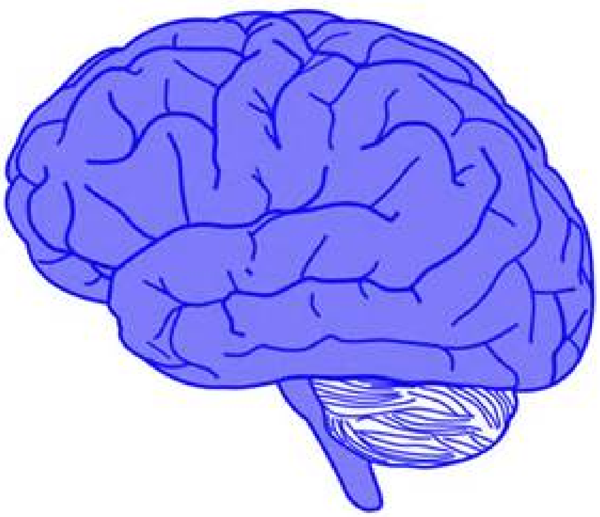
Making sense of the seneses: 'Context' matters when the brain interprets sounds

October 31 2016



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The brain's interpretation of sound is influenced by cues from other senses, explaining more precisely how we interpret what we hear at a particular moment, according to a report published in *Nature Neuroscience* online Oct. 31.

In the new study in mice, researchers at NYU Langone Medical Center found that nerve cells dedicated to hearing also rely on surrounding context to properly interpret and react to familiar sounds.

"What the brain 'hears' depends on what is 'seen' in addition to specific sounds, as the brain calculates how to respond," says study senior investigator and neuroscientist Robert Froemke, PhD, an assistant professor at NYU Langone and its Skirball Institute of Biomolecular Medicine.

Froemke says his team's latest findings reveal that while mammals recognize sounds in the auditory cortex of their brains, the signaling levels of nerve cells in this brain region are simultaneously being strengthened or weakened in response to surrounding context.

"Our study shows how the same sound can mean different things inside the brain depending on the situation," says Froemke. "We know, for instance, that people learn to respond without alarm to the honk of a car horn if heard from the safety of their homes, but are startled to hear the same honk while crossing a busy street."

If further experiments find similar activity in human brains, the researchers say their work may lead to precise explanations of situation-specific behaviors, such as anxiety brought on during math exams; sudden post-traumatic stress among combat veterans hearing a car backfire; and the ability of people with dementia to better remember certain events when they hear a familiar voice or see a friend's face.

To map how the same sense can be perceived differently in the brain, the NYU Langone team, led by postdoctoral fellow Kishore Kuchibhotla, PhD, monitored nerve circuit activity in mice when the animals expected, and did not expect, to get a water reward through a straw-like tube (that they see) after the ringing of a familiar musical note.

When mice were exposed to specific auditory cues, researchers observed patterns based on a basic divide in the nature of nerve cells. Each nerve cell "decides" whether a message travels onward in a nerve pathway. Nerve cells that emit chemicals which tell the next cell in line to amplify a message are excitatory; those that stop messages are inhibitory. Combinations of the two strike a counterbalance critical to the function of the nervous system, with inhibitory cells sculpting "noise" from excitatory cells into the arrangements behind thought and memory.

Furthermore, the processing of incoming sensory information is achieved in part by adjusting signaling levels through each type of nerve cell. Theories hold that the brain may attach more importance to a given signal by turning up or down excitatory signals, or by doing the same with inhibitory nerve cells.

In the current study, researchers found to their surprise that most of the nerve cells in auditory cortex neurons that stimulate brain activity (excitatory) had signaled less (had "weaker" activity) when the mice expected and got a reward. Meanwhile, and to the contrary, a second set of remaining "excitatory" neurons saw greater signaling activity when mice expected a reward based on exposure to the two sensory cues and got one.

Further tests showed that the activation of specific inhibitory neurons—parvalbumin, somatostatin, and vasointestinal peptide—was responsible for these changes and was in turn controlled by the chemical messenger, or neurotransmitter, acetylcholine. Chemically shutting down acetylcholine activity cut in half the number of times mice successfully went after their water reward when prompted by a ring tone. Some studies in humans have linked acetylcholine depletion to higher rates of Alzheimer's disease.

Froemke, who is also a faculty scholar at the Howard Hughes Medical Institute, says the team next plans to assess how the hormones noradrenaline and dopamine affect auditory cortex neurons under different situations.

"If we can sort out the many interactions between these chemicals and brain activity based on sensory perception and context, then we can possibly target specific excitatory and inhibitory neurological pathways to rebalance and influence behaviors," says Froemke.

More information: Parallel processing by cortical inhibition enables context-dependent behavior, *Nature Neuroscience*, DOI: 10.1038/nn.4436

Provided by New York University School of Medicine