Limits to sustained energy intake. XIII. Recent progress and future perspectives

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Summary

Several theories have been proposed to explain limits on the maximum rate at which animals can ingest and expend energy. These limits are likely to be intrinsic to the animal, and potentially include the capacity of the alimentary tract to assimilate energy – the 'central limitation' hypothesis. Experimental evidence from lactating mice exposed to different ambient temperatures allows us to reject this and similar ideas. Two alternative ideas have been proposed. The 'peripheral limitation' hypothesis suggests that the maximal sustained energy intake reflects the summed demands of individual tissues, which have their own intrinsic limitations on capacity. In contrast, the 'heat dissipation limit' (HDL) theory suggests that animals are constrained by the maximal capacity to dissipate body heat. Abundant evidence in domesticated livestock supports the HDL theory, but data from smaller mammals are less conclusive. Here, we develop a novel framework showing how the HDL and peripheral limitations are likely to be important in all animals, but to different extents. The HDL theory makes a number of predictions – in particular that there is no fixed limit on sustained energy expenditure as a multiple of basal metabolic rate, but rather that the maximum sustained scope is positively correlated with the capacity to dissipate heat.

Key words: sustained energy expenditure, central limitation, peripheral limitation, heat dissipation limit theory, heat transfer, lactation, metabolic theory of ecology, sustained metabolic scope, milk production.

Background

All biochemical, physiological and behavioural processes require energy. An axiomatic assumption, first articulated during the 1930s, is that the supply of energy to fuel these processes cannot be limitless (Fisher, 1930). Therefore, animals must make evolutionary and individual choices in the priorities they place on different activities, because doing everything simultaneously is energetically unfeasible. This is the classic resource allocation framework that has dominated the approach to life history strategies for at least the last 80 years (Stearns, 1976; Stearns, 1977; Gittleman and Thompson, 1988; Stearns, 1989; Glazier, 1999; Garland and Rose, 2009), and it pervades thinking in many other areas of biology, such as our understanding of the evolution of ageing (the disposable soma theory) (Kirkwood, 1977; Kirkwood and Holliday, 1979). While this framework is based on the fundamental assumption that available resources are limited, the exact nature of this limitation is often not addressed. Yet the nature of the limit may ultimately be as important as the assumption of its existence, because the type of constraint will dictate the actual form of the trade-off function and available solutions.

Ingested food is the sole energy source providing resources that permit the key processes characteristic of life. In many circumstances, the amount of energy that can be ingested may be limited by its availability in the environment (e.g. Speakman et al., 2003). This is particularly the case in seasonal environments in the temperate zone that alternate between warm and cold seasons during which energy may be highly abundant in the warm season, when plants are growing, but restricted in availability during the cold non-growing season. Animals respond to seasonal reductions in food availability in different ways. However, the main responses include migration away from the area where productivity is low and reducing the demand for energy by entering some form of

metabolic arrest. Reducing energy demand can be accomplished by hibernation in mammals, which involves regulation of body temperature at a much lower level than during euthermy (Heldmaier and Klingenspor, 2000), and metabolic shut-down in ectothermic organisms, where body temperature is unregulated and the body may be allowed to freeze in 'freeze-tolerant' organisms, or to cool without freezing in 'freeze-intolerant' organisms (Storey, 2004).

Whether food is also limited during the season when primary productivity is increased and animals breed is open to question, but has often been presumed to be so (Arim et al., 2007) and in some cases it clearly is (Bozinovic et al., 2005; Bozinovic et al., 2007). Several lines of evidence, however, indicate that resources at this time may often not be limited. Perhaps the best evidence comes from studies of animal responses to food supplementation, when the environmentally available food has been added to by an artificial source of food. Boutin (Boutin, 1990) reviewed 138 studies of food supplementation in vertebrates and 129 of them were in endotherms. The responses of these animals to such manipulations follow a consistent pattern across studies. The most common changes are that animals start to breed earlier. In 39 studies where time of first breeding was reported, 33 indicated an advance in the start of the breeding season. This is consistent with the initiation of breeding being constrained by food supply. The second very common response is that animals greatly reduce the size of their home range. In 23 studies reviewed by Boutin (Boutin, 1990), 19 involved reductions in home range size. This is not consistent with the idea that food supply from the environment prior to supplementation was limited. If the supply was environmentally limited, one might anticipate that animals would continue to exploit their existing home range but increase their food intake to overcome the previous limitation. What appears instead

to happen is that animals feed to satisfy a demand that is limited by some other process. If they can achieve this by feeding for less time in a smaller home range they will do so, and this is what appears to happen when their food supply is supplemented. Feeding for less time may also be beneficial because of reduced exposure to predators and unfavourable environmental conditions. Finally, most animals do not respond to supplementation by substantially elevating their productivity. In only 9 of 21 studies reviewed by Boutin (Boutin, 1990) did the animals respond by increases in brood or litter sizes, and in all these cases the increases in the number of offspring produced were relatively small. This response again indicates that total energy intake was not limited by the environmental food supply, but rather by some other process. These modest increases in productivity could be interpreted as using the energy that had been saved by exploiting a much smaller home range. These food supplementation studies indicate that while energy supply from the environment may be limited at some times of year (e.g. in temperate zone winters), during the breeding season environmental supply of energy is probably not limited.

Intrinsic limitation of energy supply

Energy in the form of fats, carbohydrates and proteins is assimilated in the alimentary tract from ingested food, and then distributed around the body by the circulatory system – sometimes including periods of temporary storage as glycogen or triglycerides. One suggestion for the main factor limiting the amount of energy that animals can expend on biochemical, physiological and behavioural processes is the capacity of the alimentary tract to absorb energy – the 'central limitation' hypothesis (Drent and Daan, 1980; Weiner, 1989; Peterson et al., 1990; Hammond and Diamond, 1992; Weiner, 1992; Bacigalupe and Bozinovic, 2002). Another more recent suggestion is that energy utilisation is limited by the fractal distribution network of the circulatory system – the 'metabolic theory of ecology' (MTE) (Brown et al., 2002; Brown et al., 2004; Allen and Gillooly, 2007). Although relevant in this context, the MTE has seldom been invoked directly to consider limitations on sustained rates of energy intake or expenditure. One interesting idea to emerge from the central limitation hypothesis was that as the system limiting the sustained rate of expenditure (i.e. the alimentary tract including associated processing organs such as the liver) is widely regarded to be expensive to maintain (Daan et al., 1989; Daan et al., 1990; Elia, 1992; Konarzewski and Diamond, 1995; Selman et al., 2001; Brzęk et al., 2007) and makes a substantial contribution to the basal rate of energy expenditure (BMR), increasing sustained rates of expenditure would only be feasible by increasing BMR as well (Konarzewski and Diamond, 1995; Mueller and Diamond, 2001). Consequently, there is predicted to be a limiting ratio between the maximum sustained and basal rates of metabolism – called the 'maximum sustained metabolic scope'. The presence of this limiting ratio has been more easily agreed than its value, with some favouring a maximum sustained metabolic scope around $4\times$ BMR (Drent and Daan, 1980; Weiner, 1989; Weiner, 1992), while others suggest around $7\times$ BMR (Peterson et al., 1990; Hammond and Diamond, 1997). This difference may be because the former refer to the ratio between sustained energy expenditure and BMR, while the latter refer to the ratio between sustained energy intake and BMR.

