Comparison of Body Composition between Spontaneous Dwarf and Wild-type Rats during Aging—A Quantitative X-ray Computed Tomographic Study

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Received November 22, 2015
Accepted March 9, 2016

A growth hormone deficiency is associated with increases in body fat. However, it currently remains unclear whether subcutaneous- or/and intra-abdominal adipose tissues are markedly elevated in dwarf obesity. Experiments were conducted on the spontaneous dwarf rats (SDRs) and normal Sprague-Dawley (SD) rats using an X-ray computed tomography scanner to determine body composition. A longitudinal study of aging was also conducted to track age-related changes in body composition using same animals.

We succeeded to estimate the subcutaneous and intra-abdominal adipose tissue mass in rat by X-ray CT. SDRs demonstrated the dwarf obesity, but SDs did not. SDRs developed dwarf obesity due to the accumulation of subcutaneous-abdominal adipose tissue, but not intra-abdominal adipose tissue. Age-dependent increases in the abdominal adipose tissue were observed in both SDRs and SDs. However, age-dependent increases in intra-abdominal adipose tissue were greater than in subcutaneous-abdominal adipose tissue.

Key Words: Aging, body fat, growth hormone, spontaneous dwarf rat, X-ray CT

1. Introduction

A growth hormone (GH) deficiency in adults is associated with increases in body fat1). GH replacement therapy has been shown to improve this abnormal body composition.2) However, it currently remains unclear whether fat tissue, subcutaneous-, or intra-abdominal adipose tissue is markedly elevated in dwarf obesity. Furthermore, the mechanisms by which dwarfism affects age-related changes in body composition have not yet been elucidated.

We previously demonstrated that the spontaneous...
dwarf rat (SDR), which was isolated from a closed colony of Sprague-Dawley rat (SD), exhibited enhanced resistance to oxidative stress and had an extended lifespan.\(^3\) The level of GH as determined by radioimmunoassay was significantly lower in SDRs (0.96±0.41 ng/mL) than in SDs (2.03±0.47 ng/mL).\(^3\) A GH deficiency in SDRs was indicated to be responsible for dwarfism.\(^3\) The body weight and waist size are used as index of the body fat weight, but it is not necessarily body fat-specific. The gold standard for accurate index in human is imaging using X-ray computed tomography scanner (X-ray CT) or magnetic resonance.

In the present study, experiments were conducted on SDRs and SDs using an X-ray CT to determine body composition. A longitudinal study of aging was also conducted by repeated X-ray CT scans in the same animals in order to investigate age-related changes in body composition.

2. Experimental

2.1 Animals

Four-week-old male SDRs (n=5) and SDs (n=5) from Japan SLC (Hamamatsu, Japan) were introduced into the animal center of the Tokyo Metropolitan Institute of Gerontology. Two rats in each group were placed in a 44×29×18 cm polycarbonate chamber with ad libitum access to water in drinking bottles and autoclaved pellet food. Bedding was used and changed weekly with the cage. Temperature was kept constant at 22±2°C and relative humidity was maintained at 50±20%. The photoperiod condition for animals was controlled under a 12-h light and dark cycle. SDRs and SDs were maintained in our animal facility until they reached 2, 6, 12, and 24 months of age. The animal experiment protocol entitled "Analysis of oxidative stress resistance and lifespan extension in the spontaneous dwarf rat" was approved by the Tokyo Metropolitan Institutes of Gerontology Animal Care and Use Committee on March 30, 2011, with the approval number 11019. All procedures performed on animals were in accordance with the Tokyo Metropolitan Institutes of Gerontology Guide for the Care and Use of Laboratory Animals.

