Pregnancy alters body-core temperature response to a simulated open field in rats

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Fewell, James E., and Patricia A. Tang. Pregnancy alters body-core temperature response to a simulated open field in rats. J. Appl. Physiol. 82(4): 1406–1410, 1997.—Exposure of a rat to a novel environment (e.g., a simulated open field) induces a transient increase in body-core temperature, which is often called stress-induced hyperthermia. Although pregnancy is known to influence thermoregulatory control, its effect on stress-induced hyperthermia is unknown. Therefore, 24 Sprague-Dawley rats (8 nonpregnant and 16 pregnant) were tested to study the hypothesis that pregnancy would alter the development of stress-induced hyperthermia after exposure to a simulated open field. Body-core temperature index increased significantly after exposure to a simulated open field in nonpregnant and gestation day-10 rats but not in gestation day-15 and day-20 rats. Thus our data provide evidence that pregnancy influences the body-core temperature response of rats exposed to a simulated open field in a gestation-dependent fashion. The functional consequences as well as the mechanisms involved remain to be determined.

stress-induced hyperthermia; thermoregulation

Numerous Physiological changes occur during the maternal adaptation to pregnancy. In rats, these changes include reversible alterations in thermoregulatory control. For example, baseline 24-h body-core temperature (Tbc) in rats decreases as gestation advances and then increases around the time of parturition (13). Furthermore, there are different thermoregulatory responses to cold (15) and to pyrogens such as bacterial endotoxin (20), interleukin (IL)-1β (IL-1β; Ref. 28), and prostaglandin (PG) E1 (PGE1; Ref. 30) in near-term pregnant rats compared with those observed in nonpregnant rats.

Exposure of a rat to a novel environment induces a transient increase in Tbc of ~1.5°C (7). This response is often called stress-induced hyperthermia. Several laboratories have provided evidence that stress-induced hyperthermia results from a regulated thermoregulatory response and shares some common mechanisms with fever in response to bacterial pyrogens (5, 29). Considering this and the aforementioned information on pregnancy and fever in response to pyrogens, the present experiments have been carried out to test the hypothesis that pregnancy would alter the Tbc response to a simulated open field in rats.

Methods

Experiments were carried out on 8 nonpregnant and 16 pregnant Sprague-Dawley rats (aged 8–11 wk) undergoing their first pregnancy (Charles River Breeding Laboratories, St. Constant, Quebec, Canada). The rats were housed individually in Plexiglas cages at 22 ± 1°C in a 12:12-h light-dark cycle, with lights on from 0700 to 1900. To familiarize the animal with the investigator, rats were handled at least three times before an experiment. All animals had continuous access to food (Lab Diet 5001) and tap water.

Surgical preparation. No sooner than 3 days before an experiment, each rat was anesthetized by inhalation of halothane (4.0% for induction and 1.5–2.0% for maintenance) in oxygen. A paramedian laparotomy was done, and a free-floating battery-operated biotelemetry device (VM-FH; MiniMitter) was inserted into the peritoneal cavity for later measurement of Tbc. The skin was sutured to close the wound.

All surgical and experimental procedures were carried out in accordance with the “Guide to the Care and Use of Experimental Animals” provided by the Canadian Council on Animal Care and with the approval of the Animal Care Committee of the University of Calgary.

Conditions of observations. Our laboratory contains two environmental chambers: a home environmental chamber in which the animals are housed on a day-to-day basis and an experimental environmental chamber that houses a simulated open field. The simulated open field consists of a 30-in. (wide) × 60-in. (length) × 24-in. (high) white acrylic finish box that is illuminated by two hanging fluorescent lights.

Each rat underwent three experiments on consecutive days: a home-cage experiment, a sham experiment, and an open-field experiment. The home-cage, sham, and open-field experiments were carried out in a random order with each animal in each of four groups of rats. The nonpregnant rats were studied on three consecutive days (group 1). The pregnant rats were studied on days 9, 10, and 11 (group 2); days 14, 15, and 16 (group 3); or days 19, 20, and 21 (group 4) of gestation (term = ~22 days). All experiments were carried out between 0800 and 1200 to avoid any possible circadian effects on the response.

During a home-cage experiment, each rat was left in her cage in the home environmental chamber. For a sham experiment, each rat was carried in her cage from the home environmental chamber to the experimental environmental chamber, her cage was placed on the floor, and she was picked up out of her cage for ~10 s. She was then returned to her cage, and the cage was carried back to the home environmental chamber. For an open-field experiment, each rat was carried in her cage from the home environmental chamber to the experimental environmental chamber. Her cage was placed on the floor, and she was picked up out of her cage and placed in the center of our simulated open field.

During measurement of Tbc, both the animal cage in the home environmental chamber as well as the simulated open field in the experimental environmental chamber were placed on platform antennas (RLA1020 Receiver, Data Sciences International) that received the output frequency (Hz) from the biotelemetry device. The received output was then fed into a peripheral processor connected to an IBM computer for determination of Tbc.

Experimental protocol. Tbc was measured at 2-min intervals during a control period and at 10-min intervals for 3 h after the home-cage, sham, or open-field manipulation. A
suitable control period was defined as one in which five consecutive measurements of $T_{bc}$ did not vary by $0.1^\circ$C.

**Statistical analysis.** Statistical analysis was carried out using a three-factor multivariate analysis of variance (MANOVA) for repeated measures followed by a Newman-Keuls multiple-comparison test to determine whether time (control; 10-, 20-, 30-min, etc.), experiment type (home cage, sham, or open field), or gestation (nonpregnant, days 9–11, 14–16, or 19–21 of gestation) affected $T_{bc}$. In addition, a two-factor MANOVA for repeated measures, followed by a Newman-Keuls multiple-comparison test, was used to determine whether experiment or gestation affected the $T_{bc}$ index, which was expressed as area under the $T_{bc}$ curve in degrees, centigrade per hour after the home cage, sham, or open field manipulation. All results are presented as means ± one SD. $P < 0.05$ was considered to be of statistical significance.

