The Etiology of Anorexia Nervosa and Bulimia Nervosa

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Abstract

Proper nutrition is an important concept that is enforced over and over by parents, teachers, coaches and the government. Nutrition effects every system in the body and can dramatically alter someone's personal state of health. However, society presents a picture of bodily perfection that combined with genetic predisposition can result in the manifestation of an eating disorder. Eating disorders occur on a continuum, ranging from extreme obesity to anorexia. Of the many eating disorders, anorexia and bulimia have been most extensively studied. They both occur predominately in females and the onset is usually during teenage years, and in both, the defining symptom is an intense sense of fear to gain weight.

This paper reviews some of the major recent research on the etiology of anorexia and bulimia. Both disorders are examined from a physiological, genetic and behavioral/social aspect in an attempt to clarify the influence that each has on etiology of anorexia and bulimia. The knowledge of these disorders is growing in the field of science as well as in society. With the advancements, anorexia and bulimia have become more treatable, but remain incurable. A deeper knowledge of the etiology of these eating disorders is necessary in order to get closer to finding improving treatment.

Introduction

In today's society, eating disorders are becoming more uniformly accepted as serious psychological disorders. Initially thought to be social disorders, the improvement in knowledge of genetics is beginning to suggest that there is also a physiological basis that contributes to the etiology of eating disorders. It is commonly accepted that eating disorders occur on a continuum, with intense restriction of food at one end and extreme overeating at the other end. Currently, there is an obesity epidemic occurring in America. Easily accessible food that is high in fat and hectic daily routines that do not allow time for exercise are effecting this country's health. As obesity is receiving more attention from the media and researchers, the opposite end of the spectrum is also peaking the interest of the medical society. Although eating disorders are not as prevalent as obesity, they are very dangerous disorders. Eating disorders are threatening for many reasons. Firstly, eating disorders are complex. They derive from environmental and genetic factors, and are often accompanied by one or more psychological disorders. The prevalence rate for both anorexia and bulimia is low, 0.1%-1% for anorexia and 1%-2% for bulimia.. These numbers are good, however, the rate of relapse after treatment is between 8% and 62% within the first 5 years of recovery (Bulick, 2005). The prevalence rates for anorexia and bulimia must be approached cautiously. The data is based on those patients who have been diagnosed, meaning those who have sought the help of a doctor or psychologist. Partial cases of anorexia and bulimia may go unnoticed and untreated, while others may refuse to seek medical help. Lastly, research has shows that the mortality rate for patients with eating disorders is much higher. As compared to a healthy population, the mortality rate for patients with eating disorders is 6.0 to 12.82 times higher. The seriousness of eating disorders is very evident. Despite the low

prevalence rate, the high relapse rate, high mortality rate and the complexity of the disorder have prompted an increase of research in this field .

Both disorders largely affect young females age 12-22, however the diagnosis in males is becoming more common. Currently it occurs in males 10% as often as it occurs in females. Researchers are running a wide range of experiment that explore the possible physiological, genetic and environmental causes of eating disorders. Presently, the treatment of an eating disorder requires an expansive medical team. The various causes, symptoms, side effects and treatment of eating disorders often require a dietitian, psychologist, psychiatrist, and other medical specialists to properly treat the disorder. Whether inpatient or outpatient the overall therapeutic goal is to have the patient gain weight and maintain it by removing the fear of weight gain and terminating the behavior that resulted from that fear. Appetitive behavior is influenced by neurotransmitters, hormones, genes, personality, mood, environment, and so much more. Each of these different aspects must be explored in an attempt to learn as much as possible about these disorders.

As research in this field progresses, so does the hope that a more effective form of treatment and preventative measures will soon be found. This paper reviews the current literature on the physiology, genetic and behavioral/social component that contribute to anorexia and bulimia. Research specific to both disorders will be cited in order to gain understanding about each disorder individually. Though the two disorders are very similar in appearance, their etiology is slightly different. The similarities and differences of these two disorders as well as the possible implications of each will be discussed.

The Etiology of Anorexia Nervosa

Since the recognition of anorexia nervosa as a psychological disorder, the medically accepted definition of the disorder has changed. The currently accepted DSM-IV definition of a full syndrome anorexic patient will display all of the following symptoms: A refusal to maintain normal body weight, so that their body weight is less than 85% of that which is expected; an intense fear of gaining weight despite being underweight; abnormalities in the way one perceives his/her own body, extreme influence of body weight on self perception and/or denial of the seriousness of low body weight. In postmenstral females, amenorrhea is often apparent and males show a severe decrease in circulating hormones. Younger patients who experience an earlier onset of the disorder may not reach their full potential height due to nutritional deficiencies. A patient who meets some but not all of the requirements, or does not meet the requirements to the point that they are preventing him/her from leading a normal lifestyle, often receive a partial diagnosis. In addition to the physical symptoms and side effects of the disorder, many patients also deal with mood disorders such as depression, bi-polar disorder, and anxiety disorders such as obsessive-compulsive disorder. One disorder does not cause the other, however there is a strong correlation between the presence of one with the other.

There are two forms of anorexia. The first is the restricting type, defined as a period when the patient severely restricts his/her caloric intake and does not engage in binging or purging behavior. In this state patients classify types of foods as either good or bad, allowing themselves to eat none of the bad and very little of the good. Once emaciated, an anorexic patient may become satisfied with his/her body, but will continue to not eat in order to prevent weight gain. An anorexic patient is most dangerous, however, when he/she does not become

satisfied with his/her body and continues to try to lose weight. Instead of maintaining a low unhealthy body weight, they continue to allow their weight to drop even lower, resulting in hospitalization and forced feeding. The second form of anorexia is the binging/purging type. This occurs when a patient suffering from anorexia binges on food and then purges in order to lose the calories. Purging can be defined as over-exercising, misuse of laxatives and diuretics, vomiting, or fasting. This cycle can occur one day a week or up to several times a day. Binging/purging cycles are seen as phases that restrictive anorexics go through when at a very low point and are very desperate to lose weight. Not all anorexics experience binging/purging cycles, however it is very common for recovering anorexics to relapse into stages of binging and purging.

