

## Scared of the wrong things: Lack of major enzyme causes poor threat-assessment in mice

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Do you run when you should stay? Are you afraid of all the wrong things? An enzyme deficiency might be to blame, reveals new research in mice by scientists at the University of Southern California.

In a paper appearing in the October 2011 issue of the *International Journal of Neuropharmacology*, USC researchers show that <u>mice</u> lacking a certain enzyme due to genetic mutation are unable to properly assess threat. The mice exhibited defensive behaviors (such as biting or tail rattling) in the presence of neutral stimuli, such as <u>plastic bottles</u>.

Conversely, in the presence of true danger cues such as predator urine or an anesthetized rat, the mice with the enzyme mutation were less cautious and defensive than their littermates, even climbing on the unconscious rat.

Mice without the enzyme also took longer to leave an open chamber, indicating reduction in exploratory and escape tendencies.

"Taken together, our findings suggest that <u>monoamine oxidase</u> A deficiency leads to a general inability to appropriately assess contextual risk, as indicated by the inappropriateness of their defensive behaviors," said senior author Jean C. Shih, University Professor and Boyd and Elsie Welin Professor of pharmacology and <u>pharmaceutical sciences</u> in the USC School of Pharmacy.



Monoamine oxidase A is the main enzyme in the brain that breaks down serotonin, norepinephrine and dopamine, which have been shown to contribute to the "fight or flight" impulse by raising heart rates and increasing blood and <u>oxygen flow</u>. Previous research in Shih's lab and elsewhere has shown that deficiency in monoamine oxidase A causes aggression in mice and humans, but this study is among the first to clarify that what was perceived as <u>aggressiveness</u> may more accurately be described as an inability to properly adapt and respond to environmental cues.

"Mice without monoamine oxidase A exhibited a distinct inability to attune their response to the situation," said Sean Godar, a post-doctoral research associate at the USC School of Pharmacy and co-lead author of the study. "The paradoxical responses to neutral and fear-inducing stimuli are markedly reminiscent of deficits in facial affect processing in schizophrenia and autism."

The researchers found no significant differences in sensory ability between the mice with a monoamine oxidase A deficiency and their littermates — both groups found buried mini-chocolate cereal chips at about the same rate, on average, and were similarly able to traverse a ledge and recognize objects.

"When compared to the broader, multi-faceted behavioral repertoire of other mice, the behavior observed in mice without monoamine oxidase A may reflect a limited range of emotional responses and flexibility," said Marco Bortolato, co-lead author of the study and research assistant professor of pharmacology and pharmaceutical sciences at the USC School of Pharmacy.

The researchers suggest that the strange defensive behavior exhibited by the enzyme-deficient mice may actually reflect a limited range of adaptive responses and lack of emotional flexibility — the mice may



only have one gear for fear.

**More information:** Godar et al., "Maladaptive defensive behaviors in monoamine oxidase A-deficient mice." *International Journal of Neuropharmacology*: October 2011.

## Provided by University of Southern California

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