

Chapter 16

Physiological Responses to Fasting in Bats

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16.1 Introduction

The evolution of powered flight in bats (Order Chiroptera) took place more than 50 million years ago (see summary in Speakman 2001) and afforded them the opportunity to fill in ecological niches void of non-volant mammals, a circumstance that might explain their remarkable diversity in terms of number of species, diet, and habitat types that they occupy. With over 1,000 species, bats are the second most diverse mammalian order, outnumbered only by rodents (Altringham 1996). Generally, bats are considered small mammals, most having body masses (m_b) ranging from less than 2 g in the bumblebee bat, *Craseonycteris thonglongyai*, to 100 g, but some are larger, the largest being the Giant golden-crowned flying fox, *Acerodon jubatus*, with a m_b in excess of 1 kg. Bats eat a wide variety of diets; many species are insectivorous, others are frugivorous, nectarivorous, carnivorous, piscivorous, omnivorous, or hematophagous. Moreover, bats are found in almost all climatic zones, and they are distributed worldwide, except for the polar regions.

Besides its clear ecological advantages, the evolution of powered flight brought about high energetic costs for bats; bats in flight increase metabolic rate (MR) 15 times over MR at rest (Austad and Fischer 1991; Harrison and Roberts 2000; Munshi-South and Wilkinson 2010; Szewczak 1997), but compensate for this enormous expense through a variety of energy-saving thermoregulatory patterns. Many species become torpid on a daily basis and have relatively short periods of activity, almost invariably at night (Speakman and Thomas 2003). Some species that feed on resources not available throughout the year, such as insects, cope with reduced prey availability by hibernating in winter. Thus, bats

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need to rely on their endogenous energy reserves on a regular basis, sometimes for very long periods. In this regard, bats are remarkable in that the size of their endogenous energy stores may vary dramatically on seasonal, daily, and even hourly timescales (Kronfeld-Schor et al. 2000; Kunz et al. 1998; Weber and Findley 1970). One might envision that bats have evolved mechanisms that allow them to make efficient use of their endogenous reserves, thus maintaining energy balance in periods of food shortage. However, surprisingly little is known about the responses of bats to fasting. In this chapter, we summarize the known responses of bats to fasting, suggest new directions for future studies, and discuss hypotheses concerning the physiological responses of bat species to fasting.

16.2 Physiological Responses of Bats to Fasting

Vertebrates that consume different diets often differ in the way they store and mobilize body energy reserves, and therefore one might expect different species to have different responses to fasting. Among all mammalian orders, bats have the largest variety of diets (Neuweiler 2000a). Although most bats are insectivorous, there is also a significant number of bat species that feed exclusively on fruit, or nectar and pollen, and others can feed on small vertebrates, and even blood of other mammals and of birds (Neuweiler 2000a). Many species of bats spend relatively short times foraging and drinking during their daily activity cycle (up to 4 h) and spend the remainder of the day in sheltered roosts (Bassett 2004), where they neither eat nor drink. Therefore, short- and long-term fasting are regular occurrences in the life cycles of bats. Accordingly, bats lend themselves to the investigation of how different diets affect physiological mechanisms, such as endurance of fasting.

16.2.1 *Frugivorous Bats*

Fruit eating bats have specialized gastrointestinal tract structure and function that allow them to digest carbohydrate-rich diets efficiently and rapidly (Keegan 1977; Okon 1977). Both the Egyptian fruit bat, *Rousettus aegyptiacus*, and the great fruit-eating bat, *Artibeus lituratus*, have high rates of paracellular absorption of carbohydrates that apparently compensate for their relatively short intestinal tract (Caviedes-Vidal et al. 2007, 2008; Tracy et al. 2007). This mechanism allows fruit bats to store relatively large amounts of hepatic glycogen (Fig. 16.1; Protzek et al. 2010).

Two species of microchiropteran fruit bat, the above-mentioned *A. lituratus* and the Jamaican fruit bat, *A. jamaicensis*, maintain relatively high blood glucose levels after short-term fasting (2–6 days) (Pinheiro et al. 2006). These species tend to have large hepatic glycogen stores that likely play a role in maintaining blood glucose levels when food is absent (Pinheiro et al. 2006). Because of their large hepatic glycogen stores, *A. lituratus* can endure 2–6 days with no food and still

