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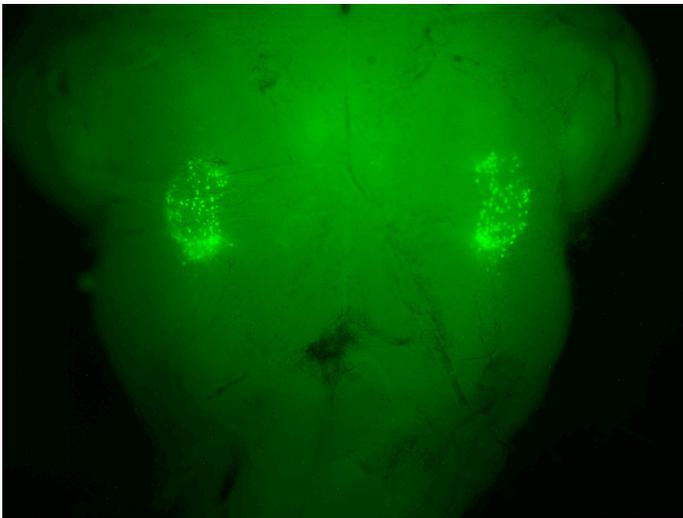
Scientists Pinpoint Brain Chemical Linked to the Sigh

Study finds neurons connected to sighing; breathing pattern thought a vital process that maintains overall health

By KAT LONG

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<http://www.wsj.com/articles/scientists-pinpoint-brain-chemical-linked-to-the-sigh-1454947258>



Shakespeare cautioned ladies to [“sigh no more”](#) over unfaithful lovers. But scientists say that’s easier said than done.

Exploring the biology of the sigh, researchers at the University of California, Los Angeles and Stanford University said they have pinpointed the neural structures that tell the brain when and how to sigh. The researchers said their findings, reported Monday in the journal *Nature*, support the theory that [sighing isn’t just an emotional outlet](#); it’s a vital biological process necessary for maintaining overall health.

Researchers are just starting to grasp why and how we sigh, and what happens when we don’t. In the brain, sighs stimulate neural activity, signal changes in behavior and reset breathing rates. In the respiratory system, sighs clear airways and help the lungs absorb oxygen. Too much or too little sighing can lead to neurological diseases, scientists say.

“A sigh is the ultimate arousal” for the brain, said Nino Ramirez, director of the Center for Integrative Brain Research at the Seattle Children’s Research Institute, who wasn’t involved in the new study. Humans breathe “restorative sighs” about once every five minutes, often without noticing. The double inhalation activates the brain’s cortex, the portion responsible for emotions, speech, recognition, reasoning and other higher functions, Dr. Ramirez said.

In the lungs, tiny air sacs called alveoli absorb oxygen and exchange it with the body’s carbon dioxide, which is eliminated through exhalation. During periods of normal breathing, the alveoli gradually

deflate “like wet balloons,” said Jack Feldman, distinguished professor of neurobiology at the University of California Los Angeles’ David Geffen School of Medicine and co-author on the new paper.

Collapsed alveoli can’t absorb enough oxygen, and regular breaths are too weak to inflate them. Sighs—triggered when the brain senses inadequate oxygen—pop the sacs open again.

In the new research, a team led by Dr. Feldman and Mark Krasnow, a professor of biochemistry at the Stanford University School of Medicine, screened more than 19,000 gene expressions in rats’ brain cells. They identified two bundles of neurons that produced two particular neuropeptides, chemicals that let brain cells talk to one another, that they thought could be associated with sighing.

To test the theory, the team injected the neuropeptides into another group of neurons in the rats’ brains called the Pre-Bötzinger complex, which sets the breathing rate and determines the types of breaths. Right away, the rats’ normal sighing rate switched into overdrive, jumping from about 40 to 400 times per hour. When the researchers removed the neuropeptides, the rats stopped sighing altogether.

“It was immediate and dramatic,” Dr. Krasnow said, adding that the experiment didn’t change the rats’ normal breathing.

Many neurological conditions, such as anxiety, sleep apnea and sudden infant death syndrome, are linked to improper breathing. For example, people with panic disorders may sigh too much, overstimulating the brain’s cortex and leading to problems like insomnia.

“There are a number of syndromes characterized by excess sighing. Now that we know which neurons are linked to sighing, and which neuropeptides trigger them, we can reduce the number and the rate of sighs,” Dr. Krasnow said.

In the future, Dr. Krasnow said, drugs that increase sighing could be developed for hospital patients who would otherwise need to go on ventilators to breathe. The finding could also mean that other neurons within the brain’s breathing circuitry may control yawning, coughing, laughing or gasping.

“The paper shows one pathway,” said Dr. Ramirez, “but I think there will be more. Knowing the pathways will help us unravel the sigh.”