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The Relationship Among the Contributing Factors to Anorexia Nervosa

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Introduction

Anorexia nervosa is now being viewed as a multidimensional disorder in terms of predisposing factors such as genetics, biology, and environment. Results from twin studies suggest that part of a susceptibility to AN may lie in genetic factors (Holland et al., 1984, 1988; Treasure and Holland, 1991). However, the nature of a genetic contribution, if any, remains unclear. Neurochemical alterations have been found to be associated with AN, but it is difficult to assess what role these neurochemical changes play in the etiology of the disorder since they may precipitate, accompany, or follow weight loss (Fava et al., 1989). Abnormal family interactions (Humphrey et al., 1986; Kog and Vandereycken, 1989) and cultural practices of diet and exercise (Epling and Pierce, 1988) have also been implicated as contributing factors to AN. The cultural and familial models are deficient, however, in that they do not account for individual susceptibility (Treasure and Campbell, 1994). Further, issues of nature versus nurture have not been fully examined in family models. The lack of understanding in the exact nature and role of the contribution of these factors to the development of AN, and the further complex relationship among these factors present a problem for researchers in understanding the aetiology of the disorder.

The purpose of this paper was to examine the contribution of each of these aforementioned factors to AN. Genetic studies, biological correlates, and family and biobehavioral perspectives on the disorder will be reviewd. Further, the present author attempted to establish an understanding of the relationship among these contributing factors in order to develop a possible profile

of vulnerability for AN.

A Case for Genetics

Available evidence is consistent with the premise that AN aggregates in families. Studies show that at a rate greater than the population base rate or chance alone, siblings are affected by AN. Gershon et al. (1983) conducted a study testing first degree relatives of anorexic probands and normal controls. The risk for relatives of anorexic probands was 2% compared to 0% for the normal population. Similarly, Strober (1990) conducted a study testing first degree female relatives of anorexic probands. He found the rate of risk for relatives of affected probands to be 4.1% compared to a rate of 1.1% for the normal population. Further, Holland et al. (1988) found 4.9% to be the rate of risk for first degree relatives, 1.16% for second degree, and .1% for the normal population. These studies suggest that AN is 8 times more common in female first degree relatives of anorexic probands as compared to the general population (Lask and Bryant-Waugh, 1992).

Additionally, data from twin studies are consistent with the suggestion that genetics may play a role in the development of anorexia nervosa. Schepank (1981) found 6 in 8 monozygotic twins to be concordant for AN, while none of the five dizygotic twins were concordant. Similarly, Holland et al. (1984) studied 30 female twin pairs and found that 9 out of the 16 (55%) monozygotic twins were concordant for AN, whereas, only 1 of the 14 (7%) dizygotic twin pairs were concordant. Further, Holland (1988) found a 56% rate of concordance among 25 female monozygotic twins, compared to a 5% rate of concordance for 20 female dizygotic twin

pairs. Holland also gave an estimate of heritability in this study for monozygotic and dizygotic twins, as well as first and second degree relatives. The estimate of heritability for twins was found to be .98 (±.12) leaving .02 to account for the variance in familial non-genetic effects. Lastly, the estimate for first and second degree female relatives was found to be between .86 and .97. The results from the different analyses used in this study suggest that "'heritability' accounts for at least 80% of the variance" in liability to genetic factors (p.567).

Holland (1988) also suggested that heritability may be a factor in "the drive for thinness" and "body dissatisfaction" (566). Research by Yager et al. (1986) demonstrated that the lack of information regarding one's body size relative to others' evident among girls with early blindness does not preclude the development of AN. This seems to confirm Holland's implication of a genetic basis for these factors.

The assertion that genetics contribute significantly to the etiology of anorexia nervosa has been disputed by some investigators. Some studies have not produced a significant difference in monozygotic and dizygotic concordance rates in twin studies, which is contrary to Holland (1984, 1988) and others. One argument against twin studies is that a rate of 100% concordance has not been found for monozygotic twins. Garfinkel and Shaw (1990) discuss the various methodological problems in research related to eating disorders. Further, Ledoux, Choquet and Flament (1991) attribute variance in reported rates as being due to: "the use of different assessment methods to define 'caseness'; the diversity of the groups surveyed; the variety of diagnostic criteria used" (Lask and Bryant-Waugh, 1992, p.283).

