/m^2). Analysis will also explore how predictors function using a dichotomous "overweight + obesity" variable as well using a BMI of 25 kg/m^2 or above as a cutoff point.

Variables – Key Independent Measures

Gene Alleles

Genetic data were collected and analyzed using respondent's saliva. Polymorphisms within five candidate genes were identified using a buccal sampling and DNA extraction procedure, where the salivary buccal cells containing DNA were isolated and genotyped (Harris et al. 2006). Included in the five genes are two of the polymorphisms described earlier that are particularly relevant to obesity: a 43-basepair insertion/deletion polymorphism (5-HTTLPR) in the promoter of the serotonin transporter (SLC6A4), and a 30-basepair VNTR polymorphism in the promoter of the monoamine oxidase A (MAOA) gene. Both of these genes will be used in obesity analysis independently, but also in conjunction as a single cumulative plasticity allele.

Both the MAOA and 5-HTT variables will be created using framework established in previous research (Fuemmeler et al. 2008; Hu et al. 2005; Sabol et al. 1998). The MAOA alleles will be classified into two groups: low activity (3 repeats of the 30-bp sequence) and high activity (3.5 or 4 repeats). MAOA is a sex-linked gene allele located on the X-chromosome, meaning that males only have a single copy while females have two. To be considered in the low activity MAOA group, individuals must have any short allele (S for males, S/S or S/L for females). The final MAOA variable is coded (0) high activity (having only long alleles) and (1) low activity (having any combination of short alleles).

The 5-HTT polymorphism will consist of three classifications based on short or long lengths of alleles: S/S, S/L, and L/L. The 5-HTT short alleles are the gene variations with 14 repeats of the 43-bp sequence whereas the long alleles have 16 repeats. As previously mentioned, extra-long alleles were also genotyped (anywhere from 17 to 22 repeats) but insufficient information exists as to the role and function of these gene variations. An extremely small portion of the sample was found to possess any extra-long 5-HTT alleles (N=116), so these individuals were excluded from the analysis. Both males and females inherit two copies of the gene. The categories will be regrouped in a process similar to that in the process of creating the MAOA variable, where low activity 5-HTT is defined as the presence of any short allele combination and high activity is the presence of only long alleles. The final 5-HTT variable is coded (0) high activity (L/L only) and (1) low activity (S/S or S/L).

Low activity MAOA and 5-HTT alleles have been associated with higher rates of obesity in past research (Fuemmeler et al. 2009; Fuemmeler et al. 2008; Need et al. 2005; Camarena et al. 2004). It is this particular variation of the gene that is referred to as the risk/plasticity (R/P) allele. Using the traditional diathesis-stress model, these low activity alleles are risk alleles. In the case of obesity, these alleles would be exacerbating only the negative effects of an individual's environment, and in turn, increasing risk of obesity. In terms of differential susceptibility, the low activity allele is a plasticity allele and may be responsible for both increased risk of obesity (given an obesity-prone environment) *and* a decreased risk of obesity (given an obesity-deterring environment).

Social-Environmental Variables

The relationship between socioeconomic status and obesity is well established. It remains one of the most important predictors of obesity in sociological obesity studies, and it is the key predictor of obesity in this study as well. Socioeconomic status is generally denoted by some combination of income, education, and/or occupational measures. A variety of composite indices have been created to best measure this concept, such as Duncan's index (occupation by income/education), material deprivation, and the Living Conditions Index (see Fotso and Kuate-defo 2005 for a full discussion of socioeconomic measures). One difficulty of creating SES indices is the combination of multidimensional variables. There is a general lack of consensus on how to weight and aggregate measures, which in turn produces a wide range of personalized measures, each very different from the next (Krishnan 2010).

Using income and education variables, a generic SES composite measure was initially created. The first issue with this particular measure was the combination of different levels of measurement. Education is not technically continuous, but is instead grouped into 13 brackets ranging from less than 8^{th} grade education to post-bachelor's professional degree. The measure was simply the summation of both variables after each had been standardized (using z-scores). Unfortunately the standardized education and income measures did not converge well. While there was a significant correlation between measures, it was very weak (r = .174) and the composite measure itself had very weak reliability (Cronbach's α = .297). Both income and education were included in logistic regression models, but used separately and without standardization or modification. In goodness-of-fit analysis, education and income were recoded into

grouped variables: education based on practical cut points (i.e. highschool, associate's degree, college graduate, etc) and income based on quintiles.

Metabolic Modifiers – Physical Activity and Eating Habits

Physical activity was based on a self-reported recollection of the activities individuals engaged in over the course of the previous week. The 7-day recall methodology is a standardized method of measuring physical activity that has been used and validated in many large-scale studies (Nelson et al. 2006). Godin and Shepard (1985) created a specific questionnaire to be used for the purpose of physical activity analysis using 7-day recall and measuring energy output. Activities, such as running, yoga, or playing particular sports, are filtered into groups based on the amount of energy expended in each activity. In the end, all activities are reclassified as being strenuous, moderate, or mild forms of exercise. Each category is assigned a specific metabolic equivalent (MET) value used to approximate how many calories were spent through physical activity: 9 METs for strenuous, 5 METs for moderate, and 3 METS for mild (Godin and Shepard 1985) .

Add Health contains eight questions that ask respondents about physical activity habits in a 7-day recall format. Each group was assigned a MET value and an index was created through summation of all measures. The resulting leisure-time activity scale was continuous, with values ranging from 0 to 301. Three categories were created from the scale based on the individual's level of activity (related to health benefits): low, moderate, or high. Two dummy variables (low activity and moderate activity) were created, using high activity as a reference category simply due to most individuals indicating that they engage in high amounts of physical activity.

Very few questions inquired about respondent's eating habits in Wave IV of the Add Health study. Only one question was relevant to this study, and it asked individuals to recall how on how many occasions they had eaten fast food in the past week. Other eating measures included frequency of soda and/or diet soda consumption; however these were not included for this analysis. Only the fast food measure will be used for this study.

Controls

Both sex and race/ethnicity were controlled for in this study, with females and those who identified as white non-Hispanic as reference groups. In addition, neighborhood type was also controlled for (rural, suburban, or urban). The physical environment has proved important in past obesity studies and will be accounted for here as well (Black and Macinko 2008; Burdette and Whitaker 2003).

Analysis and Procedure

The Add Health sample was the product of a stratified random sampling technique that used 80 clusters based on region, urbanicity, school size, school type, and racial/ethnic composition to obtain a representative sample (Chantala and Tabor 1999). This cluster sampling survey method selected individuals with an unequal probability of selection. To ensure that the sample and analysis results remain representative, researchers working with Add Health data must use multiple sample weights (individual, region, and cluster). Software packages like SPSS and SAS are unsuited for analyses runs using multiple weights. Using these more common software packages would result in biased estimates (Chantala and Tabor 1999). Stata (v.12) was used for this study as it allows for the use of multiple weights (Chantala and Tabor 1999).

