論 文 要 旨

Circadian rhythm of PERIOD2::LUCIFERASE expression in the trigeminal ganglion of mice

Yukie Shirakawa

Introduction: The trigeminal nerve conveys delicate sensations such as warmth, pain, and tactile pressure in the oral and facial regions, and most trigeminal afferent cell bodies are located in the trigeminal ganglion. Our previous study has shown that sensations in trigeminal nerve innervated areas, specifically in the maxillofacial region, exhibit diurnal variation and that sensitivity changes time-dependently. In this study, we aimed to clarify the rhythm of expression of clock gene in the trigeminal ganglion of mice to elucidate the mechanism of circadian regulation in the same area.

Methods: Immunohistochemistry examined the expression of the PER2 protein in the suprachiasmatic nucleus and trigeminal ganglion of wild-type mice. To measure gene expression as bioluminescence, PERIOD2::LUCIFERASE knock-in (PER2::LUC) mice were used. Unilateral trigeminal ganglion and brain sections including the suprachiasmatic nucleus were incubated *ex vivo*. Bioluminescence levels were then measured using a highly sensitive photodetector. The same experiments were then conducted with *Cry1* gene-deficient ($Cry1^{-/-}$) or *Cry2* gene-deficient ($Cry2^{-/-}$) mice.

Results: In the trigeminal ganglion, immunohistochemistry localized PER2 protein expression within the neuronal cell body. Mouse trigeminal ganglion *ex vivo* tissues showed distinct circadian oscillations in PER2::LUC levels in all genotypes, wild-type, $Cry1^{-/-}$, and $Cry2^{-/-}$. The period was shorter in the trigeminal ganglion than in the suprachiasmatic nucleus; it was shorter in $Cry1^{-/-}$ and longer in $Cry2^{-/-}$ mice than in the wild-type mice.

Conclusion: The expression of *Per2* in neurons of the trigeminal ganglion in *ex vivo* culture and the oscillation in a distinct circadian rhythm suggests that the trigeminal ganglion is responsible for the relay of sensory inputs and temporal gating through autonomous circadian oscillations.