A Review of the Physiological Causes and Effects of Eating Disorders: Current Research & Future Directions

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ABSTRACT

In today's media-driven culture promoting an ideal body thinness, eating disorders have become more rampant than ever before. Previous research has explored the various causes and effects of disordered eating in an attempt for medical practitioners to better define the different disorders as well as to better treat those suffering with the disorder. By analyzing previous studies along with the emerging data, this work has reviewed the most up-to-date eating disorder classifications, the potential causal components, and the physiological effects of eating disorders to highlight where more research is needed. The findings of this work highlight a significant genetic component, among other factors, that may contribute to the development of disordered eating. Moreover, this paper calls attention to the serious adverse effects associated with those suffering and recovering from eating disorders.

INTRODUCTION

Eating disorders have been defined generally as mental health conditions, characterized by a disorder in eating patterns that can result in serious and potentially life threatening physical and mental health implications (Arcelus, 2011). With the rise in the media's ideal body thinness for both men and women, but particularly for young women, the prevalence of eating disorders has become increasingly apparent. Accordingly, the incidence of anorexia and bulimia has increased in the past fifty years in females between the ages of 15 and 24. Combining the results of several studies, researchers found that between 0.9% and 2.0% of females and 0.1% to 0.3% of males will develop anorexia as well as that between 1.1% and 4.6% of females and 0.1% to 0.5% of males will develop bulimia (Statistics & Research on Eating Disorders, 2022).

As the Diagnostic and Statistical Manual of Mental Disorders, the handbook for healthcare providers, continues to improve their definition of the signs and symptoms of different

eating disorders, medical practitioners have been able to better their diagnostic measures. The Anxiety and Depression Association of America (ADAA) cites six major types of eating disorders: anorexia nervosa, binge eating disorder, other specified feeding and eating disorders, avoidant restrictive food intake disorder, rumination disorder, and unspecified feeding or eating disorder.

There has been much discussion regarding the various genetic and environmental components that may put an individual at risk for developing unhealthy eating patterns. Though there have been some linkage associations with specific genetic markers and with eating disorders, various environmental factors such as media, personality, neurocognitive effects, and parents also play an important causal role. Moreover, recent findings have found several populations with a unique risk for developing an eating disorder, including women, men, transgender people, diabetics, athletes, and members of the Jewish community.

Research has explored the varying physiological effects of disordered eating both when exhibiting symptoms of the eating disorder and when in recovery from the disorder. Eating disorders can manifest in varying ways, including oral and salivary, gastrointestinal, endocrine, and bone metabolism. Eating disorder manifestations can have serious consequences. According to the National Eating Disorder Association, adolescents between the ages of 15 and 24 with anorexia have ten times the risk of dying when compared to their peers (Statistics & Research on Eating Disorders, 2022).

Though the adverse physiological effects of eating disorders have become better understood, the prevalence of eating disorders have continued to rise, which suggests that there is more research to be done, especially in analyzing the potential causal components. With a better

comprehension of what may cause individuals to be at risk for developing an eating disorder, better preventative measures can be taken.

TYPES AND CLASSIFICATIONS

Over the past few decades, it has been challenging for researchers and practitioners to find clear and accurate definitions that distinguish one eating disorder from the others. Most medical professionals rely on the categories defined by the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), the most up-to-date version describing the signs and symptoms associated with each category of eating disorders.

According to the DSM-5, the most widely recognized eating disorder is anorexia nervosa, which can be further subdivided into restrictive and binge eating/purging. To further categorize, binge eating is characteristic of bulimia nervosa and binge eating disorder (Association, Diagnostic and Statistical Manual of Mental Disorders (5th ed.), 2013). These categorizations have only been recognized recently. In fact, in the Diagnostic and Statistical Manual of Mental Disorders, third edition (DSM-3), binge eating disorder was not formally recognized in its own category as in the DSM-5 (Association, Diagnostic and Statistical Manual of Mental Disorders (3rd ed.), 1980).

The Anxiety and Depression Association of America (ADAA) further categorizes eating disorders, which may aid diagnosticians in better identifying differences between eating disorder types. The ADAA cites six major types of eating disorders: anorexia nervosa, binge eating disorder, other specified feeding and eating disorders, avoidant restrictive food intake disorder, rumination disorder, and unspecified feeding or eating disorder. The ADAA notes that some complex eating disorders may not meet the diagnostic criteria included in the DSM-5 but should nonetheless be taken seriously and dealt with accordingly.

The first eating disorder listed, and arguably the most overt eating disorder regarding its signs and symptoms, is anorexia nervosa (AN). AN is characterized by "difficulties maintaining an appropriate body weight for height, age, and stature," usually via food restriction. According to a study combining statistics from several sources, between 0.9% and 2.0% of females and 0.1% to 0.3% of males will develop anorexia. Males have been found to comprise 25% of individuals with AN, and men have found to be at a higher risk of dying as they are often diagnosed later, if at all, since it is assumed that only women have eating disorders (Statistics & Research on Eating Disorders, 2022). Many with this disorder have a distorted body image and typically restrict their caloric intake and types of foods consumed. For some, the disorder also includes exercising to an unhealthy level, vomiting, and binge eating. Some common signs and symptoms include dramatic weight loss, preoccupation with food and calories, and maintaining a strict exercising regime.

According to this categorization, bulimia nervosa (BN) is defined as a subcategory of anorexia nervosa and consists of a cycle of binge eating and purging, which can include self-induced committing and self-administering laxatives. According to a study combining findings from several sources, between 1.1% and 4.6% of females and 0.1% to 0.5% of males will develop bulimia (Statistics & Research on Eating Disorders, 2022). Even though eating disorders are usually relatively covert diseases, patients with BN have reduced salivary flow, which can cause an enlargement of salivary glands and thus presents as noticeable facial swelling.

Another eating disorder listed by the ADAA is binge eating disorder (BED), which is a "severe, life-threatening, and treatable eating disorder" that includes repeating episodes of eating large amounts of food. According to a study combining statistics from several studies, between

0.2% and 3.5% of females and 0.9% and 2.0% of males will develop binge eating disorder. Of those with the disorder, 40% are comprised of men. Moreover, 30% of individuals seeking to lose weight show signs of BED (Statistics & Research on Eating Disorders, 2022), which is more prevalent than ever due to the pressures and widespread nature of diet culture. Oftentimes, people with BED have their episodes in secrecy, experience intense discomfort, shame, and guilt following each episode, and may purge to compensate for overeating. According to the ADAA, BED is the most common eating disorder in the United States.

Other specified feeding and eating disorders (OSFED), previously known as eating disorder not otherwise specified, was created to include those who have an unhealthy relationship with food but may not meet the criteria for anorexia nervosa or bulimia nervosa. OSFED includes signs and symptoms such as episodes of consuming large amounts of food and then purging, binge eating, having issues with body image, exhibiting strict dieting behavior, and using laxatives or diuretics to prevent weight gain.

