

Mouse calls help search for emotion-controlling genes

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Scientists have long known that emotions and other personality traits and disorders run together in families. But finding which genes are most important in controlling emotions has proven difficult. Humans and mice have similar numbers of genes, but mice are valuable because their genes can be deleted or added. Many researchers have begun to study mouse behaviors to try to link genes with complex behaviors.

A new report by Wang et al., to be published in *PLoS ONE* on April 2 found that male mice make high-frequency vocalizations during sexual interactions with female mice. These high-frequency calls are associated with approach behaviours, and with genes that control positive emotions.

“This work has supported the theory, proposed by Jeffrey Burgdorf and Jaak Pansepp, that 50-kHz calls reflect positive affect in rats, and extended that theory to higher-frequency mouse calls,” Wang said.

These high-frequency calls are inaudible to humans, but can be measured using special microphones and computer programs. The complex calls have “chirp-like” syllables and structure like bird songs. The number and density of different types of vocalizations and squeaks of male and female mice can be used to index the emotional responses of mice.

The team of researchers include Haoran Wang, John Yeomans and Shuyin Liang at the University of Toronto, and Jeffrey Burgdorf at

Northwestern University in Chicago.

In the courtship phase, before mounting, males usually made simple whistles or modulated calls. After mounting the females, however, the males shifted to more complex “chirp-like” vocalizations. The male vocalizations increased in number and complexity as intensity increased.

Wang et al. found a marked reduction of male calls when single genes were deleted. In particular, they studied genes related to the transmitters, dopamine and acetylcholine, both of which are important for emotional expression in humans and rats. Two acetylcholine receptor gene deletions (for the M5 and M2 muscarinic receptors) reduced the number of calls. Furthermore, M2 and M5 receptor deletions changed the duration, frequency and bandwidth of the calls. However, M4 muscarinic receptor mutations (contributed by Jurgen Wess of NIH along with the M2 mice) and D2 dopamine receptor mutations were not found to change the number of calls. D2 dopamine receptor mutations changed the duration of the calls.

Furthermore, Wang found that, amphetamine, a street drug activating the brain dopamine system, can induce “chirp-like” calls at very low doses, indicating a role for dopamine. However, this induction was lost in male mice lacking M5 receptor genes, known to be important for activating dopamine neurons.

These findings provide a new method for screening emotion genes, and for developing drugs for controlling emotions, drug abuse and mood disorders.

Citation: Wang H, Liang S, Burgdorf J, Wess J, Yeomans J (2008) Ultrasonic Vocalizations Induced by Sex and Amphetamine in M2, M4, M5 Muscarinic and D2 Dopamine Receptor Knockout Mice. PLoS ONE 3(4): e1893. doi:10.1371/journal.pone.0001893

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