Another argument against the possibility of a genetic risk factor for AN is the contemporary increase in general prevalence of AN cases as described by Szmukler (1985) and Plehn (1990). However, Lask and Bryant-Waugh (1992) suggest a cautious approach when interpreting the literature which purports to demonstrate a rise in the number of cases in the population. Williams and King (1987) attributed the rise in case reports to an increase in number of females in the population, as opposed to an increase in risk morbidity. They further suggest that an increase in rates of re-admission gives the appearance of an increase in case incidence. A 45-year period study was conducted in Minnesota by Lucas, Beard, O'Fallon and Kurland (1988) and the results failed to demonstrate a significant rate of increased evidence of anorexia nervosa.

What might be inherited in anorexic patients?

The available research evidence is consistent with the thesis that anorexia nervosa aggregates in families. That rate of occurrence is higher in monozygotic twins than in dizygotic twins, and higher in first-degree relatives of affected probands, compared to second-degree relatives. Knowledge of what may actually inherited is still unclear. However, available evidence suggests a significant correlation between AN, obsessive-compulsive disorder, and depression.

Researchers have demonstrated that patients with anorexia nervosa tend to have obsessional traits present in their premorbid personalities (Dally, 1969; Kay and Leigh, 1954; King, 1963; Morgan and Russell, 1975; Norris, 1979). Holden (1990) reviewed seven studies and found four that reported high rates of obsessive-compulsive personality, in terms of premorbid and

intercurrent personalities among anorexic individuals. Kay and Leigh (1954) studied 38 anorectics and estimated that 50% had obsessional traits in their pre-morbid personalities. Similarly, King (1963) examined 12 cases of AN and found these traits present in all twelve. Further, Norris (1979) stated that parents reported obsessional character as present in the pre-morbid personality of 31 out of the 54 cases (60%) examined.

Available evidence suggests that what is at the heart of AN is low-self esteem, which leads to body-image distortion. In turn, this leads to ruminations about perceived fatness, food avoidance, and ritualized behavior (Holden, 1990; Garfinkel and Garner, 1982; Gormally, 1984; Wardle, 1987). Rastam (1992) suggested that ruminations about perceived fatness are strongly correlated with the presence of obsessive-compulsive disorders. This evidence infers a need for additional studies into whether obsessive-compulsive traits may compose part of a genetic contribution to anorexia nervosa, since some forms of OCD have been found to have a genetic basis (Murray et al., 1983; Holden, 1990).

Research has also shown reports that depression is correlated with AN. Further, evidence consistently demonstrates increase rates of mood disorders among first and second-degree relatives of anorexics (Hudson, 1983; Strober, 1990). Gershon (1983) and Logue, Crow, and Bean (1989) demonstrated that among relatives of anorexics, an increased risk for mood disorders was present, which was not contingent upon the diagnoses of depressive disorder in the proband.

Evidence regarding the prevalence of obsessional traits in anorexia should not be interpreted as contrary to evidence

regarding the prevalence of affective disorders. These traits are certainly not mutually exclusive. Rothenberg (1988) found both depressive and obsessive-compulsive symptoms to be rated most frequently as accessory symptoms among eleven anorexic patients. AN is an independent disorder from OCD and affective response disorders, but an underlying feature may be "genotypic personality structures that predispose the individual to rigid and perserverative avoidance behaviors with marked obsessional, anxious-depressive coloring" (Strober, 1991, p.11).

These possible components of a genetic contribution seem to be synonymous with symptoms found in food avoidance emotional disorder, a childhood "atypical" eating disorder. Lask and Bryant-Waugh (1992) describe this disorder as one in which "food avoidance is a prominent symptom, but other symptoms such as depression, anxiety, phobias of obsessional behaviour also predominate" (p. 282). Other "atypical" childhood eating disorders are listed, none of which meet the full criteria for anorexia nervosa.

Food avoidance emotional disorder seems to be the characteristic component of the premorbid personalities of AN individuals that have been discussed. This "atypical" disorder may well be representative of the genetic contribution to the etiology of some forms of anorexia nervosa. It is true that this disorder doesn't meet the full criteria for AN, however, the problem may lie in the existing criteria.

Johnson-Sabine, Wood, Patton, Mann and Wakeling (1988) and Ledoux et al. (1991) conducted school-based surveys in which they were unable to identify any cases of anorexia nervosa. Similarly, King (1989) conducted a study of 720 subjects age 16-35 in a

general population and found no cases of anorexia nervosa. Bunnell, Shenker, Nussbaum, Jacobson and Cooper (1990) discuss the problem of underestimating the number of individuals with symptoms of an eating disorder because of the rigidity of the DSM-III-R criteria and further imply that "younger subjects in particular may experience considerable emotional difficulty and expose themselves to significant physical risk whilst not meeting formal criteria" (Lask and Bryant-Waugh, 1992, p.283).

