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Is There a Disorder of Aggression?

Posted Rob Mitchum at 9:47 AM CT, June 14, 2010

Everyone gets angry from time to time. But there's angry, and there's *angry* - wall-punching, object-throwing, call-the-police angry. The latter type of tantrum, if it's a



recurrent problem, could be a symptom of a psychiatric condition currently known as intermittent explosive disorder, or IED. Though it has appeared in every edition of the Diagnostic and Statistical Manual of Mental Disorders (albeit under different names), IED remains a hazy sort of diagnosis to many both inside and outside psychiatry. But over the last 20 years, Emil F.



Coccaro, M.D. (right), Chair and the E.C. Manning Professor of Psychiatry and Behavioral Neuroscience at the University of Chicago Medical Center, has built up a diverse body of research defining the causes, consequences, and best available treatments for IED.

Coccaro's research group is currently in the midst of a flurry of publications that break down IED from a number of angles: its familial nature, its association with other negative health outcomes, its correlation with brain activity. So I sat down with him to talk about what is currently known about the disorder, what distinguishes a person from IED from a person with "a temper," and how it is currently treated by psychiatrists. Coccaro was blunt about the history of the disorder, saying that some of the mystery surrounding the disease is due to early difficulties defining it.

"There have been controversies about it because people have wondered how much of it is out there and does it really exist," Coccaro said. "The criteria in DSM-3 and DSM-4 were never that good."

The problem, he said, was in the dynamics of the disorder. While it was clear that patients with IED had recurring, out-of-proportion episodes of aggression, the original criteria stated that the patient would be relatively "even-keeled" between. But Coccaro said that psychiatrists have come to understand that IED - which may appear in between 4 and 7 percent of the United States population - is more likely to reflect quieter impulsive aggressive "rumblings" between the big "blow-ups".

"People who have this explosive problem are not like Bruce Banner where they get angry and become this monster and then come back to baseline," Coccaro said. "They'll have big explosions, but at baseline they are a bit irritable, still, and are at high risk for blowing up when somebody frustrates or angers them."

More specific criteria have not only helped psychiatrists diagnose the disorder, it has also allowed for more thorough research. A breakthrough finding by Coccaro in 1989 was that the function of the serotonin system - a neurotransmitter also known to be involved in depression - correlated with aggressive behavior. People with lower serotonin function were, on average, more aggressive and impulsive, a relationship that only strengthened as diagnoses of IED became more accurate.

The finding also suggested an obvious treatment to try on IED patients - fluoxetine, aka Prozac®, which works by increasing the amount of serotonin in the brain. And it worked, according to a series of studies conducted by Coccaro and colleagues, reducing IED patients baseline score on an aggression scale. However, drug treatment can only accomplish so much and may need to be paired with other therapies designed to help patients cope with stressful situations, Coccaro said.

"What the drugs tend to do is increase the threshold to explode," Coccaro said. "Another treatment modality - cognitive-behavioral therapy - works on arousal and how people react to the stimuli coming at them. This is important because the drugs won't help with issues in the here and now."

But it remains to be seen whether both types of treatment are needed in every patient, or whether therapy can be more individualized for each patient. Understanding the disease in more detail would help make those decisions, and Coccaro has also used genetic linkage and brain imaging to search for the underlying causes. The clues are mounting:

- A study published in May in the Journal of Psychiatric Research found that IED is highly familial; if a person has been diagnosed with the disorder, family members are three times as likely to also qualify. This is consistent with data from twin studies that demonstrate that aggression is under substantial genetic control.
- A recent fMRI study found that the amygdala - a brain region associated with emotion - is over-responsive to pictures of angry faces in IED subjects compared to controls, while the frontal lobe regions - the "brakes" upon impulsivity - are less responsive.
- Impulsive behavior is also correlated with blood cortisol levels and aggressive behavior is directly correlated with history of cigarette smoking and with history of even minor brain injury.

Furthermore, the negative effects of IED go beyond property damage and potential legal trouble resulting from angry, aggressive explosions. A paper just published with colleagues from University of Chicago and the University of Southern Mississippi found that medical conditions such as coronary heart disease, diabetes, arthritis, and chronic

pain are elevated in IED subjects. Coccaro speculates that the root cause of these maladies stem, most likely, from the same abnormal stress response that lead to the extreme temper of those with IED.

"It's how you react to stress, and these people don't react well to stress. They're blowing up," Coccaro said. "It's an epidemiological story that leads to other questions you can then formulate specific studies around."

For an emotional disorder that may previously have been dismissed as a vague "foul temper" that couldn't be helped, it's encouraging that such studies are gaining greater clarity. The origin of both extreme and normal emotions in the brain remains a young area of research, whether it's anger or depression or mania. But the incremental successes in understanding what causes IED and how it can be fixed suggest that some emotions gone wild can be corrected.

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