| Press Release

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International Institute for Integrative Sleep Medicine, University of Tsukuba

Quality of prior waking experience is shown to greatly influence sleepiness

Research Results: Key Findings

1. In general, a simple positive correlation between sleep need and level of arousal (or more simply, sleepiness *1) has been thought to exist, with sleep need as well as sleepiness increasing the longer we are awake. However, a detailed experimental study about this relationship has not yet been conducted.
2. It has been found that sleepiness and sleep need can be regulated independently (or rather, dissociated from one another).
3. In addition, through a phospho-proteomic approach (*2), separate CNS (central nervous system) biochemical signatures associated with these behavioral parameters were identified.

Dr. Masashi Yanagisawa, Director of the International Institute for Integrative Sleep Medicine, and his research group conducted experiments on mice using two different methods of 6-hour sleep deprivation, in which a dissociation of sleep need (ease of falling into a deep sleep) and level of arousal, or sleepiness, (ease of falling asleep) are observed. Sleepiness has been proven to vary depending on various experiences during waking. In addition, through a phosphor-proteomic approach, the research team has succeeded in identifying separate CNS biochemical signatures associated with sleep need and sleepiness.

These findings indicate that the quality of prior wakeful experience greatly influences sleepiness, even under conditions where levels of sleep need are the same. It is therefore surprising that such an obvious phenomenon seen in daily life has never been precisely and systematically studied at behavioral and biochemical levels in experimental animals until now. This paper proceeds to provide important insights into the way sleepiness is regulated, a fundamental question with general interest in neuroscience.

In collaboration with the University of Texas Southwestern Medical Center's Ayako Suzuki, Christopher M. Sinton, and Robert W. Greene (also a principal investigator at IIIS), this research was published in the Proceedings of the National Academy of Sciences in the United States of America (PNAS) on June 18, 2013.

Research Background

Sleep-wakefulness is precisely regulated according to the physiological needs of the individual by the sleep history of the recent past through a “homeostatic control mechanism”. In addition, it is also regulated by the body’s internal biological clock “Circadian mechanism”, along with environmentally influenced waking experiences. In general, the longer the waking hours last, the shorter the time is takes to fall asleep, and easier it is to fall asleep (as sleep need is high). However, the details of how sleepiness and sleep need effect the quality of the wakeful experience remain a mystery.

Summary of Resesarch Findings

In this study, it was thought that feelings of sleepiness reflected in the electroencephalography (EEG) patterns would differ even in mice that have similar sleep requirements. To investigate this hypothesis, the authors deprived mice of sleep for 6 hours either by gentle handling (*3) or cage changes. While the mice experienced similar degrees of sleep loss (Figure B) and exhibited similar EEG patterns, with low-frequency non-REM brain waves (*4), during 2 hours of uninterrupted recovery sleep, the authors found that mice woken by cage changes seemed less sleepy (Figure A) and took significantly longer than other mice to fall asleep. A proteomic screen uncovered two putative markers of arousal and sleep requirements – a presynaptic neuronal protein called dynamin 1 and a glial protein (*5) known as N-myc downstream regulated gene 2, respectively – that are phosphorylated differently according to the mouse’s sleepiness (sleep latency *6) and sleep needs, the authors report. According to the research team, the findings suggest that the quality of our prior waking experiences may significantly influence how awake we feel and how long it takes to fall asleep, a finding that could have implications for sleep disorders such as insomnia.

Future Developments

Despite sleep being a very familiar phenomenon, the regulatory mechanisms are still shrouded in mystery. In the future, along with pursuing a detailed analysis of the biochemical markers identified in this study, the kind of effects that the quality of prior wakeful experiences have on functions of sleep, such as memory fixation, etc. for example, will be investigated.

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Reference Figures

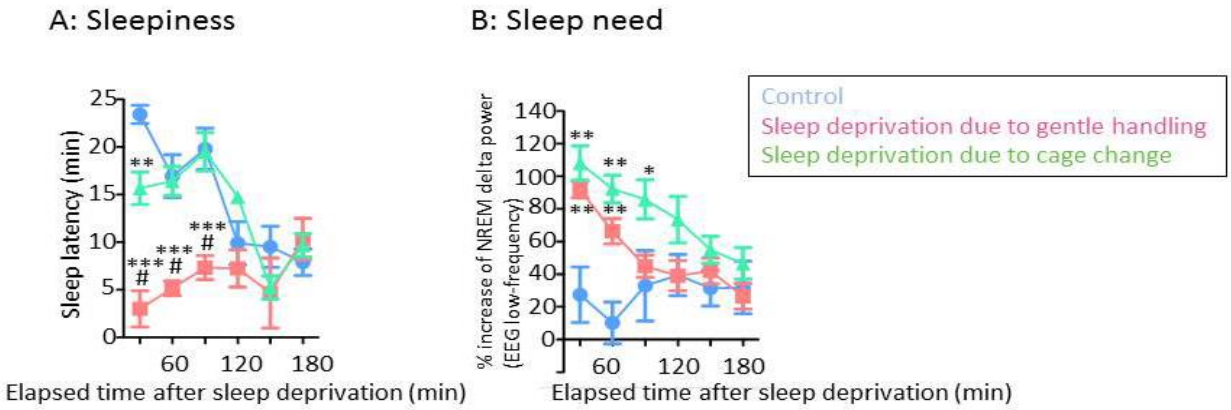

Figure) Mice were deprived of sleep for 6 hours by 1) gentle handing or 2) cage changes. Afterwards, the time taken to fall asleep (sleep latency) and the increases in the EEG low frequency component were measured. (30-min cycle was repeated six times)

Glossary of Terms

＊1 Sleep need and sleepiness

Sleep need is not necessarily subjective, as it depends on the level of sleep required by the brain. The level of sleep need can be guessed from the amount of the EEG component of non-REM sleep. Sleepiness is the level of how sleepy you consciously feel. The degree of sleepiness is measured in the time it takes to fall asleep (sleep latency).

＊2 Phospho-proteomic approach

Protein phosphorylation is particularly important in the post-translational modification of proteins. Through the proteomic analysis, it is possible to obtain the information about the changes in the phosphorylation level of proteins by the degree of sleepiness and sleep need.

＊3 Gentle handling

Deprivation of sleep by gently touching the cages when the mice started to recline and lower their heads.

＊4 EEG low-frequency component of non-REM sleep (EEG delta power expressed during sleep)

The strength of the low-frequency component of the EEG is characteristic of non-REM sleep. It is the most reliable indicator of sleep need at that time.

＊5 Glial cell

The sustaining cells that do not constitute the nerve cells (neurons) of the nervous system. It has recently been revealed that they are also involved in the regulation of neuronal activity.

＊6 Sleep latency

It is a direct indicator of the strength of “sleepiness”. Through using of the multiple sleep latency test (MSLT), measurements of how long it takes to fall asleep are made.

Article Citation

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