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13. ABSTRACT *(Maximum 200 words)*

The implantation of a biotelemetry transmitter for core body temperature (Tc) and motor activity (MA) measurements is hypothesized to have effects on growth and circadian rhythmicity depending on animal body:transmitter (B:T) size ratio. This study examined the impact of transmitter implantation (TM) on body weight (BW), food intake (FI), water intake (WI) and circadian Tc and MA rhythms in mice (23.8+ 0.04g) and rats (311.5+ 5.1g) receiving no treatment (NT), anesthesia (ANEST), laparotomy (LAP) and TM. The B:T size ratio was 6:1 and 84:1 for mice and rats, respectively. In mice, BW required 14 days to recover to pre-surgical levels and never attained the level of the other groups. FI recovered in 3 days whereas WI never reached pre-surgical levels. Rat BW did not decrease below pre-surgical levels. FI and WI recovered to pre-surgical levels in rats by day 2 post-surgery. Anesthesia decreased mouse BW for 1 week, but was without effect in rats. LAP significantly decreased BW for 5 days in mice and 1 day in rats, showing a significant effect of the surgical procedure in the absence of TM in both species. Circadian Tc and MA rhythms were evident within the first week in both species, indicating dissociation between circadian rhythmicity and recovery of growth variables. Cosinor analysis showed a TM effect on Tc min, Tc max, mesor, amplitude and period of mice, while only the amplitude of the rhythm was affected in rats. These data indicate that a large B:T size ratio is associated with minimization of the adverse effects of surgical implantation. We recommend that B:T size ratio, recovery of pre-surgical BW and display of a robust circadian Tc and MA rhythm be established prior to collection of biotelemetry data under an experimental paradigm

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Biotelemetry transmitter implantation in rodents: impact on growth and circadian rhythms

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Leon, Lisa R., Larry D. Walker, David A. DuBose, and Lou A. Stephenson. Biotelemetry transmitter implantation in rodents: impact on growth and circadian rhythms. *Am J Physiol Regul Integr Comp Physiol* 286: R967–R974, 2004. First published January 15, 2004; 10.1152/ajpregu.00380.2003.—The implantation of a biotelemetry transmitter for core body temperature (T_c) and motor activity (MA) measurements is hypothesized to have effects on growth and circadian rhythmicity depending on animal body-to-transmitter (B:T) size ratio. This study examined the impact of transmitter implantation (TM) on body weight, food intake (FI), water intake (WI), and circadian T_c and MA rhythms in mice (23.8 ± 0.04 g) and rats (311.5 ± 5.1 g) receiving no treatment (NT), anesthesia, laparotomy (LAP), and TM. The B:T size ratio was 6:1 and 84:1 for mice and rats, respectively. In mice, body weight required 14 days to recover to presurgical levels and never attained the level of the other groups. FI recovered in 3 days, whereas WI never reached presurgical levels. Rat body weight did not decrease below presurgical levels. FI and WI recovered to presurgical levels in rats by *day* 2 postsurgery. Anesthesia decreased mouse body weight for 1 wk, but was without effect in rats. LAP significantly decreased body weight for 5 days in mice and 1 day in rats, showing a significant effect of the surgical procedure in the absence of TM in both species. Circadian T_c and MA rhythms were evident within the first week in both species, indicating dissociation between circadian rhythmicity and recovery of growth variables. Cosinor analysis showed a TM effect on T_c min, T_c max, mesor, amplitude, and period of mice, whereas only the amplitude of the rhythm was affected in rats. These data indicate that a large B:T size ratio is associated with minimization of the adverse effects of surgical implantation. We recommend that B:T size ratio, recovery of presurgical body weight, and display of a robust circadian T_c and MA rhythm be established before collection of biotelemetry data collection under an experimental paradigm.

body temperature; body weight; food intake; water intake; surgery

BIOTELEMETRY IS A VALUABLE tool for the study of physiological functioning in laboratory animals. Biotelemetry permits remote sensing of body temperature (T_c; 5), motor activity (MA; 16), biopotentials (EEG, ECG, and electromyogram; 2), and other physiological and behavioral variables (e.g., blood pressure; 20) in conscious, freely moving animals throughout the circadian cycle. The main advantage imparted by biotelemetry over conventional methods is the elimination of confounding stress effects introduced by handling, restraint, and anesthesia. The insertion of rectal probes or attachment of thermocouples for T_c measurements introduces potentially confounding stress effects that complicate study interpretation. Changes in T_c, MA, heart rate, and blood pressure are well-characterized responses to stress (10, 22) that may be eliminated with telemetry. Anesthesia induces hypothermia through the inhibition of several thermoregulatory mechanisms, thus making the study of T_c difficult under these conditions (9, 18, 21).

A potential disadvantage of biotelemetry is the requirement for an invasive surgical procedure for implantation of the transmitter device. Transmitter weights range from 3.3 to 3.9 g for small rodents (body wt ~20 g), 7 to 11 g for large rodents (body wt ~175 g), and 20 to 49 g for larger animals (body wt ~2.5 kg), with the size of the transmitter depending on the application or variables being measured. Transmitter volumes are also variable, ranging from 1.75 to 33 ml^2. On the basis of the recommended nominal body weights for implantation by the manufacturer (www.transomamedical.com), the transmitter may represent up to ~19, ~7, or ~2% of the animal's body weight. Thus it is expected that transmitter implantation will have different effects on animal behavior and physiological functioning depending on animal body-to-transmitter (B:T) size ratio.

