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Research reveals first glimpse of brain circuit that helps experience to shape perception

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Odors have a way of connecting us with moments buried deep in our past. Maybe it is a whiff of your grandmother's perfume that transports you back decades. With that single breath, you are suddenly in her living room, listening as the adults banter about politics. The experiences that we accumulate throughout life build expectations that are associated with different scents. These expectations are known to influence how the brain uses and stores sensory information. But researchers have long wondered how the process works in reverse: how do our memories shape the way sensory information is collected?

In work published today in *Nature Neuroscience*, scientists from Cold Spring Harbor Laboratory (CSHL) demonstrate for the first time a way to observe this process in awake animals. The team, led by Assistant Professor Stephen Shea, was able to measure the activity of a group of inhibitory neurons that links the odor-sensing area of the brain with brain areas responsible for thought and cognition. This connection provides feedback so that memories and experiences can alter the way smells are interpreted.

The inhibitory neurons that forge the link are known as granule cells. They are found in the core of the olfactory bulb, the area of the mouse brain responsible for receiving odor information from the nose. Granule cells in the olfactory bulb receive inputs from areas deep within the brain involved in memory formation and cognition. Despite their importance, it has been almost impossible to collect information about how granule cells function. They are extremely small and, in the past,

scientists have only been able to measure their activity in anesthetized animals. But the animal must be awake and conscious in order to for experiences to alter sensory interpretation. Shea worked with lead authors on the study, Brittany Cazakoff, graduate student in CSHL's Watson School of Biological Sciences, and Billy Lau, PhD a postdoctoral fellow. They engineered a system to observe granule cells for the first time in awake animals.

Granule cells receive information from neurons involved in memory and cognition and relay it back to the olfactory bulb. There, the granule cells inhibit the neurons that receive sensory inputs. In this way, "the granule cells provide a way for the brain to 'talk' to the sensory information as it comes in," explains Shea. "You can think of these cells as conduits which allow experiences to shape incoming data."

Why might an animal want to inhibit or block out specific parts of a stimulus, like an odor? Every scent is made up of hundreds of different chemicals, and "granule cells might help animals to emphasize the important components of complex mixtures," says Shea. For example, an animal might have learned through experience to associate a particular scent, such as a predator's urine, with danger. But each encounter with the smell is likely to be different. Maybe it is mixed with the smell of pine on one occasion and seawater on another. Granule cells provide the brain with an opportunity to filter away the less important odors and to focus sensory neurons only on the salient part of the stimulus.

Now that it is possible to measure the activity of granule cells in awake animals, Shea and his team are eager to look at how sensory information changes when the expectations and memories associated with an odor change. "The interplay between a stimulus and our expectations is truly the merger of ourselves with the world. It exciting to see just how the brain mediates that interaction," says Shea.

More information: *Nature Neuroscience* DOI: 10.1038/nn.3669