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Quantity not composition of dietary fats represents the dominant contributor to experimental obesity: Relevance to human pathophysiology

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ABSTRACT

Plant fats are low in saturated fats but high in unsaturated fats compared to animal fats, and are supposedly less obesogenic. This study compared the obesogenic effects of plant and animal derived fatty diets in Wistar rats. Rats of each gender were divided into three dietary (standard chow (SC), high fat diet rich in animal fat (HFDaf) and a high fat diet rich in plant fat (HFDpf)) groups of ten each and fed for 17 weeks. Anthropometric, Adiposity and nutritive variables were assessed using standard methods. Comparing HFDpf to HFDaf: Abdominal circumference (AC),initial feed intaken (IFI), final feed intake(FFI), final body weight (FBW), white adipose tissue (WAT) were increased but brown adipose tissue (BAT) decreased in male rats fed with HFDpf; also, there were increased body length, IFI, FFI but decreased AC, FBW, BAT in female rats fed with HFDpf. Comparing male to female rats: Thoracic circumference, IFI, FFI, energy intake were increased while Adiposity index decreased across diet groups in male rats; the AC, FBW increased while WAT, BAT decreased in HFDpf fed group, also, BAT was increased but AC, FBW decreased in HFDaf fed group in male rats. Palatability and high feed efficiency of consumed diets were more associated with obesogenic risk than just the level of saturation. Therefore, Obesogenic effects of fatty diets in both genders is more dependent on the quantity (amount) of fatty diet consumed than the dietary fat composition alone.

1. Introduction

Obesity which WHO pointed as one of the most important non-communicable diseases is characterized by excessive body fat accumulation [1]. Overconsumption of a diet high in energy has a higher probability of a positive energy balance which eventually leads to overweight and in extreme cases obesity [2]. Considerable interest has been shown in the effect of consumption of dietary fat with varying degrees of saturation/unsaturation [3]. A high fat diet usually contains both saturated and unsaturated fat depending on the fat source. Diets high in saturated fats compared to unsaturated fats have been shown to either increase, decrease or have no effect on body weight [3–5] and body fat storage [6–8]. On the other hand, diets high in unsaturated fats especially polyunsaturated fats were shown to increase total energy expenditure [9], resting metabolic rate, thermic effect of food [10], fat oxidation in humans [11], norepinephrine stimulation of lipolysis in white adipose tissue of rats [12] and increase sensitivity of the adipocyte β adrenergic receptors [13]. Despite the cut down on saturated fat consumption, obesity and its comorbidities are still on the increase pointing to a possibility that consumption of food rich in saturated fat may not be the sole malefactor in obesity and its related issues. This study intends to do a comparative analysis of anthropometric variables, adiposity index, energy evaluation and nutritional variables in male and female Wistar rats fed with two different high fat diets containing either Lard (animal fat rich in saturated fatty acids) and Groundnut oil (plant fat rich in unsaturated fatty acid) to investigate which of the two diets is more obesogenic and also to evaluate the effect consumption of these diets' have on gender.

2. Materials and methods

2.1. Animals and experimental protocol

This study was approved by the University of Ibadan Animal Care and Use Research Ethics Committee (UI-ACUREC). For the study, 30

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male and 30 female weanling Wistar rats (28 days of age), with weights ranging between 40–50 g, were purchased from the Animal House of the College of Medicine, University of Ibadan, and used. During the study, the animals were kept in wire mesh cages with access to food and water *ad libitum*. They were acclimatized for one (1) week after which they were randomly divided into three equal groups, (n = 10; 5males and 5 females), and fed for seventeen (17) weeks. Group 1 (SC) were control male and female rats fed with standard rat chow. Group 2 (HFDaf) were male and female rats fed with a high fat diet, with the fat component gotten from an animal source. Group 3 (HFDpf) were male and female rats fed with high fat diet, with the fat gotten from plant source. Body Weight was recorded weekly, feed intake was recorded daily, while body length (BL), abdominal circumference (AC) and thoracic circumference (TC) were recorded at the beginning and end of the experiment. The rats were anesthetized with sodium pentobarbital (50 mg/kg BW, intraperitoneally), and BL, TC, and AC were measured before dissection while white adipose tissue (WAT) mass, brown adipose tissue (BAT) mass, energy intake (EI), feed efficiency (FI) were measured/estimated after dissection.

2.2. Proximate analysis and energy evaluation

Proximate analysis and energy evaluation were carried out on the diets. Proximate analysis of the diets was carried out chemically and metabolizable energies of the diets were estimated using the Atwater system [14]. The proximate analysis of each feed were as follows;

- Control group: Crude protein 22.7%, Crude fat 3.6%, Crude fiber 8.6%, NFE 49.6%, ASH 6.2%, Moisture 9.3%, M.E 3.2%
- HFDaf group: Crude protein 25.9%, Crude fat 31.0%, Crude fiber 3.1%, NFE 30.8%, ASH 4.3%, Moisture 5.0%, M.E 5.1%
- HFDpf group: Crude protein 22.3%, Crude fat 16.3%, Crude fiber 3.6%, NFE 42.8%, ASH 5.2%, Moisture 9.4%, M.E 4.1%

Where NFE refers to Nitrogen–free Extract; M.E metabolizable energy

2.3. Anthropometric parameters

The abdominal circumference (AC) (immediately anterior to the forefoot), thoracic circumference (TC) (immediately behind the foreleg), body length (nose-to-anus or nose–anus length) were determined in all rats at the beginning and end of the 17 week. The body weight (BW) and body length at the end of the experiment were used to determine;

1) Body mass index (BMI) = Body weight (g)/Body length^2 (cm^2).
2) Mean Cumulative body weight gain = Total accumulation of body weight in 17 weeks (grams)
3) Percentage gain = (actual measurement – initial measurement)/ initial measurement $\times$ 100

2.4. Adiposity index

The adipose tissue fat pads were dissected and weighed. White adipose tissue (WAT) or Total body fat was measured as the sum of the following individual fat pad weights: epididymal fat + retroperitoneal fat + visceral fat. Brown adipose tissue was measured as the amount of fats in grams present at the back of the neck region known as the interscapular region. The adiposity index was calculated as (total body fat/final BW) $\times$100 [15]. The adiposity index was used as a measure of adiposity, because the degree of fat tends to increase gradually with obesity [16]

Table 1
Comparison of Body length (cm), Thoracic Circumference (cm), Abdominal Circumference (cm), Body Weight (grams) of Male and Female rats feed with SC, HFDaf and HFDpf for 17 weeks.