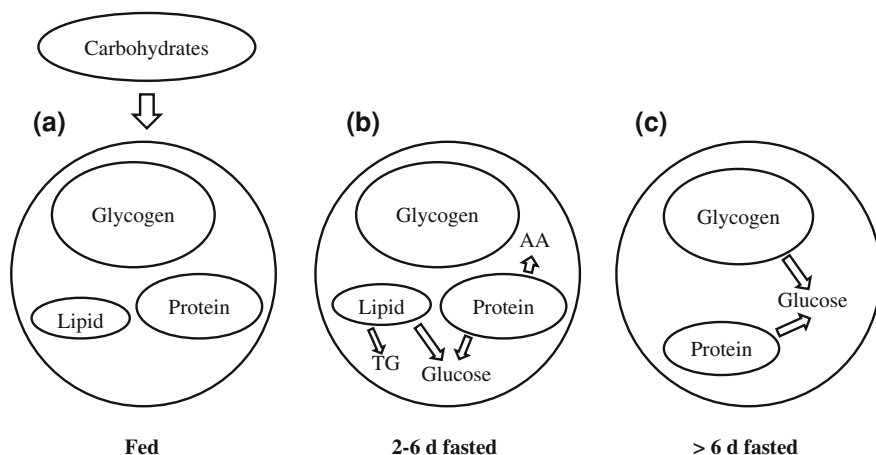


Fig. 16.1 Nutrient use by fasting frugivorous bats. **a** When bats eat their normal carbohydrate-rich diet, they accumulate large glycogen reserves, mainly in the liver. **b** During a short of fast, glycogen reserves remain intact, and bats oxidize body fat and use gluconeogenesis from amino acids to maintain a high blood glucose level. **c** If the fast is longer, frugivorous bats eventually deplete their glycogen stores. *TG* triacylglycerides, *AA* amino acids

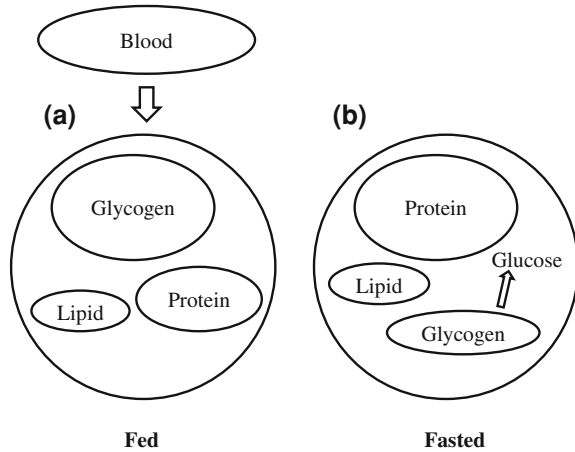
maintain normal levels of blood glucose (Pinheiro et al. 2006), an ability rarely seen among mammals. This phenomenon is peculiar given that insulin levels remain similar in both fasted and fed *A. lituratus* (Protzek et al. 2010). Although hyperinsulinemia is characteristic of insulin insensitivity (Modan et al. 1985), *A. lituratus*, which possesses a comparatively high number of pancreatic β -cells (Protzek et al. 2010), also has high insulin sensitivity and high blood glucose tolerance. Consequently, glycogenolysis does not seem to be used as a mechanism of short-term fast resistance in other fruit bat species, as indicated by their limited use of hepatic glycogen during this period (Freitas et al. 2010; Pinheiro et al. 2006). For example, *R. aegyptiacus* has large variations in its blood glucose levels, and its total blood N increases when faced with a shortage of food (Keegan 1977; Korine et al. 1999), suggesting that these bats use triacylglycerides and proteins as fuels while at rest by day (Korine et al. 1999).

Frugivorous bats face a challenge in maintaining water balance while they fast since the bulk of their water intake comes from their diet and since they have relatively high rates of mass-specific evaporative water loss (EWL) (Studier 1970) and poor urine-concentrating abilities (Studier and Wilson 1983); thus frugivorous bats are exposed to a greater risk of dehydrating than similar sized, non-volant mammals (Bakken and Sabat 2007). Bakken et al. (2008) reported that when deprived of food and water for 12 h, glomerular filtration rate (GFR) in Pallas's long-tongued bats, *Glossophaga soricina*, decreased to 90% less than when fed and watered adequately (Bakken et al. 2008), which they interpreted as a water saving mechanism.

Fig. 16.2 Nutrient use by hematophagous bats.

a Vampire bats do not accumulate large quantities of glycogen, as opposed to other mammals that eat diet protein-rich diets.

b Hematophagous bats do not tolerate fasting for long periods. They are unable to mobilize fat or protein efficiently, and they deplete their small glycogen stores quickly



16.2.2 Hematophagous Bats

Although animals that eat foods with high protein content usually store large amounts of hepatic glycogen (see Harlow, [Chap. 17](#)), vampire bats are apparently an exception (Fig. 16.2). These bats lose m_b rapidly when they do not eat, and are unable to survive more than 3 days of fasting (McNab 1973). For example, the common vampire bat, *Desmodus rotundus*, fails to maintain adequate blood glucose levels when fasting, and its hepatic glycogen stores are at least 40% smaller than those of other mammal species (Freitas et al. 2003, 2005; Kettelhut et al. 1980). Vampire bats are apparently unable to build up fat stores (Breidenstein 1982) as seen in other species and seem to lack the ability to mobilize fat rapidly. When vampire bats do not eat, the small decrease in their lipid stores is not accompanied by a significant increase in free fatty acid concentration in the blood (Freitas et al. 2003, 2005) as has been reported for other species. Moreover, no measurable change in muscle (heart, limb, and breast) and liver proteins has been found in fasting vampire bats, suggesting that they are unable to catabolize protein when deprived of food (Freitas et al. 2003, 2005). A plausible explanation for *D. rotundus* being able to fast for the reported 3 days is that they have highly elastic stomachs capable of distending and storing large quantities of blood (Freitas et al. 2003; Rouk and Glass 1970). This characteristic could mask the fact that these animals may be postabsorptive and therefore are not truly fasting. Further, *D. rotundus* has a unique behavioral adaptation to cope with fasting; related bats participate in reciprocal food sharing through regurgitation of blood to one another, allowing unsuccessful foragers to survive the night (Wilkinson 1984).

