Function of protein that helps control breathing explored

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(Medical Xpress)—A team made up of members from several research institutions in the U.S. has found evidence of a protein exerting some

control over the breathing process in mice. In their paper published in the journal *Nature*, the team describes their multi-pronged study of the protein Piezo2 and the part it plays in regulating breathing. Christo Goridis with Institut de Biologie de l'Ecole normale supérieure in France offers a News & Views piece on the work done by the team in the same journal issue outlining what the team was looking for, how they went about their experiments and what they found.

As Goridis notes, prior research has shown that many animals including humans have what is known as the Hering–Breuer reflex. It is the automatic mechanism that stops the intake of breath when the lungs have filled, preventing them from overfilling, which would cause damage. But to date, little is known about the mechanisms involved in the process. To learn more, the team began by looking at vagal sensory neurons in mouse airways, which prior research has shown play a role in conducting breathing—they convey information regarding lung conditions to the brain. Prior research has also shown that the protein Piezo2 was also involved in the process, though it was not clear how. In this new effort, the researchers sought to learn more about where in the pulmonary system the protein was expressed, and what their role was.

The team examined all of the parts involved in breathing in mice—doing so showed that Piezo2 was expressed in the nodose ganglion and the jugular ganglion, some spinal sensory neurons, and perhaps most importantly, in lung tissue. To find out what the purpose of the protein was in the different regions, the team disabled the relevant genes responsible for expressing the protein. They found that a lack of Piezo2 in jugular and dorsal-root neurons caused newborns to die of respiratory distress. Turning off production of the protein in just the nodose neurons allowed the mice to grow to adulthood but prevented the activation of the Hering–Breuer reflex—the mice also took in abnormal amounts of air during normal breathing. The researchers also engineered some of the nerves involved to respond to light, allowing activation and deactivation

of the expression of Piezo2 on demand. Doing so allowed the researchers to cause an incidence of Hering–Breuer reflex just by turning on a light.

The researchers sum up their findings by suggesting that Piezo2 is clearly an essential part of the breathing process, though they note that much more work needs to be done to gain a clearer understanding of how the entire breathing process works.

More information: Piezo2 senses airway stretch and mediates lung inflation-induced apnoea, *Nature*, nature.com/articles/doi:10.1038/nature20793

Respiratory dysfunction is a notorious cause of perinatal mortality in infants and sleep apnoea in adults, but the mechanisms of respiratory control are not clearly understood. Mechanical signals transduced by airway-innervating sensory neurons control respiration; however, the physiological significance and molecular mechanisms of these signals remain obscured. Here we show that global and sensory neuron-specific ablation of the mechanically activated ion channel Piezo2 causes respiratory distress and death in newborn mice. Optogenetic activation of Piezo2+ vagal sensory neurons causes apnoea in adult mice. Moreover, induced ablation of Piezo2 in sensory neurons of adult mice causes decreased neuronal responses to lung inflation, an impaired Hering–Breuer mechanoreflex, and increased tidal volume under normal conditions. These phenotypes are reproduced in mice lacking Piezo2 in the nodose ganglion. Our data suggest that Piezo2 is an airway stretch sensor and that Piezo2-mediated mechanotransduction within various airway-innervating sensory neurons is critical for establishing efficient respiration at birth and maintaining normal breathing in adults.

Press release