Avoidant restrictive food intake disorder (ARFID), previously known as selective eating disorder, is similar to anorexia nervosa as they both involve strict limitations in caloric intake and types of foods consumed. One study with adolescents with eating disorders found that 14% had ARFID, and those affected were most likely to be younger and male (Statistics & Research on Eating Disorders, 2022). ARFID is distinct from anorexia nervosa in that those with the disorder are not concerned with their body image. Those with ARFID do not consume enough calories to grow and develop properly; for children with the disorder, this can manifest as delayed weight gain or height growth, while for adults, this manifests as varying degrees of weight loss. Pica is a subcategory of ARFID and is a disorder that “involves eating items that are not typically thought of as food and that do not contain significant nutritional value” that

includes hair, paint chips, and paper. Similar to other eating disorders, ARFID and pica involve a lot of shame, which can result in the disorder being concealed until there is a life-threatening emergency as a result of the disorder.

Rumination disorder, another disorder listed by the ADAA, is an eating disorder that is characterized by at least one month of frequent regurgitation of food that is then split out, rechewed, or re-swallowed. This disorder does not typically involve effort to regurgitate the food.

Finally, unspecified feeding or eating disorder (UFED) includes those with symptoms of eating disorders that "cause[s] clinically significant distress or impairment in social, occupational, or other important areas of functions" but do not meet the full criteria for other eating disorders or if there is not enough information to diagnose the eating disorder more specifically (Types of Eating Disorders, n.d.).

POTENTIAL CAUSES

GENETIC COMPONENT

Difficulties in Isolating

There is much discussion about genetic predisposition as a key risk factor in the development of an eating disorder. New technology has allowed for researchers and medical practitioners to better understand the role of genetics in eating disorders. Since studies have only been exploring this relationship relatively recently, however, many findings have been found to be contradictory, which shows that there is still more research to be done. With a better comprehension of the role genetics might play in causing the onset of an eating disorder, medical practitioners can properly account for the heritability of the disorder and treat accordingly.

As research has only begun to scratch the surface, researchers have found it difficult to isolate the genetic and environmental causal components involved in eating disorders. One review study compiled the complex causes of eating disorders and found that both genetic and environmental factors contribute as factors (Culbert, Racine, & Klump, 2015). The line between the genetic and environmental components, however, is still blurry and most researchers have concluded that while both influence eating disorders, the unique contributions are not well understood.

Twin studies have played an instrumental role in attempting to isolate various potential genetic and environmental factors that may play a role in the development of unhealthy eating patterns. These twin studies, however, have still had difficulty in isolating the genetic and environmental influences on eating disorders. One study analyzing adoption situations between siblings, however, found that the effects of a shared environment tend to be negligible, which indicates a stronger genetic causal component (Klump, Suisman, Burt, McGue, & Iacono, 2009). Since other studies contradict this conclusion, it is plausible to conclude that there is not enough research to truly isolate the magnitude of genetic and environmental influences. As more data emerges, more current research has assumed that genetic and environmental causes are too complex to be separated and have been considered as one general factor that significantly contributes to risks for eating disorders.

Another factor that makes it difficult to isolate the genetic component of eating disorders is that these disorders do not follow traditional Mendelian genetics and are influenced by both one's genes and the environment. The results of one study indicate that it is not most likely not one gene for AN or one gene for BN; rather, it is more likely that there are several genes that contribute to the development of unhealthy eating patterns (Mazzeo & Bulik, 2009). This study

suggests that if the genetic component alone is complex and must consider several genes for each type of eating disorder, then it only makes it more difficult to isolate the genetic component from other potential factors.

Heritability

Most review studies on the potential genetic causal component focus on AN, BN, and BED as they are the most widely studied on a genetic and epidemiological level (Watson, et al., 2021). Heritability, or a measure of how genetically transmittable something is, has been measured for various eating disorders to attempt to isolate the genetic causal component. In one study using 672 17-year-old twin pairs, researchers analyzed the heritability of AN through interviews and self-report questionnaires and found that the total genetic effect on AN was approximately 74%. Overall, this finding indicates that a huge portion of factors that contribute to the onset of AN is genetically related. This study noted several limitations, however, including the relatively small sample size and the limiting age of the participants at 17-years-old (Klump, Miller, Keel, McGue, & Iacono, 2001).

To limit the pitfalls from the previous study, one twin study used a much larger cohort of 34,142 Danish twins who were screened for eating disorders via a self-reporting questionnaire. The researchers found that rates for eating disorders varied among monozygotic and dizygotic twins and concluded that BN had a heritability of 61% and AN had a heritability of 48% to 52% (Kortegaard, Hoerder, Joergensen, Gillberg, & Kyvik, 2001). Similarly, one twin study found that AN had a heritability of 58% (Wade, Bulik, Neale, & Kendler, 2000). These findings suggest that the majority of the factors that contribute to the onset of AN and BN are genetically related. Overall, studies of the heritability of AN and BN clearly indicate that genetics play a large role in contributing to the onset of eating disorders.

Studies have also investigated the relationship between genetic factors and BED. In one twin study, BED was found to have an estimated heritability of 57% and was found to be more common within families (Javaras, et al., 2008). Both the high heritability percentage and the fact that when one family member had BED, other family members were likely to have the disorder as well, highlights the significant genetic component of eating disorders. Furthermore, using self-report measures and criteria from the DSM-4, the incidence of both twins having BED was found to be greater for monozygotic twins than dizygotic twins, citing evidence that there may be multiple genetic loci influencing eating disorders (Mitchell, et al., 2010). Multiple genetic loci for BED not only makes the disorder more complex but also suggests multiple means for inheritance, which opens the door for much needed future research.

Aside from isolating the impact of genetics, potential genetic links between different eating disorders have also been analyzed. Researchers found a significant correlation between AN and BN, meaning that those with one of these disorders are more likely to have the other disorder as well. 66% of the correlation is attributable to genetics and 55% of the correlation is attributable to the environment, indicating that while both genetics and the environment play a role in the overlap of multiple disorders, genetics may have a slightly larger influence (Yao, et al., 2021). This study is one of several, however, and as more data emerges, it becomes clearer that the research is contradictory and inconclusive. Considering the significant finding that once someone has one eating disorder, they are more likely to have another eating disorder, it is more likely that some eating disorders may be misdiagnosed or underdiagnosed. This poses major significance in a clinical setting as clinicians should be aware of the overlap between AN and BN as well as for the potential for overlap between other eating disorders.

Genome-Wide Association Studies

Genome-wide association studies (GWAS) have been used as a tool to allow for an unbiased and broad overview of all potential genetic correlations to eating disorders. GWASs involve "rapidly scanning markers across the complete sets of DNA, or genomes, of many people to find genetic variations associated with a particular disease." Once associates between genes and disorders have been identified, researchers are able to better detect and treat genetically related diseases. These types of studies have only been possible recently with the completion of the Human Genome Project in 2003, which maps out the entire human genome (Genome-Wide Association Studies Fact Sheet, n.d.). While these studies have been instrumental in uncovering the relationship between genetics and eating disorders, conflicting findings and small sample sizes suggest a need for more research to be done.