Group Variable	SC	HFDaf	HFDpf
Body Length			
Male	71 ± 3.1	77 ± 2.6	$83 \pm 1.7^{*}$
Female	69 ± 2.8	68 ± 1.8	71 ± 0.65^{c}
Thoracic Circumference			
Male	85.3 ± 3.9	$117.2 \pm 5.6^{*}$	$130.9 \pm 8.3^{*}$
Female	$42 \pm 5.3^{*}$	$62.7 \pm 4.5^{\#, a}$	$74.6 \pm 5.7^{\#, c}$
Abdominal Circumference			
Male	76.6 ± 1.8	$101.7 \pm 2.1^{*}$	$120.9 \pm 4.5^{*, a}$
Female	64.3 ± 2.7	$120.6 \pm 2.2^{\#, a}$	$94.2 \pm 3.4^{\#, b, c}$
Final body weight			
Male	360 ± 15.0	$216.1 \pm 6.1^{*}$	$439 \pm 15.0^{*, a}$
Female	366.3 ± 11.7	$434.6 \pm 7.8^{\#, a}$	$346 \pm 11.0^{b, c}$

Values are expressed in percentage changes from starting point of Mean ± S.E.M. n = 5 “p<0.05 differ significantly from female rats when, “*” is compared to SC (male); “#” is compared to SC (female); “a” is compared to HDFaf (male); b is compared to HDFaf (female) and c is compared to HDFpf (male) respectively.

2.5. Nutritional analysis

Food consumption was measured daily, and BW was monitored once per week. Weekly caloric intake was calculated as the product of the average weekly food consumption and the caloric value of each diet. Based on food and caloric intake, the following nutritional parameters were calculated [17]:

a.) Feed intake (g/day) = Mean daily food consumption during the 17weeks
b.) Mean Cumulative Feed intake (g) = Mean total accumulation of food during the 17 weeks
c.) Energy intake (kJ/day) = mean food consumption x dietary metabolizable energy [18]
d.) Mean Cumulative Energy intake (KJ) = Mean total accumulation of Energy during the 17 weeks
e.) Feed efficiency (FE; %) = (mean body weight gain (g) x 100)/energy intake (kcal)

2.6. Statistical analysis

Data obtained were expressed as mean ± standard error of mean (mean ± SEM). The significance of the results for dietary groups within each generation was evaluated using analysis of variance (ANOVA) and the means were compared using Tukey-Kramer Multiple comparison Test. $P < 0.05$ was regarded as statistically significant.

3. Results

3.1. Anthropometric variables

There was significant increase in the body length of HFDpf male group when compared to SC male and HFDpf female respectively (Table 1). Male and Female rats in HFDaf and HFDpf groups had increased TC and AC compared to their SC groups (Table 1). Also, the males had higher TC compared to female rats in all diet groups (Table 1). An increase in male rats but a decrease in female rats AC diameter was observed in the HFDpf group when compared to their respective HFDaf group (Table 1). The male rats had decreased HFDaf but increased HFDpf AC diameter compared to their female counter-part (Table 1). FBW increased in the HFDpf group but decreased in HFDaf group when compared with the SC in male rats. In female rats, FBW increased in HFDaf group but no significant difference in the HFDpf group when compared to SC. HFDpf had FBW

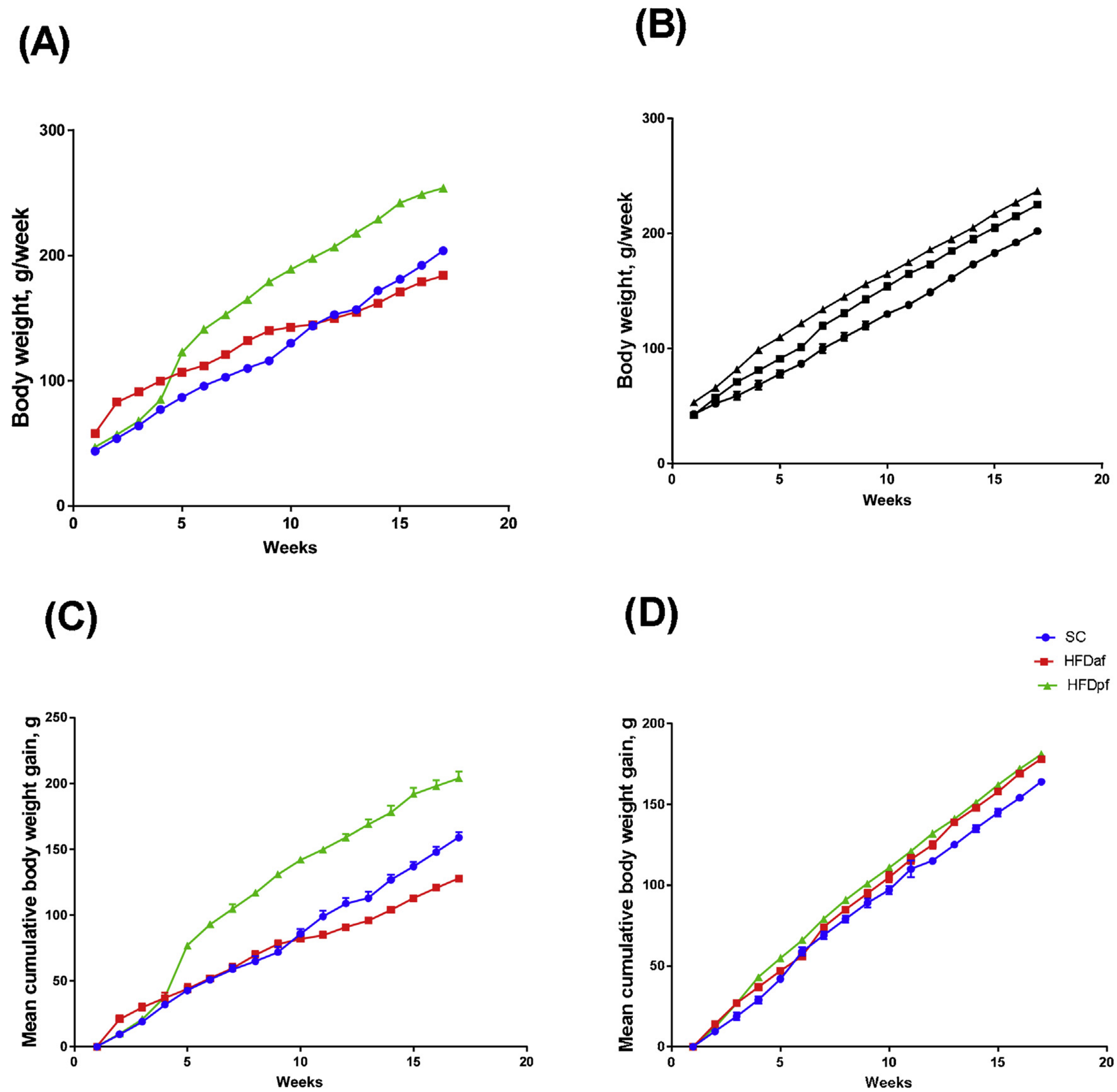

Fig. 1. Body weight of male (a) and female (b); Mean Cumulative body weight male (c) and female (d) of ● = SC, ■ = HFDaf, and ▲ = HFDpf Wistar rat groups during 17 weeks. n = 5.

increased in male but reduced in female rats when compared to their respective HFDaf groups (Table 1 and Figs. 1 and 2). Male rats were found to have greater FBW gain in HFDpf but reduction in HFDaf than the female rats (Table 1 and Figs. 1 and 2).