This section of the paper examines the research that is being done in many different fields in an attempt to learn more about anorexia nervosa. Physiological aspects, genetic components and social and environmental factors all contribute negative components that result in the manifestation of an anorexia. Research is working to determine the magnitude of effect that each factor has and how it creates that effect.

Physiology of Anorexia Nervosa

The physiological research being done on anorexia nervosa has focused mainly on neurological abnormalities and their effects on emotion and behavior. As knowledge of the brain grows, researchers are looking to neurotransmitter and hormonal deficiencies as the cause of eating disorders. Serotonin, dopamine, ghrelin, leptin, and brain derived neurotrophic factor have all been individually researched. Each of these possibilities will be explored using

evidence from some of the most recent studies.

Serotonin has been a neurotransmitter targeted in the research on eating disorders for multiple reasons. Firstly, patients with anorexia tend to demonstrate abnormal serotonin processes involving receptors and transporters. Secondly, many comorbid personality and affective disorders that accompany anorexia, such as anxiety, harm avoidance, and depression are known to be negatively effected by abnormalities in 5-HT as well as 5-HT transmitters. And thirdly, symptoms of anorexia have been slightly ameliorated by treatment with medications known to affect 5-HT pathways (Kaye et al, 2005; Kaye et al,2005). Research has shown that 5-HT is involved in moderating appetitive behavior. Studies conducted by Takimoto and his colleagues showed that 5-HT distributes some control over postprandiasl satiety. A decrease in hypothalamic 5-HT leads to an increase in carbohydrate intake and impairment of the normal levels of satiety. Other research on anorexia has shown through the use of PET scans that there is reduced 5-HT2A receptor activity in parts of the cingulate cortex and temporal and parietal cortical areas of the brain in anorexia (Bailer et al, 2004). Both of these studies were conducted on recovered anorexic patients, and despite no longer being ill, they sill showed these discrepancies in 5-HT2a receptor activity. In addition to th abnormal function of the 5-HT2a receptor, it has also been found that discrepancies from the norm also occur in the 5-HT1a receptor and the 5-HT transporter. Even though there have been a couple of studies to show no significant effect in symptoms with the administration of SSRI's, other research has shown a significant improvement in inpatient anorexics after the administration of fluoxetine and other antidepressants (Kaye et al, 2005: Attia et al, 1988; Strober et al, 1999; Kaye et al, 2001).

Researchers such as Kaye et al, and Uher use both PET and SPECT scans in order to determine the activity level of 5-HT in the different areas of the brain (Kaye et al, 2005; Uheret

al, 2005). In a study by Uher et al, brain activity was monitored using functional magnetic resonance imaging. Healthy women and women with eating disorders were shown pictures of underweight, normal weight, and overweight women. The subject also rated their level of fear and disgust on a scale of 1-7 when presented with the drawings. The subjects ratings and recorded brain activity were analyzed and compared. Healthy women and female anorexic patients both showed activation in the later fusiform gyrus, inferior parietal cortex and lateral prefrontal cortex. The difference was found in the strength of the responses. This effect and/or cause of this difference is unclear. It is possible that the decreased 5-HT response was present pre-diagnosis and contributed to the development of the disorder. Or, the disorder could have resulted in the damage of brain tissue, causing the decreased response. Overall, the anorexic patients rated all of the images as more aversive on the both the scale of fear and disgust. They were unable to find any body image to be satisfactory. The researchers were able to find a correlation between the ratings of aversiveness to activity in the right medial apical prefrontal cortex. Previous studies (Bailer et al, 2005) have also, through the use of MRI and PET scans, identified potential alterations in temporal lobe. The temporal lobe functions in abstract behavior, problem solving, movement and others. This study by Bailer et al was also able to show that the altered 5-HT activity in the temporal and frontal lobe of the brain was present while suffering from anorexia and after recovery from anorexia. The fact that this abnormality persists after recovery insinuates that the low 5-HT activity is making the subject vulnerable to anorexia.

More evasive research is being conduced using animal models. In a study by Hillebrand et al (2005), research was conducted on rats with activity-based anorexia. Activity-based anorexia is accepted as the animal model of anorexia. It can be inflicted on an animal with the

combination of scheduled feeding and voluntary wheel running. This combination results in an increase in running time, decreased feeding, extensive body weight loss and increased activity of the APA axis. Scientists believe that the melanocortin system could be the cause of this irregular behavior. The melanocortin system works to suppress appetite and in rats can be overstimulated by using a-MSH treatment. When given an a-MSH treatment, the rats increased running in the running wheel, decreased food intake, and decreased body weight. It is possible that the over activation in humans would result in similar activities.

Other appetitive-modulating hormones and neurotransmitters such as ghrelin, brain derived neurotrophic factor, leptin, and dopamine, have been studied for a possible link to anorexia. Levels of ghrelin in anorexic and healthy subjects have been compared. Ghrelin in an appetite stimulant that is present in large quantities before a meal and then decreases after a meal. Anorexic patients do not eat, therefore their body is in a constant state of needing nutrition. Whether the patients' feel intense hunger or not the circulating levels of ghrelin are going to be high because the necessary nutrition is not there to decrease production of ghrelin. When a patient is treated and weight is gained, ghrelin levels return to normal.

