How dopaminergic systems in fruit flies create reward-seeking behaviors despite adverse consequences

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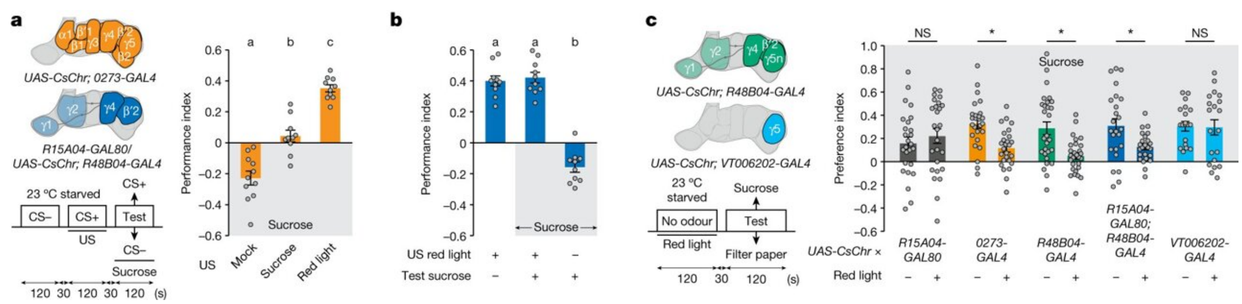

Reward DAN activity reduces subsequent need seeking. a, Left, schematics and experimental protocol. Right, starved flies trained with 0273-neuron activation (orange) disregard sucrose to seek the CS+ odor predicting artificial reward, whereas flies trained with sucrose exhibit no preference, and mock-trained flies prefer sucrose (left to right: n = 11, 10 and 10). b, Starved flies trained with activation of β′2&γ4 DANs also disregard sucrose to seek artificial reward (n = 10, unconditioned stimulus is the red light protocol from a and genotype corresponds to the schematic with blue regions in a). Different letters above bars in a,b indicate groups that are significantly different from each other. c, Left, schematics and protocol. Right, activation of 0273 neurons, R48B04 DANs, or β′2&γ4 DANs in an odorless tube decreases subsequent sucrose approach in starved flies (left to right: n = 26, 26, 26, 26, 28, 28, 24, 24, 20 and 20). Credit: *Nature* (2023). DOI: 10.1038/s41586-023-06671-8

A team of biomedical researchers at the University of Oxford's Center for Neural Circuits and Behavior has discovered how dopaminergic systems in fruit flies can instill reward-seeking behaviors despite adverse consequences.

In their study reported in the journal *Nature*, the group used neurogenetic tools to learn more about how dopamine release in the "mushroom body" of the fruit fly brain impacts both reward and punishment-aversion behaviors. Kristin Scaplen and Karla Kaun with Bryant University and Brown University, respectively, have published a News & Views piece in the same journal issue, outlining the history of research involving learning more about unconstrained reward seeking and the work done by the team on this new effort.

Prior research and anecdotal evidence have shown that humans (and sometimes other animals) will engage in or endure seemingly risky, painful or destructive behavior to gain a reward. Such behavior appears to involve overriding processes in the brain that are supposed to help with risk avoidance. Stealing things to sell for money to buy and use drugs is one example in humans.

Another example is fruit flies' willingness to walk on a material that will give them an electric shock in response to an odor that in the past has led them to a reward of alcohol. Such behavior is known as unconstrained reward seeking, and scientists would like to know what goes on in the brain of a creature engaging in it as a means to prevent such behavior in humans. For this new study, the research team studied fruit flies due to their relatively primitive nature.

The researchers focused on a part of the fruit fly brain known as the mushroom body—a part so well studied that scientists can manipulate individual neurons to gain desired results. They manipulated dopamine-releasing neurons for this experiment—prior research has shown that they are involved in behavior modification and memory retention.

To learn more about the role such neurons play in unconstrained reward seeking, the team studied gene-expression patterns in the neurons and artificially activated those that were found to be involved in reward or punishment-aversion behavior. By activating certain neurons, the researchers were able to instigate unconstrained reward-seeking behaviors.

They also discovered a natural reward–punishment system where some rewarded dopamine neurons not only gave the fruit fly a rewarding feeling, but impaired the functioning of neurons that were involved in punishment avoidance—thereby driving unconstrained reward seeking.

More information: Kristijan D. Jovanoski et al, Dopaminergic systems create reward seeking despite adverse consequences, *Nature* (2023). DOI: 10.1038/s41586-023-06671-8

Kristin M. Scaplen et al, Dopamine determines how reward overrides risk, *Nature* (2023). DOI: 10.1038/d41586-023-03085-4