Ears ringing? Scientists ID the brain's own clarion

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Brain scientists at Johns Hopkins have discovered how cells in the developing ear make their own noise, long before the ear is able to detect sound around them. The finding, reported in this week's *Nature*, helps to explain how the developing auditory system generates brain activity in the absence of sound. It also may explain why people sometimes experience tinnitus and hear sounds that seem to come from nowhere.

The research team made their discovery while studying the properties of non-nerve cells in the ears of young rats. These so-called support cells were thought to be silent bystanders not directly involved in nerve communication. However, to the researchers' surprise, these cells showed robust electrical activity, similar to nerve cells. Further, this activity occurred spontaneously, without sound or any external stimulus.

"It's long been thought that nerve cells that connect auditory organs to the brain need to experience sound or other nerve activity to find their way to the part of the brain responsible for processing sound," says the study's lead author, Dwight Bergles, Ph.D., an associate professor of neuroscience at Hopkins. "So when we saw that these supporting cells could generate their own electrical activity, we suspected they might somehow be involved in triggering the activity required for proper nerve wiring."

To figure out how these cells were generating electrical pulses, Bergles' team suspected that a chemical might be involved; so they applied a number of different candidate drugs and chemicals to the developing cochlea ¯ the small, hollow and liquid-filled chamber in the inner ear that converts sound waves to electrical signals ¯ hoping to block the mystery trigger. The few drugs that altered the electrical output all disabled ATP (adenosine triphosphate), a chemical most often used as a cell's energy currency but also, as in this case, as a signal to communicate with other cells.

According to Bergles, a breakthrough came when it was discovered that ATP also caused the supporting cells to change their shape. By simply videotaping the developing cochlea, the team was able to monitor where and when ATP was released. After studying these movies, they found that ATP was being released near hair cells, the cells that are responsible for transferring sound information to auditory nerves. It was known that hair cells have receptors for ATP, so they might also be affected by the ATP released from the supporting cells. Indeed, the team found that hair cells also showed spontaneous electrical activity, which occurred at the same time as the responses in neighboring support cells and was blocked by drugs that block ATP receptors.

In a domino-like effect, ATP then signals the hair cells to release another chemical, glutamate, which then activates the nerve cells that project into the brain. "It is as if ATP substitutes for sound when the ear is still immature and physically incapable of detecting sound," says Bergles, adding that "the cells we have been studying seem to be warming up the machinery that will later be used to transmit sound signals to the brain."

"We think that only a few cells release ATP at one time," says Bergles. "And that small amount of free-floating ATP then activates only a few nearby hair cells." This may help associated nerve cells, far away in the depths of the brain, figure out who and where their neighbors are.

Bergles acknowledges that his experiments beg the question of why a human or any animal would need to "hear" before birth. He speculates that the ability to hear subtle differences, like the inflection in one's voice, "requires a lot of fine-tuning based on where in the brain the nerves connect. It could be that brief bursts of electrical activity in just a few nerve cells at a time help do that fine-tuning so the system works well."

While this activity likely is essential for the auditory system's proper development, it could be bad in the adult, mature nervous system as it would trigger electrical signals in the absence of sound. However, as the ear matures during the first two weeks of a rat's life, most of the cells that release ATP disappear so that by the time the rat can hear sound, all the spontaneous electrical activity in its ears has stopped.

Although there is no ATP floating around at that point, the hair cells continue to be able to respond to it, and exposure to loud sounds can trigger ATP release in the ear. Bergles suspects that "if ATP were released by the remaining support cells, it may cause the sensation of sound when there is none," a condition known as tinnitus or ringing in the ears. Alternatively, he notes that bursts of activity might trigger changes in the connectivity of neurons in the brain, just like it does during development, eventually leading to abnormal activity that is perceived as sound.

Source: Johns Hopkins Medical Institutions

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