A second small areal of emphasis deals with the neurotrophic factor. Brain derived neurotrophic factor is responsible for neurodevelopment, plasticity and survival, especially during the initial creation of the brain. In research, BDNF has been removed from rats after birth (Rios et al, 2001). When subjected to stressful stimuli, the rats were anxious and hyperactive. More importantly, the mice had a dramatic increase in body weight, increased linear growth, and higher than normal levels of leptin, insulin, glucose ad cholesterol. All of these factors contributed to early onset obesity. In humans, circulating serum levels of BDNF were measured and shown to be significantly decreased in anorexic patients. This is interesting because the

absence of BDNF in rats was highly correlated with obesity, but in humans, you have the opposite effect. It is possible that measuring the serum BDNF levels is measuring something different than simply measuring the BDNF levels. Or it could be that there is a threshold level that exists between no BDNF and low BDNF. Whatever the reason, the low levels of BDNF is also significant because the same low levels can be found in patients suffering from depressive symptoms. From this data, it is evident that BDNF levels have some effect on eating behavior. The genetic significance of low BDNF levels will be discussed later.

Leptin is a peptide hormone that is excreted by adipose tissue. It suppresses appetite and burns fat stored in adipose tissue by acting on the hypothalamus (Misra et al, 2005). The greater the number of adipose cells, the higher the level of leptin. Therefore, with the extreme low levels of adipose tissue in anorexic patients, you would expect anorexic patients to also have low levels of leptin. However, because of the amazing ability that anorexics have to refrain from eating, one can also speculate that there may be abnormally high levels of leptin, over-suppressing appetite. In a study by Misra et al, leptin levels in anorexic patients were significantly lower than in healthy patients. In addition to suppressing appetite, leptin has been shown to assist in the regulation of the levels of hormones such as growth hormone, cortisol, thyroid-stimulating hormone, and luteinizing hormone that can be effected by a person's nutritional state. This connection is very reasonable considering some of the symptoms of anorexia in adolescents. The low growth hormones attribute to the stunted growth that appears in early onset anorexia. Similarly, low levels of luteinizing hormone, and thyroid-stimulating hormone can be linked to the high prevalence of amenorrhea that occurs in female anorexic patients.

Dopamine has also been studied, though not as extensively as serotonin. A study (Frank

et al, 2005) used C-raclopride, a diagnostic aid with PET scan to determine the density of D2 (dopamine 2) receptors. This measure combined with magnetic resonance imaging show that in anorexic patients, there is a decrease in the amount of intersynaptic dopamine and upregulation of D2 and D3 receptors. Dopamine is involved in fine motor co-ordination, immune function, motivation, insulin regulation, physical energy, thinking, short term memory and emotion. An imbalance in dopamine could affect any of these systems. For example, the shown disproportionality of dopamine and dopamine receptors in areas regulating physical energy, emotions and motivation could be a leading cause of the harm avoidance and extreme amounts of physical activity that often characterize anorexic patients. Similarly, discrepancies in dopamine involving thinking and motivation could contribute to the disturbance of reward mechanisms. This disturbance would reward patients when they did not eat, reinforcing the behavior. Dopamine's influence on fine motor coordination is also altered in anorexic patients. There is a possible connection between this function of dopamine and the constant movement, and excessive amounts of exercise exhibited by anorexic patients.

In a similar study by Want et al (2004), researchers found decreased D2/D3 receptor binding. This finding strengthens the argument for dopamine's influence on weight control. It is possible that there is an inverse relationship between D2/D3 levels and weight and eating. The Wang et al study was conducted on recovered subjects. Increased D2/D3 receptors in recovered patients can mean one of two things. Firstly, it could mean that the increase of D2/D3 receptors is caused by the disorder and after recovering fully, it could mean that this abnormality contributed to the onset of the disorder. Frank et al also found increased C-roclopride binding potential, meaning an increase of D2/D3 receptors in the antero-ventral striatum area of the brain is responsible for reward, reinforcement and addiction. Decreased dopamine function in patients

with addictions, has been shown to cause decreased sensitivity to non-drug stimuli. Frank et al hypothesizes that the overactive dopamine system in anorexic patients causes inappropriate response to intense stimuli. This difference between addicts and anorexics shows that anorexia is more than a difference in dopamine function in the anteroventral striatum. Even though patients are rewarded by restricting food intake, this reward is different than the reward delivered to addicts after partaking in their drug. As we learn more about eating disorders and addictions we may be able to apply some of the treatment procedures used on addictive patients on anorexic patients, or alter current treatment.

Genetic Etiology of Anorexia Nervosa:

The genetic evidence for anorexia nervosa is the strongest of all the subtypes of eating disorders. An experiment by Siegfried et al (2005) examined, using twin studies, that genetic influence is around 59%, about the same heritability level as bipolar disorder and schizophrenia. Genes can be influential in two different was. In Mendelian disorders, there is an alteration in ne gene which causes the disorder. The second is more genetically complex. Most mental illnesses including anorexia are influenced by multiple genes acting with and against each other. This makes understanding of the disorder and treatment of the disorder much more difficult. Anorexia has a definite genetic component to it, and for those who have a history of eating disorders in their family, it could also increase the negative influence of their environment. Children of parents who have or have had eating disorders are not only at risk to inherit genes that influence chances for developing anorexia, but they may also be exposed to environments that are shaped by the parental genotype, increasing the likelihood of expression of the

underlying risk genotype. Having the genetic component plus living in an environment that promotes eating disorders is called double disadvantage. Researchers are working to determine what genes and alleles are involved in the manifestation of anorexia. It is difficult because there is not one gene that contributes solely to the development of this disorder. This paper discusses the role of BDNF, cannabinoid receptor gene and different hormone regulating genes as some of the most promising areas of research.