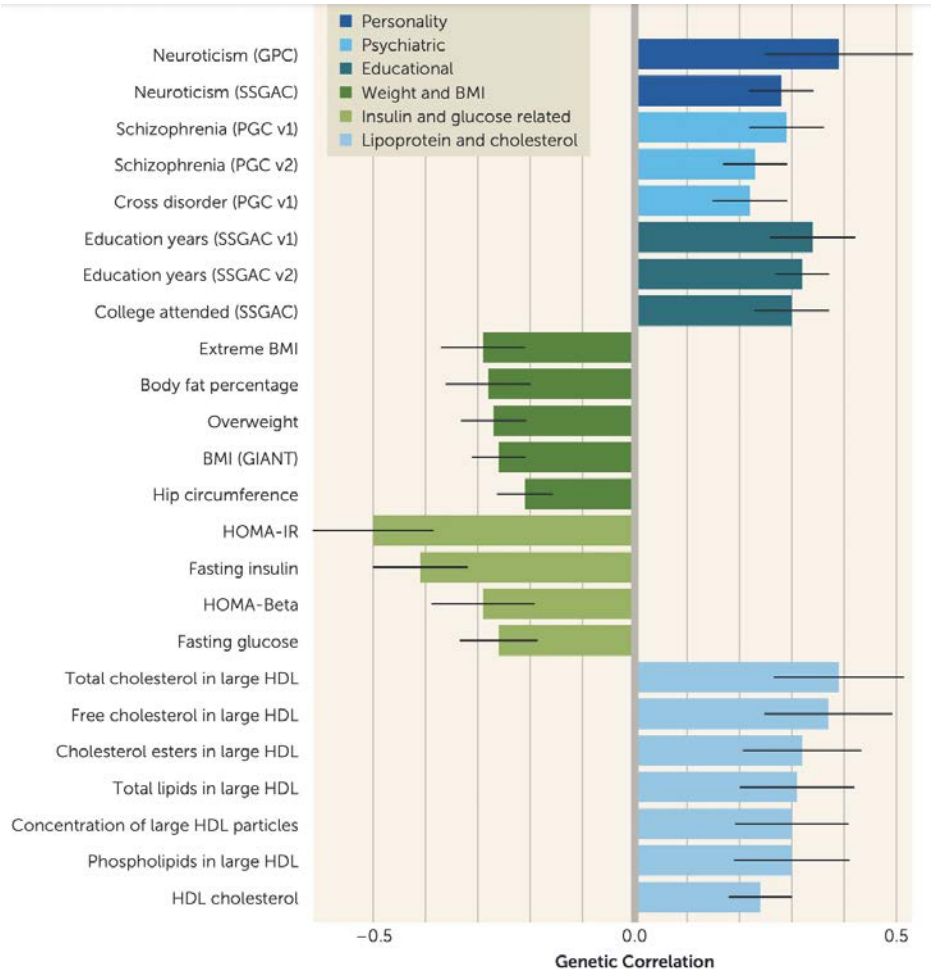
There have been several eating disorder GWASs, which have all been focused on AN as its symptoms are the most overt. Early GWASs had relatively small sample sizes that contributed to finding only a small number of significant genetic causal markers for disordered eating. The earliest GWAS (320 AN cases, 341 controls) revealed that 9 of 10 highly polymorphic microsatellite marker candidates were associated with AN. Comparing common single-nucleotide polymorphisms (SNP) in patients with AN compared to normal patients, researchers were able to further narrow down to two loci: 1q41 and 11q22 (Nakabayashi, et al., 2009). This indicates something on the genetic level that has a unique association with AN. Interestingly, amplification in one of the loci, 11q22, has been associated with lymph node metastasis, which indicates that malfunction of the immune system on a genetic level may be associated with the onset of eating disorders (Bhosale, et al., 2017). One GWAS (3495 AN cases, 10982 controls) supported this relationship, finding a significant locus on chromosome 12 that had genetic tags for type 1 diabetes and other autoimmune disease (Duncan, et al., 2017). The

relationship between the immune system and eating disorders requires further research, but the implications of such a relationship could be massive. Autoimmune disorders, such as type 1 diabetes, have been extensively researched and clinicians are well-versed in the treatment; if such a relationship exists between immune system malfunctions and eating disorders, then perhaps treatment of the immune disorder can play a role in the treatment of eating disorders or the preventing of worsening of an already existing eating disorder.

Some subsequent studies, including one study with 1033 AN cases and 3733 controls, did not find any SNPs associated with AN (Wang, et al., 2011), which undermines the results of Bhosale, et al.'s 2017 study. Though this is most likely due to the relatively small sample size of AN patients since other studies have found clear associations, the conflicting findings suggest a need for more research on the subject.

GWASs have allowed the relationship between eating disorders and other factors to be better understood, but unclear findings suggest the need for further research. One GWAS (3,495 AN, 10,982 controls) tested 159 phenotypes and plotted 24 of them using the color-coded categories, including the factors of personality, psychiatric, educational, weight & body mass index (BMI), insulin & glucose related, and lipoprotein & cholesterol. These factors were ranked in terms of genetic correlation with AN with negative values indicating negative correlation and positive values indicating positive correlation (Figure 1). The study found varying degrees of positive genetic correlation between AN and personality traits, psychiatric disorders, educational attainment, and high-density lipoprotein cholesterol. Genetic links between AN and personality and psychiatric disorders are interesting as they also have a strong overall link, which will be discussed in a later section. Interestingly, the greater one's formal educational attainment, the more likely one may be to develop an eating disorder, suggesting that the stress often associated

with higher education may negatively impact one's self-esteem and contribute to the onset of an eating disorder. High-density lipoprotein cholesterol, known to many as the 'good' cholesterol that absorbs cholesterol to bring to the liver, is also found in great levels with patients with AN, which is surprising as other forms of malnutrition do not have similar effects. This implies that though patients with AN lack proper nutrition, perhaps they still contain free cholesterol that needs to be absorbed. Additionally, negative genetic correlations were observed between AN and insulin & glucose as well as weight & BMI. It is logical that those with lower fasting insulin and fasting glucose have a correlation with greater risk for AN since over time, the body gets used to low nutrient intake and adjusts accordingly. The negative correlation regarding BMI, however, was surprising as almost every definition characterizes AN as being associated with low BMI. This finding may suggest a limitation of the study, indicating a need for more research to explore this relationship (Figure 1) (Duncan, et al., 2017).



[a] The 24 correlations depicted here (of 159 phenotypes tested) have a false discovery rate <0.05. Error bars indicate standard error. BMI=body mass index; GIANT=Genetic Investigation of Anthropometric Traits; GPC=Genetics of Personality Consortium; HDL=high-density lipoprotein cholesterol; HOMA-Beta=homeostatic model assessment of beta cell function; HOMA-IR=homeostatic model assessment of insulin resistance; PGC=Psychiatric Genomics Consortium; SSGAC=Social Science Genetic Association Consortium.