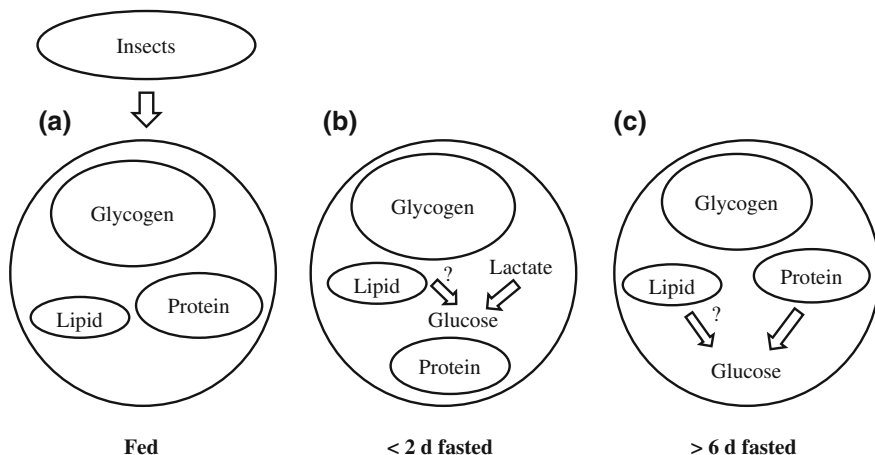


Fig. 16.3 Insectivorous bats can survive the longest periods of fasting among bats. **a** When feeding, they accumulate large quantities of glycogen in the liver and the muscles. **b** During short-term fasting, they make use of body fat reserves and activate gluconeogenesis from skeletal muscle lactate for energy, and to maintain normoglycemia. **c** When the fast is longer, insectivorous bats begin catabolizing protein, but they continue to retain large amounts of hepatic glycogen

16.2.3 Insectivorous Bats

Approximately 70% of all bat species are insectivorous (Neuweiler 2000a), and they probably have the highest resistance to long fasts among chiropterans. Freitas et al. (2010) found that male Pallas's mastiff bat, *Molossus molossus*, maintained blood glucose levels constant during 48 h of fasting, while free fatty acid concentrations did not increase in their blood. These observations suggest that these bats did not shift to phase II of fasting (*sensu* Cherel et al. 1988) even after 48 h of food deprivation. This response is further supported by the small decrease in their hepatic glycogen stores, indicating that they did not completely exhaust their glycogen stores within this period (Fig. 16.3; Freitas et al. 2010).

It is thought that insectivorous bats maintain normal levels of blood glucose in the initial 48 h of fasting by gluconeogenesis. The concentration of plasma lactate was found to decrease in response to fasting, suggesting that lactate from skeletal muscle might be one of the main substrates for gluconeogenesis in fasting bats (Corssmit et al. 2001; Pinheiro et al. 2006). Following 24 h of fasting, plasma urea levels did not change in the pallid bat, *Antrozous pallidus*, (Bassett 2004), indicating that there is no change in protein catabolism in response to short-term food deprivation. However, after longer periods of fasting (48–72 h), incorporation of amino acids into the liver, particularly alanine, seems to increase; these amino acids are used for gluconeogenesis (Corssmit et al. 2001; Pinheiro et al. 2006).

McGuire et al. (2009) reported that plasma triacylglyceride concentrations are positively correlated with changes in m_b , and can be used to infer differences in short-term m_b changes and feeding activity of insectivorous bats, a relationship analogous to that found in birds (e.g., Jenni-Eiermann and Jenni 1994). However, the concentrations of triacylglycerides are surprisingly low in Mexican free-tailed bat, *Tadarida brasiliensis* (McGuire et al. 2009; Widmaier et al. 1996). It is possible that this species has unique mechanisms for rapid clearance of lipids from the blood, such as secretion in the milk of lactating females (Widmaier et al. 1996). However, because low levels of triacylglycerides were also observed in non-lactating individuals, it is more likely that the mechanism responsible for these levels involves secretion through the skin or a high blood concentration of protein lipases that rapidly catabolize the triacylglycerides (Widmaier et al. 1996). Morris et al. (1994) reported that Gould's long-eared bat, *Nyctophilus gouldi*, store some digesta in the rectum during short fasts (Morris et al. 1994), where little absorption may occur (Warner 1981). Many microchiropteran species cope with long periods of food shortage or deprivation by becoming torpid daily, and all temperate species hibernate during the winter in response to food scarcity and cold temperatures (Speakman and Thomas 2003).