A polymorphism in the gene that transcribes BDNF being researched because of its role in neuron development. BDNF plays a critical role in regulating neural survival, development functions, and plasticity in the brain. A study by Hashimoto et al (2005) reviewed the role of BDNF, its influence on the pathophysiology of eating disorders and the BDNF gene susceptibility gene for eating disorders. Low levels of BDNF have been found in patients with eating disorders and experimentally induced low levels of BDNF in rats, has resulted in abnormal eating behaviors. Researchers in Hashimoto's study worked to isolate those patients with the gene BDNF 196G/A polymorphism. A 196G/A polymorphism converts a valine to a methionine on the BNF gene. Whereas this alteration does not effect the function of mature BDNF protein, it does significantly effect the secretion of mature BDNF protein. Decreasing the secretion of mature BDNF protein, the polymorphism has the greatest impact on the hippocampus which is critical for memory and learning (Egan, 2005). It is still unclear why there is a strong correlation. Researchers are working to understand how this polymorphism contributes to the development of anorexia.

The Cannabinoid Receptor Gene is another genetic variation that has been studied. Endocannabinoids increase feeding, while cannabinoid receptor blockage has been shown to suppress eating. Using animal models, Di Marzo et al (2001) found that when leptin levels are

experimentally increased, endocannabinoid levels decrease. They also noted high endocannabinoid levels in genetically obese animals. Cannabinoids have also been known for their partial responsibility for inducing reward effects, such as pleasure from eating foods. Researcher speculate that the reward pathway involving endocannabinoids and their receptors become altered in coping strategy for anorexic patients. Trinucleotide repeats are a type of a mutation and therefore could be a marker for a neuropsychiatric disorder. Siegfried et al searched for trinucleotide repeats in CNR1 gene. He conducted research on 52 families where the daughter suffered from an eating disorder. Eight different alleles were identified in each of the subjects and searched for polymorphisms. Overall, the results were inconclusive. When split into categorical disorders, the transmission of some alleles were more prominent than others, but none had strong enough transmission to be significant. This experiment should be repeated with a larger subject group. The transmission of some alleles were very close to being significant. A larger sample would give more strongly conclusive results.

In addition to the cannabinoid receptor gene and the brain derived neurotrophic factor, genetic research is also working to find the genes that contribute in abnormal serotonin and dopamine systems. These two systems have been shown to contribute to the symptoms of anorexia. A better genetic understanding of these two systems could indirectly lead to an increased understanding of eating disorders. Also, research for other disorders such as OCD, bi-polar disorder, depression and schizophrenia is constantly being done and built upon. Because of anorexia nervosa's tendency to be accompanied by another psychological disorder, genetic information learned about these other disorders could also be related back to anorexia. The similarities in symptoms and manifestation between anorexia and other psychological disorders such as OCD, bi-polar and depression may imply genetic similarities.

Behavioral/Social:

Historically, eating disorders have been classified as social disorders. More recently, with the advancement in the field of genetics, the extent of societal acceptance and its role on the development of eating disorders has been questioned. Even as the field of genetics is increasing there has been no allele or gene identified as having a strong influence on the development of eating disorders. Therefore, anorexic patients are considered to have similar to psychological disorders such as bipolar disorder and schizophrenia. In order for the disorder to manifest itself, this genetic predisposition must be accompanied by social and behavioral pressures. As previously mentioned, genetic studies are now predicting that the contribution of genetic factors to the manifestation of eating disorders in a patient is between 58% and 76% (Siegfried et al, 2003). That leaves 30-50% of the influence to come from environmental stimuli. Research is being conducted to find out what those stimuli that lead to the development of anorexia. Twin studies, historical research, and correlational studies are all being conducted in order to isolate the confounding factors. Historical research see how the prevalence, severity, and understanding of eating disorders has changed over the years were as research targeting personality types has allowed correlations to be made between personality types.

According to research in health psychology and body image, societal pressures to be thin have increased. Researcher are interested to know whether or not the prevalence of anorexia has increased with the rise of societal pressure. Various historical studies have been conducted that analyze the number of documented cases of anorexia in the 20th century, some that analyze the number of documented cases of anorexia dating back to the 17th century, some that analyze the

number of documented cases of anorexia that occur cross-culturally. This research is not experimental, and therefore there are many confounding factors that must be controlled for as much as possible. Firstly, the definitions of anorexia has changed over the years and are also different across cultures. As a result, ne case that may be considered full anorexia in Europe in 1940 may not be considered anorexia in the US in 1988. Researchers can not look solely at the diagnoses but must also examine the patients's medical records to see if the description of the symptoms corresponded with the present definition of anorexia. Secondly, the way that the incidence of the disorder is calculated can alter the percentage so that they are either too high or too low population must be estimated while controlling for increases or decreases in the population. If the number of adolescent females (the population most often affected by these disorders) is increasing or decreasing it can skew the results so that a too high or too low percentage is found as compared to the population size. The number of documentaries, amount of press coverage, and public awareness have all increased. As a result, patients with the disorder may be more likely to seek help, be treated and therefore increasing the percentage of cases documented. The Monroe County study was a longitudinal study. It showed that from 1960-1969 to 1970-1976 the incidence of adolescents receiving treatment for anorexia rose from .35 to .64 per 100,000 population per year, but the overall number of adolescents receiving some form of psychiatric treatment also rose from 348 to 662 per 100,000 population. It is difficult to separate whether there was a real increase in the cases of anorexia or if the increase was a result of the increase of cases reported.

