Torpor in lactating Siberian hamsters subjected to glucoprivation

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Stamper, Juliet L., Irving Zucker, Daniel A. Lewis, and John Dark. Torpor in lactating Siberian hamsters subjected to glucoprivation. Am. J. Physiol. 274 (Regulatory Integrative Comp. Physiol. 43): R46–R51, 1998.—Daily torpor has never been reported for any rodent species during lactation. To test whether torpor and lactation are incompatible processes, we administered 2-deoxy-d-glucose (2-DG), a glucose analog that interferes with cellular glycolysis, to Siberian hamsters during the 2nd wk postpartum. 2-DG (2,500 mg/kg of body mass) induced torpor in lactating as well as nonlactating females. Although depth of torpor did not differ between groups, duration of torpor tended to be shorter in lactating animals. Evidence of new milk bands suggests that pups were able to obtain milk from torpid dams. By contrast, dams subjected either to a combination of brief food deprivation and subsequent food restriction or just food restriction failed to display torpor, but instead cannibalized one or more pups. We conclude that torpor is possible during lactation; whether lactating dams in nature become torpid in response to energy shortages or cannibalize or abandon one or more of their offspring remains unknown.

Torpor: a state of reduced body temperature, metabolic rate, and metabolic fuel consumption that occurs in many small mammals during the rest phase of the daily activity cycle (9, 11). Torpor in lactating Siberian hamsters during the 2nd wk postpartum is induced by lactating rodent or other mammal, except for one genus of bats (14, 27). Procedural circumstances as well as functional relations may account for this observation. On one hand, few rodent species have been observed during lactation in laboratory settings conducive to torpor (i.e., short day lengths and low T_a). On the other hand, the hormone prolactin (secretion of which is elevated during lactation) inhibits torpor (22) and may prevent lactating females from entering torpor. Torpor bouts lasting several hours may compromise pup viability in altricial species such as Siberian hamsters whose immature offspring depend on their mothers for food, waste elimination, and possibly protection from predators. Although a torpor bout of 4- to 8-h duration, during which dams would be incapable of normal support of their young, may be disadvantageous, even very young altricial rodents in the midst of a huddle with littermates are capable of activating thermogenesis in response to declining T_b (reviewed in Ref. 10, p. 145). Finally, pregnant and lactating Siberian hamsters have elevated daytime T_b values that obscure the usual circadian changes in T_b (25). This increased baseline T_b during the rest phase of the daily cycle during which torpor normally occurs, may compromise the ability of the lactating hamster to enter torpor.

The metabolic fuel inhibitor 2-deoxy-d-glucose (2-DG) reliably induces torpor within 60 min of treatment in Siberian hamsters (3, 4). 2-DG is a more potent activator of torpor than food restriction, although both are presumed to trigger a hypometabolic state by decreasing glycolysis in selected target tissues (3). 2-DG treatment allows a convenient means to test whether lactation and torpor are incompatible states. Manifestation of torpor in response to glucoprivation during lactation would establish the compatibility of these processes, and failure to elicit torpor would support the opposite conclusion. The display of torpor by lactating hamsters in response to 2-DG treatment would not imply that dams manifest torpor under natural circumstances, where glucoprivation is presumed to be less severe than that induced by 2-DG. Torpor, for example, may have been selected against

by decreased food availability and by exposure to low T_a decreases by 45–90% when compared with intakes of nonpregnant, nonlactating females (29). One might therefore expect that daily torpor would be employed by lactating rodents to combat shortages in food and reduced T_a and perhaps more generally to reduce thermoregulatory energy expenditure that could be redirected to support the costs of milk synthesis.

