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BRIEF COMMUNICATION

Measurement of Temperature in the Rat by Rectal Probe and Telemetry Yields Compatible Results

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DILSAVER, S. C., D. H. OVERSTREET AND J. A. PECK. *Measurement of temperature in the rat by rectal probe and telemetry yields compatible results.* PHARMACOL BIOCHEM BEHAV **42**(3) 549–552, 1992.—The change in body temperature of the rat is commonly measured using biotelemetry or the rectal probe. The authors report that the two methods yield qualitatively similar but quantitatively different results in two experiments. In Experiment 1, both methods detected a salicylate-affected reduction in handling-induced hyperthermia. In Experiment 2, both methods were useful in detecting the hypothermia induced by the muscarinic agonist oxotremorine. In both Experiments 1 and 2, measurements of baseline temperature were higher when measured with the rectal probe. Baseline temperature is measured with biotelemetry prior to handling animals, whereas the act of measuring baseline temperature with the rectal probe necessitates handling. The investigators hypothesized that a rise in baseline temperature produced by handling at least partially accounts for the greater hypothermic response obtained in Experiment 2 using measurements obtained with the rectal probe. In Experiment 3, baseline temperature was measured with biotelemetry after animals were handled. Handling produced an increase in baseline temperature. The hypothermic response to oxotremorine was increased when the higher posthandling baseline temperature was used to calculate the hypothermic response of animals. The authors conclude that differences in baseline temperature and hypothermic response obtained with the two methods are related to an effect of handling.

Core body temperature Mini-Mitter Rectal probe Salicylate Oxotremorine

CHANGE in body temperature is used as a dependent variable in basic and clinical studies. A rectal probe and biotelemetry are commonly used to measure this parameter in animals. Overstreet and associates of the Flinders University of South Australia use a rectal probe (1,9,10,13) and Dilsaver and colleagues from The Ohio State University use telemetry (2,3, 5,6,7). These groups have consistently reported differences in baseline temperature of about 1°C. They have also reported large differences in the magnitude of the hypothermic response to similar doses of the muscarinic agonist oxotremorine (1,2,3,13). The groups, therefore, met to conduct experiments designed to compare their methods.

The results of three experiments are reported. In the first, the ability of the two methods to detect the antipyretic effects of sodium salicylate (8,12) was assessed by measuring its capacity to blunt the hyperthermic response to routine handling (manual manipulation, weighing, and injection of a substance). In the second, the ability of the two methods to detect the hypothermic response to oxotremorine was measured. In the final experiment, biotelemetry was used to assess the influence of prior handling on baseline temperature and the relationship of this parameter to the magnitude of hypothermic response to oxotremorine.

METHOD

Measurement of Temperature

Telemetric measurements were obtained using an intraperitoneally implanted Mini-Mitter (Mini-Mitter Co., Sun River,

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OR). The Mini-Mitter consists of a thermosensor and hearing-aid-battery-powered radio transmitter. Animals are allowed a minimum of 5 days to recover from the implantation surgery before use in an experiment.

The Mini-Mitter functions reliably for a period of 4 or more months at 37–38°C. It is sensitive to a change in temperature of 0.1°C. The model of the Mini-Mitter used emits amplitude-modulated (AM) radio waves. The rate of emission increases as temperature rises. A transistor radio set to an AM frequency and attached to a digital frequency counter (Universal Instruments, Model 5001, New Haven, CT) served as the receiver (2,3).

Calibration and thermistor probe. The calibration of VM Mini-Mitters requires that the rate of emission of AM waves at three or more temperatures be measured. Reliability of the calibration procedure has been demonstrated (4). Two investigators independently calibrated 10 Mini-Mitters in a Model 50 precision water bath set for 34C, 35C, 36C, 37C, and 38°C. Each investigator measured the time to emit 10 sounds using a digital display stopwatch (Fisher Scientific, Fair Lawn, NJ, Model 14-649-5) until they obtained four measurements within 0.04 s of one another. These measurements were then averaged. This yielded five pairs of time and temperature. Two linear regression equations were calculated. The slopes of the regression equations are directly proportional to change in temperature per unit time. The first equation was based on the emission rate of the instruments at 34C, 36C, and 38°C. The second set of equations was based on their emission rates at 34C, 35C, 36C, 37C, and 38°C.

The slopes were statistically indistinguishable for all 10 instruments based on calibration using either three or five temperature points.

Calibration of rectal thermometer. Rectal temperature was measured by the insertion of a thermistor probe about 6 cm into the rectum and recording the output on a Telethermometer (YSI Model 43TF, Yellow Springs Instrument, Yellow Springs, OH) (10).