Anorexia nervosa is not a disorder affecting otherwise normal individuals. It is plausible to assume that those exhibiting tendencies to both OCD and affective response disorders have a food avoidance emotional disorder that often goes unnoticed or untreated. Given certain environmental stressors, such as sexual abuse, familial dysfunction, certain career choices (e.g., ballet, modeling, pressures from the media, etc.), this "atypical" disorder may exacerbate into anorexia nervosa. On the other hand, it is also likely that those exhibiting signs of a food avoidance emotional disorder, but living in a "protected" environment, may never progress into anorexia nervosa. This may be a reason for the cultural differences seen in the number of reported cases for anorexia. Further research is needed in order to determine the nature of the genetic tendency. However, available evidence implies that those exhibiting tendencies to both OCD and affective response disorders will be more likely to have AN. Knowledge of a possible nature of genetic contribution to the etiology of some forms of anorexia nervosa and results demonstrating a higher occurrence of the disorder in women as compared to men has led researchers to re-examine the biological hypothesis for AN (Treasure and Campbell, 1994).

Biological Correlates

The environment can be conducive to an individual choice to diet. However, not all people who diet develop anorexia nervosa. In order for the full disorder to emerge, an individual appears to need an additional vulnerability (Goodwin, 1990). Researchers have speculated that this additional vulnerability is reflected in hypothalamic functioning.

The possibility that AN may involve a central hypothalamic defect is supported by various research. Russell (1985) asserted that AN involves a hypothalamic disorder that is expressed through endocrine disturbance involving the hypothalamic-anterior-pituitary-gonadal axis. Further, studies by Gold et al. (1986) and Hoffer et al., (1986) show that ACTH and cortisol response to CRF are blunted in anorectic individuals and are only restored to normal after long-term weight restoration. Newman and Halmi (1988) also showed that ovarian function can be restored in AN individuals before weight restoration with the administration of luteinizing hormone (LH).

Proponents of the view that AN is caused by a central hypothalamic defect have not been free from criticism. A study conducted by Goodwin (1990) demonstrated that major endocrine changes in AN could be easily mimicked by experimental dieting. Now, researchers such as Kaplan and Woodside (1987) suggest that anorexia nervosa involves abnormalities in certain central-nervous-system amines that act as neurotransmitters and control the release of hormones from the hypothalamus. Presently, researchers have turned to looking at changes in three major systems containing these CNS amines that have been found to be

highly correlated with AN, the noradrenergic, serotonergic, and opiod systems. These systems are also implicated in symptoms such as anxiety and depression that are commonly observed in anorexic individuals (Fava et al., 1989).

Noradrenergic

Norepinephrine is a neurotransmitter known to play a role in feeding behavior (Kaplan and Woodside, 1987). This neurotransmitter when active in the medial hypothalamus and paraventricular nucleus stimulates feeding, and conversely, when active in the lateral hypothalamus, inhibits feeding (Liebowitz, 1983). Liebowitz and Brown (1980) found that feeding becomes inhibited when ß-adrenergic agonists are applied to the perifornical region of the hypothalamus.

Norepinephrine turnover has been suggested to be reduced in AN since studies report lower levels of MHPG and CSF norepinephrine in anorexic individuals (Gross et al., 1979). Further, a defect in norepinephrine metabolism has been implicated as a "trait" marker of AN based on a study by Kay et al. (1984) demonstrating that weight restored anorexic individuals continued to show a 50% lower CSF norepinephrine level compared with normal controls. Kaplan and Woodside (1987) also found lower levels of CSF norepinephrine in weight recovered anorexic individuals compared with normal controls. Further, Berger et al. (1985) found that AN in animals with hypothalamic damage is reversed by noradrenalin. The results from these studies seem to indicate that low norepinephrine turnover is a precipitating biological factor in AN. The contribution of this system to the development of AN supports the idea mentioned earlier that obsessive-compulsive personality and depression are possibly involved in the

genetic contribution to AN, since researchers have found that the noradrenergic system plays a role in anxiety and depression (Charnery and Heninger, (1985); Price, Charney, Rubin et al., 1986).

Serotonergic

Serotonin is another neurotransmitter known to play a role in feeding behavior (Kaplan and Woodside, 1987). Liebowitz (1983) found that serotonin induces satiety and inhibits feeding . Other researchers have also stated that 5-HT is critically important in appetite (Blundell and Hill, 1991; Curzon, 1992). However, 5-HT control of appetite seems to be pronounced in females as compared to males (Treasure and Campbell, 1994).

