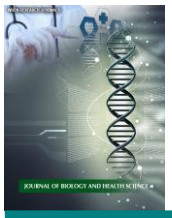

Journal of Biology and Health Science

ISSN: 3108-0189

Research Article

WRJBHS-24-010

Brown Adipose Tissue Reduction and Overfeeding Impact on Adipose Cellularity

Orien L Tulp*

Department of Medicine, University of Science Arts and Technology, Olveston, Montserrat

***Correspondence:** Orien L Tulp, Department of Medicine, University of Science Arts and Technology, Olveston, Montserrat, E-mail: o.tulp@usat.edu; DOI: https://doi.org/10.56147/jbhs.1.2.10

Citation: Tulp OL (2024) Brown Adipose Tissue Reduction and Overfeeding Impact on Adipose Cellularity. J Biol & Heal Sci 1: 10.

Abstract

Cafeteria overfeeding of normally lean rats during early postweaning growth results in hyperplasia and increased thermogenesis in Brown Adipose Tissue (BAT). Most studies have focused on the Interscapular BAT depot, which represents approximately one third of the total BAT in lean rats. To determine the effects of overnutrition *via* a Café overfeeding regimen combined with removal of the thermogenic potential of the Interscapular Brown Adipose Tissue (IBAT) depot on Adipose Tissue (AT) cellularity, groups (n=6 rats/group) of normally lean 4-week-old Sprague-Dawley rats were maintained on a Purina Chow diet (CHOW) or offered a cafeteria diet (Café) supplement for 52 days during postweaning growth and development. An additional group of the Café diet groups was subjected to surgical removal of their IBAT at 4 weeks of age and continued on the Café diet regimen (Café-IBAT). Measures of body weight (BW) and biometry were obtained at periodic intervals. At the end of the study, abdominal and subcutaneous adipose tissue depots were dissected in their entirety and measures of adipose tissue cellularity determined. BW of Café >CHOW and BW of Café were similar to Café-IBAT. Torso length was similar in all groups, but mid-abdominal girth and Girth to Torso ratios were similarly increases in Café and Café-IBAT. The mass of Epididymal (EPI), Retroperitoneal (RP), Mesenteric (MES), Dorsal (DOR) and Inguinal (ING) fat pads of Café- >>CHOW-fed rats, with further increases in DOR, ING and total fat pad mass in the Cafe-IBAT group. The AT cell number of Café > CHOW in DOR, ING and RP and unchanged by diet regimen in EPI. Adipocyte lipid content of Café >CHOW in all depots and increased further in DOR, EPI and RP, while differences in cell diameter were similar to the measures of cell lipid content. In addition, surgical reduction of IBAT resulted in further increases in the mass, cell size and cell lipid content of the ING subcutaneous depot. These results indicate that overfeeding results in greater adiposity characterized by differential cellular effects in abdominal and subcutaneous depots, with the greatest increase in diet induced adipocyte hyperplasia in the inguinal, dorsal and retroperitoneal depots. In conclusion, while adipocyte hypertrophy occurred in all depots studied, the partial reduction of BAT mass following IBAT removal resulted in an only modest additional impact on overall adiposity during overfeeding, with the greatest impact in the ING subcutaneous depot and thereby consistent with potential thermogenic compensation in other BAT depots to minimize the impact of the Café feeding regimen on developing adiposity.

Keywords: Obesity; Brown adipose tissue; Overnutrition; Adipose cellularity; Rat

Received date: December 07, 2024; **Accepted date:** December 10, 2024; **Published date:** December 31, 2024

Introduction

The metabolic effects of brown adipose tissue on the expression of Non-Shivering Thermogenesis (NST) responses to alterations in diet and environment are well established, implying a possible role of BAT on energy balance by dissipating excess caloric intake as heat while minimizing energy retention in adipose tissues [1,2]. Several authors have reported that surgical reduction of brown adipose tissue resulted in decreases in the capacity for NST in addition to a greater propensity to develop

