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Daily Rhythms of Serum Lipids in Dogs: Influences of Lighting and Fasting Cycles

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Circadian clocks organize a wide array of metabolic functions in a coherent daily schedule and ensure synchrony of this schedule with environmental rhythms. Daily rhythmicity of lipid metabolism occurs in rodents and ruminants. We examined daily level variations of serum lipids (nonesterified fatty acids [NEFA], triglycerides, phospholipids, total cholesterol and total lipids) in healthy dogs, particularly focusing on their temporal relationship to lighting and fasting cycles. Whereas serum NEFA levels did not change across the day, levels of total lipids, total cholesterol, phospholipids, and triglycerides occurred in dogs maintained under 12:12-h light:dark cycles and fed a single meal daily. Only the rhythmic pattern of triglycerides responded to a 6 h delay in light onset, suggesting a cardinal role of a light-entrained circadian oscillator in its generation. To investigate whether temporal variations in serum lipids depend to physiological postprandial changes, we measured lipid levels in fasted dogs. Rhythms of total lipids, total cholesterol, phospholipids, and triglycerides vanished when dogs were food-deprived, indicating that these rhythms are driven by the digestive process. Levels of serum NEFA patterns were significantly higher during fasting than after food intake. The increase of NEFA concentrations during fasting may reflect the mobilization of adipose tissue NEFA mediated by the decrease in insulin with its lypolitic effects. Elucidating the daily rhythmicity of lipid levels is fundamental to understanding the metabolism of the dog, an animal model frequently used for research in metabolic pathophysiology.

Abbreviation: NEFA, nonesterified fatty acids

Circadian clocks are autonomous internal daily timekeeping mechanisms that allow organisms to adapt to external daily rhythms of many environmental factors.[31] The adaptive importance of circadian timekeeping has been illustrated in several model systems.[10] Fundamental properties of circadian oscillators are that they produce a rhythm with a free-running period that can be synchronized by periodic environmental cues.[27,32] The most pervasive environmental signals for the mammalian circadian system are the natural light–dark cycle and food availability. Photic entrainment is entirely dependent on light input through the eyes to the suprachiasmatic nuclei of the anterior hypothalamus. Bilateral eye-enucleated mammals do not show any behavioral entrainment by light–dark cycles.[40] Because feeding entrainment persists in animals with lesions of the suprachiasmatic nucleus,[26,36-38] it may be regulated by a different circadian system. The dorsomedial nucleus of the hypothalamus recently was reported to play an important role in feeding entrainment.[15]

The circadian clock reportedly regulates metabolism and energy homeostasis in the liver and other peripheral tissues by mediating the expression or activity of various metabolic enzymes and transport systems involved in cholesterol, glycogen, and glucose metabolism.[8,17,24,43] The importance of circadian timekeeping for metabolism is shown clearly by the metabolic phenotypes associated with mice carrying mutations in clock genes.[22,35,39]

Daily rhythmicity of lipid metabolism has been described in different mammalian orders. For instance, the plasma concentrations of nonesterified fatty acids (NEFA), triglycerides and cholesterol displayed daily variations in rodents[13,22,] and ruminants.[1,5,29,42]

Elucidating the daily rhythmicity of lipid levels is a fundamental necessity for understanding the metabolism of the dog, an animal model frequently used for research in the pathophysiology of diabetes mellitus. However, circadian investigations of the metabolism of dogs have been scarce. Previous investigations showed diurnal variations of various metabolic and neuroendocrine activities in dogs in association with feeding–fasting cycles.[16,19] However, these studies did not use canonical experimental protocols, which are necessary for the identification of rhythmicity.

Here we examined daily level variations of serum lipids (nonesterified fatty acids [NEFA], triglycerides, phospholipids, total cholesterol, and total lipids) in healthy dogs, particularly focusing on their temporal relationship to lighting and fasting cycles. The goals of this study were to determine whether levels of these plasma lipids show circadian variation, and, if so, whether the variations related to the lighting cycles, reflect simple postprandial changes, or are under the control of a circadian clock.

Materials and Methods

Animals and housing. Five clinically healthy purebred Beagles (*Canis familiaris*, male, 2 y old, mean body mass = 13 kg) were used. During tests the animals were housed in individual pens (140 × 200 cm) equipped with a darkened opening and an airflow system. The visual and acoustic isolation of each dog from conspecifics prevented social entrainment of circadian behavioral rhythms.[9] Animal room temperature and relative humidity

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