Baumans et al. (1) examined body weight and behavior of 24–28 g Balb/c and 129/Sv mice intraperitoneally implanted with 3-g dummy transmitters. The size of the transmitter, equivalent to ~12% of mouse body weight, significantly decreased body weight gain for 4 days postsurgery compared with sham-operated mice that did not receive a transmitter. Body weight did not return to presurgical levels until *day 14* (1). Effects on behavior were also shown, with the frequency of climbing, grooming, and locomotion significantly decreased in implanted mice. An effect on biotelemetry measures was not assessed, due to the use of an inactive (dummy) transmitter.

T_c and MA are two common biotelemetry measurements used for physiological studies in rodents. The establishment of a robust circadian T_c and/or MA rhythm is often cited as an indication of surgical recovery from transmitter implantation. Gegout-Pottie et al. (6) showed 4 days of postsurgical recovery as sufficient for establishing a regular circadian T_c cycle in rats and suggested this interval as a requirement before biotelemetry experimentation (transmitter represented ~3% body wt). In many biotelemetry studies, specific surgical recovery times are noted, with no reference to circadian T_c or MA rhythmicity (e.g., 7, 11, 14, 17, 19). Given the smaller size of the mouse relative to the rat, there will likely be differences in surgical recovery time after implantation of the same size transmitter.

This study was designed to assess the impact of intraperitoneal transmitter implantation on growth and circadian rhythmicity of T_c and MA in mice and rats. We examined three

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aspects of surgical implantation, including anesthesia, laparotomy, and physical presence of an intraperitoneal transmitter. The goal of this study was to determine the recovery rate of factors that affect growth (body weight and food and water intake) and circadian T_c and MA rhythms relative to one another. We sought to address the question: what is the relationship between the recovery of presurgical body weight and food and water intake vs. recovery of circadian T_c and MA rhythms after intraperitoneal transmitter implantation in mice and rats? We also determined the applicability of transmitter devices designed for use in mice for the measurement of T_c and MA rhythms in rats to test the hypothesis that B:T size ratio is the determining factor in surgical recovery rates.

MATERIALS AND METHODS

Animals. Adult C57BL/6J male mice (Jackson Laboratories, Bar Harbor, ME) and Sprague-Dawley male rats (Harlan; Indianapolis, IN) were used. Animals were individually housed in transparent polycarbonate cages fitted with HEPA-filter cage tops and wood chip bedding (Pro-Chip, PWI). Rodent laboratory chow (Harlan Teklad, LM-485, Madison, WI) and water were provided ad libitum under standard laboratory conditions (25 ± 2°C, 12:12-h light-dark cycle, lights on at 0600). In conducting research using animals, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council.

Body weight, food, and water intake measurements. Body weight, food intake (FI), and water intake (WI) were measured between 0800 and 1000 each day on a top-loading balance accurate to ±0.1 g. Care was taken to correct for food spillage into the bottom of the cage. Fresh cages, food, and water were provided the day before surgery in mice and the day of surgery in rats. Fresh food induced increased food consumption in mice but was without effect in rats. Therefore, to obtain accurate baseline measurements in mice, changes in body weight, FI, and WI were calculated by subtracting each day's value from the value obtained 2 days before surgery (before receiving fresh cages, food, and water). Thus *day −2* represents baseline body weight, FI, and WI values in mice. *Day 0* represents baseline rat measurements. Body weight, FI, and WI were measured through *day 14* and *day 9* in mice and rats, respectively. WI was determined by weighing water bottles daily. Water spillage during the weighing procedure was determined as <0.1 ml/bottle. Body weights were corrected for transmitter weights.

Surgical procedures. Isoflurane anesthesia (2.5% induction, 1% maintenance in 100% O_2, flow rate = 0.5 l/min) was used for all surgical procedures. Surgical preparation consisted of shaving the abdominal fur and scrubbing the shaved area with Betadine and alcohol. An ~1-cm incision was made through the skin and abdominal muscle layer using aseptic technique. A battery-operated free-floating transmitter (model TA10TA-F20, Data Sciences International, St. Paul, MN) weighing 3.7 g with a volume of 1.75 cc was inserted into the abdominal cavity. The transmitter was able to freely move among the peritoneal organs, because it was not attached to the peritoneum. Animals receiving laparotomy had the transmitter inserted into the peritoneal cavity and immediately removed. The peritoneal muscle and skin layers were closed with interrupted sutures (3–0 Silk, Ethicon, Somerville, NJ), and surgical glue (cyanoacrylate, Nexabond brand) was applied to the skin layer. Immediately after surgery, each animal was returned to its home cage with ad libitum food and water for the duration of the study. Analgesics were not used in this study, because injection procedures induce significant stress effects and treatment of drinking water may have influenced water intake, which was an outcome measurement. Each transmitter was magnetically activated >24 h before implantation to ensure accurate T_c and MA measurements.