greater mass and fatness in white adipose tissue depots [3-7]. As noted above, the BAT has also been proposed as a potential buffer to maintain energy balance against excess weight gain following episodes of excess caloric intake or macronutrient imbalance [8]. In addition, deficits in BAT energy expenditure as occur in the obese phenotype of several rodent strains are likely metabolic contributors to the excess weight gain and early onset adiposity in those animal strains [9-12]. The current increasing prevalence of obesity and its numerous pathophysiologic sequelae in Westernized societies represents a serious challenge to the effectiveness, availability and capacity of treatment resources to manage the disorders linked to the obesity-linked stigmata [13,14]. Adipose tissue is now known to contribute a broad range of hormonal activities, in addition to the roles of insulin, catecholaminergic, thyroidal and glucocorticoid regulation [15-19]. The nutritional and metabolic factors that contribute to the current epidemic of obesity and overweight conditions in Western society typically include factors of diet, environment, lifestyle, often combined with metabolic and genetic predisposition [18,19]. The therapeutic measures to treat the disorders linked to obesity and overweight conditions typically address one or more of the adaptive or heritable contributors but often may be only partially effective due to the complex nature of the conditions.

The discovery of brown adipose tissue in humans and animals goes back several centuries, but its physiologic role in energy metabolism has been discovered only more recently [1,2,20,21]. Brown adipose tissue morphology and function differs remarkably from that of white adipose tissue [21]. Both tissue types occupy specific anatomic domains that are suited to their physiologic functional role in homeostasis and energy balance [15]. In white adipose tissue, the primary function is linked to energy storage in the form of triglycerides, which become deposited in mature preadipocytes as a single large lipid droplet, surrounded with a thin layer of cytoplasm, a flattened nucleus located in the cytoplasmic ring, accompanied with cellular organelles common to somatic cells to carry our basic cellular functions including cellular metabolism to maintain cellular viability. In times of caloric excess, the lipid droplet may expand to contain up to 1 μg or more of lipid content in response to hormonal and substrate influences, while in states of caloric deprivation, the lipid droplet may be mobilized along its outer surfaces to release free fatty acids to contribute to the energy demands of peripheral tissues. Adipocytes from white adipocyte tissue may develop from preadipocytes *via* hyperplasia and hypertrophy and remain viable and responsive to accommodate increases or decreases in energy intake and serving as an energy reserve from the stored triglycerides and fatty acids throughout adolescence and much of the adult lifespan. Of significant concern, the onset of overweight and obese conditions is now occurring earlier in the lifespan than in previous generations, more often in children and adolescents where it can contribute to an earlier onset of the comorbidities commonly associated with the overweight and obese conditions [14].

In contrast, the cellular morphology and physiological functions of brown adipose tissue vary considerably from those of white AT [1,2,22]. Brown adipocytes are typically smaller, round structures with a round, centrally placed nucleus. The main function of brown adipose tissue is to contribute to heat generation, accomplished *via* a large cellular density of specialized mitochondria and strategically located in close proximity to abundant vascular tissues. Brown adipose tissues can effectively dissipate the heat energy to peripheral tissues to facilitate the regulation of homeostatic body temperatures [1,2]. Brown adipocytes can mobilize the heat generation process rapidly, *via* specialized β-neuroadrenergic membrane-bound receptors. Because the lipid in brown adipocytes is contained in multiple small locules distributed throughout the cytoplasm, it provides a greater metabolizable surface area to lipid content ratio. Thus, surface area is an important consideration that contributes to the efficiency of their energy producing functions. The locules are strategically distributed throughout the cytoplasmic compartment, thereby creating a larger surface area per unit of lipid than occurs in white adipocytes, thereby facilitating a more rapid mobilization of the contained lipid since lipid mobilization in both tissue types occurs along the outer surface area of the lipid droplet or locule. Additionally, because the brown adipocytes contain a centrally located spherical nucleus, surrounded by all essential organelles required to maintain cellular functions, the ease of morphologic distinction from other surrounding cells and tissues is readily discerned.

Brown adipose tissue develops via hyperplasia and limited hypertrophy prior to adulthood in the rat, while white adipose tissue in most depots may continue to increase by hyperplasia from preadipocytes and limited hypertrophy throughout much of the lifespan in rodents [21]. Once formed, both brown and white adipocytes appear remain present thereafter and where they may continue to expand in response to caloric status. Once formed, differentiated adipocytes of either type can remain active as lipid storage depots virtually indefinitely, to accommodate the energy needs of the organism as needed during both energy privation and excess. Both tissues regulate their lipid stores and metabolic status *via* hormonal actions including those inspired by insulin and catecholamines. In contrast, pharmacologic ablation *via* inhibition of β-adrenergic functions results in increases in locule diameter and lipid content in isolated brown adipocytes, consistent with decreased thermogenic activity [22].

