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Research Article

The Effect of Using a Downdraft Table Versus a Standard Treatment Cart on the Rectal Temperature of Anesthetized Rhesus Macaques (*Macaca mulatta*) and Cynomolgus Macaques (*Macaca fascicularis*)

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Abstract

Downdraft tables protect personnel against airborne hazardous materials. One concern during manipulations on a downdraft table is an animal's temperature reduction and the increased risk of hypothermia, because of the high airflow resulting from the negative pressure across the work surface. Hypothermia causes bradycardia, prolonged recovery, impaired coagulation, and affects immune defense mechanisms. We evaluated the effect of a downdraft table on the rectal temperature of anesthetized nonhuman primates. Ten anesthetized cynomolgus and ten rhesus macaques, (4 to 10 y; 11 males and 9 females), were assigned to a standard treatment cart or a downdraft table, allowing a washout period of 5 to 7 days between events. Rectal temperatures were recorded every 5 minutes for 30 minutes. Among rhesus macaques, significant effects of the downdraft table on rectal temperature were observed at 5, 10, and 25 minutes (P=0.0452, P=0.0440, and P=0.0440, respectively), with downdraft table animals displaying mean rectal temperatures between 0.63 °F and 0.90 °F lower than the standard treatment cart. No association between table type and rectal temperature was observed in cynomolgus macaques, althougha significant number with low rectal temperatures requiring thermal support was observed. In conclusion, thermal support for these animals during extended sedation should be provided, regardless of table type. Earlier thermal support during downdraft table operations, could prevent additional heat loss leading to cold stress and hypothermia. Thermal support for ananesthetized nonhuman primate, especially during downdraft table operations, is arefinement that would improve animal welfare, research outcomes, and reproducibility in animal studies.

ABBREVIATIONS

NHP: Nonhuman Primate; **BSC:** Biological Safety Cabinet; **LEVD:** Local Exhaust Ventilation Device; **SIV:** Simian Immunodeficiency Virus; **STLV-1**: Simian T-Lymphotropic Virus-1; **SRV:** Simian Retrovirus; **IACUC:** Institutional Animal Care and Use Committee; **PHS:** Public Health Service; **MM:** *Macaca mulatta*; **MF:** *Macaca fascicularis*; **ANOVA:** Analysis of Variance; **ANCOVA:** Analysis of Covariance; **SD:** Standard Deviation; **CL:** Confidence Limit

INTRODUCTION

Biosafety control measures and precautions protect both workers and the community from accidental exposure to infectious materials, pathogenic organisms and/or toxins, and prevents their release into the environment [1,2].New biosafety technologies and guidelines have significantly improved the ways to safely handle biological materials and facilitated our ability to apply appropriate biosafety practices and controls [3]. Primary containment barriers provide the first layer of protection, usually in direct contact with, or immediately surrounding the biohazardous material or infected animal[1].Secondary barriers are provided by physical and engineering controls and may include physical separation of laboratory areas from public areas, specialized ventilation systems, and airlocks, in order to contain potential hazards [4,5].

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Downdraft tables are a type of engineering control used for personal protection and to handle hazardous materials that can become airborne[6-8]. They are considered a local exhaust ventilation device (LEVD), drawing contaminated air away from the user. They are commonly used in laboratory animal research facilities to control waste anesthetic gases [9,10] and provide protection during necropsies, surgeries, specimen dissections, and other animal manipulations [11]. Downdraft tables have grilles on the table surface through which the air and particulates are drawn under negative pressure by a fan through a filter bank [11,12] the contaminated air is then vented through an exhaust system, protecting both personnel and the working environment [11]. Although downdraft tables are useful in capturing aerosols, they are not as efficient as a biological safety cabinet (BSC), are not considered primary containment [13], and the effective height is usually only up 6 to 8 inches from the surface above the grille [14]. The design of the downdraft table and positioning of the animal or materials on the table can influence the ability to collect particulates because air velocities vary across the surface. The recommended air flow across the table surface is 150-250 cubic feet per minute (cfm) per square foot of table surface area [12].