Studies show that the role of 5-HT in decreasing feeding is more pronounced in females. Rowland (1986) found that infusion of fenfluramine in rats had a greater hypophagic effect in females as opposed to males. Goodwin et al. (1987) found that weight loss enhances the release of prolactin in response to L-tryptophan in women but not in men. These studies suggest, as Holland et al. (1984) asserted, that women might be more vulnerable than men to the effects of dieting because of the sexual dimorphism in the response of the 5-HT mediated release of prolactin to dieting.

Researchers have also found changes in the serotonergic system to be correlated with anorexia nervosa. Morely and Blundell (1988) asserted the possibility that 5-HT and corticotrophin-releasing hormone were important candidates involved in the neurochemical aetiology of AN. Donohoe (1984), Dourish et al. (1987), and Kennett et al. (1987) have proposed an animal model of immobilization-stress anorexia involving 5-HT pathways as an analogue for human anorexic conditions. However,

contrary to the results of low norepinephrine turnover, researchers such as Morely et al. (1986) and Morey and Blundell (1988) suggest that a "trait" marker in AN appears to be an increase in hypothalamic release of 5-HT. Kaye et al. (1991) showed that long-term weight restored anorexic subjects have elevated concentrations of CSF 5-HIAA compared with controls. However, results from various studies on changes in the serotonergic system are unclear. Brewerton et al. (1990) and McBride et al. (1991) suggest that AN individuals have decreased 5-HT mediated prolactin release.

Knowledge regarding the genetic contribution to the etiology of some forms of anorexia nervosa may support the implication of overactivity of 5-HT pathways in AN individuals. Treasure and Campbell (1994) state that this overactivity may lead to the behavioral inhibition and control in AN. This behavioral inhibition is representative of the obsessional aspect of perfectionism found in the premorbid personalities of AN individuals. Overactivity of the 5-HT pathways contrasts the suicidal behavior associated with low levels of 5-HIAA and blunted 5-HT neuroendocrine functions (Traskamn et al., 1981; Linniola et al., 1983; O'Keane, 1992). Weight loss does lead to a decrease in serotonin level which may be one of the reasons AN individuals experience heightened depression. Treasure and Campbell (1994) further suggest that this decrease due to weight loss obscures the underlying abnormality of increased 5-HT mediated responses in AN.

Taken together, the profile of vulnerability seems to consist of low norepinephrine turnover and overactivity of the 5-HT pathways. These predisposing biological factors may contribute to the behaviors seen in the premorbid personalities of anorexic

individuals. Low levels of CSF norepinephrine may very well lead to the depression some anorexic individuals have before the onset of the disorder, and increased 5-HT mediated responses may lead to the inhibited behavior present in the premorbid personalities of AN individuals. Thus, the biological factors are related to the genetic in that they may set the stage for the development of the behaviors that, when combined, represent the genetic contribution to the etiology of some forms of anorexia nervosa. However, the opiod system needs to be considered as a possible contributing factor to vulnerability.

Opiod

Kaplan and Woodside (1987) assert that opiods are linked to eating behaviors. Opiod levels have been found to be elevated in obese rats (Margules, Moisset, Lewis, Shibuya, and Pert, 1978). Grandison and Guidotti (1977) demonstrated that when injected into the ventromedial hypothalamus, endorphins stimulated intake in satiated rats. Naloxone, an opiod antagonist, has been shown to decrease food intake in food deprived and obese rats (Holtzman, 1974), and to also cause weight and appetite loss in humans (Hollister et al., 1981).

Kay and Woodside (1987) reported elevated CSF total opiod activity has been found in AN individuals. Kay, Pickar, Naber, and Ebert (1982) found higher levels of opiod activity in patients with AN. These same researchers further found that current anorexics had higher CSF opiod activity compared to weight restored and weight recovered counterparts.

Kay, Pckar, Naber, and Ebert (1982) suggest that the increase in opiod activity may be due to opiod appetite stimulation. They further suggest that this is the increase responsible for the

exacerbation of obsessive behavior concerning food in AN individuals. This increase in opiod level may be one reason anorexics continue to exhibit obsessional behavior even though serotonin levels become lowered. The implication of these researchers seems to suggest that increased opiod level is secondary to starvation. However, the opiod system still contributes to the profile of vulnerability because it is part of the biobehavioral process leading to human anorexias triggered by cultural practices of diet and exercise (Epling, Pierce, and Stefan, 1983).

