Smaller organ mass with greater age, except for heart

Qing He,1,2 Stanley Heshka,1,2 Jeanine Albu,2 Lawrence Boxt,3 Norman Krasnow,4 Marinos Elia,5 and Dympna Gallagher1,2

1New York Obesity Research Center, St. Luke’s-Roosevelt Hospital; 2Institute of Human Nutrition and Department of Medicine, College of Physicians and Surgeons, Columbia University; and Departments of 3Radiology and of 4Cardiology, St. Luke’s-Roosevelt Hospital, New York, New York; and 4Institute of Human Nutrition, University of Southampton, Southampton, United Kingdom

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The aim of this study was to investigate the association between age and the weight of specific high-metabolic-rate organs in vivo, including brain, heart, kidneys, liver, and spleen measured by MRI in healthy African-American and Caucasian men and women, and how the association will be influenced by sex and race.

METHODS

Subjects

Study volunteers were recruited through advertisements in local newspapers, on radio stations, and flyers posted in the local community. Based on self-report, only persons with all four grandparents of either African-American or European Caucasian ancestry were selected. Inclusion criteria required that volunteers be nonsmoking, ambulatory, not vigorously exercising, weight stable (weight change < 2.5 kg within past 6 mo), and not taking any medications or with any known medical condition that could potentially affect the variables under investigation. A body mass index (BMI) < 37 kg/m² was set as a requirement for participation to accommodate MRI scanner limitations. A screening test that included physical examination and blood tests was conducted on each potential subject. Only healthy individuals without serious medical diagnoses or medical conditions that would affect body composition, organ size, and with normal thyroid hormone and cortisol values were finally enrolled. The age range for the study population was 19–88 yr of age. The study was approved by the Institutional Review Board of St. Luke’s-Roosevelt Hospital, and each subject gave written consent to participate.

Body Composition Measurement

All body composition evaluations were carried out within a 2-wk period. On the test day, the subject reported to the laboratory in the morning after an overnight fast, and the tests were conducted with the subject clothed in a hospital gown and wearing foam slippers.

Anthropometry. Body weight was measured to the nearest 0.1 kg (Weight Tronix, New York) and height to the nearest 0.5 cm using a stadiometer (Holtain; Crosswell, United Kingdom).

MRI. Subjects were positioned on the 1.5-T scanner (General Electric, 6X Horizon, Milwaukee, WI) platform with their arms extended above their heads. All MRI tests were carried out without prior sedation in a postabsorptive state. All organ volume values (in liters) were converted to mass (in kg) using the assumed density for autopsy data as a reference for in vivo organ mass include a significant loss of organ weight that occurs during the first 15 min after being freed from the surrounding tissue (9). It is also unclear how the mass of these organs changes from a living to a cadaver state. An organ weight measured in vivo is likely more meaningful to guide clinical practice for treatment of a patient and evaluation of disease progression. The availability of imaging techniques, such as MRI, allows for the in vivo determination of organ weight (5, 6, 17).

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AGING OF ORGANS AND TISSUES is of clinical and research interest. Elucidating the extent of organ and tissue atrophy has important implications for understanding resting energy expenditure (REE) changes with age and REE-related diseases such as obesity (2, 18). Although the combined weight of the brain, heart, kidneys, and liver is less than 6% of total body weight, these four high-metabolic-rate organs account for 60–70% of REE in adults (3, 5, 10).

The in vivo weight of these organs and tissues may serve as a reference when evaluating the stage of a patient’s disease. In normal (disease free) aging, the degree to which organ and tissue atrophy correlates with functional decline varies by organ and tissue. Most reference data for organ weights have been derived from autopsy studies (1, 9, 12, 20). Autopsy data have shown a linear decline in organ weight with increasing age for brain, liver, and kidneys, while the weight for heart increased with age (9). Limitations associated with the use of
each organ, 1.05 kg for liver, kidneys, and spleen and 1.03 kg for heart and brain (21). The MRI protocol has no known health risks to the subjects such as radiation, and it provides a measurement to quantify body composition at the organ level.

LIVER, KIDNEY, SPLEEN, AND BRAIN MEASUREMENT. Liver, kidney, and spleen volumes were measured using an axial T1-weighted spin echo sequence with 5-mm slice thickness, no interslice gap, and a 40 × 40 cm² field of view. For brain volumes, two protocols were used during the course of the study: an axial orientation for data collected before 2001 and a coronal orientation for data collected after 2001. Approximately 29 brain images acquired using the axial protocol were produced using a body coil with a fast-spin echo T2-weighted sequence with 5-mm contiguous axial images and a 40 × 40 cm² field of view with a matrix of 256 × 256 and number of excitations of 1. For the coronal protocol, a transaxial T1-weighted sequence with 1.5-mm slice thickness was acquired in a coronal plane orthogonal to the anterior commissure-posterior commissure (AC-PC) plane over the whole brain with the acquisition time of 11 min. To estimate organ volume from MRI-derived volume to the coronal volume as previously described (8).

