Molecular tag explains differences in brain's response to anger, fear

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When people perceive anger and fear in others, a region of the brain called the amygdala sends signals throughout the rest of the brain that allow us to prepare for potentially threatening situations.

Interestingly, people differ in the way that their brain responds to these cues. For example, some people may over-respond to relatively non-

threatening signals, which may be an inefficient use of costly bioenergetic resources.

Researchers at the University of Virginia have now uncovered a chemical tag on DNA that can be drawn from the blood and used to understand these differences. Their findings are reported online this week in the *Proceedings of the National Academy of Sciences* Early Edition.

The chemical tag - called DNA methylation - is found on the oxytocin receptor gene. This receptor is important for allowing the cell to respond to a molecule called oxytocin. Oxytocin, sometimes called the "love hormone," is linked to a variety of human behaviors - relationship forming, caring, bonding and trust, among others. In short, the hormone is important in regulating the way we socialize and respond to kindness or threats. Individuals low in DNA methylation on the oxytocin receptor may be better able to utilize this important hormone.

Using a study sample of 98 healthy Caucasians aged 18 to 30 who provided blood samples and underwent functional MRI brain scans while looking at pictures of angry and fearful faces, the researchers identified a relationship between the level of DNA methylation in an individual and activity in the amygdala and other parts of the brain responsible for emotion processing.

According to study co-author James P. Morris, a U.Va. assistant professor of psychology, individuals with lower DNA methylation show diminished brain response to angry and fearful faces and greater communication between brain regions important for regulating emotion.

The research team hypothesizes that this may be important for understanding the state of the disrupted or diseased brain as individuals with autism spectrum disorder, psychopathy, depression and anorexia

nervosa all display high degrees of DNA methylation at the oxytocin receptor.

"Defining biomarkers like this epigenetic tag associated with the oxytocin receptor may help us to predict future social developmental problems and inform interventions for those with social deficits," said co-author Jessica J. Connelly, a U.Va. assistant professor of psychology.

"While our findings certainly have clinical implications, we show that even in a healthy population these markers are variable and may partially explain what makes each of us unique in how we respond in social situations," said the study's lead author Meghan Puglia, a Ph.D. candidate in psychology at U.Va.

The investigators believe it is possible that eventually a blood test could be developed that would, in effect, predict how a person would behave in various social situations. Connelly and her colleagues are sorting through the complexities of epigenetics - the nature -and-nurture question of how both genetics and environment affect psychological development.

More information: Epigenetic modification of the oxytocin receptor gene influences the perception of anger and fear in the human brain, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1422096112

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