16.2.3.1 Use of Torpor

Many animals face periods of fasting in which they have to rely on stored nutrients (McCue 2010). In endothermic vertebrates, maintenance of a high, constant body temperature (T_b) is the main determinant of depletion of endogenous reserves in periods of fasting (Bennett and Ruben 1979; see also Hohtola, Chap. 10; Ullrey, Chap. 18). Thus, endotherms that decrease costs of thermoregulation while fasting are at an advantage over those that do not (Geiser 2004). Bats are the only mammals that have evolved powered flight, an ability that imposes higher energetic cost than incurred by other mammals; moreover, bats have high surface to volume ratios, which increases rates of heat dissipation (Speakman and Thomas 2003). To minimize energy expenditure when food is restricted or absent, many species of bats make use of torpor, and reduce T_b to values close to ambient temperature (T_a). Torpor allows bats to reduce significantly the cost of thermoregulation and subsequently overall energy expenditure during fasting.

Among bats there is a continuum of thermoregulatory patterns, from species that strictly defend euthermic T_b , to others which regulate T_b at temperatures as low as 20°C, and even 5°C (Speakman and Thomas 2003). Insectivorous bats from temperate regions are probably the most thermolabile species, hibernating during the cold winter when food availability is low, and regularly entering torpor during their daily inactive phase throughout the year (e.g., Turbill et al. 2003; Willis et al. 2005). In insectivorous bats, a temporary decline in food availability can induce torpor even when the T_a is relatively high (Neuweiler 2000b). For example, fasting Gould's Long-eared bat, *Nyctophilus gouldi*, entered torpor even at T_a of 30°C (Neuweiler 2000b). Although the decline in T_b and MR is less pronounced during

short bouts of torpor that are used throughout the year, than during the long bouts that characterize hibernation (Geiser and Ruf 1995; Wojciechowski et al. 2007), even small reductions in T_b and MR lead to significant savings of energy (Heldmaier et al. 2004). For instance, a bout of daily torpor may last up to 12 h during which MR is reduced to about 25% of the active MR (Heldmaier et al. 2004). As a result, total daily energy requirements may decline by 40% (Heldmaier et al. 2004). In the long-term, energy budgets of animals that enter torpor regularly may only be two-thirds of the energy requirements of normothermic individuals (Ortmann et al. 1997; Ruf and Heldmaier 1992; Schmid et al. 2000). Therefore, daily torpor is an important strategy for a substantial reduction of an animal's total energy requirements, thereby saving endogenous reserves in periods of food restriction or fasting.

16.2.3.2 Hibernation and Arousal

Insectivorous bats can endure fasting when food availability is low by their ability to hibernate, a characteristic common among the temperate members of the Vespertilionidae and Rhinolophidae (Altringham 1996). Hibernation in bats is not a constant state of reduced metabolism and T_b , rather it consists of repeated cycles of torpor and arousal. Arousals occur periodically, roughly every 12–15 days, and account for more than 85% of energy used throughout the winter (Wang 1978) and do so to drink, eat or both (Boyles et al. 2006).

During winter both food supply and T_a decline, and while some species of bats escape this energetic bottleneck by migrating, others hibernate (Speakman and Thomas 2003). Prior to both hibernation and migration, bats generally accumulate up to 25% of their m_b in fat (Speakman and Thomas 2003; Widmaier et al. 1996) that serves as metabolic fuel during hibernation and migration (Dark 2005; Guglielmo 2010). Both of these energetically challenging periods are dependent upon a high capacity for fatty acid mobilization, and therefore the bats' survival is affected by adaptive changes in fatty acid transport proteins (Eddy and Storey 2004; Guglielmo et al. 1998). In addition, fatty acid composition is also important in lipid mobilization since fatty acids are preferentially mobilized when they are short, less saturated, and have double bonds located close to the terminal methyl group of the chain (Groscolas and Herzberg 1997; see also Price and Valencak, Chap. 15).

Since hibernating bats decrease their metabolism, enter prolonged fasting, and rely almost solely on lipids as fuel, it is not surprising that hibernation results in modifications in the composition of triglycerides, fatty acids, amino acids, ketones, and other blood metabolites (Arevalo et al. 1990; Dark 2005; Wells et al. 1965). The major changes in metabolic physiology during hibernation are probably the switch from primarily carbohydrate to primarily lipid metabolism, reduction in protein synthesis and protein degradation (Van Breukelen and Carey 2002; Van Breukelen and Martin 2001; Yacoe 1983), and increased gluconeogenesis during periodic arousals (Burlington and Klain 1967).

Lipids fuel basal metabolism during torpor, non-shivering thermogenesis by oxidation in brown adipose tissue (BAT), and shivering thermogenesis by skeletal muscle that rewarm the animal during arousals (Geiser 1988). Since lipids supply most metabolic fuel during hibernation, hibernating mammals should optimize mobilization and oxidation of lipids (see Harlow, Chap. 17). One factor significantly affecting lipid mobilization is the activity and concentration of fatty acid binding proteins that play an important role in intracellular transport of fatty acid (Stewart 2000). The little brown bat, *Myotis lucifugus*, has been reported to undergo modifications in fatty acid binding proteins during hibernation that may increase the efficiency of lipid mobilization (Eddy and Storey 2004). In addition, the fatty acid composition of adipose tissue in hibernating bats undergoes changes as well (Arevalo et al. 1990; Geiser and McMurchie 1984; Widmaier et al. 1996). Wells et al. (1965) found a greater proportion of unsaturated fatty acids in the tissues of hibernating *M. lucifugus* than in non-hibernating animals. A higher proportion of unsaturated fatty acids might enable longer torpor bouts, lower T_b , and thus reduce MR, because the relatively lower melting point of unsaturated fatty acids will maintain the fluidity of cell membranes in such a way that energy can be produced even when T_b is low (Munro and Thomas 2004; Ruf and Arnold 2008).