**RESULTS**

$T_{bc}$ index increased significantly after exposure to a simulated open field in nonpregnant and gestation day-10 rats but was not different from that observed during a home-cage experiment on days 15 and 20 of gestation (Fig. 1). On being placed into the center of the simulated open field, all rats moved to a wall of the box, circled the perimeter once or twice, and then settled in a corner where they usually stayed for the duration of the experiment. There was no effect of pregnancy on this behavior.

In nonpregnant animals, exposure to a simulated open field produced a rapid increase in $T_{bc}$ of $0.9^\circ$C that peaked at 20 min. $T_{bc}$ was significantly increased above control level at 10 min after exposure to a simulated open field and continued to be elevated for 80 min (Fig. 2). In day 10 gestation rats, exposure to a simulated open field produced a more gradual increase in $T_{bc}$ of $0.7^\circ$C that peaked at 60 min. $T_{bc}$ was increased by 10 min but remained elevated for the duration of our recordings (i.e., 180 min). On day 15 of gestation, $T_{bc}$ was elevated only at 40 min after exposure to a simulated open field; and on day 20 of gestation, $T_{bc}$ did not change after exposure to a simulated open field. During a sham experiment, $T_{bc}$ was elevated only in nonpregnant rats (Fig. 3). The magnitude of the response as well as the duration of the response, however, were attenuated compared with

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**Fig. 1.** Body-core temperature index during home-cage (open bars), sham (hatched bars), and open-field (solid bars) experiments in nonpregnant (NP, $n = 8$), gestation day 10 (d10, $n = 6$), gestation day 15 (d15, $n = 5$), and gestation day 20 (d20, $n = 5$) rats. Data are means ± SD. *$P < 0.05$ vs. home-cage experiment; **$P < 0.05$ vs. sham experiment at given gestation by multivariate analysis of variance (MANOVA) and Newman-Keuls test.

**Fig. 2.** Body-core temperatures during an open-field experiment in nonpregnant (A), gestation day 10 (B), gestation day 15 (C), and gestation day 20 rats (D). Data are means ± SD. *$P < 0.05$ vs. C (control) by MANOVA and Newman-Keuls test.
that observed during an open field experiment. No changes in Tbc occurred during a home-cage experiment in any of the groups (Fig. 4).

**DISCUSSION**

Our experiments provide new and important information about the maternal adaptation to pregnancy in rats. A novel finding in our study was that pregnancy altered the Tbc response of rats after exposure to a simulated open field; this response was gestation dependent.

 Exposure of a rat to a novel stimulus (whether it be restraint, handling, a loud noise, or a novel environment) causes a rise in Tbc (see Ref. 22 for recent review).
After exposure to a novel environment, an increase in Tbc occurs, which is often called stress-induced hyperthermia. This increase is thought to result from a regulated thermoregulatory response because it occurs when the animals are studied in a cold environment as well as when they are studied in a warm environment (4, 6, 19), and it is accompanied by activation of heat-producing (27) and heat-conserving mechanisms (5, 6). Although the mechanisms that initiate stress-induced hyperthermia are not clear, prostaglandins (5, 29) and endogenous opioids (3, 25) appear to play important roles in mediating the Tbc response, and glucocorticoids appear to play an important role in modulating (21, 23) the Tbc response. Circulating inter- 
gluco- 
glucocorticoids appear to play an important role in vasopressin into the ventral septal area of the rat 
Albert (26) have shown that administration of arginine 
nuclei in rats near term of pregnancy (9, 17). Ruwe et 
vactivated in plasma (17) and in a number of hypothalamic 
substrate in the central nervous system (16), is ele-
tral morbidity and mortality.

These possible mechanisms require further investiga-

Regardless of the mechanism of the altered stress-
induced hyperthermic response on exposure to a simu-
lated open field near term of pregnancy in rats, what 
are the possible consequences for the fetus? From the 
standpoint of oxygen supply and demand, it may be of 
advantage to the fetus for the mother not to develop 
stress-induced hyperthermia for several reasons. One 
reason is that stress-induced hyperthermia may cause 
circulatory adjustments such that blood flow from 
internal body organs, including the uterus and pla-
centa, shifts toward thermogenic organs (e.g., brown 
adipose tissue). Under conditions of maximal stimula-
tion, brown adipose tissue, which usually represents 
<1% of body weight, can receive up to 60% of the 
cardiac output (24). A decrease in uteroplacental blood 
flow can compromise placental gas exchange, with a 
resulting decrease in fetal oxygen supply. Another 
reason is that during stress-induced hyperthermia, 
fetal Tbc, which is normally 0.4–0.8°C higher than 
maternal Tbc (1), would most likely increase in parallel 
with the rise in maternal Tbc with a resulting increase 
in oxygen demand secondary to the temperature coeffi-
cient of metabolism (i.e., Q10). A moderate increase in 
Tbc during the latter part of gestation may be detrimen-
tal to the fetus not only by increasing oxygen demand 
but also by causing a rightward shift of the oxyhemoglo-in dissociation curve, thereby decreasing oxygen affinity 
and hemoglobin oxygen saturation. Furthermore, in 
conditions in which fetal oxygen availability is severely 
limited (e.g., asphyxia during birth), an increase in Tbc 
may exacerbate neuronal injury (8) and increase perina-
tal morbidity and mortality.

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