2.2 Food intake study

The food intake study was performed using 12-month-old male SDRs (n=6) and SDs (n=6). The autoclaved standard rat chow (CRF-2; Oriental Yeast Co., Ltd., Tokyo, Japan) was weighed and given to each rat for 7 days. Body weight was recorded every day. The remaining food including crumbs was recovered, weighed, and the daily food intake estimated. Feces were also collected every day, air-dried, and weighed. Calorie contents in the feces and food were determined using an automatic bomb calorimeter (Shimadzu, model CA-4, Kyoto, Japan). Food intake was expressed as net total calorie absorption and calculated by subtracting calories excreted in feces from calories ingested. Daily calorie intake was expressed per rat (kJ/day/rat), per gram body weight (kJ/day/g body), and per gram body weight to the power of 0.67 (kJ/day/g\(^{0.67}\) body).\(^5\)

2.3 X-ray CT of rats

Age-dependent changes in the body composition of SDRs and SDs and their bone structures were analyzed using an X-ray CT scanner for experimental animals (LaTheta LCT-100, Hitachi-Aloka Medical Co., Mitaka, Tokyo, Japan). The X-ray tube voltage was set at 50 kV with a constant 1-mA current. SDRs and SDs that reached 2, 6, 12, and 24 months of age in our animal facility were anesthetized with an intraperitoneal injection of sodium pentobarbital (45 mg/kg body weight) and their weights were measured. Anesthetized animals were placed supine in the acrylic animal holder. In order to avoid artificial movement during the scan, the body was extended and fixed to a holder via the front teeth and hind
limbs.

A whole-body scan was performed, and scout images were acquired to confirm the area of the imaging view. In the abdominal adipose tissue (subcutaneous adipose tissue plus intra-abdominal adipose tissue) analysis, an X-ray CT scan was performed from the bottom line of the thoracic diaphragm to that of the scrotum at a slice pitch of 2 mm. The voxel size was 250 ¿m x 250 ¿m x 250 ¿m. After X-ray CT scanning, image data were transferred to a workstation. Subcutaneous adipose tissue, intra-abdominal adipose tissue, and lean tissue were discriminated using embedded software, and this automatic procedure required numerous manual corrections. The regions of interest (ROI) were defined as subcutaneous adipose tissue, intra-abdominal adipose tissue, and lean tissue. Different tissues were discriminated from each other based upon their Hounsfield units (HU), an X-ray attenuation coefficient embedded in the manufacturer’s software. The scanned area was divided into ten equal widths along an axis and axial slices located from 3/10 to 6/10 of the scanned area were used for the body composition analysis. The quantification of abdominal tissue weights was performed using embedded software with the following density factors; 0.92 g/cm³ for subcutaneous and intra-abdominal tissues, and 1.06 g/cm³ for lean tissue. The weight percentages of the body and subcutaneous and intra-abdominal adipose tissues were calculated according to the following formulae:

Body adipose tissue (\%)
\[ \frac{V_f \times D_f}{V_f \times D_f + V_{sf} \times D_{sf} + V_i \times D_i} \times 100 \]

Subcutaneous adipose tissue (\%)
\[ \frac{V_{sf} \times D_{sf}}{V_f \times D_f + V_{sf} \times D_{sf} + V_i \times D_i} \times 100 \]

Intra-abdominal adipose tissue (\%)
\[ \frac{V_i \times D_i}{V_f \times D_f + V_{sf} \times D_{sf} + V_i \times D_i} \times 100 \]

where \( V_f, V_{sf}, V_{i}, \) and \( V_i \) represent adipose mass (cm³), subcutaneous-abdominal adipose tissue mass (cm³), intra-abdominal adipose tissue mass (cm³), and lean mass (cm³), respectively, while \( D_f \) and \( D_i \) represent adipose tissue density (g/cm³) and lean tissue density (g/cm³), respectively. Animals repeatedly underwent X-rays for body composition analyses when they reached 2, 6, 12, and 24 months of age.

2.4 Plasma thyroid hormone measurement

Thyroxine (T₄) was analyzed by the SRL Inc. (Tokyo, Japan) using an electrochemiluminescence immunoassay with plasma samples from 12-month-old male SDRs (n=5) and SDs (n=5).

