

Clock gene dysregulation may explain overactive bladder

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If you think sleep problems and bladder problems are a fact of life in old age, you may be right. A new report appearing in the November 2014 issue of *The FASEB Journal*, shows that our sleep-wake cycles are genetically connected to our bladder, and disruptions to one may cause problems with the other. This discovery builds on the hypotheses that under normal circumstances, a primary clock located in the brain controls several other peripheral clocks located throughout the body. These peripheral clocks, in turn, control the activity of functional proteins and receptors, including those in the bladder.

"We hope our study will stimulate further progress in understanding circadian control of body physiology and aging-related dysfunction and ultimately lead to new strategies of treatment by targeting the circadian regulatory process, including non-drug treatment approaches," said Changhao Wu, M.D., Ph.D., a researcher involved in the work from the Department of Biochemistry and Physiology at the University of Surrey in the United Kingdom.

To make this discovery, scientists used genetically modified mice in which a special wavelength of light was emitted when the clock proteins were produced in isolated [bladder](#) tissue. This light reported real-time clock expression and acted directly as a measure of peripheral clock expression. Over 24 hours, changes in clock expression were recorded in the presence and absence of the receptor activators. Rhythmic clock activities occurred in the bladder wall with a cycle around 24 hours and peaked at about hour 12. Application of these receptor activators shifted

the peak of the clock expression to an earlier time. In older mice, the clock expression and its response to the activators were significantly dampened. Bladder contractions also exhibited circadian rhythms, similar to changes of the clock expression. The contractile function in the bladder can be regulated by the local circadian clocks, which are in turn under the feedback control of the output receptors. This reciprocal control of clock function represents an important mechanism for maintaining physiological function in the peripheral hollow organs and its dysregulation may contribute to abnormal motility in age-related disorders such as [overactive bladder](#).

"It's hard to appreciate how much of a problem an overactive bladder can be," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*. "It disrupts many aspects of life, from the obvious, like sleep and travel, to the less obvious, like exercise and entertainment. This study helps us understand what's causing the problem, and points the way to a solution."

More information: Changhao Wu, Guiping Sui, Simon N. Archer, Paolo Sassone-Corsi, Karen Aitken, Darius Bagli, and Ying Chen. Local receptors as novel regulators for peripheral clock expression. *FASEB J.* November 2014 28:4610-4616; [DOI: 10.1096/fj.13-243295](https://doi.org/10.1096/fj.13-243295)

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