Orthogonal to the anterior commissure-posterior commissure (AC-PC) was used to analyze all MRI images in the Image Reading Center (New York). The coefficient of variation for the same five measures of organ weight from MRI, and fat mass and FFM from DXA, were not compared. The relationship between organ mass and age (unadjusted for covariates) is presented in Fig. 1, A–E. Except for the LVM, the mass of all other organs was smaller with increasing age.

Association Between Age and Organ Mass

Multiple regression analysis was used to examine the associations between the mass of each organ (kg) and age after adjustment for other variables: weight and height (Table 2). No statistically significant two- or three-way interactions were found among age, sex, and race in any regression analysis. Significant negative relationships between organ mass and age were seen in brain \((P < 0.0001)\), kidneys \((P = 0.01)\), liver \((P = 0.001)\), and spleen \((P < 0.0001)\), indicating per year decreases of 0.002 kg for brain, 0.001 kg for kidneys, 0.003 kg for liver, and 0.001 kg for spleen. For LVM, a nonstatistically significant positive relationship was found with age \((P = 0.15)\). This finding was the same when the analysis was run using the method (echocardiography vs. cardiac gated MRI) as a covariate (results not shown here). The SEs of estimate for the regression equations were 0.107 kg for brain, 0.026 kg for LVM, 0.143 kg for kidneys, 0.188 kg for liver, and 0.319 kg for spleen. Similar results were found using FFM and fat mass as covariates instead of weight and height for body size (Table 3). Organ weights were positively related to fat mass, except for the brain volume. The coefficient of variation for the same five measures of organ weight from MRI, and fat mass and FFM from DXA, were not compared. The relationship between organ mass and age (unadjusted for covariates) is presented in Fig. 1, A–E. Except for the LVM, the mass of all other organs was smaller with increasing age.

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Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>African-American ((n = 41))</td>
<td>Caucasian ((n = 34))</td>
</tr>
<tr>
<td>Age, yr</td>
<td>48.1 ± 22.3</td>
<td>45.2 ± 17.2</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>72.4 ± 15.3</td>
<td>62.1 ± 9.1</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.62 ± 0.06</td>
<td>1.63 ± 0.05</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.30 ± 5.04</td>
<td>23.41 ± 3.60</td>
</tr>
<tr>
<td>Brain (MRI), kg</td>
<td>1.05 ± 0.11</td>
<td>1.11 ± 0.11</td>
</tr>
<tr>
<td>LVM (MRI), kg</td>
<td>0.14 ± 0.03</td>
<td>0.12 ± 0.02</td>
</tr>
<tr>
<td>Kidneys (MRI), kg</td>
<td>0.31 ± 0.06</td>
<td>0.31 ± 0.05</td>
</tr>
<tr>
<td>Liver (MRI), kg</td>
<td>1.36 ± 0.26</td>
<td>1.39 ± 0.17</td>
</tr>
<tr>
<td>Spleen (MRI), kg</td>
<td>0.13 ± 0.06</td>
<td>0.16 ± 0.07</td>
</tr>
<tr>
<td>Fat mass (DXA), kg</td>
<td>26.48 ± 11.27</td>
<td>19.51 ± 7.92</td>
</tr>
<tr>
<td>Fat-free mass (DXA), kg</td>
<td>45.91 ± 6.44</td>
<td>41.89 ± 3.99</td>
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Values are means ± SD. BMI: body mass index; MRI: magnetic resonance imaging; LVM: left ventricular mass; DXA: dual-energy X-ray absorptiometry.

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brain; and age did not modify this relationship as the interaction between fat mass and age was not significant in all models. The SEs of estimate for the regression equations were 0.106 kg, 0.026 kg, 0.145 kg, 0.185 kg, and 0.322 kg for brain, LVM, kidneys, liver, and spleen, respectively. In summary, age explained 10% of the variance for brain, 1% for LVM, 4% for kidneys, 5% for liver, and 11% for spleen in the weight and height model (Table 2). Similar values were found (1–11%) in the FFM and fat mass model (Table 3).

**DISCUSSION**

To our knowledge, this is the first study to present in vivo values for brain, liver, kidneys, spleen, and LVM in healthy African-Americans and Caucasians across the adult age range (19–88 yr). These findings confirm and expand our knowledge of organ weights from previous autopsy studies, i.e., older people have a smaller mass of brain, kidneys, liver, and spleen, but not the heart, compared with younger subjects.