2.5 Statistical analysis

All data were expressed as the mean±SD. The significance of differences was determined by the Student’s t-test when there were only two comparative groups, and by a two-way analysis of variance (ANOVA) with Tukey’s test when there were multiple comparative groups.

3. Results

3.1 Comparison of body weights, daily energy intakes, and plasma T₄ levels between SDRs and SD rats

SDRs displayed the typical characteristics of dwarf animals with a diminutive body size (Figs. 1, 2). The body weights of SDs increased with age, whereas those of SDRs were maintained at 23~35% that of SDs (Fig. 1). Food intake, expressed as net total calorie absorption per rat, was 65.4% lower (\( p<0.01 \)) in SDRs (113±20 kJ/day/rat) than in SD rats (327±85 kJ/day/rat), but was not significantly different from SDs when expressed per gram body weight (0.486±0.107 kJ/day/g body for SDRs and 0.471±0.113 kJ/day/g body for SDs) and per gram body weight to the power of 0.67 (2.94±0.60 kJ/day/g⁰.⁶₇ body for SDRs and 4.19±0.92 kJ/day/g⁰.⁶₇ body for SDs). Plasma T₄ levels were significantly
lower (p<0.01) in SDRs (2.88±0.52 µg/dL) than in SDs (4.33 ± 0.21 µg/dL).

3.2 Age-dependent changes in body composition in SDRs and SDs

The total adipose tissue area in the abdominal region was significantly lower in SDRs than in SDs (Figs. 3 and 4); however, when this area was expressed as a percentage of the total abdominal region, it was significantly higher in SDRs than in SDs (Fig. 5). The higher percentage of the abdominal adipose tissue area in SDRs was dependent on the subcutaneous-abdominal adipose tissue mass, but not intra-abdominal adipose tissue.

The abdominal adipose tissue area increased with
Fig. 3 Representative X-ray CT images of the abdominal region of SDRs and SDs of different ages. Individual tissues were categorized as subcutaneous adipose tissue (SAT) (yellow), intra-abdominal adipose tissue (IAAT) (pink), lean (blue), and bone (white/gray) (Color online).

Fig. 4 Age-dependent changes in (a) cross-sectional abdominal adipose tissue (AT), (b) subcutaneous-abdominal adipose tissue (SAT), (c) intra-abdominal adipose tissue (IAAT), and (d) lean tissue areas in SDRs and SDs. Each value represents the mean±SD. Significant differences between SDRs and SDs were determined by a two-way analysis of variance (ANOVA) with Tukey’s test (p<0.01** and p<0.05* from respective SDs, p<0.01†† and p<0.05† from 2-month-old rats, and p<0.01## from 6-month-old rats).
age-dependent elevations in body weight in SDRs and SDs (Fig. 4). The intra-abdominal adipose tissue area in SDRs and SDs also increased with age-dependent elevations in body weight. Similar increases were observed in the subcutaneous-abdominal adipose tissue area in SDRs and SDs, which were inconsistent with the elevations observed in their body weights (Fig. 4). The percentage of the abdominal adipose tissue area (subcutaneous- plus intra-abdominal adipose tissues) was higher in SDRs than in SDs, and increased with age (Fig. 5). The percentage of the intra-abdominal adipose tissue area in SDRs significantly increased with age, and was similar to that observed in SDs. The percentage of the subcutaneous adipose tissue area was significantly higher in SDRs than in SDs, whereas age-dependent increases in subcutaneous-abdominal adipose tissue were small in SDRs and SDs (Fig. 5).