Several studies have been performed that allow us to reject both the central limitation and MTE ideas as factors determining the sustained energy intake and hence expenditure. The main studies have been performed using lactating mice as an experimental model (e.g. Hammond and Diamond, 1992). The reason for choosing mice

at peak lactation to test these ideas is that during this time the animals have an enormously elevated food intake. Moreover, lactation is probably the most energy-demanding period in the lives of most female mammals (Millar, 1977; Millar, 1979; Innes and Millar, 1981; Glazier, 1985; Speakman, 2008), and therefore understanding limits at this stage has wide ecological relevance. Intake at this time also appears to be limited. For example, food intake in the MF1 outbred mouse eating regular laboratory chow increases very rapidly over the first 10 days of lactation from around 6 g on the last day of pregnancy to about 23 g on day 10 of lactation. Over the last 8 days of lactation, however, until the pups are weaned at day 18, there is no further increase in intake (Johnson et al., 2001a). Because the incoming food is the only source of energy for the lactating female to synthesise milk, this fixed intake leads to a fixed level of milk production. Consequently, if the female is raising more offspring, there is less milk to go around, and this contributes to the familiar trade-off between the litter size and the size of the individual offspring at weaning (König et al., 1988; Johnson et al., 2001a; Johnston et al., 2007; Garland and Rose, 2009). The same trade-off is observed in many mammals (e.g. Fiorotto et al., 1991; Speakman, 2008). Female mice were unable to increase either their food intake or their milk output if the number of pups they raised was experimentally increased (Hammond and Diamond, 1992; Johnson et al., 2001a); similar responses were also observed in guinea pigs (*Cavia porcellus*) (Künkele, 2000). These data have at least two implications. First, pups would drink more milk and grow larger if it was available, given they do so when they are members of a smaller litter. Consequently, their growth and the supply of milk are not regulated by offspring growth capacity, but rather by the female's ability to supply milk. Second, the female must be limited in her capacity to either intake food or synthesise milk (or both), because smaller pups derived from larger litters are at a distinct disadvantage relative to larger pups weaned from smaller litters. This disadvantage can be traced to several effects. Smaller individuals fare less well in aggressive interactions with larger individuals, and hence would be expected to be less competitive for food and mates (Wolff and Sherman, 2007). Additionally, smaller offspring often undergo subsequent catch-up growth, and this has large negative effects on their fitness (e.g. Rauw et al., 1999; Metcalfe and Monaghan, 2001; Metcalfe and Monaghan, 2003). Moreover, with extremely large litters females fail to raise their offspring at all because insufficient milk is supplied to keep all pups alive (Hammond and Diamond, 1992). If the female was able to synthesise additional milk to enable pups in large litters to grow larger, or in very large litters to enable them to survive, then she would have a fitness advantage. This limitation is consistent with the central limitation hypothesis and the MTE. Another interesting observation is that when litter size is experimentally decreased (as must be performed to provide pups to enlarge other litters), food intake at peak lactation is not scaled back until the litters are quite small (Johnson et al., 2001a). Females probably do not ingest the same peak amount of food to supply milk to these very small litters because at some point the capacity of the pups to convert this milk to growth becomes the limiting factor. Pup demand may also be the primary factor determining the mothers' food intake during the first phase of lactation between days 0 and 10, when they eat less than the peak intake.

Several manipulations of this system have been made to give lactating females additional energetically expensive tasks to perform. These manipulations included making lactating mice simultaneously pregnant (Johnson et al., 2001c), forcing them to

run to obtain their food (Perrigo, 1987), and artificially extending the duration of lactation by preventing offspring from weaning (Hammond and Diamond, 1994). The same manipulation to extend lactation has also been performed in guinea pigs (Laurien-Kehnen and Trillmich, 2003) along with a cross-species fostering experiment (Rehling and Trillmich, 2008). In all cases, the food intake was not elevated above that observed at peak lactation in natural large litters, and in response the mice made various adjustments in their energy budgets, in some cases killing some of their offspring rather than eating more food. These manipulations therefore supported the central limitation idea. A study involving manipulation of dietary composition, which was suggested to support the central limitation hypothesis, was performed in brown hares (Hackländer et al., 2002). In this experiment, hares were fed a diet that was low in fat relative to their normal diet. Hares partially compensated by increasing their intake but this was insufficient to offset the reduced energy density of the diet. The inability to completely compensate was suggested to be in part because of digestive constraints and the time taken for the gut to respond to changed diet composition.

Although these experiments were generally supportive of the central limitation hypothesis (and retrospectively the MTE), one manipulation that did result in a significant elevation of both the food and energy intake was to expose mice during lactation to the cold (Johnson and Speakman, 2001; Hammond et al., 1994). This observation was subsequently replicated in several other species including cotton rats (*Sigmodon hispidus*) (Rogowitz, 1998), deer mice (*Peromyscus maniculatus*) (Hammond and Kristan, 2000) and Brandt's voles (*Lasiopodomys brandtii*) (Zhang and Wang, 2007). It was further shown that if lactating mice are exposed to hot conditions (30°C), then their intake is limited at a much lower level (Król and Speakman, 2003a; Król and Speakman, 2003b; Król et al., 2003); this effect was also replicated recently in Brandt's voles (Wu et al., 2009). These data comprehensively showed that the central limitation (and MTE) ideas cannot be correct, because during cold exposure the mice could increase their food intake above the level that at 21°C appeared to be limiting – even to the extent that females would be prepared to kill their own offspring rather than eat more food. The phenomenal flexibility of the alimentary tract to respond to changes in demand during lactation by structural and capacity alterations probably explains why it is not limiting on intake (Green and Millar, 1987; Speakman and McQueenie, 1996; Derting and Austin, 1998; Hammond and Kristan, 2000; Derting and Hornung, 2003; Naya et al., 2007a; Naya et al., 2007b; Naya et al., 2008).

To explain the accumulated data, it was suggested that the food intake at peak lactation is dictated by a combination of demands arising from peripheral tissues – the 'peripheral limitation' hypothesis (Hammond et al., 1994). The idea that there might be a link between the basal and sustained metabolic rate that defines a maximum sustained metabolic scope could also apply under this hypothesis, as long as the peripheral tissue that limits expenditure (in this case the mammary glands) continues to be a major factor influencing BMR.