During the lengthy fast of hibernation, there is a decrease in both blood glucose and liver glycogen (Burlington and Klain 1967), and thus the capacity to induce carbohydrate catabolism is apparently retained (Hannon and Vaughan 1961). The only sources of glucose available to fasting hibernators are glycogenolysis and gluconeogenesis. Yacoe (1983) found that fasting big brown bats, *Eptesicus fuscus*, undergo significant decreases in lean mass, pectoral muscle mass, and in total pectoral muscle protein, suggesting significant oxidation of tissue protein. Studies of hibernating Syrian hamsters, *Mesocricetus auritus*, and 13-lined ground squirrels (*Citellus tridecemlineatus*) may suggest an explanation for this; during arousal, their respiratory quotient approaches 1.0 (Mokrasch et al. 1960), evidence that protein catabolism is used for gluconeogenesis (Lyman and Leduc 1953).

During arousal, after two months of hibernation with no access to food, the rate of gross protein synthesis in the liver of *E. fuscus* was similar to that found in the liver of active bats after an overnight fast during the summer (Yacoe 1983), suggesting that the source of the amino acids used for synthesis of new proteins must be endogenous, i.e., from breakdown of tissue protein. This contrasts what was found in hibernating 13-lined ground squirrels, *Spermophilus tridecemlineatus*, in which hepatic polyribosomes are disaggregated (Whitten et al. 1970), and there was significantly lower protein synthesis in *in vitro* cultures of liver samples collected in winter than in summer samples from the same species (Klain and Whitten 1968). These observations contradict what one might expect in animals that have fasted for two months, since during prolonged periods of fasting protein metabolism declines due to decreased levels of mRNA (McNurlan et al. 1979), and low protein degradation levels lead to low amino acid availability (Cahill 1976; Gan and Jeffay 1967).

Similar to other fasting-adapted species, urea does not accumulate in the blood of *E. fuscus* during bouts of torpor lasting up to 12 days (Castellini and

Rea 1992; Yacoe 1983). The concentration of plasma urea does not differ between torpid and normothermic bats, perhaps the result of a low accumulation rate, and corresponds to only 0.01% loss of total protein per day (Yacoe 1983). A massive use of protein occurs during arousals when pectoral muscle and liver protein catabolism are similar to the rates in normothermic bats in summer. Since glycogen stores are small (Dodgen and Blood 1956) and the contribution of glycerol is coupled to the rate of fat oxidation, the increased demand for glucose during arousals must be met by gluconeogenesis from tissue protein. The relatively large loss of pectoral muscle and liver protein, together with increased hepatic gluconeogenic capacity (Klain and Whitten 1968) and high production of urea during arousals, suggest that during periodic arousals tissue protein is used to supply gluconeogenic demand. This is in contrast to what happens during torpor, when the rates of tissue protein synthesis and degradation are very low (Yacoe 1983). Fuel use during prolonged fasts is well documented in the literature, and the switch between different metabolic fuels is known to occur in three distinct phases (Cherel et al. 1988), therefore the switch back and forth between metabolic fuels during torpor and arousal in hibernating bats is remarkable.

16.2.3.3 Hormonal Control

Almost all of the endocrinological studies done on fasting bats focused on hibernation, when bats do not feed for several weeks or even months at a time (Roy and Krishna 2010; Srivastava and Krishna 2008, 2010). Therefore, our discussion focuses on hormonal control of prolonged fasting in hibernating bats (Fig. 16.4).

In all mammals, there is a complex system that regulates fuel stores and energy balance (Friedman and Halaas 1998). This system allows the storage of sufficient quantities of energy-dense triglyceride in adipose tissue to survive periods of food deprivation encountered during the lifetime of the animal; tight regulation of fuel stores also helps avert the presence of excess adipose tissue that can be maladaptive (Friedman and Halaas 1998; see also Zhang et al., Chap. 13). Leptin, a hormone secreted by adipose tissue, and its receptors, are integral components of this system, and have been the focus of most studies on hormonal control of fasting during hibernation. Leptin, mainly via the hypothalamus, controls and modulates the nutritional status of the animal by inhibiting appetite (Friedman and Halaas 1998; Kronfeld-Schor et al. 2000). Leptin levels decline during hibernation in the greater Asiatic yellow bat, *Scotophilus heathi*, and in *M. lucifugus* (Kronfeld-Schor et al. 2000; Roy and Krishna 2010; Srivastava and Krishna 2008; Widmaier et al. 1997), which is consistent with the general finding that leptin levels decrease during fasting. Although the functions of leptin are not yet well understood, it is known that low leptin levels induce metabolic and endocrinological changes resulting in frugal use of energy, enhancing the survival of the bats during the long, challenging fast in winter.