3.2. Adiposity evaluation

There was significant increase in the BMI of HFDpf and HFDaf when compared to SC but no observable difference when the BMI of HFDpf was compared with HFDaf group in both sexes (Table 2). There was significant increase in AI and WAT mass in HFDaf and HFDpf when compared to SC in both sexes (Table 2). There was no significant difference in AI when HFDpf was compared to HFDaf in both sexes (Table 2). In the females, there were higher accumulation of WAT mass in the HFDpf group than the HFDaf group (Table 2) but no change in WAT mass amongst the fatty groups was observed in the male rats (Table 2). Female rats had higher AI compared to their male counter-part in both high fat diets (Table 2). Also, females accumulated more WAT mass that the males only in HFDpf group (Table 2). HFDaf and HFDpf groups respectively in female rats had high BAT mass compared to the SC, also, HFDaf had higher BAT mass than HFDpf diet group (Table 2). There was an increase in BAT mass in the males compared to the females in HFDaf group but a reversed occurred in HFDpf group were the females had higher BAT than the males (Table 2).

3.3. Nutritional and energy evaluation

In female rats, the initial feed intake showed a reduction in feed intake in HFDaf diet group when compared to SC group. Also, there was a decrease in feed consumption in HFDaf group when it was compared to HFDpf in female rats (Table 3 and Fig. 3b and d). There was a significant decrease in the final feed intake in HFDaf but an increase in HFDpf when compared to SC. The decrease was also observed in HFDaf when compared to HFDpf (Table 3 and Fig. 3b and d). In the male rats, there was significant increase in initial feed intake in HFDpf rats when compared to SC rats. Also, rats in HFDaf groups consumed lower amount of fed when compared to HFDpf at their first exposure in both sexes (Table 3 and Fig. 3a and c). The final feed intake in male rats showed decreased feed consumption in HFDaf and HFDpf rats when compared to SC rats, also in males, a reduction in feed intake was observed in HFDaf rats when compared to HFDpf rats (Table 3 and Fig. 3a and c). Regardless of the group, male were observed to consume more feed than the females

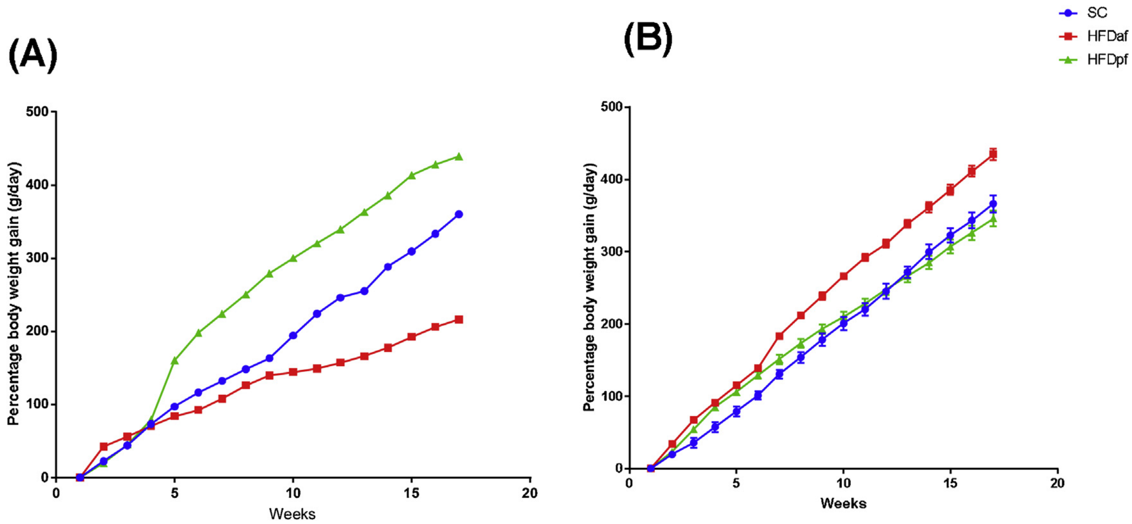

Fig. 2. Percentage Body weight gain of male (a) and female (b) of ● = SC, ■ = HFDaf, and ▲ = HFDpf Wistar rat groups during 17 weeks. n = 5.

Table 2
Comparison of Body Mass Index (g/cm^2), Adiposity Index (%), White Adipose Tissue (g) and Brown Adipose Tissue (g) of Male and Female rats feed with SC, HFDaf and HFDpf for 17 weeks.

Group Variable	SC	HFDaf	HFDpf
Body Mass Index			
Male	8.6 ± 0.22	11 ± 0.39*	12 ± 0.42*
Female	8.5 ± 0.16	11 ± 0.35#	11 ± 0.37#
Adiposity Index			
Male	1.6 ± 0.12	3.8 ± 0.14*	3.2 ± 0.12*
Female	1.7 ± 0.1	5.3 ± 0.18#, a	4.9 ± 0.14#, c
White Adipose Tissue			
Male	2.9 ± 0.12	9.5 ± 0.56*	8.9 ± 0.67*
Female	3.3 ± 0.26	9.7 ± 0.72#	14 ± 0.75#, b, c
Brown Adipose Tissue			
Male	0.61 ± 0.02	1.4 ± 0.03*	0.6 ± 0.05a
Female	0.55 ± 0.06	1.2 ± 0.03#, a	0.79 ± 0.04#, b, c

Values are expressed as Mean ± S.E.M. n = 5 "p<0.05 differ significantly from female rats when, "*" is compared to SC (male); "#" is compared to SC (female); "a" is compared to HDFaf (male); b is compared to HDFaf (female) and c is compared to HDFpf (male) respectively.

Table 3
Comparison of Initial Feed Intake (g/day), Final Feed Intake (g/day), Energy intake (KJ/day) and Feed Efficiency (%) of Male and Female rats feed with SC, HFDaf and HFDpf for 17 weeks.