One concern with the use of downdraft tables during animal manipulations is whether, the temperature of an animal could be reduced due to the high airflow around the body resulting from the negative pressure across the work surface. Due to this increased airflow, there is a higher risk of hypothermia when using downdraft tables, chemical fume hoods, or biosafety cabinets, especially in small animals [15]. Yang et al. (2015) examined a similar concern in a study involving anesthetized people undergoing surgical procedures in laminar airflow conditions. He concluded that the use of a laminar airflow operating room, in addition to advanced age, were significant risk factors for developing intraoperative hypothermia - suggesting that the increased airflow increases the risk of hypothermia in anesthetized patients [16]. In a laminar airflow system, the air in the operating room recirculates between 20 to 300 times per hour. These ceiling-to-floor systems are commonly used in modern operating rooms because they help reduce dust, maintain positive pressure to reduce the number of microorganisms in the air, and help to prevent intra- and post-operative wound infections [16].

Body temperature is one of the fundamental parameters assessed when determining the health status of an animal in both the clinical and research settings [17]. In most mammals, the core body temperature is tightly regulated and protected by a thermoregulatory defense mechanism which can lead to hypothermia, if it becomes impaired or overwhelmed [18]. Nonhuman primates (NHPs) exhibit a wide range of variation in their basic physiological parameters both between and within species. For example, in rhesus and cynomolgus macaques, the normal range for body temperature is 98.6-103.1 °F (37.0-39.0 °C) [19]. In NHPs, hypothermia can cause bradycardia, low cardiac output, and delayed recovery from anesthesia [20] and is frequently observed in New World monkeys, as well as in young, aged, debilitated, and anesthetized animals [19]. In small NHPs such as marmosets, hypothermia can be life-threatening and should be avoided by using supplemental warming devices [21]. In NHPs, hypothermia is worsened when the core body temperature falls below 94.0 °F (34.0 °C), since the body's thermoregulatory system becomes impaired below this temperature [20]. One of the recommendations to minimize further heat loss in NHPs, is to ensure that animals are kept away from locations with increased drafts, such as near supply or exhaust ducts [19].

One of the important parameters often studied during infectious disease research, is the clotting cascade and coagulation parameters. Hypothermia can lead to impaired coagulation through an increased prothrombin time and partial thromboplastin time, disrupting the clotting cascade and exacerbating blood loss [22-24]. It has also been shown that only 3.4 °F (1.9 °C) of hypothermia can adversely affect antibody- and cell-mediated immune defense mechanisms, [22,23] which is of particular importance during vaccine and therapeutics research. In humans, hypothermia has been shown to cause dysfunctions in the heart, kidneys, and the brain [25]. In summary, not only can hypothermia adversely affect animal health and welfare, but it could also affect animal survival and reproducibility of experiments.

The objective of this study was to evaluate if the rectal temperature in anesthetized rhesus and cynomolgus macaques would be reduced by using a downdraft table for 30 minutes compared to a standard treatment cart. The hypothesis of this study was that the animals maintained on the downdraft table would demonstrate a decrease in rectal temperature as time progressed, compared to those animals maintained on the standard treatment cart, because of the increased airflow around the animal due to the sustained negative airflow generated by the downdraft table.

MATERIALS AND METHODS

Animals and husbandry

The study population consisted of 10 cynomolgus macaques (*Macaca fascicularis*) and 10 rhesus macaques (*Macaca mulatta*), (n=20; age, 4 to 10 y; weight, 3.3 to 9.8 kg; 11 males and 9 females). All animals were of Chinese origin, were housed in the same corridor in four different rooms, and were singly or pair-housed. The study animals were deemed to be in good health, had been confirmed seronegative for SIV, STLV-1, B virus, and SRV, and were tested twice annually by tuberculin skin testing and remained negative throughout the study. Research was conducted under an IACUC-approved protocol in compliance with the Animal Welfare Act, PHS Policy, and other Federal statutes and regulations relating to animals and experiments involving animals. The facility where this research was conducted is accredited by AAALAC, International and adheres to principles stated in the *Guide for the Care and Use of Laboratory Animals*, National Research Council, 2011.