Treatment groups. Animals were body weight matched on arrival and assigned to one of the following groups: *1*) no treatment (NT), *2*) anesthesia (Anest), *3*) laparotomy (LAP), or *4*) transmitter (TM). NT group received no treatment but was exposed to the surgical suite [ambient temperature (T_a) = 25 ± 2°C] for the duration of surgical treatment of the other groups. Anest group received surgical preparation (shaved abdomen with Betadine and alcohol scrub) and was exposed to 27 ± 2 min of isoflurane anesthesia, which is equivalent to the duration of anesthesia exposure during transmitter implantation. LAP group had the transmitter inserted and immediately removed from the abdominal cavity. TM group was intraperitoneally implanted with a biotelemetry transmitter that measured T_c and MA. All animals remained in their home cage with food and water in the surgical suite until the last treatment was completed, at which time they were returned to the animal room for the duration of the study.

T_c and MA. T_c (±0.1°C) and MA were continuously monitored using the Dataquest A.R.T. system (Data Sciences International). The signal emitted by the transmitter is proportional to T_c. MA (counts) is obtained by counting the number of impulses, detected by changes in signal strength, per unit time. The signal is received by an antenna under each animal's cage and transferred to a peripheral processor connected to a personal computer. The frequency emitted by the transmitter is converted to T_c values using predetermined calibration values. All transmitters were calibrated before surgery and at the completion of experimentation to ensure validity of biotelemetry measurements. T_c and MA values were collected at 5-min intervals in unrestrained, conscious animals starting at 1800 on the day of surgery. Raw T_c and MA data are graphically presented as 1-h averages for ease of presentation.

Circadian T_c analysis. Automated analysis of circadian core temperature data (CIRCAD; 4) was used to calculate minimum, maximum, mesor, amplitude, and period of the T_c data for each 24-h period after transmitter implantation through *day 12* postsurgery. Cosine curves with a set period length of 24 h (1800–0600) were fit to a 36-h window within the data set for analysis of T_c 5-min data. Any missing values were eliminated from analysis. This analysis was not available for MA data.

Statistical analysis. Results are presented as means ± SE. Data were analyzed by ANOVA with repeated measures followed by Tukey's test for multiple comparisons. $P < 0.05$ was considered significant.

RESULTS

Figure 1 shows the size relationship between transmitter devices recommended for the measurement of T_c and MA in mice (Fig. 1, *top*; TA10TA-F20 model) and rats (Fig. 1, *bottom*; TA10TA-F40 model). The TA10TA-F20 transmitter is recommended for implantation in animals weighing >20 g, whereas the TA10TA-F40 transmitter is designed for use in animals weighing >175 g. We implanted the TA10TA-F20 transmitter into mice and rats to determine the effect of transmitter presence on growth and circadian T_c and MA values, assuming that these species would be differentially affected due to differences in the B:T size ratio. The B:T ratio was 6:1 and 84:1 for mice and rats, respectively.

Tables 1 and 2 show the baseline characteristics of mouse and rat treatment groups, respectively. Baseline values were obtained 2 days before surgery in mice. This time point represents a more reliable measurement of baseline FI and WI, because fresh food and water, provided the day before surgery, increased food consumption in mice that is not representative of baseline intakes. Baseline values were obtained immediately

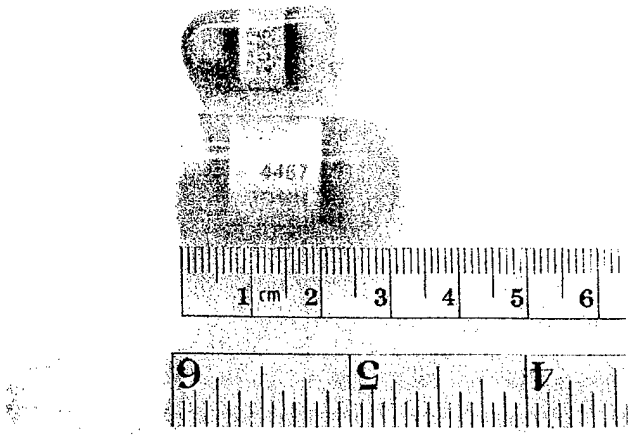

Fig. 1. Size comparison of TA10TA-F20 (*top*) and TA10TA-F40 (*bottom*) transmitters designed for the measurement of core body temperature (T_c) and motor activity (MA) in mice and rats, respectively.

before surgery in rats, because fresh food and water had no effect on consumption. Baseline age, body weight, FI, and WI were virtually identical between treatment groups (Tables 1 and 2). Body weight was 23.8 ± 0.04 g for all mouse groups and 311.5 ± 5.1 g for all rat groups. Both mice and rat body weight were greater than the manufacturer's recommended nominal body weight of 20 g for implantation of the TA10TA-F20 transmitter (http://transomamedical.com).

Changes in mouse body weight are depicted in Fig. 2*A*. NT mice gained 5.5 ± 0.6 g over the entire observation period (*day −20* through *day 15*). The Anest group showed a significant reduction in body weight compared with NT mice from *day 2* through *day 7* (ANOVA, $P < 0.05$). On *day 2*, Anest body weight was reduced ~0.1 g/day, whereas a 0.7 ± 0.02 g increase for NT mice was noted. LAP mice showed a more pronounced body weight decrease than the Anest group, with a maximum loss of 1.0 ± 0.2 g on *day 2* (ANOVA, $P < 0.01$). Body weight of LAP mice was virtually indistinguishable from Anest mice by *day 5* but did not recover to NT levels until *day 15*. Transmitter implantation significantly decreased body weight compared with all other groups from *day 1* through *day 15* (ANOVA, $P < 0.001$). The maximum decrease in BW was 3.5 ± 0.1 g observed on *day 2*. Postsurgical body weight reached presurgical levels by *day 13*.

