Constant Lighting May Disrupt Development of Preemie's Biological Clocks

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Keeping the lights on around the clock in neonatal intensive care units may interfere with the development of premature babies' biological clocks. That is the suggestion of a new study reported in the Aug. 21 issue of the journal *Pediatric Research*.

The study, which was headed by Douglas McMahon, professor of biological sciences at Vanderbilt University and an investigator at the Vanderbilt Kennedy Center for Research on Human Development, reports that exposing baby mice to constant light keeps the master biological clock in their brains from developing properly and this can have a lasting effect on their behavior.

"We are interested in the effects of light on biological clocks because they regulate our physiology extensively, and also have an important effect on our mood," McMahon said. "This study suggests that cycling the lights in NICUs may be better than constant lighting for premature babies' from the perspective of developing their internal clocks."

Every year about 14 million low-weight babies are born worldwide and are exposed to artificial lighting in hospitals.

"Today, we realize that lighting is very important in nursing facilities, but our understanding of light's effects on patients and staff is still very rudimentary," said William F. Walsh, chief of nurseries at Vanderbilt's Monroe Carrel Jr. Children's Hospital. "We need to know more. That is why studies like this are very important."

Although older facilities still use round-the-clock lighting, modern NICUs, like that at Vanderbilt, cycle their lighting in a day/night cycle and keep lighting levels as low as possible, Walsh said. Also, covers are kept over the isolets that hold the babies in an effort to duplicate the dark conditions of the womb.

The finding that exposure to constant light disrupts the developing biological clock in baby mice provides an underlying mechanism that helps explain the results of several previous clinical studies. One found that infants from neonatal units with cyclic lighting tend to begin sleeping through the night more quickly than those from units with constant lighting. Other studies have found that infants placed in units that maintain a day/night cycle gain weight faster than those in units with constant light.

The research is a follow-up from a study that the McMahon group published last year which found that long periods of constant light disrupt the synchronization of the biological clock in adult mice. In all mammals, including mice and humans, the master biological clock is located in an area of the brain called the suprachiasmatic nuclei (SCN). It influences the activity of a surprising number of organs, including the brain, heart, liver and lungs and regulates the daily activity cycles known as circadian rhythms.

The SCN is filled with special neurons that are wired in such a way that their activity varies on a regular cycle of roughly 24 hours. In a normal brain, the activity of these clock neurons is synchronized to a single cycle which is set by the 24-hour day/night cycle.

McMahon's previous study found that the SCN neurons in adult mice begin drifting out of phase after a mouse is exposed to constant light for about five months and that this is accompanied by a breakdown in their ability to maintain their normal nocturnal cycle.

“After we got this result, my post-doctoral fellow, Hidenobu Ohta, who is now a pediatrician at Tohoku University Hospital in Japan, wanted to study the impact of constant light on newborn mice because he was interested in finding out whether the use of constant light in NICUs may be having a similar effect,” McMahon said.

Newborn mice provide a good model for premature human infants because baby mice are born at an earlier stage of development than humans, a stage closely equivalent to that of premature babies.

“We found that the newborn mice were even more vulnerable to the effects of constant light than the adults,” McMahon said.

The researchers took two groups of newborn mice. One group was exposed to a normal cycle of 12 hours of light and 12 hours of darkness for the first three weeks of life. The second group was exposed to constant light for the same period. They used a special transgenic strain of mouse with an artificial gene that produces a green fluorescent protein under the control of one of the genes associated with the biological clock. As a result, when the neurons are active they produce a bright glow.

This allowed the scientists to determine that the SCN neurons in the baby mice who were exposed to a normal light cycle quickly became synchronized. By contrast, the clock neurons in baby mice exposed to constant light were unable to maintain coherent rhythms. However, when the constant-light mice were exposed to a day/night light cycle, the clock neurons rapidly fell into lock-step.

To get an idea whether the constant light exposure had any lasting impact, the scientists also exposed some of the mice to constant light for an additional four weeks and monitored their behavior. They found that two-thirds of the mice initially exposed to constant light were unable to

establish a regular activity cycle during this extended period as measured by their use of the exercise wheel.

“We know that infants are strongly influenced by the rhythms of their mothers,” said McMahon. “But, even though the mothers maintained a regular cycle during the constant light period, the stimulatory effect of the light was strong enough to overcome their influence.”

In a separate study, newborn mice who had spent their first three weeks in a day/night cycle were exposed to constant light for an extended period were able to maintain their circadian rhythm for three to five months before their activity patterns became disrupted.

“This is a new area of research,” said McMahon, “so there are a lot of unanswered questions. For example, could disruption of a baby’s biological clock increase their vulnerability to associated mood disorders like depression and seasonal affective disorder? Could it make it harder for someone to adjust to shift work or suffer more from jet lag? All this is speculative at this point. But, certainly the data would indicate that human infants benefit from the synchronizing effect of a normal light cycle.”

Vanderbilt undergraduate Amanda Mitchell contributed to the study.

Source: Vanderbilt University