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Nighttime dying linked to sleep apnea from brain cell loss

UCLA study scrutinizes loss of cells in brain's breathing command-post

Aim to grow old and die peacefully in your sleep? Be careful what you wish for. A new UCLA study suggests that some people die in their sleep because they stop breathing due to a cumulative loss of cells in the brain's breathing command-post. The online edition of Nature Neuroscience reports the findings on Aug. 7.

"We wanted to reveal the mechanism behind central sleep apnea, which most commonly affects people after age 65," explained Jack Feldman, principal investigator and Distinguished Professor of Neurobiology at the David Geffen School of Medicine at UCLA. "Unlike obstructive sleep apnea – in which a person stops breathing when their airway collapses -- central sleep apnea is triggered by something going awry in the brain's breathing center."

Feldman's team had earlier pinpointed a brainstem region they dubbed the preBötzinger complex (preBötC) as the command post for generating breathing in mammals, and identified a small group of preBötC neurons responsible for issuing the commands. This time, the researchers studied the role of the preBötC neurons in generating breathing during sleep, and what would happen if these brain cells were destroyed.

The scientists injected adult rats with a cell-specific compound to target and kill more than half of the specialized preBötC neurons. Then the team monitored the rats' breathing patterns. After four or five days, the results proved visibly dramatic.

"We were surprised to see that breathing completely stopped when the rat entered REM sleep, forcing the rat to wake up in order to start breathing again," said Leanne McKay, postdoctoral fellow in neurobiology. "Over time, the breathing lapses increased in

severity, spreading into non-REM sleep and eventually occurring when the rats were awake, as well."

Because mammals' brains are organized in a similar fashion, the scientists believe that the rat findings are relevant to the human brain. Rats possess 600 specialized preBötC cells, and Feldman theorizes that humans have a few thousand, which are slowly lost over a lifetime.

"Our research suggests that the preBötzinger complex contains a fixed number of neurons that we lose as we age," said Feldman. "Essentially, we sped up these cells' aging process in the rats over several days instead of a lifetime."

Long before the rats had difficulty breathing when awake, they developed a breathing problem during sleep. The UCLA team suspects the same thing happens as people grow older.

"We speculate that our brains can compensate for up to a 60 percent loss of preBötC cells, but the cumulative deficit of these brain cells eventually disrupts our breathing during sleep. There's no biological reason for the body to maintain these cells beyond the average lifespan, and so they do not replenish as we age," said Feldman. "As we lose them, we grow more prone to central sleep apnea."

When elderly but otherwise healthy people die during sleep, physicians commonly record the cause of death as heart failure. The UCLA team believes that the loss of preBötC neurons sparks central sleep apnea, causing elderly people whose lungs and heart are already weaker due to age, to stop breathing and succumb to death in their sleep. Their true cause of death remains unknown.

The scientists suspect central sleep apnea also strikes people suffering the late stages of neurodegenerative disorders, such as Parkinson's disease, Lou Gehrig's disease and multiple system atrophy, all serious conditions that lead to movement problems.

"People with these diseases breathe normally when they are awake, but many of them have breathing difficulties during sleep," said Wiktor Janczewski, assistant researcher in neurobiology. "When central sleep apnea strikes, they are already very ill and their sleep-disordered breathing may go unnoticed.

"As the patients grow sicker, their nighttime threshold for wakefulness rises," he added. "Eventually, their bodies reach a point when they are unable to rouse themselves from sleep when they stop breathing, and they die from lack of oxygen."

The UCLA team will repeat their research with elderly rats in order to learn why central sleep apnea first strikes during REM sleep. The group also plans to analyze the brains of people who die from neurodegenerative diseases to determine whether these patients show damage in their preBötzinger complexes.

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