The metabolic regulation of lipid stores in man and animals revolves primarily around Insulin, catecholamines and macronutrient energy intake in addition to numerous other secondary factors *via* both direct stimulatory and

Journal of Biology and Health Science

ISSN: 3108-0189

permissive effects [15]. Insulin exhibits both glycemic and lipogenic actions in peripheral tissues *via* stimulating glucose uptake, stimulating lipogenesis and lipid uptake of preformed lipids, while impeding lipid mobilization and ketogenesis from white adipose tissue stores. Thus, it is a primary hormone in the peripheral management of energy stores over time. Catecholamines can bring about the mobilization of glycogen and lipid stores during instances of duress, negative energy balance and/or food depravation. While the metabolic effects of insulin actions may persist for hours, the responses to catecholamine are initiated on the plasma membrane and the positive effects on energy balance are more immediate and give rise to the common phrase 'fight or flight' response. Plasma glucose can become significantly elevated with minutes in response to catecholaminergic stimulation, while in the presence of insulin resistance, plasma glucose and processes of glucose disposal in peripheral tissues may persist for hours to recover after the adrenergic challenge [23].

Brown adipocytes have specialized β3-adenalreceptors, in addition to individual neural synapses to facilitate highly specialized and virtually instantaneous responses to activation [2]. In white adipose tissue, insulin can impede lipoprotein lipase activity, thereby limiting the mobilization of free fatty acids and diglycerides from stored triglycerides [15]. Thus, the overall integrated regulation of energy stores from carbohydrate and lipid sources is a complex and ongoing process that continues throughout the lifespan of the individual or animal species. In humans, the presence of brown adipose tissue has been noted for many generations, with the earliest observations during cadaveric dissections some 1500 years ago and histologic evidence in humans throughout the lifespan more recently [20,21-25]. While the existence of BAT in mammalian species has been known for many years, the biochemical processes of energy generation in brown adipose tissue and its presence in adult humans have been established more recently [1,2,21]. Thus, the purpose of the present study was to determine if partial reduction of brown adipose tissue, which represent approximately one third of the total BAT mass in rats but the depot that is most surgically accessible, would result in measurable changes in adiposity and energy storage in a normally lean rat model of hyperphagia.

Material and Methods

Groups of weanling Sprague-Dawley Rats (n=6-8 rats/group, 40 g-42 g BW each) were obtained from Charles River Laboratories and acclimated to plexiglass shoebox cages in littermate pairs and fed Purina Chow and house water, *ad libitum*. At 4 weeks of age, two groups were offered a highly palatable Cafeteria diet in addition to the Purina chow regimen. At 4 weeks of age, one group of the Café diet regimen was subjected to surgical removal of the Interscapular brown adipose tissue depot under pentobarbital-ketamine anesthesia as describes elsewhere and continued on the café diet regime thereafter [3,6,7]. Recovery from the surgery was uneventful and complete within a few days. Body weights were monitored periodically throughout the study. After 52 days of the dietary regimens' animals were sacrifices *via* cervical dislocation and measures of biometry including torso length and girth diameter determined with an anthropometry tape. The epididymal, retroperitoneal, mesenteric, inguinal and dorsal adipose tissue depots dissected in their entirety, weighed to the nearest mg and prepared for measures of adipose tissue cellularity *via* the osmium fixation methods of Hirsch and Gallian [24,26,27]. Tissue lipid content determined gravimetrically *via* the method of Dole and Meinertz as conducted in our laboratory [28]. Measures of adipocyte diameters were determined microscopically with a stage micrometer *via* light microscopy at 45X magnification [22]. Data were analyzed by ANOVA corrected for multiple comparisons where indicated, and descriptive analysis via standard statistical procedures [29,30]. The study was approved by the Institutional Animal Care and Use Committee.

Results

Measures of biometry after 52 days of the chow or café regimens are depicted in **figure 1** and indicate that the Café diet resulted in greater final body weights in both the Café and the Café-IBAT groups, although significant differences in final body weight between the Café ad Café-IBAT groups were not apparent. Measures of torso length were similar in all groups, indicative of adequacy in nutrient intake when fed the Café diet. Measures of mid-abdominal girth and Girth to torso length ratio were greater in the Café fed group and were similar in both Café and Café-IBAT groups.