Analysis began with a univariate analysis of all study variables. Bivariate analyses, focusing on relationships between obesity, socioeconomic status, and gene alleles, will then help to establish preliminary relationships between our outcome measure and predictors of interest. The core of the analysis will be conducted using a binary logistic regression technique predicting the odds of obesity among study participants. Use of interaction terms will also be employed in an effort to capture the nuanced gene-by-environment relationship that is anticipated. Lastly, chi-square goodness-of-fit tests will be used to see how the distribution of obese individuals into socioeconomic status groups varies based on risk/plasticity alleles.

CHAPTER VI

Results

Table 1. Descriptive Statistics

	Percentage/Mean	S.E.	Variable n
Controls:			
Male	50.7%	---	14,800
White (reference)	67.1%	---	14,408
Black	15.4%	---	14,408
Hispanic	12.3%	---	14,408
Asian	3.0%	---	14,408
Multiracial	1.8%	---	14,408
Neighborhood:			
Suburban (reference)	45.1%	---	12,803
Urban	32.6%	---	12,803
Rural	22.4%	---	12,803
Socioeconomic Status:			
Income	$34,593	911.87	14,066
Education	5.53	.086	14,796
Physical Activity and Diet:			
High activity (reference)	49.5%	---	14,780
Moderate activity	15.3%	---	14,780
Low activity	35.2%	---	14,780
Fast food frequency (week)	2.36	.062	14,720
MAOA Gene:			
Low activity (R/P) allele	49.5%	---	13,590
5-HTTLPR Gene:			
Low activity (R/P) allele	66.5%	---	13,978
Obesity (≥30kg/m^2):			
Obese	31.9%	---	14,568
Overweight+Obesity (≥25kg/m^2):			
Overweight+	63.8%	---	14,573

Descriptive statistics in Table 1 indicate that demographically the sample is evenly split male and female, and over two-thirds of the population identify as white non-Hispanic. Most respondents live in suburban neighborhoods (45.07%), followed by urban

Table 2. Obesity and Overweight+Obesity by MAOA Gene Alleles

	MAOA Alleles	
	Low Activity (R/P)	High Activity (No R/P)
(0) Not Obese	67.21%	69.12%
(1) Obese	32.79%	30.88%

Differences between low activity and high activity for obese: $\chi^2 = 5.6572$; $F=3.117$ ($p < .10$)

(0) Not Overweight	35.90%	35.30%
(1) Overweight	64.10%	64.70%

Differences between low activity and high activity for overweight: $\chi^2 = 0.6130$ (not sig)

residential (32.58%) and then a rural setting (22.35%). In terms of socioeconomic status, average income for respondents is about $35,500 annually and average education (5.53) falls midway between the (4) and (5) groups: some college/completion of an Associate's degree and college graduate. Nearly half of all respondents reported engaging in vigorous physical activity, although 35% of the remaining individuals reported little to no activity at all. On average, respondents ate out at fast food restaurants about twice per week.

A large change in the proportion of people who are classified as obese versus overweight is apparent here as well. A substantial majority of respondents are considered overweight (63.84%) whereas only about 32% are considered obese, meaning that nearly a third of all individuals fall between the 30 kg/m^2 and 25 kg/m^2 BMI thresholds. The sample is evenly split for low activity (risk/plasticity) and high activity MAOA alleles, although two-thirds of the sample possess the 5-HTT risk/plasticity allele.

Table 3. Obesity and Overweight+Obesity by 5-HTTLPR Gene Alleles

	5-HTT Alleles	
	Low Activity (R/P)	High Activity (No R/P)
(0) Not Obese	67.79%	68.11%
(1) Obese	32.21%	31.89%

Differences between low activity and high activity for obese: $\chi^2 = 0.1370$; F=0.087 (not sig)

(0) Not Overweight	36.12%	35.79%
(1) Overweight	63.88%	64.21%

Differences between low activity and high activity for overweight: $\chi^2 = 0.1447$; F=0.054 (not sig)

Table 4. Obesity by Cumulative Risk/Plasticity Allele Measure

	Risk/Plasticity Allele Combinations				
	Both	MAOA	5-HTT	Neither	Total
(0) Not Obese	67.54%	66.50%	68.57%	70.38%	68.17%
(1) Obese	32.46%	33.50%	31.43%	29.62%	31.83%

Differences between allele combinations for obesity: $\chi^2 = 8.8012$; F=1.548 (not sig)

Table 3 reveals that the association between the 5-HTT risk/plasticity allele and both overweight and obesity weight classifications is not significant. Table 2 however indicates that the relationship between MAOA risk/plasticity alleles and obesity is marginally significant however ($p<.10$) and in the anticipated direction. Individuals with the MAOA risk/plasticity allele were about 2% more likely to report being obese.

Table 5. Overweight+Obesity by Cumulative Risk/Plasticity Allele Measure

	Risk/Plasticity Allele Combinations				
	Both	MAOA	5-HTT	Neither	Total
(0) Not Overweight	36.86%	35.31%	35.58%	37.03%	36.17%
(1) Overweight	63.14%	64.69%	64.42%	62.97%	63.83%

Differences between allele combinations for overweight: $\chi^2 = 2.990$; F=0.517 (not sig)

Both genes were used in tandem as a cumulative plasticity allele to explore associations with overweight and obesity. Tables 4 and 5 indicate that no significant difference exists between weight status based on the combination of MAOA and 5-HTT risk/plasticity alleles an individual has. In other words, having additional low activity alleles is not associated with an increase or decrease in either weight status.

Table 6 reveals a number of important predictors of obesity and overweight. In both cases, odds of obesity or overweight were significantly predicted by race/ethnicity , type of neighborhood, educational level, physical activity, and having the MAOA plasticity allele. Individuals who identified as black or Hispanic were 54.7% and 43.7% more likely to be obese respectively, while those who identified as Asian were 37.1% less likely to be considered obese compared to white. Individuals living in rural settings were 41.3% more likely to have been classified as obese compared to those living in a suburban environment. Respondents with the MAOA risk/plasticity allele were 10-11% more likely to be obese or overweight. This finding was significant for overweight+obese, but only marginally significant in the case of obesity.