Two additional but conflicting pieces of information are available – one of which strongly supports the peripheral limitation hypothesis based on the synthetic capacity of the mammary glands, and a second which strongly refutes it. Hammond and colleagues (Hammond et al., 1996) sought to test the peripheral limitation hypothesis directly by surgically removing some of the mammary tissue from Swiss-Webster outbred mice. It was argued that if the mammary glands were not working at maximal capacity, then by removing some of the glands, the mouse would be able to increase her milk production in the remaining tissue to meet the demands of the pups. Alternatively, if the peripheral limitation idea was correct and the glands were working at maximal capacity, she would be unable to increase milk output after this manipulation. The data strongly supported the idea that the mammary tissue was working at maximal capacity. If Hammond and colleagues (Hammond et al., 1996) were correct that mammary gland production was always at maximal capacity and that when exposed to different temperatures mice were simply responding to the thermoregulatory demands in other tissues, milk production would be constant across the different temperatures and pup growth might be anticipated to be independent of temperature. Alternatively, if pup energy demands increased in the cold, those in the cold would be expected to be smaller than those raised at room temperature or under hot conditions. In fact, neither situation proved to be the case when these parameters were measured in MF1 mice. Milk production was increased as the temperature got colder (Johnson and Speakman, 2001) and decreased in hot conditions (Król and Speakman, 2003b), and pups raised in the cold were consequently the largest and those under hot conditions were the smallest (Johnson and Speakman, 2001; Król and Speakman, 2003a; Speakman et al., 2004). Note that these studies were performed in two different strains of mice. Moreover, adding to the confusion, in cotton rats exposed to the cold, milk production was no different to that for rats in the warm (Rogowitz, 1998).

New ideas on limits to sustained energy intake

We (Speakman and Król, 2005) outlined three new hypotheses that might explain the available data at that time. These were the 'saturated neural control' hypothesis, the 'seasonal investment' hypothesis and the 'heat dissipation limit' (HDL) theory (see also Speakman and Król, 2010a). The saturated neural control hypothesis was based on our expanding knowledge about factors in the brain that regulate the intake of food (Schwartz et al., 2000; Woods et al., 2000; Mercer and Speakman, 2001). It is known that during lactation intake is regulated by a number of neuropeptides in the hypothalamus – including neuropeptide Y (NPY) (Malabu et al., 1994; Pickavance et al., 1999; García et al., 2003; Chen and Smith, 2004), agouti-related peptide (AgRP) (Chen et al., 1999; Phillips and Palmiter, 2008), pro-opiomelanocortin (POMC) (Smith, 1993) and cocaine- and amphetamine-regulated transcript (CART), which are strongly expressed in the arcuate nucleus and dorsomedial hypothalamus (Brogan et al., 2000). These neuropeptides interact with melanocortin receptor populations in the paraventricular nucleus (Chen et al., 2004) as well as systems in the brain stem and reward centres of the dopaminergic system in the nucleus accumbens (Gammie et al., 2005; Xiao et al., 2005). The argument in the saturated neural control hypothesis was that this regulatory system in the brain may be stimulated by a number of peripheral signals. For example, in lactation there is a profound reduction in circulating leptin levels (Pickavance et al., 1998; Brogan et al., 1999; Kunz et al., 1999; Woodside et al., 2000), which potentially stimulates food intake *via* inhibition of neurons expressing POMC and CART (Elias et al., 1998) and stimulation of neurons expressing NPY and AgRP (Crowley et al., 2004; Crowley et al., 2007). There is a limit, however, to how much this system can be stimulated – in the case of leptin, for example, it is impossible to stimulate intake more than can be achieved by reducing the hormone levels to zero. It may be that during lactation there are only a limited number of signals available [for potential signals additional to leptin see e.g. Josephs et al. (Josephs et al.,

2007), Woodside (Woodside, 2007) and Xu et al. (Xu et al., 2009)], and that once these have been maximally recruited, no further stimulation of intake is possible. Processes that signal to the brain *via* the same compounds would then be unable to further stimulate food intake (for example exercise), but processes that tapped into new signalling pathways (for example cold) might be able to stimulate additional intake. Although our knowledge about food intake regulation in rodents during lactation is expanding (Li et al., 1998a; Li et al., 1998b; Chen et al., 1999; Li et al., 1999a; Li et al., 1999b; Brogan et al., 2000; Chen and Smith, 2004; Chen et al., 2004), the available information is not sufficient to test this idea. In support of the general concept, however, it appears that lowered leptin concentration may be an important factor leading to increased food intake in the cold (Abelenda et al., 2003; Tang et al., 2009) (but see Zhang et al., 2009), while in lactation it may be a contributory factor, but not the primary driver of elevated food intake (Woodside et al., 2000; Smith and Grove, 2002; Vernon et al., 2002; Denis et al., 2003). Interestingly, mice selected for high voluntary locomotor activity have low levels of circulating leptin relative to their fat contents (Girard et al., 2007), and this may underpin the inability of mice to combine exercise and lactation (Perrigo, 1987).

The seasonal investment hypothesis suggests that all the decisions made by the female about what to invest in, and at what level, reflect evolutionary trade-offs moulded by seasonality in the wild. By this argument, it is suggested that females at 21°C are physiologically capable of increasing their food intake and their investment in larger litters so that the individual offspring could grow larger, but that they 'choose' not to make this investment based on deep-rooted selective pressures in their evolutionary history. Trade-off decisions are presumed to result in lower levels of food intake than physiological limits, which are therefore seldom reached. One reason why female mice may have variable investment patterns at different ambient temperatures is perhaps related to the reproductive value of offspring that are born at such temperatures in the wild (Bronson and Perrigo, 1987). For example, pups that are born early in the year at the start of the breeding season, when it is coldest, have the greatest reproductive value because they are able to mature and breed before the season ends. However, pups born late in the season, when it is hottest, have the least reproductive value because they are unable to mature and breed before the breeding season ends. They must then survive through the non-breeding season before they can contribute to the population. It makes evolutionary sense therefore for females to invest substantially more into offspring born under cold conditions than in hot conditions. This hypothesis does not, however, explain why females do not elevate their food intake when faced with other competing demands at a fixed ambient temperature (for example exercise or being simultaneously pregnant). Moreover, if it is optimal to generate pups that weigh a certain amount when weaned at a given temperature, it is unclear why females choose to invest less than this when raising large litters, and ultimately as litters get very large why they choose to produce so little milk that the litters die. Both these latter observations suggest that the total investment by a female is constrained by some additional factor(s).

