

Brain cortex may regulate the need for sleep

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Researchers at the University of Oxford have now uncovered a new target for sleep investigations within the mammalian brain—the cerebral cortex. The paper was published today in *Nature Neuroscience*.

The cerebral cortex makes up about 80% of the brain's volume and is responsible for many complex phenomena, including perception, thought, language, attention and memory. While activity in the cortex is



normally used in <u>sleep studies</u> to record sleep/awake patterns, the latest study from Oxford has found that processes within the cortex itself may actually be responsible for sleep control, such as how long to sleep for and how deeply to sleep.

The study monitored <u>brain activity</u> in <u>laboratory mice</u>, which have fundamental brain similarities to humans in terms of anatomy and sleep mechanisms. Neurons in two areas of the cortex—neocortical layer 5 and a part of the hippocampus—were 'silenced' in the mice's brains. When the neurons in these areas of the brain were deactivated, the lab mice suddenly stayed awake for at least three hours longer every day. To put this into perspective, an average mouse lives for approximately two years, which means they gained three full months of 'awake' time in over their lifespans. In human terms, this would equate to about 10 years.

Though the mice were awake longer, their need for <u>deep sleep</u> did not appear to be affected. Normally, when mice (and humans) stay awake longer than usual and get more tired, we sleep more deeply to compensate. This study in lab mice found that they did not sleep any more deeply than usual. Their body clock did not appear to be affected at all by the extra waking hours in their days.

Dr. Lukas Krone of the Department of Physiology, Anatomy and Genetics, University of Oxford, and lead author on the study, said, "Our finding that the cortex is part of the sleep-regulating system opens new perspectives for sleep medicine. It might be possible to use alreadyestablished non-invasive <u>brain</u> stimulation techniques to alter cortical activity and thereby moderate sleep for therapeutic purpose, such as for the treatment of sleep disorders."

Professor Vladyslav Vyazovskiy, Head of Sleep, Brain and Behaviour Laboratory in the Department of Physiology, Anatomy and Genetics and a member of Sleep and Circadian Neuroscience Institute (SCNi), a co-



corresponding author on the paper, said, "The cortex is a highly <u>complex</u> <u>structure</u>, both anatomically and functionally, and is therefore difficult to study; and this is why we think its role in sleep control was previously overlooked. The effects on sleep of cortical silencing offers a novel and fresh perspective on the mechanisms of sleep control, and has the strong potential to transform the field of sleep neurobiology."

Professor Zoltán Molnár, Head of Cerebral Cortical Development and Evolution Laboratory in the Department of Physiology, Anatomy and Genetics and co-corresponding author on the paper said, "Much effort and funding over the last decades has been spent on clarifying the role of subcortical structures in sleep regulation and the <u>cerebral cortex</u> was not the focus of attention. When we first performed our 'silencing' study on different cortical projection neurons, I expected such phenotype from another neuronal population and not from layer 5 and hippocampus. For me, the discovery of its effect on the mice's sleep was a great surprise."

While this study is an important first step, more work needs to be done. "We hope that many other research groups will now be investigating how exactly the cortex contributes to sleep regulations," said Dr. Krone. "A <u>multidisciplinary approach</u> will help us to fully understand the cellular mechanisms and neuronal circuits through which the <u>cortex</u> regulates sleep."

More information: Lukas B. Krone et al, A role for the cortex in sleep–wake regulation, *Nature Neuroscience* (2021). <u>DOI:</u> <u>10.1038/s41593-021-00894-6</u>

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