Scientific Research

Neural Mechanisms Underlying Age-Related Decline in Circadian Rhythm

Material below summarizes the article, Age-Related Changes in the Circadian System Unmasked by Constant Conditions, *published on August 27, 2015 in* eNeuro *and authored by Takahiro J. Nakamura, Wataru Nakamura, Isao T. Tokuda, Takahiro Ishikawa, Takashi Kudo, Christopher S. Colwell, and Gene D. Block.*

Circadian rhythms are altered by the aging process in humans and many other organisms. In people, we see this most commonly with changes in our sleep/wake cycle, with many elderly experiencing a shift to earlier bedtimes and difficulty staying asleep throughout the night. The circadian system governs the temporal patterns of processes throughout our body, and aging impacts the daily patterning of behavior, physiology, and even gene expression. In our work, we have been exploring how aging impacts the core circadian clock that drives these daily rhythms.

In rodents, aging alters the cycle length (period) of circadian rhythms and decreases the amount of activity and the coherence of locomotor activity. As in people, an aged mouse will display a less robust sleep/wake cycle. Since the 1990s, research aiming to clarify “the point of action of age-related changes in the biological clock” on these physiological phenomena has been conducted in rodents. In 2011, our group found an age-related decline of the neuronal activity rhythms in the master circadian clock in the suprachiasmatic nucleus (SCN) of hypothalamus (Nakamura et al., 2011). Importantly, this study demonstrated a decline in the circadian output from the SCN, but did not find an age-related decline in the intra-SCN molecular clockwork which drives circadian oscillations.

In the present study, using an electron multiplying charge-coupled device camera, our group created a system to record faint bioluminescence in high resolution over a long period of time. With this system, we observed the expression rhythm of clock genes in the SCN at the cellular level.

We discovered that the SCN cellular rhythms for aged mice (20–24 months old) were not much different from the young mice (3–5 months old) when seen at the level of individual cells, but that the rhythm within the SCN as a whole had become scattered and less synchronized. This observation suggests that the neural connections among SCN cells weaken with age. Furthermore, these age-related changes were smaller for mice housed in environments with 12 hours of light and 12 hours of darkness, compared to mice housed in all-day darkness (constant darkness). These findings indicate that in the environment without light, the effect of the aging on the biological clock is more readily detected. Additionally, these findings provide evidence that the light environment can preserve circadian function even in advanced age.

In our recent investigation using female mice, our group found evidence that age-induced infertility may be influenced by which a light environment is incompatible with the biological clock (Takasu et al., 2015). Furthermore, many other laboratories have reported that a robust light/dark cycle is effective in increasing attentiveness and improving quality of sleep in older individuals. Thus, our group plans to continue investigating the mechanism of the molecules involved in the reduction of neural connections among SCN cells.

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Age-Related Changes in the Circadian System Unmasked by Constant Conditions. Takahiro J. Nakamura, Wataru Nakamura, Isao T. Tokuda, Takahiro Ishikawa, Takashi Kudo, Christopher S. Colwell, and Gene D. Block. *eNeuro*. Aug 2015, 2 (4). **DOI:** 10.1523/ENEURO.0064-15.2015.

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