Scientists decode how the brain senses smell

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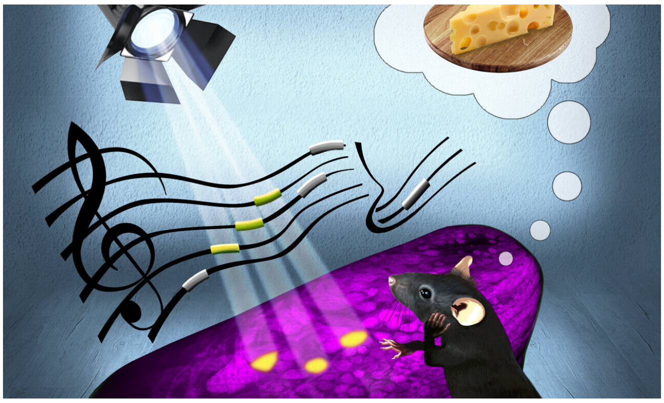

Artistic rendering related to research. Credit: Dancing Lemon Studio

Scientists have further decoded how mammalian brains perceive odors and distinguish one smell from thousands of others.

In experiments in mice, NYU Grossman School of Medicine researchers have for the first time created an electrical signature that is perceived as an odor in the brain's smell-processing center, the olfactory bulb, even though the odor does not exist.

Because the odor-simulating signal was manmade, researchers could manipulate the timing and order of related nerve signaling and identify which changes were most important to the ability of mice to accurately identify the "synthetic smell."

"Decoding how the brain tells apart odors is complicated, in part, because unlike with other senses such as vision, we do not yet know the most important aspects of individual smells," says study lead investigator Edmund Chong, MS, a doctoral student at NYU Langone Health. "In facial recognition, for example, the brain can recognize people based on visual cues, such as the eyes, even without seeing someone's nose and ears," says Chong. "But these distinguishing features, as recorded by the brain, have yet to be found for each smell."

The current study results, published online in the journal *Science* on June 18, center on the olfactory bulb, which is behind the nose in animals and humans. Past studies have shown that airborne molecules linked to scents trigger receptor cells lining the nose to send electric signals to nerve-ending bundles in the bulb called glomeruli, and then to brain cells (neurons).

The timing and order of glomeruli activation is known to be unique to each smell, researchers say, with signals then transmitted to the brain's cortex, which controls how an animal perceives, reacts to, and remembers a smell. But because scents can vary over time and mingle with others, scientists have until now struggled to precisely track a single smell signature across several types of neurons.

For the new study, the researchers designed experiments based on the availability of mice genetically engineered by another lab so that their brain cells could be activated by shining light on them—a technique called optogenetics. Next they trained the mice to recognize a signal generated by light activation of six glomeruli—known to resemble a pattern evoked by an odor—by giving them a water reward only when they perceived the correct "odor" and pushed a lever.

If mice pushed the lever after activation of a different set of glomeruli (simulation of a different odor), they received no water. Using this model, the researchers changed the timing and mix of activated glomeruli, noting how each change impacted a mouse's perception as reflected in a behavior: the accuracy with which it acted on the synthetic odor signal to get the reward.

Specifically, researchers found that changing which of the glomeruli within each odor-defining set were activated first led to as much as a 30 percent drop in the ability of a mouse to correctly sense an odor signal and obtain water. Changes in the last glomeruli in each set came with as little as a 5 percent decrease in accurate odor sensing.

The timing of the glomeruli activations worked together "like the notes in a melody," say the researchers, with delays or interruptions in the early "notes" degrading accuracy. Tight control in their model over when, how many, and which receptors and glomeruli were activated in the mice, enabled the team to sift through many variables and identify which odor features stood out.

"Now that we have a model for breaking down the timing and order of glomeruli activation, we can examine the minimum number and kind of receptors needed by the olfactory bulb to identify a particular smell," says study senior investigator and neurobiologist Dmitry Rinberg, Ph.D.

Rinberg, an associate professor at NYU Langone and its Neuroscience Institute, says the human nose is known to have some 350 different kinds of odor receptors, while mice, whose sense of smell is far more specialized, have more than 1,200.

"Our results identify for the first time a code for how the brain converts sensory information into perception of something, in this case an odor," adds Rinberg. "This puts us closer to answering the longstanding question in our field of how the brain extracts sensory information to evoke behavior."

More information: E. Chong el al., "Manipulating synthetic optogenetic odors reveals the coding logic of olfactory perception," *Science* (2020). science.sciencemag.org/cgi/doi … 1126/science.aba2357

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