The HDL theory provides an alternative mechanism that may limit food intake. All energy intake that is not used for growth, storage or export ultimately appears as heat. Under this theory, it is suggested that animals are limited in their capacity to get rid of this heat by physical constraints, combined with an inability to store the heat internally because of the risks of hyperthermia. Severe hyperthermia is well established to be fatal. In the USA, for example, a child dies every 10 days because it is left in a car that overheats (McLaren et al., 2005; Null, 2010). However, even non-lethal hyperthermia can lead to a whole range of detrimental effects, which include elevated protein damage, increased inflammatory responses, apoptosis, increased DNA damage in germ cells, oxidative stress, mitochondrial dysfunction, liver damage, cerebral ischaemia, disrupted blood–brain barrier function and embryonic death in pregnant females (e.g. Arnaud et al., 2002; McAnulty et al., 2005; Yan et al., 2006; Chang et al., 2007; Lee et al., 2008; Hansen, 2009). In contrast, mild hypothermia appears to bring a range of benefits including neuroprotection (Salerian and Saleri, 2006; Cheng et al., 2008; Salerian and Saleri, 2008) and enhanced lifespan (Conti et al., 2006; Conti, 2008). The HDL theory suggests that at a given ambient temperature, the capacity to dissipate heat is limited by the physics of heat transfer across the animal surface (Speakman and Król, 2010a). Hence, when animals are given additional tasks to perform at peak lactation, such as running to get their food or being simultaneously pregnant, or if lactation is artificially extended, they cannot elevate their food intake because this would necessitate an increase in heat production that they are physically incapable of dissipating. Similarly, increased litter sizes do not stimulate the female to generate more milk, enabling the pups to grow larger, because the female cannot increase milk production without the heat production that accompanies milk synthesis, which would necessitate greater heat dissipation. However, exposing a female mouse to the cold at peak lactation does not give her an extra burden, but rather removes the constraint on her ability to dissipate heat. This removed constraint allows her to ingest more food, synthesise more milk and wean larger pups (Johnson and Speakman, 2001; Speakman et al., 2004). Conversely, putting the lactating female into hot conditions has exactly the opposite effect (Król and Speakman, 2003a; Król and Speakman, 2003b). It reduces her capacity to dissipate heat, enforces a reduction in food intake and milk synthesis and leads to stunted offspring.

One factor that radically affects the capacity to dissipate body heat is body size, because as animals get larger their surface to volume ratio gets lower (Rubner, 1883). The HDL theory therefore predicts that problems with dissipating heat at peak lactation will be more evident in larger animals (Speakman and Król, 2010a; Speakman and Król, 2010b). This is indeed the case, and there is a rich literature predating the HDL theory, showing that heat dissipation is a primary factor influencing lactation performance in many large domesticated mammals such as pigs, sheep, goats and cattle (Quiniou et al., 2000; Renaudeau and Noblet, 2001; Renaudeau et al., 2001; Lacetera et al., 2003; Renaudeau et al., 2003; Cam and Kuran, 2004; Berman, 2009; Silva et al., 2009). In fact, amelioration of heat stress in lactating dairy cows is a major issue in the dairy industry, and reduced milk production and increased mortality during heat waves cost many millions of dollars. In addition to this strongly supportive evidence for the HDL theory from large domesticated mammals, there is also a diverse literature on factors that affect maternal suckling behaviour in rodents. These data indicate that a key factor influencing maternal suckling duration is the risk of the mother overheating during the suckling bout (Leon et al., 1978; Leon et al., 1983; Bates et al., 1985; Leon et al., 1985; Adels and Leon, 1986; Newkirk et al., 1998). Further support for the HDL theory comes from comparisons of the reproductive performance of mice selectively bred to enhance their capacity to dissipate heat (Nielsen et al., 1997a; Nielsen et al., 1997b; Kgwatalala et al., 2004; McDonald

and Nielsen, 2006). These mice have elevated milk production and raise heavier litters (McDonald and Nielsen, 2007).

An alternative explanation of the trends in maternal food intake with ambient temperature is that they reflect effects of temperature on the pups rather than on the mother. To test the HDL theory, we (Król et al., 2007) experimentally manipulated MF1 mice during lactation to elevate their capacity to dissipate heat, independent of changes in ambient temperature, by shaving off their dorsal pelage. This targets the capacity of the female to dissipate heat, independent of effects on the offspring. In line with the HDL theory, the shaved mice at 21°C elevated their food intake, and used this extra intake to synthesise more milk and wean larger offspring relative to unshaved mice at the same ambient temperature. In sheep (*Ovis aeries*), a similar experiment in late gestation (sheared on day 100 of gestation and the removed pelage maintained through lactation) also resulted in a greater milk yield relative to unsheared controls (Cam and Kuran, 2004). Moreover, shaving off the dorsal pelage in rats (*Rattus norvegicus*) resulted in an increase in suckling duration of the mothers, although in that study milk production was not measured (Adels and Leon, 1986).

Testing the heat dissipation limit theory

The HDL theory was established by examination of the factors limiting performance of laboratory mice that have been selected over time for high litter sizes and good parental performance. One potential problem with using these animals is that they may be physiologically exceptional, and working at rates of milk production that are abnormally high. Consequently, they may become limited by heat dissipation, as we demonstrated (Król et al., 2007) in our shaving experiment, but this limit would not normally apply in wild animals working at much lower rates of productivity. To explore this idea, Wu and colleagues (Wu et al., 2009) measured the responses of Brandt's voles to increased ambient temperatures during lactation. Brandt's voles have litters of between 2 and 9 offspring, which is substantially fewer than the MF1 mouse (average weaned litter size 11.3) (Johnson et al., 2001a). Wu and colleagues (Wu et al., 2009) found that at high ambient temperatures there was a decrease in milk production, and hence pup growth, until about day 12 of lactation, when the pups started to self feed. Overall, these data support the HDL theory; however, this effect was most profound in mothers with the largest litters, and in very small litters there was no significant effect. This study raises the question therefore whether small rodents that have exclusively small litters would be affected by heat dissipation limits, and hence the wider validity of the HDL theory.

Simons and colleagues (Simons et al., 2011) explored the effects of ambient temperature and shaving on the performance of common voles (*Microtus arvalis*), which routinely raise between 1 and 6 pups (modal litter size 3). They found that food intake in lactation, and across litters of different sizes, reached an asymptote of about 12–14 g per day at 21°C. When these voles were exposed to 30°C, their intake at peak lactation fell to about 7 g per day and this was correlated with decreased milk production. These data are consistent with the HDL theory. However, an alternative explanation is that the reduced food intake of the mothers was driven primarily by reduced pup demand. This seems unlikely, however, because, as was observed in mice, the pups raised at 30°C were stunted relative to those raised at 21°C, suggesting that they had been relatively starved of resources. To address the possibility that the reduced intake reflected lower pup demand rather than a decreased capacity to dissipate heat by the female, Simons and colleagues (Simons et al., 2011) shaved the females during lactation

at 30°C. As predicted by the HDL theory, this led to a small but significant increase in pup growth. Although maternal food intake and milk production showed a trend in the right direction (both upwards), they did not reach statistical significance. Overall, this study provides support for the wider validity of the HDL theory even in small mammals that raise small litters.

