

MS01-1 Introduction of chronotherapy and physiological importance of peripheral clocks

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Since the discovery of clock gene in 1997, molecular mechanism of circadian oscillation and daily entrainment has been elucidated. When the expression profile of clock genes such as Per1 and Per2 is examined in the whole body, almost all organs such as kidney liver, lung, and skeletal muscle clearly show the circadian rhythms, suggesting that peripheral clock may operate the local clock function. For example, Glut2 and Glut5 are highly and daily expressed in the small intestine, and expression time of these genes is well corresponded to the time for absorption of sugar when animals take food. Morning light is important entrainment signals for entrainment circadian rhythm. On the other hand, daily restricted feeding entrains the circadian rhythm of mouse clock gene expression in the central nervous system excluding the suprachiasmatic nucleus (SCN), as well as in the peripheral tissues such as the liver, lungs, and heart. In addition to entrainment of the clock genes, daily restricted feeding induces a locomotor activity increase 2-3 h before the restricted feeding time. The increase of activity is called the food anticipatory activity (FAA). Food volume and fasting period are key factors for food-induced entrainment, and a balanced diet such as adequate percent of carbon hydrate and protein is suitable for peripheral entrainment. At present, the precise mechanisms for restricted feeding-induced entrainment of activity and liver clock are still unknown. On the other hand, abnormality of clock function such as clock gene mutation and shift of light-dark cycle causes the obesity, high cholesterol, and cancer growth.