Researcher have found cases of self-starvation dating back to the 5th and 8th centuries. These cases were thought to be the result of demonic possession and were said to e cured by exorcism. With advancements in society and science, the cause and reasoning behind food

refusal changed as well. The motivation that prompted individuals to refrain from eating changed with society, and as a result the validity of the diagnosis became unclear. Fasting became elevated by religion and by society. With the revered status that was given to those who refrained from eating, it s possible that some who were diagnosed were actually faking it in order to receive the admiration. For example, in the late 1800's according to studied sone by Bemporad (1996) and Brumbert (1989) fasting was seen as being an action that revered the saints and it gained the females great amounts of attention nationally and internationally. They cited specific cases where the emaciation of the patients attracted people from all over who marveled at their ability and their dedication to the refusal of food. There was also a case of females who were though to have the amazing ability to eat nothing, and yet retain a healthy weight. Discrepancies such as this make it very difficult to draw conclusive evidence about whether or not the cases were legitimate. As a result, it makes it difficult to determine how the prevalence of eating disorders has changed.

When looking cross-culturally, studies show the existence of anorexia in developed, westernized nations as opposed to underdeveloped nations not effected by western culture. The main difference cross-culturally is the reason that patients have for not eating. The most common reason in western culture is the fear of gaining weight. Contrastingly, a 1993 study conducted in Hong Kong by S. Lee et al (1993) showed that 50% of the patients diagnosed with anorexia blamed their restricted diet on digestive discomfort. The same researcher from Hong Kong hypothesized that with the westernization of their culture, the number of anorexic patients who fear weight gain would increase. When a follow-up study was done in 2000, they did find an increase in fear being cited as the cause of food restriction as compared to digestive discomfort being cited as the cause.

Personality types have also been studied as contributing to the etiology of anorexia. Perfectionism, obsessive-compulsive traits, narcissism, sociotropy, and autonomy are all outstanding characteristics that are commonly found in restricting anorexics (Cassin et al, 2005). Perfectionism is characterized by the setting of extreme goals or ideals and working incessantly to reach them, despite negative consequences that may affect the patient, or those associated with the patient. There are three forms of perfectionism; self-oriented, other-oriented, and socially prescribed perfectionism. In a study conducted by Bastiani et al. (1995), using the Multidimensional Perfectionism Scale, the researcher found that the perfectionism most commonly displayed by restricting anorexic patients tended to be self-oriented and socially prescribed perfectionism. Obsessive-compulsive traits are easily found in patients with eating disorders. Anorexics are continuously obsessing over their bodies and their weight, knowing and being uncomfortable about everything that goes into their mouth. Not eating or over-exercising acts as a compulsion by alleviating some of the obsessions temporarily. A form of narcissism is also often found in anorexic patients. It is not the tradition form of narcissism where a person has an intense love for their body, but instead, these subjects have an intense love and intense drive to improve their body image. In both cases, the narcissist has a deep preoccupation with his/her own body. A final characteristic is either sociotropy, being concerned with acceptance, or autonomy, being very independent and purpose driven. Anorexia patients usually display one or the other. These personality traits, may be a result of environment or genetics or both. Either way, they can help to expedite the onset of an eating disorder, enhance the severity of the disorder, and linger after recover, increasing the number of relapses.

Anorexia is a complicated disorder. Genetic and environmental factors cause abnormalities in physiological systems which lead to the development of the disorder. Research

is being done on the physiological systems to learn what abnormalities exist and what the resulting complications are. Genetic Research approaches the problem differently. Researchers look for abnormalities in the genes that are encoded for the physiological systems. And finally, the role that the environment pays is explored using experimental methods as well as linear studies. The more knowledge we have about the different aspects of the disorder, the better and more effective the treatment can be. With continued Research in all three areas, advancements will continue to be made.

The Etiology of Bulimia Nervosa

Bulimia nervosa is characterized by a constant cycle of binging and purging. A bulimic patient will partake in a binge session of uncontrollable eating that can last up to two hours in which they may consume as many as 21,000 calories. Afterwards the patient will purge by means of vomiting, excessive exercise or laxatives in order to get ride of the calories and the guilt that accompanies binge sessions. This cycle will happen at least twice a week for three months or more. Bulimia is often difficult to detect because the patient usually maintains normal body weight. However, body weight is seen by the patient as being excessive and causes the patient to have very low body image of his/herself. As a result, her or she obsesses over weight loss and dieting. This paper reviews some fo the most recent research that is being done one on bulimia. It discusses the environmental influences, genetic influences and the resulting physiological abnormalities. First research concerning specific abnormalities that occur in the nervous system are discussed. Then the genetic and environmental causes of those abnormalities as supported through research will be presented. Even though the precise etiology of the

disorder is unknown, there is a lot of information that allows researchers to make educated guesses.

Physiology of Bulimia Nervosa:

Physiological factors that effect bulimia are very similar to those that affect anorexia. Serotonin, ghrelin and other hormones have all been examined in search of information about bulimia. Bulimia is often seen as a more social disorder than anorexia. However some of the same physiological abnormalities are present in both disorders. Researchers have found deviations from the normal in the serotenergic system, ghrelin levels, BDNF levels, lipid levels, noradrenaline levels and leptin levels. Unlike in anorexia, researchers have found no variation in the dopamine system of bulimic patients. All of these different abnormalities could be the result of or cause of the disorder. Most research is conducted in recovered patients and research can not be done on a patient before the onset of the disorder. Therefore, there is no baseline to compare the subjects in order to determine when and why the abnormality occurred. The research presented in ths paper deals with some of the most promising hypothesis about what abnormalities contribute to the development and maintenance of bulimia.

