

Supplementary Material:

Cerebral blood flow rates in recent great apes are greater than in *Australopithecus* species that had equal or larger brains

Computational approaches to evaluate blood flow rate from foramen size

This study uses a new, empirical approach to calculate internal carotid artery (ICA) blood flow rate from the radius of the carotid canal. So it is worthwhile to compare this “empirical equation” with the previous one based on the Poiseuille-derived “shear stress equation”. The techniques used to measure the canal size (CT scans, microphotographs and impression casting) are comparable, and a sensitivity analysis of the shear stress equation reveals reasonable accuracy (Qiaohui Hu et al. MS submitted). However, there are two assumptions that weaken the foramen technique and use of the shear stress equation: the arterial wall thickness-to-lumen radius ratio is assumed a constant (Assumption 1) and the scaling of wall shear stress is calculated from the body mass of the animal (Assumption 2).

Assumption 1: The arterial wall thickness-to-lumen radius ratio being a constant is reasonable. Larger arteries develop thicker walls because average wall cross-sectional stress is normalized according to the Principle of Laplace that requires the wall thickness to increase in proportion to blood pressure and the radius of the vessel [1, 2]. Central mean arterial blood pressure is practically independent of body mass in mammals the size of primates [3]. The thickness of large arterial walls increases mainly by adding more elastic layers in the tunica media such that the wall stress is roughly constant, for example, the aorta of a rat has ~8 media layers while a aorta of a human has ~60 layers, each layer opposing similar stresses and normalizing overall wall stress [4]. However, the value of the ratio for the ICA ($w = 0.40$), used originally [5] and subsequently was not derived from any human ICA. Instead, it was derived from one value of 0.40 in the canine ICA [6], one value of 0.40 in the human common carotid artery (CCA) [7] and an ignored value of 0.36 in the rat posterior communicating artery [8]. The present investigation sought more studies of the wall thickness-to-lumen radius ratio for the human ICA and CCA, eventually finding 14 studies and obtaining a more exact value of $w = 0.30$.

Assumption 2: The shear stress equation is derived from hydrodynamic theory based on the Poiseuille-Hagen equation: $\dot{Q} = (\Delta P \pi r_i^4)/(4 L \eta)$, where \dot{Q} is the flow rate of blood ($\text{cm}^3 \text{s}^{-1}$) of given viscosity (η ; dyne s cm^{-2}), in response to a pressure difference (ΔP ; dyne cm^{-2}) along a vessel of known length (L ; cm) and internal known radius (r_i ; cm). The shear stress equation eliminates ΔP and L and replaces them with a variable that accounts for wall shear stress (τ ; dyne cm^{-2}): $\dot{Q} = (\tau \pi r_i^3)/(4 \eta)$ [9]. While ΔP is nearly impossible to evaluate on short real vessels, evaluating τ is also difficult to assess without knowing the velocity profile within the vessel. Although once thought to be a constant within the circulatory system regardless of species and artery size, shear stress is not a

constant, but decreases in larger vessels in a non-linear way [10]. Shear stress decreases in individually named arteries with increasing body mass [10-13], and allometric exponents must be found empirically. Published data for ICA lumen radius and flow rate in two species (humans and rats) in relation to body mass (M_b ; g) yielded the original empirical equation, $\tau = 167 M_b^{-0.20}$ [5], which was used subsequently in several studies of primates [5, 14-17]. Our equation was justly criticized for the low sample size and low predictive value [18]. Another problem with the evaluation of wall shear stress is that there is no obvious reason why it should be functionally related to body mass and not blood vessel size alone. Finally, the flow regimes in large arteries may not conform to Poiseuille flow theory, that is, in proportion to radius cubed, as the shear stress equation assumes. Because of these problems, we sought to find the relationship between blood flow rate and arterial lumen size directly and empirically, without reliance on theory, hydrodynamic equations, or calculation of wall shear stress. Recent imaging studies supplied 57 data points for blood flow rate and artery radius in seven cephalic arteries (common carotid, internal carotid, vertebral, basilar, anterior cerebral, middle cerebral and posterior cerebral arteries) in six genera of resting mammals (*Mus*, *Rattus*, *Oryctolagus*, *Canus*, *Homo*, *Equus*) [10]. The data result in a power equation, $\dot{Q} = 155 r_i^{2.49}$, which we call the “empirical equation” to distinguish it from the “shear stress equation”. The empirical equation can calculate blood flow rates from any cephalic foramen and the results compared with calculated values from the shear stress equation. The range of lumen radius covered by the empirical equation is 0.02 – 0.5 cm, which includes the range of measured radii of all haplorhine primates included in this study and the literature (from *Tarsius* sp., $r_i = 0.02$ cm, to *Homo sapiens*, $r_i = 0.24$ cm). This permits an independent re-evaluation of the allometric relationships among extant primates and fossil hominin species.

ICA blood flow calculated with the shear stress and empirical equations

The major determinant of \dot{Q}_{ICA} is arterial lumen radius, because it is raised to the power of 3.0 in the shear stress equation and 2.49 in the empirical equation. Therefore a reduction in the wall thickness-to-lumen radius ratio from 0.40 to 0.30 results in a 25% increase in \dot{Q}_{ICA} in hominins (Fig. S2). Because wall shear stress is lower in larger arteries [10-13], it is lower in the same named arteries in larger animals, which tends to reduce \dot{Q}_{ICA} calculated with the shear stress equation in animals with larger brains. Thus the effect of the wall shear stress factor is to counterbalance the cubic exponent of lumen radius in the shear stress equation to some extent. However, the compensation is not complete. For full compensation, the scaling exponent of wall shear stress with body mass would need to be -0.51, not -0.20. ($2.49 - 3.0 = -0.51$). Therefore, we expect a lower exponent when using the empirical equation compared to the shear stress equation. However, when the revised wall thickness-to-lumen radius ratio and empirical equation are applied to the \dot{Q}_{ICA} hominin data, there is no significant difference in exponent ($F_{2, 30} = 0.062$; $P = 0.94$), but a significant increase elevation ($F_{2, 32} = 3.53$; $P = 0.04$) (Fig. S2).

The shear stress equation and $w = 0.40$ was used to calculate Q_{ICA} in primates [17]. The scaling equation from their tabled data is not significantly different from the empirical equation and $w = 0.30$, either in exponent ($F_{1,48} = 0.034$; $P = 0.85$) or elevation ($F_{1,49} = 1.431$; $P = 0.24$), but there is a slight improvement in the coefficient of determination.

The scaling of \dot{Q}_{ICA} on endocranial volume in haplorhine primates produces an exponent of approximately 1.0 regardless of whether we use the shear stress equation or new empirical equation (Fig. S3), ICA foramen size from two separate studies (Fig. S4), or regional tissue volumes (Fig. 3). This exponent is very high compared to the exponent of 0.75 expected from “Kleiber’s Law” for whole body metabolic rate and body mass or the actual exponent, which is significantly lower [19]. Cardiac output in resting mammals scales with an exponent higher than basal metabolic rate, approximately 0.80 [20, 21], and the exponents are 0.80 for the femoral artery, 0.74 for the infrarenal aorta and 0.80 for the common carotid artery [10]. All of these are significantly lower than the exponent of \dot{Q}_{ICA} in haplorhine primates. We conclude that the high exponent represents an unusually high rate of perfusion to the cognitive parts of the haplorhine brain.