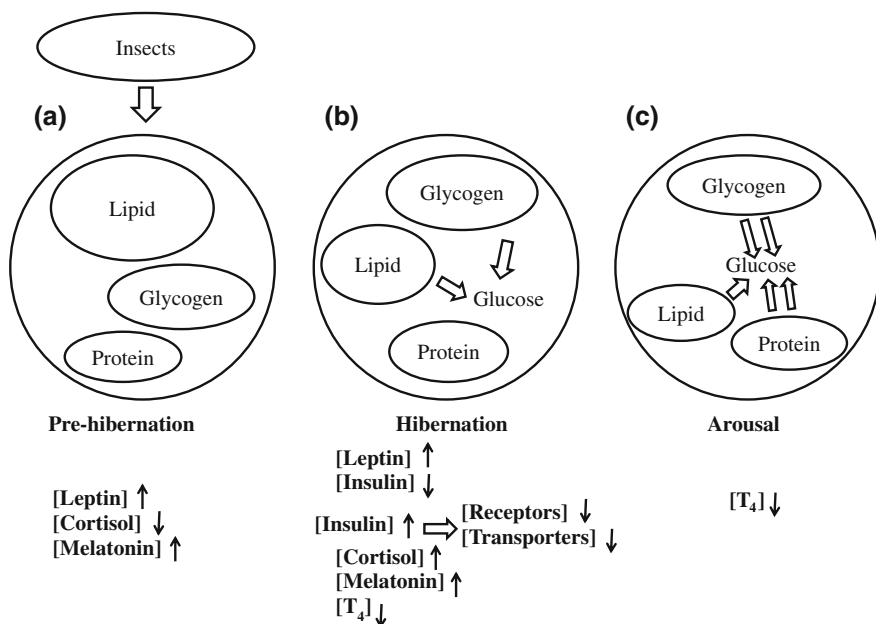


Fig. 16.4 Nutrient use and hormonal changes during the hibernation cycle of insectivorous bats. **a** Prior to hibernation, bats accumulate large amounts of body fat, which will become the main source of metabolic fuel during hibernation. While fattening, bats have high blood levels of leptin and melatonin, and low levels of cortisol, which favors the storage of nutrients. **b** During hibernation, bat blood glucose levels are relatively low, and, for energy, they switch from carbohydrate to fat catabolism. Leptin, insulin, and melatonin all seem to play a crucial role in this switch. In some species, insulin levels are high in the blood, but cells are not responsive since the expression of receptors and glucose transporters is down-regulated. Blood T₄ is high before hibernation, but decreases gradually during this period. **c** Torpor bouts during hibernation are interrupted by periodic arousals, which account for 85% of the energy used in winter. During arousals, bats use fat to rewarm, but after that, they burn hepatic glycogen for energy. Much synthesis and degradation of proteins take place during this period. The levels of plasma T₄ are low during arousals, indicating that the concentration of T₄ in the blood might act as a signal for bats to arouse

Lord et al. (1998) and Srivastava and Krishna (2008) hypothesized that a decline in leptin levels triggers numerous neuroendocrine responses to fasting, such as suppression of reproduction, thermogenesis, and immune defense, and also the stimulation of the stress response. According to this function, leptin levels should be high during the fattening period when bats prepare for migration and/or hibernation. As expected, in hibernating *M. lucifugus*, plasma levels of leptin are high prior to the fattening period, but decrease during the late fattening period (Kronfeld-Schor et al. 2000). However, it was shown that in these bats leptin plasma levels and adiposity are dissociated (Kronfeld-Schor et al. 2000), suggesting a possible state of gradual leptin insensitivity in target organs early in the prehibernatory period (Kronfeld-Schor et al. 2000; Townsend et al. 2008).

Gavrilova et al. (1997) hypothesized that the dissociation is achieved by plasma leptin being sequestered by circulating leptin binding-proteins, as appears to be the case in mice during the hyperleptinemic period of pregnancy. Whether such binding proteins exist in bats is not yet known.

One might expect insulin levels to decrease during winter hibernation, and, indeed, that was found in *Scotophilus heathi* (Srivastava and Krishna 2008), leading to the notion that leptin and insulin may work in synergy to stimulate fat mobilization in winter and to provide the bats with a satiety signal during their seasonal dormancy (Srivastava and Krishna 2008). However, plasma insulin remained high during hibernation in *M. lucifugus* (Bauman 1990; Srivastava and Krishna 2010). The cause of high plasma insulin during hibernation is yet unknown, but it might be a consequence of an increase in blood melatonin (see below). Despite the high concentrations of insulin in the plasma, the down-regulation of insulin receptors and glucose transporter 4 (GLUT-4) ensures reduced insulin sensitivity of cells during hibernation (Srivastava and Krishna 2010).