Bulimia has recently been associated with increased levels of serum lipids, specifically cholesterol (Monteleone et al, 2004). Cholesterol is a circulating lipid. Abnormally high cholesterol levels have been found in patients with bulimia. Using the Eating Disorder Inventory II, a psychological assessment test for eating disorders, Monteleone found a positive correlation between cholesterol levels and a subject's desire to be thin, awareness of their feelings and impulse regulation. This high level of cholesterol contributes to the already unhealthy lifestyle.

Abnormal cholesterol levels have also been shown to play a role in symptoms that appear in some psychological disorders such as impulsivity, aggression, hostility, depression and suicidal tendencies (Agargun 2002; Apter et al 1999). Cholesterol causes behavioral problems by effecting the fluidity of cell membranes, making the process of information exchange more difficult. By increasing he difficult of neurotransmitter transmission, neurotranmsission signaling become altered. Altered neurological activity is one of the strongest hypothesis concerning the cause of abnormal eating behavior. Cholesterol levels also have an effect because of the role of its' protégée. Cholesterol is the precursor of prenenolone, a hormone that once metabolized into a steroid, regulate certain processes such as mood, anxiety, aggression and feeding. These characteristics can be related to bulimia as well as the psychological disorders that often coexist with bulimia. As neuroactive steroid that effects feeding and anxiety could be a contributing factor to an eating disorder that is characterized by a normal eating pattern and anxious behavior. The control of mood and aggression is a trait that becomes altered in disorders such as depression and bipolar disorder. It is accepted in the scientific field that high levels of cholesterol is not the cause of bulimia. However it is being researched as a possible component to the maintenance of the disorder. The binging initially causes and maintains the high cholesterol levels, which in turn contributes to the symptoms of bulimia.

Not surprisingly, increased postsynaptic activity (Kaye et al2005) and low transcription of the 5-HT transporter protein (Steiger et al, 2005) has been found in recovered bulimics as well as in patients still suffering from bulimia. The abnormalities have been found in many different areas of the brain, depending on the focus of the particular study. One study (Kaye et al, 2005) identified unusual serotonin activity in the frontal, cingulate, temporal, and parietal cortical regions of the brain. They also showed the effectiveness of antidepressant medications of the

treatment of bulimia. Takimoto et al (2004) found evidence that decreases in hypothalamic 5_HT lead to increased carbohydrate intake and impairment of unusual levels of satiety. If this conclusion is confirmed by other researchers, it could create a strong correlation between 5-HT levels and th uncontrollable binging of bulimia. Solid evidence has been found confirming a decrease of sensitivity of hypothalamic sensitivity. Researchers do agree that there is abnormalities in 5-HT function, but the role that this abnormality plays in the development and persistence of the disorder is unknown.

The study of ghrelin has often resulted in conflicting data. Ghrelin is a gastrointestinal peptide hormone that regulate food behavior by stimulating appetite and food intake in humans as well as metabolism. An experiment lead by Nakazato (2004) recorded serum levels of ghrelin in bulimic patients between 11am and 12 pm. His results reported no difference in circulating serum levels of ghrelin between patients with bulimia and the control healthy patients (Nakazato et al, 2004). Contrastingly, a previous study by Papezova et al, (2005) had conducted their measurements in the morning after a night of fasting. This experiment showed the circulating serum ghrelin levels of bulimics to be higher than normal controls (Papezova et al, 2005). Fasting increase the concentration of circulating ghrelin and feeding deceases it. Papezova's study suggests that bulimics have sharper increases in ghrelin levels as a result of fasting than controls do. A third study (Monteleone, 2005) introduces peptide YY, which is inversely proportional to ghrelin. Peptide YY (PYY) increases after a mean and then decreases as a result of fasting. These two work together to regulate the beginning and ending of feeding. This third study by Monteleone et al measured PYY and ghrelin levels in bulimics and control subjects before a meal and found no significance difference. They measured again after the meal. In the control subjects, there was a normal increase in PYY and normal decrease in ghrelin. In the

bulimic patients, the level of circulating ghrelin decreased only slightly and remained high as compared to the control and the PYY levels increased only slightly and remained low as compared to the control. The blunted increase/decrease of PYY and ghrelin suggests that in a bulimic patient, eating does not cause the normal level of fullness. As a result they are able to eat more, to an extreme, creating the binge episode. The binge always leads to a purge episode.

Neurotransmission abnormalities are the focus of most research. In addition to 5-HT, noradrenaline (norepinephrine) has been extensively studied. Norepinephrine was the first neuronal system to be studied in research for eating disorders. When injected into the hypothalamus, norepinephrine produced feeding in both satiated and hungry animal models. In humans, norepinephrine levels in the cerebral spinal fluid have been shown to be lower than in bulimic patients, but the basal plasma levels of norepinephrine do deviate from the normal levels. Researchers believe the difference in central versus peripheral norepinephrine levels is a result of the different function of norepinephrine in the two systems (Takimoto et al, 2003; Kaye et al, 1990; Buckholtz et al, 1988). The contrasting results found between the animal model and the human subjects is interesting. In the rats, increased levels of norepinephrine stimulated eating, even when the rats were not hungry. This behavior is very similar to a binge episode. However bulimics were shown to have lower than normal levels of norepinephrine. The phase of the disorder that subjects were in when tested could be a possible cause for the discrepancy. Repeat experiments are necessary to determine why this discrepancy between physiological abnormalities and physical symptoms exists. Research on leptin levels and dopamine levels have also been explored in regards to bulimia. However, much of the resulting data has been inconclusive. There is a possibility that dopamine and leptin do have an affect and the technology or innovation is not there to allow us to discover at this time.