Table 6. Logistic Regression Models Predicting Odds of Obesity and Overweight+Obesity

	Obesity (n = 10,691)		Overweight (n = 10,694)	
	OR	*SE*	*OR*	*SE*
Controls				
Male	0.971	.0743	1.723***	.1114
White	---	---	---	---
Black	1.547***	.1382	1.668***	.1525
Hispanic	1.437***	.1315	1.546***	.1405
Asian	0.629*	.1223	0.607*	.1231
Multiracial	1.203	.2878	0.958	.1815
Neighborhood				
Suburban	---	---	---	---
Urban	1.047	.0693	0.938	.0699
Rural	1.413***	.1020	1.269**	.0952
SES				
Income	0.999	.0000	0.999	.0000
Education	0.938***	.0135	0.936***	.0130
Physical Activity				
High activity	---	---	---	---
Mod. activity	1.173†	.0954	1.011	.0890
Low activity	1.402***	.0919	1.241***	.0813
Fast Food	0.998	.0120	0.974*	.0099
Risk/Plasticity Alleles				
MAOA	1.102†	.0634	1.111*	.0535
5-HTT	1.058	.0536	1.036	.0699

† $p \leq .10$, * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$

Sex was not a significant predictor of obesity, but was one of the strongest predictors of overweight. Males were 72.3% more likely than females to be considered overweight. In addition, the frequency of fast food consumption was a significant predictor of overweight but not obese. An inverse relationship between fast food consumption and overweight exists here which was not anticipated.

Table 7. 5-HTT Allele Interaction Models Predicting Odds of Obesity and Overweight+Obesity

	Obesity (n = 13,761)		Overweight (n = 13,379)	
	β	*SE*	*β*	*SE*
Education	-0.063**	.0205	-0.081**	.0232
5-HTT	0.256†	.1908	0.704	.1760
Education x 5-HTT	-0.045†	.0846	-0.015	.0282
Constant	-0.413		1.034	

† p ≤ .10, * p ≤ .05, **p ≤ .01, ***p ≤ .001

Table 8. MAOA Allele Interaction Models Predicting Odds of Obesity and Overweight+Obesity

	Obesity (n = 13,379)		Overweight (n = 13,386)	
	β	*SE*	*β*	*SE*
Education	-0.972***	.0154	-0.063***	.0174
MAOA	0.029	.1273	0.297*	.1729
Education x MAOA	0.013	.0706	-0.053*	.0214
Constant	-0.285		0.924	

† p ≤ .10, * p ≤ .05, **p ≤ .01, ***p ≤ .001

Interaction models were used to explore the potential nuanced relationship between socioeconomic status, plasticity genes, and weight status. Table 7 indicates marginally significant interaction between 5-HTT risk/plasticity alleles and education when used to predict the odds of obesity. No significant interaction exists when predicting overweight. Table 8, using the MAOA risk/plasticity allele, depicts a relationship opposite to what is found with 5-HTT alleles. A significant interaction term was found when using education and MAOA risk/plasticity interaction to predict overweight, but not obesity. In both cases where the interaction terms were significant, the interaction term itself provided a slight decrease to obesity or overweight, but the net overall effect of the gene alleles was an increase in obesity rates.

Table 9. Male Only Models Predicting Odds of Obesity and Overweight+Obesity

	Obesity (≥ 30 kg/m^2)		Overweight (≥ 25 kg/m^2)	
	OR	*SE*	*OR*	*SE*
Controls				
White	---	---	---	---
Black	1.002	.1314	1.169	.1532
Hispanic	1.450**	.1734	1.485**	.2111
Asian	0.882	.2253	0.678	.1779
Multiracial	1.431	.3947	1.308	.4181
Neighborhood				
Suburban	---	---	---	---
Urban	0.949	.1086	0.878	.0972
Rural	1.322**	.1249	1.177	.1234
SES				
Income	1.000	.000	1.000	.0000
Education	0.955*	.0191	0.978	.0222
Physical Activity				
High activity	---	---	---	---
Mod. activity	1.151	.1458	0.802†	.1049
Low activity	1.538***	.1301	1.234*	.1247
Fast Food	0.994	.0156	0.965**	.0127
Risk/Plasticity Alleles				
MAOA	1.189*	.0921	1.105	.0890
5-HTT	0.961	.0793	0.918	.0890

† p ≤ .10, * p ≤ .05, **p ≤ .01, ***p ≤ .001

Due to the significance of sex as a predictor of overweight+obese, but not solely obesity, in the logistic regression models, separate sex models were additionally run. Table 9 contains the results of the male-only model predicting obesity. Hispanic males were 45% more likely the report being obese compared to white males, and Hispanic race/ethnic identification was significant in predicting both obesity and overweight. Additional predictors of odds of obesity were rural (versus suburban), education, low physical activity (versus high) and possessing the MAOA

Table 10. Female Only Models Predicting Odds of Obesity and Overweight+Obesity

	Obesity (≥ 30 kg/m^2)		Overweight (≥ 25 kg/m^2)	
	OR	*SE*	*OR*	*SE*
Controls				
White	---	---	---	---
Black	2.340***	.2805	2.333***	.2492
Hispanic	1.455**	.1993	1.618**	.2438
Asian	0.396***	.1116	0.523*	.1545
Multiracial	0.973	.3856	0.717	.2044
Neighborhood				
Suburban	---	---	---	---
Urban	1.173†	.1100	1.020	.0861
Rural	1.465***	.1524	1.349**	.1389
SES				
Income	0.999***	.0000	0.999***	.0000
Education	0.929***	.0201	0.906***	.0155
Physical Activity				
High activity	---	---	---	---
Mod. activity	1.154	.1462	1.206	.1414
Low activity	1.236*	.1229	1.225*	.0969
Fast Food	1.006	.0155	0.991	.0135
Risk/Plasticity Alleles				
MAOA	1.023	.0817	1.125	.0872
5-HTT	1.177*	.0898	1.161†	.0922

† $p \leq .10$, * $p \leq .05$, **$p \leq .01$, ***$p \leq .001$

risk/plasticity allele. Besides Hispanic racial/ethnic status, only physical activity differences and fast food consumption predicted odds of overweight among males.

Logistic regression models for females indicate strikingly different results. Significant predictors of odds of obesity and overweight include: race/ethnicity (black, Hispanic, Asian), rural neighborhood (versus suburban), income, education, low physical activity (versus high), and possessing the 5-HTT risk/plasticity allele. African American females were more than twice as likely to be classified obese than white females. At the

Table 11. Differences in the Distribution of Only Obese Individuals with 5-HTT and MAOA Risk/Plasticity Alleles by Education (Goodness-of-Fit Test)

Education	5-HTT		MAOA	
	R/P Allele	*No R/P Allele*	*R/P Allele*	*No R/P Allele*
Less than HS	10.4%	9.3%	9.1%	10.7%
Highschool	20.4%	18.9%	18.8%	20.9%
Associates	48.7%	49.5%	49.9%	48.3%
Bachelors	13.5%	14.3%	14.5%	13.2%
Masters	5.4%	6.1%	5.9%	5.0%
PhD or Professional	1.6%	1.9%	1.7%	1.8%
Total N	2911	1573	2317	2023

5-HTT:χ^2 = 13.1674; F=1.008 (not sig); MAOA:χ^2 = 29.4897; F=0.455 (not sig)

same time, Asian females were about 60% less likely to be classified obese than white females. Women living in a rural environment were disproportionately more obese. For obesity, living in an urban environment was also a marginally significant predictor.