Cortisol levels were reported to decrease during activity and to increase during hibernation (Gustafson and Belt 1981). These results were interpreted to suggest that the activity of the adrenal cortex increases during hibernation (Gustafson and Belt 1981; Krutzsch and Hess 1961). In addition, levels of corticotrophin releasing hormone (CRH) were reported to decrease significantly in *M. lucifugus* when they fast (Widmaier et al. 1997). Therefore, the mobilization of fatty acid from deposited fat correlates with elevated glucocorticoid levels. However, the opposite was found in *S. heathi*, possibly due to different types of glucocorticoids measured in the different studies (Gustafson and Belt 1981; Srivastava and Krishna 2008; Widmaier et al. 1997).

The insectivorous species *S. heathi* and the long-winged tomb bat, *Taphozous longimanus*, had higher plasma concentrations of T_3 and T_4 in winter than in summer (Singh et al. 2002; Srivastava and Krishna 2008). Fasting may increase the secretion of hypothalamic TRH, although a mechanism is not yet known (Decuypere and Kuhn 1985). However, in *M. lucifugus* plasma T_4 levels were lowest at the beginning of hibernation and reached a maximum at the time of arousal (Damassa et al. 1995). It is possible that the increased T_4 plasma levels result from increased synthesis and release of T_4 during late hibernation and/or reductions in the uptake and clearance of this hormone that signals the time of arousal in this bat (Damassa et al. 1995).

Photoperiod is also a key determinant of the metabolic processes occurring prior to and during winter fasting in hibernating mammals. The pineal gland, through melatonin, the hormone it secretes, is a major regulator of seasonal changes in animals, informing the brain of the need for metabolic changes required to meet the approaching challenges (see also Ulrey, Chap. 18). These observations have led to intensive research of the effects of melatonin on seasonal metabolic changes, and several studies have reported that melatonin influences insulin secretion, lipid, and glucose metabolism (Hoyos et al. 2000; Nishida et al. 2002; Peschke 2008). In hibernating *S. heathi* plasma melatonin concentration increases with fat accumulation and attains a peak level during the period of maximum body

fat deposition. Remarkably, melatonin levels remained high even during hibernation, when blood glucose levels were low (Srivastava and Krishna 2010). The authors found that in bats deprived of food for 36 h, until glycogen stores are depleted, high concentrations of exogenous melatonin were associated with an increase in the level of blood glucose (Srivastava and Krishna 2010). They concluded that the high melatonin level in combination with high insulin concentrations during hibernation may be facilitating gluconeogenesis, as observed in rabbit kidney cultures (Derlacz et al. 2005). Melatonin might inhibit glycogen breakdown, thus sustaining a slow release of glucose during a long fast. Other studies support the role of melatonin in preserving glycogen stores (Mazepa et al. 2000; Mustonen et al. 2002). High melatonin levels during winter also elevate the use of fat as the major metabolic fuel, activating lipolysis, which is a primary source of energy during hibernation (Srivastava and Krishna 2010). In support of this observation, it was found that pinealectomy directly affects lipid metabolism causing a severe alteration in the balance between lipogenesis and lipolysis (Borges-Silva et al. 2005).

16.2.3.4 Migration

Many species of bats migrate, either to avoid food shortage (e.g., *T. brasiliensis*, straw-colored fruit bat, *Eidolon helvum*) or to an area with T_a 's more conducive to hibernation (Bisson et al. 2009). During migratory flight, many bats are unable to feed, yet they have very high energy demands. Migration, as documented in the avian literature, requires several physiological adaptations, such as premigratory fat deposition, increased muscle activity, and even changes in the digestive system (McWilliams et al. 2005; Popa-Lisseanu and Voigt 2009). However, while migration was intensively investigated in birds (see Bauchinger and McWilliams, Chap. 12; Jenni-Eiermann and Jenni, Chap. 11), there is little information about physiological adjustments in migratory bat species, and it is not yet known whether they undergo similar physiological adaptations (McGuire and Guglielmo 2009). There is, however, some evidence that Brazilian free-tailed bats, *Tadarida brasiliensis*, increase fat stores prior to migration (O'Shea 1976), but most bats that migrate hibernate first, and it is likely that the fat that is deposited in autumn is completely exploited during hibernation (Kunz et al. 1998).

Because of the very high metabolic cost of flight, while flying, bats must mobilize and oxidize metabolic fuels efficiently. It is still not clear how bats fuel flight. The differences in fuel use between birds and bats during flight are manifested in some aspects of protein catabolism. While small, passerine birds use some protein from the muscle and digestive organs to obtain energy and water, and end their migratory flights with less digestive system muscle mass (Karasov and Pinshow 2000; McWilliams and Karasov 2001), bats stop to feed between relatively short flights and insectivorous species can feed on the wing and are thus expected to have intact digestive systems at feeding stops between flights (McGuire and Guglielmo 2009). However, during hibernation, when the bats face

prolonged fasts, there is a reduction in the mass of the digestive system as well as a decline in gut enzyme concentrations (Carey et al. 2003).