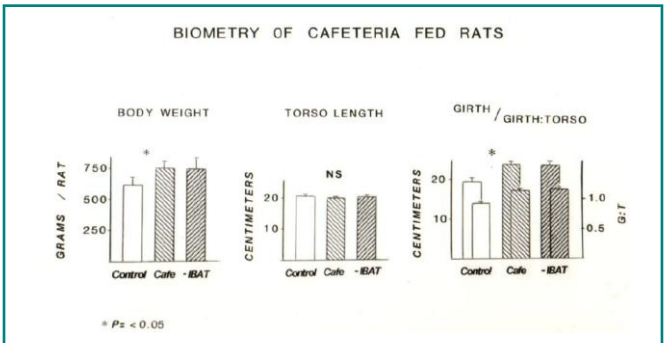

Figure 1: Biometry of cafeteria fed rats. Data are mean ± 1 SEM, n=8 rats/group. *=p=<0.05 (ANOVA).

Measures of adipose tissue mass in multiple depots is depicted in **figure 2** and indicates that the mass of Epididymal (EPI), Retroperitoneal (RP), Mesenteric (MES), Dorsal (DOR) and Inguinal (ING) fat pads were >in Café fed rats, with further increases in depot mass in the DOR, ING and total fat pad mass in the Café-IBAT group. AT cell number of Café >CHOW in DOR, ING and RP and unchanged in EPI. Adipocyte lipid content of Café > CHOW in all depots and increased further in DOR, EPI and RP, while

Journal of Biology and Health Science

ISSN: 3108-0189

differences in cell diameter were similar to the measures of cell lipid content. In addition, surgical reduction of IBAT resulted in further increases in the mass, cell size and cell lipid content of the ING depot **(Figures 3,4 and 5)**.

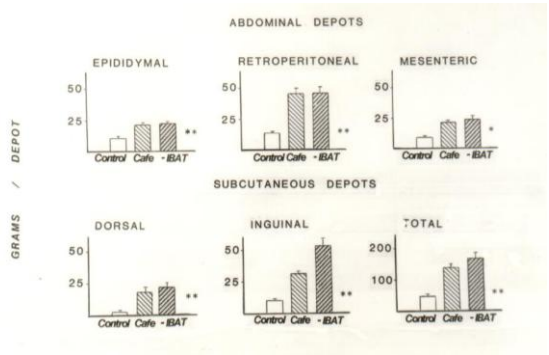

Figure 2: Effect of the Café diet on fat pad mass in abdominal and subcutaneous depots. Data are mean ± 1 SEM, n=8 rats/group. *: p=<0.05; **: p=<0.01 (ANOVA).

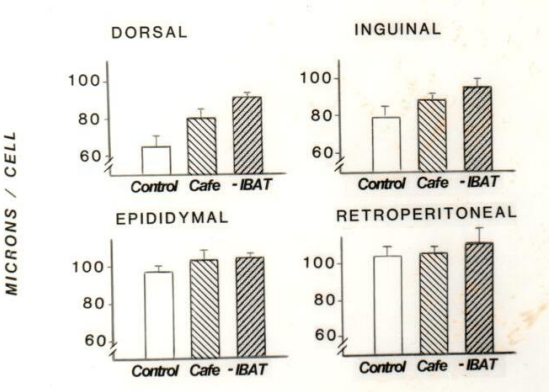

Figure 3: Effect of the Café diet on adipocyte diameters in abdominal and subcutaneous depots. Data are mean ± 1 SEM, n=8 rats/group. *: p=<0.05; **: p=<0.01 (ANOVA).

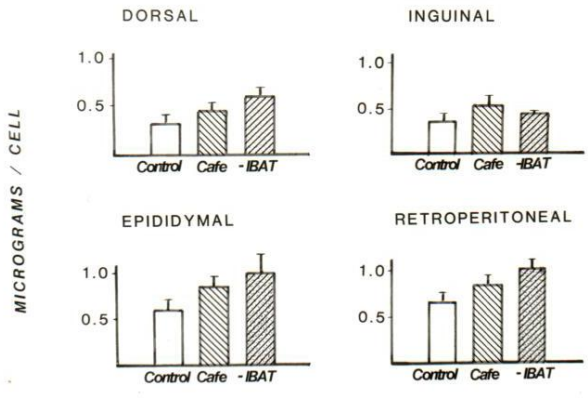

Figure 4: Effect of the Café diet on adipocyte lipid content in abdominal and subcutaneous depots. Data are mean ± 1 SEM, n=8 rats/group. *: p=<0.05; **: p=<0.01 (ANOVA).

