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Discovery of a Gastric Food Clock

The master pacemaker, located in the suprachiasmatic nucleus (SCN) of the hypothalamus, serves as a circadian biological clock in mammals. This clock influences a wide array of daily rhythms, including sleep-wake cycles, body temperature, cardiovascular activity, and physiology of the gastro-intestinal tract. Peripheral organs such as the liver or kidney, heart and pancreas contain "clock genes" that normally are synchronized to the rhythms of the SCN. However, when food is restricted to the daytime in nocturnal rodents, the phase of peripheral circadian genes such as *Per1* and *Per2* mRNA are reset to the new feeding time (Damiola et al., 2000). It is not know whether peripheral circadian genes are distributed throughout the tissues, or are associated with specific neuronal or endocrine cells. In the present studies, I demonstrate the localization of rhythmic circadian genes in specific cells of the stomach. PER1 and PER2 proteins are expressed in the X/A like cells of the gastric luminal oxyntic glands, which also express ghrelin, a hormone that regulates food intake and energy homeostasis, and is thought to be a signal for meals (Kojima & Kangawa, 2005). In mice maintained in a 12:12 light dark cycle, and provided with food *ad libitum*, I found a diurnal rhythm in ghrelin, PER1 and PER2. In a food-shift paradigm, food was restricted to 6 h/day for 14 days and was presented either at the beginning of the dark phase (zeitggeber time, ZT12-18) or in the middle of the light phase (ZT6-12). For the night fed animals, the rhythm in ghrelin, PER1 and PER2 remained as in controls. For the day fed animals, the rhythms of grhelin, PER1 and PER2 phase advanced, indicating that expression of both the gastric hormone and the circadian genes are controlled by the feeding schedule, and not by the light-dark cycle. In both night fed and day fed animals, the levels of ghrelin were lower immediately before the time of food presentation than 6 h earlier, indicating that ghrelin release anticipated scheduled food presentation. This suggests that the secretion of ghrelin is clock controlled rather than food controlled, and that ghrelin may be directly part of the circadian mechanisms controlling rhythms of food intake.