The rhesus macaques (MM) were housed in two rooms maintained at an average temperature of 70.0 °F with an average relative humidity of 42.2 % during the month leading up to the experiments. The cynomolgus macaques (MF) were housed in two rooms maintained at an average temperature of 70.7 °F with an average relative humidity of 42.0 % during the month leading up to the experiments. All rooms were maintained on a

12:12-h light: dark cycle. A commercial diet (2050 Teklad Global 20 % Protein Primate Diet, Envigo, Frederick, MD) was provided to each nonhuman primate (NHP) twice daily, as well as fresh produce once a day. Chlorinated and filtered municipal water was provided ad libitum through an automated watering system (Edstrom Industries, Waterford, WI). A variety of toys and manipulanda were used as part of the environmental enrichment program.

Equipment and Thermometry

Each animal was fasted for a minimum of 6 – 12 hours and anesthetized with tiletamine-zolazepam (Telazol, Zoetis, Parsippany, NJ) 5 mg/kg injected intramuscularly in the cranial or caudal thigh. We chose tiletamine-zolazepam, since in our facility, it is commonly used as an injectable anesthetic in macaques for routine procedures such as blood collection and physical examinations, and is more frequently used in containment studies for these macaque species.

Once the animal was adequately anesthetized, the animal was weighed and was placed, according to the randomization order, either on a standard treatment cart (Model: Flex, Metro, Wilkes-Barre, PA) or a downdraft table (Model: FT3048, DualDraw, Denver, CO), both lined by a disposable absorbent underpad (Henry Schein, Melville, NY) (Figure 1). The standard treatment cart used in this study is a type of medical treatment cart constructed of a lightweight polymer that provides ample work surface and is commonly used at our institution for NHP routine procedures such as physical exams, blood collection, and tuberculin skin testing. The airflow on the downdraft tables was constant during the study; the fan speed for the downdraft table is not variable and remained constant throughout the study. This speed is set by the manufacturer to ensure adequate air flow across the working surface and is not adjustable by the end user. The air flow of the downdraft tables used in our study was 50 to 100 feet per minute, set by the manufacturer. The absorbent underpad was placed on the downdraft table in such a way to avoid covering more than 50 % of the total work surface during operations.

Rectal temperatures were taken between 0800 and 1200 to minimize the effect of normal circadian variations on the data using a digital rectal thermometer (SureTemp Plus, Welch-Allyn, Skaneateles Falls, NY) covered by a protective plastic cover and a lubricant. The thermometer had a temperature range of 80 °F (26.7 °C) to 110 °F (43.3 °C), an accuracy of ± 0.2 °F (± 0.1 °C) and a measurement time of approximately 10 seconds. The rectal thermometer was advanced approximately 1-inch and thermometry measurements were collected beginning at time=0 (immediately after the animal was placed on the appropriate table and the rectal probe was introduced) and recorded every 5 minutes for the duration of the experiment for a total time of 30 minutes. Oxygen saturation and heart rate were monitored and recorded every 5 minutes for 30 minutes by using a pulse oximeter (Model: H100, Edan USA, San Diego, CA) attached to the tongue, opposite cheek, or the pinna as part of the anesthesia monitoring. In the event that the temperature of an NHP was below 97.0 °C (36.1 °C) at the end of the procedure, the NHP was then provided thermal support during recovery using forced-air warming blankets (3M Bair Hugger, St Paul, MN) and/or conductive fabric warming blankets (HotDog, Eden Prairie, MN) until the temperature had reached 99.0 °F or the NHP was awake enough to be safely placed back in the home cage. Each NHP continued to be monitored for appropriate recovery in their home cage after each anesthetic event. Each animal was anesthetized two times, once while on the standard treatment cart and once on the downdraft table. The thermometers, pulse oximeters, and downdraft tables were used according to the manufacturer's instructions.

Study design

A 2×2 crossover study design was used to compare the table types. Animals were randomized to receive one of the two possible treatment sequences, stratified by sex and species. Animals were either, monitored on a standard treatment cart first, followed by the downdraft Table 1, or the animals were monitored on a downdraft table first, followed by the standard treatment cart. A minimum washout period of 5 to 7 days between anesthetic events was allowed.

