Genetic variation cues social anxiety in monkeys and humans

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A genetic variation involving the brain chemical serotonin has been found to shape the social behavior of rhesus macaque monkeys, which could provide researchers with a new model for studying autism, social anxiety and schizophrenia. Humans and macaques are the only members of the primate family to have this particular genetic trait.

"We have found very similar gene-based disruptions in social rewards shared by monkeys and by humans," said Michael Platt, Ph.D., associate professor of neurobiology at Duke University Medical Center and an expert in neuroeconomics.

The study appears in the online journal *PLoS One* on Jan. 13.

Platt's research group at Duke studied behavior and social anxiety in two groups of monkeys with variations in the serotonin transporter gene, crucial to regulating emotion. Based on earlier observations in humans, the scientists knew that humans carry two versions of the gene, long and short. Some people have two long versions (L/L), but the people with one of each (S/L) are known to experience a higher incidence of social anxiety and other behaviors.

In a series of experiments, the S version of the gene in monkeys was found to influence their risk-taking when faced with particular social stimuli.

"Based on work in humans, we interpreted this to reflect an induction of

a fearful emotional state, which often leads people to become risk averse," said Karli Watson, Ph.D., of the Duke Department of Neurobiology, lead author on the paper.

In human populations of European ancestry, 48% are S/L and 36% are L/L. The rest are S/S. The S allele is more common in Asian populations, Watson noted.

The authors conducted three experiments with male monkeys that had been genotyped for the S/L or L/L variants to learn how genetic variation might influence their responses to social rewards and punishments. They found that monkeys with one copy of the short gene spent less time gazing at images of the face and eyes of other monkeys, were less likely to engage in risk-taking behavior, and less likely to want to view a picture of a high-status male.

"For both human and non-human primates, faces and eyes are a rich source of social information, and it's well established that both humans and macaques tend to direct visual attention to faces, especially the eye region," Platt said. "Rhesus monkeys live in highly despotic societies, and convey social rank information by making threats and showing dominant and submissive behaviors."

In the eye imaging experiment, the monkeys were observed while being shown images of the faces or scrambled faces of familiar monkeys. In addition to spending less time looking at faces and eyes, the S/L monkeys also had larger pupil diameters when gazing at photos of high-status male macaques, indicating higher arousal.

"Their brains set off alarms," Platt said. "In human studies, people with the short version of the gene often show hyperactive amygdalas, a part of the brain involved in detecting threats in the environment. In autism, too, people often don't look people directly in the eye, which may point to a

new avenue of research."

In a second experiment, the S/L monkeys were less willing to take risks after they were primed with the faces of high-status males. They more often chose a "safe" option of a fixed volume of juice, rather than the chance for a greater or lesser amount, the "risky" choice. Previous studies have found that inducing fear in human subjects makes them more risk-averse. "Our findings showed that faces of high-status males cause greater fear in the S/L monkey," Platt said.

The final experiment was a pay-per-view set-up. The monkeys could have a juice reward paired with an image or a juice reward without any image. The images were of high-status male faces, low-status male faces, female genitals or a gray square. The S/L monkeys actually had to be paid juice to view the dominant males, while the L/L monkeys gave up juice for a look at these faces.

"Heightened sensitivity to social threats may prove to be helpful in many ways, because success in a social group depends on seizing opportunities while avoiding any potential harmful, antagonistic interactions," Watson said.

"Altogether, our data show that genetic variation in serotonin function does contribute to social reward and punishment in macaques, and thus shapes social behavior in both humans and rhesus macaques," Watson said. "This study confirms rhesus monkeys can serve as a model of what goes on in our brains, even in the case of social behavior."

Source: Duke University Medical Center