Although the HDL theory explains many facets of the experimental work previously performed on limits to sustained energy intake and expenditure, as well as patterns of maternal suckling behaviour in rodents and lactating performance of domestic animals, one experimental result that it cannot explain is the failure of Swiss-Webster mice to upregulate their intake of food and their milk production when their mammary glands were surgically manipulated at room temperature (Hammond et al., 1996). This may suggest that fundamentally different factors are limiting the capacity to generate milk and regulate food intake in different strains of mice (Fig. 1). Supporting this suggestion, a study has been performed recently on Swiss mice that attempted to replicate the shaving experiment we had performed on MF1 mice (Król et al., 2007). This work revealed an effect of shaving on food intake, but did not result
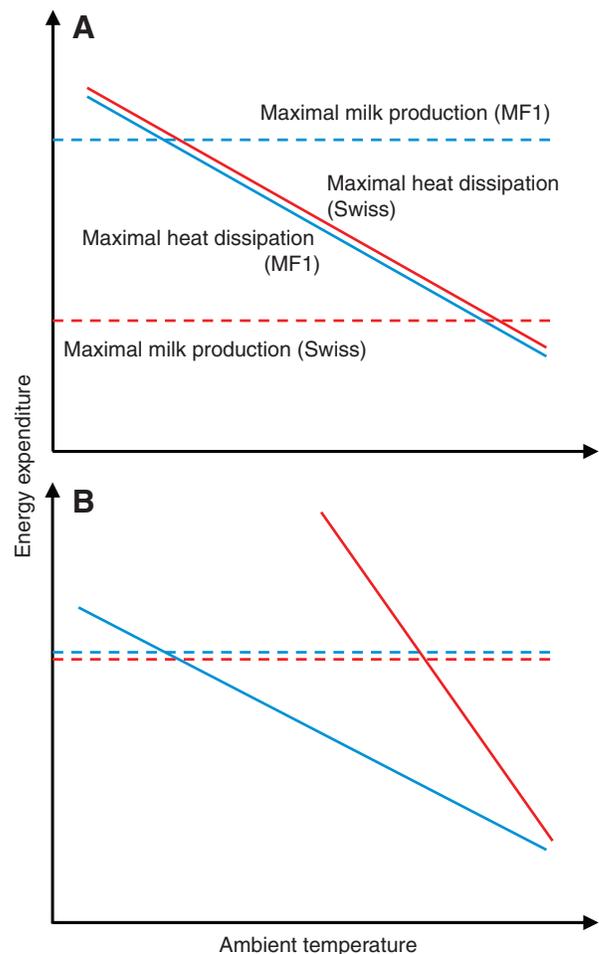

Fig. 1. Two alternative scenarios explaining the different responses of MF1 (blue) and Swiss (red) mice to manipulations of their energy budgets at peak lactation. In A, the two strains have similar maximal capacities to dissipate heat as a function of ambient temperature (solid lines), but their maximal capacities to synthesise milk (dashed lines) differ. In B, their maximal capacities to synthesise milk (dashed lines) are similar, but their maximal heat dissipation capacities (solid lines) are different. Actual data from Table 1 suggest that scenario A is more likely.

in any increase in pup growth (Zhao and Cao, 2009). However, this result is not a strong refutation of the HDL theory, because milk production was not measured. It is theoretically possible that the female mice did increase their milk production, but for some reason the offspring did not translate this increased production into greater growth. To counter this argument, the experiment has been repeated (Zhao et al., 2010) and the same effects on food intake were reported. When milk production was quantified, there was no significant elevation as a result of shaving. The power to detect a significant effect in this sample was 94.5%, suggesting that the responses of the Swiss mice to shaving were indeed very different from those of the MF1 mice (Król et al., 2007).

There are two potentially different interpretations of the strain differences that might contribute to the contrasting results between the studies. First, the two strains may differ in their maximum capacity to synthesise milk, but have similar maximum capacities to dissipate heat in relation to ambient temperature (Fig. 1A). Consequently, when the MF1 mice were shaved they could use the elevated capacity to dissipate heat to increase milk production, because they were well below their maximum milk production capacity. In contrast, Swiss mice had elevated heat loss, reflected in their increased feeding time and greater food intake (Zhao and Cao, 2009), but an inability to upregulate their milk production (Zhao et al., 2010), because their maximal milk production capacity is low relative to their capacity to dissipate heat. An alternative scenario is that the two mouse strains have similar maximum milk production capacities but divergent maximum capacities to dissipate heat (Fig. 1B), with MF1 mice having poor heat dissipation capacity (good insulation). In this case, shaving the MF1 mice would again elevate their low heat production capacity and allow them to generate more milk, but in Swiss mice their heat production capacity already well exceeds their milk production capacity, and shaving would have no impact.

Examination of the detailed energetics data from the responses to shaving in the two strains (Table 1) suggests that the gross intake of energy is similar, but that the digestive efficiency of the MF1 strain is about 10% higher, meaning that the metabolisable energy intake in the MF1 mouse is 38.3–43.8 kJ day^{-1} higher. Daily energy expenditure data of control mice of the two strains were also very similar (121.8–125.0 kJ day^{-1}). This suggests that the mice had similar maximal heat dissipation capacities. The biggest differences in the energy budgets were in the milk production (Table 1). Swiss mice exported between 41.8 and 58.9 kJ day^{-1} less energy in milk and were less efficient at this production. Hence, in MF1 mice, the gross efficiency of milk production was about 55%, but in Swiss mice it was only about 43%. These data suggest that the model most likely to explain the differences between strains is that illustrated in Fig. 1A, rather than in Fig. 1B. Despite these inefficiencies and the fact that the Swiss mothers produce on average only 64.6–71.1% of the amount of milk energy produced by the MF1 mouse, a surprising result of this comparative exercise was that weaned litter masses of the two strains were about the same [Swiss control litters were 1.5 g (1.9%) heavier than their MF1 counterparts and litters from Swiss shaved mice were 6.8 g (7.7%) lighter than litters raised by shaved MF1 mice]. This suggests much greater efficiency in milk utilisation by the Swiss pups. Exact figures for the efficiency cannot be calculated as energy content of the Swiss pups is unavailable, but assuming no large differences in pup energy content between strains would suggest that Swiss pups are around 30% more efficient at converting ingested milk into growth. This may be an adaptive response to the poor milk production capabilities of their mothers, and emphasises that caution is required before estimating maternal milk production from pup growth data. Until data are available in the same detail for other species, it remains unclear whether the high milk production capacities of the MF1 mouse, or the low milk production capacities of the Swiss mouse are more typical among other mammals. Data for the Brandt's vole (Wu et al., 2009) are also presented in Table 1. It is clear from these data that the Brandt's vole has a profile more similar to that of the Swiss mouse. It has an efficiency of digestion around 63% and an efficiency of milk production of only 28–33%. Yet despite this profile, an experimental manipulation that involved exposure to hot conditions (30°C) in lactation supported the HDL theory (Wu et al., 2009), because milk production in this circumstance was suppressed (Table 1). In contrast, in the same species, exposure to cold conditions (5°C) resulted in elevated food intake, but a reduction in litter growth (Zhang and Wang, 2007), perhaps indicating a failure to upregulate milk production, which was not measured directly.