Total brain blood flow calculated with the shear stress and empirical equations

This study focuses on the ICA, but it is now possible to apply the empirical equation to the radius of the vertebral artery (VA) that passes through the transverse foramen of the cervical vertebrae. With the best available information, Boyer and Harrington [17] have estimated that the VA lumen radius averages 51% of the foramen radius in nine mammal species. This value is equivalent to an effective wall thickness-to-lumen radius ratio of $w = 0.96$, although in this case the “wall” is not only the arterial wall but also a large surrounding venous plexus. The veins are negligible in the carotid canal, so the ratio for the ICA is much lower, $w = 0.30$. Using Boyer and Harrington’s tabled values of lumen radii for the VA and ICA, we can use the empirical equation to estimate \dot{Q}_{VA} , \dot{Q}_{ICA} and \dot{Q}_{TOTAL} for haplorhine primates (Fig. S5). We see significantly different exponents for \dot{Q}_{VA} and \dot{Q}_{ICA} . The VA and ICA supply equally in haplorhines with brains smaller than 15 ml, but the role of the VA progressively diminishes until it supplies about 26% of total perfusion in a 1400 ml human brain. This corresponds well to the fraction measured in imaging studies of humans [22-27]. The exponent for \dot{Q}_{TOTAL} in haplorhines is 0.95 ± 0.06 when using the empirical equation (Fig. S5) and 0.87 ± 0.06 when using Boyer and Harrington’s data calculated with the shear stress equation and their assumptions of effective wall thickness [17]. The equations are marginally not significantly different in exponent ($F_{1,44} = 3.585$; $P = 0.06$), but significantly different in elevation ($F_{1,45} = 0.695$; $P = 0.41$). Interestingly, the exponent of total flow for all 49 species of euarchontans is 0.95 calculated with their protocol and 1.04 with the empirical equation. The equations for these regressions are significantly different in exponent ($F_{1,94} = 6.394$; $P = 0.013$), and the \dot{Q}_{TOTAL} below an V_{br} of 55 ml are significantly lower with the empirical equation. In either case, there is a greater than expected total perfusion in larger brains.

Roles of the internal carotid arteries (ICA) and vertebral arteries (VA) in total brain perfusion in haplorhine primates

The entire brain is supplied by both the ICAs and VAs in haplorhine primates. However, unlike the ICAs that fill the carotid foramina, the VAs run through transverse foramina of the cervical vertebrae accompanied by substantial veins that are part of the spinal venous plexus [28, 29]. In humans, for example, the lumen of the vertebral artery occupies only 38% of the transverse foramen area of cervical vertebra C3 [30]. Venous blood from the brains of erect rhesus monkeys flows almost entirely in the venous plexus, with almost none going through the jugular veins [31, 32]. After passing through the cervical vertebrae, the VAs enter the skull through the foramen magnum with the spinal cord and other vessels, which does not inform us about their size.

Nevertheless, Boyer and Harrington [17] determined the relationship between VA lumen radius and transverse foramen radius and evaluated the contribution of the VAs to total blood flow rate, using the shear stress equation. There is an increasing role of \dot{Q}_{ICA} , and a decreasing role of \dot{Q}_{VA} , in determining overall \dot{Q}_{TOTAL} , as V_{br} increases in haplorhine primates. This is evident in the converging scaling regressions for $\dot{Q}_{TOTAL} (\propto V_{br}^{0.87})$ and $\dot{Q}_{ICA} (\propto V_{br}^{0.98})$. Because $\dot{Q}_{TOTAL} \approx \dot{Q}_{ICA} + \dot{Q}_{VA}$, it is apparent that \dot{Q}_{VA} must be approximately proportional to $V_{br}^{0.77}$. According to these relationships, \dot{Q}_{ICA} accounts for only 34% of total flow in the 3.3 ml brain of *Tarsius*, 59% in the 450 ml brain of *Gorilla* and 67% in the 1400 ml brain of *Homo sapiens*. Based on foramen radius data presented by Boyer and Harrington [17], the new empirical equation confirms converging regressions, and with similar exponents. The revised haplorhine equations are, $\dot{Q}_{ICA} = 0.0065 V_{br}^{1.01}$, $\dot{Q}_{VA} = 0.0083 V_{br}^{0.84}$, and $\dot{Q}_{TOTAL} = 0.0143 V_{br}^{0.95}$ (Fig. S5).

Roles of the ICAs and VAs in total brain perfusion in hominins

In humans, the ICAs supply approximately 75%, and the VAs only 25%, of total brain perfusion (\dot{Q}_{TOTAL}) [22-27]. Although the arteries communicate within the Circle of Willis, the ICAs supply 88% of cerebral flow, and the VAs 12% (unpublished flow data from a meta-analysis of 19 human imaging studies of seven major cephalic arteries by the authors). Thus the ICAs are relied upon for servicing almost all of the cognitive parts of the human brain. The VAs supply mainly the upper spinal cord, brainstem and cerebellum.

Unfortunately, we cannot yet evaluate \dot{Q}_{VA} in fossil hominins, because the foramina that the VAs flowed through have not been measured. However, because $\dot{Q}_{TOTAL} \approx \dot{Q}_{ICA} + \dot{Q}_{VA}$, we can ask what the exponent of \dot{Q}_{VA} on V_{br} would be in hominins, if we know that $\dot{Q}_{ICA} = 0.00028 V_{br}^{1.41}$. Assuming that V_{br} varies between 300 and 1400 ml in hominins, \dot{Q}_{ICA} is 75% of \dot{Q}_{TOTAL} in the 1400 ml human brain, and $\dot{Q}_{TOTAL} \propto V_{br}^{0.95}$ (as it is in haplorhines), then the scaling of \dot{Q}_{VA} can be estimated. The analysis is not as simple as adding or subtracting exponents, because allometric power equations deal precisely with factors, but not terms. Therefore power equations for \dot{Q}_{TOTAL} and \dot{Q}_{ICA} will not result in a power equation for \dot{Q}_{VA} , but it will be close.

Here we start the model with the hominin \dot{Q}_{ICA} equation $\dot{Q}_{ICA} = 0.00028 V_{br}^{1.41}$ and force the power equation for \dot{Q}_{TOTAL} through a point 4/3 times the value of \dot{Q}_{ICA} when V_{br} is 1400 ml for the human brain. We assume arbitrarily a scaling exponent of 0.95 for \dot{Q}_{TOTAL} , because that is the exponent for haplorhine primates according to Boyer and Harrington [17]. This defines the allometric equation for total brain perfusion: $\dot{Q}_{TOTAL} = 0.01047 V_{br}^{0.95}$. \dot{Q}_{VA} is then calculated as the difference $\dot{Q}_{TOTAL} - \dot{Q}_{ICA}$ and plotted (Fig. S6). The equation for this result is described exactly as a polynomial, $\dot{Q}_{VA} = 1.8 \times 10^{-6} V_{br}^2 + 3.98 \times 10^{-3} V_{br} + 0.486$. The best fit power equation is, $\dot{Q}_{VA} = 0.872 V_{br}^{0.36}$ ($R^2 = 0.87$). The model shows that if \dot{Q}_{TOTAL} is assumed proportional to $V_{br}^{0.86}$, then \dot{Q}_{VA} scales as $V_{br}^{0.22}$. If \dot{Q}_{TOTAL} is assumed proportional to $V_{br}^{0.73}$, then \dot{Q}_{VA} scales as $V_{br}^{0.00}$.