The decrease in organ mass with aging (except for the heart) is an important finding. The finding of no significant interaction between age, sex, and race in any of the analyses that we report indicates that, within the power of this sample size to detect differences (sex or race) in rate of decline, none are seen. It is well known that muscle mass decreases with aging (4, 11, 15, 16); here we also see a disproportionate decrease in organ mass, even after adjusting for FFM. The reasons for organ mass decrease and associated functional implications are worthy of future studies. One possible reason for the failure of the heart to decrease with age is that blood pressure increases with age, which means that the heart has to work harder to maintain its cardiac output. This would predispose to cardiac hypertrophy, an increase in heart mass.

Fig. 1. A: the relationship between the mass of brain and age (scatterplots of the raw data). B: the relationship between left ventricular mass (LVM) and age (scatterplots of the raw data). C: the relationship between the mass of kidneys and age (scatterplots of the raw data). D: the relationship between the mass of liver and age (scatterplots of the raw data). E: the relationship between the mass of spleen and age (scatterplots of the raw data). Symbols: ●, African-American men; ■, Caucasian men; ▲, African-American women; ×, Caucasian women.
It is observed based on the $R^2$ values from the multiple regression equations that age, race, sex, and weight and height (or FFM and fat mass) explain only about one-half of the variability in organ size. Most of the variation not explained by regression analysis is due to interindividual variation, e.g., differences in musclearity either through training or constitition; one is more muscular than the other (i.e., ratio of muscle to FFM will be affected). The same could apply to organs. The effect of alcohol on liver size is complex and depends on the presence of fat at least in some individuals. It is not so meaningful to compare our MRI-derived organ weight with those autopsy data. First, organs after death are not healthy,” which were judged based on the statement from the general practitioner or relatives of the deceased (9), whereas the other study used “free of pathological changes” as an inclusion criterion to derive organ weight for healthy subjects (1).

All previously published data on organ weight have come from autopsy studies. These data are useful for pathologists as a reference for understanding whether specific organs under investigation in autopsy show pathological changes based on the size. A comparison of organ weights across autopsy-derived databases is difficult given that these studies had quite different inclusion criteria for healthy subjects. For example, one study used the inclusion of “healthy” and “apparently healthy,” which were judged based on the statement from the general practitioner or relatives of the deceased (9), whereas the other study used “free of pathological changes” as an inclusion criterion to derive organ weight for healthy subjects (1).

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the same in nature as the organs during life. To evaluate the clinical significance of a patient’s organ weights, it is important to know the normal range of these organs in a living condition. Second, the methodology on the inclusion of associated tissues in an organ mass from the in vivo MRI analysis may be slightly different from the autopsy dissection. Table 4 shows the organ weights derived from our MRI measure (Caucasian subjects only) and the autopsy data cited from Garby et al. (Ref. 9; the majority of their subjects are white). Generally, the MRI organ weights were less than the autopsy organ weight. One of the explanations for this difference is that associated tissues were included in the autopsy measurement. For example, liver mass from MRI analysis did not include portal and inferior vena cava, gall bladder, and biliary ducts; however, all or a portion of these tissues were included as liver mass when measurements were made during autopsy. Another example is that the volumes of intraventricular fluid and blood within the chambers of heart were not included in the MRI measurements; however, autopsy calculation included these volumes in the total weight of the heart. The causes of death were not provided in the study by Garby et al. (9), which may have included unexpected deaths, accident, homicides, suspected crimes, etc., as these were the main reasons for requiring an autopsy in accordance with Danish law (9). Accordingly, the following reasons could result in the autopsy organ weights being greater than the in vivo MRI organ weights: death having occurred after fluid administration (before and after admission to hospital); heart failure that results in venous congestion and hepatomegaly; head injury that results in cerebral edema; and injury to other organs, which can cause them to swell.

**Study Limitations**

1) This study is limited by its cross-sectional design. Ideally, elucidation of the effect of aging on features of interest should be based on serial measures of the same individuals as they progress through adulthood.

2) An assumed organ density was used in calculating mass for each organ and it is unclear whether the density of individual organs changes with increasing age or whether densities are similar across race/ethnic groups. We acknowledge that there may be individual differences in density, e.g., due to lipid in liver. We convert MRI measurement of organ volume to mass using an assumed density because this makes the units more comparable with other data (body weight, the DXA variable of FFM or autopsy organ weights). However, since the MRI measurements are of organ volume, and the conversions to mass are based on multiplying volume by a constant, at a minimum, the observed age-related changes can be applied to organ volumes. We acknowledge that this problem is not totally avoided by using volume because fatty infiltration of the liver is likely to affect liver volume also.

**Summary**

Our findings demonstrate that age has a significant effect on brain, kidneys, liver, spleen, and heart mass. The effect of age is consistent across sex and across the race groups studied.

**GRANTS**

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**REFERENCES**