Identifying the physiological abnormalities is not overly difficult. However determining how those abnormalities were produced and how they effect the different areas of the nervous system and consequently behavior is complex. There are many physiological factors that contribute to the modulation of eating behavior. This paper discussed norepinephrine, ghrelin, peptide YY, 5-HT and serum lipids. Abnormalities in any of these could cause disturbances in eating behavior. A combination of appetitive disturbance result in the manifestation of an eating disorder. In order to determine that combination, research must continue on the individual factors that contribute to the abnormalities that occur.

Genetic Etiology of Bulimia Nervosa:

Bulimia does not have the same strong genetic contribution that anorexia has. However, there is still some genetic influence involved in the production of personality, neurotransmitter systems and other systems involved in eating behavior. Much of the genetic research conducted on bulimics is explored in conjunction with another disorder that often occurs simultaneously. By doing this, researchers are able to play of the knowledge of both disorders and compare results. Twin studies are also conducted to allow researchers to compare the strength of environmental influences to the strength of genetic influence. This paper sites researchers who study genetic abnormalities that influence different components of the serotenergic system. Papers comparing symptom similarities with genetic similarities between OCD and bulimia and bipolar disorder and bulimia will also be discussed. There are many more studies that deal with the genetic influence on bulimia, however, due to the limitation of this paper, they will not be discussed.

Serotonin is one of the most extensively studied systems that effects bulimia. Focusing on the serotonin -1DB receptor gene, a study looked at the G861C polymorphism on the G allele as a possible contributor to the prevalence of OCD in bulimia. There has long been a correlation between patients with bulimia and OCD. Parts of the G allele have been previously studied and has been shown to contribute to the presence of OCD in a person. This study did not find any strong evidence that the G861Cpolymorphis is in involved in bulimia because there was not a significant occurrence of the polymorphism in bulimia. However, it did show a strong relationship between the presence of the G allele and the severity of obsessions in those bulimic patients with OCD. In this study of 165 bulimic patients, 33 had full OCD and 12 had partial syndrome OCD. Obsessions are manifested in bulimia through the patients preoccupation with food. It is possible that this mutation that increases the intensity of obsessions in OCD has a similar effect on the severity of bulimia.

As to be expected, researchers have also found an abnormality in the serotonin transporter gene - (Steiger et al, 2005). An abnormality in the promoter region of this allele has been associated with low transcription of the 5-HT transporter protein, increased depression, and with clinical symptoms that often accompany bulimia. The study showed that variations in this allele had more effects on the clinical symptoms of eating disorders such as affective instability, and insecure attachment. There was not correlation found between variance in this allele and the frequency of binge episodes, eating attitudes, body dissatisfaction or BMI. This implies that there is something else causing the obscure appetitive disturbances. It is possible that there is a third factor that is causing both the disturbances in the 5-HT system and personality imbalances. This study and others show that the abnormal serotonin transporter gene does not cause bulimia. Previous studies have also shown that the personality symptoms of bulimia are often present

before the onset of bulimia. This is evidence against the idea that the nutritional deficiencies cause the clinical symptoms. This leaves the possibility that there is a 3rd component causing both the 5-HT abnormalities as well as the personality disorders and that these two characteristics of bulimia are linked genetically.

Researcher have found a possible relationship between bipolar illness and bulimia. In a study (Ramacciotti et al, 2005) 51 patients being treated for bipolar disorder, 14 met the criteria for an eating disorder, 5 of the 14 had bulimia. In all of the patients, the bipolar preceded the onset of bulimia. The majority of the eating disorders begin during a depressive episode. Of the 51 patients, 10% had bulimia - this percentage is well above the occurrence rate in a normal population. The high occurrence of bulimia in bipolar patients is another example of a patient with bipolar disorder's ability to control his/her behavior. There is a relationship b/t these two disorders, however it is not very strong. Ramacciotti study was conducted using bipolar patients. It would be interesting to conduct the same experiment using bulimic patients to find the occurrence of bipolar disorder. A comparison of the two studies may lead to the better understanding of what genetic factor links the two disorders.

Behavioral etiology of Bulimia Nervosa

Societal pressure are much more influential in the development of bulimia than in anorexia. Anorexia has a strong genetic influence and the role of society is a secondary or tertiary contributor to the onset of anorexia. The evidence for bulimia has not been as straightforward as that for anorexia. One study may demonstrate a strong genetic influence while another study may demonstrate minimal genetic influence with a strong environmental influence. Despite the conflicting data, it is mostly accepted that bulimia has a stronger

environmental influence than anorexia. Experiments resulting in both sides of the conflicting data will be presented.

Duncan et al, conduced a family study where the prevalence of eating disorders in the parents was compared the the prevalence rate in the children who had eating disorders. Of the 122 children with eating disorders, 115 came from families with eating disorders. From this data, there is clear evidence that there is a distinct genetic component. However, this was a family study and it did separate the eating disorders into subgroups. Those children who shared 50% of their genes with each of their parents also shared the same environment with them. Many other psychological disorders were fond to comorbidly exist in the bulimic patients, such as depression, anxiety and addictions. Research on all of these disorders have found genetic influence on their manifestation. However, it is easy to find a strong environmental contributor. A mother or father who once suffered from an eating disorder is more likely to put pressure on his/her child to be thin. Even if they do not put pressure on the child, the child may still observe the pressure the adult puts on his/herself and learn from observing. Also, parents who previously had problems with body image may pass on their personality traits which often include perfectionism, impulsivity, and obsessionality. These personality traits combined with the stressful environment created by the parents greatly increase the child's likelihood of acquiring an eating disorder his/herself.