4. Discussion

X-ray CT is regarded as the best modality for longitudinally and non-invasively determining body composition, bone mass, and bone density in small animals. Aloka X-ray CT has been used to automatically categorize body composition and subcutaneous, intra-abdominal adipose, and lean tissues. In the present study, the relative abdominal fat area estimated by X-ray CT was higher in SDRs than in SDs. The storage of energy primarily as body fat is affected by energy expenditure and intake. The administration and deficiency of GH has been shown to increase7) and decrease8) oxygen consumption, a marker of energy expenditure, respectively. In the present study, plasma T4 concentrations were lower in GH-deficient SDRs than in SDs. This result indicates that the energy metabolic rate is lower in SDRs because thyroid hormones are the main regulator of the metabolic rate, and plasma concentrations of these hormones affect the basal metabolic rate.9, 10) In our previous study, we also found that the energy metabolic rate was lower in SDRs based on the findings of low plasma insulin and IGF-1 concentrations with lower plasma GH in these animals.3) Insulin, IGF-1, and GH are anabolic hormones that construct or synthesize molecules from smaller components, a process that generally requires energy.10, 12) Lower serum insulin and IGF-1 concentrations decrease oxygen utilization, oxidative metabolism, and energy expenditure.9) Ghrelin is a GH-releasing peptide that plays a role in the central regulation of feeding.12) The administration of ghrelin has been shown to stimulate food intake and body weight gain.13) We previously reported that ghrelin levels were increased in SDRs.3) However, food intake, which was
expressed as per rat (kJ/day/body), per gram body weight (kJ/day/g body), and per gram body weight to the power of 0.67 (kJ/day/g^{0.67} body) did not increase in SDRs beyond that in SDs. Thus, the greater accumulation of adipose tissue in SDRs may be explained by energy expenditure being less than energy intake.

Ghrelin regulates peripheral lipid metabolism. The effects of the administration of ghrelin on lipid metabolism in lipogenic tissues has been investigated in GH-deficient Lewis rats, and the findings obtained indicate that the central administration of ghrelin stimulates a gain in body weight and adipose tissue (visceral and omental) mass as well as in lipid storage-related enzymes in white adipose tissues. The enhanced lipid storage-related enzymes are also mentioned as another likely explanation for obesity in SDRs.

The effects of a GH deficiency on obesity and the mechanisms by which subcutaneous- and intra-abdominal adipose tissue accumulate in GH-deficient animals currently remain unknown. A genetic model of a GH deficiency, the “Little” mouse, exhibited obesity and lower serum IGF-I levels than its normal littermates. A previous study reported that dwarf GH receptor knockout mice and GH antagonist-expressing mice had an increased percent body fat with most of the excess fat mass accumulating in the subcutaneous region. GH transgenic mice have been shown to become significantly leaner than controls by 4 months in males and 6 months in females, whereas younger GH mice have a higher fat mass than their normal littermates. A conflicting research finding of the absence of fat accumulation in the dwarf rat has also been reported. Visceral fat mass was previously shown to be significantly less in dwarf rats than in wild-type rats. Fat mass was determined in Ames dwarf and normal mice at the ages of 2, 4.5–6, and 18 months using dual X-ray absorptiometry, and the percentage of body fat was found to be lower in adult dwarfs than in the corresponding normal controls. As described above, although a GH deficiency in humans is associated with increases in body fat, it currently remains unclear whether subcutaneous- and/or intra-abdominal fat masses are markedly elevated in dwarf obesity. A GH deficiency has been shown to induce an increase in the relative mass of fat, predominantly in the visceral region.

Another study indicated that subcutaneous and visceral fat masses were not higher in GH-deficient patients than in control subjects, whereas GH replacement therapy resulted in similar relative decreases in subcutaneous and visceral fat masses. However, this result did not necessarily accord with previous results in dwarf animals and humans. At this time, the reasons are still not clear. The diet has been implicated as one of the main speculative reasons for increases in body fat, which is predominant in the subcutaneous region of SDRs. Another reason is speculated that the higher energy consumption in GH-deficient animals leads to an increase in the relative mass of fat, predominantly in the subcutaneous region. In the rate of living theory, small warm-blooded vertebrates expend more mass-specific metabolic rate, but at a declining rate with increasing body mass, because, more metabolic rate might be needed in small warm-blooded vertebrates compared to big vertebrates to compensate for a lost heat from the body surface. An adaptive response to keep the body temperature of small body mass might be involved in the increased relative mass of subcutaneous fat in SDRs.

