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Exploring the Potential Shared Pathology of Eating Disorders and Addiction: A Behavioral Neuroscience Approach

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ABSTRACT

This literature review will examine the potential overlapping neural contributions to eating disorders and addiction from a behavioral neuroscience perspective. The major similarities between eating disorders and alcohol abuse are related to dopamine (DA) activity within structures of the prefrontal cortex. Specifically, abnormal DA and other neurochemical function and structural differences are evident within the medial orbitofrontal cortex, ventromedial prefrontal cortex, nucleus accumbens, and ventral striatum. Differences in these regions and their circuits appear to contribute to the impulsive and reinforcing behaviors that are exhibited in both types of disorders. For instance, commonalities found between eating disorders and addiction include the sensitization of DA systems and high medial prefrontal cortex activation in response to food or during drug cravings. Research seems to suggest that these similarities can increase the likelihood of someone with an eating disorder developing substance abuse, but not vice versa. Additionally, evidence suggests that the pathology of bulimia nervosa may be more similar to that of alcoholism and other substance abuse disorders than the pathology of anorexia. Thus, there may be a greater probability of bulimics developing alcoholism and other substance abuse disorders than anorexics; however, the structural and functional similarities still suggest risk in all eating disorders.

1 INTRODUCTION

Eating disorders and alcoholism are two extremely prevalent, and damaging, disorders from which millions of Americans suffer. Approximately 30 million Americans of all ages, genders, ethnicities, and classes struggle with an eating disorder at some point in their life (Hudson et al., 2007; Le Grange et al., 2012), while 40 million Americans are victims of addiction (Altman, 2012). These disorders are often presented comorbidly. In fact, up to 50% of people who suffer from an eating disorder also abuse alcohol or illicit drugs at some point in their lifetime, a rate that is five times greater than that of the general population (Califano, 2012). This staggering statistic suggests that there may be behavioral and biological similarities between the two disorders since its comorbidity is so common. Behaviorally, abnormal eating behaviors and alcohol abuse may serve as a coping mechanism for the disorders' shared risk factors, including family history, low self-esteem, depression, anxiety, and social pressures (Schrieber et al., 2013). Biologically, the behaviors exhibited from these disorders are reinforced and maintained due to altered neurotransmitter activity as well as abnormal prefrontal function and structure ((Avena, 2007; Frank, 2013; Kaye et al., 2013; Uher et al., 2004). This paper will focus on the neurobiological mechanisms that drive these abnormal behaviors. In particular, there are similarities between eating disorders and alcohol abuse in terms of dopamine activity within structures of the prefrontal cortex. These similarities may contribute to the impulsive and reinforcing behaviors that are exhibited in both disorders.

2 EATING DISORDERS: ANOREXIA NERVOSA AND BULIMIA NERVOSA

Individuals with eating disorders exhibit an obsessive preoccupation with food that can be presented in symptoms such as food avoidance, purging, or binging. These disorders are often comorbid with other psychological disorders such as depression, anxiety, and substance abuse (Wonderlich & Mitchell, 1997). Eating disorders affect more women than men, but still affect a small percentage of the population: 1% of women and less than 0.5% of men (Nevid et al., 2018). The eating disorders that will be evaluated in this review are anorexia nervosa and bulimia nervosa.

People with anorexia nervosa experience distorted body image and excessive fears of gaining weight, which is combated with extreme calorie restriction and food avoidance (Kaye et al., 2013). According to the American Psychiatric Association, anorexia nervosa is characterized by extreme emaciation, an intense fear of gaining weight or becoming fat despite a low body weight, a disturbed perception of weight and shape or a denial of the seriousness of low body weight, and amenorrhea, or the absence of a menstrual period. Anemia, dry skin, thin hair, cardiovascular complications, and constipation may also arise (Nevid et al., 2018).

Anorexia typically develops during adolescence and, in the case of females, shortly after menarche. It is common for a girl to notice sudden weight gain after her first menstrual period and insist on losing it. However, the girl plans to lose the weight by unhealthy and extreme calorie restriction and/or exercise regimens instead of healthy weight loss strategies. These dangerous behaviors often continue after the initial weight loss goal is achieved (Nevid et al., 2018).