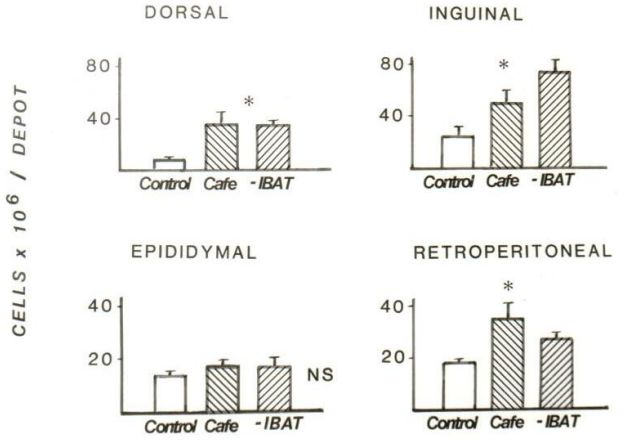

Figure 5: Effect of the Café diet on fat pad mass in abdominal and subcutaneous depots. Data. Data are mean ± 1 SEM, n=8 rats/group. *: p=<0.05; **: p=< 0.01 (ANOVA).

In the Café diet IBAT cellularity determination resulted in greater depot cell numbers in the dorsal, retroperitoneal and inguinal depots. The café-IBAT group demonstrated greater cell numbers in the Café-IBAT inguinal depot, while depot cell numbers in the Café-IBAT retroperitoneal group were also elevated at a level intermediate between the chow and Café groups.

Discussion

The presence of brown adipose tissue in hibernating and other animals had previously been reported, but its relationship to energy balance and diet-induced adaptive thermogenesis in mammalian species and humans remained unknown for many years [1,2]. In the 20th Century, Sims et all were among the first to describe the phenomena of luxus consumption in humans' in recent history, which they observed in human volunteers in the Vermont Study of Obesity [31]. Healthy, normal weight and predominantly sedentary volunteers consumed up to 10,000 excess calories/day without becoming obese and lost the modest extra weight they had gained quickly upon return to normal energy intakes [31]. Rothwell and Stock later demonstrated the apparent presence of brown fat activity following adrenergic activation and also further linking the thermogenic response to dietary and environmental factors [21]. While the presence of brown adipose tissue in hibernating animals and in humans had long been known, the biochemical mechanisms implicated and the physiologic contributions have now been elucidated by Himms-Hagen and others. The thermogenic mechanism was found to revolve around specialized BAT mitochondria capable of generating heat from the hydrolysis of high energy phosphate bonds from ATP, a process sometimes referred to as 'uncoupled oxidative phosphorylation. The process results in heat generation of ~7 kcal/mole of high energy phosphate bonds, but without

being linked to biosynthetic processes [1,2]. The effects of pharmacologic inhibition of BAT thermogenesis *via* β-adrenergic blockade resulted in enlargement of the lipid locule diameters indicative of decreased thermogenic activity, while attempts to document excess weight gain and greater adiposity following surgical removal of IBAT have yielded variable results [3-5,7,8,22].

The results of this study indicate that café- induced overfeeding results in depot specific increases in adiposity including increases in body weight, abdominal circumference and in adipose tissue cellularity in abdominal and subcutaneous depots. The results obtained herein are qualitatively similar to those that have been reported by other authors [7,8,12]. In the present study, the increases in adipose tissue cellularity occurred by a combination of hyperplasia and hypertrophy of adipocytes that were expressed differently in different depots. In the epididymal depot, adipocyte hyperplasia is likely complete by puberty and increases in depot mass beyond puberty occur *via* limited hypertrophy. Epididymal cell diameters and cell lipid content exhibited only a modest trend toward greater lipid content following the Café diet in either Café group and Café-IBAT were without additional effect. Likewise, adipocyte number in the dorsal, retroperitoneal and inguinal depots increased significantly when fed the café diet, but the cell number in the Café-IBAT group was greater only in the Inguinal depot. The reasons for the differential effects of overfeeding on differential depot specific alterations in adipose tissue cellularity are unclear but may be secondary to depot specific differences in insulin sensitivity, lipogenic actions and chronological differences in lipid accretion in the different depots. Effects on linear growth were not observed, suggesting that the Café diet as offered in combination with their chow regimen likely provided adequate nutrition to accommodate lean tissue growth and development. In contrast, the differences in adiposity correlated more with net energy intake, including refined carbohydrates and processed food items of less nutritional value. While measures of adipocyte number in the IBAT were not measured in the present study, parallel studies in both rats and mice reported a 3-fold increase in IBAT mass and cellularity after an analogous 52-day or shorter feeding regimen [6,7,23,27,32-34].