The main factor limiting mobilization of extramuscular lipids in mammals is their transport across muscle membranes (Vock et al. 1996). Bats, unlike their nonflying mammals of similar m_b , seem to overcome this problem by increasing the concentration of fatty acid binding proteins (Eddy and Storey 2004). In addition, bats may have increased muscle oxidation activity due to modifications in muscle fiber morphology and physiology (Foehring and Hermanson 1984; Hermanson and Foehring 1988). In fact, the oxidative enzymes in the pectoral muscle of *M. Lucifugus* have the highest activity among vertebrates (Armstrong et al. 1977).

16.3 Conclusions

Bats are fascinating model for exploring physiological responses to fasting for numerous reasons. For example, bats dedicate a very small portion of their daily activity cycle to forage and drink. Therefore, fasting is a regular part of their life cycle and all bat species are adapted to cope with short-term fasting on a daily basis. In Table 16.1 we summarize what is known. Apparently, there is a great variation in the ability of bats to undergo long periods of fasting, which seem to be associated with their respective diets. At one extreme are hematophagous species that are unable to fast longer than 72 h due to its apparent inability to store and mobilize endogenous fuels. Interestingly, these bats seem to have evolved behavioral responses that allow them to cope with several foodless days. At the other extreme are insectivorous vespertilionid and rhinolophid species that can fast for several months. They are able to endure these long periods of fasting due to several different physiological mechanisms. First, they are thermolabile and are thus able to significantly reduce their T_b and metabolism, save energy and minimize the use of endogenous stores. Second, they have a specialized machinery (e.g., transport proteins) that allows them to mobilize fuels efficiently. Third, they are able to double their m_b and store significant amount of fat in preparation for periods of shortage. Last, some species migrate long distances in search of food and/or an environment less challenging or more conducive to torpor or hibernation.

Despite their ecological importance, far less is known about fasting adaptations in bats than non-volant mammals or birds. Many questions remain open regarding the physiology, endocrinology, biochemistry, and energetics of fasting in bats. For example, substantial differences in the life histories of females and males of the same species may significantly affect their seasonal responses to fasting and their ability to withstand periods of fasting. Another question of importance is how do bats switch between different fuel types compared with other species that fast. While migration is a well-studied phenomenon in birds, very few studies focused on bats. The comparison between these two taxa is highly interesting; because of

Table 16.1 List of studies exploring physiological responses to fasting in bats

Species	Suborder/chiroptera	Body mass (g)	Diet	References	Characteristics studied
<i>Desmodus rotundus</i>	Micro-	42	Blood	McNab (1973); Freitas et al. (2003), (2005); Rouk and Glass (1970); Wilkinson (1984)	Energetics; fuel use in fasting; reciprocal food sharing; gastric histology
<i>Diaemus youngi</i>	Micro-	43	Blood	McNab (1973)	Energetics
<i>Diphylla ecaudata</i>	Micro-	34	Blood	McNab (1973)	Energetics
<i>Rowsettus aegyptiacus</i>	Mega-	160	Fruits	Keegan (1977); Caviedes-Vidal et al. (2007); Korine et al. (1999)	Carbohydrate assimilation; plasma nitrogen levels
<i>Eidolon helvu</i>	Mega-	280	Fruit	Okon (1977)	Gastric histology
<i>Artibeus lituratus</i>	Micro-	70	Fruits	Caviedes-Vidal et al. (2007, 2008); Pinheiro 2006; Protzek et al. (2010)	Carbohydrate assimilation; fuel use in fasting; hormone levels
<i>Artibeus jamaicensis</i>	Micro-	50	Fruit	Pinheiro et al. (2006)	Fuel use in fasting
<i>Glossophaga soricina</i>	Micro-	11	Fruit	Bakken et al. (2008)	Renal function in fasting
<i>Tadarida nigeriae</i>	Micro-		Insects	Okon (1977)	Gastric histology
<i>Myotis velifer</i>	Micro-	12	Insects	Rouk and Glass (1970)	Gastric histology
<i>Antrozous pallidus</i>	Micro-	21	Arthropods	Rouk and Glass (1970); Bassett (2004)	Gastric histology; renal function in fasting
<i>Molossus molossus</i>	Micro-	11	Insects	Freitas et al. (2010)	Fuel use in fasting
<i>Tadarida brasiliensis</i>	Micro-	12	Insects	Widmaier et al. (1996); Rouk and Glass (1970)	Plasma triacylglycerides; gastric histology
<i>Nyctophilus gouldi</i>	Micro-	9	Insects	Morris et al. (1994)	Reabsorption from rectum
<i>Scotophilus heathi</i>	Micro-	33	Insects	Srivastava and Krishna (2010); Roy and Krishna (2010)	Hormone levels in fasting
<i>Myotis lucifugus</i>	Micro-	10	Insects	Bauman (1990); Kronfeld-Schor et al. (2000); Townsend et al. (2008); Eddy and Storey (2004)	Hormone levels in fasting; fuel mobilization
<i>Eptesicus fuscus</i>	Micro-	20	Insects	Yacoe (1983)	Protein catabolism
<i>Leptonycteris sanborni</i>	Micro-	22	Nectar	Rouk and Glass (1970)	Gastric histology

their flight ability, these two groups have similar selection pressures, but their physiological and biochemical machineries are different. We hope this review will stimulate others to address the many questions and gaps in our knowledge to which we have called attention.

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