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Allometric scaling of cardiomyocyte number, mitochondria and myofibril volume in mammals of different size

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Introduction

Small mammals have a higher heart rate and, relative to body weight (bw), a higher metabolic rate than large mammals. In contrast, heart weight and stroke volume scale linearly with bw. With mitochondria filling approximately 50% of a shrew cardiomyocyte—space unavailable for myofibrils—it is unclear how small mammals generate enough contractile force to pump blood into circulation (Fig. 1). Here, we investigated cardiac mitochondria and myofibrils and whether the number of cardiomyocytes per unit bw shows an allometric relationship.

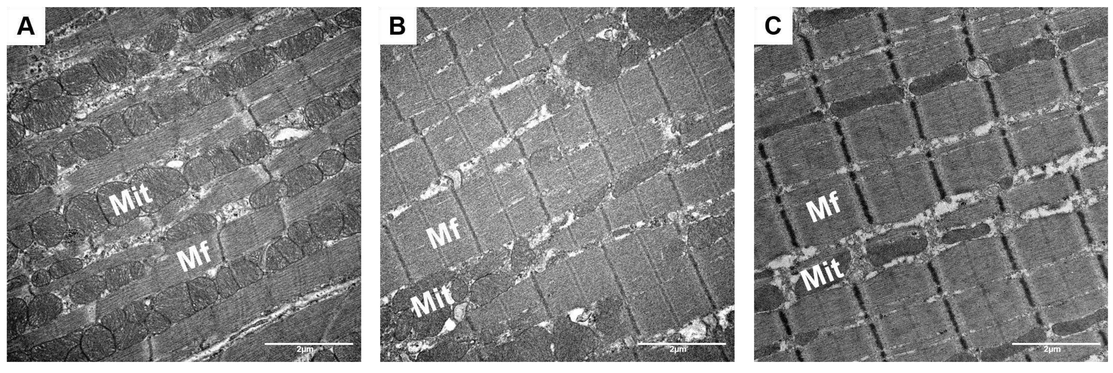

Fig. 1: Electron micrographs of cardiomyocytes of Etruscan shrew (A), dog (B) and horse (C) taken with Morgagni 268 (FEI, Eindhoven, NL). The volume fraction of mitochondria (Mit) is highest in the Etruscan shrew (**A**) and lowest in the horse (**C**) while volume fraction of myofibrils (Mf) is highest in the horse and lowest in the Etruscan shrew.

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Methods

Through statistical analysis of data from 25 stereologic studies with 19 different healthy mammalian species with bw spanning seven orders of magnitude (2.2g to 920kg), we determined how number, volume density and total volume of cardiomyocytes, mitochondria, and myofibrils in the left ventricle depend on bw (Fig. 2).

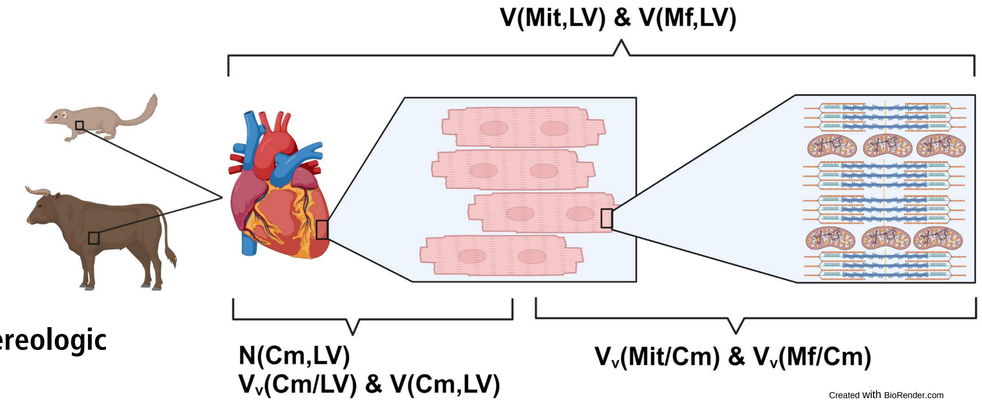

Fig. 2: Stereologic analysis

Results

The number [N(Cm,LV)] and volume [V(Cm,LV)] of cardiomyocytes in the left ventricle increases linearly with increasing bw (i.e. isometrically) (Fig. 3A,C).

The volume density of mitochondria [Vv(Mit/Cm)] decreases (inverse allometry) and that of myofibrils [Vv(Mf/Cm)] increases (negative allometry) with increasing bw (Fig. 4A,C).