Figure 2*B* shows the effect of surgical intervention on changes in FI. Baseline (*day −2*) food consumption was ~3.3 g in all groups (Table 1). All groups showed transient increases in FI on *days −13*, *−6*, *−1*, *8*, and *15*, reflecting the response to fresh food placed into the cage the previous day. NT and Anest groups did not differ on any day pre- or postsurgery (Fig. 2*B*). Before surgery on *days −15* and *−7*, LAP mice showed

Table 1. *Baseline characteristics of mouse surgical recovery groups*

	NT (n = 9)	Anest (n = 9)	LAP (n = 12)	TM (n = 28)
Age, days	63	63	63	63
Body wt, g	23.4±0.7	23.9±0.5	23.9±0.4	24.1±0.2
Food intake, g	3.3±0.1	3.4±0.2	3.2±0.2	3.4±0.1
Water intake, ml	4.5±0.3	4.8±0.2	5.3±0.3	4.8±0.2

Values are means ± SE. All measurements were made 2 days before surgery to eliminate the confounding influence of fresh cages, food, and water the day before surgery. Sample sizes are indicated in parentheses at the top of each group column. NT, no treatment; Anest, isoflurane anesthesia; LAP, laparotomy; TM, transmitter implantation.

Table 2. *Baseline characteristics of rat surgical recovery groups*

	NT (n = 6)	Anest (n = 6)	LAP (n = 6)	TM (n = 6)
Age, days	62	62	62	62
Body wt, g	310.5±7.9	311.2±4.4	310.9±4.0	312.2±3.5
Food intake, g	20.7±0.5	22.5±0.4	21.4±0.7	22.4±0.8
Water intake, ml	35.3±1.3	33.8±1.4	30.5±0.8	38.2±3.4

Values are means ± SE. All measurements were made immediately before surgery. Sample sizes are indicated in parentheses at the top of each group column.

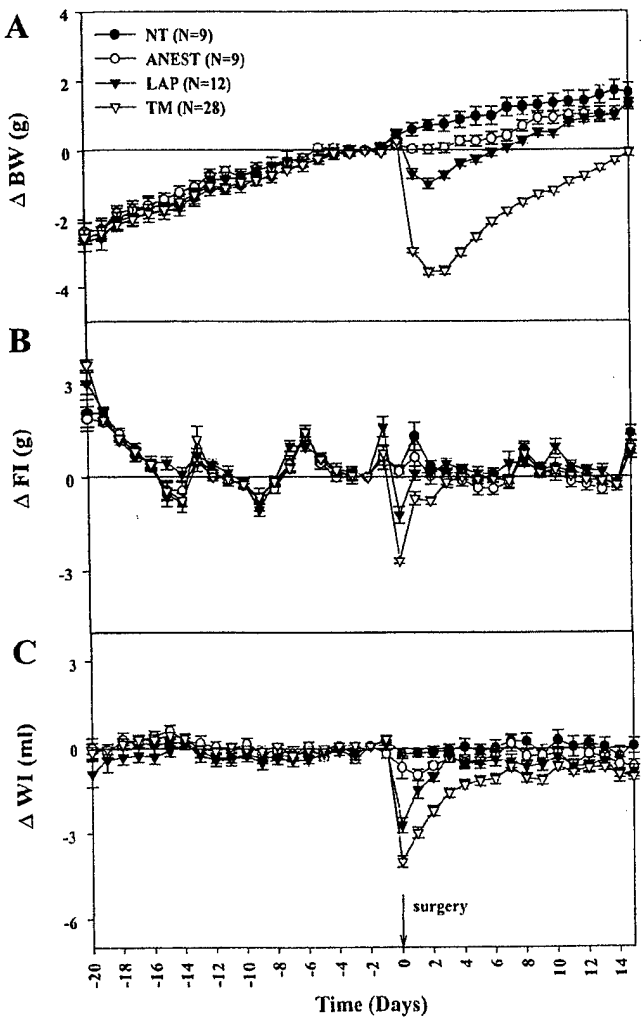

Fig. 2. Change in body weight (BW; *A*), food intake (FI; *B*), and water intake (WI; *C*) in C57BL/6J male mice receiving no treatment (NT), isoflurane anesthesia (Anest), laparotomy (LAP), or transmitter implantation (TM). All values are relative to 2 days before surgery. *Day 0* represents the day of surgery. Sample sizes are indicated in parentheses. Differences are significant at $P < 0.05$.

increased FI compared with all other groups (ANOVA, $P = 0.01$). The reason for this effect is unknown. LAP mice reduced FI by 1.2 ± 0.3 g in response to surgery on *day 0*, which differed significantly from NT and Anest groups (ANOVA, $P < 0.001$). LAP group FI returned to presurgical levels and was similar to NT and Anest values the following day. TM mice decreased FI by 2.7 ± 0.1 g on *day 0*, which was significantly different from all other groups (Fig. 2*B*; ANOVA, $P < 0.001$). TM group FI recovered to presurgical levels and was no longer different from the other groups by *day 3*.