Statistical analysis

For the primary analyses of rectal temperatures, a two-way repeated measures ANOVA was fit to each time point, taking table type as the within subject, and species as the between subject factor. Subgroup analysis on the effect of sex was carried out by fitting a two-way repeated measures ANOVA separately for each time point and species, taking table type as the within subject, and sex as the between subject factor. To analyze the interaction between age and table type, a repeated measures ANCOVA model was fit and estimates of the effect of table type at 60 and 120 months of age were obtained as single degree of freedom

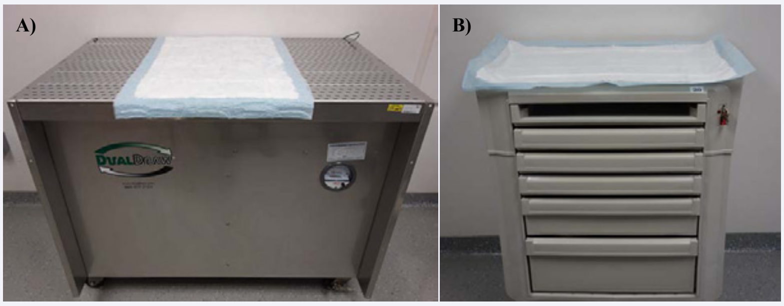

Figure 1 DualDraw Model: FT3048 Flat Top Downdraft Table; (B)–Metro Model: FlexStandard Treatment Cart.

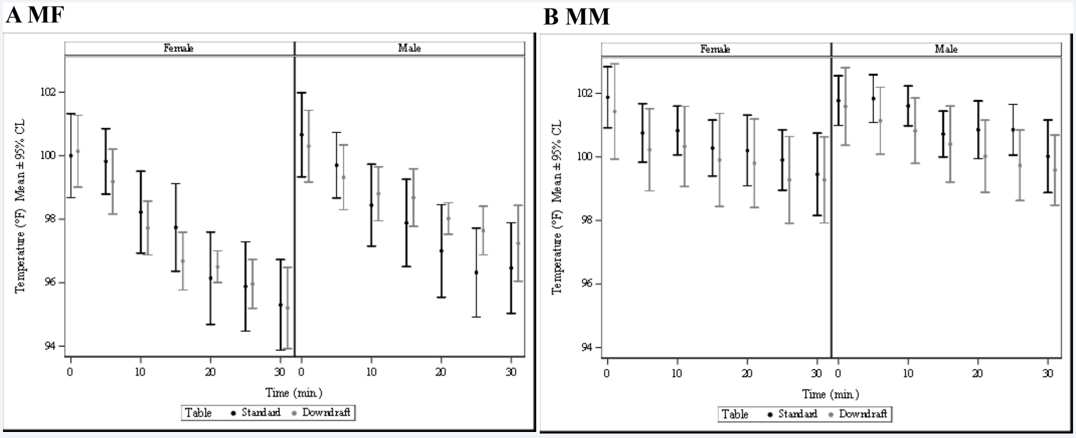

Figure 2 Association of sex and table type with mean rectal temperature in (A) cynomolgus macaques and (B) rhesus macaques.In cynomolgus macaques (MF), as time progressed, a greater separation in rectal temperatures by sex was noted (A). Among rhesus macaques (MM), the difference between rectal temperatures by sex remained relatively constant (B).