A scaling exponent of 0.36 for \dot{Q}_{VA} would require the VA lumen radius to scale as $V_{br}^{0.14}$ (0.14 is 0.36 divided by 2.49, which is the exponent of VA lumen radius in the empirical equation). The exponent 0.14 is less than half of the isometric exponent of 0.33. In other words, to achieve the 1.41 exponent for hominin \dot{Q}_{ICA} , the radius of the VA would have to shrink, not absolutely, but relative to the size of the brain. This is doubtful, and becomes even more doubtful if we assume that $\dot{Q}_{TOTAL} \propto V_{br}^{0.86}$, as assumed for mammals in general. We hypothesize that, if $\dot{Q}_{VA} \propto V_{br}^{0.84}$ in hominins (as it is in haplorhines), \dot{Q}_{TOTAL} would be approximately proportional to $V_{br}^{1.22}$, a strongly hyperallometric relationship, similar to the hyperallometric scaling of \dot{Q}_{ICA} .

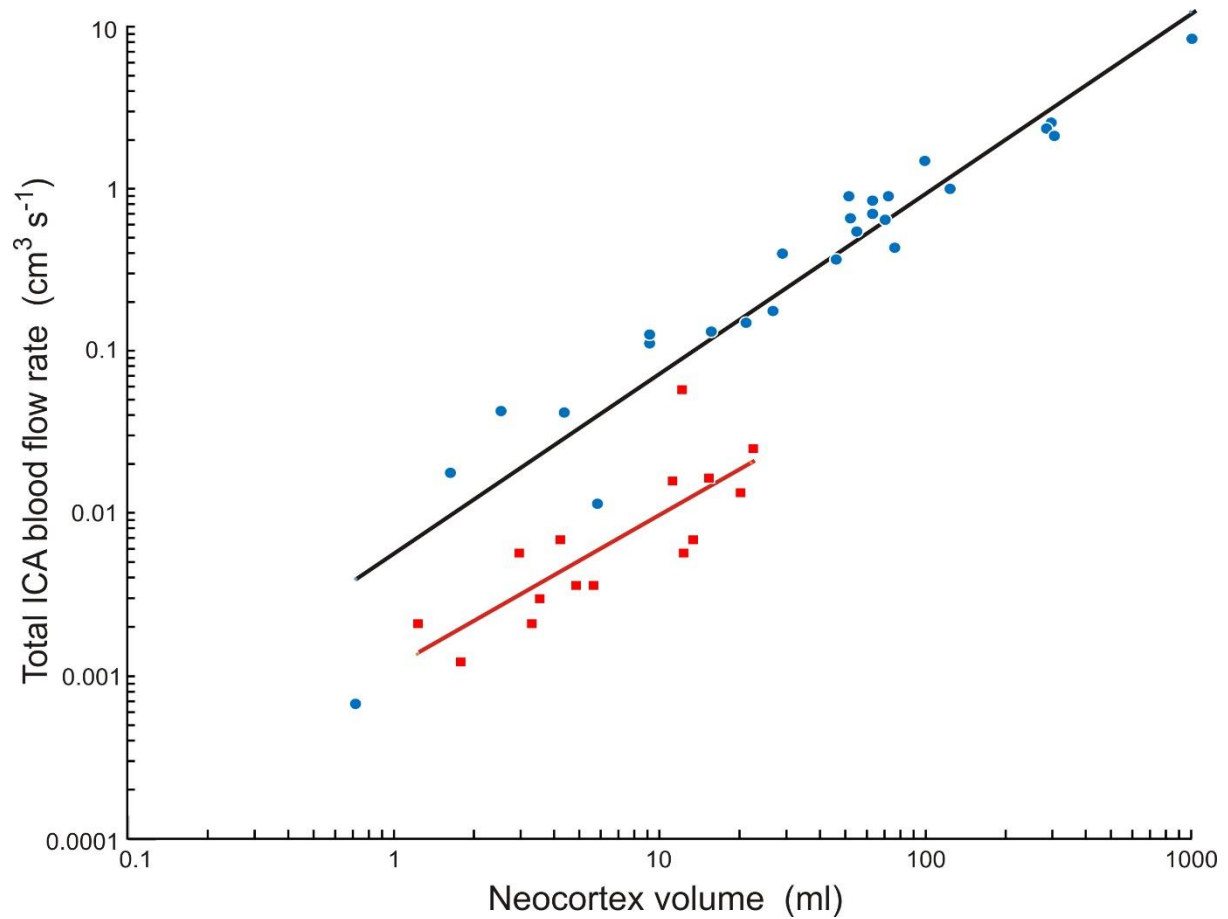


Figure S1. Relationship between total blood flow rate of both ICAs (\dot{Q}_{ICA}) and neocortex volume (V_{neo}) in 26 species of haplorhine primates (blue circles) and 15 species of strepsirrhine primates (red squares). Blood flow rates are calculated with the “empirical equation” and $w = 0.30$ from foramen sizes listed in Seymour et al (2015) [5] and Boyer and Harrington (2019) [17], and neocortical volumes are from dataset 2 in Miller et al. (2019) [33]. The equations are, $\dot{Q}_{ICA} = 0.0062 V_{neo}^{1.12 \pm 0.15 \text{ CI}}$ ($R^2 = 0.91$) for haplorhines and $\dot{Q}_{ICA} = 0.0012 V_{neo}^{0.96 \pm 0.42 \text{ CI}}$ ($R^2 = 0.66$) for strepsirrhines. See Table S5 for data.