Age-related changes in intra-abdominal adipose tissue and subcutaneous-abdominal adipose tissue in humans have been investigated using X-ray CT. Cross-sectional data revealed that intra-abdominal adipose tissue increased with age up to approximately the 7th decade in men and roughly the 8th decade in women, whereas age-related increases were observed in subcutaneous-abdominal adipose tissue among women, reaching a peak around the 7th
decade of life, with a subsequent decline thereafter. However, subcutaneous-abdominal adipose tissue remained relatively stable in men across the adult life-span. Similarly, a comparison between old and young subjects showed that intra-abdominal adipose tissue was greater in older subjects, whereas subcutaneous-abdominal adipose tissue mostly remained at the same level. There is emerging evidence to support the differential roles of visceral and subcutaneous white adipose tissues in the maintenance of health. Sensitivity to oxidative stress was previously reported to be lower in subcutaneous white adipose tissue than in visceral white adipose tissue. The progressive loss of subcutaneous and gain in visceral fat throughout life has been demonstrated. While subcutaneous fat responds to the equilibrium between energy needs and fuel supply, visceral fat acts in a dysfunctional manner. Visceral fat does not appear to be optimal for fat storage. Previous studies identified intra-abdominal adipose tissue as a major risk factor for insulin resistance, cardiovascular disease, stroke, and metabolic syndrome. Reductions in abdominal adipose tissue especially intra-abdominal adipose tissue have been suggested to prevent or delay age-related diseases and increase longevity. Laron syndrome (primary GH insensitivity or resistance) results from a dysfunction in the GH receptor, which leads to lower insulin and IGF-1 levels. These patients display the typical characteristics of dwarfism with a diminutive lean body, low serum IGF-1 levels, and the progressive development of obesity. The long-term treatment of these patients with IGF-1 resulted in a significant decrease in subcutaneous fat. Large cohort studies have been performed on the longevity of patients with Laron syndrome. It currently remains unclear whether the lifespan of Laron syndrome patients is prolonged. However, these patients are known to be protected from the development of cancer. In a previous study, we demonstrated that the lifespan of SDRs was longer than that of SDs, and this extension in lifespan was attributed to decreases in the incidence of pituitary tumors and severe chronic nephropathy. Interestingly, SDR has much in common with the Laron syndrome.

5. Conclusions

In the present study, the relative area of intra-abdominal adipose tissue in SDRs significantly increased in an age-dependent manner, similar to that in SDs, whereas the relative area of subcutaneous adipose tissue was significantly higher in SDRs than in SDs through their lifespan. As previously demonstrated, SDRs had an extended lifespan. Thus, subcutaneous adipose tissue in SDRs is not negatively associated with longevity.

Acknowledgments

Dr. Hiroshi Kondo is a coauthor of this study. He sadly passed away recently. We are honored to have had the opportunity to work with him. We appreciate the support of Japan SLC for providing SDRs, and Mr. Yasushi Tachikawa (Hitachi Aloka Medical) for his technical advice.

References

1) Egger, A., Buehler, T., Boesch, C., Diem, P., Stettler, C. and Christ, E. R., The effect of GH replacement therapy on different fat compartments: a whole-body magnetic resonance imaging study, Eur. J. Endocrinol., 164, 23–29 (2011)
2) Boguszewski, C. L., Meister, L. H., Zaninelli, D. C. and Radominski, R. B., One year of GH replacement therapy with a fixed low-dose regimen improves body composition, bone mineral density and lipid profile of GH-deficient adults, Eur. J. Endocrinol., 152, 67–75 (2005)
3) Kuramoto, K., Tahara, S., Sasaki, T., Matsumoto, S., Kaneko, T., Kondo, H., Yanabe, M., Takagi, S. and Shinkai, T., Spontaneous Dwarf Rat (SDR): a novel model for aging research, Geriatr. Gerontol. Int., 10, 93–100 (2010)
4) Sasaki, T., Tahara, S., Shinkai, T., Kuramoto, K.,
Matsumoto, S., Yanabe, M., Takagi, S., Kondo, H. and Kaneko, T., Lifespan extension in the spontaneous dwarf rat and enhanced resistance to hyperoxia-induced mortality, *Exp. Gerontol.*, 48, 457–463 (2013)