Group Variable	SC	HFDaf	HFDpf
Initial Feed Intake			
Male	49 ± 0.80	53 ± 0.72	68 ± 0.7*, a
Female	41 ± 0.75	31 ± 1.1#, a	42 ± 0.4b, c
Final Feed Intake			
Male	102 ± 0.59	74 ± 0.93*	96 ± 0.65*, a
Female	69 ± 0.71*	53 ± 0.4#, a	75 ± 0.23#, b, c
Energy intake			
Male	1006 ± 41	1447 ± 38*	1409 ± 45*
Female	816 ± 31	972 ± 33#, a	1068 ± 42#, c
Feed Efficiency			
Male	31 ± 4.2	21 ± 2.6	33 ± 4.2
Female	41 ± 5.9	38 ± 5.2	36 ± 4.7

Values are expressed as Mean ± S.E.M. n = 5 "p<0.05 differ significantly from female rats when, "*" is compared to SC (male); "#" is compared to SC (female); "a" is compared to HDFaf (male); b is compared to HDFaf (female) and c is compared to HDFpf (male) respectively.

(Table 3). In all gender, HFDaf and HFDpf groups had higher energy intake when compared with the SC groups (Tables 3 Fig. 4). The male rats had higher energy intake than the female rats in all groups (Table 3). There was no significant difference in the feed efficiency across all groups in both male and female rats and gender has no influence on feed efficiency of rats (Table 3 and Fig. 5).

4. Discussion

A lot of factors have been implicated in the aetiology and pathogenesis of obesity. This include such as dietary intake [19], lack of exercise [20] and sleep [21,22] hormonal imbalance [23] and metabolic disorders [24,25]. Lifestyle changes, such as a change in dietary fat-type consumption, are often used as therapies in the prevention and management of obesity and associated metabolic disorders [26,27]. This has contributed in large part to the age-long controversy regarding saturated fat, which is normally referred to as bad fat and unsaturated fat also referred to as good fat [28]. This study points to the likelihood that consumption of diets high in energy over a long period may be the major factor responsible for obesity and its comorbidities.

Total body weight depends on the body water mass [29], protein mass [30] and bone mass [31], in addition to fat mass [32]. Any increase in these factors would lead to an increase in the body weight. Increased adipose tissue content was observed in this study and this can be directly correlated and adduced to have been responsible for the noticeable increase in body weight in the test groups. Weight gain due to prolonged exposure to high calorie fatty diets has been reported in several studies [33,34], and in some studies, the justification for the weight increase from the high calorie diets was protein mass depletion and an increase in adipose tissue mass [35,36]. Contrary reports by other researchers state a similarity in weight between animals fed a fatty diet and those fed on a normal diet over a long period [37]. This present study, like previous studies, has clearly shown that high intake of fatty diets over a long period of time will lead to an increase in adipose tissue mass which in turn will contribute to an increase in total body weight. A combination of both high protein and fat contents in the fatty diets would result in increased protein and fat tissue masses which would invariably lead to increased weight as observed in the test group. The HFDaf female group, whose diet had a protein content of 25.9% and although not significant, had the highest numeric feed efficiency value of 38% showing that its consumed feed was the most efficiently utilized in the body, must have contributed to the increase in body weight observed despite the low feed intake and **white** adipose tissue mass.

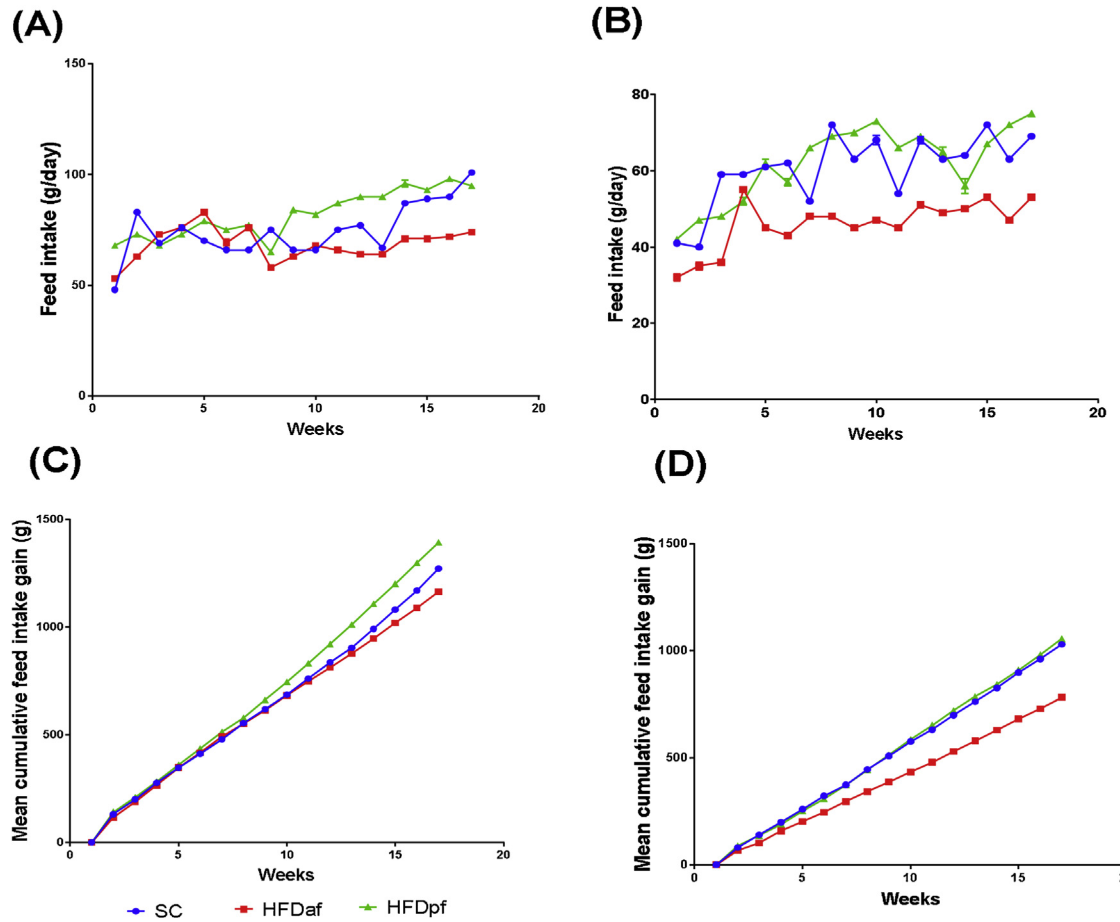

Fig. 3. feed intake in male (a) and female (b); Mean Cumulative feed intake in male (c) and female (d) of (●) = SC, (■) = HFDaf, and (▲) = HFDpf Wistar rat groups during 17 weeks. n = 5.

