



Effect of Heat Stress on the Core Body Temperature in Normal Adults Rats
The Study was Carried out At Makerere University, College of Health Sciences, Mulago

K. ALI, K. J. JOSEPH, O. A. SHABAN, A. WALUSANSA

Islamic University In Uganda.

Received 10th June 2018 and Revised 15th September 2018

Abstract: Globally, rats are among the most important non-human mammals in both the natural ecosystems and Laboratory settings; they are the most commonly used models in assessing essential drugs and other substances that can subsequently be used safely in humans. At present, Sub Saharan Africa, and Uganda in particular, faces scarcity of rats, especially laboratory grown strains. This could probably be attributed to the ongoing climate change characterized by global warming. Core body temperature is a major factor that controls life processes in biological systems by affecting enzymatic activities. Hence, environmental factors that alter core body temperature can hinder metabolic processes, leading to adverse effects such as; dizziness, madness, impairment of the brain function, reduced response to stimuli, improper impaired coordination, locomotion, and heart beat, and may eventually lead to death of the organism. Among such factors, temperature stress has been documented as being key in altering core body temperature of organisms. Core body temperatures can be altered by factors such as; environmental temperatures, drugs, disease.

Though much research has been done about the effect of heat stress on core body temperature of mammals, especially man in Sub Saharan Africa, little is known about rats and other essential mammals that lack sweat glands and have furred bodies. This study assessed the effect of temperature stress on the core body temperature in normal adult rats (*Rattus norvegicus*) living in Sub Saharan Africa, taking those in Uganda as the case study, to avail data that can guide to improved availability and conservative utilization of rats in this region. A total of sixty rats (60) divided into three treatment groups each containing twenty (20). Twenty (20) rats subjected to hypothermia (10 °C) another twenty (20) hyperthermia (41 °C) while the rest kept at the prevailing room temperature of 25°C maintained constant by the thermostat. In each case the rectal temperature measurement estimated the core body temperature by inserting the digital thermometer into the anus before and after treatment. The results indicated that the core body temperature significantly decreased on exposure to hypothermia and insignificantly increased in hyperthermia. Therefore, it was concluded that the core body temperature was affected by hypothermia and not hyperthermia. Thus, hypothermia renders the use *Rattus norvegicus* ineffective experiment models to represent human beings.

1. INTRODUCTION

Temperature stress refers to the situation whereby the environmental temperature becomes too low or too high which could result into the body temperature being elevated or lowered. Either condition affects the normal body functioning and would be lethal to the organism (Axelrod and Diring, 2008; Vinkers *et al.*, 2013).

Among the factors that are known to affect the core body temperature includes; changes in environmental temperatures, disease, exercises, age, sex, body size , drugs among other (Bradshaw, 2007, -Juarez, *et al.*, 2010). The available literature on the factors affecting core body temperature in humans cannot be generalized to other mammals. This is because there are some differences between humans and other mammals in regard to mechanisms of temperature regulations (Campbell, *et al.*, 2000; Guihong, *et al.*, 2016). For example humans regulate their core body temperature stress through sweating alongside a number of behavior

mechanisms but information on how it fares in non-sweating and furred mammals is scanty. Therefore taking the rat as an example there is need to assess how the core body temperature of furred mammals respond to environmental.

Hypothermia is a condition in which the body's core temperature drops below that required for normal metabolism and body functions (Petrovic, *et al.*, 2008). This is generally considered to be less than 35 °C (Gisele, *et al.*, 2011) Mild condition of hypothermia is characterized by symptoms like shivering and mental confusion and severe condition lead into madness, heart complications among others (Guihong *et al.*, 2016; Mancini, *et al.*, 2011). Decreased temperatures have been reported to increase the activities of the thyroid hormones which play a pivotal role in temperature regulation, stimulation of thermo genesis, regulation of cellular metabolism and hence more food is needed by the endotherms in maintaining the core body

temperature (Sean *et al.*, 2016). Thus, decreased environmental temperature puts a lot of burden on the survival of human as a species. However, the literature on how furred mammals like rats respond to decreased temperature most especially those living in Sub-sahara Africa remains a major question of discussion.