Figure 1: Genetic Correlation Between Anorexia Nervosa Patients and Various Phenotypes. Genetic correlations between anorexia nervosa and diverse phenotypes reveal overlap across psychiatric, educational, weight, insulin, lipoprotein, and cholesterol phenotypes**.** Bars are ± standard error. Adapted from Duncan, et al., 2017.

Since GWASs proved to be a useful method for analyzing the genetic component of eating disorders, additional studies were conducted using a better research design. The most recent GWAS had the largest sample size to date (16992 cases, 55525 controls) and as such found eight significant loci. Using a Manhattan plot, researchers concluded that eight

chromosomal loci have a significant correlation to AN, with AN, with chromosome 3 containing the most correlated locus. In this plot, the $-\log_{10}(P)$ values for the association tests (two-tailed) are shown on the y-axis and the chromosomes are ordered on the x-axis. The most frequent variant is indicated by a green diamond. The red and blue colors are helpful in distinguishing between adjacent chromosomes (Figure 2). Overall, these GWAS studies indicate that AN is polygenic and as sample sizes grow, so too will the number of genome-wide loci related to AN (Stahl, et al., 2019).

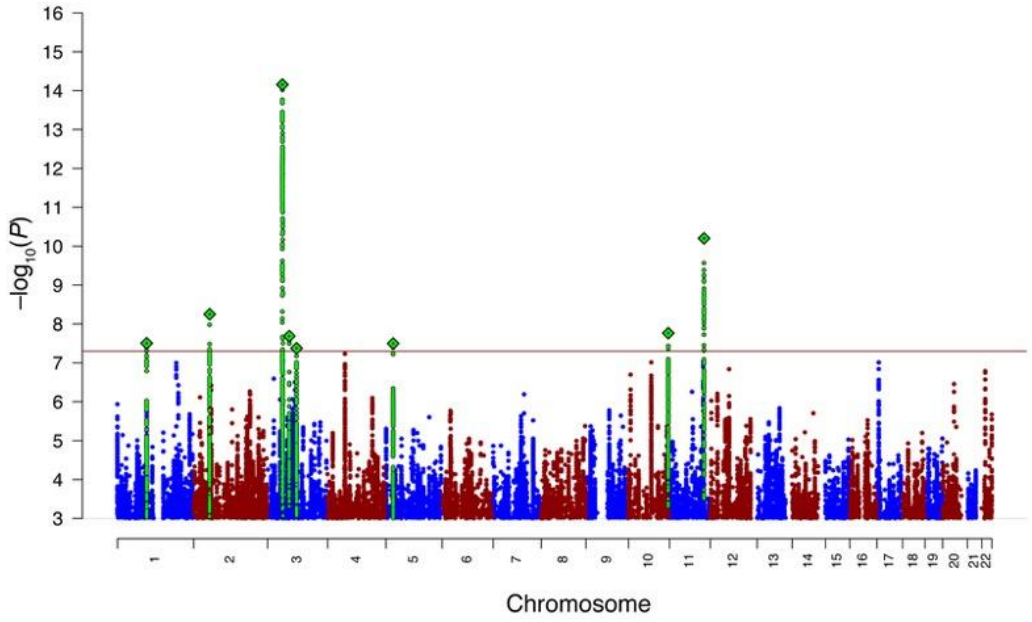


Figure 2: Manhattan Plot Showcasing Significant Loci from Genome Wide Association Study. The Manhattan plot for the primary genome-wide association meta-analysis of anorexia nervosa with 33 case-control samples. Eight genetic loci surpassed genome-wide significance ($-\log_{10}(P) > 7.3$). Adapted from Stahl, et al. 2019.

Overall, the current research and the emerging research implies a strong genetic component influencing the onset of eating disorders. Even though it is difficult to isolate the genetic from the environmental influence, larger studies have proven to be more accurate and

more successful. In addition to the genetic factor in general involved in disordered eating, there have been some GWASs that have isolated specific chromosomes and chromosomal loci with a potential correlation with eating disorders. Though there have been several GWASs, all have only considered AN, which proves to be a major limitation in all the studies. Additionally, the current research has been somewhat conflicting and has not been conclusive. More research is required to better understand the role that specific genes play in influencing the development of an eating disorder.

ENVIRONMENTAL COMPONENT

Despite the challenges that come with isolating the genetic and environmental component, one's upbringing and surroundings impact how one perceives oneself, which can lead to the development of an eating disorder. Though it is difficult to quantify how much one's environment contributes to the development of an eating disorder, research suggests that various factors, such as media, personality traits, neurocognitive processes, and parenting, have been correlated with disordered eating.

Media

In today's technologically and media-driven era, culture and media play a big role in promoting the ideal body type for both men and women. It is well known that over the past decades, the cultural idealization of a thin body has been associated with AN and has promoted AN tendencies (Culbert, Racine, & Klump, 2015). In one study, media exposure of an ideal thinness was found to predict increased levels of unhealthy relationships with food (Bearman, Presnell, Martinez, & Stice, 2006). This shows a clear association with unrealistic body standards and the onset of disordered eating. Specifically, research indicates that this media exposure can predict increased eating disorders in adolescent and young girls

(Martınez-Gonzalez, et al., 2003), which displays that women may be uniquely vulnerable to the ideal body thinness set forth by the media.

Twin studies have been conducted in an attempt to isolate the effect of environmental factors. In one twin study, researchers concluded that the internalization of an ideal thinness is accounted for both genetically and environmentally, indicating that though some may have a genetic predisposition for the disorder, one's surroundings play a key role in determining one's risk for developing disordered (Suisman, et al., 2014). This finding has major implications, suggesting that not only do genetics contribute to unhealthy eating patterns but also the intense influence of the media.

Personality Traits

In addition to media promoting an ideal body type, the development of personality traits can contribute to the onset of disordered eating. While personality does contain some genetic components, much of one's personality is influenced through social interaction and the desire to fit perceived social norms. Negative emotionality and neuroticism can predict the potential for an eating disorder (Cervera, et al., 2003), specifically placing one at risk for AN (Bulik, et al., 2006) and BN (Tyrka, Waldron, Graber, & Brooks-Gunn, 2002). Both negative emotionality and neuroticism cause an individual to pessimistically internalize their surroundings, which can be detrimental to one's self-image and can promote unhealthy eating patterns.

Another major personality trait that plays a key factor in contributing to eating disorders is the desire to achieve perfectionism. In one study, those with traits of perfectionism were found to have higher incidents and increased risk of BN in late adolescent and young adult females. These results, however, were only applicable among participants who also had low self-esteem and had the perception that they were overweight, suggesting that the trait of perfectionism may

not be directly correlated to eating disorders (Polderman, et al., 2015). There is a direct relationship, however, between the trait of perfectionism and issues with one's self-esteem; perfectionism often leads to self-esteem issues with one's body and can cause a fixation on one's weight, ultimately putting one more at risk for unhealthy eating patterns (Boone, Soenens, & Luyten, 2014). It is worth noting that the most research regarding the association between personality traits and eating disorders has involved studying AN and BN, indicating a need for more research to be done with the other types of eating disorders.