The rectal probe is tested for accuracy by comparing its measurements of water temperature against those obtained using a standard laboratory thermometer.

Experiment 1

Twelve adult, male Sprague-Dawley rats, weighing approximately 400 g, were divided into two groups of six. The baseline temperature of each rat was measured using telemetry prior to being touched. Groups 1 and 2 then received IP injections of 1 ml/kg normal saline and 1 ml/kg sodium salicylate (220 mg/ml), respectively. Four days later, the groups initially given saline received sodium salicylate and vice versa.

A preliminary experiment indicated that the effect of sodium salicylate on handling-induced hyperthermia was only apparent during the second 60-min period following its injection. Therefore, measurements were restricted to the second 60-min period following an injection of saline or sodium salicylate. Sixty minutes (t = 60) after initial injection, all rats received 1 ml/kg normal saline by IP injection. Baseline was defined as the temperature of each rat just prior to this second injection of saline. This was immediately followed by the measurement of temperature using the rectal probe. Temperature was measured using telemetry both at baseline (60 min) and 120 min after the initial injection. Temperature by telemetry was also measured at 10-min intervals between min 60–120.

Experiment 2

Experiment 2 required the measurement of the hypothermic response of the same group of 12 rats to 0.25 mg/kg (IP) oxotremorine 6 days later. As indicated above, the Australian and American groups have reported highly different hypothermic responses to 0.25 mg/kg oxotremorine. This difference in response could result from an elevation of baseline temperature. A given dose of oxotremorine may not allow the rat's temperature to fall beneath a set point if there is a "floor effect."

The investigators anticipated that use of the rectal probe would be associated with a (a) higher mean baseline body temperature, (b) greater mean hypothermic response, and (c) greater magnitude of effect. However, it was also anticipated that the two methods of measurement would lead to the same conclusion.

Experiment 3

This experiment was designed to address the question of whether the hyperthermic response produced by handling the rat might be related to the magnitude of the hypothermic response to oxotremorine using only telemetry. The baseline temperature of 17 male Sprague-Dawley rats with a mean weight of 240.3 ± 6.6 g was measured prior to being touched. Each rat then received 1.0 mg/kg scopolamine methylnitrate. Thirty minutes later, the postscopolamine methylnitrate base-

TABLE 1

MAGNITUDE OF HYPERTHERMIC RESPONSE TO HANDLING BASED ON USE OF MINI-MITTER AND RECTAL PROBE

	Mean Temperatures (°C)		
Time	Mini-Mitter (n = 12)	Rectal Probe (n = 12)	Difference
Baseline (t = 0)	37.25 ± 0.10	38.45 ± 0.06	1.20*
60 Min postsaline	38.05 ± 0.07†	38.91 ± 0.03†	0.86*
Change from baseline	+0.80 ± 0.07	+0.46 ± 0.06	−0.34*
Postsalicylate (t = 120)	37.76 ± 0.10†‡	38.52 ± 0.16‡	0.74*
Change from baseline	+0.53 ± 0.07	+0.07 ± 0.03	−0.46*

†Significantly higher than baseline, $p < 0.01$.
‡Significantly lower than saline, $p < 0.01$.
*Significant difference between methods, $p < 0.01$.

TABLE 2

MAGNITUDE OF HYPOTHERMIC RESPONSE TO OXOTREMORINE BASED ON USE OF MINI-MITTER AND RECTAL PROBE

	Mean Temperature (°C, n = 12)		
Time	Mini-Mitter	Rectal Probe	Difference
Baseline (t = 0)	37.35 ± 0.09	38.20 ± 0.05	0.85*
60 Min	36.56 ± 0.13	36.85 ± 0.14	0.29
Change from baseline	−0.80 ± 0.14†	−1.36 ± 0.15†	0.56*

*Significant difference between methods, $p < 0.01$.
†Significantly different from baseline, $p < 0.01$.

line temperature was measured. Immediately thereafter, oxotremorine (0.25 mg/kg base) was injected IP. Temperature was then measured at 10-min intervals for 120 min.

Data Analysis

Paired t-tests were used to analyze the data. In addition, correlation coefficients were also obtained to provide an estimate of the qualitative similarity of the methods.

All measures of variance refer to the SEM.

RESULTS

Table 1 compares telemetry and rectal probe under several conditions. It can be seen that the temperatures recorded by the rectal probe are always substantially and significantly higher than those recorded by telemetry. In contrast, the change in temperature from baseline after injection of saline and/or salicylate is smaller when the rectal probe is used than when the Mini-Mitter is used (Table 1). Finally, both methods clearly demonstrate the antipyretic effects of salicylate, as the measurements of temperature after receiving this drug are lower than those after receiving saline (Table 1). In fact, there was a high positive correlation between the two methods for the change in temperature after salicylate (r = +0.83, t = 2.97, $p < 0.05$).