Table 1. Comparative energetics of peak lactation in dorsally shaved (S) and unshaved control (C) MFI mice and Swiss mice exposed to ambient temperatures of 21°C and 23°C, respectively

	MF1 mice (21°C)			Swiss mice (23°C)			Brandt's voles	
	C	S	S–C	C	S	S–C	21°C	30°C
Reproductive performance								
BM (g)	46.0	45.7	−0.3	49.5	49.2	−0.3	53.4	52.9
Litter size (N)	11.4	11.3	−0.1	10.6	10.2	−0.4	7.3	7.8
LM (g)	79.6	91.8	12.2	81.1	85.1	4.0	–	–
Energy flux (kJ day^{-1})								
GEI	333.3	372.4	39.1	317.5	355.5	38.0	249.0	173.2
MEI	266.3	297.2	30.9	227.7	253.4	25.7	158.8	105.6
DEE	121.8	130.8	9.0	125.0	145.9	20.9	105.7	75.7
MEO	144.5	166.4	21.9	102.7	107.5	4.8	53.1	29.9
Efficiencies (dimensionless)								
MEI/GEI	0.799	0.798		0.717	0.713		0.64	0.61
MEO/MEI	0.543	0.559		0.451	0.424		0.334	0.283

Data for MF1 mice (Król et al., 2007) and Swiss mice (Zhao et al., 2010) were obtained from previous studies. Data for unshaved Brandt's voles lactating at 21 and 30°C are also shown (Wu et al., 2009).

BM, female body mass at peak lactation; LM, total litter mass at weaning; GEI, gross energy intake; MEI, metabolizable energy intake (GEI minus energy in faeces and urine); DEE, daily energy expenditure; MEO, milk energy output; MEI/GEI, digestive efficiency; MEO/MEI, milk production efficiency; S–C, difference between shaved and control mice.

These data suggest that different limits are likely to come into play under different conditions in different species (Fig. 2), and hence acceptance or rejection of the two theories (peripheral limitation and heat dissipation) will depend entirely on whether the species in question has a high, medium or low maximal milk production capacity, compared with a high medium or low maximal heat dissipation capacity, and exactly what experimental protocol is used to test between them. For an animal with high maximal milk production capacity and a low heat dissipation capacity, the animal will always be constrained by its capacity to dissipate heat and hence will be expected to increase its milk production when transferred from warm to cold conditions, and decrease its milk production when transferred from warm to hot conditions. Shaving this animal to convert it from a low to a medium heat dissipation capacity will also result in elevated milk production, because the heat dissipation capacity is always lower than the maximum milk production capacity (black dots in Fig. 2C). This is probably the situation pertaining in the MF1 mouse. In contrast, if we consider an animal with a low maximal milk production capacity, this animal

will always be constrained by its milk production capacity whatever its capacity to dissipate heat (high, medium or low). Hence transferring such an animal from warm to hot, or from warm to cold, or shaving it, will not lead to elevated milk production, because the maximal milk production constraint always lies below the maximal capacity to dissipate heat (red dots in Fig. 2C). This is perhaps the situation pertaining in Swiss mice, although the experimental exposure to hot temperatures has not yet been performed in these animals. Finally, consider an animal with medium capacity to produce milk and high heat dissipation capacity. In this case, transferring the animal from warm to hot conditions will result in reduced milk production, consistent with the HDL theory, but transferring it from warm to cold conditions will not elevate milk production, consistent with the peripheral limitation hypothesis (green dots in Fig. 2C). This is probably the situation in Brandt's voles and perhaps also in cotton rats. Common voles may be similar to Brandt's voles or to MF1 mice, but the exposure to low ambient temperatures to distinguish which they are more similar to has not yet been performed.
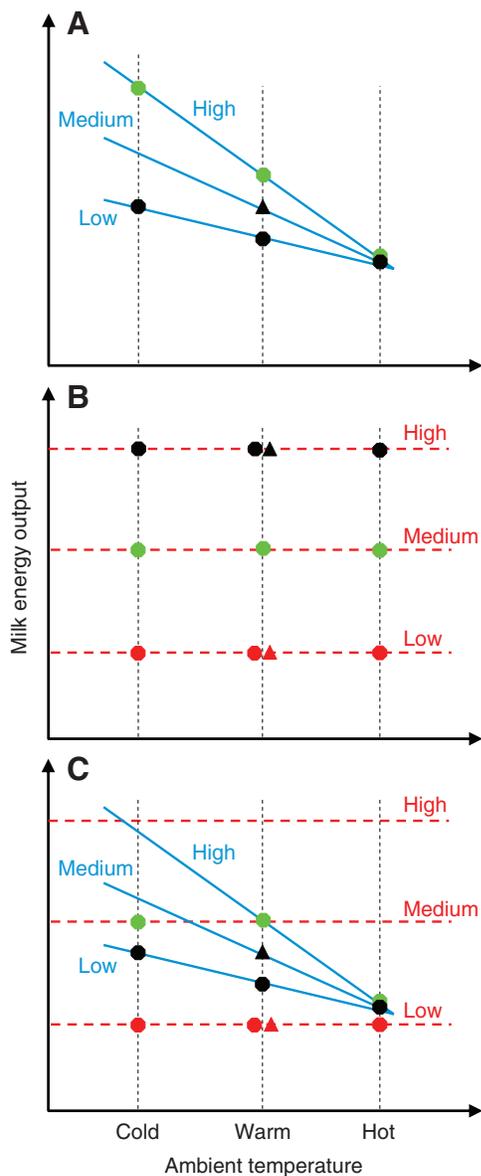

Fig. 2. A theoretical framework for understanding the relationship between the heat dissipation and peripheral limitation theories. The x-axis is ambient temperature with three temperatures indicated. In experiments with small rodents cold has been equated to 5–8°C, warm to room temperature (21–23°C) and hot to thermoneutral temperatures (30°C). The y-axis is milk energy export. In A, the animals are constrained in their milk energy output only by their capacity to dissipate heat. Three different capacities to dissipate heat are illustrated by solid blue lines. If the only constraint on milk energy export is capacity to dissipate heat, then this model predicts that animals will increase their milk production as it gets colder (illustrated by the black points for an animal with low heat dissipation capacity and green dots for one with high heat dissipation capacity). If an animal with low heat dissipation capacity is shaved to increase its capacity to dissipate heat, this will also increase its capacity to generate milk (black triangle). In B, the only factor constraining milk production is the capacity of the mammary glands. Three different levels of maximal milk production capacity are indicated by dotted red lines. In each case this is a theoretical maximum, limited only by the capacity of the mammary tissue, which is independent of ambient temperature. Milk production is consequently independent of ambient temperature (illustrated by the red dots for an animal with low milk production capacity, green dots for one with medium capacity and black dots for one with high milk production capacity). Shaving a mouse has no impact on its capacity to produce milk (red triangle for a shaved mouse with low milk production capacity, and black triangle for a shaved mouse with high milk production capacity). In C, these two different constraints are combined. Actual milk export in relation to temperature then depends on the combination of mammary capacity and heat dissipation capacity. For some animals mammary capacity will constrain milk export before heat dissipation, and for others the reverse will be the case. Three different animals are illustrated with coloured dots and triangles that represent the milk energy production at different ambient temperatures. The black dots are for an animal with a high milk production capacity, but low heat dissipation capacity. If this animal is shaved to convert it to an animal with a medium heat dissipation capacity the result is the black triangle. This animal increases milk production as temperature falls and responds positively to shaving. The red dots are for an animal with low mammary capacity to produce milk. In this case, it does not matter what the heat dissipation capacity is because the animal is always constrained by mammary capacity. If this animal is shaved the result is the red triangle. This animal shows no response in milk production to either temperature or shaving manipulations. The green dots are for an animal with medium dissipation capacity and medium milk production capacity. For this animal at high temperatures milk production is heat limited, but at low temperatures it is limited by mammary capacity. Consequently, exposing it to cold has no effect on milk production, but exposing it to high temperatures suppresses milk production.