Overconsumption of a diet high in energy has a higher probability of a positive energy balance which eventually leads to overweight and in extreme cases obesity [38]. Overconsumption has being attributed to the high palatability of high energy diets (in most cases high fatty diets) in comparison to other diets [39–41]. This study reports a positive correlation between feed intake and energy intake. Diets with very high energy values above the body requirements lead to accumulation of excess energy in the form of body fat. The energy intake observed in the HFDaf and HFDpf of both male and female rats was in accordance to the findings of Wang et al., who proved that dietary fats contain about double the energy found in protein and carbohydrates [42]. The contribution of caloric intake to obesity development in the two models elicited significant differences in body fat, fat pad mass, body mass index and the adiposity index between the obese (HFDaf and HFDpf) and SC groups. These results are consistent with several studies that induced obesity in rats by HFD-feeding [43–45]. Studies have shown that both obese and lean rats are sensitive to the palatability of the food [46,47] with fatty food being known to be more palatable than other food types [48]. Other studies are of the view that high fat diets are consumed in lesser amount than the control diet [34,37]. In this study, there was high consumption of fatty food in the first week of introduction of the feed but with subsequent exposure to the fatty feed (Fig. 1a and b), a decline was noticed and it can be assumed that continuous exposure of the body to fatty diet stimulated a mechanism that causes reduction in its palatability and consumption, although this mechanism was not investigated.

Several studies have examined the possible health implication of increased thoracic circumference ever since Vague [49], proposed that those who have fat predominantly accumulated in the upper body rather than the lower body are more susceptible to metabolic disturbances. The fatty diets in this study caused an increase in thoracic circumference in both male and female rats. Among several anthropometric measurements, waist circumference has been shown to be the best predictor of intra-abdominal fat thickness in normal subjects, and therefore of central obesity in humans [50]. Prolonged feeding on the fatty diets would lead to increased abdominal adipose tissue accumulation, which would explain the increase abdominal circumference observed in this study. A similar result reporting an increase has been reported by [51].

Body-mass Index (BMI) has been the most commonly used measure of overall obesity to reflect total body fat, although the index cannot distinguish between muscle and fat mass [52]. From our study, the BMI was higher in rats that consumed both fatty diets. Previous studies made attempts at adducing the increase in BMI to an observed decrease in body length [51,53,54]. No observable differences in body length were observed in our study, although it was noted that the body length was not directly proportional to the increase in body size.

High fatty diets, especially those rich in animal fats, are very palatable compared to fatty diets rich in plant fat. Research has been on for decades to determine which of the two fatty diets sources is more obesogenic. Earlier studies in animals showed that models fed with high fat diet enriched with plant fat gain less body energy and had lower fat content in their carcasses than high fat diet enriched with animal fat [3,9]. Also, Rolland et al. [55], in their study observed that food intake and body weight in butter-fed Zucker rats where higher than those fed with soybean oil. Our results were contrary

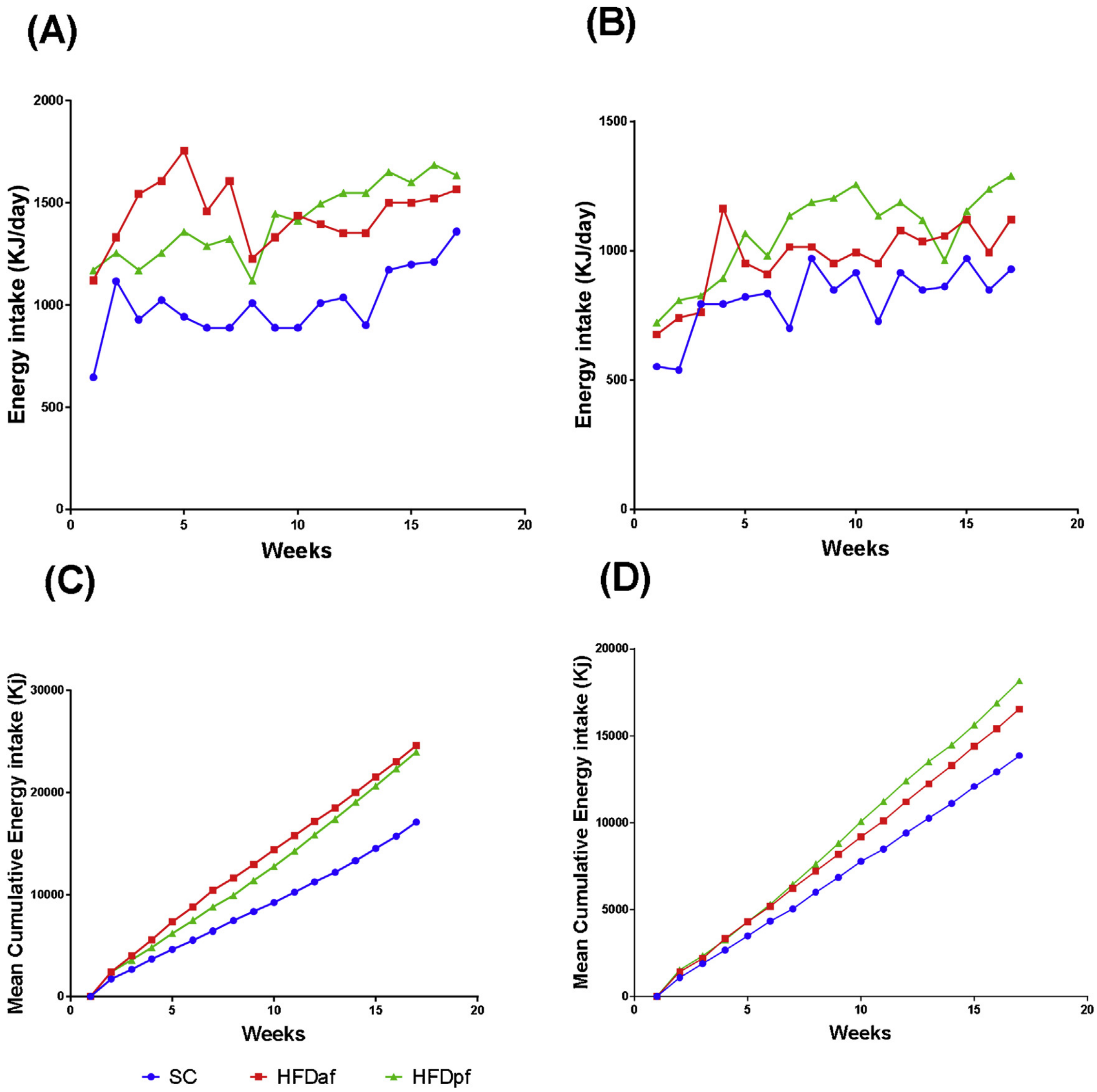

Fig. 4. Energy intake in male (a) and female (b); Mean Cumulative Energy intake in male (c) and female (d) of ● = SC, ■ = HFDaf, and ▲ = HFDpf Wistar rat groups during 17 weeks. n = 5.