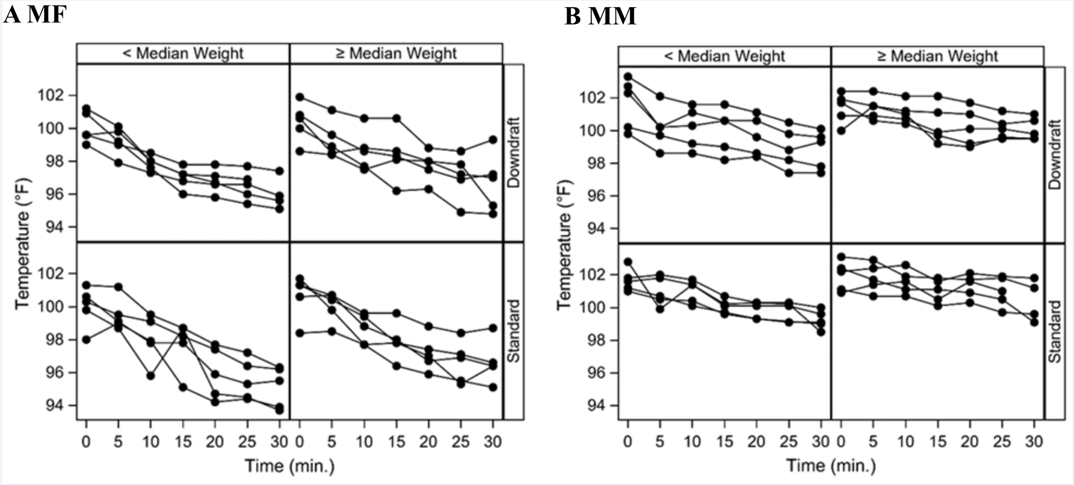

Figure 3 Association between weight and rectal temperature by table type and time in (A) cynomolgus macaques (MF) and (B) rhesus macaques (MM). Animals are categorized as being the heaviest (≥ Median weight) and lightest (< Median weight) animals in the study. Heavier animals maintained higher rectal temperatures relative to lighter animals regardless of table type, and, as time progressed, the association between weight and rectal temperature became more pronounced.

contrasts. No adjustment was applied for multiple comparisons. For the baseline rectal temperatures, ages, body condition scores and weights, P-values between species were based on *t*-test. The comparison of temperatures to historical control was based on paired *t*-test. Statistical significance was set at a P-value of less than 0.05.Analysis was implemented in SAS Proc mixed, SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Summary statistics on historical and baseline rectal temperatures, as well as baseline ages, body condition scores (BCS), and weights for the study population are presented in Table 1. Historical rectal temperatures were obtained from animal medical records by evaluating routine physical exams performed during the previous 5 years. These temperatures were obtained rectally from anesthetized study animals on a standard treatment cart using a digital rectal thermometer during previous routine physical examinations. For study purposes, a review of animal medical records for the study animals was performed and these previous rectal temperature values were used to calculate mean historical rectal temperatures by species and sex. Since the historical temperature values used span the previous 5 years, these values were averaged for each animal, and therefore they represent values from different ages and different weights for each animal during this time period. A significant difference in historical baseline rectal temperatures between species was observed, with the rhesus macaques maintaining a higher baseline rectal temperature, historically, compared to the cynomolgus macaques under similar conditions (P=0.0011). In our study population, rhesus macaques started, on average, at a higher baseline rectal temperature than cynomolgus macaques on both the standard and the downdraft tables (P=0.0055 and P=0.0196, respectively). There was also a significant difference in age between the rhesus and cynomolgus macaques, with

Table 1: Historical and baseline rectal temperatures, age, body condition score and weight comparison of study population.

	MF (n=10)[c]		MM(n=10)		MM vs MF
	Female (n=5)	**Male (n=5)**	**Female (n=4)**	**Male (n=6)**	**(P-Value)[a]**
Temperature (°F)					
Historical	101.18 (0.43)	100.43 (1.06)	102.40 (0.54)	101.96 (0.69)	0.0011
Downdraft Table Baseline	100.14 (0.91)	100.30 (1.25)	101.43 (1.11)	101.58 (1.40)	0.0196
vs Historical (P-Value)[b]	0.1050		0.1094		-
Standard Table Baseline	100.00 (1.24)	100.66 (1.32)	101.88 (0.85)	101.77 (0.82)	0.0055
vs Historical (P-Value)	0.1938		0.1043		-
Age (months)	92.20 (26.12)	65.40 (6.39)	112.50 (1.73)	87.67 (14.92)	0.0443
Body Condition Score	3.90 (0.82)	2.80 (0.91)	3.00 (0.41)	3.08 (0.38)	0.3924
Weight (kg)	5.17 (1.34)	6.98 (1.52)	7.27 (1.94)	7.37 (1.62)	0.1212

[a] Result of *t*-test.
[b] Comparison to historical control is based on paired *t*-test.
[c] Displayed values indicate Mean or Mean (SD), unless otherwise noted.
Abbreviations: MF=cynomolgus macaque, MM=rhesus macaque, SD=standard deviation

Table 2: Mean rectal temperatures by time, species and table type.