Physical activity rates were the strongest predictors of obesity and overweight odds for men, but were one of the weakest for females. Females who reported low levels of physical activity were between 22 and 24% more likely to be classified overweight or obese respectively. MAOA risk/plasticity alleles did not significantly predict odds of either weight status for women, but 5-HTT alleles did. Women with the 5-HTT risk/plasticity allele were 17.7% more likely to be classified obese and 16.1% more likely to be classified overweight (although 5-HTT was marginally significant in the overweight model).

In order to compare and contrast the different theoretical frameworks, the effects of risk/plasticity alleles on obesity needed to be examined more closely. Table 11 displays the distributions of obese individuals only, broken down into groups based on risk/plasticity allele possession and grouped education levels. In order for results to

Table 12. Differences in the Distribution of Only Obese Individuals with 5-HTT and MAOA Risk/Plasticity Alleles by Income (Goodness-of-Fit Test)

	5-HTT		MAOA	
Income (Quintiles)	*R/P Allele*	*No R/P Allele*	*R/P Allele*	*No R/P Allele*
Q1 ($0-10,500)	22.9%	21.8%	25.1%	20.3%
Q2 ($10,501-25,000)	22.6%	29.3%	26.9%	22.4%
Q3 ($25,001-35,000)	19.9%	18.6%	19.2%	19.6%
Q4 ($35,001-50,000)	19.8%	15.9%	16.2%	20.9%
Q5 ($50,001+)	14.7%	14.3%	12.6%	16.9%
Total N	2783	1497	2205	1944

5-HTT:$\chi^2 = 87.3090$; $F=4.305$ ($p < .01$); MAOA:$\chi^2 = 152.3963$; $F=5.984$ ($p < .001$)

support a diathesis-stress model, individuals with the low activity *risk* alleles should have significantly higher obesity rates than those without it in the lower education brackets. At the same time, individuals with higher education levels in either allele group should have nearly identical distributions. This would indicate that having a risk allele results in vulnerability to obesity among the less educated, or that only the individuals with either MAOA or 5-HTT alleles are more prone to becoming obese but are unaffected by factors that would deter obesity.

The alternative interpretation posited by differential susceptibility advocates is that *plasticity* alleles affect individuals on both ends of the spectrum. In other words, having a MAOA or 5-HTT plasticity allele would make an individual more susceptible to the negative forces that increase obesity, but also less susceptible when the positive forces that discourage obesity are present. Unfortunately, Tables 11 indicates that no significant differences were found in the distributions of obese individuals into educational groups based on either MAOA or 5-HTT risk/plasticity alleles.

Table 13. Males Only: Differences in the Distribution of Only Obese Individuals with 5-HTT and MAOA Risk/Plasticity Alleles by Income (Goodness-of-Fit Test)

	5-HTT		MAOA	
Income (Quintiles)	*R/P Allele*	*No R/P Allele*	*R/P Allele*	*No R/P Allele*
Q1 ($0-10,500)	13.3%	13.3%	17.1%	11.4%
Q2 ($10,501-25,000)	18.6%	24.5%	24.1%	17.8%
Q3 ($25,001-35,000)	20.2%	18.7%	17.4%	20.7%
Q4 ($35,001-50,000)	24.7%	20.2%	18.5%	26.2%
Q5 ($50,001+)	23.2%	23.4%	22.9%	23.9%
Total N	1259	642	754	1105

5-HTT: $\chi^2 = 86.7449$; $F=1.732$ (not sig); MAOA: $\chi^2 = 260.7320$; $F=3.935$ ($p < .01$)

Using income (in quintiles) as an indicator of socioeconomic status and repeating the same procedure produced a very different result. Table 12 shows the differences in the distribution of obese individuals based on income and risk/plasticity alleles. Those with 5-HTT risk/plasticity alleles had significantly higher rates of obesity in all income brackets with the exception of the $10,501 to $25,000 income bracket. That particular income bracket also has the greatest difference in the distributions of individuals, 29.3% obesity in the no risk/plasticity allele group compared to only 22.6% in the risk/plasticity group. Results also indicate that individuals with the MAOA risk/plasticity allele were significantly more obese in lower income brackets *and less* obese at higher incomes than those without the allele.

While education was a significant predictor in nearly every model of obesity or overweight, income was only significant in the female model. Due to the important role gender may play, male-only and female-only distributions were also created. Table 13 displays the results of the male only distributions of obese individuals based on income and risk/plasticity allele. Results are similar to those found in the male only logistic

Table 14. Females Only: Differences in the Distribution of Only Obese Individuals with 5-HTT and MAOA Risk/Plasticity Alleles by Income (Goodness-of-Fit Test)

	5-HTT		MAOA	
Income (Quintiles)	*R/P Allele*	*No R/P Allele*	*R/P Allele*	*No R/P Allele*
Q1 ($0-10,500)	32.2%	29.5%	30.2%	33.7%
Q2 ($10,501-25,000)	26.5%	33.7%	28.6%	29.4%
Q3 ($25,001-35,000)	19.8%	18.5%	20.3%	17.8%
Q4 ($35,001-50,000)	15.0%	12.2%	14.8%	12.9%
Q5 ($50,001+)	6.5%	6.1%	6.2%	6.2%
Total N	1524	855	1451	839

5-HTT:χ^2 = 87.1677; F=2.192 (p < .10); MAOA:χ^2 = 33.1693; F=0.734 (not sig)

regression models, where MAOA, but not 5-HTT, plays a significant role. In this case, obese males with the MAOA risk/plasticity allele were disproportionally overrepresented in the low income quintiles and disproportionally underrepresented at the highest incomes. The distributions of obese males based on 5-HTT in were not significantly different.

Results of the female only models in Table 14 also mirror the relationships established in the female only logistic regression models. Findings indicates that obese females with the 5-HTT risk/plasticity allele had a marginally significant overrepresentation in all income brackets relative to those without the allele except the $10,501 to $25,000 income bracket, which was found in the non-gender specific model as well. Obese females with the MAOA risk/plasticity allele were not significantly difference that those without the allele in their distribution among income quintiles.

CHAPTER VII

Discussion

Weight Status and Gene Alleles

Statistical analysis of obesity and overweight+obese established sociological predictors, and their interaction effects, had mixed results. Preliminary analysis of the association between obesity and overweight and the gene alleles of interest failed to reveal significant association in any of the four models ($p < .05$), although marginal significance was found between MAOA and obesity. Both MAOA and 5-HTT gene alleles have been repeatedly associated with obesity in a variety of studies, including many using previous iterations of Add Health data (Fuemmeler et al. 2009, Fuemmeler et al. 2008).