Hyperthermia is elevated body temperature due to failed thermoregulation that occurs when a body produces or absorbs more heat than it dissipates (Giuliano *et al.*, 2000). Extreme temperature elevation can result into serious medical emergency requiring immediate treatment to prevent disability or death due to denaturation of active sites of the enzymes that drives life processes like respiration, digestion, cell division to mention but a few (Giuliano *et al.*, 2000). According to (Nelson and Habibi, 2009) acute temperature elevation may be caused by exposure to excessive heat, or combination of heat and humidity, overwhelms the heat-regulating mechanisms by affecting the normal functioning of central nervous system that play a role pertaining temperature regulation (Silvestri, *et al.*, 2016). This is the response of humans to hyperthermia and yet they used number behavioural methods to minimize temperature rise when it is too hot in addition to sweating as a mean of dissipating excessive. The situation could turn to be even worse in furred mammals including rats which hardly sweat and have limited behavioural mechanism in response to hot conditions but the literature on this is still limited.

The effect of temperature stress on core body in man has been extensively investigated. The available findings have indicated that decreased environmental temperatures resulted into decreased core temperature in the extremities; like the ears, feet and finger (Vinkers *et al.*, 2013; Guihong *et al.*, 2016) also investigated the effect of on the peripheral body temperatures and their finding indicated that stress decreased intestinal temperature, figure print but did not affect the arterial temperature (Mancini *et al.*, 2011). The available literature on humans may not be directly applicable to other mammal's since there are some differences in thermoregulation. For example man sweat and is less furred unlike other mammals and employs a variety of behavioural mechanisms in response environmental stress. With global climatic changes there is need to assess how these animals would respond to temperature extremes otherwise it would become difficult to conserve both domesticated and wild animals. This does not only put risk on the nutritional status of man in regards to animal protein most especially of mammals which must survive only after a relatively constant body temperature to the set point (Gisele *et al.*, 2011). Animal like fish which are exothermic and live in water which

has a high specific heat capacity and would maintain the water temperature irrespective of globe. This could serve as an alternative source of animal protein is increasingly becoming very expensive since they are acting as one of the export for the country's revenue to where the study was conducted. This does not only make them readily available but also unaffordable most especially to people who survive on the less than a dollar a day (Bahiigwa, Mugambe, and Keizire, 2003). Thus, any factor that is detrimental to survival of animal both domesticated and wild could devastate the economic status of individuals and the country at large. For example death of these animals in response to temperature extremes would not only result in reduction in export for foreign exchange but also affects tourism industry as well as reduction of income for the agriculturalist. This could turn even worse in countries like Uganda where the study was conducted which relies entirely on agriculture as its back bone (Bahiigwa *et al.*, 2003; FAO, 2003). Thus, it would render it impossible sustainability of Millennium Development Goals in such countries.

2. MATERIALS AND METHODS

2.1. Type of study

The study was a laboratory experimental horizontal study on eight-months old normal adult rats, housed in same cages for at least one month to avoid light variations and their effects on thyroid function. Constant food and water were supplied to the animals, right from the time they were weaned and throughout the experimental period to avoid the effects of starvation and fasting on thyroid function. The food was constituted by rat pencils bought from Nuvita Feeds and assumed to contain a balanced diet. Animals were kept in the Small-animal laboratory at the Physiology Department at College of Health Sciences, Makerere University Kampala. Rats were kept at room temperatures at 25 °C, using a thermostat that switches on cooling fan or heater automatically to avoid the effect of cold or increased temperature on the core body temperature on rats prior to the experiment.

2.2 Scope of the Study

The study was only restricted to a total of sixty (60) adult normal rats of species *Rattus norvegicus*. It specifically assessed the effect of temperature stress on the core body temperature basing on the rectal temperatures. Rats were kept subjected to only two temperature extremes i.e. high and lower temperatures at 41 °C and 10 °C respectively were used in this study with respect to the control kept at prevailing room temperature of 25 °C regulated by a thermostat. The whole exercise took a period of six months from proposal development to manuscript production.