Time (min.)								
Species	**Table Type**	**Baseline**	**5**	**10**	**15**	**20**	**25**	**30**
MF (n=10)	**Downdraft**	100.22 (99.47 , 100.97)	99.25 (98.55 , 99.95)	98.26 (97.59 , 98.93)	97.68 (96.83 , 98.53)	97.26 (96.57 , 97.95)	96.80 (96.05 , 97.55)	96.29 (95.39 , 97.19)
	Standard	100.33 (99.63 , 101.03)	99.76 (99.13 , 100.39)	98.33 (97.67 , 98.99)	97.81 (97.12 , 98.50)	96.57 (95.77 , 97.37)	96.10 (95.34 , 96.86)	95.88 (95.03 , 96.73)
	Downdraft vs Standard	-0.11 (*P*= 0.7282)	-0.51 (*P*= 0.0986)	-0.07 (*P*= 0.8235)	-0.13 (*P*= 0.7587)	0.69 (*P*= 0.0839)	0.70 (*P*= 0.0989)	0.41 (*P*= 0.3478)
MM (n=10)	**Downdraft**	101.52 (100.77 , 102.27)	100.77 (100.07 , 101.47)	100.62 (99.95 , 101.29)	100.20 (99.35 , 101.05)	99.93 (99.24 , 100.62)	99.55 (98.80 , 100.30)	99.46 (98.60 , 100.32)
	Standard	101.81 (101.11 , 102.51)	101.40 (100.77 , 102.03)	101.29 (100.63 , 101.95)	100.54 (99.85 , 101.23)	100.59 (99.79 , 101.39)	100.45 (99.66 , 101.25)	99.77 (98.89 , 100.65)
	Downdraft vs Standard	-0.29 (*P*= 0.3643)	-0.63 (*P*= 0.0452)	-0.67 (*P*= 0.0440)	-0.34 (*P*= 0.4253)	-0.66 (*P*= 0.0971)	-0.90 (*P*= 0.0440)	-0.31 (*P*= 0.4727)
MM or MF	**Downdraft vs Standard**	-0.20 (*P*= 0.3760)	-0.57 (*P*= 0.0131)	-0.37 (*P*= 0.1080)	-0.23 (*P*= 0.4356)	0.01 (*P*= 0.9558)	-0.10 (*P*= 0.7287)	0.05 (*P*= 0.8717)

[a] Displayed values indicate mean (95% CL) or mean difference (P-Value) for comparisons.
Abbreviations: MF=cynomolgus macaque, MM=rhesus macaque, CL=confidence limit

Table 3: Difference in mean rectal temperatures by species, table type, age and time points.

	MF				**MM**			
	Age (months)				**Age (months)**			
	60		**120**		**60**		**120**	
Time (min.)	**Downdraft – Standard (F)[a]**	**P-Value**	**Downdraft – Standard**	**P-Value**	**Downdraft – Standard**	**P-Value**	**Downdraft – Standard**	**P-Value**
0	0.07938	*P* = 0.8538	-0.5250	*P* = 0.4603	-0.6922	*P* = 0.4337	-0.05037	*P* = 0.9313
10	0.5855	*P* = 0.1707	-1.5065	*P* = 0.0441	-1.5589	*P* = 0.0149	-0.1405	*P* = 0.6907
20	1.4136	*P* = 0.0121	-0.8957	*P* = 0.2431	-1.9005	*P* = 0.0358	0.07903	*P* = 0.8804

[a] Estimated difference in mean temperatures on downdraft versus standard table.
[b] Negative values indicate a reduction in body temperatures on the downdraft table.
Abbreviations: MF=cynomolgus macaque, MM=rhesus macaque

the cynomolgus species having a younger median age of 69.5 months versus 103.5 months for the rhesus species (P=0.0443). No significant difference was observed in body condition scores between species or by sex within each species. The median weight for the rhesus macaques was 7.37 kg and 6.41 kg for the cynomolgus macaques, such that there was no significant difference between their baseline weights.

Mean rectal temperatures by time, species and table type are presented in Table 2. The effect of using the downdraft table relative to the standard treatment cart on rectal temperature was larger among rhesus macaques. Among rhesus macaques, significant effects of table type on mean rectal temperatures were observed at 5, 10, and 25 minutes (P=0.0452, P=0.0440, and P=0.0440, respectively), with the animals on the downdraft table displaying mean rectal temperatures between 0.63 and 0.90 °F lower than the animals on the standard table at the same time points. In contrast, cynomolgus macaques were not found to have a significant association between table types and mean rectal temperatures.