The non-significant association between both gene alleles and obesity/overweight is expected for a few important reasons. Harris et al. (2013) explain that the relationship between variation in genetic makeup and any social outcome of interest is difficult to pinpoint and capture. They emphasize the importance of utilizing the longitudinal data in Add Health and delicately accounting for changes over time, which this study does not do. If researchers understand genetics to be an intermediate influence between social predictors and outcomes, it would make sense that the relationship between genetics and outcomes outright may not always yield significant results. Other studies using Wave IV Add Health data have also failed to find a substantial and significant direct effect of genetic variation on BMI (Wickrama, Walker-O'Neal, and Lee 2013).

In order to corroborate the differential susceptibility framework, a significant association between outcome and gene allele should not exist outright. Belsky and

colleagues (2007) proposed stepwise criteria for distinguishing true differential susceptibility from other types of interaction. One of the preliminary steps in differential susceptibility evaluation is a test of association between the susceptibility factor (MAOA or 5-HTT in this case) and the outcome (obesity or overweight). Belsky and colleagues explain that if a significant association exists there is no need for further analysis. In that case, evidence would suggest that the relationship between outcome, predictor, and susceptibility factor is that of a dual-risk model where both the predictor and susceptibility factor are affecting obesity rates (Belsky et al., 2007). In the context of this research, a significant relationship between gene alleles and obesity outright would indicate both socioeconomic status and gene alleles are both independently predicting obesity. In order for differential susceptibility to prove true, gene alleles must moderate the relationship between socioeconomic status and obesity instead.

The distribution of obese individuals within educational groups did not significantly differ based on plasticity and non-plasticity allele groups in either direction. While it appears that individuals with the 5-HTT plasticity allele are more obese than those without the allele at low levels of education *and* less obese than those without at high levels of education, the difference is not statistically significant. The implication of this is that neither diathesis-stress nor differential susceptibility frameworks are supported when observing education, obesity, and MAOA/5-HTT despite education continually reappearing as a significant predictor of obesity and overweight in regression models.

The distribution of obese individuals within income quintiles yielded much more interesting results. In general, there were significantly more obese individuals in all income groups (with one exception) for those who had the 5-HTT plasticity allele relative

to those who did not. A very different relationship existed for those with MAOA allele. Significantly more obese respondents with the MAOA risk/plasticity allele were found in the lower two income quintiles, while significantly less fewer were found in the upper two income quintiles. Results of the 5-HTT models lend themselves to a diathesis-stress framework, where genetic predisposition amplifies negative environmental influences that increase obesity rates regardless of income. On the other hand, MAOA models further validate differential susceptibility frameworks, where genetic predisposition increases overall susceptibility to environmental influences, both increasing and decreasing obesity rates.

Gene Interaction

Analysis of the interaction between plasticity alleles and socioeconomic status when predicting odds of obesity and overweight did yield interesting results. Education remained a significant predictor in all models regardless of the outcome (obesity or overweight) or the gene allele and interaction action term included (MAOA or 5-HTT). The MAOA plasticity allele and interaction was only significant in the overweight model, while the 5-HTT plasticity allele and interaction was only marginally significant in predicting obesity.

The disparity in the relationships between allele type and weight status provide rather compelling evidence against the use of cumulative plasticity allele indices which are currently and often used in gene-environment studies (Wickrama et al. 2013; Belksy and Beaver 2011; Guo et al. 2008). Statistical significance of associations between 5-HTT and MAOA alleles and weight status differ substantially for on sex. The sex-moderated models revealed that MAOA was a significant predictor for males, but not for

females. For females, 5-HTT plasticity alleles were a significant predictor, but not for males. It is not surprising that a cumulative plasticity allele using MAOA and 5-HTT revealed no significant relationship to either weight status in this study.

Sex

Sex disparities in both weight status models are prominent. Sex was the strongest predictor of overweight status in the preliminary regression models, but were not significant in obesity models. Earlier blocks of the obesity model did reveal sex as a significant predictor, but its significance was later accounted for when neighborhood type and socioeconomic status variables were added. From the descriptive statistics we know that nearly a third of the sample was classified overweight (BMI > 25kg/m^2), but not obese (BMI < 30 kg/m^2). This portion of the sample clearly differs from those who are considered obese, which could use additional exploration.

For males, physical activity was the strongest predictor of obesity, specifically the difference between individuals who reported low levels of activity relative to those who were vigorously active. This is a logical difference due simply to the direct effect exercise has on an individual's weight. The second strongest predictor of obesity was Hispanic ethnic identification. All other race/ethnic categories did not significantly predict odds of obesity or overweight for males. Fuemmeler et al. (2008) produced findings that mirror these, where white and Hispanic men had significantly higher rates of overweight and obesity. In that study no significant findings were produced among females.

For females, all race/ethnicies with the exception of the multi-race category were strong predictors of both obesity and overweight. African American females in particular

had the highest increased odds of obesity out of all models (135% more likely to be classified obese). Physical activity, while significant, was not as strong of a predictor of obesity or overweight for females as it is for males. One additional factor that became marginally significant in the female model was urban environment (versus suburban). The significance of both rural and urban environments in predicting weight status reflects much of the literature that details limited food access and availability in both settings, although many studies focus predominantly on urban food scarcity (Morland and Evenson 2009; Black and Macinko 2008). With regard to both variables in this study, living in rural and urban environments disproportionately increased odds of obese and overweight classification.

The differences in the gender-specific distributions of obese individuals by income and gene alleles support both diathesis-stress and differential susceptibility frameworks, but also signal the important role gender plays as well. The 5-HTT allele was marginally significant for females, but not significant for males. The opposite relationship exists between genders when using the MAOA allele. Studies have shown that changes in estrogen levels in women, typically among aging women, can decrease the expression of the MAOA gene (Gundlah, Lu, and Bethea 2002; Smith et al. 2004). The net effect of this change is an increase in the serotonin levels among these women, which in turn would increase the amount of pleasure derived from things such as eating. At the time this data was collected female cohort participants were in their late 30s, and it is possible that some of them are already experiencing hormonal changes which could affect eating behaviors and mask the effect of the MAOA allele among women in this study.

In general, however, findings regarding the role gender plays in gene-by-environment obesity studies are mixed. Sookoian et al. (2008) found that the 5-HTT allele was associated with increased obesity rates among men, but did not have a female sample to compare to. Wickrama and colleagues (2013) find that woman report greater increases in obesity over time than men even when accounting for cumulative risk/plasticity alleles, including 5-HTT and MAOA among others. Fuemmeler et al. (2008) find that both 5-HTT and MAOA are associated with obesity and overweight+obesity only among men, while other studies suggest that only MAOA is significantly related to obesity for men (Marmorstein and Hart 2011). While the current findings with regard to gender are supported in some past research, it is clear that the role gender plays needs additional attention.

Research Questions

Genetics-informed social research clearly has a place, although additional work is necessary for distinguishing how and to what degree genetic variability influences social outcomes. The relationship genes have with various outcomes is not often direct or explicit, but is instead enmeshed in the relationships between the outcome and its known predictors, as is the case here. Understanding the predictors of obesity is a necessary component to exploring gene-environment interactions so that this complex relationship can be properly unfolded.