Neurocognitive Processes

Not only do personality traits play a role in causing eating disorders, but the development of certain neurocognitive processes, or lack of proper development, can contribute to the onset of unhealthy eating patterns. Cognitive flexibility, or the ability to shift between different tasks or mental sets, is localized in the prefrontal cortex, anterior cingulate cortex, and posterior parietal cortex. In one study, compared to controls, adults with AN were found to have not performed as well on tasks requiring cognitive flexibility, suggesting that there is a correlational relationship between eating disorders and lack of cognitive flexibility (Wu, et al., 2014). Though a causal relationship is not well understood, the correlation between these factors makes sense: those who are unable to break free from societal expectations and unhealthy mental states are more prone to developing a fixation on food and may be more likely to develop disordered eating.

Parenting

There has been much to say about parenting and the environment in one's childhood home being a big determining factor for the development of eating disorders. Most research indicates that parenting is not solely to blame for causing eating disorders. Parents do, however, play a tremendous role in influencing the tendencies of their children, which can result in parents

with eating disorders to model unhealthy eating behaviors and attitudes. The modeling behaviors of parents likely contributes to the environmental causal component of disordered eating (Mazzeo & Bulik, 2009).

Various case studies indicate that parenting style plays a factor not only in the potential for modeling eating disorders but that parents may force their eating habits onto their children. Parents, specifically mothers, with eating disorders may similarly be over concerned about their children's weight even when it is well within normal limits (Russell, Treasure, & Eisler, 1998). This finding indicates a practical application for clinicians that when a parent has an eating disorder, specifically a mother, the children should be screened as well. In one study, the weight concerns of the mothers were positively associated with the amount of restriction they imposed on their daughters' eating (Francis, Hofer, & Birch, 2001), suggesting that mothers play a huge role in determining the development of eating disorders. Though many with disordered eating cite their upbringings as one of the factors that may have contributed to the onset of the disorder, there is still more research needed to explore this relationship, especially the role of the father and the extent of the impact of parenting.

POPULATIONS AT RISK

Women

Most studies have concerned disordered eating patterns in women, primarily because women seemingly have been the main subject of the ideal body type presented in the media. In this regard, women are more susceptible to internalizing the body thinness standard of the media. In one study, researchers tested the Feminine Gender Role Stress scale, which was used to determine if there was a link between eating disorders and women's perceptions of certain situations as stressful because of their desire to conform to the traditional feminine gender role.

Researchers indicated that this stress placed on females may be a missing link between cultural values of femininity and vulnerability for disordered eating (Martz, Handley, & Eisler, 1995). With a huge pressure for women to remain thin and feminine, the current research has concluded that women are most at risk for developing an eating disorder.

Women are also particularly at risk for developing an eating disorder because of the changes in the sex hormones estradiol and progesterone. The fluctuation of estradiol and progesterone can predict changes in emotional eating and/or binge eating, which ranges between individuals based on various personal factors (Klump, et al., 2013). More research is needed to better understand how hormone fluctuations present a unique risk for women to develop unhealthy eating patterns.

Men

Though women have traditionally been thought to be more at risk for having unhealthy eating patterns, recent studies have shown the unique vulnerability of men. One review study on populations at risk points out that most eating disorder studies concern women because women take eating disorders more seriously and perceive it as being common among their peers (Mond & Arrighi, 2011). Society's perception that women are the majority of those affected by eating disorders does not actually prove that women are more prone to developing an eating disorder, rather it only points to the fact that there are limitations to the data on men and eating disorders.

Additionally, the emerging research has shown that men are not as well-educated about eating disorders, which may cause them to be at a unique risk. In a survey study, male and female undergraduate and postgraduate students responded to fictional situations of women who suffered from AN or BN. Men responded much less emphatically to the scenarios and did not view symptoms of disordered eating as a big deal, suggesting that there is a strong need to target

male perception of eating disorders (Mond & Arrighi, 2011). Without proper knowledge and understanding that eating disorders are more common than one may think, men may not be able to properly diagnose and seek treatment for unhealthy eating behaviors.

Studies have only recently come out to explain that men make up a larger percentage of those with disordered eating than one may think. One study found that 25% of individuals with AN are comprised of men and that men are at a higher risk of dying from the disorder. The researchers partially credit the higher mortality rate of men with regards to eating disorders because men are typically diagnosed later as many people assume males do not have eating disorders (Statistics & Research on Eating Disorders, 2022). Overall, the stigma surrounding men with eating disorders have proven to be detrimental to the men affected, indicating a strong need for more research to be done in this field.

Transgender People

Many transgender people suffer from body dysmorphia, which may place them at greater risk for developing unhealthy eating behaviors. In one study examining the relationship between gender identity, sexual orientation, and eating disorders in college students, researchers found that transgender people were indeed at a greater risk for developing disordered eating. Across all genders and sexual orientations, transgender people were most likely to have self-reported eating disorders with many reported using diet pills and vomiting or laxatives in the past month (Diemer, Grant, Munn-Chernoff, Patterson, & Duncan, 2015). More research is needed to better understand the implications of eating disorders in the transgender community.

Diabetics

According to one review article, those with diabetes were at greater risk for developing an eating disorder because they had a chronic medical condition that directly concerns a focus on

diet and dietary restraint. Additionally, the use of insulin results in a higher BMI, which may also put those with diabetes at greater risk for developing an unhealthy relationship with food. In a study comparing preteen and early teenage girls with and without type 1 diabetes, researchers found that diabetics were more likely to binge eat, to excessively exercise, and to have a combination of eating disorders (Colton, Olmsted, Daneman, Rydall, & Rodin, 2004). Diabetics are more at risk for developing disordered eating, but more research may be needed to better understand the relationship between diabetes and eating disorders.

Athletes

With a huge pressure to be in shape and maintain a thin physique, athletes face a unique risk of developing an eating disorder. Compared to other individuals, athletes may be more prone to over-exercising or developing unhealthy eating patterns, specifically female athletes. In a study with Division 1 NCAA athletes, over one-third of female athletes reported attitudes and symptoms placing them at risk for AN. In another study with female high school athletes involved in aesthetic-related sports, 41.5% reported disordered eating. Moreover, the study found that female athletes with eating disorders were eight times more likely to be injured than athletes in aesthetic sports who did not report disordered eating, indicating the adverse effects of athletes with eating disorders (Statistics & Research on Eating Disorders, 2022). Overall, the relationship between athletes and eating disorders is relatively poorly understood, especially in male athletes.

