Review Provides New Insights into the Causes of Anorexia

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New imaging technology provides insight into abnormalities in the brain circuitry of patients with anorexia nervosa (commonly known as anorexia) that may contribute to the puzzling symptoms found in people with the eating disorder. In a review paper published on line in *Nature Reviews Neuroscience*, Walter Kaye, MD, professor of psychiatry and director of the Eating Disorders Program at the University of California, San Diego, and colleagues describe dysfunction in certain neural circuits of the brain which may help explain why people develop anorexia in the first place, and behaviors such as the relentless pursuit of dieting and weight loss.

"Currently, we don't have very effective means of treating people with anorexia," said Kaye. "Consequently, many patients with the disorder remain ill for years or eventually die from the disease, which has the highest death rate of any psychiatric disorder."

A better understanding of the underlying neurobiology - how behavior is coded in the brain and contributes to anorexia - is likely to result in more effective treatments, according to the researchers.

Childhood personality and temperament may increase an individual's vulnerability to developing anorexia. Predisposing factors, some suspected to be inherited, such as perfectionism, anxiety, or obsessive-compulsive tendencies may precede the onset of an eating disorder. These traits become intensified during adolescence as a consequence of many factors such as hormonal changes, stress and culture.

"Adolescence is a time of transition, when individuals must learn to balance immediate and long-term needs and goals in order to achieve independence," said Kaye. "For such individuals, learning to cope with mixed societal messages and pressures may be overwhelming, exacerbating underlying traits of anxiety and a desire to perfectly achieve."

Once a patient develops anorexia, starvation and malnutrition cause profound effects on the brain and other organ systems. Such changes include neuro-chemical imbalances, which may, in turn, exaggerate the preexisting traits and accelerate the disease process.

"Individuals with anorexia tend to report that dieting reduces anxiety, while eating increases it," said Kaye. "This is very different from most individuals, who experience hunger as unpleasant." The powerful drive to avoid being anxious drives actually weight loss in anorexia nervosa, triggering the out-of-control spiral that results in severe emaciation and malnutrition.

In addition, people with anorexia nervosa tend to not experience pleasure or live "in the moment." They often have exaggerated and obsessive worry about the consequences of their behaviors, looking for rules when there are none, and are overly concerned about making mistakes. Co-author Julie L. Fudge of the Department of Psychiatry & Neurobiology and Anatomy at the University of Rochester Medical Center, notes that imaging studies suggest that individuals with anorexia have an imbalance between circuits in the brain that regulate reward and emotion (the ventral or limbic circuit) and circuits that are associated with consequences and planning ahead (the dorsal or cognitive circuit).

"Brain-imaging studies also show that individuals with anorexia have alterations in those parts of the brain involved with bodily sensations, such as sensing the rewarding aspects of pleasurable foods," said co-author Martin Paulus, UC San Diego professor of psychiatry, who heads UC San Diego's Laboratory of Biological Dynamics and Theoretical Medicine. "Anorexics may literally not recognize when they are hungry."

One such brain region is the anterior insula, which is critically important for interoception, or the self-awareness of internal body signals. In addition to a failure to respond appropriately to signals of hunger, symptoms of anorexia - such as distorted body image and diminished motivation to change - could be related to disturbed interoceptive awareness.

"Anorexia is very complicated, and there needs to be a paradigm shift in understanding its underlying cause," said Kaye. "We're just beginning to understand how the brain is working in people with this disorder."

Kaye noted that the temperament and personality traits that may create a vulnerability to develop anorexia may also have a positive aspect. These traits include attention to detail, concern about consequences, and a drive to accomplish and succeed. "It's my clinical experience that many individuals who recover from anorexia do well in life," he said.

Under Kaye's leadership, the eating disorders treatment program at UC San Diego is developing treatments based on understanding the temperament and personality that drives anorexia, and helping patients to use such traits in constructive, rather then self-defeating ways.

Symptoms of the disease anorexia nervosa, more commonly known as anorexia, include the patient's refusal to maintain body weight at or above a minimally normal weight for age and height; and intense fear of gaining weight or becoming fat, even when the individual is underweight. Although anorexia is characterized as an eating disorder, it remains unknown whether there is primarily a disturbance of appetite, or whether change in appetite is secondary to other issues such as anxiety or obsessional preoccupation with weight gain. When malnourished and emaciated, individuals with the disease have widespread and severe alterations of the brain and other organs. As it is unclear whether these changes are the cause of consequence of severe weight loss, individuals who have recovered from anorexia have been studied. While approximately 50% to 70% of affected individuals eventually recover, a significant proportion of patients develop a chronic illness or die, making anorexia the number one cause of death among psychiatric diseases.

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