Torpor is not observed in any lactating rodents, other mammals, except for one genus of bats (14, 27). Procedural circumstances as well as functional relations may account for this observation. On one hand, few rodent species have been observed during lactation in laboratory settings conducive to torpor. On the other hand, the hormone prolactin (secretion of which is elevated during lactation) inhibits torpor. Torpor bouts lasting several hours may compromise pup viability in altricial species such as Siberian hamsters whose immature offspring depend on their mothers for food, waste elimination, and possibly protection from predators. Although a torpor bout of 4- to 8-h duration, during which dams would be incapable of normal support of their young, may be disadvantageous, even very young altricial rodents in the midst of a huddle with littermates are capable of activating thermogenesis in response to declining T_b (reviewed in Ref. 10, p. 145). Finally, pregnant and lactating Siberian hamsters have elevated daytime T_b values that obscure the usual circadian changes in T_b. This increased baseline T_b during the rest phase of the daily cycle during which torpor normally occurs, may compromise the ability of the lactating hamster to enter torpor.

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Winter conditions represent a significant energetic challenge to small mammals in temperate and boreal regions. High metabolic rates, an inability to store large energy reserves in the form of fat, increased energetic demands imposed by low ambient temperatures (T_a), and decreased food availability all compromise survival and limit reproduction during winter (1). Energy requirements for lactation greatly exceed those of pregnancy; typically, lactating dams consume twice as much food as nonpregnant, nonlactating females. In lactating Siberian hamsters, energy consumption increases by 45–90% when compared with intakes of nonpregnant, nonlactating females. One might therefore expect that daily torpor would be employed by lactating rodents to combat shortages in food and reduced T_a and perhaps more generally to reduce thermoregulatory energy expenditure that could be redirected to support the costs of milk synthesis.
under field conditions in lactating females, because both the dam and pups could be subject to increased predation when the dam is hypothermic and lethargic. Thus, even if physiologically possible, torpor may be contraindicated and may not be employed by lactating females facing food scarcity. As a test of this hypothesis, we determined whether lactating females maintained at low temperatures and confronted with reduced food availability would engage in torpor.

MATERIALS AND METHODS

Experiment 1

Animals. Thirty-eight adult female Siberian hamsters from our colony were maintained in a long photoperiod (16:8-h light-dark cycle, lights on 0800 Pacific Standard Time) at TBM 23 ± 2°C. At weaning, hamsters were group housed with same-sex siblings in polycarbonate tub cages with wood shavings for bedding; food (Purina rodent diet 5015) and water were available ad libitum. Animals were housed individually before the onset of testing. Measurement of TBM. Radiofrequency transmitters (model VM-FH or VM-FH-LT, Mini-Mitter, Sunriver, OR) were implanted into the peritoneal cavity under pentobarbital sodium anesthesia (80 mg/kg body mass) through a single midline incision. The wound was closed with sterile sutures and treated with 0.1% nitrofurazone ointment (Furacin). Postsurgical discomfort was alleviated by providing a 1.0% solution of acetaminophen (Tylenol) and codeine phosphate in the drinking water for 2–3 days. Individual cages were placed over receiver boards, and TBM was recorded telemetrically every 10 min and stored by computer as previously described (3, 4).

2-DG treatments. 2-DG is a nonoxidizable glucose analog that disrupts cellular glycolysis (30). Lactating females were injected intraperitoneally with either 2,500 mg/kg 2-DG (volume 2 ml/kg) or distilled water vehicle on day 6 or 7 of lactation. A cohort of eight nonlactating females also was injected with 2,500 mg/kg 2-DG.

Criterion for torpor. Torpor is usually defined as a decrease in TBM to <31°C for at least 30 min (3, 11), which represents an average decrease in TBM of ~6°C from euthermic values. Because the baseline TBM of lactating females was elevated relative to that of control females, the criterion for torpor in this experiment was a decrease in minimum TBM (TBMmin) >6°C for at least 30 min after 2-DG treatment, compared with TBMmin the preceding day. TBM data were analyzed for proportion of animals demonstrating torpor, mean decrease in TBM of animals undergoing torpor (TBMmin the day before treatment minus TBMmin the day of treatment), and duration of torpor (duration of TBM decrease >6°C).