We also explored the relationship between variables such as sex, weight, age, and rectal temperature changes using both the downdraft table and the standard treatment cart. Figure 2 depicts the association between sex and table type with mean rectal temperatures for both species. In both species, the relative effects of the downdraft table versus the standard treatment cart were comparable within each of the sexes; however, female macaques had a lower rectal temperature throughout the study, regardless of species. While the difference between rectal temperatures of males and females remained relatively constant among rhesus macaques, there was a significant trend in the cynomolgus macaques toward a greater separation in rectal temperatures between the sexes as time progressed, with significant differences starting at 15 minutes and continuing through 30 minutes ($P<0.05$ at each time point by repeated measures ANOVA). In cynomolgus macaques, there was a larger decrease observed between mean baseline and final rectal temperatures regardless of table type.

Figure 3 depicts the association between weight and rectal temperature by table type and time. There was a significant trend toward animals above or equal to the median weight, maintaining higher rectal temperatures at each time point relative to animals below the median weight, on both the downdraft and the standard tables ($P<0.05$ by linear regression). Moreover, the association between weight and rectal temperature became stronger as time progressed, regardless of table type ($P<0.05$, by linear regression). Animals with a BCS above or equal to 3.0, generally maintained higher rectal temperatures regardless of table type and, as time progressed, the association between BCS and rectal temperature became more pronounced.

The differences in mean rectal temperatures by species, table type, age, and time points are summarized in Table 3. Among cynomolgus macaques, there was a significant increase in rectal temperatures for the younger age group on the downdraft table at 20 minutes (P=0.0121) and a significant reduction in rectal temperatures for the older age group on the downdraft table at 10 minutes (P=0.0441). Among rhesus macaques, there was a significant reduction in rectal temperatures for the younger age group on the downdraft table at 10 and 20 minutes (P=0.0149 and P=0.0358, respectively).Finally, the differences in mean rectal temperatures by species, table type, weight, and time points are summarized in Table 4. Among rhesus macaques, there was a significant reduction in rectal temperatures for lighter animals (< median weight) on the downdraft table at 10 minutes (P=0.0340) and for heavier animals (≥ median weight) at 20 minutes (P=0.0348). No statistically significant differences were observed between table types within either weight class of cynomolgus macaques.

DISCUSSION

Downdraft tables are a commonly used form of engineering control in research facilities to protect the worker from airborne particulates generated. Several studies have repeatedly shown the consequences of inadvertent hypothermia during anesthesia to include prolonged recovery, prolonged duration of action of drugs, increased incidence of surgical infections, impaired antibody- and cell-mediated immune defense mechanisms and an increased incidence of postoperative adverse myocardial events [18,26]. In addition to the animal welfare considerations arising from the adverse physiological effects that cold stress and hypothermia may have, hypothermia could also confound results by affecting survival and the reproducibility of animal studies [27]. The main objective of this study was to evaluate if the rectal temperature in anesthetized rhesus and cynomolgus macaques would be reduced by using a downdraft table for 30 minutes compared to a standard treatment cart.

Among rhesus macaques on the downdraft table, we found that mean rectal temperatures were between 0.63 °F and 0.90 °F lower than on the standard treatment cart at the same time points - suggesting an effect of the downdraft table on the rectal temperature, likely related to the increased downdraft airflow. Even though the rhesus macaques on the downdraft table displayed mean rectal temperatures between 0.63 and 0.90 °F lower than those on the standard treatment cart, a reduction in temperature of this magnitude is not expected to affect any physiologic functions on healthy animals. However, New World monkeys and small NHPs such as marmosets as well as young, aged, and debilitated animals may be more sensitive to subtle changes in temperature and should be more closely monitored and be provided supplemental thermal support. In contrast, we found no significant association between table type and rectal temperature changes in the cynomolgus macaques. Interestingly, the cynomolgus macaques consistently maintained a lower temperature regardless of table type throughout the study and a larger decrease was observed between mean baseline and final rectal temperatures, with 45 % (9/20) falling below 97.0 °F at the end of the procedure, thus, requiring thermal support during the recovery period. None of the rhesus macaques displayed a rectal temperature below our lower limit of 97.0 °F at the end of the procedure or required thermal support during the recovery period. In contrast, rhesus macaques maintained higher rectal temperatures throughout the study, regardless of table type, which could be explained by a normal species variability or their circadian rhythm since their historical rectal temperatures showed similar results. We established a temperature lower limit of 97.0 °F as the temperature at which the animal would receive thermal support at the end of the procedure, to avoid a severe reduction in the rectal temperature of these animals.