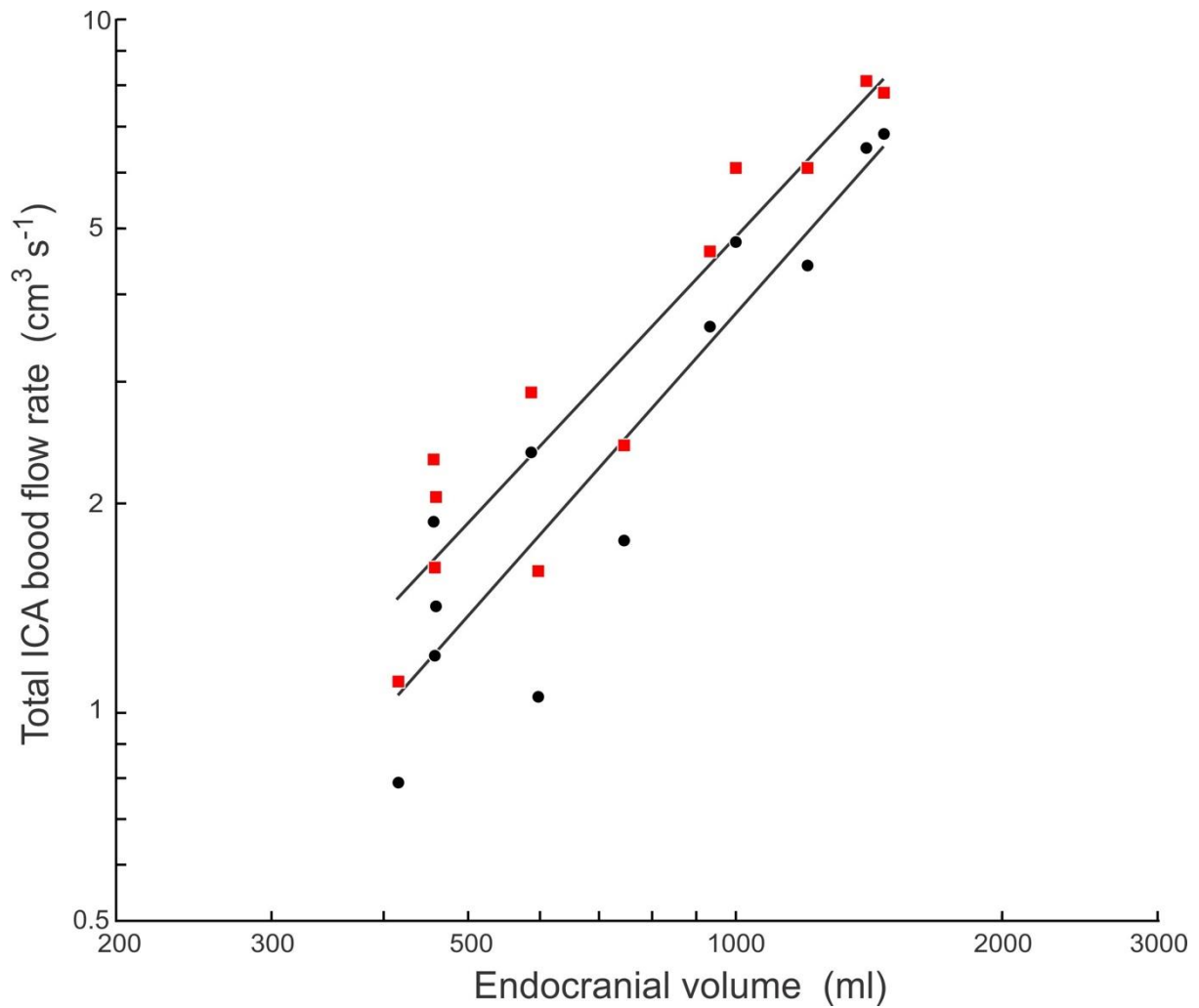


Fig. S2. Comparison of total blood flow rate of both ICAs (\dot{Q}_{ICA}) as a function of endocranial volume (V_{br}) in 11 hominin species (Early and Late *H. erectus* are given individual points) calculated from ICA foramen size according to the shear stress equation and assuming $w = 0.40$ (black circles), and calculated according to the new “empirical equation” and assuming $w = 0.30$ (red squares). The equations are, $\dot{Q}_{ICA} = 0.000170 V_{br}^{1.45}$ and $\dot{Q}_{ICA} = 0.000373 V_{br}^{1.37}$ respectively. ICA foramen data are from Seymour et al. (2017) [15] and do not include *Ardipithecus ramidus*.

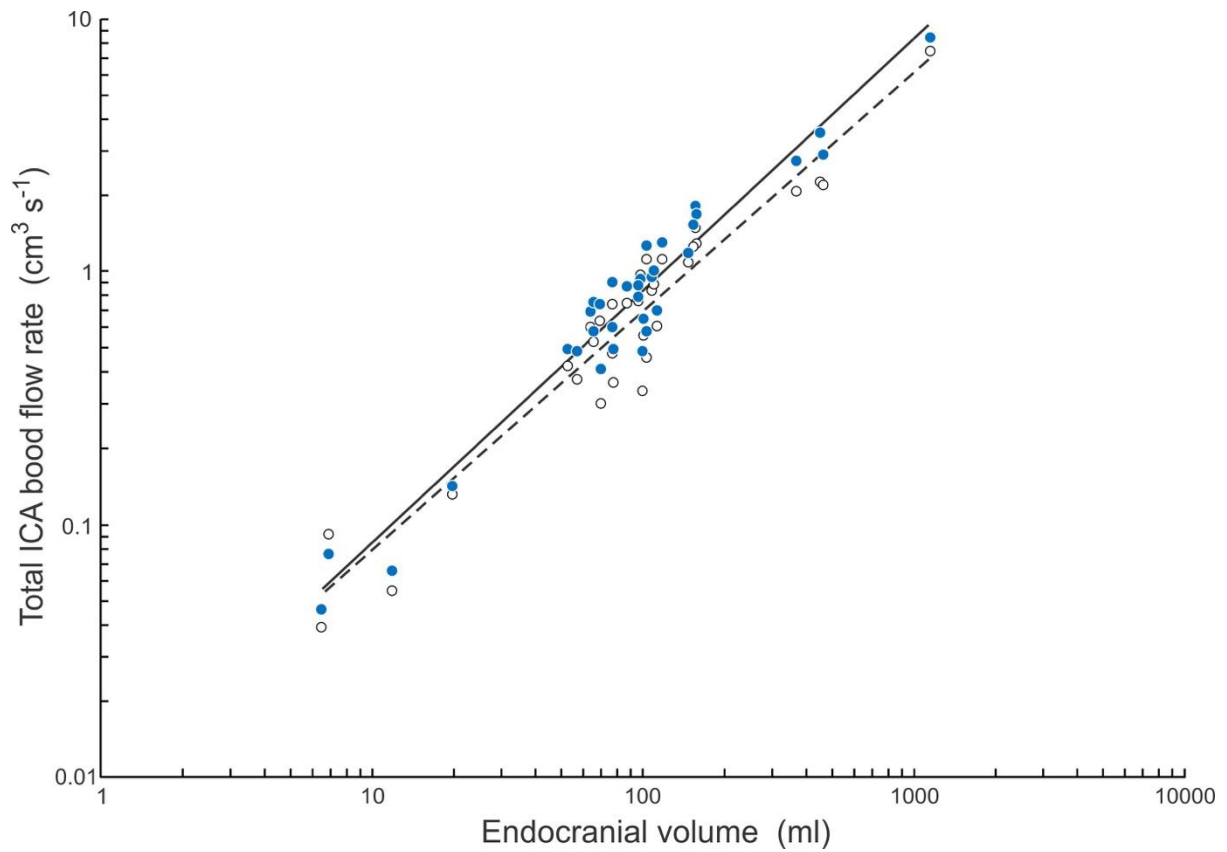


Fig. S3. Comparison of total blood flow rate of both ICAs (\dot{Q}_{ICA}) as a function of endocranial volume (V_{br}) in 34 haplorhine species calculated from ICA foramen size. Results from the “empirical equation” and assuming $w = 0.30$ (blue circles) are compared to results from the shear stress equation and assuming $w = 0.40$ (open circles). The equations are $\dot{Q}_{ICA} = 0.0084 V_{br}^{1.00}$ and $\dot{Q}_{ICA} = 0.0088 V_{br}^{0.95}$, respectively. ICA foramen data are from Seymour et al. (2015) [5].

