*Physiol. Res. 43: 201–204, 1994*

SHORT COMMUNICATION

# Cold-Activated Growth of Rat Brown Adipose Tissue in the Neonatal Period

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*Received March 4, 1993*
*Accepted January 26, 1994*

## Summary

Repeated exposure of newborn rats to a short-term cold load between day 10 and 30 after birth stimulates the physiological growth rate of the brown adipose tissue. This indicates that in the neonatal period the brown adipose tissue has no reserve thermogenic capacity to compensate an additional cold load and therefore the rate of tissue growth must be activated.

**Key words**

Brown adipose tissue – Newborn rats – Cold stress

The thermogenic role of brown adipose tissue (BAT) in newborn and hibernating animals is well established (see Nichols and Locke 1984). Brown adipose tissue appears in the rat during the last days of embryonal development (Drahota *et al.* 1985). This can be demonstrated by immunochemical detection of the uncoupling protein, localized only in the inner membrane of brown adipose tissue mitochondria (Ricquier *et al.* 1983).

The thermogenic function of BAT is most important for mammals during the early neonatal period when other thermogenic and thermoregulatory mechanisms are not yet fully developed (see Janský 1973). In agreement with this fact are observations which demonstrate that the growth activity of BAT occurs only during the suckling period (Vízek *et al.* 1972) and that lipids from maternal milk are the main source of energy for heat production (Hahn and Koldovský 1966, Drahota *et al.* 1968, Drahota *et al.* 1970). The growth activity of BAT is highly depressed in rats older than 30 days and the physiological function of BAT as a thermogenic organ disappears. However, even in the suckling period the growth rate of brown adipose tissue is very low in comparison with the growth rate of other organs or total body weight (Sbarbati *et al.* 1991). In adult rats, the growth activity of brown adipose tissue may be again activated by cold stress (Foster and Frydman 1979, Bukowiecki *et al.* 1986), by norepinephrine administration (Desautels and Himms-Hagen 1979) or overfeeding (Rothwell and Stock 1979).

There are indications that growth of brown adipose tissue in the neonatal period may be activated (Dawkins and Hull 1964, Sutter 1969). However, there are no data evaluating to which extent the physiological growth rate of BAT of young animals is regulated by changes in environmental temperature. There are also no data indicating to what extent the involution of BAT in young rats may be prevented by an increased cold load. In our experiments, we therefore applied an additional limited cold load every day between day 10 and 30 of postnatal life and we measured changes in fat-free dry weight and tissue lipids in control and cold-exposed animals.

Wistar rats were fed a standard diet *ad libitum* and maintained at 12 h light cycle at 24 °C. In each litter nine newborn rats of the same weight were selected. Cold exposure started the 10th day after birth and was performed in such a way that five animals from each litter were used as control animals and remaining four animals were exposed every day for 4 hours to 8 °C. From each litter one animal was killed on day 10 and then one control and one cold-exposed rat at day 15, 20 and 30 after birth.

