Scaling of organ masses in mammals: implications for metabolic rate scaling

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Abstract The continual enigma that is sublinear (increasing slower than linearly) scaling of the whole-body metabolic rate should be solved on both the ultimate and proximate levels. The proximate mechanism likely involves superlinear scaling of metabolically inert tissue/organ masses, sublinear scaling of metabolically expensive organ masses, a decrease in mass-specific metabolic rates or, more likely, a combination of these three things. Surprisingly, studies on the scaling of tissue/organ masses are very scarce. Here, we analyse the scaling of tissue/organ masses in a sample of 100 mammalian species with a phylogenetically informed method (PGLS). Metabolically inert adipose tissue scales isometrically, but the masses of energetically expensive visceral organs scale sublinearly, with the exception of lungs, with the lowest slope occurring for the brain. As discussed, such sublinear scaling together with the decrease in the mass-specific metabolic rate with body mass explains the sublinear scaling of the whole-body metabolic rate in both mammals and birds on the proximate level. However, in birds, the role of the decrease in the mass-specific metabolic rate seems more important.

Introduction

The slower than linear increase in metabolic rate with body mass, referred to as a negative or sublinear mass-scaling, has fascinated biologists since the time of the publications of Rubner (1908) and Kleiber (1947). Technically, this phenomenon is studied by examination of the slope (*b*) in a linear regression log metabolic rate = *a* + b log body mass, which takes a value <1 under a sublinear scaling. Although the existence of a universal value for *b* has been contradicted in recent decades (e.g. Harrison 2018 and citations there), the ubiquity of the sublinear scaling requires explanation on two levels: ultimate and proximate. There is no agreement on the ultimate causes, but the proximate mechanism is clear but not always invoked: the size of metabolically inert parts must increase with body mass faster than linearly, the size of energy-demanding organs must increase with body mass slower than linearly, the mass-

specific metabolic rate of organs must decrease with body mass or, most likely, all of these phenomena occur simultaneously (Krebs 1950; Wang et al. 2001). Therefore, evidence of the interspecific scaling of organ masses is crucial for explaining the sublinear scaling of the whole-body metabolic rate on the proximate level, but such data are scarce. Wang et al. (2001) estimated organ sizes and their energy demands for 5 mammalian species spanning a wide range of body sizes: rat, rabbit, cat, dog and human. Log organ masses increased sublinearly with log body mass with different slopes: 0.76 for the brain, 0.85 for the kidneys, 0.87 for the liver and 0.98 for the heart. However, conclusions that are based on a few arbitrarily chosen species and that neglect the effect of phylogeny are currently unacceptable. Much more is known about the scaling of the brain mass (see Discussion).

Here, we used published data to estimate body mass-scaling for the mass of the brain, heart, liver, kidneys, lungs, spleen, digestive tract and its components (stomach and intestine) and the adipose deposits in 100 mammalian species with phylogenetic-informed methods. We address possible reasons why different organs can show different mass-scaling.

Methods

Data for whole body mass, fat-free body mass, adipose deposits and sizes of organs, as well as a phylogenetic tree for 100 mammalian species were taken from the supplemental material of Navarrete et al. (2011). Their dataset comprises one species of Didelphimorphia, 3 species of Diprodontia, 3 species of Artiodactyla, 28 species of Carnivora, 3 species of Chiroptera, one species of Erinaceomorpha, two species of Lagomorpha, 23 species of Primata, 29 species of Rodentia, one species of Scandentia and 6 species of Soricomorpha. Scaling parameters for adipose deposits and sizes of organs were calculated in R software (R CoreTeam 2019) with an ordinary least squares regression (OLS) and with a phylogenetic generalized linear model (PGLS) from the caper package (Orme et al. 2018). Body mass or fat-free body mass were independent variables. All analysed data were log transformed prior to the analysis.

