

論文の内容の要旨

論文題目

SCOP/PHLPP1 β in the basolateral amygdala regulates circadian expression of mouse anxiety-like behavior
(扁桃体基底外側核に存在するSCOP/PHLPP1 β によるマウス不安様行動の概日制御)

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The daily solar cycle enables organisms to synchronize their internal circadian rhythms and subsidiary bodily functions according to their temporal niches. Circadian regulation of physiology extends to higher brain functions including cognition and memory, while disruption of the circadian clock triggers a spectrum of affective abnormalities ranging from mania to depression. While evidence linking clock gene mutations and the resulting affective disorders is emerging, the physiological roles of the circadian clock in affect regulation remain unexplained. Here, in order to more fully understand how the clock maintains affective behaviors at physiological levels, I characterized the time-of-day-dependent regulation of anxiety-like behavior in *Mus musculus*. I show that mouse anxiety-like behavior is expressed in a circadian manner and demonstrate that the circadian clock machineries in the dorsal telencephalon (dTel) are required for the rhythmic expression of anxiety-like behaviors. I identify SCOP (suprachiasmatic nucleus circadian oscillatory protein; also known as PHLPP1 β , pleckstrin homology domain leucine rich repeat protein phosphatase 1 β) as an essential intracellular signaling molecule mediating the regulation of anxiety-like behaviors downstream of the clock. Using viral-mediated, basolateral amygdala (BLA)-specific knockout of *Scop*, I demonstrate that SCOP in the BLA serves an anxiogenic function on the elevated plus maze. Collectively, I conclude that the circadian expression of SCOP in the BLA plays a pivotal role in generating the circadian rhythmicity in the anxiety-like behavior. My results demonstrate SCOP as a novel regulator of affect and reveal its key roles in the anxiogenic functions of the BLA and, together with the identification of dTel clock machineries in affect regulation, provide important insights into the mechanisms governing mammalian affective behaviors as well as into the pathology of affective disorders.