Bulimia nervosa is similar to anorexia in that both involve excessive fear of weight gain and body dysmorphia. However, bulimia is distinguished by frequent and persistent episodes of uncontrollable consumption of large amounts of food, compensatory behavior to prevent weight gain (e.g., purging, laxative abuse, or over-exercise), and an extreme preoccupation of weight and body shape as a determinant of self-worth (Avena, 2007; American Psychiatric Association, 2013). During a binge-eating episode, the person may consume 5,000 to 10,000 calories in a 30-60 minute time span (Nevid et al., 2018). These binge-eating episodes and compensatory behaviors occur at least once a week for at least three months, according to the DSM-V (American Psychiatric Association, 2013).

3 ALCOHOLISM AND THE ROLE OF REINFORCEMENT IN ADDICTION

People use alcohol and addictive substances for multiple reasons. Some may drink or turn to drugs to relieve boredom, strain, anxiety, or pain; others may use substances to feel relaxed or euphoric, or even as a result of social pressure (Bechara et al., 2019). Regardless of the specific reason for using, alcohol and drugs are used to achieve a certain purpose for the user. Victims of addiction probably have comparatively lower impulse control in relation to the substance, or ability to moderate consumption in order to avoid the negative social, psychological, and physical health effects of that substance (Bechara et al., 2019).

Reinforcement appears to be a significant contributor for persistent use of alcohol and other drugs of abuse. Specifically, positive reinforcement encourages further alcohol use due to the pleasant experiences derived from it (Bechara et al., 2019). Eventually, after prolonged and regular use of the drug, withdrawal symptoms arise and begin to get in the way of the user's daily functioning; thus, the drug is taken as negative reinforcement to eliminate the unpleasant experience of withdrawal.

4 DOPAMINERGIC ACTIVITY IN ANOREXIA AND BULIMIA NERVOSA

Dopamine Release in the Nucleus Accumbens

Dopaminergic release differs between restrictive- and binge-type eating disorders, but in both, dopamine (DA) neurotransmitter release acts as a way of reinforcing an abnormal relationship with food. Dopaminergic systems appear to be a key component in motivation, specifically the desire to seek rewarded outcomes, in a wide range of species including humans (Frank & Fossella, 2011). In cases of starvation or very low body weight, people become more sensitive to the reinforcing properties of DA as food restriction enhances the release of basal DA (Avena, 2007). This extracellular DA reinforces people with anorexia to continue to restrict their eating, providing them with a rewarding feeling when they can achieve any of their disordered eating goals, such as an aim to stay under a low daily calorie limit or to avoid a meal. This reinforcing property in people with low body weight is also seen in drugs of abuse, including alcohol (Pothos et al., 1995).

Clinical literature reveals that patients with bulimia have altered DA activity. Rat studies have revealed an increase in DA release in the nucleus accumbens in rats with a normal body weight after bingeing on sugar (Avena, 2007). Increased DA release due to feeding is also regulated glutamate, an excitatory neurotransmitter (Taber & Fibiger, 1997). Glutamatergic neurons originating from the prefrontal cortex innervate the mesolimbic DA system (Taber & Fibiger, 1997), therefore influencing DA release.

Changes in accumbens acetylcholine (ACh) levels may be similarly involved in the pathology of binging behavior. Cholinergic signaling is involved in satiety, so that when someone is finishing their meal, ACh is released; consequently, purging after a large meal greatly reduces ACh release (Avena, 2007). In cases of bulimia, when a binge-eating episode is followed by purging, the compensatory behavior is reinforced by the DA release without any ACh (Avena, 2007). The unbalanced relationship of DA and ACh could be a significant neurochemical contributor to the binging-purging behaviors that are exhibited in bulimia.