Table 2 summarizes the results of the study with oxotremorine. The baseline temperatures recorded by rectal probe were higher than those using the Mini-Mitter. Both methods reliably detected the hypothermic response to oxotremorine. However, the decrease was significantly greater for the rectal probe. The final temperatures (60 min after oxotremorine) recorded by the two methods were not significantly different (Table 2). Given that (a) baseline temperature is higher when measured using the rectal probe and (b) the final temperature following the injection of oxotremorine does not differ between methods of measurement, (c) the magnitude of the hypothermic response was greater using the rectal probe. Nevertheless, there was a very high positive correlation between the two methods for the hypothermic response to oxotremorine (r = +0.93, t = 7.75, $p < 0.001$).

In the third experiment, the temperature of rats after being touched (37.2 ± 0.2°C) was significantly higher than their original baseline (37.2 ± 0.2°C; t = 4.65, $p < 0.001$). Consequently, the mean thermic responses to oxotremorine (-0.3 ± 0.1°C for unhandled; −0.8 ± 0.1°C for handled) were also significantly different (t = 3.77, $p < 0.001$). Thus, as predicted, the higher baseline contributed to a greater hypothermic response to oxotremorine.

DISCUSSION

These findings provide support for numerous previous reports on the antipyretic effects of salicylate (1,12) and the hypothermic effects of oxotremorine (9,10,13). More importantly, they indicate that both the telemetry and the rectal probe methods were able to demonstrate these effects and there were high positive correlations between the two methods.

Nevertheless, the present results also clearly demonstrate quantitative differences between the two methods that cannot be ignored when surveying the literature. Under most conditions, the rectal probe led to higher measurements of temperature than did telemetry. Our suspicion that differences in baseline temperature obtained with the two methods are partially due to an effect of handling is supported by the results of Experiment 3. Handling produced an increase in the measurements of baseline temperature obtained with the Mini-Mitter. The increment in hypothermic response was equal to the increment in baseline temperature. The results of Experiment 3 are consistent with the hypothesis that the magnitude of temperature change induced by any agent might be dependent on the baseline temperature.

In general, the magnitude of the handling-associated hyperthermia was greater when based on measurements using the Mini-Mitter. However, the magnitude of oxotremorine-induced hypothermia was greater when based on measurements using the rectal probe. Both these findings could be due to the lower baseline temperatures obtained using the Mini-Mitter. These results also raise the possibility that the thermic response to cholinergic agonists such as oxotremorine might have two components: One is the well-established hypothermia; a second might be the inhibition of systems promoting hyperthermia. Only further, more sophisticated studies will be able to confirm this hypothesis.

The fact that the two methods are qualitatively similar (highly correlated results) suggests that either could be used for most studies of temperature regulation. However, we recently reported that telemetry seems more appropriate for studies of undisturbed circadian rhythms (11). As reported in this article, the temperatures recorded by rectal probe were higher than those recorded by telemetry; more importantly, however, the amplitude of the rhythm was much smaller with the rectal probe so it was not possible to obtain valid estimates of the rhythm parameters. In sum, telemetry and the rectal probe produce quantitatively different but qualitatively similar findings. Regardless of which method is used, investigators must be aware of the substantial handling-induced hyperthermia, which could interfere with the interpretation of their findings.

Measurements of temperature obtained with a rectal probe are contingent upon it being inserted the appropriate distance and the allowance of sufficient time for the temperature of the probe to come into equilibrium with the surrounding tissue.

The Mini-Mitter will provide reliable measurements of temperature if its function is unaltered by structural defect or a low cell and its location *does not* substantially change. Grayson and Mendel (6) studied the distribution of temperature in the normal rat. Thermocouples were placed in the liver (n = 35), mesentery (n = 21), and lower abdomen (n = 15). In general, no more than three thermocouples were implanted into the same animal. The mean ($\pm$SEM) temperatures in these regions were 39.3 $\pm$ 0.24, 39.1 $\pm$ 0.24, and 38.5 $\pm$ 0.20°C, respectively. The difference between the mean temperature in the liver and lower abdomen constitutes a trend ($p < 0.10$). However, despite failing to reach statistical significance the difference is important. The Mini-Mitter may move within the peritoneal cavity. Substantial differences in baseline temperature may result from this movement. This was most striking when on one occasion the Mini-Mitter moved in the scrotum. The baseline temperature led us to doubt its functional integrity until we discovered its location.

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