2.3. Experimental Procedure

The characteristics of the study population are summarized in **(Table 1)**. Sixty (60) were used in this study and divided into three groups each containing twenty (20). One group of the animals were subjected to heat stress conditions for two hours i.e. they were put in the same well aerated chamber that had a thermostat set at 41 °C with an incubator fixed with a respirator tube used to supply the necessary air. The second group of 20 rats was subjected to cold stress conditions for two hours by putting them in a cold chamber at temperatures of 10 °C, also fixed with a respirator tube to supply the necessary air. Rats in the third group that served as control were left in their cages at the prevailing room temperature of 25°C maintained by a thermostat.

2.4: Measurement of Body Mass

The mass of each rat was taken and recorded by wrapping each rat in a black polythene bag and then weighed on the digital scale. The mass of the polythene bag was later taken and deducted from the total mass and so the remaining mass was for the rat.

2.5: Temperature Measurement

In all groups, each animal's rectal temperature was used to estimate the core body temperatures, before and after exposure to the temperature stress conditions. A digital thermometer with a small probe was inserted into the rectum via the anus. This estimated the core body temperature.

2.6: Data Analysis

Data was analyzed by use of computer program of STATISTICS for XL-STAT 2008 VERSION. A t- test was then carried out to find out whether there was any significant increase or decrease in the core body between control and hypothermia and hyperthermia.

3. RESULTS OF THE STUDY

As seen from the **(Table-2)** lower temperatures decreased the core body temperature from a mean value of 36.945 °C to 24.765 °C for the Control. The maximum and minimum temperatures registered for the Control and hypothermia were 38.600 °C and 23.700 °C, respectively. A statistical analysis (t-test) at $\alpha=0.05$ for the difference between the mean body temperature before and after exposure to hypothermia taken after 2 hours indicated a significant decrease ($p = 0.0001$). Hence the core body temperature in normal adult rats is significantly decreased by low temperature extremes. Higher temperatures on the other hand however, slightly increased the core body temperature from 36.925 °C for the control to 38.150 °C. A statistical analysis (t-test), showed that the mean core body temperature before and after hyperthermia taken after 2 hours of exposure showed no significant increase ($p = 0.774$). Hence, the core body temperature in normal adult rats is not affected by higher temperature extremes.

4. DISCUSSION OF THE FINDINGS

The findings show that very low environmental temperatures decreased the core body temperature from 36.945 °C to 24.765°C as shown in **(Table 2)**. A statistical analysis (t-test) at $\alpha=0.05$ for the difference between the core body temperature before and after 2-hours exposure to hypothermia, showed a significant decrease ($p = 0.0001$). These results are in line with those of (Nedergaard and Bengtsson, 2014) who found out that the core body temperature in mice was significantly reduced to 26.50 °C on exposure to 15 °C, and on prolonged period and they eventually died. This was attributed to reduction in the core body temperature caused by low environmental temperatures that block the hypothalamus thermo-receptors which later on

Table 1: Characteristics of the Study Population

Total population of the study	Hypothermia (10 °C)	Hyperthermia (41 °C)	Control (25 °C)	Body mass (g)	Diet	Genetic factor
60	20	20	20	28.87	Rat pencils	9 (total) 3 (each)

Table2: Effect of Temperature Stress (Hypothermia and Hyperthermia) on the Core Body Temperature

Variable	Observation (°C)	Minimum (°C)	Maximum (°C)	Mean	Standard deviation	Change in temperature (°C)
Control	20	36.200	37.800	36.950	0.201	
Hypothermia	20	23.700	25.500	24.765	0.635	Decreased
Hyperthermia	20	36.500	38.600	38.150	0.237	Increased

resulted into failure of the thermoregulatory centre to maintain a constant body that eventually offsets below the set point. The death of the organism was due inactivation of the enzymatic activity which controls life processes such as respiration, cell division, digestion needed in maintenance of life in organisms. However, to a small extent it differed from the current study. For example whereas in their study the experimental animal died was not the case to this study. This was because in their study the experimental animals were exposed to cold stress for prolonged period of time, unlike in the current study where the period of exposure was only one hour.

Similar observations were made by (Nelson and Habibi, 2009) where the body temperature in dogs was seen to decrease after hypothermia followed by an increase and eventually reaching the normal body temperature of 36 ± 0.2 after 96 hours after hypothermia. Body temperatures of dogs differed significantly from normal values during this period ($p=0.0001$). Thus, it appears that the core body temperature vary considerably depending on the nature and duration of exposure to environment temperature stress.