A Biobehavioral Perspective

Essential to the understanding of a biobehavioral perspective of anorexia nervosa is the understanding of the importance of cultural factors in the development of the disorder. According to Epling and Pierce (1988) stereotypes of the "perfect" body are frequently conveyed by the media. Individuals use these cultural standards as a basis by which they form a prototype image of the ideal person. In order to meet these cultural requirements for health and thinness, individuals are encouraged to exercise and change eating patterns. (Epling and Pierce, 1988).

The anorexic cycle begins with cultural practices of dieting and exercise. The appetite becomes suppressed when an organism engages in strenuous exercise (Epling and Pierce, 1988). Pierce, Epling and Boer (1986) state that this suppression of appetite leads to a decline in body weight and food intake because the value of food reinforcement decreases. The motivational value of activity increases as a function of body weight decline which further reduces the value of food reinforcement and increases that

of physical exercise (Epling and Pierce, 1988). Epling and Pierce (1988) further state that "once initiated this cycle is 'self-maintaining' and resistant to change" (p. 476).

The idea of activity-based anorexia is supported by laboratory research. Researchers of AN have frequently noted the importance of excessive activity to the onset of anorexia (Blitzer, Rollins, and Blackwell, 1961; Crisp 1965; Halmi, 1974; King, 1963; Kron et al., 1978; Slade, 1973; Thoma, 1967). Routennberg(1968) and Routennberg and Kuzenof (1967) demonstrate that animals place themselves at risk of dying from "self-starvation" when allowed to run on an activity wheel and fed only a single daily meal. Epling and Pierce (1988) list studies that demonstrate a reduction of caloric intake in humans as a function of increased exercise.

The physiological mechanisms responsible for the increased reinforcement value of running due to food deprivation may be the endogenous opiates which mediate running and eating (Epling and Pierce, 1988). Davis, Lamb, Yim, and Malven (1985) found that injecting 2-deoxy-D-glucose in exercise-trained rats reduces food intake. This same result has been noted by Sanger and McCarthy (1980) when animals are injected with morphine. Human research also supports this premise. Moore, Mills and Forster (1981) found that anorexics will gain weight when given the opiate antagonist naloxone. Thus, increased levels of endorphins act to decrease appetite in food deprived animals (Epling and Pierce, 1988).

Some researchers question whether an animal model demonstrating an activity-based anorexia can be generalized to humans on the basis that rats are imposed to restrict food intake whereas humans are not (Epling and Pierce, 1988). Bachrach,

Erwin, and Mohr (1965) and Hallsten (1965) argue that humans do not "willfully" restrict food intake. These researchers assert that societal pressures act to impose food restriction on humans in the same manner that experimenters impose food restriction on rats. The biobehavioral model thus suggests that "choosing to diet or exercise is determined by biological and environmental conditions" (Epling and Pierce, 1988, p. 482).

Conclusion

Anorexia nervosa is a disorder that emerges from a variety of contributing factors. Available evidence is consistent with the premise that AN aggregates in families. Research has demonstrated that obsessive-compulsive tendencies and abnormal affective response patterns may compose part of a genetic susceptibility to anorexia nervosa.

Earlier researchers also hypothesized individual susceptibility may partially lie in a central hypothalamic defect. Since then, researchers have begun to focus less on the abnormal functioning of the hypothalamus as a cause. Rather, they see it as an effect of changes in certain central-nervous-system amines. Further, research has demonstrated that two of these CNS amines, norepinephrine and serotonin may be "trait" markers of the disorder.

Biobehavioral processes have been demonstrated as well as contributing to some forms of anorexia nervosa, more specifically, activity-based anorexia. Researchers have demonstrated that cultural practices of diet and exercise initiate a self-maintaining anorexic cycle. Exercise leads to weight loss, weight loss increases endorphin levels, and body weight and food intake

further decline.

In order to propose a profile of vulnerability for AN, it is necessary to understand the relationship among these contributing factors. The present authors conclude from the available research evidence that the biological "trait' markers, low norepinephrine turnover and overactivity of 5-HT pathways, may give rise to the obsessive-compulsive and depressive behaviors seen in the premorbid personalities of AN individuals. This aspect of vulnerability relates to the biobehavioral perspective in that AN individuals who possess these neuroendocrine abnormalities are more susceptible to the activity-based anorexia cycle. This cycle further changes neuroendocrine function which enhances the maintenance of the disorder and the cycle's resistance to change.

Further research is needed in order to understand the complex relationship among the contributing factors to anorexia nervosa. The available evidence, however, suggests that the complex relationship determines a profile of vulnerability that makes some individuals more susceptible to the development of anorexia nervosa than others.

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