Baseline WI was virtually identical in all groups at 4.8 ± 0.2 ml (Table 1). WI of NT mice was virtually identical for all days of observation (Fig. 2*C*). Anest had no effect on WI. LAP induced a 2.7 ± 0 ml decrease in WI on *day 0*, which recovered to presurgical values by *day 3*. WI of LAP mice was similar to Anest mice by *day 1* but differed from NT mice on *days 0, 1, 2, 8*, and *15* (ANOVA, $P < 0.001$). TM decreased WI by 4.0 ± 0.2 ml on *day 0*. WI of TM mice never reached presurgical or NT group levels but was virtually indistinguishable from LAP mice by *day 6* (ANOVA, $P < 0.001$).

Figure 3 depicts changes in rat body weight, FI, and WI. NT rats gained ~136 g over the observation period (Fig. 3*A*; *day −13* through *day 9*). In contrast to mice, anesthesia had no effect on body weight in rats. Laparotomy induced a significant reduction in body weight compared with NT rats on *days 1, 2*, and *3* through *9* (ANOVA, $P < 0.001$). Transmitter surgery induced a significant reduction in body weight compared with NT rats from *day 1* through *day 9* (ANOVA, $P < 0.001$). Postsurgical body weight of the rat TM group did not match that of the rat NT group at any time point. However, body weight of the TM group did not significantly decrease below presurgical BW at any time point.

Figure 3*B* shows changes in rat FI for the four treatment groups. Baseline (*day 0*) food consumption was ~22 g in all groups (Table 2). There were no differences in food consumption before surgery between any of the treatment groups. Anesthesia had no effect on FI compared with the NT group. Laparotomy induced a significant reduction in FI compared with NT rats on *day 1* only (ANOVA, $P < 0.001$). The TM group showed a significant reduction in FI compared with NT rats on *days 1* through *4* and *days 6* through *9* (Fig. 3*B*; ANOVA, $P < 0.001$). The reduction of FI in the TM group on *day 1* was significantly greater than the LAP group (ANOVA, $P < 0.001$). FI of the LAP and TM groups recovered to presurgical levels by *day 2*.

Changes in WI of the rat treatment groups are depicted in Fig. 3*C*. No differences were detected between groups before surgery. Anesthesia had no effect on WI. Laparotomy and transmitter surgery induced a significant reduction in WI on *day 1* compared with the NT group (ANOVA, $P < 0.001$). TM rats showed a greater reduction in WI than LAP rats on *day 1*. LAP and TM WI recovered to presurgical levels by *day 2*.

Circadian T_c and MA rhythms of the mouse and rat TM groups are graphically presented as 1-h averages in Fig. 4, *A* and *B*, respectively. The absence of an implanted transmitter in NT, Anest, and LAP groups prevented a comparison of circadian rhythms between groups. TM groups were placed onto receiver boards at 1800 the day of surgery and continuously monitored through *day 12* of recovery with minimal disturbance. Weighing induced an ~1-h increase in T_c and MA at

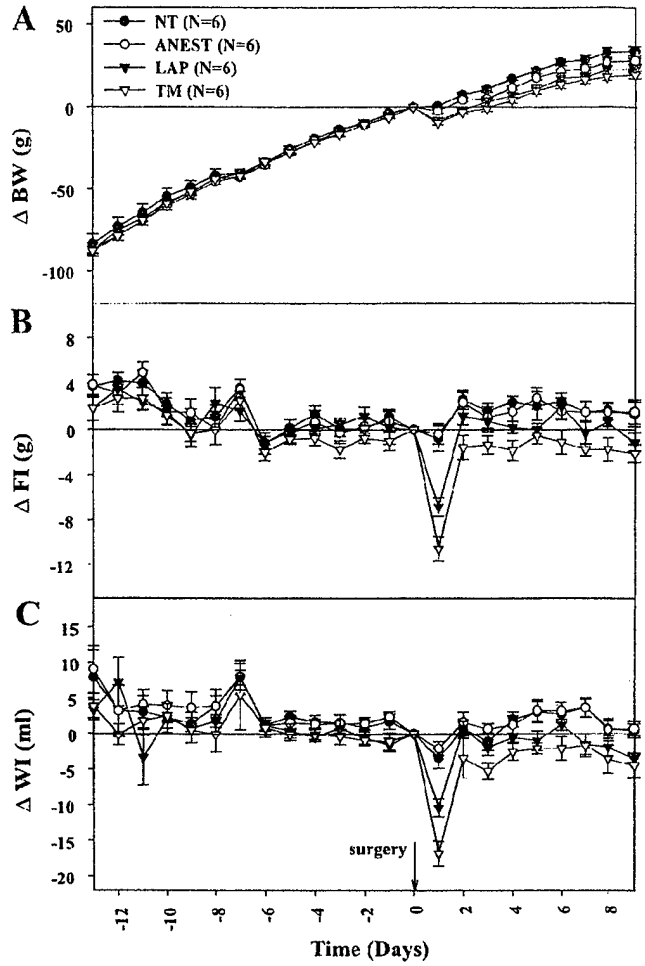

Fig. 3. Change in BW (*A*), FI (*B*), and WI (*C*) in Sprague-Dawley male rats receiving NT, Anest, LAP, or TM. All values are relative to the value obtained immediately before surgery. *Day 0* represents the day of surgery. Sample sizes are indicated in parentheses. Differences are significant at $P < 0.05$.

~0830 each day, indicative of stress-induced hyperthermia. This response was more pronounced on *day 7* due to cage changes in addition to weighing on that day. By *day 5* in mice (Fig. 4*A*) and *day 3* in rats (Fig. 4*B*), a circadian T_c and MA rhythm could be detected with low daytime and high nighttime values that remained similar throughout the observation period.