Jewish Community

With a culture that is centered both around meals and the expectation of staying thin to attract potential marriage suitors, the Jewish community is particularly at risk for developing unhealthy eating patterns. The stigma within the community surrounding discussions of eating disorders as well as a general lack of resources and education regarding eating disorders may

contribute to the community's unique risk. Another note of importance is that there are several fast days in the Jewish religion, which may promote the act of restricting one's calories and ultimately leading to the development of disordered eating. The National Eating Disorder Association (NEDA) acknowledges that there is no scientifically proven reason why the Jewish community would be at a greater risk, but it is clear from their cultural practices that they are at a unique risk. NEDA highlights that a Jewish individual with an eating disorder or a predisposition for the disorder may restrict their calories during the week to indulge in the Sabbath delicacies (Eating Disorders in the Jewish Community, n.d.). This indicates that observant Jews may use religious practice as an unintended excuse for their unhealthy eating patterns.

One study that used the Eating Attitudes Test, a self-reporting survey aiming to differentiate between individuals with and without eating disorders, confirmed that Jewish adolescent females were more at risk for developing eating disorders compared to their non-Jewish peers. The researchers in the study also noted that they did not find clear reasons for this distinction but that this is a step towards discovering the relationship between the Jewish community and eating disorders (Pinhas, Heinmaa, Bryden, Bradley, & Toner, 2008). Though more research is needed to understand eating disorders within the Jewish community, understanding the potential correlation is important for medical practitioners to acknowledge.

PHYSIOLOGICAL MANIFESTATIONS

In addition to the various causal components of disordered eating, eating disorders can present as a variety of physiological manifestations. Both those actively suffering with the disorder as well as those who are recovering from the disorder face serious adverse effects due to their unhealthy eating patterns. Though malnutrition impacts almost every aspect of human

physiology, this paper will discuss the oral and salivary, gastrointestinal, endocrine, and bone metabolism manifestations.

ORAL AND SALIVARY

As a result of nutritional deficiencies and self-induced vomiting, many with eating disorders have oral and salivary complications. Potential dental issues include dental erosion, tooth decay, and gum tissue, or periodontal, disease. Erosion of tooth enamel is further worsened when those with eating disorders compensate with sugary and acidic foods and beverages, caffeinated or carbonated beverages, or sugary chewing gum.

The acidity of vomit involved in purging can erode the teeth and mouth area. As opposed to other gastrointestinal issues, which affects the posterior teeth, eating disorder-related vomiting manifests as erosion of the anterior teeth (Preetha, Sujatha, Patil, & Hegde, 2015). Being able to identify where tooth enamel erosion is occurring can aid medical practitioners in differentiating between gastrointestinal issues, such as reflux, and eating disorder-related purging. Additional erosion from the acidic vomit can cause the development of ulcers in the soft palate of the mouth, which can be incredibly painful and potentially cause infection.

The malnutrition associated with eating disorders can have serious implications for dental health. Primarily, the dehydration involved in some disordered eating can result in dry mouth, which can cause additional tooth decay and mouth sores (Dental Complications of Eating Disorders, n.d.). Moreover, deficiencies of various vitamins due to purging can cause perioral and periodontal disease. Specifically, vitamin C deficiency is associated with impaired collagen synthesis and gingival inflammation, and vitamin B deficiency, especially vitamin B1, B6, and B12, can impair epithelial cell turnover (Bern, Woods, & Rodriguez, 2016). Lack of iron can result in mouth sores, lack of vitamin B3 can cause bad breath and canker sores, and lack of

calcium can cause tooth decay and gum disease (Dental Complications of Eating Disorders, n.d.). Not only does malnutrition affect dental health because of a lack of proper vitamins, but it also can cause opportunistic infections in the mouth area due to the development of a weakened immune system.

GASTROINTESTINAL

As briefly mentioned in the context of oral health, there is a lot of overlap between the symptoms of purely gastrointestinal issues and gastrointestinal complications due to disordered eating, which makes it difficult for medical practitioners to distinguish between the two. To this point, when analyzing the relationship between eating disorders and gastrointestinal symptoms, one study found that in patients with restrictive eating and/or purging disorders, one-third complained of esophageal issues, such as heartburn, chest discomfort and difficulty swallowing (Wang X. , Luscombe, Boyd, & et al., 2014). It is worth mentioning that AN is more easily distinguishable from other gastrointestinal issues as it causes severe malnutrition while BN and BED are harder to distinguish as their symptoms are more covert.Understanding the differences between purely gastrointestinal issues and adverse gastrointestinal effects due to eating disorders will help medical practitioners in properly diagnosing individuals.

Esophageal

Those with an eating disorder that engage in self-induced vomiting have regular contact between the lining of the esophagus and the regurgitated acidic gastric contents, which can cause esophageal inflammation and abnormal growths. In one study, patients who reported purging due to their disordered eating present similarly to those with achalasia, a disorder that damages the esophageal nerves and makes it difficult for those affected to swallow (Bern, Woods, & Rodriguez, 2016). To a similar effect, researchers performing endoscopies on 37 patients with

BN found that their stomach and esophagus appeared normal for 23 of the patients, but the rest of the patients presented with gastrointestinal abnormalities. Though a relatively small sample size, their findings suggest that purging has the potential to cause damage to the gastrointestinal tract, but the damage is variable in each person. The extent of the damage, particularly to the esophageal region, depends on how long and how much the affected individual purges (Kiss, Wiesnagrotzki, Abatzi, & et al., 1989). In extreme cases, studies have found that extended periods of purging can even cause the onset of esophageal cancer (Shinohara, Swisher-McClure, Husson, & et al., 2007).

Stomach

A review of the scientific literature reveals that the nutritional deficiencies and the emptying of the stomach through purging has variable effects. Many with BN and AN complain of bloating, nausea, epigastric discomfort, and fullness. These symptoms can be the result of impaired motility of the gastrointestinal contents due to the disorder, but it can also be the result of a purely gastrointestinal disorder (Hadley & Walsh, 2003). Impaired motility of gastric contents can cause poor nutrient reabsorption and constipation among other things.

Small and Large Intestine

With the largest surface area in the gastrointestinal tract, the small and large intestine can develop problems due to purging. For instance, one study with patients with restrictive eating and/or purging disorders found that 53% had irritable bowel syndrome, functional bloating, or constipation (Wang X. , Luscombe, Boyd, & et al., 2014). Researchers studied the gastrointestinal tract in animal models and found that when starved, the animals had reduced absorptive surface area, reduced cell proliferation, and increased risk for infection. This was confirmed in another study regarding women with AN who were found to have decreased

permeability of the intestines. These findings suggest that caloric deficiencies may cause one's body to train itself to reduce the need to absorb nutrients over a large surface area so that it can focus its attention on absorbing whatever little nutrients are available (Bern, Woods, & Rodriguez, 2016).

