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Brain's sensitivity to different types of regret may impact mood disorders

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Researchers from New York's Icahn School of Medicine at Mount Sinai Hospital found that the way the brain processes the complex emotion of regret may be linked to our ability to cope with stress and be changed in psychiatric disorders.



The study was just published in the American Association for the Advancement of Science's open-access journal, *Science Advances*. Titled "Distinct forms of regret linked to resilience versus susceptibility to stress are regulated by region-specific CREB function in mice," it reveals that rodents show sensitivity to two distinct types of regret and that these different thought processes likely stem from different parts of the brain.

The team, headed by Dr. Brian Sweis, an instructor in the department of neuroscience and a resident in the department of psychiatry at Icahn Mount Sinai, was the senior author of the study.

The team found that a genetic marker that predisposes maladaptive stress response traits and vulnerability to depression was linked to sensitivity to one type of regret, while healthy and stress-resilient animals were instead sensitive to a second type of regret. These novel findings could have broad implications for multiple fields, including psychiatry, psychology and behavioral economics, and could affect the future design of targeted therapies for mood disorders in humans, said Sweis.

"Is regret exaggerated and do individuals hyper-ruminate on past decisions, or are those with depression numb to this emotion? Is this adaptive or maladaptive, and are individuals unable to learn from their mistakes? For patients struggling with depression, there has been no clear description of regret as a defining feature of the condition," he added.

Building on previous work demonstrating that rats and mice are capable of processing regret-like thoughts, the Mount Sinai Hospital study pushes the boundaries of what can be captured in rodent models used for the study of mental illnesses. The authors reached this goal by combining sophisticated approaches in behavioral economics and chronic stress procedures with viral gene therapy to study the neural and molecular basis of complex decision-making in animals.

This methodology was built on principles of neuroeconomics, which is the study of how the physical limits of the brain give rise to biases we have when making decisions. This approach made it possible for the researchers to capture how complex choices made in one's past can impact subsequent decisions and, importantly, how the way in which individuals process or realize missed opportunities is capable of interacting with affective states when influencing future choices – the basis of regret.

The team trained mice on a decision-making task termed "Restaurant Row" during which the rodents navigated a maze foraging for their sole source of food. Mice were given only a limited amount of time each day to invest in rewards of varying costs (delays randomly selected from one to 30 seconds signaled by the pitch of a tone) and subjective value (unique flavors tied to four separate locations or "restaurants").

Mice chose to enter or skip each restaurant depending on the cost and flavor presented. If mice accepted an offer by entering the restaurant, they were tasked to wait out a countdown to earn the reward before moving on to the next one. They showed stable preferences of willingness to wait depending on each restaurant's flavor.

Among the major findings: the existence of two distinct types of regret that are not generic but are connected to separate parts of the brain, depending on the exact nature of the missed opportunity being processed. Both types involve animals making mistakes.

But type-one regret was defined as an "economic violation" in which animals walked away from a good opportunity only to "get burned" on subsequent trials. Conversely, type-two regret was defined as decisions in which animals made poor choices to invest their limited time in offers they typically could not afford. Thus, the first type was framed by the rodents' realization that they missed a favorable opportunity, while the second type was characterized by facing the decision to cut their losses and move on.