Results

The results of the phylogenetically informed PGLS and ordinary least squares regression (OLS) model, with log body mass as the independent variable, are presented in Figure 1, together with the corresponding confidence intervals. The log masses of the brain, heart, liver, kidneys, digestive tract as a whole, and intestine scale sublinearly for both the PGLS and OLS. Scaling of the spleen and stomach masses are sublinear according to the OLS, but PGLS analysis does not exclude isometry. Scaling of the lung and adipose deposit masses are isometric for both the OLS and PGLS. The results of the same analyses with log fat-free body mass are given in the Supplemental material; because the increase in adipose deposits is almost ideally isometric (PGLS slope 1.00, OLS slope 1.03), the scalings for log body mass and for log fat-free body mass are almost identical. A substantial difference between the PGLS and OLS results is visible in only the scaling of the brain mass (PGLS slope 0.70, OLS slope 0.81), which demonstrates the strongest phylogenetic signal (Pagel's lambda=0.923). Interestingly, slightly weaker but still strong phylogenetic signals observed for the scaling of the stomach and spleen masses affect neither the slope nor the intercept, which suggests that phylogeny influences mainly slopes in the case of the brain and intercepts without a grade shift (nonrandom distribution of clades with high or low intercepts on log body mass axis (Martin et al. 2005)) in the case of the stomach and spleen. The scaling of the liver, intestine and adipose deposit masses do not show any phylogenetic signals. The scattering of species-specific points around regression lines is very low (r^2=0.97-98) in most visceral organs and low for brain (r^2=0.93, PGLS), spleen (r^2=0.81), stomach (r^2=0.94) and adipose tissues (r^2=0.88).

Discussion

The mass of the adipose deposits scale with the log body mass isometrically. Isometry of this metabolically inert tissue (1.90 kJ kg^{-1} h^{-1} in humans, (Gallagher et al. 1998)) precludes its role in shaping the sublinear scaling of whole-body metabolism in mammals. The slope for fat in birds equals 0.94 for 22

species (Daan et al. 1990), which also precludes such a role in birds. Scattering of species data points around the regression line is substantial for the mass of adipose tissue.

Interestingly, the lung mass also scales isometrically with body mass. In birds, the scaling of this organ is also almost isometric (0.975, Daan et al. 1990). According to Hoppeler and Weibel (1998), lungs in mammals have very low developmental and training plasticity, and they are built with significant excess structural capacity in non-athletic mammals but may limit the maximal metabolic rate in athletic species.

The heart mass, responsible for the distribution of both oxygen and nutrients, has a slope of 0.92 with PGLS and 0.94 with OLS analysis. Wang et al. (2001) reported a higher slope of 0.98 (OLS) for their very limited set of 5 mammals, and Daan et al. (1990) reported a slope of 0.98 (OLS) for birds. The liver mass scales with a slope of 0.89 (PGLS) or 0.90 (OLS), almost identical to the value given by Wang et al. (2001), and lower than that in birds (0.97, Daan et al. 1990). Similarly, the slope for the kidney mass, equal to 0.84 (PGLS) or 0.85 (OLS), is almost identical to the slope given by Wang et al. (2001) and much lower than that in birds (0.95, Daan et al. 1990). The similarity of slopes for the liver and kidney from our two analysis methods and Wang et al.'s (2001) phylogenetically non-informed results is not surprising because phylogenetic signals are not significant for these organs. The sublinear scaling of the masses of energy-demanding visceral organs must significantly contribute to the sublinear scaling of the whole-body metabolic rate in mammals, but this sublinear scaling only slightly contributes to the same in birds for which the scaling is very close to isometric.

The mass of the digestive tract as a whole scales sublinearly (0.92 for PGLS and 0.91 for OLS), while in birds, the scaling is even slightly positive (the slope 1.07, Daan et al. 1990). The stomach mass in our data set scales with a slope of 0.96 (both PGLS and OLS) and the intestinal mass with a slope of 0.89 (PGLS) or 0.88 (OLS).

Because of the expensive brain hypothesis, linking the relative brain size with the life history-based pace of life (Aiello and Wheeler 1995), more is known about the scaling of the brain mass. The observed 0.70 PGLS slope is lower and the 0.81 OLS slope is higher than the 0.77 slope (OLS, r=0.98; the same slope for 14 order averages) given by Martin (1996) for a set of 477 mammals. According to a recent analysis of 1552 species of mammals, the OLS slope for brain mass equalled 0.75 (CI 0.742, 0.758) with a very strong phylogenetic signal (Burger and George 2019); according to PGLS analysis, the slope was very low at only 0.57. However, the analysis on the level of orders resulted in variable slopes (0.24 to 0.81) with a median value of 0.64, differing from both OLS and PGLS slopes for all mammals. These results provide a warning that PGLS analysis does not solve the problem of the lack of phylogenetic independence if grade shifts exist, i.e., if branches of a tree differing in the slopes or intercepts of a scaling are not randomly distributed along the log body mass axis (Martin et al. 2005). Although the realistic value of the slope is still uncertain, the scaling of brain mass in mammals is much lower than one. It is also very low in birds (0.57, Daan et al. 1990).