A second study (Speranza et al, 2005) tried to find a correlation between alexithymia and bulimia. Alexithymia is characterized by not truly understanding your feelings or being able to describe them. It is possible that binge/purging episodes are a way of dealing with the stressful situation of not understanding feelings and emotions like anger, stress and loneliness. A study with 98 bulimic patients measured the correlation between depression and bulimia and found that

all bulimic patients had higher than normal levels of depression according to the Beck Depression Inventory. They also have higher levels of alexithymia. Pointing to alexithymia as a contributor of bulimia could strengthen the argument that bulimia has a genetic basis because alexithymia is a result of physioloigical abnormalities. However, environmental factors could also result in an ability to understand one's feelings.

Historical research shows a stronger environmental component than the previously mentioned studies. The incidence of bulimia has increased over time (Keel & Klump, 2003). Information of this sort poses the same questions as with anorexia. How is the way the prevalence rate is gathered effecting the data? With the popularization of the disorder, are people more willing to come forward to get treatment now? Is the change due to a chance in the definition of the disorder? Cross-culture research showed bulimia to be a much more culture-bound syndrome than anorexia. There has been no evidence of any cases of bulimia arising without the influence of Western culture (Keel & Klump, 2003). Attempts to find historical cases of bulimia were also largely unsuccessful. Does this information discredit the possibility of a genetic predisposition towards bulimia? It is possible that people with bulimia have a genetic predisposition to other psychological disorders such as OCD, Perfectionism, alexithymia, and addictions. This in turn could make them more vulnerable to the societal pressures of western culture.

Supporting the previous study by Keel and Klump, another by Cotrufo et al (2005) has shown that the severity of eating disorder cases has progressively decreased as the prevalence of eating disorders has increased. This is evidence that more cases are the result of societal pressure as opposed to strict genetic factors. If genetics was a sole contributor, or even a major contributor, the severity of the eating disorders and the prevalence of eating disorders should

remain constant. Bulmics appear to be more affected by the pressures of society, and in conjunction with psychological disturbances that make them more susceptible to these types of pressures, they develop bulimia in an attempt to deal with other issues.

Bulimia is more common than anorexia. It is seen in conjunction with athletics such as running, wrestling and ballet. In these activities the pressure to be a certain size is very strong and vital to the level of competition. Societal pressures and environmental situations contribute a great deal to the manifestation of bulimia. As a result it is easier to treat and there are less relapses than occur during recovery from anorexia. Even with the strong environmental contributions, it appears that in order to develop a full case of bulimia, there are genetic components that must be present. The imbalances in the different physiological systems are evident that there are serious neurological abnormalities that are causing the manifestation of this disorder. With continued research into the genetic and environmental components of bulimia, treatment of the resulting physiological abnormalities will become more advanced and effective.

Discussion:

There are many similarities in the anorexia and bulimia. Of the two, anorexia is the most severe. It has more of a genetic component and therefore is the most difficult to treat and has the severest reproductions. While doing the research, it seemed that bulimia shared a great deal of qualities with obsessive compulsive disorder. Bulimic patients obsess about food and staying thin. In order to ameliorate the emotions and caloric intake that occurs during the obsessive periods, bulimics partake in compulsions such as excessive exercise and vomiting. Just as repeatedly locking a door helps to calm an OCD patients with paranoid obsession, purging calms

and relieves the guild of binging in a bulimic patient. Could bulimia be a form of OCD that has been molded by the environmental pressure of society?

Anorexia seems to have more genetically in common with serious psychological disorders such as bipolar disorder and schizophrenia. Both disorders allow the patient to find comfort and take pleasure in food deprivation. We know the areas of the brain that are stimulated when we find something pleasing emotionally or physically. It is here that researchers will determine a way to treat eating disorders. Some sort of drug that will artificially reassure the patients so that they are capable of living comfortable and healthy lives being content with their bodies. However, this could create a problem because the patients would become dependent on the medicine and it would more than likely be abused. Also there is a definite behavioral component to both anorexia and bulimia. Personality, genetic and environment all lead to the manifestation of the disorders. The complexity of the disorders can not be fixed by artificially stimulating the pleasure zone in the brain.

The increase in the prevalence in bulimia but not anorexia shows that society is putting more and more pressure on females to fit a stereotypical mold. Societal acceptance is more important in bulimia than anorexia. This difference is demonstrated in the side span of discrepancy between actual and ideal body weight in bulimics than in those with anorexia. Even though cases of anorexia do not obsess about weight, once they are very underweight and emaciated, their main focus is not to lose weight but to keep it off. Bulimics are usually at normal or just below average body weight, leaving them from the very thin and almost emaciated body type that they aspire to.

It seems that as more knowledge is gained bout these disorders, more people, instead of taking it as a warning, are taking it as a suggestion and using the techniques of a bulimic

individual in order to meet the standards set by society. This is the compete opposite of what the spread of knowledge is supposed to do. Now researchers are faced with two problems. Initially, they must determine the etiology of anorexia and bulimia in order to know the best way to treat it, but they must also devise a plan that will allow them to attack the spread of the popularity of eating disorders among adolescents. There are serious medical reproductions for putting your body through the pain and fatigue that is brought on by bulimia and anorexia. Hopefully in the next few years progress will be made in both of these areas.

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