While the inclusion of the allele data into statistical models did not aid in the understanding of weight status outright in most cases, the variation in significance for each of the genes individually and the disparities between significant predictors within models inform future gene-environment study in a variety of ways. Past studies have

utilized cumulative risk/plasticity measures by creating indices with multiple genetic alleles under the assumption that all alleles function together as a vulnerability (in diathesis-stress models) or susceptibility factor (using differential susceptibility). It is evident here that MAOA and 5-HTT gene alleles have different effects on obesity and/or overweight and function in different ways. While both alleles may be associated with obesity, the use of both alleles combined in a single measure seems unwarranted.

Successful preliminary testing revealed that genetic alleles were often marginally or non-significant in additive models or in association with obesity and overweight+obesity, which is an important step in providing evidence for the moderating nature of genes in both diathesis-stress and differential susceptibility theoretic frameworks. A closer analysis of the plasticity allele groups by education levels, however, revealed that there was little to no difference in the distribution of obesity on either end of the educational spectrum between groups. Evaluation of differential susceptibility and diathesis-stress theories using education predictor of obesity did not produce any significant results. Both frameworks were supported, however, using income as a predictor and were additionally nuanced when sex was included. There is no clear consensus as to why this difference exists or to the specific role gender plays in gene-by-environment obesity studies in the current literature.

Limitations and Future Research

Although this study has important implications and contributes to the growing gene-environment literature, there are limitations that future researchers should consider. Data used for this study was used cross-sectionally, a disadvantage for many studies but one that is particularly detertrimental for genetic-informed social research as Harris et al.

(2013) have described. The relationship between genes and social outcomes is complexly layered and due diligence is required of those in pursuit of further exploring this relationship. Harris et al. (2013) discuss the benefits of using Add Health data longitudinally, and in models that adequately considered changes over time, at length. Each factor influencing an outcome works at multiple levels, at times in conjunction with other factors, and no single factor solely determines the outcome. Sufficient knowledge of genetics, the predictors related to the outcome of interest, and advanced statistical methodology is required to accurately depict any given gene-environment relationship.

In the current study different measures of weight status produced disparate results, highlighting the role and importance of measurement choice when working with weight. Running separate obesity and overweight models indicated that a variety of predictors existed in only one of the two models. These differences were further accentuated when analyses were subdivided into models based on sex. Additional weight status measures are also available and are used in other obesity and overweight studies. BMI is often used in analysis in raw score form, kg/m^2 (Wickrama et al. 2013; Fuemmeler et al. 2009), but can also be used after z-score standardization (Richardson et al. 2013; Marmorstein and Hart 2011) and in a percentile rank variable (Guo et al. 2012).

The gender findings presented here may serve as an important starting point for researchers. Many of the most recent Add Health genetic studies exploring obesity have produced results that are often significant for only one gender. No studies have currently focused solely on interaction between gender, gene alleles, and/or predictors when studying obesity or overweight, although many have recommended it as an area where

future research is necessary (Marmorstein and Hart 2011; Fuemmeler et al. 2009; Fuemmeler et al. 2008).

REFERENCES

Appelhans, Bradley M., Matthew C. Whited, Kristin L. Schneider, Yunsheng Ma, Jessica L. Oleski, Philip A. Merriam, Molly E. Waring, Barbara C. Olendzki, Devin M. Mann, Ira S. Ockene, and Sherry L. Pagoto. 2012. "Depression Severity, Diet Quality, and Physical Activity in Women with Obesity and Depression." *Journal of the Academy of Nutrition and Dietetics* 112(5):693-698.

Bearman, Peter. 2008. "Exploring Genetics and Social Structure." *Journal of Sociology* 114(S1):v-x.

Belcher, Britni R., David Berrigan, Kevin W. Dodd, B. Adar Emken, Chih-Ping Chou, and Donna Spuijt-Metz. 2010. "Physical Activity in US Youth: Impact of Race/Ethnicity, Age, Gender, & Weight Status." *Medicine and Science in Sports and Exercise* 42(12):2211-2221.

Belsky, Jay, and Kevin M. Beaver. 2011. "Cumulative-Genetic Plasticity, Parenting, and Adolescent Self-Regulation." *Journal of Child Psychology and Psychiatry* 52(2):619-626.

Belsky, Jay, C. Jonassaint, Michael Pluess, M. Stanton, B. Brummett, and R. Williams. 2009. "Vulnerability Genes or Plasticity Genes?" *Molecular Psychiatry* 14:746-754.

Belsky, Jay and Michael Pluess. 2009. "Beyond Diathesis Stress: Differential Susceptibility to Environmental Influences." *Psychological Bulletin* 135(6):885-908.

Belsky, Jay, Marian J. Bakermans-Kranenburg, and Marinus H. van IJzendoorn. 2007. "For Better and For Worse: Differential Susceptibility to Environmental Influences." *Current Directions in Psychological Science* 16(6):300-304.

Belsky, Jay. 1997. "Variation in Susceptibility to Rearing Influence: An Evolutionary Argument." *Psychological Inquiry* 8:182-186.

Beydoun, May A., and Youfa Wang. 2010. "Pathways Linking Socioeconomic Status to Obesity Through Depression and Lifestyle Factors Among Young US Adults." *Journal of Affective Disorders* 123:52-63.

Black, Jennifer L. and James Macinko. 2008. "Neighborhoods and Obesity." *Nutrition Reviews* 66(1):2-20.

Blazer, Dan G., Sandra Moody-Ayers, Jennifer Craft-Morgan, and Bruce Burchett. 2002. "Depression in Diabetes and Obesity: Racial/Ethnic/Gender Issues in Older Adults." *Journal of Psychosomatic Research* 53(4):913-916.

Bodenlos, Jamie S., Stephenie C. Lemon, Kristin L. Schneider, Madeline A. August, and Sherry L. Pagoto. 2011. "Associations of Mood and Anxiety Disorders with Obesity: Comparisons by Ethnicity." *Journal of Psychosomatic Research* 71:319-324.

Booth, Katie M., Megan M. Pinkston, and Walker S. Carlos Poston. 2005. "Obesity and the Built Environment." *Journal of the American Dietetic Association* 105(5):S110-S117.

Bowman, Shanthy A. and Bryan T. Vinyard. 2003. "Fast Food Consumption of U.S. Adults: Impact on Energy and Nutrient Intakes and Overweight Status." *Journal of the American College of Nutrition* 23(2):163-168.

Brosnahan, Jennifer, Lyn M. Steffen, Leslie Lytyle, Joan Patterson, and Ardys Boostrom. 2004. "The Relation Between Physical Activity and Mental Health Among Hispanic and Non-Hispanic White Adolescents." *Archives of Pediatrics & Adolescent Medicine* 158(8):818-823.