The heart, kidney, liver and brain are expensive organs. In humans, they contribute 0.5, 0.4, 2.6 and 2.0 % of the body mass, respectively, but as much as 8.7, 8.2, 21.6 and 20.2 % of the total resting metabolic rate (calculated from Gallagher et al. 1998). Altogether, these organs constitute only 5.5 % of the body mass, but their metabolic rates constitute as much as 59 % of the metabolic rate (calculated from Gallagher et al. 1998). With isometric scaling, skeletal muscles (Muchlinski et al. 2012; Raichlen et al. 2010) constitute 40 % of body mass and use only 22 % of energy at rest in humans (Gallagher et al. 1998), and adipose tissue constitutes 21 % of body mass, using 15 % of the energy. Thus, the sublinear scaling of visceral organs controls 59 % of the metabolic rate in humans and over 50 % of that in mice (Konarzewski and Diamond 1995), which should explain a large part of the sublinear scaling of the whole-body metabolic rate. Additionally, the mass-specific metabolic rate of these organs decreases with body mass, with a slope of -0.12 for the heart, -0.27 for the liver, -0.08 for the kidneys (Wang et al. 2001), and

-0.14 for the brain (Karbowski 2007). Interestingly, in birds, scaling of all visceral organs except the brain is steeper than that in mammals and close to isometric (Daan et al. 1990), but scaling of the whole-body metabolic rate is shallower (Glazier 2008). Because the brain mass of birds (1.7 % of body mass for 1 kg bird, (Daan et al. 1990)) is much lower than that of mammals (5.5 % of body mass for 1 kg mammal, (Burger and George 2019)), shallower scaling of brain mass in birds cannot compensate for the steeper scaling of other visceral organs. This means that the mass-specific metabolic rate of visceral organs in birds must decrease with body mass at a faster rate than that in mammals. Thus, the relative role of proximate mechanisms of the sublinear scaling of the metabolic rate differs between these two classes of vertebrates.

Metabolism takes place in cells that form different tissues/organs. Unfortunately, researchers usually measure total body masses and whole-body metabolic rates. Such state-of-the-art results do not originate from a well-developed research strategy but from the ease of taking these measurements. If we want to resolve the still-enigmatic sublinear scaling of metabolism, we should refocus on body composition and organ-specific metabolic rates.