Also findings conducted by (Berry, *et al.*, 2003) in lactating cows revealed that hypothermia significantly decreased core body temperature and but hyperthermia insignificantly increased it. Thus, it appears that the response to environmental stress on the core body temperature in furred mammals are similar irrespective of the body size. This is because in mammals the core body temperature is controlled by the thermoregulatory centre of the brain, the hypothalamus whose effects are blocked by too low temperature. Higher temperature on the other hand has less effect on the hypothalamus. However, response in humans most especially to hyperthermia would differ from the rest of mammals (Campbell *et al.*, 2000). This could be attributed to less fur on human body and sweat in response to heat stress and additionally use a variety of behavioural means to regulate body temperature unlike other mammals.

Observations made by (Petrovic *et al.*, 2008) also indicated that small and poorly insulated mammals have the highest and area-specific conductance and are likely to face condition of high energy demand in maintaining body temperature which may not be readily available especially in winter conditions due to limited resources and as such could not maintain a constant body temperature. Instability of core body temperature due to exposure temperature extremes have been studied mostly in humans (Toor *et al.*, 2008). For example hypothermia of more than 20°C results in loss of the brain in the coordination of locomotory performance, impairment of physiological function and loss of

consciousness. Hypothermia of more than 5°C could often results in death. Thus, for many small and poorly insulated animals, survival mechanisms have evolved that allow them temporarily to abandon tight thermoregulatory control. Thus, exposure of animals to prolonged exposure does not only affect the core body temperature but also has an effect the entire brain functions which is lethal

5. CONCLUSION

- The core body temperature was significantly decreased in hypothermia but higher temperature insignificantly affected it. Thus, exposure of normal adult rats living in Sub-Sahara Africa to low temperature had an effect on core body temperature.
- Therefore, rat exposed to very low temperatures are not recommend to be used as experimental models because their normal physiology is altered and hence falsifying and cannot be used to represent humans' situation.

Areas for Future Research

On basis of the findings of this study, the research recommends that the following area would be suitable for further research;

- A vertical study may be conducted of the heat stress on core body using varying age groups of rats.
- A study on the effect of temperature stress on the core body temperature in primates living Sub-Sahara may also be conducted.

Declaration of Areas of Interest

I declare that there is no conflict of interests that could be perceived as prejudicing and impartiality of this manuscript. This research was purely meant for academic purposes and has nothing to do with employment and consultancies, grant fees and honoraria, ownership of stock among other.

Funding

The current area of study was entirely funded by the researcher.

Authors' Contributions

Some work on the effect of temperature stress on core body temperature on various mammals like humans have been documented. Yet there are some differences between humans and other mammals in regard to their response to environmental and temperature regulations. For example humans sweat and less furred and additionally employ various behavioural mechanisms in temperature regulation unlike other mammals. This alone suggests that finding on response of human species to temperature stress may not necessary be reflective enough to what prevails in other organisms generally. Even then the available literature that exists is on other mammals and especially on diseased ones and those living in the Mediterrean areas

which are relatively colder than Sub-Sahara Africa. Thus, the findings reported by the previous researchers may be falsifying to the prevailing conditions in Sub-Sahara Africa most especially when using rats as experimental models. The current study provided a basis of effect of heat stress on core body temperature in normal adult rats, living in sub-Saharan Africa. Therefore, researcher recommended that rats under extreme temperatures stress should not be used as experimental models because their physiology is altered and results obtained would be falsifying if extrapolated to represent human situations

6. ACKNOWLEDGEMENTS

I would like to extend my sincere appreciation to Dr. Kisakye John Joseph and Kasozi Hannington of Makerere University for their tremendous guidance in the course of this work.

Special thanks goes to Dr. Sarah Nachuha, Dean Faculty of Science, (IUIU), Professor B. Makanga, Dr. Ssekimpi PSN, Head of Department, (Biological Sciences), Shaban Okurut, Mr. Jamil E. Ssenku, Mr. Twaha Ssemogerere and Mr. Ejotre Imran for their tireless guidance, encouragement and support (IUIU).

Special thanks go Ms. A. Mulumba of Makerere University, Medical School-Mulago for assistance given during the collection of data, Mr. Brian Isabirye Makerere University, Department of statistics for his guidance rendered during analysis of data. Further still special thanks goes to Makerere University Medical School for rearing the Rats right from the beginning of this study to the end.