Summary and Conclusions

The results of this study showed that feeding a Café diet supplement to normally lean rat during the post-weaning growth period resulted in depot-specific increases in mass and cellularity characteristics in lean, Sprague-Dawley rats. Partial surgical reduction of BAT mass by removing the Interscapular depot in its entirety resulted in modest additional depot specific increases in adiposity, but the net increases were not proportionate to the proportion of BAT removed. Whether other BAT depots may have compensated by additional increases in cellularity or thermogenic functions remain unclear, however in an earlier study, resting and norepinephrine simulated thermogenic responses were only modestly decreased following a similar surgical reduction of IBAT [5-7]. Thus, overfeeding *via* the Café regimen in a strain of normally lean rats is an effective method to bring about modest physiological changes in adiposity and adipose tissue cellularity in white adipose tissue depots *via* differential depot-specific effects on adipocyte hyperplasia and hypertrophy.

Acknowledgements

The author thanks the University of Science Arts and Technology, Montserrat for the Institutional resources to complete this study.

References

1. Himms-Hagen J, Desautels M (1978) A mitochondrial defect in brown adipose tissue of the obese (ob/ob) mouse: reduced binding of purine nucleotides and a failure to respond to cold by an increase on binding. Biochem Biophys Res Commun 83: 628-634. [Crossref] [Google Scholar] [Indexed]

2. Cannon B, Nedergard J (2004) Brown adipose tissue: function and physiological significance. Physiol Ruc 84: 277-359. [Crossref] [Google Scholar] [Indexed]

3. Stephens DN, Nash SC, Proffitt C (1981) Dietary obesity in adult and weanling rats following removal of interscapular brown adipose tissue. Pflugers Arch 392: 7-12. [Crossref] [Google Scholar] [Indexed]

4. Tulp OL (1981) The development of brown adipose tissue during experimental overnutrition in rats. Int J Obes 5: 579-91. [Google Scholar] [Indexed]

5. Tulp OL, Gregory MH, Danforth E Jr. (1982) Characteristics of diet-induced brown adipose tissue growth and thermogenesis in rats. Life Sci 30: 1525-30. [Crossref] [Google Scholar] [Indexed]

6. Tulp OL Blaisdell cafeteria feeding and effect of long-term regional brown fat removal on development of obesity in rat. Clin Res 30: 248A, 1982.

7. Tulp OL, Clark M, Engert J, Blaisdell L, Tatelman H (1982) Effect of brown adipose tissue reduction and chronic overfeeding on body composition and adipose cellularity in rats. Proc Maine Biomed Assoc: 25.

8. Kozak LP, Koza RA, Anunciado-Koza R (2010) Brown fat thermogenesis and body weight regulation in mice: Relevance to humans. Int J Obes: S23-27. [Crossref] [Google Scholar] [Indexed]

9. Tulp OL, Einstein GP (2021) Thermogenesis, aging and obesity in the LA/Ntul//-cp (corpulent) rat. Adv Obes Weight Manag Control 11: 37-43. [Google Scholar]

10. Tulp OL, Awan AR, Einstein GP, DeBolt SP (2021) Enhanced caloric efficiency contributes to adiposity in LA/N//-cp corpulent rats. Experimental Biology 35. [Crossref] [Google Scholar]

11. Greenhouse DD (1980) New models of genetically obese rats for studies in diabetes, heart disease and complications of obesity. ILAR J 21: 1-5.

