'Second-guessing' is a hard-wired behavior, study suggests

May 24 2023, by Julie Kiefer

University of Utah Health scientists have found that genes bias decision-making, even decisions that seem irrational. Credit: Cornelia Stacher-Hörndli, PhD

Have you ever made a decision that in hindsight seemed irrational? A new study with mice, which could have implications for people, suggests that some decisions are—to a certain extent—beyond their control. Rather, the mice are hard-wired to make them.

"This research is telling us that animals are constrained in the decisions they make," says Christopher Gregg, Ph.D., a neurobiologist at University of Utah Health and senior author of the study that recently published in *iScience*. "Their genetics push them down one path or another."

Gregg and his research team started investigating decision-making after noticing mice repeatedly making what appeared to be an irrational decision. After finding a stash of hidden seeds, rather than staying put to eat them, mice kept returning to a (different) location that had had food in it the day before. Only on this day, the original location was empty.

"It was as if the mice were second-guessing whether the first location really had no food," Gregg says. "Like they thought they had missed something."

To Gregg and the study's co-authors, the behavior didn't make any sense. The animals ended up eating less because of the time spent continuously returning to the empty food patch. If that kind of behavior causes mice to eat less in the wild, it could spell trouble, Gregg explains, because not getting enough calories can be detrimental for a mouse.

The real surprise came after discovering that mice lacking a specific gene didn't "second-guess" where to go and instead were more likely to stay and eat the food they found. As a result, they consumed more calories overall. This was the first evidence the scientists found that genes could bias decision-making, even decisions that did not seem logical, at least to a human. In this case, the gene Arc appeared to be

important for compelling the mice to continue searching for food even when it didn't appear to be necessary.

"We all have a clear sense of what it is like to second-guess something, but who would have thought that this type of behavior could be so profoundly affected by one gene?" says Cornelia Stacher-Hörndli, Ph.D., neurobiologist and co-author. "This raises the question 'Are other cognitive biases under genetic control?'"

Decoding behavior

To the human eye, a mouse's life seems pretty simple. When placed in a naturalistic setting in Gregg's lab, they left home, explored their surroundings, searched for food, ate a little, and made stops back home in between. But the view looked quite different after a machine learning algorithm deconstructed their journeys.

Machine learning algorithms showed that as mice foraged for food, they strung together a finite number of stereotyped behavioral sequences like building blocks, interspersing them with spontaneous behaviors to construct more complex behavior patterns. Credit: Cornelia Stacher-Hörndli, PhD

A custom program built by Gregg and study co-author Jared Emery analyzed 1,609 foraging excursions and saw that the mice repeated 24 behavior sequences over and over. As the mice foraged, they strung together the sequences like building blocks, interspersing them with spontaneous behaviors to construct more complex behavior patterns. One of them was the second-guessing behavior. "To a certain extent, you could predict the future," Gregg remarks.

That future changed for mice missing the gene, Arc. Six of the 24 behavior sequences were altered, and together, those differences short-circuited the second-guessing behavior. Previous research had shown Arc is involved in learning and memory. But overall, analysis showed that the mice's memory—and their other behaviors—were largely intact. The implication is that the effect on those six behaviors was specific.

"One intriguing idea is that the animals evolved to make those decisions because they were somehow advantageous in the wild," Gregg says. He explains one possibility: When mice go back and forth to evaluate previous food locations, it helps them create a mental map that might help them find food faster the next time around. "Genetically controlled cognitive bias may allow for effective decision-making during foraging," he says.

The question remains, is there a biological basis for other types of cognitive bias? And could genes guide decision-making in humans? More research will tell. "I believe that this research is foundational for a new field that we are calling 'decision genetics,'" Stacher-Hörndli says.

In addition to Gregg and Stacher-Hörndli, additional co-authors are Alicia Ravens, Susan Steinward, and Jason Shepherd from University of Utah Health and Jared Emery from Storyline Health, Inc.

More information: Alicia Ravens et al, Arc regulates a second-guessing cognitive bias during naturalistic foraging through effects on discrete behavior modules, *iScience* (2023). DOI: 10.1016/j.isci.2023.106761

Provided by University of Utah Health Sciences