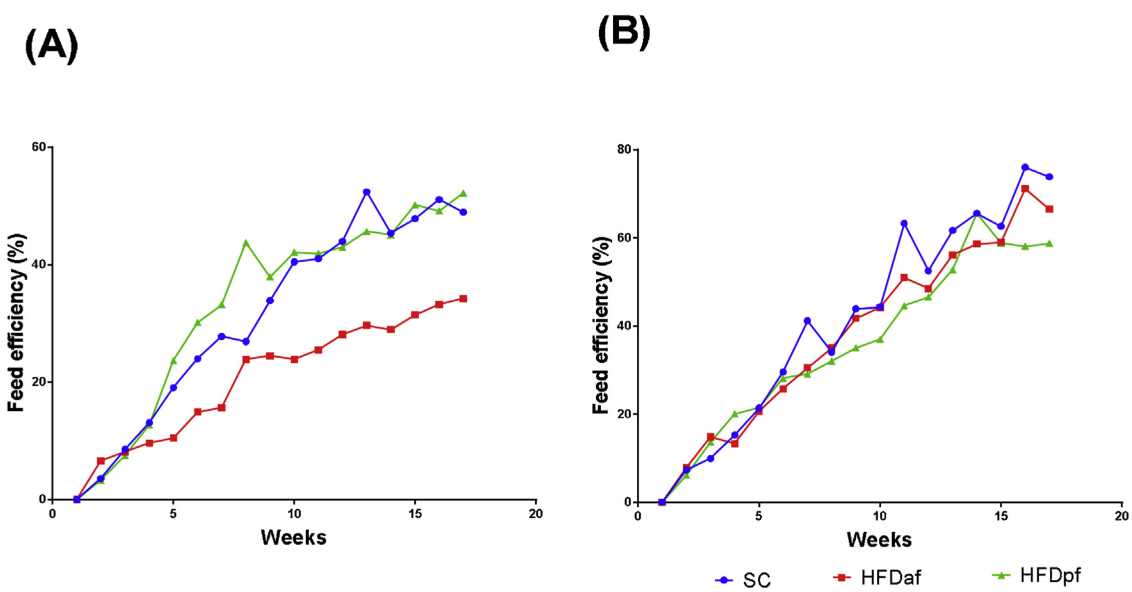

Fig. 5. Feed efficiency in male (a) and female (b) of ● = SC, ■ = HFDaf, and ▲ = HFDpf Wistar rat groups during 17 weeks. n = 5.

to previous reports, as fatty diet derived from plant sources were observed to be more palatable (due to the amount consumed) than those from animal sources. This palatability in turn resulted in the higher abdominal circumference, body weight, and feed intake in the fatty diet group rich in plant fat in comparison with the fatty food rich in animal fat. The BMI, body length, thoracic circumference, adiposity index, WAT, energy intake and feed efficiency were either similar or not clearly consistent in the male and female rats to be considered significant. Even though results of studies were contradictory to our study, one factor remain common to all study, food intake was highest amongst all animal groups that showed a significant difference in any of the above variables. This suggests that the quantity of diet consumed plays a big role, in addition to the quality of the diet.

Females in the past where shown to be more likely to become obese than men [56], current research has however gone contrary to this finding [57,58], both observed that the body weight gain (g) was higher in males compared to their female counterparts. Male rats have been shown by several reports to consume more food, which directly means they consume higher calories compared to female rats [57]. Similar results were replicated in this study across the three dietary groups, clearly showing that gender has a big role to play in eating behavior and obesity. Males usually have higher thoracic circumference than their female counterparts [59], this sexual dimorphism could be due to females having smaller lung volume values than males of the same height and age [58,60]. This study also showed the males having higher thoracic circumference than females in all diet groups. Khalid et al. [57], in their study observed that the food consumed (g/day), energy intake (KJ/day), and body length (cm), were all higher in control male Wistar rats compared to females. The findings of Kautzky-Willer et al. [61], was that the deleterious effect of increasing adiposity, as indicated by increased BMI, on insulin sensitivity, is sex specific, being stronger in males than in females. Rats fed on our diets showed no sexual dimorphism in BMI. Influence of sex on BMI has been controversial, with some studies being of the opinion that men had lower BMI than their female counterparts [58], while other studies suggesting the opposite [57,61].

5. Conclusion

High consumption of fatty diet predisposes rats to obesity and probably its comorbidities, irrespective of the nature of the fatty diet or energy content of the fatty diet. Sexual dimorphism was observed in majority variables checked and could be said to influence feeding patterns. High consumption of diets that directly correlates with feed efficiency (that is, the effective utilization of the diet by the body), puts the animal at greater risk of developing obesity than just the quality of the diets. Therefore, obesogenic effects of fatty diets come from the quantity (amount) of fatty diet consumed and not the quality (level of saturation).

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Declaration of Competing Interest

None.

