

ABERRANT BODY TEMPERATURE REGULATION IN OBESE YELLOW (A^y/a) MICE *

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INTRODUCTION

Mice heterozygous for the A^y allele at the agouti locus have several phenotypic characteristics which distinguish them from littermates without this allele. A^y homozygosity results in death early in gestation (Eaton and Green, 1962). The most obvious feature of heterozygotes, a yellow coat, has been shown to result from a lack of eumelanin formation by the melanocytes (Geschwind, Huseby and Mishioka, 1972). However, in skin culture, pigment-forming cells of yellow (A^y/a) mice are capable of producing the dark eumelanin characteristic of black (a/a) littermates (Cleffman, 1963). Another characteristic, which becomes obvious after A^y/a mice reach 50 days of age, is obesity; mean body weight of adult A^y/a animals is nearly twice that of a/a littermates.

Few attempts to identify metabolic or physiologic differences between A^y/a mice and their non- A^y/a littermates have been reported. Bartke and Gorecki (1968) measured rate of oxygen consumption, but were able to demonstrate differences between genotypes only at low environmental temperatures and/or in mice older than 50 days. However, alterations of respiratory rate have been found in pre-obese mice, suggesting that a metabolic alteration may be present preceding the increase in adiposity (Cizadlo, 1976). Knowledge of another indicator of metabolic alteration, body temperature, may be useful in postulating mechanisms resulting in the A^y/a phenotype.

Turner (1948) measured body temperature in "obese" and "thin" yellow mice and the ability of these animals to adjust to different environmental temperatures in an attempt to implicate disturbed hypothalamic function in the yellow mouse syndrome. She noted thermoregulatory differences between the two groups of yellows, but did not include any non-yellow littermates in her report. Body temperature of animals classified as "obese" was lower than those classified as "thin" at thermoneutral temperatures; in addition, obese yellows were less able to compensate for low environmental temperatures. The present study was conducted

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to evaluate body temperature in A^y/a and a/a littermate mice within their thermoneutral zone both before and after yellow animals became obese.

MATERIALS AND METHODS

Experimental animals were selected from a colony of C57BL/6J- A^y/a or $-a/a$ mice derived from breeding stock originally obtained from The Jackson Laboratory (Bar Harbor, Maine). Animals were grouped 2 to 6 per plastic cage with free access to Purina Mouse Chow and water. Bedding was changed once and water bottles twice weekly. An 8-hr. night:16-hr. day was maintained by an automatic light timer.

A total of 92 yellow (37 male, 55 female) and 80 black (41 male, 39 female) mice were utilized in this study. Of these, 27 yellow animals were younger than 50 days and 65 were older than 50 days. Age groups of black mice included 28 younger than 50 days and 52 older than 50 days.

In order to minimize diurnal variation, all measurements were made between 10:00 and 12:00 A.M. Environmental temperature during the measurement period varied between 22.5 and 31 C. Rectal temperature was obtained once in each animal by inserting the lubricated, alcohol-sterilized thermistor probe of an electronic thermometer (YSI Model 44 Tele-Thermometer and Model 402 Probe) 1.4 cm into the rectum and recording the temperature to the nearest 0.1 degree after one minute of stabilization. During the measurement, animals were restrained in a 4x8 cm plexiglass rectangle. Between each reading, the probe was placed in a waterbath at approximate body temperature to allow faster stabilization.

Data were analyzed for significant differences by Student's *t*-test. Relationships of body temperature with age and body weight were analyzed by linear regression and correlation.

RESULTS AND DISCUSSION

Results are summarized in Table 1. Body temperature was not different between sexes within genotypes. Mean (\pm SE) body temperature of a/a males ($n = 41$) was 36.3 ± 0.1 C, while that of a/a females ($n = 39$) was 36.2 ± 0.1 C. Mean temperature of A^y/a males ($n = 37$) was 36.1 ± 0.1 C, and that of A^y/a females ($n = 55$) was 36.0 ± 0.1 C. Combination of data obtained from all a/a mice ($n = 80$) resulted in a mean body temperature of 36.3 ± 0.1 C; that of all A^y/a animals ($n = 92$) was 36.0 ± 0.1 C ($P < 0.01$).

McLaren (1961) observed no change in body temperature with age in C57BL mice, but found a significant decrease in the C3H strain. Body temperature of animals sampled for the present sur-

¹Yellow Springs Instrument Co., Inc., Yellow Springs, Ohio.

TABLE 1
Rectal Temperature of Yellow (A^y/a) and Black (a/a) Mice

Genotype	Sex	Age	Number	Body Weight (g) (Mean \pm SE)	Body Temperature (C) (Mean \pm SE)
A^y/a	Female	<50 Days	17	17.7 \pm 0.6	36.1 \pm 0.1
A^y/a	Female	>50 Days	38	40.6 \pm 1.7	35.9 \pm 0.1
a/a	Female	<50 Days	12	16.0 \pm 0.5	35.9 \pm 0.2
a/a	Female	>50 Days	27	26.0 \pm 1.3	36.4 \pm 0.1
A^y/a	Male	<50 Days	10	18.2 \pm 1.3	36.2 \pm 0.1
A^y/a	Male	>50 Days	27	39.1 \pm 1.1	36.0 \pm 0.1
a/a	Male	<50 Days	16	19.0 \pm 1.0	36.7 \pm 0.1
a/a	Male	>50 Days	25	28.8 \pm 0.5	36.1 \pm 0.2

vey remained constant over the range of ages studied; correlation of age and temperature was low in both genotypes (correlation coefficient, r : $a/a = 0.08$; $A^y/a = 0.27$). Similarly, correlation of body temperature and body weight indicated little relationship (r : $a/a = 0.17$; $A^y/a = 0.16$).

Results of this study indicate that, in addition to deficient thermoregulation at low environmental temperatures, A^y/a mice have a lower body temperature than a/a littermates at environmental temperatures within the thermoneutral zone. Defective thermoregulation has been demonstrated in another genetic obesity of mice, ob/ob (Trayhurn, Thurlby and James, 1977). These authors suggest that the increased metabolic efficiency of ob/ob animals may be due to a decreased contribution of the total energy expenditure to thermogenesis. The result is an increase in the amount of energy available for storage as fat. Since the phenotype of A^y/a mice differs considerably from that of ob/ob animals, it is presumed that a different metabolic defect is responsible for the two obesities. However, since defective thermoregulation is present in animals of both genotypes, a general relationship may exist between increased metabolic efficiency and defective thermogenesis. A block in intermediary metabolism which forces energy substrate into lipid storage, regardless of the animal's energy demands, may limit the energy available for thermogenesis. Therefore, investigation of the major energy-producing pathways of genetically obese mice may prove beneficial in defining the mechanism responsible for the apparent increase in efficiency.

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