Briefly evaluating the effect of weight on rectal temperature by table type, there was a significant trend toward heavier animals being able to maintain higher rectal temperatures throughout the study, suggesting that weight had a protective effect against low temperature. Heavier animals have a smaller surface area relative to their body mass and are comparatively inefficient at radiating their body heat off into the surroundings, which is protective against hypothermia [28]. Heavier animals are also thought to be able to use brown adipose tissue (BAT), a fat tissue specialized in non-shivering thermogenesis, to assist them in retaining their heat after cold exposure relative to lighter animals [28]. This could have helped the rhesus macaques maintain their temperature better throughout the procedure since they had, on average, slightly larger weights than the cynomolgus macaques. In rhesus macaques, BAT is primarily found in the cervical and the axillary regions, similar to adult humans [29], and in cynomolgus macaques, BAT has been identified in the axillary, interscapular, subscapular, and cervical regions [30].

When evaluating the effect of age on rectal temperature by table type, our study suggests that a younger age appears to have a protective effect on rectal temperature. Previous research studies have shown that elderly individuals have an impaired ability to maintain body temperature when exposed to cold temperatures and are, therefore, more susceptible to the effects of hypothermia, most likely due to an age-related decrease in thermoregulatory vasoconstriction [24]. This impaired ability to efficiently thermoregulate during cold temperatures, not only has been established in elderly humans, but also in aged laboratory animals [31]. Since the cynomolgus macaques were of younger age and we did not see a significant association between table type and rectal temperatures on these animals, it is possible that a younger age might have played some role in the increased resistance to the effects of the downdraft table.

One of the limitations of this study is the effect of anesthetics on thermoregulation. Many anesthetic agents have been shown to alter thermoregulation most likely through the inhibition of the thermoregulatory centers in the central nervous system, which suppresses both shivering and vasoconstriction [24]. In a study comparing the effects of ketamine-acepromazine and tiletamine-zolazepam on body temperature, tiletamine-zolazepam produced a more profound hypothermia in a group of cynomolgus macaques [32].To control for some of the effects of anesthetics, we used a single anesthetic agent (tiletamine-zolazepam) at the same dose (5 mg/kg) for each animal during each anesthetic procedure.

CONCLUSION

To our knowledge, this was the first study evaluating the effect of the use of a downdraft table in the temperature of an anesthetized NHP. We hypothesized that the animals maintained on the downdraft table would demonstrate a decrease in rectal temperature as time progressed as compared to those animals maintained on the standard treatment cart, because of the increased airflow around the animal generated by the sustained negative airflow from the downdraft table. In summary, our study showed that the effect of using the downdraft table was, in general, larger among rhesus macaquesas demonstrated by the lower rectal temperatures as time progressed relative to the animals on the standard treatment cart. However, after analyzing subgroup variables, our study showed that the effect of the downdraft table on the rectal temperature was not always consistent and variables such as species, sex, weight, and age of the animal are important considerations when operating this type of table during live animal manipulations. In cynomolgus macaques, there was a significant reduction between starting and ending rectal temperatures with many requiring thermal support regardless of table type. Therefore, based on the results of our studyand because anesthesia impairs the ability of an animal to maintain body temperature, we recommend that thermal support be provided during extended sedation events for these animals regardless of the table type used. Additionally, the use of thermal support earlier during the operation of downdraft tables should be considered in these animals to prevent additional heat loss that could potentially lead to hypothermia on these species. Finally, our results also suggest that a younger age might have played a role in the increased resistance of the cynomolgus macaques to the effects of the downdraft table as seen with the rhesus macaques.

In terms of the type of thermal support method recommended while operating downdraft tables for live animal manipulations, conductive-fabric warming devices are the preferred method, since the airflow caused by a forced-air warming blanket could potentially disrupt or interfere with the downdraft airflow necessary to protect both the user and the working environment. In accordance with Russell and Burch's three Rs (refinement, reduction, and replacement) of animal research, [33] providing thermal support to NHPs not only during the use of a standard table but especially during downdraft table operations, is an important refinement that would help improve not only animal welfare, but research outcomes and reproducibility as well.

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