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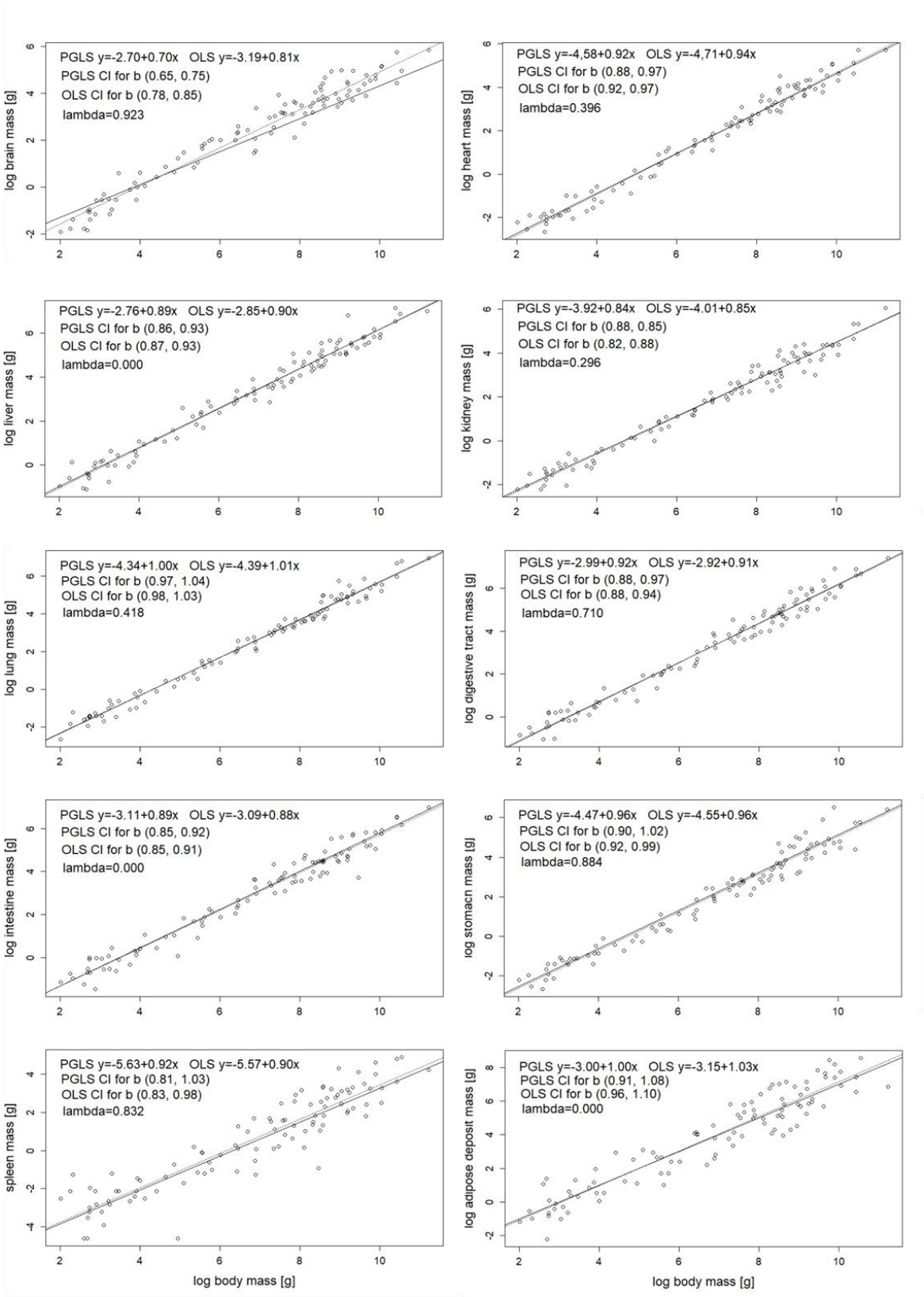
181 **Figure legend**

182 Figure 1. PGLS and OLS interspecific scaling of tissue/organ masses in mammals, with log body mass as
183 the independent variable. For the scaling with log fat-free-body mass as an independent variable, see the
184 Supplemental material.

185

Figure 1.


PGLS y=-2.70+0.70x OLS y=-3.19+0.81x
PGLS CI for b (0.65, 0.75)
OLS CI for b (0.78, 0.85)
lambda=0.923
log brain mass [g]
PGLS y=-4,58+0.92x OLS y=-4,71+0.94x
PGLS CI for b (0.88, 0.97)
OLS CI for b (0.92, 0.97)
lambda=0.396
log heart mass [g]
PGLS y=-2.76+0.89x OLS y=-2.85+0.90x
PGLS CI for b (0.86, 0.93)
OLS CI for b (0.87, 0.93)
lambda=0.000
log liver mass [g]
PGLS y=-3.92+0.84x OLS y=-4.01+0.85x
PGLS CI for b (0.88, 0.85)
OLS CI for b (0.82, 0.88)
lambda=0.296
log kidney mass [g]
PGLS y=-4.34+1.00x OLS y=-4.39+1.01x
PGLS CI for b (0.97, 1.04)
OLS CI for b (0.98, 1.03)
lambda=0.418
log lung mass [g]
PGLS y=-2.99+0.92x OLS y=-2.92+0.91x
PGLS CI for b (0.88, 0.97)
OLS CI for b (0.88, 0.94)
lambda=0.710
log digestive tract mass [g]
PGLS y=-3.11+0.89x OLS y=-3.09+0.88x
PGLS CI for b (0.85, 0.92)
OLS CI for b (0.85, 0.91)
lambda=0.000
log intestine mass [g]
PGLS y=-4.47+0.96x OLS y=-4.55+0.96x
PGLS CI for b (0.90, 1.02)
OLS CI for b (0.92, 0.99)
lambda=0.884
log stomacn mass [g]
PGLS y=-5.63+0.92x OLS y=-5.57+0.90x
PGLS CI for b (0.81, 1.03)
OLS CI for b (0.83, 0.98)
lambda=0.832
spleen mass [g]
PGLS y=-3.00+1.00x OLS y=-3.15+1.03x
PGLS CI for b (0.91, 1.08)
OLS CI for b (0.96, 1.10)
lambda=0.000
log adipose deposit mass [g]
log body mass [g]
log body mass [g]