Alteration of gene may disrupt our bodies internal rhythm, causing sleep disorder

May 16 2012, By Frances Dumenci

(Medical Xpress) -- Researchers at Virginia Commonwealth University have found that a gene known as RAI1 controls one of the most important genes in circadian rhythm, CLOCK.

Earlier studies identified that mutation or deletion of the RAI1 gene results in Smith-Magenis Syndrome, a complex disorder characterized by obesity, sleep disturbances, negative behaviors and developmental delays.

“How this disruption of RAI1 causes Smith-Magenis Syndrome is not fully understood,” said Sarah H. Elsea, Ph.D., associate professor in the VCU Departments of Pediatrics and Human and Molecular Genetics in the VCU School of Medicine. “One of the hallmarks of Smith-Magenis Syndrome is severe sleep disturbance, and through our current work, we have found that alteration of the expression or function of RAI1 disrupts the expression of other molecular clock genes, dysregulating circadian rhythm.”

Circadian rhythms are physical, mental and behavioral changes that follow a roughly 24-hour cycle, responding primarily to light and darkness in the environment. In this current study, Elsea, graduate student Stephen Williams, Ph.D., and the research team have identified a novel and important function of RAI1 in circadian rhythm.

While this is the first study to identify a key regulator of CLOCK that is also associated with a neurodevelopmental genetic syndrome, it also

highlights the importance of circadian biology in neurodevelopment and behavior.

“The data reported in this study lay the foundation to support Smith-Magenis Syndrome as a primary circadian rhythm disorder, wherein sleep, metabolism and behavior are all intertwined and tightly connected to the circadian rhythm of the individual,” said Elsea. “Better understanding of the function of RAI1 leads to better understanding of the molecular underpinnings of the syndrome, which can then lead to appropriate, targeted therapy.”

The results of the current study were published online May 10 and will appear in the June print issue of The American Journal of Human Genetics.

According to Elsea, the identification of RAI1 as a primary regulator of circadian rhythm is key not only for individuals with Smith-Magenis Syndrome, but also for the general population that is affected with sleep disorder.

“Sleep problems affect millions of people around the world, and these issues can impact many aspects of one’s life, including body weight, metabolism, productivity and emotional state,” said Elsea. “Understanding fully how circadian rhythm functions is of great importance to all of us. Our work adds another piece to the puzzle of circadian rhythm and may one day help to alleviate the sleep issues of individuals with Smith-Magenis Syndrome.”

Provided by Virginia Commonwealth University

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