Statistics. Mean differences (±SE) between groups were analyzed using Student's t-test, and differences in proportion between groups were compared using Fisher's Exact Test (SigmaStat, Jandel, San Rafael, CA). Criterion for statistical significance was P < 0.05.

Procedure. At 4 mo of age hamsters were implanted with transmitters, housed individually, and transferred to an environmental chamber maintained at TBM 17°C and with an identical long photoperiod. After an initial adaptation period of several days, 30 females were paired with males of proven fecundity. Males were removed after 18 days to avoid postpartum mating. The remaining eight females were treated identically but were not paired with males. Rodent chow was supplemented with sunflower seeds beginning 12 days after pairing. Daily inspections for the presence of pups were initiated 18 days after pairing. On the day of birth, body mass of the dam and number of pups in the litter were recorded. The day of birth was designated the first day of lactation. Lactating females were injected with 2-DG (n = 11) or vehicle (n = 7) between 0900 and 1030 on day 6 or 7 of lactation; nonlactating females (n = 8) were injected with 2-DG at the same time of day. Body mass of the dam, presence of milk bands in the pups, number of pups in the litter, and collective pup mass were recorded at the time of the injection. These measures were repeated 3 h after 2-DG treatment and, except for the milk band measure, again at weaning. TBM data were analyzed for characteristics of torpor as previously described.

Experiment 2

Animals. Adult female hamsters kept in a long photoperiod as described above were housed individually at 4 mo of age and were paired with males of proven fecundity. Additional females were treated identically but were not paired with males.

Data collection and analysis. Food intake was measured by providing a preweighed quantity of food that was reweighed daily. TBM was recorded telemetrically via surgically implanted transmitters as previously described. Differences between groups were compared using analysis of variance with Student-Newman-Keuls post hoc tests (where appropriate), Student's t-test, and Fisher's Exact Test.

Procedure. When pups were 11–12 days old, eight lactating hamsters were deprived of food for 18–24 h and then restricted to 70% of their predeprivation average daily ad libitum food intake. Another seven lactating hamsters were restricted of food to 70–80% of ad libitum food intake without being subjected to the food deprivation regimen, and eight lactating hamsters were fed ad libitum. Eight nonlactating females also were deprived of food for 18 h and then restricted to 70% of their ad libitum food intake. Food-restricted hamsters were provided their daily ration 2–3 h before the onset of the dark phase. Body mass of the dams, number of pups per litter, and total mass of the pups were recorded during the week before food restriction and the week after restriction.

RESULTS

Experiment 1

Average litter size at birth was 4.1 ± 0.4 pups. TBM the day before injection was ~1.0°C higher in lactating (37.8 ± 0.1°C, n = 18) than nonlactating (36.7 ± 0.3°C, n = 8) females (P < 0.001). Body mass also was higher in lactating than nonlactating females (37.2 ± 0.7 vs. 34.7 ± 0.7 g, P < 0.05).

None of the lactating animals injected with the vehicle became torpid (n = 7). 2-DG induced torpor in lactating and nonlactating hamsters (Fig. 1); the percentage of hamsters that decreased TBM by >6°C after treatment did not differ significantly between the groups (64 vs. 100%, Fisher's Exact Test, P > 0.05, n = 11 and 8, respectively). The mean decrease in TBM during torpor bouts did not differ between nonlactating and lactating hamsters (P > 0.05, Table 1). Although duration of torpor tended to be longer in nonlactating than lactating females (203 vs. 146 min), this difference also was not statistically significant (P > 0.05, Table 1).
litter size and pup mass did not differ between the groups (P > 0.05), and new milk bands were seen on pups of torpid dams, as well as those injected with vehicle; by this time dams treated with 2-DG had lost more weight than dams treated with vehicle (−1.2 ± 0.2 vs. −0.4 ± 0.2 g, P < 0.005). At weaning, body mass of dams in the two treatment groups did not differ (P > 0.05), but, surprisingly, litter mass was −25% greater for offspring of dams treated with 2-DG than those given vehicle (14.0 ± 0.6 vs. 11.1 ± 0.1 g, P < 0.05).