References

[1] J. Owen, E. Reisin, Non-communicable disease: a welcome and long needed addition to the WHO's 2012 World Health Statistics, Curr. Hypertens. Rep. 14 (6) (2012) 475–477, http://dx.doi.org/10.1007/s11906-012-0303-6.
[2] B. Swinburn, G. Egger, Preventive strategies against weight gain and obesity, Obes. Rev. 3 (4) (2002) 289–301.
[3] Y. Shimumora, T. Tamura, M. Suzuki, Less body fat accumulation in rats fed a safflower oil diet than in rats fed a beef tallow diet, J. Nutr. 120 (1990) 1291–1296.
[4] D.A. Pan, L.H. Storlein, Dietary lipid profile is a determinant of tissue phospholipid fatty acid composition and rate of weight gain in rats, J. Nutr. 123 (1993) 512–519.
[5] W. Su, P.J.H. Jones, Dietary fatty acid composition influences energy accretion in rats, J. Nutr. 123 (1993) 2109–2114.
[6] J.O. Hill, J.C. Peters, D. Lin, F. Yakabu, H. Greene, L. Swift, Lipid accumulation and body fat distribution are influenced by type of dietary fat fed to rats, Int. J. Obes. Relat. Metab. Disord. 17 (1993) 223–236.
[7] F. Bourgeois, A. Alexiu, D. Lemmonier, Dietary-induced obesity: effect of dietary fats on adipose tissue cellularity in mice, Br. J. Nutr. 49 (1983) 17–26.
[8] G. Schillaber, D.C.W. Lau, Regulation of new fat cell formation in rats: the role of dietary fats, J. Lipid Res. 35 (1994) 592–600.
[9] S.W. Mercer, P. Trayhurn, 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 (1987) 2147–2153.
[10] W.D. Van Marken Lichtenbelt, R.P. Mensink, K.R. Westerterp, The effect of fat composition of the diet on energy metabolism, Z. Ernahrungswiss. 36 (1997) 303–305.
[11] P.J.H. Jones, D.A. Schoeller, Polyunsaturated:saturated ratio of diet fat influences energy substrate utilization in the human, Metabolism 37 (1988) 145–151.
[12] A.B. Awad, E.A. Zepp, Alteration of rat adipose tissue lipolytic response to norepinephrine by dietary fatty acid manipulation, Biochem. Biophys. Res. Commun. 15 (86) (1979) 138–144.
[13] C. Nicolas, D. Lacasa, Y. Giudicelli, et al., Dietary (n_6) polyunsaturated fatty acids affect β adrenergic receptor binding and adenylate cyclase activity in pig adipocyte plasma membrane, J. Nutr. 121 (1991) 1179–1186.
[14] W.O. Atwater, Principles of Nutrition and Nutritive Value of Food Farmers Bull, U.S.D.A, Washington, 1910, No. 142.
[15] B.A. Taylor, S.J. Phillips, Detection of obesity QTLs on mouse chromosomes 1 and 7 by selective DNA pooling, Genomics 34 (1996) 389–398, http://dx.doi.org/10.1006/geno.1996.0302.
[16] A.S. Leopoldo, A.P. Lima-Leopoldo, A.F. Nascimento, R.A.M. Luvizotto, M.M. Sugizaki, D.H.S. Campos, D.C.T. da Silva, C.R. Padovani, A.C. Cicogna, Classification of different degrees of adiposity in sedentary rats, Braz. J. Med. Biol. Res. 49 (4) (2016), http://dx.doi.org/10.1590/1414-431X20155028.
[17] Y.S. Diniz, L.A. Faine, C.M. Galhardi, et al., Monosodium glutamate in standard and high-fiber diets: metabolic syndrome and oxidative stress in rats, Nutri. 21 (2005) 749–755.
[18] E.L. Novelli, Y.S. Diniz, C.M. Galhardi, G.M. Ebaid, H.G. Rodrigues, Anthropometrical parameters and markers of obesity in rats, Lab Anim. (NY) 41 (2007) 111–119.
[19] D. Papandreou, K. Makedou, A. Zormpa, M. Karampola, A. Ioannou, A. Hitoglou-Makedou, Are dietary intakes related to Obesity in Children? Maced J Med Sci. 4 (2) (2016) 194–199, http://dx.doi.org/10.3889/oamjms.2016.045.
[20] P. Wiklund, The role of Physical activity and exercise in obesity and weight management: time for critical appraisal, J. Sport Health Sci. 5 (2) (2016) 151–154.
[21] J.P. Chaput, Short sleep duration as a cause of obesity: myth or reality? Obes. Rev. 12 (2011) e2–3, http://dx.doi.org/10.1111/j.1467-789X.2010.00772.x.
[22] J.P. Chaput, A. Tremblay, Insufficient sleep as a contributor to weight gain: an update, Curr. Obes. Rep. 1 (2012) 245–256, http://dx.doi.org/10.1007/s13679-012-0026-7.
[23] Kopelman PG. Hormones and obesity, Baillieres Clin. Endocrinol. Metab. 8 (3) (1994) 549–575.
[24] C.N. Lumeng, A.R. Saltiel, Inflammatory links between obesity and metabolic disease, J. Clin. Invest. 121 (6) (2011) 2111–2117, http://dx.doi.org/10.1172/JC157132.
[25] A.R. Saltiel, J.M. Olefsky, Inflammatory mechanisms linking obesity and metabolic disease, J. Clin. Invest. 127 (1) (2017) 1–4, http://dx.doi.org/10.1172/JC192035.
[26] S.S. Daskalopoulou, D.P. Mikhailidis, M. Elisaf, Prevention and treatment of the metabolic syndrome, Angio. 55 (6) (2004) 589–612.
[27] S.R.S. Stender, G.A. Burghen, J.T. Mallare, The role of health care providers in the prevention of overweight and type 2 diabetes in children and adolescents, Diabetes Spectr. 18 (4) (2005) 240–248, http://dx.doi.org/10.2337/diaspect.18.4.240.
[28] Y. Li, A. Hruby, A.M. Bernstein, S.H. Ley, D.D. Wang, S.E. Chiuve, L. Sampson, K.M. Rexrode, E.B. Rimm, W.C. Willett, F.B. Hu, Saturated fats compared with unsaturated fats and sources of carbohydrates in relation to risk of coronary heart disease: a prospective cohort study, J. Am. Coll. Cardiol. 66 (14) (2015) 1538–1548, http://dx.doi.org/10.1016/j.jacc.2015.07.055.
[29] H.P. Sheng, R.A. Huggins, A review of body composition studies with emphasis on total body water and fat, Am. J. Clin. Nutr. 32 (3) (1979) 630–647.
[30] J.S. Garrow, New approaches to body composition, Am. J. Clin. Nutr. 35 (1982) 1152–1158.
[31] A.R. Behnke, E.F. Osserman, W.C. Welham, Lean body mass: its clinical significance and estimation from excess fat and total body water determinations, AMA. Arch. Internal Med. 91 (1953) 585–601.