Burdette, Hillary L. and Robert C. Whitaker. 2003. "Neighborhood Playgrounds, Fast Food Restaurants, and Crime: Relationships to Overweight in Low-Income Preschool Children." *Preventative Medicine* 38:57-63.

Burke, Mary A. and Frank Heiland. 2007. "Social Dynamics of Obesity." *Economic Inquiry* 45(3):571-591.

Camarena, Beatriz, Haydee Santiago, Alejandro Aguilar, Elsa Ruvinskis, Jorge Gonzalez-Barranco, and Humberto Nicolini. 2004. "Family-Based Association Study Between the Monoamine Oxidase A Gene and Obesity: Implications for Psychopharmacogenic Studies." *Neuropsychobiology* 49:126-129.

Caspi, Avshalom, Karen Sugden, Terrie E. Moffitt, Alan Taylor, Ian W. Craig, HonaLee Harrington, Joseph McClay, Jonathan Mill, Judy Martin, Antony Braithwaite, and Richie Poulton. 2003. "Influences of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene." *Science* 301(5631):386-389.

Chang, Virginia W. and Diane S. Lauderdale. 2005. "Income Disparities in Body Mass Index and Obesity in the United States, 1971-2002." *Archives of Internal Medicine* 165(18):2122-2128.

Chantala, Kim and Joyce Tabor. 1999. *Strategies to Perform a Design-Based Analysis Using the Add Health Data.* Unpublished manuscript, Carolina Population Center, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Cohen-Cole, Ethan and Jason M. Fletcher. 2008. "Is Obesity Contagious? Social Networks vs. Environmental Factors in the Obesity Epidemic." *Journal of Health Economics* 27:1382-1387.

Cummins, Steven and Sally Macintyre. 2005. "Food Environments and Obesity – Neighborhood or Nation?" *International Journal of Epidemiology* 35:100-104.

Davis, Catherine L. and Stephanie Cooper. 2011. "Fitness, Fatness, Cognition, Behavior, and Academic Achievement Among Overweight Children: Do Cross-Sectional Associations Correspond to Exercise Trial Outcomes?" *Preventative Medicine* 52(S1):S65-S69.

Diez-Roux, Ana V. 2006. "Integrating Social and Biological Factors in Health Research: A Systems View." *Annals of Epidemiology* 17(7):569-574.

Dockray, Samantha, Elizabeth J. Susman, and Lorah D. Dorn. 2009. "Depression, Cortisol Reactivity, and Obesity in Childhood and Adolescence." *Journal of Adolescent Health* 45:344-350.

Durand, Emmanuelle, Philippe Boutin, David Meyre, M. Aline Charles, Karine Clement, Christian Dina, and Philippe Froguel. 2004. "Polymorphisms in the Amino Acid Transporter Solute Carrier Family 6 (Neurotransmitter Transporter) Member 14 Gene Contribute to Polygenic Obesity in French Caucasians." *Diabetes* 53(9):2483-2486.

Ewing, Reid, Tom Schmid, Richard Killingsworth, Amy Zlot, and Stephen Raudenbush. 2003. "Relationship Between Urban Sprawl and Physical Activity, Obesity, and Morbidity." *American Journal of Health Promotion* 18(1):47-57.

Fotso, Jean-Christophe and Barthelemy Kuate-Defo. 2005. "Measuring Socioeconomic Status in Health Research in Developing Countries: Should We Be Focusing on Households, Communities, or Both?" *Social Indicators Research* 72:189-237.

Freese, Jeremy. 2008. "Genetics and the Social Science Explanation of Individual Outcomes." *American Journal of Sociology* 114(S1):S1-S35.

Freese, Jeremy and Sara Shostak. 2009. "Genetics and Social Inquiry." *Annual Review of Sociology* 35:107-128.

Fuemmeler, Bernard F., Tanya Agurs-Collins, F. Joseph McClernon, Scott H. Kollins, Melanie E. Garrett, Allison E. Ashley-Koch. 2009. "Interactions Between Genotype and Depressive Symptoms on Obesity." *Behavioral Genetics* 39:296-305.

Fuemmeler, Bernard F., Tanya D. Agurs-Collins, F. Joseph Mcclernon, Scott H. Kollins, Melanie E. Kali, Andrew W. Bergen, and Allison E. Ashley-Koch. 2008. "Genes Implicated in Serotonergic and Dopaminergic Functioning Predict BMI Categories." *Obesity* 16(2):348-356.

Giles-Corti, Billie, Sally Macintyre, Johanna P. Clarkson, Terro Pikora, and Robert J. Donovan. 2003. "Environmental and Lifestyle Factors Associated with Overweight and Obesity in Perth, Austrailia." *American Journal of Health Promotion* 18(1):93-102.

Godin, Gaston and Roy J. Shepard. 1985. "A Simple Method to Assess Exercise Behavior in the Community." *Canadian Journal of Applied Sport Sciences* 10(3):141-146.

Gundlah, Chrisana, Nick Z. Lu, and Cynthia L. Bethea. 2002. "Ovarian Steriod Regulation of Monoamine Oxidase-A and B mRNAs in the Macaque Dorsal Raphe and Hypothalmic Nuclei." *Psychopharmacology* 160:271-282.

Guo, Guang, Kari E. North, Penny Gorden-Larson, Cynthia M. Bulik, and Seulki Choi. 2012. "Body Mass, DRD4, Physical Activity, Sedentary Behavior, and Family Socioeconomic Status: The Add Health Study." *Obesity* 15(5):1199-1206.

Guo, Guang, Yuying Tong, and Tianji Cai. 2008. "Gene by Social-Context Interactions for Number of Sexual Partners Among White Male Youths: Genetics-Informed Sociology." *American Journal of Sociology* 114:S36-S66.

Heitmann, B. L. 2010. "Obesity and Gender." Pp 58-64 in *Clinical Obesity in Adults and Children*. Wiley-Blackwell.

Harris, Kathleen Mullan, Carolyn Tucker Halpem, Jon Hussey, Eric A. Whitsel, Ley Killeya-Jones, Joyce Tabor, Glen Elder, John Hewitt, Michael Shanahan, Redford Williams, Ilene Siegler, and Andrew Smolen. 2013. "Social, Behavioral, and Genetic Linkages from Adolescence to Adulthood." *American Journal of Public Health* 103(S1):S25-S32.

Harris, Kathleen Mullan, Carolyn Tucker Halpern, Andrew Smolen, and Brett C. Haberstick. 2006. "The National Longitudinal Study of Adolescent Health (Add Health) Twin Data." *Twin Research and Human Genetics* 9(6):988-997.

Harris, Kevin C., Lisa K. Kuramoto, Michael Schulzer, and Jennifer E. Retallack. 2009. "Effect of School-Based Physical Activity Interventions on Body Mass Index in Children: A Meta-Analysis." *Canadian Medical Association Journal* 180(7):719-726.

