Scientist pursuing new treatments for impulsive aggression

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(Medical Xpress)—Most of us get a little angry, and perhaps even aggressive, now and then. And in most cases, that's perfectly OK.

But for individuals with pathological impulsive aggression, getting angry can be an altogether different—and dangerous—experience. Their aggression is characterized by impulsive outbursts of violence and anger. These outbursts are typically disproportionate to whatever triggered them, and in many cases, they're associated with deficits in self-control, along with defiant or hostile behavior.

"We're talking about uncontrolled and potentially violent outbursts that can have devastating effects for the aggressive individual and those around them," said University of Kansas neuroscientist Marco Bortolato. "Unfortunately, science hasn't yet provided adequate tools to really understand and treat the full spectrum of impulsive-aggressive disorders."

That's why Bortolato, an assistant professor of pharmacology and toxicology in the School of Pharmacy, is examining the neurobiological basis of impulsive aggression. His goal is to unlock the condition's underlying mechanisms and ultimately develop treatments for it.

"Like many behavioral disorders, impulsive aggression is currently diagnosed based on symptoms and qualitative descriptors," Bortolato said. "But we're looking for biomarkers —biologically based indicators—or other measurable indices that can help us better identify

and treat the entire spectrum of pathological aggression disorders."

The social impact of pathological aggression is substantial, accounting for 60 percent of the 4.5 million violent crimes committed each year in the United States. It's also a key factor in suicide among male adolescents. The economic toll is equally significant. According to the World Health Organization, the overall costs of impulsive aggression total $200 billion per year when including costs such as medical expenses, legal services and incarceration.

"There's clearly a significant social and economic cost," Bortolato said, "which is why we need to better understand and treat it."

Searching for biomarkers

In recent years, researchers have begun making headway in their search for biologically based indicators of aggression.

A large body of research, including past work by Bortolato, has zeroed in on the enzyme monoamine oxidase A (MAO A) as a possible biomarker for aggression. Specifically, Bortolato and others have shown that the combination of MAO A deficiency and extreme stress or abuse at a young age can cause pathological aggression in mice and adult males.

In 2011, Bortolato and his colleagues built on these findings by developing the first animal model of this genetic-environment interaction. In particular, he developed a new transgenic line of mice with very low levels of MAO A and then subjected them to early life stress that simulated child neglect and abuse. As expected, the mice demonstrated increased aggression.

In 2012, Bortolato and his colleagues made a breakthrough discovery when they identified a critical neurological factor in aggression: a brain

receptor that malfunctions in overly hostile mice. When the researchers shut down the brain receptor, which also exists in humans, the excess aggression disappeared.

Earlier this year, Bortolato used his models to demonstrate that the combination of low MAO A and early life stress can impact learning and memory. Those findings appear in the July 2013 edition of *PNAS*, the journal of the *Proceedings of the National Academy of Sciences*.

And most recently, Bortolato used his mice models to demonstrate that the combination of low MAO A and early life stress can increase perseverative behaviors—the repetitive, seemingly purposeless behaviors we often associate with autism. His study appears in the latest edition of the journal *Neuropharmacology*.

In total, Bortolato's recent discoveries are further demonstrating the usefulness of MAO A as a potential indicator of aggression.

"By creating these models, we're able to better identify and isolate possible biomarkers for severe aggression," he said. "In doing so, we're getting closer to better prevention, diagnosis and treatment of this condition."

Provided by University of Kansas