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Lack of fragile X and related gene fractures sleep

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Lack of both the fragile X syndrome gene and one that is related could account for sleep problems associated with the disorder, which is the common cause of inherited mental impairment, said a consortium of researchers led by scientists at Baylor College of Medicine in Houston. Their findings appear in a report in the current issue of the *American Journal of Human Genetics*.

Mice deficient in the fragile X mental retardation 1 gene (FMR1) and a similar gene called fragile X-related gene 2 (FXR2) have no rhythm to their wake and sleep pattern, said Dr. David Nelson, professor of molecular and human genetics at BCM and co-director of the Interdepartmental Program in Cell and Molecular Biology.

Normal mice have a sleep-wake cycle of just under 12 hours awake and 12 hours asleep. Exposed to light and dark, they are awake in the dark and asleep during the light because they are nocturnal animals. If they are kept in the dark, their cycle reduces by about 10 minutes per sleep-wake period but remains fairly normal. When mice do not have either FMR1 or FXR2, they have a slightly shorter cycle but the difference is not dramatic.

"However, the double-mutants (those without both genes) have no rhythm at all," said Nelson. "This has never been seen in a mouse before." The animals, usually kept in a cage with a wheel on which they run when awake, sleep a little, run a little, sleep a little – but there is no rhythm to it.

The finding is important because parents whose children have autism or fragile X report problems getting their children to go to sleep and stay asleep. Fragile X is the most common known cause of autism. While there are few studies on the topic, said Nelson, "the impression I have is that many fragile X patients have a period of time that's like an extended infancy when they don't settle into a typical sleep–wake period."

Understanding how the gene associated with fragile X affect the circadian clock or the sleep-wake cycle could help explain some of the symptoms experienced by patients, he said.

After ruling out the possibility that the animals without the two genes could not perceive light, Nelson collaborated with a group in The Netherlands to test whether the cell's "central clock" called the suprachiasmatic nucleus in the animals was normal. They concluded that the clock was normal but that somehow the expression of genes that govern it is altered in these mice.

"These genes (FMR1 and FXR2) are new players in the control of circadian (daily) rhythms," said Nelson. Currently, the genes are thought to have a role in translating RNAs (ribonucleic acids) – particularly at the receiving side of the connections between neurons called dendrites. Dendrites are characterized by the fine branches that reach out into tissue. Scientists theorize that FMR1 and FXR2 may be involved in transporting the RNAs to the areas of those branches where the synapse is present.

Source: Baylor College of Medicine