Touchscreens and milkshakes: Study reveals more about brain's reward systems

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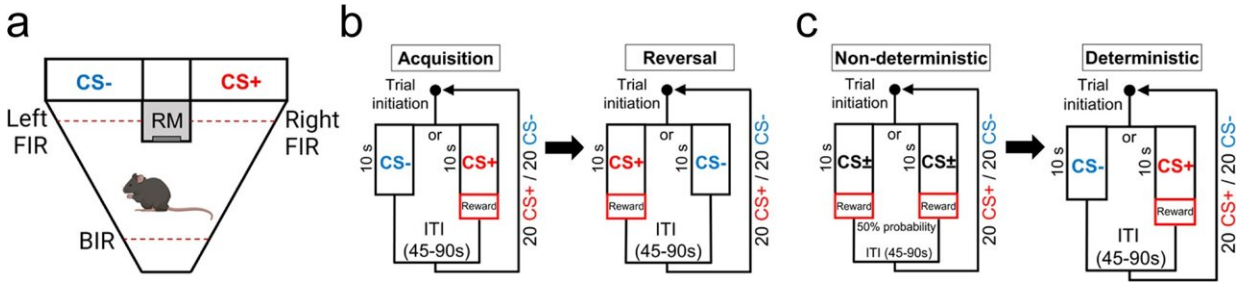

The touchscreen Autoshaping task to assess Pavlovian approach behaviors toward reward-predicting stimuli. a Layout of the Autoshaping touchscreen operant chamber depicting the two screens (left, CS-; right, CS+) and the reward magazine (RM) delivering strawberry milkshake reward (10 µl). Each chamber was equipped with a back infrared photobeam (BIR) to initiate trials, and two front infrared photobeams (FIR) on each side of the RM to record approaches to the CS screen. An infrared photobeam inside the RM (not displayed) recorded latency time to collect rewards. b Flowchart overview of the Autoshaping task during acquisition (left) and reversal (right) training sessions. (left) Following a variable ITI, a trial initiated after breaking the BIR followed by the presentation of the stimulus (CS+ or CS−) during 10 s. Upon CS+ offset a reward was delivered and a new ITI began once the mouse pulled away from the RM. Upon CS− offset, no reward was delivered, and a new ITI started. Within a single session, CS+ and CS− trials alternated pseudo-randomly. In total, each session ended after 20 CS+ and 20 CS- trials or after 60 min, whichever occurred first. (right) Following 10 acquisition sessions (1 session/day), mice undergo a total of 10 reversal sessions, in which the location of the CS+ and CS- were reversed. c (left) In contrast to the previous, both CS screens (left and right) had 50% of probability to deliver rewards in non-deterministic trials. Contingencies after

CS+ or CS- remained similar as previously described. Within a single session a total of 20 CS+ and CS- trials were presented. (right) After 10 consecutive non-deterministic training sessions, mice followed 10 consecutive deterministic training sessions as described in (b). Figure 1a was created with BioRender.com. Credit: *Nature Communications* (2022). DOI: 10.1038/s41467-022-35601-x

Using strawberry milkshakes, mouse models of disease, cutting-edge fiber optic technology and touchscreens, researchers at Schulich School of Medicine & Dentistry have gained a better understanding of our brain's reward networks. And in doing so, they are paving the way to new treatments for addiction and neuropsychiatric disease, such as schizophrenia, depression and Parkinson's disease.

"Our brains have reward systems: interconnected networks of brain cells that motivate us to seek the rewards that are basic to our survival, such as sex, food, drink, and social interactions," said Miguel Skirzewski, lead author on a new study that recently appeared in *Nature Communications*.

Much of our behavior can be traced back to activities in these networks, said Skirzewski, a research associate at Robarts Research Institute.

"These networks allow us to predict when rewards will happen, so we can design strategies and make decisions," said Skirzewski. "Understanding these networks is essential to understanding how we function in the world."

In a number of disorders, these reward networks are hijacked by addiction to drugs or alcohol, or compromised, as is the case with schizophrenia, depression and Parkinson's disease.

Strawberry milkshakes

Skirzewski and collaborators from Western's Mouse Translational Research Accelerator Platform (MouseTRAP) used a touchscreen-based mouse testing system developed by Robarts scientists Tim Bussey and Lisa Saksida to gather the data.

Mice were trained to use images presented on a touchscreen to predict when a strawberry milkshake reward would be delivered. During the exercise, researchers, using fiber optic methodologies, recorded rapid changes in specific neurochemicals used for communication between brain cells.

Some of the mouse models had deficits in the secretion of acetylcholine—a type of chemical messenger that plays an important role in learning and memory—and failed to perform in this exercise. The researchers discovered that the neurochemicals dopamine and acetylcholine—both implicated in neuropsychiatric disease—rapidly influence each other to support the prediction of a reward.

"In our study, mice learned whether certain cues, such as an image on the screen, helped them to predict rewards," Skirzewski said. "This is a basic phenomenon known as Pavlovian conditioning, which is disrupted in many psychiatric disorders, in which the circuits that underlie reward prediction are thought to be compromised."

Skirzewski said these tests can be easily adapted to humans and provide the insights needed to help understand a number of neuropsychiatric conditions.

"The brain processes information through these networks," he said. "There is interaction between these different networks, which are all constantly talking to each other and affecting behaviors. One brain network does not control only one type of behavior. With this methodology, we can detect how different brain networks interact."

The research has implications for the way drugs are developed for neuropsychiatric disease, an enterprise which has met with limited success. Skirzewski cites treatments for multiple brain diseases.

"In the past, scientists tested treatments in animals, and got a positive result, but not necessarily because they understood how these treatments worked. Most drugs in use were created by trial and error. With this approach, we can now understand mechanisms of disease at the molecular and circuit level," he said.

"By understanding what is happening in the brain from a network perspective, we are now approaching drug development in a different way. It will help make the development of new therapeutic approaches much more efficient."

More information: Miguel Skirzewski et al, Continuous cholinergic-dopaminergic updating in the nucleus accumbens underlies approaches to reward-predicting cues, *Nature Communications* (2022). DOI: 10.1038/s41467-022-35601-x

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