Hjelmborg, Jacob v.B., Corrado Fagnani, Karri Silventoinen, Matt McGue, Maarit Korkeila, Kaare Christensen, Aila Rissanen, and Jaakko Kaprio. 2008. "Genetic Influences on Growth Traits of BMI: A Longitudinal Study of Adult Twins." *Obesity* 16(4):847-852.

Hu, Xianzhang, Gabor Oroszi, Jeffrey Chun, Tom L. Smith, David Goldman, and Marc A. Schuckit. 2006. "An Expanded Evaluation of the Relationship of Four Alleles to the Level of Response to Alcohol and the Alcoholism Risk." *Alcoholism: Clinical and Experimental Research* 29(1):8-16.

Krishnan, Vijaya. 2010. *Construction an Area-Based Socioeconomic Index: A Principal Components Analysis Approach.* Unpublished manuscript. Early Child Development Mapping Project, University of Alberta, Edmonton, Alberta.

Lucki, Irwin. 1998. "The Spectrum of Behaviors Influenced by Serotonin." *Biological Psychiatry* 44(3):151-162.

Lyons-Ruth, Karlen, Bjarne M. Holmes, Maria Sasvari-Szekely, Zsolt Ronai, Zsofia Nemoda, and David Pauls. 2007. "Serotonin Transporter Polymorphism and Borderline/Antisocial Traits among Low-Income Adults." *Psychiatric Genetics* 17:339-343.

Marmorstein, Naomi R. and Daniel Hart. 2011. "Interactions Between MAOA Genotype and Receipt of Public Assistance: Predicting Change in Depressive Symptoms and Body Mass Index." *Journal of Research on Adolescence* 21(3):619-630.

Martin, Molly A. 2008. "The Intergenerational Correlation in Weight: How Genetic Resemblance Reveals the Social Role of Families." *American Journal of Sociology* 114(S1):S67-S105.

Morland, Kimberly B. and Kelly R. Evenson. 2009. "Obesity Prevalence and the Local Food Environment." *Health & Place* 15:491-495.

Morland, Kimberly, Ana V. Diez Roux, and Steve Wing. 2006. "Supermarkets, Other Food Stores, and Obesity: The Atherosclerosis Risk in Communities Study." *American Journal of Preventative Medicine* 30(4):333-339.

Morton, Lois Wright and Troy C. Blanchard. 2007. "Starved for Access: Life in Rural American's Food Deserts." *Rural Realities* 1(4):1-10.

Need, A.C., K.R. Ahmadi, T.D. Spector, and D.B. Goldstein. 2006. "Obesity is Associated with Genetic Variants that Alter Dopamine Availability." *Annals of Human Genetics* 70:293-303.

Nelson, Melissa C., Penny Gordon-Larsen, Yan Song, and Barry M. Popkin. 2006. "Built and Social Environments: Associations with Adolescent Overweight and Activity." *American Journal of Preventative Medicine* 31(2):109-117.

Richardson, A. S., K. E. North, M. Graff, K. M. Young, K. L. Mohlke, L. A. Lange, E. M. Lange, K. M. Harris, and P. Gorden-Larsen. 2013. "Moderate to Vigorous Physical Activity Interactions with Genetic Variants and Body Mass Index in a Large U.S. Ethnically Diverse Cohort." *Pediatric Obesity* [Epub ahead of print]

Sabol, Sue Z., Stella Hu, and Dean Hamer. 1998. "A Functional Polymorphism in the Monoamine Oxidase A Gene Promoter." *Human Genetics* 103(3):273-279.

Saelens, Brian E., James F. Sallis, Jennifer B. Black, and Diana Chen. 2003. "Neighborhood-Based Differences in Physical Activity: An Environmental Scale Evaluation." *American Journal of Public Health* 93(9):1552-1558.

Schwartz, Marlene B. and Kelly D. Brownell. 2004. "Obesity and Body Image." *Body Image* 1:43-56.

Simons, Ronald L., Man Kit Lei, Steven R. H. Beach, Gene H. Brody, Robert A. Philibert, and Frederick X. Gibbons. 2011. "Social Environment, Genes, and Aggression: Evidence Supporting Differential Susceptibility Perspective." *American Sociological Review* 76(6):883-911.

Smith, Lisa J., Jessica A. Henderson, Creed W. Abell, and Cynthia L. Bethea. 2004. "Effects of Ovarian Steroids and Raloxifene on Proteins That Synthesize, Transport, and Degrade Serotonin in the Raphe Region of Macaques." *Neuropsychopharmacology* 29(16):2035-2045.

Sookoian, Silvia, Tomas F. Gianotti, Carolina Gemma, Adriana Burgueno, and Carlos J. Pirola. 2008. "Contribution of the Functional 5-HTTLPR Variant of the SLC6A4 Gene to Obesity Risk in Male Adults." *Obesity* 16(2):488-491.

Sookoian, Silvia, Carolina Gemma, Silvia I. Garcia, Tomas Fernandez Gianotti, Guillermo Dieuzeide, Adriana Roussos, Miriam Tonietti, Liliana Trifone, Diego Kanevsky, Claudio D. Gonzalez, and Carlos J. Pirola. 2007. "Short Allele of Serotonin Transporter Gene is a Risk Factor for Obesity in Adolescents." *Obesity* 15(2):271-276.

Stafford, Mai, Steven Cummins, Anne Ellaway, Amanda Sacker, Richard D. Wiggins, and Sally Macintyre. 2007. "Pathways to Obesity: Identifying Local, Modifiable Determinants of Physical Activity and Diet." *Social Science & Medicine* 65:1882-1897.

Suviolahti, Elina, Laura J. Oksanen, Miina Ohman, Rita M. Cantor, Martin Ridderstrale, Tiinamaija Tuomi, Jaakko Kaprio, Aila Rissanen, Pertti Mustajoki, Pekka Jousilahti, Erikki Vartiainen, Kaisa Silander, Riika Kilpikari, Veikko Salomaa, Leif Groop, Kiimo Kontula, Leena Peltonen, and Paivi Pajukanta. 2003. "The SLC6A4 Gene Shows Evidence of Association with Obesity." *Journal of Clinical Investigation* 112(11):1762-1772.

Ulijaszek, Stanley J. and Hayley Lofink. 2006. "Obesity in Biocultural Perspective." *Annual Review of Anthropology* 35:337-360.

Via, Marc, Christopher Gignoux, and Esteban Gonzalez-Burchard. 2010. "The 1000 Genomes Project: New Opportunities for Research and Social Challenges." *Genome Medicine* 2:3-5.

Wickrama, Kandauda, Catherine Walker O'Neal, and Tae Kyoung Lee. 2013. "Early Community Context, Genes, and Youth Body Mass Index Trajectories: An Investigation of Gene-Community Interplay Over Early Life Course." *Journal of Adolescent Health* 53:328-334.