Minimum T_c of mice on *day 1* was 35.69 ± 0.06°C, which was significantly elevated above all other days (Fig. 5*A*; ANOVA, $P < 0.001$). By *day 4*, mouse minimum T_c was 35.20 ± 0.13°C, which did not change significantly on subsequent days. In rats, minimum T_c was similar on all days (36.63 ± 0.01°C; Fig. 5*B*). In mice, maximum T_c reached a plateau of 38.42 ± 0.05°C by *day 5*, but was significantly depressed at 37.92 ± 0.08°C on *day 1*, whereas in rats, maximum T_c was similar on all days at 38.61 ± 0.06°C (Fig. 5*B*). The mesor, or estimated mean T_c, showed a significant decrease in mice from *day 1* to *day 3* (ANOVA, $P = 0.022$) compared with *days 5* through *15*. By *day 5*, mesor was 36.57 ± 0.10°C and did not change significantly on subsequent days (Fig. 5*C*). Rat mesor was similar on all days at 37.50 ±

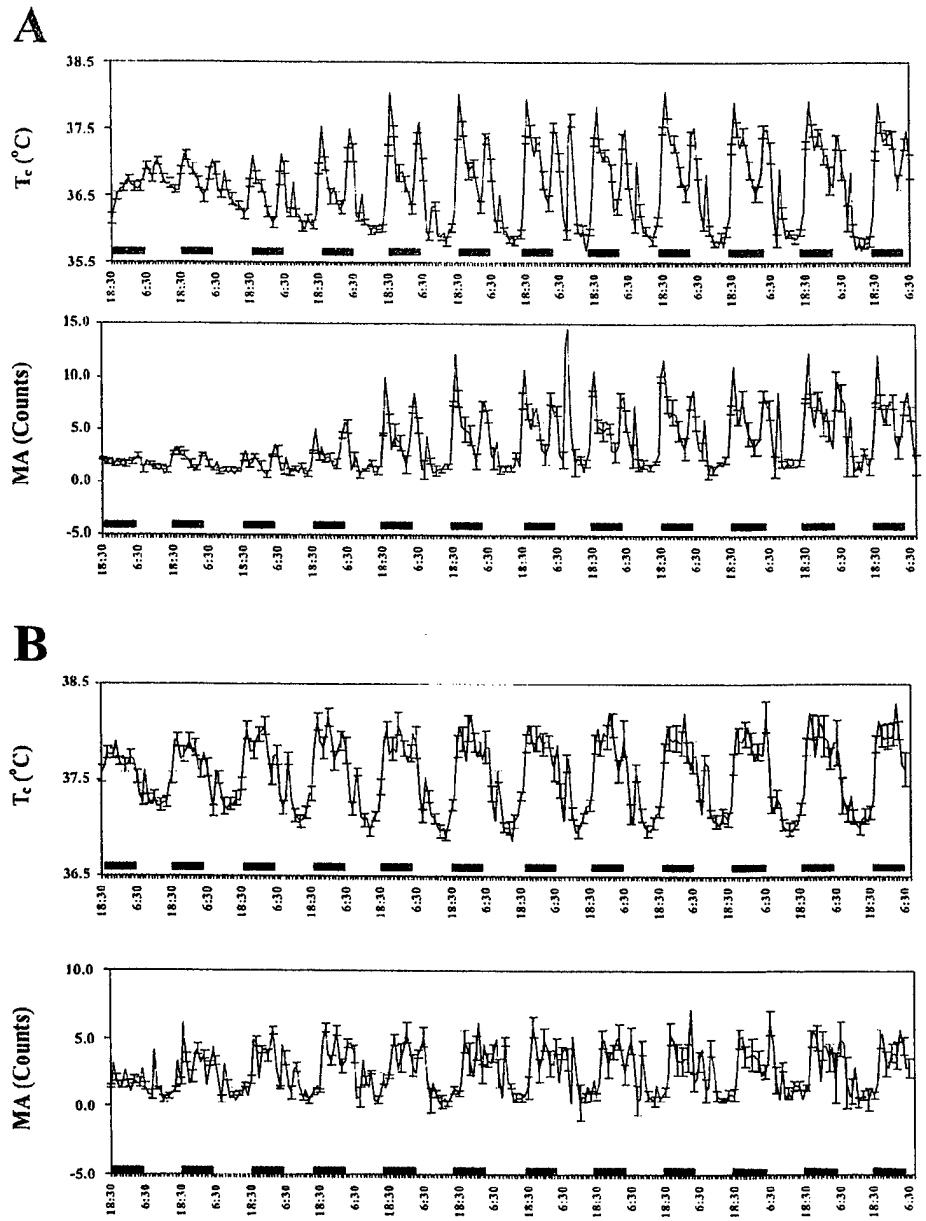

Fig. 4. One-hour averages of T_c and MA in C57BL/6J male mice (*A*) and Sprague-Dawley male rats (*B*). Data represent recovery after implantation of a biotelemetry transmitter device approximating 16 and 1% of body weight, respectively. Black horizontal bars represent the lights-off (active) period on a 12:12-h light/dark cycle with lights on at 0600.