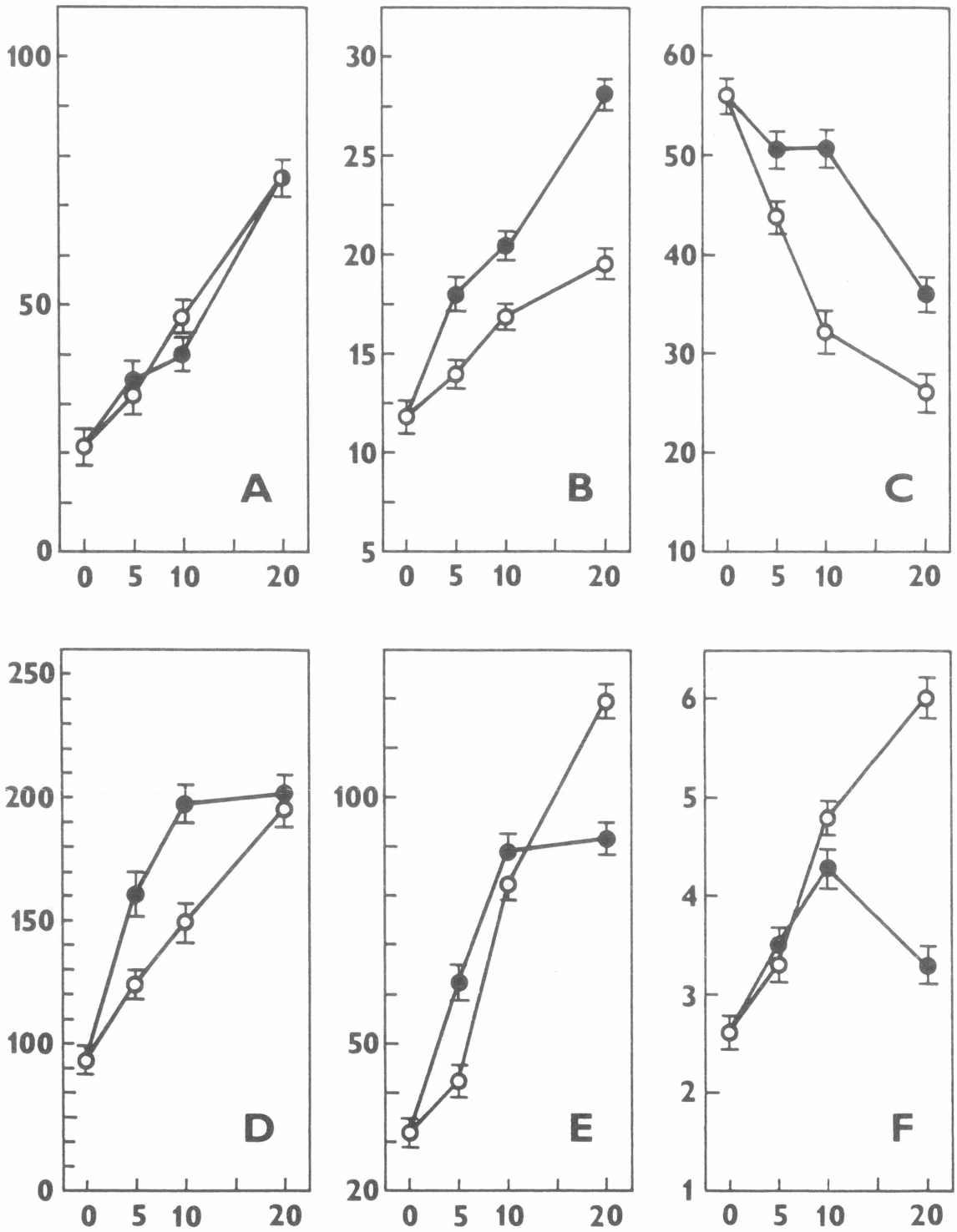


**Fig. 1**
The effect of repeated cold load on total body weight and lipid content of brown adipose tissue. Ten-day-old animals were exposed for 20 days to 8 °C for 4 hours a day as described in Methods. Abscissa indicates days of exposure. All values are means ± S.E.M. from 7 animals. Open circles show values of control animals, closed circles values of cold-exposed ones. Fig. 1A indicates changes of body weight in grams. Fig. 1B indicates changes of fat-free dry weight of brown adipose tissue in milligrams. Fig. 1C indicates changes of fat-free dry weight (in milligrams per 100 g of total body weight). Fig. 1D indicates changes of brown adipose tissue wet weight in milligrams. Fig. 1E indicates changes of total lipids in milligrams. Fig. 1F indicates changes of the total content of lipids (in milligrams per 100 mg of fat-free dry weight).

Interscapular brown adipose tissue was excised and adherent white adipose tissue and muscular tissue remnants were carefully removed. Wet weight was determined and the tissue was dried to constant weight at 80 °C. The tissue lipids were extracted with redestilled petroleum ether and their amount was determined from the difference between the weight of the total and fat-free dry weight.

Our data show that the increase in total body weight between 10th and 30th day after birth is the same in normal rats as in cold-exposed animals (Fig. 1A). During the period between the 6th and 10th day of cold exposure the growth of cold-exposed animals is reduced. However, this decrease is then compensated and no difference in body weight between control and cold exposed rats is present after 20 days of cold exposure (see Fig. 1A).

Determination of fat-free dry weight of BAT shows that there is a higher increase in BAT weight in cold-exposed animals (see Fig. 1B). The changes in BAT fat-free dry weight may also be evaluated on the basis of total body weight. Data in Fig. 1C show a high decrease in the relative weight of BAT in both groups. The decrease in cold-exposed animals is, however, smaller (see Fig. 1C).

Lipids are the main source of energy for the thermogenic function of brown adipose tissue and the content of triglycerides is therefore one of the characteristic indicators of BAT functional activity. Fig. 1F shows that, during the first period of cold exposure, the content of lipids per mg of fat-free dry weight is similar both in cold-exposed and control animals. Starting from the 10th day of cold exposure a high increase of lipids in BAT of control animals occurs, whereas in cold-exposed rats the content of lipids per mg of dry weight decreases. At this period, the content of lipids is very low in cold-exposed animals (see Fig. 1E) and due to the lipid decrease, the increase of wet weight after 10 days of cold exposure is greatly reduced (see Fig. 1D,E,F). This situation reflects the differences between the thermogenic activity of BAT in control and cold-exposed animals. The high lipid decrease in BAT of cold-exposed animals indicates that the thermogenic activity of BAT is still very high. The steady-state level of stored lipids is therefore close to that detected in control 10-day-old animals. At this age BAT has its maximum thermogenic activity (Janský 1973). In the BAT of control rats, the increase of lipids indicates lower triglyceride utilization due to the decreased thermogenic function of BAT.

We may conclude from our experiments that in the neonatal period BAT has no reserve capacity in its thermogenic function as an active thermogenic organ, and that for the compensation of a further limited cold load the growth of the tissue must be activated. The weight of the tissue and hence its thermogenic capacity is thus regulated during the neonatal period in concert with actual changes in environmental temperature. However, the increased cold load is not sufficient to abolish the large decrease in relative weight of BAT. This decrease of the relative weight as well as the high increase of lipids in control animals show that BAT of 30-day-old rats does not play such an important role in the maintenance of body thermal homeostasis as in the neonatal period, evidently because additional thermogenic and thermoregulatory mechanisms have developed.

**Acknowledgement**

This work was supported by a Research Grant of the Czech Academy of Sciences No. 71144.

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**Reprint Requests**

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