Experiment 2

Food consumption was elevated during the 1st wk postpartum in lactating compared with nonlactating females (P < 0.05, Table 2), with an even greater increase in intake during the 2nd wk postpartum (P < 0.005, Table 2). Again, Tb was affected by lactation (F = 9.84, P < 0.001, Fig. 2); it was higher in both lactating groups than in nonlactating females (Student-Newman-Keuls test, P < 0.05, week 2, Fig. 2) and was not influenced by food restriction in the lactating groups (Student-Newman-Keuls test, P > 0.05 each week, Fig. 2).

Torpor did not occur in any hamster, regardless of lactational status or food availability. Five of eight food-deprived and food-restricted females and five of seven food-restricted only females, however, cannibalized at least one of their young, whereas none of eight ad libitum-fed females displayed this behavior (Fisher's Exact Test, P < 0.05). Food rationing was terminated when it became clear that litter reduction rather than torpor was the modal response to restriction.

Body mass of dams did not differ between those that were food deprived and/or food restricted or fed ad libitum before or after the period of food restriction (F = 0.49, P > 0.05; Fig. 3, top), even though both groups lost mass during this interval (F = 8.05, P < 0.01; Fig. 3, top). Litter size was affected by food deprivation and/or food restriction (F = 7.88, P < 0.01). Litter size was reduced by cannibalization in the food-deprived and/or food-restricted group after food restriction (Fig. 3, middle), whereas the number of pups in the ad libitum-fed group was unchanged (Fig. 3, middle). Litter mass also was affected by food deprivation and/or food restriction (F = 11.50, P < 0.005). Litter mass did not differ between these groups before food restriction but was greater for ad libitum fed dams after food restriction (not illustrated). Although individual pup mass of both groups had increased by weaning (F = 63.50, P <

Table 1. Decrease in Tb of nonlactating and lactating Siberian hamsters entering torpor after 2-DG treatment and duration of 2-DG-induced torpor

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<th>Decrease in Tb, °C</th>
<th>Duration of Torpor, min</th>
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<tr>
<td>Nonlactating</td>
<td>8.5 ± 0.6</td>
<td>203 ± 33</td>
</tr>
<tr>
<td>Lactating</td>
<td>8.2 ± 0.5</td>
<td>146 ± 17</td>
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Values are means ± SE; n = 8 nonlactating and 11 lactating hamsters. Tb, body temperature; 2-DG, 2-deoxy-D-glucose (2,500 mg/kg body mass); duration of torpor, length of time Tb was decreased by >6°C.

Table 2. Food intake during the 1st and 2nd wk of lactation

<table>
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<th>Food Intake, g/day</th>
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<td>Nonlactating, week 1</td>
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<td>Lactating, week 1</td>
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<td>Lactating, week 2</td>
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Values are means ± SE; n = 8 nonlactating and 23 lactating hamsters. *P < 0.05 compared with nonlactating females. †P < 0.005 compared with 1st wk of lactation.
mean pup mass of both groups was comparable before food restriction and reduced in the food-deprived and/or food-restricted group after weaning (Fig. 3, bottom).

**DISCUSSION**

This study documents for the first time that torpor can occur during lactation in a rodent species. Inspection of pups 3 h after their dams were treated with 2-DG indicated that some litters were unable to nurse successfully while the dam was torpid, whereas others obtained milk as indicated by the presence of new milk bands. Regardless, all pups survived to weaning. Previously, the only eutherian mammals for which lactational torpor had been reported were two species of bats, *Myotis lucifugus* and *M. thysanodes* (14, 27). Spontaneous torpor also does not appear to occur in lactating marsupials (6, 7). That lactating hamsters can enter torpor is noteworthy, considering the altricial nature of their young, the inhibition of torpor by hyperprolactinemia (22), and the elevation of $T_h$ during lactation. Endogenous prolactin concentrations during lactation (25–100 ng/ml, Ref. 19), however, are considerably lower than the supraphysiological concentrations of exogenous prolactin that effectively blocked spontaneous torpor (~300 ng/ml, Ref. 22). This may account for the persistence of torpor during lactation and its elimination during infusion of very high prolactin concentrations. The endocrine milieu of lactation, per se, is not incompatible with torpor in Siberian hamsters faced with a potent glucoprivic challenge.