0.30°C (Fig. 5*C*). Amplitude represents the difference between the mesor and the maximum T_c. Significantly depressed amplitude was observed in mice on *day 2* (0.24 ± 0.02°C) compared with all subsequent days (ANOVA, $P < 0.001$). Two phases of amplitude change were observed in mice: from *days 3* through *7* and from *days 8* through *15* (Fig. 5*D*). In rats, amplitude increased from *day 1* through *day 3*. From *day 4* through the end of the observation period, no differences in amplitude were detected in rats (Fig. 5*D*). Periodicity of mouse circadian T_c rhythm was significantly decreased on *day 1* (22.3 ± 0.5 h) compared with all other days (ANOVA, $P < 0.001$; Fig. 5*E*). The increase observed on *day 6* differed from all other days except *day 3* and *day 12*. Rats showed no difference in periodicity of the circadian T_c rhythm throughout the observation period (Fig. 5*E*).

DISCUSSION

This study examined the effect of intraperitoneal implantation of a biotelemetry transmitter device on changes in growth and circadian rhythms in mice and rats. A 3.7-g biotelemetry transmitter was implanted into ~24-g mice and ~311-g rats, and the rate of recovery of body weight, FI, WI, and time required to establish circadian T_c and MA rhythms was examined. NT groups consistently gained weight and maintained stable food and water intake throughout the study, suggesting no prolonged effect of the surgical environment on normal growth. Surprisingly, Anest mice showed a reduced body weight compared with NT mice from *days 2* through *7*. Because no significant difference in FI or WI between these mouse groups was noted, the reduced body weight in the Anest

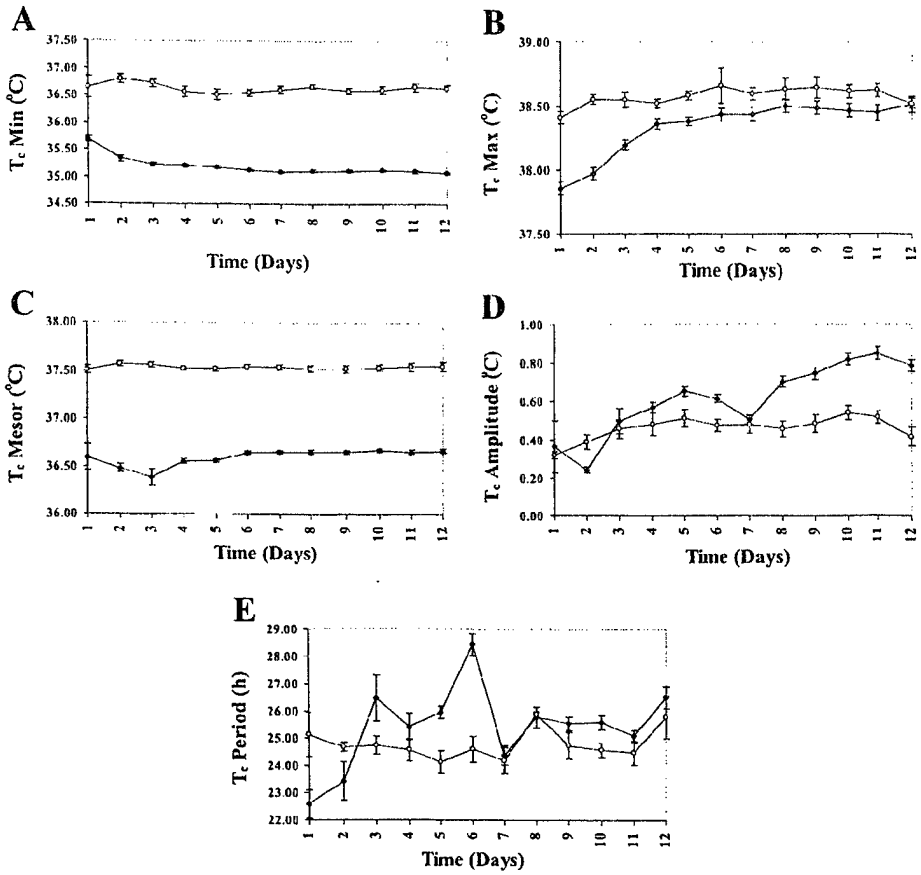

Fig. 5. Automated analysis of circadian T_c data (CIRCAD) of C57BL/6J male mice (●) and Sprague-Dawley male rats (○) during 12 days of recovery from biotelemetry transmitter implantation. T_c data summarized in Fig. 4 were analyzed using cosinor analysis of T_c data collected at 5 min intervals during a 36-h window. Minimum T_c (*A*), maximum T_c (*B*), T_c mesor (*C*), T_c amplitude (*D*), and T_c period (*E*) were determined from CIRCAD.

group suggested an effect of anesthesia on mouse basal metabolism. The lack of an effect of anesthesia on rat body weight suggests that this effect is not universal across species. The reason for this difference between rodent species is not known. Laparotomy induced a decrease in body weight, FI, and WI in both mice and rats compared with nontreated groups. TM mice required 13 days to recover presurgical body weight, despite a recovery of FI to presurgical levels within 3 days. For reasons unidentified, mouse WI never returned to presurgical levels in the TM group. We speculate that the ability to reach the water bottle immediately after recovery was hindered by the presence of the transmitter and the pain associated with the surgical wound. In rats, the effect of transmitter implantation was more transient. The larger B:T size ratio is likely responsible for this less pronounced effect of implantation in this species. Our data indicate that the use of smaller transmitter devices in rats can significantly reduce the impact of implantation on postsurgical growth, thus reducing surgical recovery times.