[32] U.G. Kyle, A. Piccoli, C. Pichard, Body composition measurements: interpretation finally made easy for clinical use, Curr. Opin. Clin. Nutr. Metab. Care 6 (2003) 387–393.
[33] F.O. Duarte, M. Sene-Fiorese, M.S. Manzoni, L.F. de Freitas, N.C. Cheik, A.C. Garcia de Oliveira Duarte, et al., Caloric restriction and refeeding promoted different metabolic effects in fat depots and impaired dyslipidemic profile in rats, Nutrition. 24 (2) (2008) 177–186, http://dx.doi.org/10.1016/j.nut.2007.10.012.
[34] M.G. Picchi, A.M. Mattos, M.R. Barbosa, C.P. Duarte, M.A. Gandini, G.V. Portari, A.A. Jordão, A high-fat diet as a model of fatty liver disease in rats, Acta Cirúrgica Brasileira 26 (2011) 25–30.
[35] D.L. Johannsen, E. Ravussin, Obesity in the elderly: is faulty metabolism to blame? Aging health 6 (2) (2010) 159–167.
[36] M. Juonala, J. Juhola, C.G. Magnussen, P. Würtz, J.S. Viikari, R. Thomson, I. Seppälä, J. Hernesniemi, M. Kähönen, T. Lehtimäki, M. Hurme, R. Telama, V. Mikkilä, C. Eklund, L. Räsänen, M. Hintsanen, L. Keltikangas-Järvinen, M. Kivimäki, O.T. Raitakari, Childhood environmental and genetic predictors of adulthood obesity: the cardiovascular risk in young Finns study, J. Clin. Endocrinol. Metab. 96 (9) (2011) E1542–9, http://dx.doi.org/10.1210/jc.2011-1243.
[37] F. Angelico, L. Loffredo, P. Pignatelli, T. Augelletti, R. Carnevale, A. Pacella, F. Albanese, I. Mancini, S. Di Santo, M. Del Ben, F. Violi, Weight loss is associated with improved endothelial dysfunction via NOX2-generated oxidative stress down-regulation in patients with metabolic syndrome, Intern Rmerg Med. 7 (3) (2012) 219–227, http://dx.doi.org/10.1007/s11739-011-0591-x.
[38] B. Swinburn, G. Egger, Preventive strategies against weight gain and obesity, Obes. Rev. 3 (4) (2002) 289–301.
[39] J. Cooling, J. Blundell, Are high-fat and low-fat consumers distinct phenotypes? Differences in the subjective and behavioural response to energy and nutrient challenges, Eur. J. Clin. Nutr. 52 (1998) 193–201.
[40] S.W. Hill, N.B. McCutcheon, Eating responses of obese and nonobese humans during dinner meals, Psychosom. Med. 37 (1975) 395–401.
[41] A. Drewnowski, J.D. Brunzell, K. Sande, P.H. Iverius, M.R. Greenwood, Sweet tooth reconsidered: taste responsiveness in human obesity, Physiol. Behav. 35 (1985) 617–622.
[42] J. Wang, D. Gallagher, J.C. Thornton, W. Yu, R. Weil, B. Kovac, F.X. Pi-Sunyer, Regional body volumes, BMI, waist circumference, and percentage fat in severely obese adults, Obesity Silver Spring (Silver Spring) 15 (11) (2007) 2688–2698.
[43] T. Akiyama, I. Tachibana, H. Shirohara, N. Watanabe, M. Otsuki, High-fat hypercaloric diet induces obesity, glucose intolerance and hyperlipidemia in normal adult male Wistar rat, Diabetes Res. Clin. Pract. 31 (1996) 27–35, http://dx.doi.org/10.1016/0168-8227(96)01205-3.
[44] C.R. Wilson, M.K. Tran, K.L. Salazar, M.E. Young, H. Taegtmeyer, Western diet, but not high fat diet, causes derangements of fatty acid metabolism and contractile dysfunction in the heart of Wistar rats, Biochem. J. 406 (2007) 457–467.
[45] J.T. Dourmashkin, G.Q. Chang, E.C. Gayles, J.O. Hill, S.K. Fried, C. Julien, S.F. Leibowitz, Different forms of obesity as a function of diet composition, Int J Obes (Lond). 29 (11) (2005) 1368–1378.
[46] S.K. Gale, T.B. Van Itallie, I.M. Faust, Effect of palatable diets on body weight and adipose tissue cellularity in the adult obese female Zucker rat (fa/fa), Metab 30 (2) (1981) 105–110.
[47] T.W. Castonguay, D.E. Upton, P.M. Leung, J.S. Stern, Meal patterns in genetically obese Zucker rat: a reexamination, Physiol. Behav. 28 (5) (1982) 911–916.
[48] A.F. Nascimento, M.M. Sugizaki, A.S. Leopoldo, A.P. Lima-Leopoldo, C.R. Nogueira, E.L. Novelli, et al., Misclassification probability as obese or lean in hypercaloric and normocaloric diet, Biol. Res. 41 (2008) 253–259, http://dx.doi.org/10.4067/S0716-97602008000300002.
[49] J. Vague, The degree of masculine differentiation of obesities: a factor determing predisposition to diabetes, atherosclerosis, gout, and uric calculous disease, Am. J. Clin. Nutr. 4 (1) (1956) 20–34.
[50] M.S. Roopakala, A. Suresh, Srinath Ashtalakshmi, Giridhar Ashok, Silvia W.D. Anand, Anthropometric measurements as predictors of intraabdominal fat thickness, Indian J. Physiol. Pharmacol. 53 (3) (2009) 259–264.
[51] J.C. Wong, K.C. Krueger, M.J. Costa, A. Aggarwal, T.L. McLaughlin, B.J. Feldman, A glucocorticoid and diet-responsive pathway toggles adipocyte precursor cell activity in vivo, Sci. Signal. 9 (451) (2016) ra103.
[52] WHO Expert Consultation. Appropriate body-mass index for Asian population and its implication for policy and intervention strategies, Lancet 363 (9403) (2004) 157–163.
[53] M. Bielohuby, M. Matsuura, N. Herbach, et al., Short-term exposure to low-carbohydrate, high-fat diets induces low bone mineral density and reduces bone formation in rats, J. Bone Miner. Res. 25 (2010) 275–284.
[54] Q. Zhang, Zhang Z-x, Su H-m, et al., Effects of high-fat feeding on growth and expression of IGF-I in young rats, Journal of Clinical Pediatrics 12 (2011) 013.
[55] V. Rolland, S. Roseau, G. Fromentin, S. Nicolaidis, D. Tome, P.C. Even, Body weight, body composition, and Energy metabolism in lean and obese Zucker rats fed soybean oil or butter, Am. J. Clin. Nutr. 75 (2002) 21–30.
[56] National Center for Health Statistics, Health, United States, 1989, Public Health Service, Hyattsville, MD, 1990.
[57] A.M. Khalid, R. Habid ur, S.Y. Muhammad, Z. Hafsa, R. Imtiaz, K.T. Sajid, A.R. Muhammad, Sub-chronic exposure to low concentration of dibutyl phthalate affects anthropometric parameters and markers of obesity in rats, Environ. Sci. Pollut. Res. Int. 24 (32) (2017) 25462–25467.
[58] D.P. Duong, K. Boncho, S. Choi, H.C. Nam, C. Seongwon, Y.K. Jong, Thoracic to hip circumference ratio as a novel marker of type 2 diabetes, independent of body mass index and waist- to- hip ratio, in Korean adults, Diabetes Res. Clin. Pract. 104 (2014) 273–280.
[59] R.A. Adedoyin, O.E. Adeleke, A.O. Fehintola, G.E. Erhabor, L.A. Bisiriyu, Reference values for chest expansion among Adult Rodents in Ile-Ife, J. Yoga Phys. Ther. 2 (3) (2012).
[60] American Thoracic Society, Lung Function testing: selecting of normal values and interpretative strategies, Am. Rev. Respir. Dis. 144 (1991) 1202–1218.
[61] A. Kautzky-Willer, A.R. Brazzale, E. Moro, et al., Influence of increasing BMI on insulin sensitivity and secretion in normotolerant men and women of a wide age span, Obesity 20 (10) (2012) 1966–1973, http://dx.doi.org/10.1038/oby.2011.384.