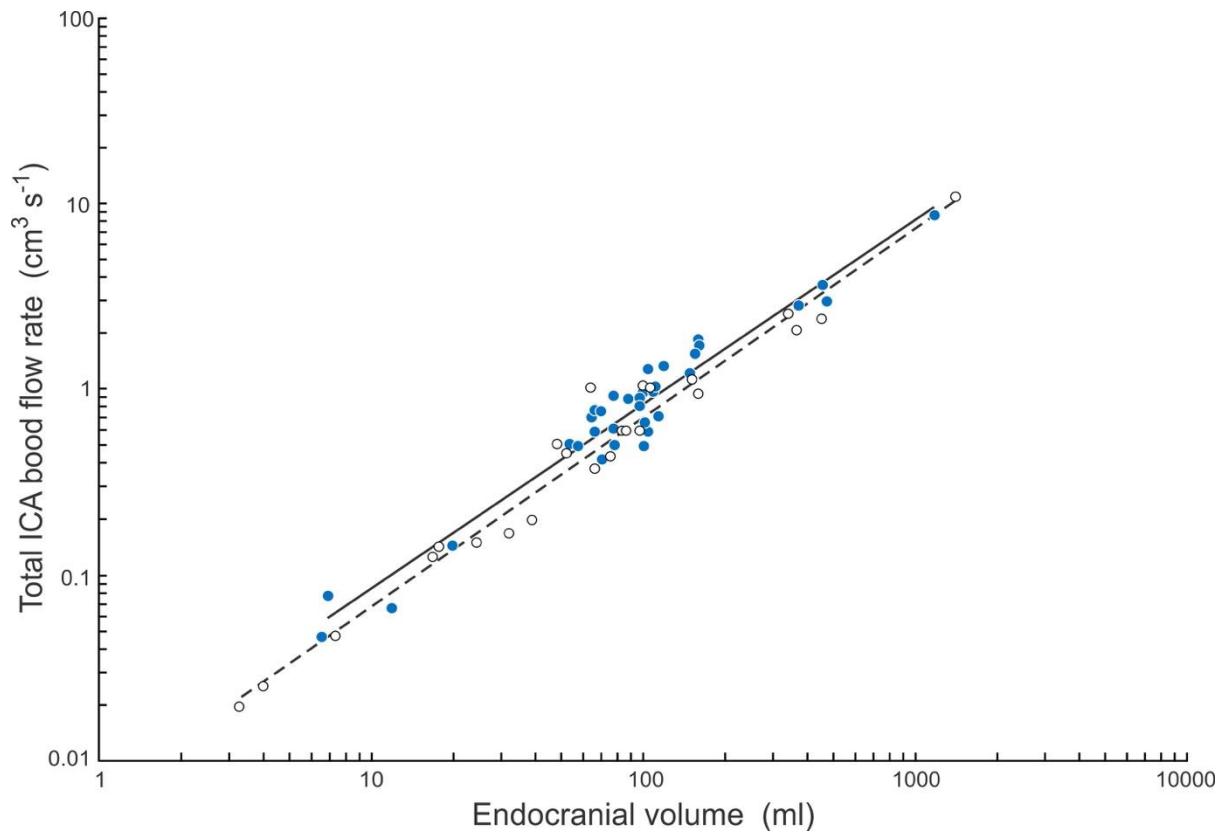


Fig. S4. Total blood flow rate of both ICAs (\dot{Q}_{ICA}) as a function of endocranial volume (V_{br}) in haplorhine primates calculated from ICA foramen radius according to the “empirical equation” and assuming $w = 0.30$. Foramen radius data are derived from 34 species measured by Seymour et al. (2015) [5] (blue circles) and 24 species measured by Boyer and Harrington (2019) [17] (unfilled circles). The equations are, $\dot{Q}_{ICA} = 0.0084 V_{br}^{1.00}$ and $\dot{Q}_{ICA} = 0.0065 V_{br}^{1.01}$, respectively.

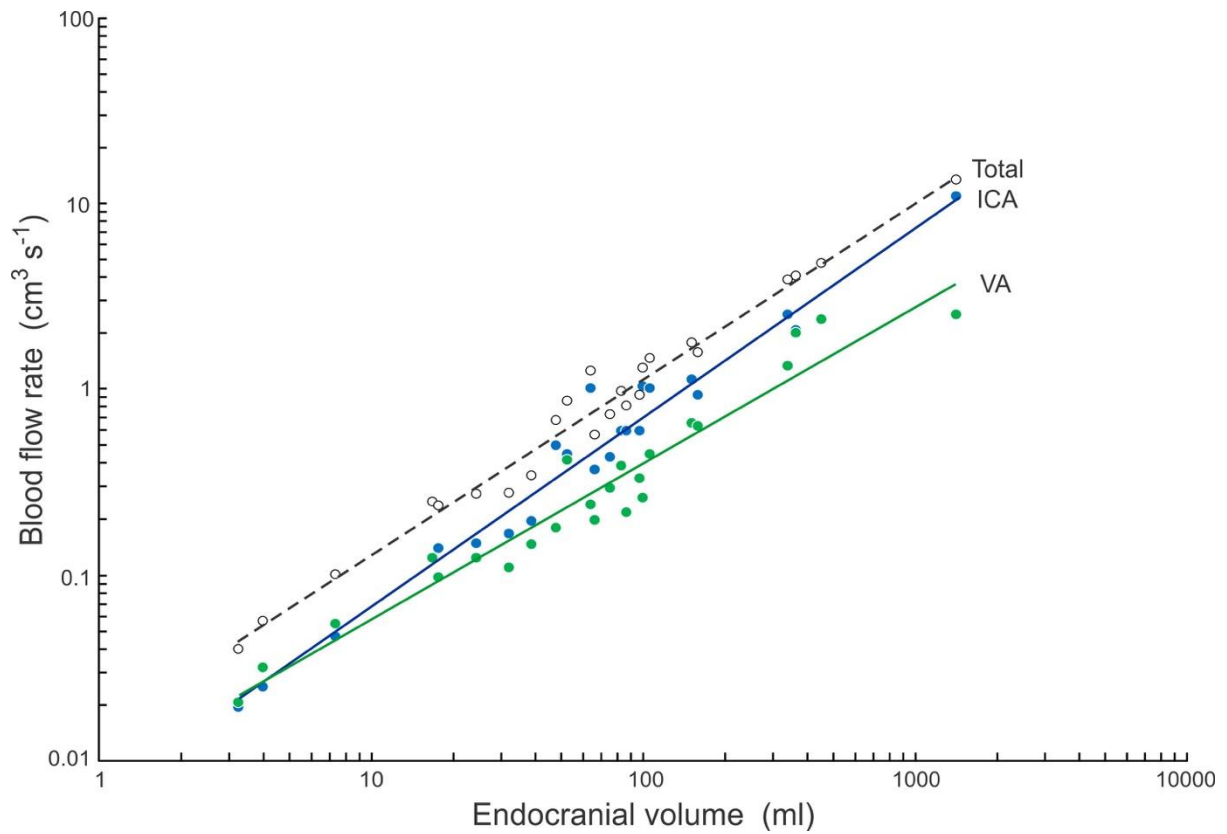


Fig. S5. Blood flow rates of the paired ICAs (\dot{Q}_{ICA}), paired vertebral arteries (\dot{Q}_{VA}), and the sum of these (\dot{Q}_{TOTAL}) plotted as a function of endocranial volume (V_{br}) in 24 haplorhine species calculated from foramen radius according to the “empirical equation” and assuming $w = 0.30$ for the ICA and $w = 0.96$ for the VA. Data are derived from foramen radius measured by Boyer and Harrington (2019) [17]. The equations are, $\dot{Q}_{ICA} = 0.0065 V_{br}^{1.01}$, $\dot{Q}_{VA} = 0.0083 V_{br}^{0.84}$, and $\dot{Q}_{TOTAL} = 0.0143 V_{br}^{0.95}$, respectively.