A single bout of torpor did not affect the litter mass 3 h after treatment but significantly reduced the mass of the dam. The energy costs of rewarming her own and the entire nest mass likely further challenged the energy reserves of the dam. A 2-DG-induced torpor bout would therefore not appear to conserve energy for lactating females but may instead exacerbate depletion of energy reserves. Nonlactating females that manifested torpor did not undergo a comparable reduction in

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**Fig. 2.** Means ± SE daily body temperature of nonlactating (n = 8), lactating (n = 8), and lactating, food-restricted (n = 15) hamsters during 1st and 2nd wk of lactation. *P* < 0.05 compared with either lactating group.

**Fig. 3.** Top: means ± SE body mass of ad libitum fed (n = 8) and food-deprived and food-restricted (FD-FR, n = 15) dams before and after interval of food restriction. Middle: litter size of each group before and after food restriction. Bottom: litter mass before and after ad libitum feeding or interval of food restriction. *P* < 0.05 compared with each group's own value before food restriction. *b*P* < 0.05 compared with females fed ad libitum.
body mass. Because energetic savings normally associated with daily torpor appear to be absent in lactating Siberian hamsters, torpor may not be a viable tactic to counter the energetic demands of lactation in a cold environment, despite the inherent ability of lactating females to successfully undergo torpor without immediate consequences for the survival of their offspring.

Food restriction that failed to induce torpor in nonlactating hamsters produced infanticide and cannibalization in lactating females. A majority of hamsters subjected to moderate food restriction, or more severe energy curtailment, cannibalized at least one of their pups. Because energetic challenges insufficient to induce torpor readily promoted infanticide, we conclude that dams faced with inadequate food resources are more likely to sacrifice some of their offspring than conserve energy by undergoing torpor. This leaves open the question of why lactating hamsters subjected to 2-DG-induced glucoprivation resort to torpor, rather than infanticide. Perhaps torpor in this case is independent of the glucoprivic action of 2-DG but instead reflects a separate effect on a specific neural substrate(s). As a result 2-DG may induce torpor, not infanticide, despite its glucoprivic activity.

Food restriction during lactation provokes cannibalization in other rodents, e.g., mice, wood rats, and Syrian hamsters (2, 15, 20, 24). In mice, cannibalization increases with the severity of food restriction (20). Mice and Syrian hamster pups that survived infanticide associated with maternal food deprivation were of normal weight at weaning (20, 24); infanticide may be a strategy in which reductions in litter size increase resources for the surviving pups that then retain normal viability. That infanticide is related to maternal energy availability is further supported by the finding that heavier Syrian hamster dams show less cannibalization than lighter ones (24), presumably because the former have greater energy reserves. Again, a difference in underlying mechanism is suggested for food restriction and 2-DG treatment in this case. The energetic challenge of food restriction brought about a reduction in litter size and a litter mass comparable to that of controls at weaning, whereas 2-DG-induced glucoprivation did not affect litter size but increased litter mass at weaning.

These experiments also confirm the elevation of $T_b$ during lactation in Siberian hamsters (cf. Ref. 25). The duration of torpor tended to be shorter in lactating than nonlactating females, which may reflect the high metabolic heat production associated with lactation and milk synthesis (cf. Ref. 28) and/or a reduced capacity for thermoregulatory cooling during lactation, as evidenced by suppression of evaporative water loss at this time (13). Nevertheless, neither factor prevented torpor of a typical depth and duration from occurring after 2-DG treatment.

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