The use of laxatives has had various effects on the intestinal tract as the ingredients change over time. Laxatives function by changing the way that fluids and electrolytes are transported and/or the rate of movement in the intestines, resulting in an increase in stool amount and frequency. Researchers have found that present day laxatives contain certain neurotoxins, such as podophyllum, that may result in cathartic colon (De Ponti & De Giorgio, 2002). Another ingredient that may be harmful is castor oil, which can damage the intestinal lining by damaging the intestinal epithelial cells (Bern, Woods, & Rodriguez, 2016)**.**

Pancreas

As another member of the digestive system, the pancreas can be impacted by the malnutrition involved in disordered eating. Acute pancreatitis, or inflammation of the pancreas over a short period of time, has been associated with patients with AN. During the nutritional rehabilitation that comes with recovered eating disorder patients, shifts in bodily fluids may cause a lack of blood flow to the pancreas, which can affect pancreatic function (Keane, Fennell, & Tomkin, 1978).

Liver

The symptoms of eating disorders can also have ranging adverse effects in the liver. Low BMI can cause damage to the liver by causing a range in elevation of liver enzymes, most importantly in hepatic transaminases. One study found an increase in liver enzymes in 4% of affected individuals (Mickley, Greenfeld, Quinlan, & et al., 1996) and another found elevation in

one-third of individuals (Tomita, Haga, Ishii, & et al., 214). Elevated levels of transaminases in the blood are signs of inflammation and damage to the liver cells. Therefore, having elevated liver enzymes in patients with disordered eating compared to controls indicates that the malnutrition associated with eating disorders can result in liver damage.

The extent of liver damage in patients with eating disorders can be determined by the severity of malnutrition: the more severe the malnutrition, the greater the risk for damage to the liver (Nagata, Park, Colditz, & et al., 2015). In one study analyzing patients with AN, the injury to the liver was found to occur because of "starvation-induced autophagy." Autophagy is a normal cellular process that occurs when a phagosome, or phagophore, consumes proteins or organelles in the cytoplasm to form a complex called an autophagosome. The autophagosome fuses with a lysosome to form an autolysosome, and this complex allows the material inside to be degraded by the hydrolase enzymes in the lysosomes (Figure 3) (Xie & Klionsky, 2007). The malnutrition resulting from AN can cause autophagy to be excessively activated in order to promote nutrient preservation and protect liver cells from being broken down. When autophagy is provoked unnecessarily, it can result in liver cells to be broken down faster than they can be formed (Kheloufi, Boulanger, Durand, & et al., 2014).

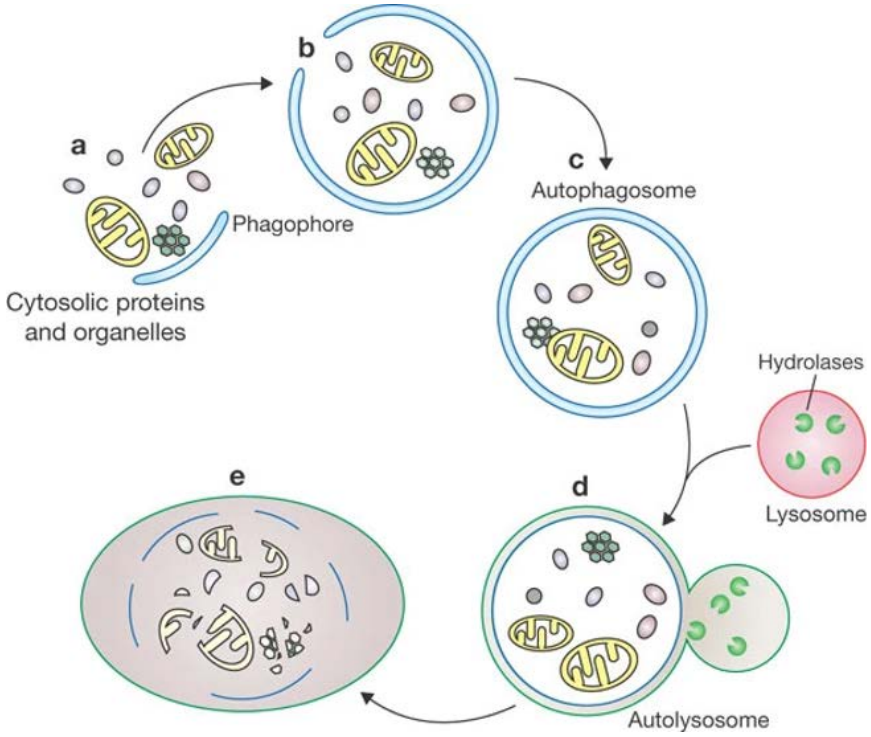


Figure 3: Schematic Depiction of Autophagy. (a, b) Cytosolic material is sequestered by an expanding membrane sac, the phagophore, (c) resulting in the formation of a double-membrane vesicle, an autophagosome; (d) the outer membrane of the autophagosome subsequently fuses with a lysosome, exposing the inner single membrane of the autophagosome to lysosomal hydrolases; (d) the cargo-containing membrane compartment is then lysed, and the contents are degraded. Taken from Xie & Klionsky, 2007.

ENDOCRINE

Reproductive Hormones

Amenorrhea, or the absence of menstruation, has been found to be associated with AN due to extreme caloric deficits. Malnutrition can cause a lack of menstruation because of an impaired release of gonadotropin releasing hormone (GnRH) from the hypothalamus, resulting in lower levels of luteinizing hormone (LH) and follicular stimulating hormone (FSH) and ultimately of the sex hormones that control menstruation (Figure 4). LH plays a crucial role in

the menstrual cycle by triggering ovulation, or the release of an egg from the ovaries, along with regulating the sex hormone progesterone. FSH is also instrumental in maintaining proper function of the menstrual cycle as it stimulates the eggs to grow in the ovaries and is involved in regulated the sex hormone estrogen. One study found that women and girls with AN have lower levels of estradiol, a type of estrogen hormone, and testosterone compared to controls, which confirms the notion that malnutrition can impact the menstrual cycle (Misra, et al., 2003). In men, LH stimulates the testes to produce testosterone, which is responsible for male secondary sex characteristics. Similarly, FSH release in men helps to control sperm production. Disruption to the hypothalamic-pituitary-gonadal axis in both women and men due to malnutrition can cause reproductive issues.

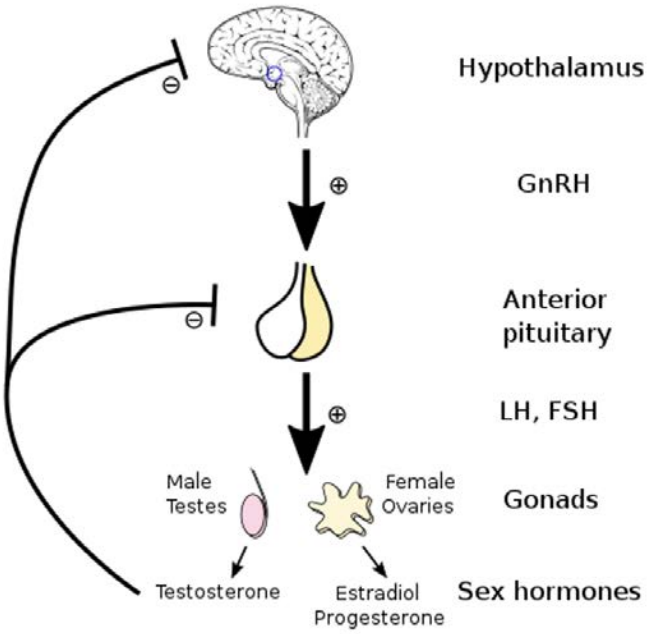


Figure 4: Schematic Representation of the Hypothalamic-Pituitary-Gonadal Axis. Positive signs indicate positive stimulation; negative signs indicate negative feedback. Adapted from Hypothalamic-pituitary-gonadal axis, n.d.