This framework in Fig. 2 generates some additional points of interest. First, whatever the capacity of the mammary glands of an animal to produce milk, and no matter how good its thermal insulation and hence how low its capacity to dissipate heat, there will always come a point when it is sufficiently cold that the capacity to generate milk will be exceeded by the capacity to dissipate heat. At that ambient temperature and all colder temperatures, the animal will be peripherally limited. The key question then is not whether the peripheral limitation or the HDL theory is correct, but rather at which ambient temperature peripheral limits become more significant than heat dissipation limits. If the transitional temperatures are generally lower than the ambient temperatures experienced by the animals in the wild during their breeding seasons, then heat dissipation will be a more important phenomenon constraining lactation. However, if the transitional temperatures are normally higher than the temperatures experienced in the wild, then peripheral limits will be the more important constraint. At present, after about 20 years of accumulated effort, we know that for MF1 mice this temperature is less than 8°C (Johnson and Speakman, 2001), for Brandt's voles (Wu et al., 2009) and cotton rats (Rogowitz, 1998) it is probably somewhere around 23°C, for common voles it is less than 21°C (Simons et al., 2011) and for Swiss mice (Zhao et al., 2010) it is above 20–22°C. The current sample is clearly too small to draw any firm conclusions and studies are needed of a wide diversity of mammals to establish the likely importance of the different limits in the wild. Ideally, such studies would include the generation of complete energy budget data (as in Table 1) for lactating females raising offspring at a variety of ambient temperatures. One prediction, however, is that larger animals will have lower mass-specific capacities to dissipate heat because of their surface to volume ratios, and all else being equal, it is likely that the transition temperatures will increase in relation to body mass, making it more probable that heat dissipation limits will be a constraining factor on endothermic animals as they get larger.

A second point to note is the predicted effects of shaving at different ambient temperatures. This model suggests that shaving at high temperatures will have a very small or no impact on milk production, while at low temperatures the effects will be magnified (unless the maximal milk production capacity is reached). This may explain why the effects of shaving observed by Simons and colleagues (Simons et al., 2011) in common voles at 30°C were relatively small, compared with the effects observed in MF1 mice shaved at 21°C (Król et al., 2007). However, there is clearly a potential species difference as well, which complicates the comparison, and it would therefore be useful to replicate our shaving experiment in mice, but expose them to 30°C rather than 21°C, to explore whether the effect of shaving is diminished. This would be a useful validation of the model in Fig. 2, if not a test of the HDL theory.

A recent study has replicated our dorsal shaving experiment (Król et al., 2007) in Siberian hamsters (*Phodopus sungorus*) and has also shown an increase in maternal food intake in the shaved females, but found no evidence of elevated pup growth, which might be indicative of them using this increased capacity to dissipate heat to increase milk production (Paul et al., 2010) – but see the above note and data in Table 1 concerning the inadequacy of using pup growth as a measure of maternal milk production. This study, however, as acknowledged by the authors in their discussion, is not a rigorous test of the HDL theory because the litter sizes of the animals were experimentally manipulated to be either 2 or 4 pups. This was substantially lower than the average litter size in

captivity of 7 pups. It is possible that these small litters were in the size range where the primary limitation is the capacity of the offspring to convert milk intake into growth, rather than the milk production capacity of the female (see above discussion of the responses to MF1 mice to litter size reductions). Supporting this view, the weaned size of the offspring was independent of litter size at two different ambient temperatures (5°C and 23°C), indicating that females with 4 pups were secreting twice as much milk as those raising 2 pups, and were hence not under any constraint in their milk production. It is perhaps not surprising, therefore, that the females that were shaved did not elevate their milk production, because the pups may have been unable to convert any increased milk production into elevated growth. Lending weight to this interpretation for a role of litter size is the observation that lactating Brandt's voles exposed to hot temperatures decreased their investment in larger litters but not in smaller ones (Wu et al., 2009). It would be interesting to know whether shaving Siberian hamsters at 23°C, when raising their usual litter sizes, leads to elevated milk production and increased pup growth, and also to know the effects of transfer of mothers raising natural litters from 23 to 30°C.

A test of the HDL theory has also recently been performed in brown hares (*Lepus europeaus*) (Valencak et al., 2010). In this study, the authors did not shave the hares but instead used features of the suckling behaviour of lagomorphs to independently manipulate offspring demands and the maternal capacity to dissipate heat. Hares only suckle their offspring for about 10 min every day. This enables a measure of milk production from the weight change of the suckled pups over the suckling period. It also permits exposure of the offspring to a different temperature from that of the mother during the rest of the day. In this experiment, there were three separate groups. In two groups, the mothers were exposed to warm conditions, and in one group they were exposed to the cold. For the two groups where the mothers were exposed to the warm conditions, the offspring were either exposed to the cold or to the warm. For the mothers in the cold, their offspring were also in the cold. The HDL theory predicts in this circumstance that at peak lactation the food intake and milk production would be dependent only on the temperature experienced by the mothers and independent of pup demands. In contrast, if the mothers were only responsive to pup demands then they would invest more milk in those pups that had been exposed to the cold, independent of the temperature they experienced themselves, since these pup demands would be greatest. The response of the hares was more complex than these simple predictions. Taking only the last part of lactation, when the hares were at peak lactation and milk production was maximised, the responses of the mothers matched exactly the predictions of the HDL theory [see figure 3 in Valencak et al. (Valencak et al., 2010)]. However, earlier in lactation, when food intake and milk production were not yet at peak levels, the pattern matched more closely the expectation based on pup demands. This pattern does not conflict with the HDL theory, since at this time the hares were not at peak food intake or milk production. Nonetheless, the authors claimed that the pattern did disprove the HDL theory, because at one point during mid-lactation the food intake of the hares raising the litters exposed to the cold was significantly higher than that at the peak lactation 3 weeks later, when the HDL theory predicted they were constrained. However, this is not a strong argument because the higher intake at mid-lactation might have been used in part to deposit fat, which would not have been detected with the sensitivity of the measures being made. This stored energy would not contribute to heat production, permitting them to have a higher intake than at peak lactation.

Without a more comprehensive assessment of the entire energy budget, these data do not conflict with the HDL theory. Overall, this experiment provides support for the HDL theory, because the pattern of intake and milk production at peak lactation, when animals were most likely limited by milk production capacity, matched exactly the theoretical predictions.

Implications of the heat dissipation limit theory

The HDL on sustained metabolic rate probably applies in many situations and is not just applicable in lactation. We have detailed elsewhere some of the broad implications of this theory for our understanding of animal energetics in general – including Bergmann's rule, latitudinal and altitudinal trends in reproductive output, the relationship between daily energy expenditure in the field and body mass, and the evolution of ageing (Speakman and Król, 2010a; Speakman and Król, 2010b). We conclude here with answers to two commonly asked questions about the theory, and provide two additional implications that were not in these previous papers.