Dopamine function in the Striatum

Evidence suggests that people suffering from eating disorders also have altered striatal DA function compared to the general population. In cases of anorexia, PET scan images reveal that there is more frequent binding of DA to D2/D3-type receptors and a greater density of DA receptors in the anterior ventral striatum, where the nucleus accumbens is located (Frank et al., 2005). This is most likely attributed to the fact that there is an increased upregulation and/or sensitization of DA for its D2/D3 receptors because those with anorexia show a reduction of homovanillic acid (HVA), a DA metabolite, in their cerebrospinal fluid (**?**). Dopamine function is proposed to be particularly different in anorexics in that its release induces feelings of anxiety, whereas DA release typically is associated with a pleasure/reward response in non-anorexics (**?**). More research needs to be done concerning the anxiogenic release of DA in anorexics and other possible DA functions in eating disorders. If DA release is anxiogenic, or anxiety-inducing, it may explain their motivation for starvation because it may be an effective means of reducing anxiety, whether it is related to food or other stressors (Kaye et al., 2013).

On the other hand, there is a significant negative association between binge and purge episode frequencies and the striatal DA response (Kaye et al., 2013). Rat models of bulimia have revealed lower DA levels in the nucleus accumbens and reduced D2 levels in the striatum via CSF HVA analyses (**?**). Reduced D2/D3 receptor density as well as low CSF HVA levels found in people with bulimia support the hypothesis that they are "addicted" to food (Kaye et al., 1999). Additionally, there is evidence of a reduction in striatal [11C]raclopride binding in bulimics which has also been found in people with substance abuse, further suggesting that these disorders share DA D2 receptor vulnerabilities (Kaye et al., 2013).

5 STRUCTURAL AND FUNCTIONAL DIFFERENCES OF THE PREFRONTAL CORTEX IN EATING DISORDERS

There is plenty of evidence suggesting that there are structural and functional differences within the prefrontal cortex in people with eating disorders. Research reveals functional differences within the orbitofrontal cortex, for instance (Frank, 2013; Uher et al., 2004). The orbitofrontal cortex is a subregion of the prefrontal cortex which is involved in decision making and also shares connections with sensory areas and limbic system structures that are involved in emotion (Bechara, Damasio, & Demasio, 2000). In anorexia and bulimia, affective states in response to food stimuli and food avoidance have been associated with medial orbitofrontal cortex activity (Frank, 2013). Since the orbitofrontal cortex shares connections to sensory areas, the orbitofrontal cortex function has a direct relationship with the experience of "taste pleasantness," suggesting a possible explanation for feelings of overstimulation by a food and its textures, taste, and consistency (Frank, 2013).

Experimental studies reveal reduced activity in the prefrontal cortex and the anterior cingulate during rest; however, during food exposure (e.g., eating cake or viewing a photo of a high-calorie drink) these areas of the brain showed abnormal increases in activity

(Uher et al., 2004). For example, fMRI scans of people with anorexia and bulimia show activity in the medial prefrontal cortex, which is important for emotional decision-making, in response to pictures of food. Increased activity in this region potentially indicates that eating disordered behaviors are driven by emotions, such as feelings of inadequacy and poor self-image, instead of rationale. This evidence suggests that the pathologies of anorexia and bulimia share similar functional neural substrates (Uher et al., 2004).

There are also structural brain differences in the orbitofrontal cortex in eating disorders. Specifically, for both ill and recovered anorexia and bulimia groups, MRIs revealed increased gyrus rectus volume in the medial orbitofrontal cortex (Frank, 2013). The larger gyrus rectus found in those with eating disorders is associated with a more intense sensory experience with food, which may explain the feeling of being overwhelmed by food and therefore the initiation of cognitive food avoidance. Past researchers also found this association with the medial orbitofrontal cortex and food avoidance, so it may be key to understanding the cause of eating disorders (Plassmann et al., 2009; Frank, 2013).