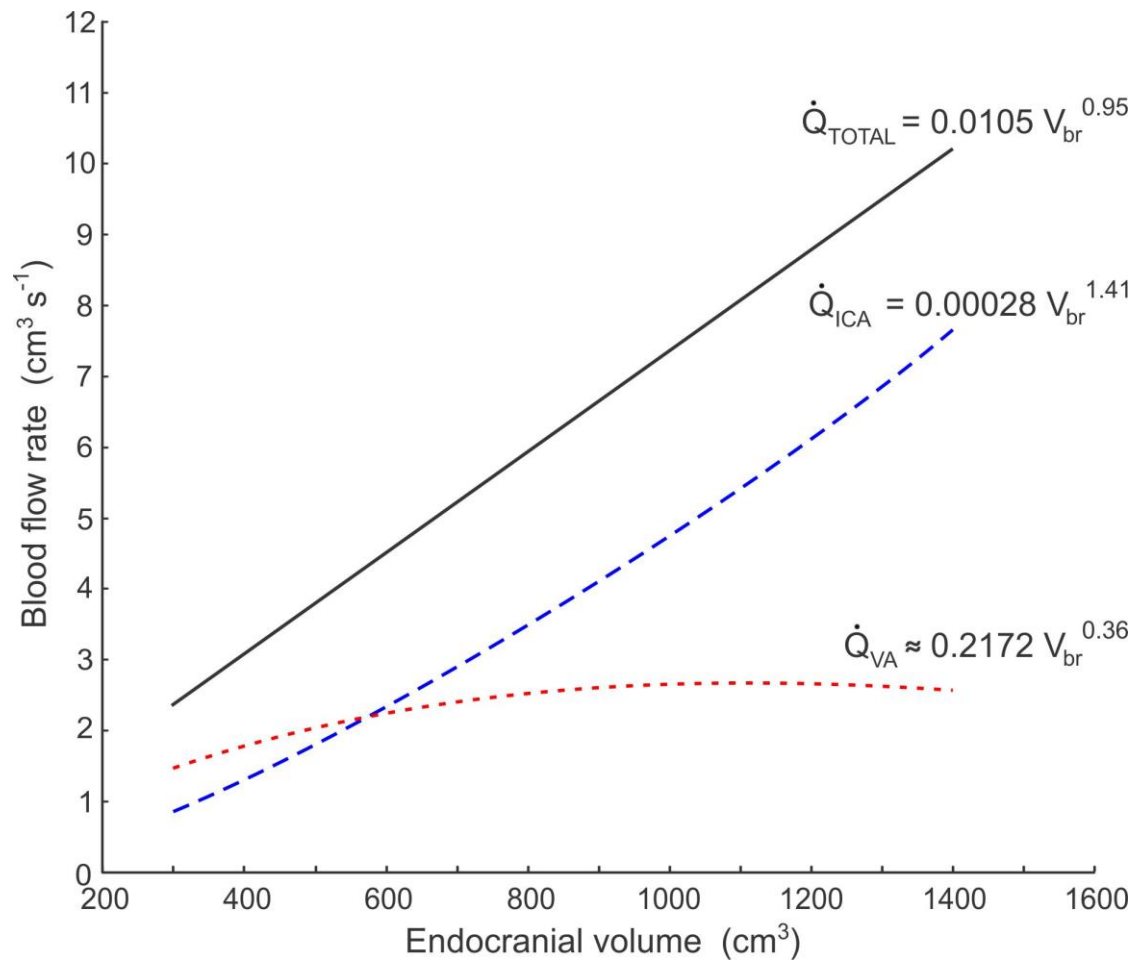


Fig. S6. Model of allometric scaling of hominin brain blood flow rate in relation to endocranial volume (V_{br}). Power equations describe the lines for total brain blood flow rate (\dot{Q}_{TOTAL}), which is the sum of blood flow rate in the internal carotid arteries (\dot{Q}_{ICA}) and vertebral arteries (\dot{Q}_{VA}). The model procedure is described in the Supplementary material text.

Table S1. Literature data for dimensions of the internal carotid artery (ICA), carotid canal and common carotid artery (CCA) in humans.

| Study | Method | Artery/canal | Outer radius (mm) | Lumen radius (mm) | Wall thickness (mm) | Wall-lumen ratio | Notes |
|----------------------|-----------------|---------------|-------------------|-------------------|---------------------|------------------|-------|
| Sommer et al. 2010 | <i>In vitro</i> | ICA | 3.17 | 2.56 | 0.61 | 0.24 | |
| Watase et al. 2018 | MRI | ICA | 4.30 | 3.40 | 0.90 | 0.26 | |
| Saam et al. 2009 | MRI | ICA | 3.98 | 3.33 | 0.64 | 0.19 | |
| Cibis et al. 2016 | MRI | ICA | 4.52 | 3.23 | 1.29 | 0.40 | |
| Qiao et al. 2016 | MRI | ICA | 4.82 | 3.81 | 1.01 | 0.26 | |
| Somesh et al. 2014 | Manual | Carotid canal | 3.60 | 2.39 | 1.21 | 0.51 | 1 |
| Calguner et al. 1997 | Manual | Carotid canal | 2.79 | 2.39 | 0.40 | 0.17 | 1 |
| Naidoo et al. 2017 | Manual | Carotid canal | 3.23 | 2.39 | 0.84 | 0.35 | 1 |
| Berlis et al. 1992 | Manual | Carotid canal | 3.38 | 2.39 | 0.99 | 0.41 | 1 |
| Aoun et al. 2013 | Manual | Carotid canal | 3.10 | 2.39 | 0.71 | 0.30 | 1 |
| Saba et al. 2013 | MDCTA | CCA | 4.55 | 3.29 | 1.26 | 0.38 | 2 |
| Saba et al. 2008 | MDCTA | CCA | 4.11 | 3.29 | 0.82 | 0.25 | 2 |
| Saba et al. 2010 | MDCTA | CCA | 4.20 | 3.29 | 0.91 | 0.28 | 2 |
| Boussel et al. 2007 | MRI | CCA | 3.91 | 3.24 | 0.67 | 0.21 | |
| | | | | | | | |

Methods: *In vitro*, direct measurements were from arteries fixed or observed at mean physiological pressure of 13.3 kPa. MRI, Magnetic Resonance Imaging. Manual, Direct measurement of bony canal. MDCTA, Multidetector Computed Tomographic Angiography.