In our mice and the mouse study by Baumans et al. (1) the decrease in body weight of the TM group approximates the weight of the implanted biotelemetry device, which is equivalent to ~15% total body weight. In contrast, in rats the body weight decrease of the TM group was ~9.6 g, representing ~3% of total body weight. Thus body weight loss is not directly related to transmitter weight but is more likely related to the impact of transmitter volume in the peritoneal cavity. In addition, the surgical procedure alone has a different impact on recovery in the two species. Whereas laparotomy induced a body weight decrease of ~1.0 g in mice, rats lost ~8.4 g of body weight. Thus the surgical procedure alone was responsible for ~30 and ~88% of the total body weight loss in the two species, respectively.

One of the main questions arising from this study is the impact of the weight vs. the size of the transmitter. It is clear from the comparison of our results in mice and rats that the B:T size ratio is an important factor in the recovery from transmitter implantation. However, the surgical site of implantation also appears to have an impact on growth and recovery. Butz and Davisson (3) showed that only 4 days of recovery are required to attain presurgical body weight in mice implanted subcutaneously with a blood pressure transmitter. These data complement our current findings in suggesting that several factors can impact surgical recovery, including the surgical site of transmitter implantation and the B:T size ratio.

Interestingly, exposure of mice to inhalational anesthesia decreased body weight, suggesting a prolonged influence of this treatment beyond the immediate anesthetic effects in this species. We chose isoflurane as the treatment based on the rapid induction and recovery time using this anesthetic. Anesthesia is known to blunt thermoregulatory control through a variety of mechanisms (9, 18, 21). We cannot discount the possibility that mice were hypothermic after anesthesia exposure such that shivering was required for return of T_c to baseline levels. An increased metabolic demand during shivering, in the absence of increased FI, may be responsible for decreased body weight in the mouse Anest group. Housing at

a T_a of 25°C may have induced increased metabolic demands on the mice due to heat loss to the environment given the high surface area-to-body mass ratio of this species. The thermoneutral zone of mice ranges from 26 to 34°C (corresponds to T_a with minimal metabolic rate; 8), suggesting that the chosen T_a for this study was close to or equivalent to the lower critical threshold for metabolic stimulation. Although the mice used in this study may have been acclimated to 25°C due to housing at this T_a for 2 wk before surgery, it is unclear if housing at 30°C or higher would have facilitated a faster recovery after treatment. The absence of an anesthesia effect in rats may be directly related to the environmental temperature of the surgical suite and animal housing room, as well. Because 25°C is within the thermoneutral zone of rats, it is expected that hypothermia would not have been as readily induced in this species.

In telemetered mice and rats, daytime (inactive period) T_c ranges from ~35 to 37°C (depending on housing conditions) and nighttime (active period) T_c is ~1 to 2°C above this range (8, 13). Whereas mouse minimum T_c the day after surgery (35.69 ± 0.06°C) was within this daytime T_c range, it was significantly increased compared with subsequent days of recovery. Maximum (nighttime) T_c of mice was significantly depressed the day after surgery but showed recovery concomitant with increases in MA. Endothermic animals use both behavioral and physiological means to achieve and maintain T_c. Whereas bursts of MA are commonly correlated with T_c changes, there are instances in which these two variables may be dissociated, such as during infection and inflammation (12, 13). Surgical injury of the abdominal region could be expected to induce inflammatory pain, with a subsequent reduction in MA. As shown in the T_c and MA profile of rats (Fig. 4*B*), this larger species did not show as prolonged a suppression of T_c and MA as mice. In fact, by *day 1* after surgery, a robust circadian T_c and MA rhythm was detectable in rats. It is interesting to note that in both species the recovery of body weight and the manifestation of circadian rhythms occurred at different rates. In mice, circadian rhythms recovered sooner than body weight, whereas in rats the opposite was shown. These data demonstrate that growth and circadian rhythmicity after transmitter implantation are dissociated events, such that reliance on one measure alone is inadequate for an accurate assessment of surgical recovery.

Our data suggest that the surgical procedure, which was identical between species, is not the only factor affecting T_c and MA rhythms. We believe it is the discomfort of the transmitter device in the mouse peritoneal cavity that hinders the resumption of normal circadian T_c and MA rhythms after surgery. Our data suggest that at least 1 wk is sufficient for manifestation of a robust circadian T_c rhythm in mice and rats. However, we recommend that circadian rhythmicity be used as only one of several criteria to indicate surgical recovery before inclusion in a biotelemetry study. We recommend that *1*) the surgical site of implantation (3), *2*) the B:T size ratio, *3*) the recovery of presurgical body weight, and *4*) manifestation of a robust circadian T_c and MA rhythm be considered in the assessment of surgical recovery from biotelemetry transmitter implantation. At the writing of this study, we have completed several studies in rats using the smaller transmitter devices originally designed for mice (TA10TA-F20, Data Sciences). These devices function well in both mice and rats and provide the benefit of minimizing the potentially confounding effects of implanting a large device into a small body cavity that may result in organ compression.

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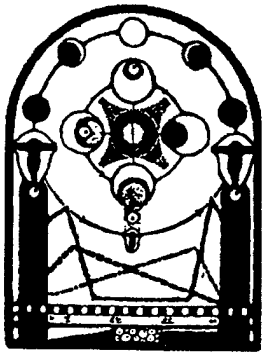
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