Neuroimaging has also allowed researchers to find an alteration in the dorsal executive/cognitive circuitry in those with eating disorders. The dorsal executive neural circuits include dorsal regions of the caudate, the dorsolateral prefrontal and parietal cortices, and other regions involved in selective attention, planning, and regulating affective states (Kaye et al., 2013). This circuit is specifically involved in inhibitory decision making processes, especially in reward-related behaviors (Kaye et al., 2013). Anorexics have a high level of self-control because of strong dorsal cognitive circuit function (Kaye et al., 2009), whereas bulimics are more vulnerable to overeating and substance abuse due to less self-regulation and impulse control; this lack of control is due to the lower utilization of cognitive control networks (Kaye et al., 2013).

In the lateral prefrontal cortex, which is involved in suppressing undesirable behaviors, there was diminished activity in bulimics which may account for the loss of control exhibited in binge-eating episodes (Uher et al., 2004). This decreased lateral prefrontal cortical activity may also account for the need for compensation via purging; in order to counteract the binge in which the person felt they had no control, they can gain control back by purging. Purging is an undesirable behavior for some bulimics, especially those in recovery, suggesting a continuous cycle of uncontrollable eating disordered behaviors.

Eating disorders have structural implications on the basal ganglia as well. In a study by Frank (2013), MRI results showed reduced caudate and putamen volume in both bulimia and anorexia groups compared to controls. Further, sensitivity to reward was positively correlated with right putamen gray matter volumes in both eating disorder groups (Frank, 2013). The dorsal striatum also exhibited a reduction in volume, which may alter reward-motivated behaviors in people with eating disorders (Frank, 2013). This region has a high density of DA receptors that illicit a reward response. The alteration in dorsal striatal volume may be related to the sensitivity to reward found in eating disorders.

6 THE NEUROBIOLOGY OF ALCOHOLISM AND ITS SIMILARITIES TO AND INTERACTIONS WITH EATING DISORDERS

Eating disorders and alcoholism are both associated with the sensitization of DA systems. Avena (2007) conducted a rat study to examine if binge-eating is an addictive behavior similar to the use of drugs of abuse. In the study, rats increased their lever-pressing behavior for sugar after 2 weeks of abstinence from binging compared to before the break. This change in the motivational impact of sugar persisted, and the intake increased when it was available again; this is known as the deprivation effect (Avena, 2007).

Rats from the study by Avena (2007) were also fed daily with irregular amounts of sugar and chow. This diet developed locomotor cross-sensitization within the rats, or an increased response to both sugar, the original stimulus, and amphetamine, the related stimulus. Sensitization between DA agonists, such as cocaine and quinpirole, and intermittent sugar access has been reported by others (Foley et al., 2006; Gosnell, 2005). Intermittent access to sugar was also shown to increase alcohol consumption in rats. These drug sensitization and neurochemical findings support that the DA system is sensitized by intermittent sugar access, revealing that enhanced mesolimbic dopaminergic neurotransmission may contribute to drug dependence and the comorbidity of substance abuse with some eating disorders (Avena, 2007).

Food deprivation or reduced body weight can enhance reinforcing properties of many drugs of abuse (Carr, 2007; **?**). Enhanced release of extracellular DA in the nucleus accumbens occurs with low basal extracellular DA that results from food restriction (Avena, 2007). During withdrawal caused by the opioid antagonist naloxone or by fasting, there is a reversal of accumbens DA-ACh balance (DA low, ACh high), which is also observed in withdrawal from drugs of abuse (Colantuoni et al., 2002). In cases of bulimia, binging and purging behaviors are reinforced by DA without ACh, which is less similar to normal eating and more similar to the effects of alcohol and other drugs of abuse (Avena, 2007). Dopamine is also associated with reward processing in response to alcohol. Volkow et al. (2007) investigated DA release in the ventral striatum in alcoholics versus controls. PET scans were used to examine DA activity using DA tracers in the prefrontal cortex. Participants took methylphenidate (MP), which blocks DA reuptake transporters, allowing researchers to indirectly assess DA activity. Dopamine increases were associated with the rewarding effects of MP (drug-liking and high) in the ventral striatum and putamen. However, this increase in DA was 70% lower in the ventral striatum of alcoholics compared to the controls, and 50% lower in the putamen of alcoholics compared to the controls (Volkow et al., 2007). Since the ventral striatum receives input from the prefrontal cortex (Groenewegen et al., 1999) these results supported their hypothesis that there is a loss of prefrontal modulation of DA cell activity and a decrease in DA activity in alcoholics.