Notes: 1, ICA lumen radius taken as the mean from 13 imaging studies [10]. 2, CCA lumen radius taken as the mean from 6 imaging studies [10].

References to be added from below:

[34-47]

Table S2. Summary data for endocranial volume (V_{br}), internal carotid artery (ICA) foramen radius (r_o) and total blood flow rate of both ICAs (\dot{Q}_{ICA}) for hominid skulls. Statistics are 95% confidence intervals.

| Species | Number | V_{br} (ml) | r_o (cm) | \dot{Q}_{ICA} ($\text{cm}^3 \text{s}^{-1}$) |
|-----------------------------------|--------|------------------|---------------|--|
| <i>Gorilla beringei</i> | 16 | 482 ± 30 | 0.223 ± 0.009 | 3.92 ± 0.44 |
| <i>Gorilla gorilla</i> | 13 | 494 ± 40 | 0.208 ± 0.020 | 3.39 ± 0.78 |
| <i>Pongo abelii</i> | 12 | 346 ± 28 | 0.205 ± 0.012 | 3.19 ± 0.49 |
| <i>Pongo pygmaeus</i> | 20 | 357 ± 17 | 0.184 ± 0.010 | 2.44 ± 0.32 |
| <i>Pan troglodytes</i> | 19 | 377 ± 23 | 0.197 ± 0.013 | 2.96 ± 0.47 |
| <i>Pan paniscus</i> | 2 | 300 | 0.178 | 2.20 |
| <i>Homo sapiens</i> | 24 | 1325 ± 79 | 0.271 ± 0.010 | 6.37 ± 0.59 |
| <i>Australopithecus africanus</i> | 8 | 499 ± 56 | 0.156 ± 0.008 | 1.60 ± 0.19 |
| <i>Australopithecus afarensis</i> | 3 | 476 ± 74 | 0.186 ± 0.020 | 2.46 ± 0.64 |

Table S3. Endocranial volume and total blood flow rate of both ICAs (\dot{Q}_{ICA}) of haplorhine and hominin primates, calculated according to the “empirical equation” (Seymour et al. 2019) [10] and a wall thickness-to-lumen radius ratio of $w = 0.30$. Data for endocranial volume and ICA foramen radius are from Seymour et al. (2015, 2016) [5, 14] and Boyer and Harrington (2019) [17], except for *Ardipithecus ramidus* which came from [48, 49].

| Species | Taxon | Endocranial volume (ml) | \dot{Q}_{ICA} ($\text{cm}^3 \text{s}^{-1}$) |
|--------------------------------|------------|-------------------------|---|
| <i>Alouatta sp.</i> | Haplorhini | 53 | 0.445 |
| <i>Aotus trivirgatus</i> | Haplorhini | 17 | 0.123 |
| <i>Ateles geoffroyi</i> | Haplorhini | 107 | 1.007 |
| <i>Cacajao calvus</i> | Haplorhini | 88 | 0.685 |
| <i>Callicebus moloch</i> | Haplorhini | 18 | 0.139 |
| <i>Callithrix jacchus</i> | Haplorhini | 7.0 | 0.046 |
| <i>Callithrix pygmaea</i> | Haplorhini | 5.5 | 0.051 |
| <i>Cebus capucinus</i> | Haplorhini | 67 | 0.367 |
| <i>Cercopithecus mitis</i> | Haplorhini | 71 | 0.413 |
| <i>Cercopithecus neglectus</i> | Haplorhini | 65 | 0.699 |
| <i>Chiropotes satanas</i> | Haplorhini | 48 | 0.496 |
| <i>Chlorocebus aethiops</i> | Haplorhini | 67 | 0.763 |
| <i>Colobus satanas</i> | Haplorhini | 79 | 0.494 |
| <i>Gorilla gorilla</i> | Haplorhini | 458 | 2.970 |
| <i>Homo sapiens</i> | Haplorhini | 1304 | 9.660 |
| <i>Hylobates lar</i> | Haplorhini | 106 | 0.798 |
| <i>Hylobates syndactylus</i> | Haplorhini | 120 | 1.313 |
| <i>Lagothrix lagotricha</i> | Haplorhini | 110 | 0.957 |
| <i>Leontopithecus rosalia</i> | Haplorhini | 12 | 0.065 |
| <i>Lophocebus albigena</i> | Haplorhini | 98 | 0.739 |
| <i>Macaca fascicularis</i> | Haplorhini | 71 | 0.544 |
| <i>Macaca maura</i> | Haplorhini | 105 | 1.272 |
| <i>Macaca mulatta</i> | Haplorhini | 78 | 0.607 |
| <i>Macaca nemestrina</i> | Haplorhini | 112 | 1.014 |
| <i>Macaca nigra</i> | Haplorhini | 150 | 1.196 |
| <i>Macaca ochreata</i> | Haplorhini | 98 | 0.799 |
| <i>Macaca radiata</i> | Haplorhini | 67 | 0.584 |
| <i>Macaca silenus</i> | Haplorhini | 89 | 0.878 |
| <i>Mandrillus leucophaeus</i> | Haplorhini | 160 | 1.376 |
| <i>Mandrillus sphinx</i> | Haplorhini | 161 | 1.696 |
| <i>Miopithecus talapoin</i> | Haplorhini | 39 | 0.194 |
| <i>Nasalis larvatus</i> | Haplorhini | 81 | 0.750 |
| <i>Pan troglodytes</i> | Haplorhini | 409 | 2.713 |
| <i>Papio anubis</i> | Haplorhini | 152 | 1.118 |
| <i>Papio hamadryas</i> | Haplorhini | 157 | 1.538 |
| <i>Ptilocolobus badius</i> | Haplorhini | 64 | 1.007 |

| | | | |
|-----------------------------------|------------|------|-------|
| <i>Pithecia pithecia</i> | Haplorhini | 32 | 0.165 |
| <i>Pongo pygmaeus</i> | Haplorhini | 372 | 2.419 |
| <i>Presbytis melalophos</i> | Haplorhini | 71 | 0.747 |
| <i>Saimiri sciureus</i> | Haplorhini | 22 | 0.145 |
| <i>Semnopithecus entellus</i> | Haplorhini | 102 | 0.488 |
| <i>Tarsius sp.</i> | Haplorhini | 3.3 | 0.019 |
| <i>Trachypithecus obscurus</i> | Haplorhini | 105 | 0.584 |
| <i>Trachypithecus vetulus</i> | Haplorhini | 58 | 0.486 |
| <i>Ardipithecus ramidus</i> | Homininae | 315 | 0.843 |
| <i>Australopithecus afarensis</i> | Homininae | 457 | 2.296 |
| <i>Australopithecus africanus</i> | Homininae | 458 | 1.600 |
| Early <i>Homo erectus</i> | Homininae | 939 | 4.588 |
| Late <i>Homo erectus</i> | Homininae | 1004 | 6.043 |
| <i>Homo habilis</i> | Homininae | 590 | 2.870 |
| <i>Homo georgicus</i> | Homininae | 600 | 1.583 |
| <i>Homo heidelbergensis</i> | Homininae | 1213 | 6.043 |
| <i>Homo neanderthalensis</i> | Homininae | 1413 | 8.068 |
| <i>Homo rudolfensis</i> | Homininae | 752 | 2.404 |
| <i>Homo sapiens</i> | Homininae | 1479 | 7.759 |
| <i>Homo naledi</i> | Homininae | 460 | 2.026 |
| <i>Homo floresiensis</i> | Homininae | 417 | 1.094 |