5) Heusner, A. A., Body size and energy metabolism, *Annu. Rev. Nutr.*, 5, 267–293 (1985)

6) Hillebrand, J. J., Langhans, W. and Geary, N., Validation of computed tomographic estimates of intra-abdominal and subcutaneous adipose tissue in rats and mice, *Obesity* (Silver Spring), 18, 848–853 (2010)

7) Jorgensen, J. O., Vahl, N., Dall, R. and Christiansen, J. S., Resting metabolic rate in healthy adults: relation to growth hormone status and leptin levels, *Metabolism*, 47, 1134–1139 (1998)

8) Akhter, N., Odle, A. K., Allensworth-James, M. L., Haney, A. C., Syed, M. M., Cozart, M. A., Chua, S., Kineman, R. and Childs, G. V., Ablation of leptin signaling to somatotropes: changes in metabolic factors that cause obesity, *Endocrinology*, 153, 4705–4715 (2012)

9) Berneis, K. and Keller, U., Metabolic actions of growth hormone: direct and indirect, *Baillieres Clin. Endocrinol. Metab.*, 10, 337–352 (1996)

10) McAninch, E. A. and Bianco, A. C., Thyroid hormone signaling in energy homeostasis and energy metabolism, *Ann. N.Y. Acad. Sci.*, 1311, 77–87 (2014)

11) Mullur, R., Liu, Y. Y. and Brent, G. A., Thyroid hormone regulation of metabolism, *Physiol. Rev.*, 94, 355–382 (2014)

12) Nakazato, M., Murakami, N., Date, Y., Kojima, M., Matsuo, H., Kangawa, K. and Matsukura, S., A role for ghrelin in the central regulation of feeding, *Nature*, 409, 194–198 (2001)

13) Wren, A. M., Small, C. J., Abbott, C. R., Dhillon, W. S., Seal, L. J., Cohen, M. A., Batterham, R. L., Taheri, S., Stanley, S. A., Ghaedi, M. A. and Bloom, S. R., Ghrelin causes hyperphagia and obesity in rats, *Diabetes*, 50, 2540–2547 (2001)

14) Sangiao-Alvarellos, S., Vázquez, M. J., Varela, L., Nogueiras, R., Saha, A. K., Cordido, F., López, M. and Diéguez, C., Central ghrelin regulates peripheral lipid metabolism in a growth hormone-independent fashion, *Endocrinology*, 150, 4562–4574 (2009)

15) Donahue, L. R. and Beamer, W. G., Growth hormone deficiency in 'little' mice results in aberrant body composition, reduced insulin-like growth factor-

I and insulin-like growth factor-binding protein-3 (IGFBP-3), but does not affect IGFBP-2,-1 or -4, *J. Endocrinol.*, 136, 91–104 (1993)

16) Berryman, D. E., List, E. O., Coschigano, K. T., Behar, K., Kim, J. K. and Kopchick, J. J., Comparing adiposity profiles in three mouse models with altered GH signaling, *Growth Horm. IGF Res.*, 14, 309–318 (2004)

17) Palmer, A. J., Chung, M. Y., List, E. O., Walker, J., Okada, S., Kopchick, J. J. and Berryman, D. E., Age-related changes in body composition of bovine growth hormone transgenic mice, *Endocrinology*, 150, 1353–1360 (2009)

18) Davies, J. S., Gevers, E. F., Stevenson, A. E., Coschigano, K. T., El-Kastl, M. M., Bull, M. J., Elford, C., Evans, B. A., Kopchick, J. J. and Wells, T., Adiposity profile in the dwarf rat: an unusually lean model of profound growth hormone deficiency, *Am. J. Physiol. Endocrinol. Metab.*, 292, E1483–E1494 (2007)

