INSELGRUPPE

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How skin temperature triggers either dreaming or muscle paralysis

For the first time, researchers at the University of Bern and Inselspital, Bern University Hospital, have shown that temperature signals from the skin are processed in the brain, influencing REM sleep and sleep-related disorders. These new findings enhance our understanding of brain-body interactions that regulate sleep and provide novel therapeutic strategies for sleep-wake rhythm disorders, such as narcolepsy.

Sleep is an essential component of our physical and mental health. The regulation of sleep is complex and influenced by numerous factors. Particularly REM sleep – the phase during which we experience intense dreaming – is closely linked to the regulation of body functions such as muscle tension and temperature. Previous studies have shown that warm thermoneutral temperatures increase REM sleep involving specific brain cells. However, the process by which temperature information is transmitted from the skin to the brain remained unclear. These mechanisms have now been investigated in more detail by examining the rare sleeping disorder narcolepsy. This chronic, incurable neurological disorder is characterized by pronounced sleepiness and sudden sleep attacks. Another characteristic symptom of narcolepsy is cataplexy, which involves brief episodes of muscle paralysis while awake and can be triggered by strong emotions, such as laughter. Narcolepsy significantly impairs everyday lives of those affected and may lead to social withdrawal, particularly due to cataplexy. Currently, only a few drug therapies are available to treat the symptoms of this disorder.

A new study led by researchers from the Department for BioMedical Research (DBMR) at the University of Bern, and the Experimental Neurology Center (ZEN) at the Department of Neurology at Inselspital, Bern University Hospital, provides evidence for the first time that skin temperature plays a central role in controlling brain states. In collaboration with the University of Lyon, the team demonstrated that the brain possesses neuronal systems that respond to skin temperature. In narcolepsy, these systems act as a switch, determining whether the brain enters the sleep state (REM sleep) or triggers muscle paralysis while the person is awake. The results were recently published in the journal *Science Translational Medicine*.

Unique translational approach

To investigate the effects of skin temperature on brain states in narcolepsy, the researchers conducted both animal and human studies. Using innovative methods, they were able to specifically change the skin temperature on the extremities, tail and ears of narcoleptic mice and thus analyze precisely how temperature changes influence sleep phases. Thanks to the collaboration with the neuroanatomy research group from Lyon, the researchers were able to incorporate a new technique to

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identify the underlying neuronal signaling pathways in the brain. "The study combines clinical sleep medicine in patients with experimental basic research in animals – a translational approach implemented by only a few centers worldwide," says Markus Schmidt, last author of the study and Head of Sleep Medicine at the Sleep-Wake-Epilepsy Center (SWEC) at Inselspital, Bern University Hospital and research group leader at the Department for BioMedical Research at the University of Bern. The expertise available at the Experimental Neurology Center (ZEN) and the University Sleep-Wake-Epilepsy Center were crucial for conducting the study. The latter was recognized in 2024 by Kosek, the coordination office for rare diseases, as a reference center for rare sleep disorders.

When subtle temperature differences make the difference

This study is the first to show that skin temperature specifically controls brain states such as REM sleep and cataplexy. The researchers found that a drop in skin temperature increases the likelihood of cataplexy both in narcoleptic patients and narcoleptic mice. Further, they could demonstrate in mice that manipulating skin temperature has a direct impact on the expression of cataplexy and REM sleep. Antoine Adamantidis, co-author of the study and Professor of Neurophysiology and Director of ZEN at Inselspital, Bern University Hospital, explains: “We assumed that warming the skin would increase both REM sleep and cataplexy, given that muscle paralysis occurs in both cases.” However, the study showed that increasing skin temperature enhances REM sleep while it suppresses cataplexy. He adds: “The fact that skin temperature controls these two similar muscle states in opposite ways came as a surprise.”

The researchers identified special nerve cells (MCH neurons) in the hypothalamus that react to skin temperature and help to control whether the brain switches to a state of REM sleep or cataplexy. Schmidt adds: “It is well known that the body influences the brain. But it is astonishing that even slight changes in skin temperature can trigger either REM sleep or cataplexy."

Prospects for people with narcolepsy

The new findings are relevant not only for basic research, but also for improving the long-term treatment of people with narcolepsy. “Our findings demonstrate the close communication between the brain and body and open up new possibilities for reducing symptoms such as cataplexy using non-medicinal, everyday approaches,” says Professor of Neurology Claudio Bassetti, co-author of the study, Dean of the Faculty of Medicine at the University of Bern, and Director of Teaching and Research at Insel Gruppe AG. The researchers now intend to examine whether and how targeted changes in skin temperature can promote REM sleep and reduce cataplexy attacks in patients.

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Experimental Neurology Center (ZEN)

The Experimental Neurology Center in the Department of Neurology at the Inselspital, Bern University Hospital is one of the leading institutions in translational research, combining clinical sleep medicine and animal sleep research. This special infrastructure enables groundbreaking studies to optimize patient care. The close integration of basic research and clinical practice results in innovative therapies that directly benefit patients and set international standards in sleep medicine.

Further information: https://neurologie.insel.ch/de/lehre-und-forschung/forschung/research-resources/standard-titel

Department for BioMedical Research (DBMR)

The Department for BioMedical Research (DBMR) of the Faculty of Medicine of the University of Bern was founded in 1994 by the University of Bern and the Inselspital, Bern University Hospital. The DBMR is divided into 13 research programmes with around 100 participating individual laboratories and several independent research laboratories whose research spans all biomedical areas. To bridge the gap between the laboratory and the bedside, the DBMR promotes clinical research with a strong emphasis on the development of translational approaches, the use of "omics" and other cutting-edge technologies, and extensive collaboration between laboratory-based and patient-centred clinical research. The DBMR is also committed to the promotion of young scientists.

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