REFERENCES:

Axelrod, Y. K., and M. N. Diringer, (2008). Temperature management in acute neurologic disorders. *Neurol*, 26(2), 585-603.

Bahiigwa, G., K., Mugambe, and B. B. Keizire, (2003). *Fiscal reforms in Uganda. A paper presented at Workshop and Exchange of Views on Fiscal Reforms for Fisheries to promote Growth Poverty Eradication and Sustainable Management*. Paper presented at the Fisheries Department, Kampala

Berry, R. J., and A. L. Schaefer, (2003). Daily Variation In Udder Temperature Variation of dairy Cow Measured by infrared Thermography Potential for Mastitis Detection. *Can. J. Anim. Sci*, 83(678-693).

Bradshaw, D. (2007). *Environmental Endocrinology Gen. Comp. Endocrinol*, 152, 125-141.

Campbell, A. N., D., Mitchell, and B. C. (Eds.). Reece, (2000). *Biology Concept connection. An Imprint of Addition*. San Francisco: Benjamin/Cumming Wesley Longman Inc.

Decherf, I., S. Seugnet, and M. Lopez-Juarez, (2010). *Thyroid Hormone Exerts Negative Feedback on Hypothalamic Type 4 Melanocortin Receptor Expressions*.-S. Clerget-Froidevaux, B. A. Demeneix *Proceedings of the National Academy of Sciences*. .

FAO. (2003). *Brief Notes on Fisheries Production Marketing and Credit Facilities in Uganda*. Paper presented at the FAO Corporate Department Geneva.

Fox, I. S. (Ed.). (1996). *Human Physiology*. London: WMC Brown Publishers.

Gisele, L., L., Giannocco, D., Maria, and N. Tereza, (2011). The Case of Thyroid Hormones: How to Learn Physiology by Solving a Detective case Camilo Lellis-Santos. *Physiology Education*, 35(2), 219-226.

Giuliano, K. K., A. J. Giuliano, E. MacLachlan, S. Elliot, (2000). Temperature Measurement in Critically ill adults: a Comparison of Tympanic and Oral Methods. *Am J Crit Care*, 9(4), 254-261.

Mancini, A., and G. P. Littarru, (2011). Hormonal influence on Coenzyme (Q10) levels in blood plasma *Int. J. Mol. Sci*, 12, 9216-9225.

Nedergaard, T., and B. C. Bengtsson, (2014). Unexpected evidence for active brown adipose tissue in adult humans. *Am. J. Physiol*, 293 (2007), 444-452.

Nelson, E. and R. H. R. Habibi, (2009). Thyroid Receptor Subtypes: Structure and Function in Fish Gen. *Comp. Endocrinol*, 161, 90-96.

Petrovic, N., I. G. Shabalina, J. A., Timmons, B. Cannon, and J Nedergaard, (2008). Thermogenically Competent Nonadrenergic Recruitment in Brown Preadipocytes by a PPAR γ Agonist *Am. J. Physiol. Endocrinol Metab*, 295 287-296.

Sean, C., I. Lema, Michelle, Chow, Emily, R., Kristin, (2016). Endocrine and Metabolic Impacts of Warming Aquatic Habitats: Differential Responses Between Recently Isolated Populations of a Eurythermal Desert Pupfish Hardy Conservation *Physiology*, 1, 47.

Silvestri, L., A., Schiavo, and F. Lombardi, (2016). Regulation of Growth Rate and Developmental Timing by Xenopus Thyroid Hormone Receptor α Luan Wen, Yun-Bo Shi Development, Growth and Differentiation. *Endocrinology*, 58(1), 106--115.

Toor, G., M. D. Pinto, A., Alessandro, D. Lèger, (2008). Mutations in the Iodotyrosine Deiodinase Gene and Hypothyroidism *J. Med.*, 358, 1811-1818.

Vinkers, C. H. I., R. Penning, J., Hellhammer, J. C. Verster, J. H., Klaessens, B. Olivier, , and C. Kalkman, (2013). The Effect of Stress on Core and Peripheral Body Temperature in Humans. *Epub*, 13(5), 520-530.