Not only can malnutrition cause amenorrhea, but also the impaired GnRH release may result in alterations in hormones that are secreted or regulated by fat, such as leptin, ghrelin, peptide YY, adiponectin, cortisol, insulin, and insulin-like growth factor-1 (IGF-1). One such hormone, ghrelin, is an appetite stimulant secreted by the stomach that reflects energy levels. High levels of ghrelin suggest that the body is low on energy and stimulates appetite; high levels of ghrelin are usually found in patients with AN as those affected are severely malnourished. Ghrelin also causes the secretion of growth hormones (GH) and has been found to be increased in patients with AN due to their extreme state of malnutrition (Misra & Klibanski, 2011).

Growth Hormone Insulin-Like Growth Factor-1 Axis

The severe malnutrition involved in AN has been associated with an acquired resistance to GHs. As previously discussed, the appetite stimulant ghrelin also stimulates the secretion of GH, and, in patients with AN, this can cause a buildup of GH and ultimately a resistance to the hormone. This resistance may manifest as elevated GH levels, decreased production of IGF-1 in the liver, decreased levels of GH receptor, or an overall decreased expression of the GH receptor (Misra & Klibanski, 2011).

Another factor contributing to GH resistance is fibroblast growth factor-21 (FGF21), which stimulates glucose uptake in adipocytes, or fat cells. In one study, FGF21 mice were found to have high GH and low IGF-1 levels; FGF21 overexpression inhibits STAT-5, a key transcription factor in the GH-signaling cascade, which ultimately explains the cause of GH resistance (Inagaki, et al., 2008). Another study confirmed a positive association between elevated FGF21 levels and GH concentrations in adolescent girls with AN and an inverse association with IGF-1 (Fazeli, Misra, Goldstein, Miller, & Klibanski, 2010). Though the

mechanism of GH-resistance has been extensively explored by researchers, applying this in a clinical setting is of utmost importance.

Hypothalamic-Pituitary-Adrenal Axis

Blood and urine levels of cortisol, the body's main stress hormone, were found to be higher in AN than controls. Cortisol is involved in gluconeogenesis and increases in individuals with AN as a counter response to the patients' reduced caloric intake to maintain normal blood glucose concentrations. High levels of cortisol may have a negative impact on gonadotropin secretion and may contribute to hypogonadotropic hypogonadism, a condition in which there is little to no secretion of sex hormones by the sex organs (Misra & Klibanski, 2011).

Hypothalamic-Pituitary-Thyroid Axis

Thyroid function, which controls metabolism functionality and particularly the T3 hormone, is associated with markers of one's nutritional status. One study indicated that girls with AN have no differences in thyroid stimulating hormone (TSH), which stimulates the release of thyroid hormones, but the total T3 and T4 count was significantly lower compared to controls (Misra, et al., 2005). Lower T3 and T4 levels are correlated with nutritional deficiency, which is expected in patients with AN or similar eating disorders.

The secretion of various hormones has an impact on thyroid hormone levels. Ghrelin inhibits the secretion of TSH, so high levels of ghrelin may be associated with low thyroid hormone levels. Leptin, on the other hand, stimulates the secretion of TSH, so high levels of leptin will be associated with high thyroid hormone levels (Misra & Klibanski, 2011). Malnutrition has various adverse effects on the many hormonal systems throughout the body; however, more research is needed to better understand the effects of eating disorders other than AN.

BONE METABOLISM

The severe malnutrition associated with eating disorders may result in those affected to be at a high risk for low bone density. The bone density of children, adolescents, and adults with eating disorders are impacted differently. Children with poor nutrition and delayed or arrested puberty may lead to an over-reporting of low bone density, which can be confused with the low bone density associated with eating disorders. Furthermore, children are most vulnerable to the effects of eating disorders on bone development as they have yet to fully develop. Adolescents with AN were consistently found to have a decrease in bone formation and resorption, indicating a low bone turnover rate and therefore are at risk for not achieving peak bone mass, which is an important determinant of bone health and fracture risk later in life. Adults with AN were also found to have a decrease in bone formation and an increase in bone resorption, but this may have less of an effect as in children or adolescents as adult bones, for the most part, are no longer growing to the same extent (Misra & Klibanski, 2011).

Hormonal levels have a direct influence on the bone density of those who are malnourished, such as those with unhealthy eating patterns. As previously discussed, those with severe cases of eating disorders may experience impaired release of sex hormones and may face amenorrhea as a result. The longer a woman or girl goes without her period can be a predictor of the extent of bone loss. Moreover, normal increases in GH and IGF-1 during puberty are crucial to properly facilitate bone formation and growth during puberty; without this vital increase in hormones, bone formation will not occur properly or to a lesser extent. Particularly, GH-resistance due to AN was found to contribute to low bone density. Even with the administration of GH in high doses, there were no markers of bone formation, which further confirms GH-resistance in patients with AN. Another hormonal influence on bone density is the

negative impact of high levels of cortisol on bone density. In patients with AN, high cortisol levels and lower bone formation confirmed this effect (Misra & Klibanski, 2011).

Even when patients recovered from their unhealthy eating patterns, the resulting low bone density was not restored to normal bone density. In one study, patients in recovery from AN did not fully restore bone formation function (Misra, et al., 2008). The administration of calcium and vitamin D, both essential in the formation of bone, was not found to be effective in restoring or increasing bone density in individuals with AN (Soyka, Grinspoon, Levitsky, Herzog, & Klibanski, 1999). Even in the stage of recovery, those with eating disorders experience long term adverse health implications that may never be reversible. More research is needed to better understand these long-term, and sometimes irreversible, effects.

CONCLUSION

Today's media-driven society has placed greater emphasis on appearance than ever before, which has played a tremendous role in the rampant cases of eating disorders. With types and classifications being categorized only recently, eating disorders have only begun to be understood. Though new technologies have allowed the genetic and environmental causal components to be better understood, conflicting conclusions suggest that researchers have only scratched the surface of the complexity of disordered eating. Specifically, more research appears to be needed in discovering the genetic component of disordered eating as it has been genetically linked to immune system malfunctions, which can have serious implications. Some groups of people appear to be at a particular risk for developing eating disorders; however, all those impacted by the disorder experience serious physiological manifestations. Though there is much research done to investigate the adverse effects of eating disorders, more research is needed to

better understand the long-term implications to better handle the proper treatment for eating disorders.

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