19) Heiman, M. L., Tinsley, F. C., Mattison, J. A., Hauck, S. and Bartke, A., Body composition of prolactin-, growth hormone, and thyrotropin-deficient Ames dwarf mice, *Endocrine*, 20, 149–154 (2003)

20) Cummings, D. E. and Merriam, G. R., Growth hormone therapy in adults, *Annu. Rev. Med.*, 54, 513–533 (2003)

21) Johannsson, G., Svensson, J. and Bengtsson, B. A., Growth hormone and ageing, *Growth Horm. IGF Res.*, 10 (Suppl B), S25–S30 (2000)

22) Speakman, J. R., Body size, energy metabolism and lifespan, *J. Exp. Biol.*, 208, 1717–1730 (2005)

23) Ng, A. C., Melton, L. J. 3rd, Atkinson, E. J., Achenbach, S. J., Holets, M. F., Peterson, J. M., Khosla, S. and Drake, M. T., Relationship of adiposity to bone volumetric density and microstructure in men and women across the adult lifespan, *Bone*, 55, 119–125 (2013)

24) Lee, Y., Shin, H., Vasy, J. L., Kim, J. T., Cho, S. I., Kang, S. M., Choi, S. H., Kim, K. W., Park, K. S., Jang, H. C. and Lim, S., Comparison of regional body composition and its relation with cardiometabolic risk between BMI-matched young and old subjects, *Atherosclerosis*, 224, 258–265 (2012)

25) Liu, R., Pulliam, D. A., Liu, Y. and Salmon, A. B., Dynamic differences in oxidative stress and the regulation of metabolism with age in visceral versus subcutaneous adipose, *Redox Biol.*, 6, 401–408 (2015)

26) Zafon, C., Fat and aging: a tale of two tissues, *Curr.
Aging Sci., 2, 83–94 (2009)

27) Finelli, C., Sommella, L., Gioia, S., La Sala, N. and Tarantino, G., Should visceral fat be reduced to increase longevity? Ageing Res. Rev., 12, 996–1004 (2013)

28) Sala, M. L., Röell, B., van der Bijl, N., van der Grond, J., de Craen, A. J., Slagboom, E. P., van der Geest, R., de Roos, A. and Kroft, L. J., Genetically determined prospect to become long-lived is associated with less abdominal fat and in particular less abdominal visceral fat in men, Age Ageing, 44, 713–717 (2015)

29) Laron, Z., Insulin-like growth factor-I treatment of children with Laron syndrome (primary growth hormone insensitivity), Pediatr. Endocrinol. Rev., 5, 766–771 (2008)

30) Laron, Z. and Klinger, B., Body fat in Laron syndrome patients: effect of insulin-like growth factor treatment, Horm. Res., 40, 16–22 (1993)

要 旨

小動物用X線CTを用いた矮小ラットの体組成の加齢変化の測定

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2015年11月22日 受付
2016年3月9日 受理

成長ホルモン分泌不全性低身長症では肥満を示すことが知られている。しかし、GH欠乏において皮下と内臓脂肪のどちらかが優位に増加するのか、また、体組成の加齢変化は明らかにされていない。本研究は自然発症矮小ラット（SDR）とその対照であるSprague-Dawleyラット（SD）の腹部の皮下と内臓脂肪量の加齢変化を、X線CTを用い同一の動物で検討した。

小型小動物用X線CT装置でラットの皮下と内臓脂肪の加齢変化を弁別して解析することができた。SDRはSDに比べて脂肪肥満傾向を示した。この肥満は皮下脂肪を主体とし、内臓脂肪にはならないことがわかった。腹部の脂肪率はSDR、SDのいずれも加齢に伴って増加した。しかし、内臓脂肪の増加率はSDR脂肪に比べて顕著であった。