Table S4. Volumes of brain regions of haplorhine primates from Navarrete et al. (2018) [50] and total blood flow rate of both ICAs (\dot{Q}_{ICA}) calculated according to the new “empirical equation” and $w = 0.30$ from ICA foramen radius measured by Seymour et al. (2015) [5] and Boyer and Harrington (2019) [17].

| Species | | Telencephalon volume (ml) | Grey matter volume (ml) | \dot{Q}_{ICA} ($\text{cm}^3 \text{s}^{-1}$) |
|-------------------------------|-----------------|---------------------------|-------------------------|---|
| <i>Cercopithecus mitis</i> | Cercopithecidae | 57 | 36 | 0.413 |
| <i>Lophocebus albigena</i> | Cercopithecidae | 78 | 48 | 0.730 |
| <i>Macaca fascicularis</i> | Cercopithecidae | 43 | 27 | 0.542 |
| <i>Macaca mulatta</i> | Cercopithecidae | 73 | 45 | 0.607 |
| <i>Macaca nemestrina</i> | Cercopithecidae | 78 | 43 | 1.014 |
| <i>Macaca nigra</i> | Cercopithecidae | 61 | 34 | 1.196 |
| <i>Macaca silenus</i> | Cercopithecidae | 79 | 51 | 0.878 |
| <i>Mandrillus sphinx</i> | Cercopithecidae | 104 | 67 | 1.696 |
| <i>Papio hamadryas</i> | Cercopithecidae | 140 | 85 | 1.538 |
| <i>Gorilla gorilla</i> | Hominidae | 342 | 174 | 2.932 |
| <i>Pan troglodytes</i> | Hominidae | 287 | 173 | 2.708 |
| <i>Pongo pygmaeus</i> | Hominidae | 263 | 164 | 2.403 |
| <i>Aotus trivirgatus</i> | Platyrrhini | 13 | 10 | 0.123 |
| <i>Callithrix jacchus</i> | Platyrrhini | 6.0 | 4.3 | 0.046 |
| <i>Callithrix pygmaea</i> | Platyrrhini | 3.2 | 2.3 | 0.046 |
| <i>Lagothrix lagotricha</i> | Platyrrhini | 76 | 48 | 0.957 |
| <i>Leontopithecus rosalia</i> | Platyrrhini | 8.7 | 6.4 | 0.065 |

Table S5. Neocortical volumes and total blood flow rate of both ICAs (\dot{Q}_{ICA}) of haplorhine and strepsirrhine primates. Neocortical volumes are from dataset 2 in Miller et al. (2019) [33]. Blood flow rate data are calculated from ICA foramen radius in Seymour et al. (2015) [5] and Boyer and Harrington (2019) [17].

| Species | Taxon | Neocortex volume (ml) | \dot{Q}_{ICA} (cm ³ s ⁻¹) |
|-----------------------------|------------|-----------------------|--|
| <i>Alouatta sp.</i> | Haplorhini | 29 | 0.445 |
| <i>Aotus trivirgatus</i> | Haplorhini | 9.2 | 0.123 |
| <i>Ateles geoffroyi</i> | Haplorhini | 73 | 1.007 |
| <i>Callicebus moloch</i> | Haplorhini | 9.1 | 0.139 |
| <i>Callithrix jacchus</i> | Haplorhini | 4.4 | 0.046 |
| <i>Callithrix pygmaea</i> | Haplorhini | 2.5 | 0.046 |
| <i>Cercopithecus mitis</i> | Haplorhini | 46 | 0.413 |
| <i>Gorilla gorilla</i> | Haplorhini | 298 | 2.932 |
| <i>Homo sapiens</i> | Haplorhini | 1002 | 9.620 |
| <i>Hylobates lar</i> | Haplorhini | 63 | 0.788 |
| <i>Lagothrix lagotricha</i> | Haplorhini | 63 | 0.957 |
| <i>Lophocebus albigena</i> | Haplorhini | 71 | 0.730 |
| <i>Macaca mulatta</i> | Haplorhini | 55 | 0.607 |
| <i>Mandrillus sphinx</i> | Haplorhini | 99 | 1.696 |
| <i>Microcebus murinus</i> | Haplorhini | 0.7 | 0.0007 |
| <i>Miopithecus talapoin</i> | Haplorhini | 27 | 0.194 |
| <i>Nasalis larvatus</i> | Haplorhini | 52 | 0.739 |
| <i>Nycticebus coucang</i> | Haplorhini | 5.8 | 0.012 |
| <i>Pan troglodytes</i> | Haplorhini | 282 | 2.708 |
| <i>Papio anubis</i> | Haplorhini | 122 | 1.118 |
| <i>Ptilocolobus badius</i> | Haplorhini | 51 | 1.007 |
| <i>Pithecia pithecia</i> | Haplorhini | 21 | 0.165 |
| <i>Pongo pygmaeus</i> | Haplorhini | 306 | 2.403 |

| | | | |
|-------------------------------------|---------------|-----|--------|
| <i>Saimiri sciureus</i> | Haplorhini | 16 | 0.145 |
| <i>Semnopithecus entellus</i> | Haplorhini | 76 | 0.488 |
| <i>Tarsius sp.</i> | Haplorhini | 1.6 | 0.019 |
| <i>Avahi laniger</i> | Strepsirrhini | 4.8 | 0.0039 |
| <i>Cheirogaleus major</i> | Strepsirrhini | 2.9 | 0.0061 |
| <i>Cheirogaleus medius</i> | Strepsirrhini | 1.2 | 0.0022 |
| <i>Daubentonia madagascariensis</i> | Strepsirrhini | 22 | 0.028 |
| <i>Eulemur fulvus</i> | Strepsirrhini | 12 | 0.0061 |
| <i>Eulemur mongoz</i> | Strepsirrhini | 12 | 0.063 |
| <i>Galago senegalensis</i> | Strepsirrhini | 1.8 | 0.0013 |
| <i>Indri indri</i> | Strepsirrhini | 20 | 0.015 |
| <i>Lemur catta</i> | Strepsirrhini | 11 | 0.017 |
| <i>Lepilemur sp.</i> | Strepsirrhini | 3.3 | 0.0022 |
| <i>Loris tardigradus</i> | Strepsirrhini | 3.5 | 0.0032 |
| <i>Otolemur crassicaudatus</i> | Strepsirrhini | 4.2 | 0.0075 |
| <i>Perodicticus potto</i> | Strepsirrhini | 5.6 | 0.0039 |
| <i>Propithecus verreauxi</i> | Strepsirrhini | 13 | 0.0075 |
| <i>Varecia sp.</i> | Strepsirrhini | 15 | 0.018 |

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