First, we will address two often asked questions. The first question is, if being shaved in lactation is advantageous, then why do lactating females not naturally lose their pelage in lactation? One factor is that the pelage plays additional roles to that of insulation (e.g. camouflage, signalling and protection from ectoparasites), which may influence the costs and benefits of shedding it. However even if we disregard these effects, the pelage thickness of the female is a compromise between the need to dissipate heat when suckling to offspring and the need to conserve heat when foraging (Speakman and Król, 2010a). The net sum of this trade-off is never likely to be at a condition where the female finds it advantageous to be completely bald in lactation, except in rare situations where the breeding female never goes out to forage – a possible example is the naked mole-rat. It might be expected, however, that in all endotherms the pelage or plumage would become substantially thinner in the warmer breeding season to facilitate heat loss and hence greater reproductive energy expenditure (Speakman and Król, 2010a). We are not aware of direct tests of this prediction. However, it is well established that animals that moult regularly shift from a thick winter coat with high insulative capacity to a much thinner summer coat, which we suggest facilitates heat dissipation in the warmer months. It is interesting to note that when female mice are shaved, their pelage does not grow back in lactation at anywhere near the rate it does in non-reproductive females (E.K., unpublished) (see also Paul et al., 2010). This seems to be because the hormonal milieu in lactation prevents hair growth. This effect is completely consistent with the HDL theory. Further support for the importance of being able to dissipate heat in lactation comes from observations that female voles build poorer insulated nests than males (Redman et al., 1999) and female American red squirrels (*Tamiasciurus hudsonicus*) utilise poorly insulated nests more often during lactation (Guillemette et al., 2009).

The second question often asked is if heat dissipation is maximised at cold temperatures, then why do animals not time their breeding to coincide with the times of year when it is coldest, rather than what they generally do, which is breed when it is warmest? We hypothesise that animals shuttle seasonally between situations where food supply is limited to situations where food supply is not limited, but where they are instead constrained by their capacity to dissipate heat. The period when food supply is constrained is generally also the time of year when it is coldest. Hence, while animals might have a greater capacity to dissipate heat in these conditions, they do not have the resources available in the environment to match these high energy expenditures. In these environmental conditions, many mammals attempt to minimise their energy requirements, utilising both morphological (thick pelage) and behavioural (reduced activity) strategies (Humphries et al., 2005; Zub et al., 2009). A second consideration is that while lactating at low temperature may be optimal for the milk production of the mother, it may be detrimental to the pups – in terms of reducing their growth capacity and also elevating their mortality. Ultimately, in the wild, fitness may then be a trade-off between the contrasting effects of temperature on pups and their mothers (Paul et al., 2010) (Simons et al., 2011).

Finally, we end with two novel implications of the HDL theory. The first concerns the function of fat loss during lactation in small rodents, and the second relates to the idea that sustained metabolic rates are linked to basal metabolism such that there is a maximal sustained metabolic scope at around 4× or 7× BMR. During lactation, many small rodents withdraw almost all of their body fat stores (e.g. Johnson et al., 2001b; Król et al., 2003). It has been widely assumed that the main purpose of this withdrawal is to provide energy that supports the elevated food intake. However, quantification of the contribution of this fat to the total energy budget in lactation in mice reveals that its significance is very minor, amounting to around 2–4% of the total energy supply (Speakman, 2008). An alternative hypothesis is that the main function of reducing body fat is to reduce levels of circulating leptin, which then contribute to the stimulation of food intake (Speakman, 2008). This idea is supported by the observation that food intake at peak lactation in Brandt's voles is negatively correlated with circulating leptin levels (Zhang and Wang, 2008). We have recently tested this hypothesis experimentally by giving exogenous leptin to lactating female Brandt's voles to bring their circulating levels back to the levels of non-reproductive animals, and examining the impact on food intake (Cui et al., 2011). These experiments suggest that about 16% of the food intake at peak lactation can be attributed to the reduction in leptin levels, over 4× greater effect on the energy intake than the contribution of the energy from the withdrawn fat. This effect was similar in magnitude to that reported in previous studies that have given leptin to lactating females (Woodside et al., 2000; Stocker et al., 2007). However, another consequence of this leptin treatment in lactation was an increase in the levels of uncoupling protein 1 (UCP1) in brown adipose tissue (BAT) (see also Xiao et al., 2004). It is well established that BAT undergoes profound changes in lactation. These include hypotrophy, downregulation of UCP1 and UCP3 and reductions in thermogenic capacity (Trayhurn et al., 1982; Trayhurn, 1985; Trayhurn and Richard, 1985; Trayhurn and Jennings, 1987; Trayhurn and Wuseman, 1987; Pedraza et al., 2001; Xiao et al., 2004). The main hypothesis for this reduction in BAT activity is that it saves energy that can be used for milk production (Trayhurn, 1985). However, a more likely interpretation in the context of the HDL theory is that downregulation of BAT thermogenesis reduces heat production (Cannon and Nedergaard, 2004; Speakman, 2008), permitting greater heat production derived from milk synthesis, within the overall heat dissipation capacity limit. Leptin clearly plays a key role in this downregulation (Xiao et al., 2004) (Cui et al., 2011), hence a third role for reducing fat levels in lactation may be to facilitate downregulation of the competitive heat production by BAT.

The second implication of the HDL theory highlighted here is its major consequence for the idea of a fixed limitation on energy budgets based on a maximum sustained metabolic scope, i.e. that

sustained limits are fixed at some multiple of BMR (Drent and Daan, 1980; Weiner, 1989; Weiner, 1992; Hammond and Diamond, 1997), which has pervaded the literature on limits for the past 30 years. Instead of a fixed limit, the HDL theory suggests that the maximum sustained metabolic scope will vary as a direct function of ambient temperature because the maximal capacity to dissipate heat, which constrains the sustained metabolic rate, varies as a function of ambient temperature. Consequently, an animal at an ambient temperature of 35°C may expend energy at 3× BMR and already be working at its maximal limit, while an animal at 0°C may be expending energy at 9× BMR and still be below its maximal limit. This explains why the calculated sustained metabolic scopes for gross energy intake of the MF1 mouse at peak lactation, based on actual resting metabolic rate measurements in the same animals (Johnson and Speakman, 2001; Johnson et al., 2001b; Król et al., 2003), are 7.5 at 30°C, 7.9 at 21°C and 9.4 at 8°C (Speakman et al., 2004). These scopes increase as temperature declines, they all exceed the previously suggested maxima (4× or 7× BMR), and they all refer to animals that appear to be working at their maximal capacity at each measurement temperature. The HDL theory therefore also provides a clear context for understanding how it is possible for migrating wading birds to expend energy continuously for protracted periods at 12× BMR (Piersma, 2011), as they fly at high altitudes where it is cold and they can dissipate the high heat loads generated in flight by convection (Ward et al., 1999; Ward et al., 2001), thereby avoiding limiting levels of hyperthermia.

Acknowledgements

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