12. Tulp OL (1990) Characteristics of thermogenesis, obesity and longevity in the LA/N –cp rat. ILAR J News 32: 32-39. [Crossref] [Google Scholar]

13. World Health Organization (2021) Obesity and overweight.

14. Prevalence of childhood obesity in the United States. Division of nutrition, physical activity and obesity. National Center for Chronic Disease Prevention and Health Promotion, CDC report.

15. Rahman MS, Einstein GP, Tulp OL (2021) Autonomic, Immunological and Endocrine influences on adipose tissue as an organ. Adv Obes Weight Manag Control 11: 48-58. [Google Scholar]

16. Tulp OL (2024) Glucocorticoid ablation restores glycemic and thermogenic parameters in obesity. Diana Loreta Păun Intech Open press. [Crossref] [Google Scholar]

17. Danforth E Jr (1981) Hormonal control of thermogenesis. Life Sci 28: 1281-1287.

18. Danforth E Jr. (1983) The role of thyroid hormones and insulin in the regulation of energy metabolism. Am J Clin Nutr 38: 1006-1101.

19. Gessner K. Historie Animalium: Lib I De. Paris: Quadrupedibus, 1551.

20. Rothwell N, Stock MJ, Rothwell NJ, Stock MJ (1979) A role for brown adipose tissue in diet-induced thermogenesis. Nature 281: 31-35. [Crossref] [Google Scholar] [Indexed]

21. Tulp OL, Root D, Frink R (1984) The effect of anti-hypertensive drug treatment on brown adipocyte diameter and locule distribution in rats. Comp Biochem Physiol 79C: 317-320. [Crossref] [Google Scholar] [Indexed]

22. Tulp OL, Gambert S, Horton ES (1979) Adipose tissue development, growth and food consumption in protein malnourished rats. J Lipid Res 20: 47-54. [Crossref] [Google Scholar] [Indexed]

23. Tulp OL (2022) The effect of phenotype on development of brown and white adipose tissue cellularity and no shivering thermogenesis in the Wistar fatty rat. Adv Obes Weight Manag Control 12: 123-130. [Google Scholar]

24. Barbee O, Stevens C, Tulp OL (1987) Thermogenesis and obesity in the diabetic fatty-Wistar rat. Fed Proc 46: 578.

25. Tanuma Y, Tamamoto M, Uto T, Yokochi C (1975) The occurrence of brown adipose tissue in perirenal fat in Japanese. Arch Hiltol Jpn 38: 43-70. [Crossref] [Google Scholar] [Indexed]

26. Hirsch J, Gallian E (1968) Methods for the determination of adipose cell size in man and animals. J Lipid Res 9: 110-119. [Crossref] [Google Scholar] [Indexed]

27. Tulp OL, Shields SJ (1984) Thermogenesis in cafeteria-fed LA/N-cp (corpulent) rats. Nutr Res 4: 325-332. [Crossref] [Google Scholar]

28. Dole VP, Meinertz H (1968) Micro determination of long chain fatty acids in plasma and tissues. J Biol Chem 235: 2595-2599.

29. Ott L (1988) An introduction to statistical methods and data analysis (3rd edtn). PWS-Kent Publihers: Boston, USA.

30. Page EB (1963) Ordered hypothesis for multiple treatments: A significance test for linear ranks. J Amer Stat Assn 58: 216-230. [Google Scholar]

31. Sims EA, Goldman RF, Gluck CM, Horton ES, Kelleher PC, et al. (1968) Experimental obesity in man. Trans Assoc Am Physicians 81: 153-170. [Indexed]

32. Mercer SW, Trayhurn P (1987) Effect of high fat diets on energy balance and thermogenesis in brown adipose tissue of lean and genetically obese ob/ob mice. J Nutr 117: 2147-2153. [Crossref] [Google Scholar] [Indexed]

33. Tanuma Y, Ohata M, Ito C, Yokochi C (1976) Possible function of human brown adipose tissue as suggested by observation on perirenal brown fats from necropsy cases of variable age groups. Arch Histol Jpn 39: 117-145. [Crossref] [Google Scholar] [Indexed]

34. Tulp OL, Hansen CT, Michaelis OE (1989) Effect of dietary carbohydrate and phenotype on thyroid hormones and brown adipose tissue locularity in adult LA/N –cp rats. Comp Bioch Physiol 94A: 225-229. [Crossref] [Google Scholar]