

Scientists discover how cells responsible for wakefulness turn on and off

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Scientists may have discovered an underlying reason why individuals who suffer from sleep apnea, the disorder characterised by pauses in respiration during sleep, wake suddenly once they stop breathing.

Waking up when breathing stops during sleep and feeling faint during hyperventilation are common experiences. In an attempt to understand their neural basis, research led by scientists at the University of Cambridge focused on "orexin neurons", brain cells recently found to be vital for normal wakefulness and breathing. The new experiments reveal that changes in brain acidity, which are tightly linked to breathing, can excite or silence these "wakefulness" cells.

Inside the brain, much of communication is electrical, and involves neurons "firing" signals that travel along biological "wires" (axons) to other neurons. In the case of orexin neurons, the signals they generate are so important for steady consciousness that without them humans and animals become narcoleptic, suffering irresistible attacks of sleep and unconsciousness.

The Cambridge and Oxford researchers found that rising levels of acid, such as those that occur during sleep apnea, released an electrical "brake" in orexin neurons. This allowed the neurons to fire faster. The brake consists of potassium pores in orexin cell membrane - when open, they stop neurons from firing. Rising acidity shuts down these pores, making orexin neurons fire very fast, while falling acidity opened the pores, silencing the firing.

In the body, rises and falls in acidity are controlled by breathing. Acid is constantly made by the body's metabolism, but is normally prevented from building up because we breathe out "acidic" carbon dioxide. However, during sleep apnea the breathing stops, leading to a dangerous build up of acid in the brain. Acceleration of orexin cell by acid

would dissipate this threat by causing awakening and increased breathing.

Denis Burdakov of the University of Cambridge, who led the study, said: "Orexin neurons are among the most exciting discoveries in neuroscience since their activity has such striking effects on wakefulness and consciousness. We are thrilled to discover how this activity can be controlled".

One of the barriers to studying orexin cells is that they are sparse and few in number. To overcome this, the scientists used genetic engineering to make orexin cells fluorescent and so easier to see.

Lars Fugger at Oxford, who carried out these genetic manipulations, said: "Our findings are important for understanding sleep disorders such as sleep apnea and narcolepsy. It is our aim to translate this research into a clinical setting that will benefit the patients afflicted by these diseases".

The paper "Control of hypothalamic orexin neurons by acid and CO₂," is scheduled for publication in this week's edition of the *Proceedings of the National Academy of Sciences* (PNAS).

Source: University of Cambridge

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