The absolute volume of mitochondria in the left ventricle [V(Mit,LV)] increased more slowly bw (negative allometry) and the total volume of myofibrils [V(Mf,LV)] showed a linear increase with bw (Fig. 4B,D). The volume density ratio of mitochondria and myofibrils [Vv(Mit/Cm)/ Vv(Mf/Cm)] was higher in small mammals (inverse allometry) (Fig. 4E).

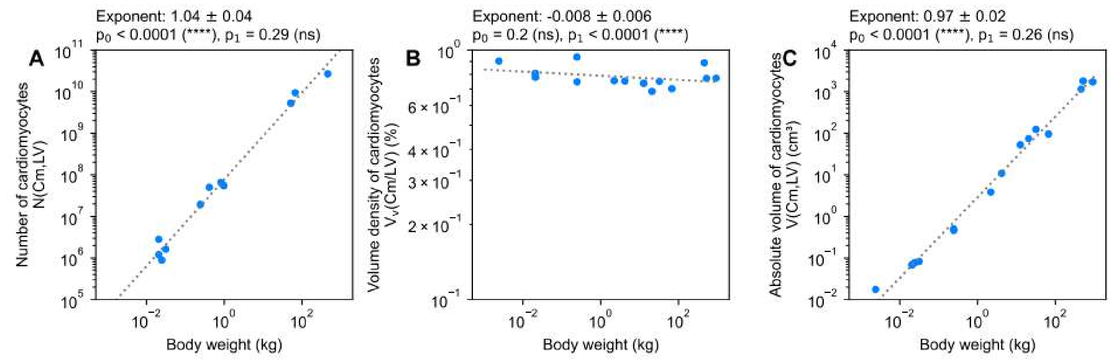

Fig. 3: Allometric relationships of number of cardiomyocytes in the left ventricle (N(Cm,LV) (A), volume density of cardiomyocytes in the left ventricle V_v(Cm/LV) (B) and absolute volume of cardiomyocytes in the left ventricle V(Cm,LV) (C) are presented in log-log-plots. The scaling exponent is shown including significant differences to a slope of 0 (p_0) and 1(p_1) (ns: no significance, *: p<0.05, **: p<0.01, ***: p<0.001, ****: p<0.0001).

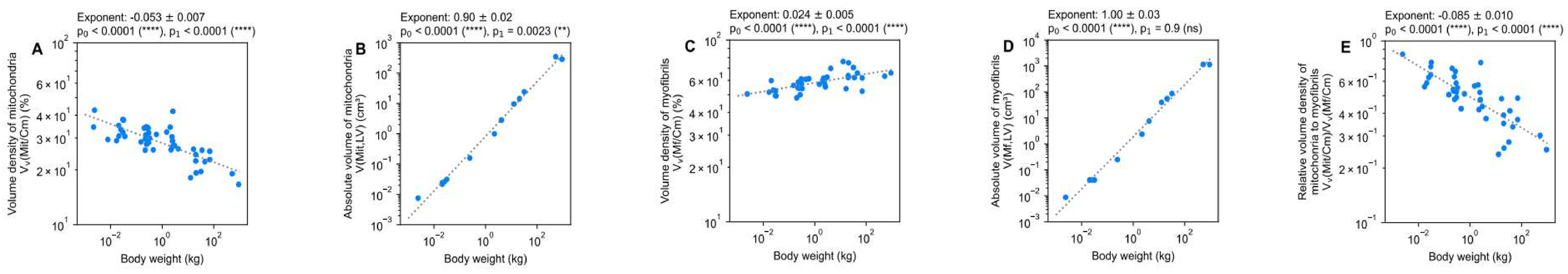

Fig. 4: Allometric relationships of volume density Vv(Mit/Cm) (A) and absolute volume V(Mit,LV) (B) of mitochondria in the left ventricle, volume density Vv(Mf/Cm) (C) and absolute volume V(Mf,LV) (D) of myofibrils in the left ventricle are presented in log-log-plots. The scaling exponent is shown including significant differences to a slope of 0 (p_0) and 1(p_1) (ns: no significance, *: p<0.05, **: p<0.01, ***: p<0.001, ****: p<0.0001).

Conclusions

The number of cardiomyocytes does not compensate for the higher heart rate and specific metabolic rate of small mammals although more mitochondria and less myofibrils are present. A slight blood pressure increase in large mammals might demand higher forces requiring a higher volume fraction of myofibrils per cardiomyocyte.

References

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