This blunted DA response in the ventral striatum and reduced reward response to the MP in alcoholics suggests that abnormal DA activity may be the reason for anhedonia, or lack of pleasure, also experienced by alcoholics. The diminished DA response may contribute to their risk for alcohol abuse because they may overconsume alcohol to compensate for their DA deficit while also using alcohol to cope with their feelings (Volkow et al., 2007).

This finding is similar to bulimia's deficit in D2/D3 receptors in the striatum discussed earlier, which accounts for the addictive qualities of both binge-eating and alcohol consumption. However, unlike bulimia, people with anorexia experience increased activity and density of D2/D3 receptors in the striatum, suggesting that anorexics may have a lesser chance of developing substance abuse (Kaye et al., 2013).

Lastly, recall that participants with anorexia and bulimia exhibited medial prefrontal cortex activity in response to symptom-provoking pictures of food (Uher et al., 2004). This neural response is similar to that found in studies of drug addiction. Drug addicts show anterior cingulate and orbitofrontal activation that is related to craving and compulsive drug-taking behaviors. Thus, both eating disorders and addiction are associated with dysfunctional activity in brain regions associated with compulsive and affective phenomena (Uher et al., 2004).

7 CONCLUSION

Eating disorders and substance abuse appear to share a common pathology in terms of DA activity within structures of the prefrontal cortex. These similarities may contribute to the impulsive and reinforcing behaviors that are exhibited in both disorders. Eating disorders show structural and neurochemical similarities to alcoholism, however research suggests that anorexia and bulimia may not share the same direction of relationship with substances; specifically Kaye and colleagues describe bulimia as more "vulnerable" to and anorexia as more "protected" from substance abuse (Kaye et al., 2013).

Specifically, people suffering from bulimia seem to have a higher likelihood of adopting abusive relationships with alcohol and other drugs than people with anorexia (Kaye et al., 2013). This probability is attributed to DA system sensitization after numerous binge episodes causing feelings of withdrawal that are similar to those experienced with drugs of abuse. Reports of withdrawal sensations in bulimia patients strengthens the argument that binge-eating is an addiction like alcoholism (Avena, 2007). Unlike alcoholism, bulimia exhibits compensatory behaviors, like self-inflicted vomiting, due to a rise in DA without ACh and feelings of guilt after a loss of control.

Depleted DA levels in the striatum result in feelings of anhedonia in alcoholics. Low DA levels are also found in people with bulimia, suggesting that bulimics may also experience anhedonia and therefore respond by binge-eating as a coping mechanism. Additionally, the increased medial prefrontal cortex activity in response to food stimuli in bulimics is similar to the medial prefrontal cortex activity associated with cravings and compulsive drug-taking behaviors found in substance abuse (Uher et al., 2004).

Prefrontal regulation and DA deficits need to be restored in alcoholics and those with eating disorders. However, solely addressing the biological mechanisms behind these disorders will not completely solve them. Medical interventions to address these issues must be combined with addiction therapy and cognitive behavioral therapy in treatment programs for best results in psychological recovery (Uher et al., 2004).

This review explored and discussed the potential shared brain mechanisms underlying eating disorders and substance abuse and addiction. These include (1) the sensitization of DA systems, (2) the reinforcement of behaviors by DA without ACh in bulimia, (3) withdrawal symptoms caused by low DA and high ACh in bulimia, which is also seen in anorexia, (4) blunted DA activity and fewer DA receptors in the ventral striatum in alcoholics and bulimics, and (5) medial prefrontal activation similarities in response to food or during drug cravings. Additional research will be able to further characterize these similarities, with the current literature suggesting a potential link between the neural underpinnings of eating disorders and addiction.

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