Engineered mice show jet lag could become a thing of the past

Anyone who has taken a long plane ride knows all too well how jet lag can adversely affect us. But a new discovery could soon make jet lag a thing of the past and cure the sleepless nights that come from traveling long distances.

In August, a team from the University of Oxford discovered that a genetic mechanism is partly responsible for regulating our sleep cycles, giving hope that scientists would one day be able to turn off this gene and prevent jet lag. Last week, a team of researchers from Kyoto University in Japan followed up that discovery by engineering mice that are immune to jet lag. According to an article posted on *National Geographic*'s Phenomena Blog, this success could help suppress the proteins that cause jet lag and one day cure jet lag entirely.

The Kyoto researchers, who published their results in early October, put mice in cages with lights designed to mimic day and night. They then altered these lights to mimic an 8-hour time difference–roughly the length of a flight from San Francisco to London. The engineered mice were able to readjust almost immediately, suggesting that hormones could prevent jet lag, which comes from a disruption of our body's natural rhythm.

The body runs on an internal clock based on the 24 hours in a day. This clock helps regulate not just our sleep schedules, but also our metabolism, blood pressure, hunger and body temperature. The proteins that control this clock are produced in greater quantities at certain parts of the day and then fall when they aren't needed, creating the circadian rhythm. These proteins are regulated by the suprachiasmatic nucleus (SCN), a collection of 10,000 neurons at the base of the brain.

The SCN is very sensitive to light, which helps it know when to produce certain proteins and stop producing others. Based on signals attained from our eyes, the SCN allows us to feel more awake during the day and tired enough for sleep at night.

When we take a long plane ride, we confuse the CSN, since it has regulated the proteins in our body based on one schedule while we demand it adjusts to a new one. Typically, it takes the CSN one day to adjust for every time zone we cross. Until it readjusts, we suffer from jet lag, which alters our sleeping habits and other basic functions.

The Kyoto team discovered that about half of the neurons in the SCN secrete a hormone, arginine vasopressin (AVP), and also detect it using receptor proteins. The researchers were able to deliver chemicals to mice that blocked these receptors and minimize the effects of disrupting the mice's circadian rhythms.

The researchers also discovered, however, that curing jet lag isn't as simple as delivering chemicals that would block the AVP receptors. Since drugs are unable to be delivered directly to the brain, the chemicals that would block AVP receptors in the brain would also do so across the entire body. Because these receptors are found in other vital organs, such as the kidneys, this solution would create more problems

than it solved.

The team thinks that a cure for jet lag lies somewhere in the way that the neurons in the SCN connect with one another. The neurons that produce and detect AVP synchronize with one another on a tight schedule. While delivering chemicals disrupts this synchronization, the process resumes after the chemicals wear off. The mice engineered by the Kyoto team showed a looser connection of these SCN neurons, which allowed them to adjust so quickly to disruptions in their natural rhythms.

But finding a way to prevent the effects of jet lag is not simply to spare travelers an annoyance. Finding a way to cure or combat circadian rhythm disruption could be particularly useful for shift-workers and other people who have inconsistent schedules. Studies have found that shift-working can lead to higher risks of high blood pressure, diabetes, heart disease and even some cancers.

Additionally, an article published in *Wired* a few years ago reported that jet lag can also have a serious impact on the ability to learn and retain memories. The article reported the results of another experiment using mice in which researchers at the University of California, Berkeley found that jet lagged mice produced about half the neurons in the hippocampus compared to regular mice, which lessened their ability to learn or remember. The mice in the study even showed inhibited learning ability after four weeks of a schedule that returned their circadian rhythms to normal.

While scientists are still years away from discovering a cure for jet lag, the recent research on the subject has helped provide a solid understanding of the genetic mechanisms that regulate our circadian rhythms. This understanding will help give scientists targets to develop drugs to battle the effects of this disorder and will likely one day make jet leg a thing of the past.

“A small interfering RNA is a neat molecular way of being able to turn off one gene within cells,” said Dr. Stuart Peirson, the study team leader and a senior research scientist at Oxford’s Nuffield Department of Clinical Neurosciences, in an article in *The Independent*. “There’s no reason you couldn’t develop specific drugs to inhibit this particular mechanism, so it should be possible in the future to develop drugs that allow us to adjust more quickly and help alleviate jet lag.”

Additional Resources:

- “Meet The Mice That Are Immune To Jet lag,” National Geographic
- “Jet lag disorder,” Mayo Clinic
- “Mother’s Genes May Be Key in Jet Lag,” ABC News