Comparative Study of Brain Ontogeny: Marsupials, Humans and Other Eutherians

Carmen De Miguel
Biological Anthropology and Comparative Anatomy Research Unit, Adelaide Medical School. University of Adelaide.
Arthur Saniotis
Department of Pharmacy, Knowledge University. Erbil, Kurdistan Region
Agata Cieslik
Department of Anthropology, Ludwik Hirszfeld Institute of Immunology and Experimental Therapy. Polish Academy of Sciences
Maciej Henneberg (maciej.henneberg@adelaide.edu.au)
Biological Anthropology and Comparative Anatomy Research Unit, Adelaide Medical School. University of Adelaide.

Research Article

Keywords: brain ontogeny, marsupials, eutherians

Posted Date: April 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-418220/v1

Abstract

The human brain is commonly considered unique in its growth pattern, especially in its fast growth in early infancy. Consequently, many researchers were encouraged to find peculiarities in the human brain and development which differentiated it from the brains of other animals. In this paper, we argue that the pattern of human brain growth is not different from that of other mammals, both marsupials and eutherians. Thus, our study, challenges the notion of the uniqueness of the human brain and its development indicating that specifically human mental abilities are not a result of brain morphology or size. In order to test our hypothesis we studied the ontogeny of brain weight relative to body weight using pouch young sample of 43 koalas *(Phascolarctos cinereus)*, 28 possums *(Trichosurus vulpecula*), and 36 tammar wallabies *(Macropus eugenii)* preserved in a solution of 10 % buffered formalin. We also analysed the growth of brain vs. body size in all eutherian species falling into this group (humans, rhesus monkeys, dogs, cats, rats and mice).

Introduction

The human brain is commonly considered unique in its growth pattern. During the 19th and 20th centuries several thinkers argued that human brain volume (especially the prefrontal cortex) was positively correlated with superior intelligence. Influential scientists such as Paul Broca (1824–1880) and Francis Galton (1822–1911) promoted this idea. Consequently, many researchers were encouraged to find peculiarities in the human brain and development which differentiated it from the brains of other animals. However, in the light of recent research, mental capacities which were historically deemed to be the province of *Homo* are ungrounded.

Moreover, it has been claimed that the human brain is different from other mammals especially in its fast growth in early infancy. Fortunately, there are several comparative studies of brain growth in eutherian and marsupial mammals[1,2,3,4,5,6]. In relation to brain composition, early comparative studies of mammalian brains deemed them to be similarly fashioned, especially with regard to cerebral cortex volume and neuron/glia density ratio[7,8,9]. Although marsupials exhibit considerable diversity in their morphology, behavior and cerebral organization, their neocortical arrangement and cellular composition is not as well understood as in eutherian mammals[5,7]. An exception is a commentary on low neocortical neuronal density in the opossum (*Didelphis virginiana*)[8].

Due to their distinct reproductive method marsupials allow us to study growth of the pouch young and thus to easily observe stages of growth corresponding to intrauterine stages in eutherians[10,11,12,13]. Although earlier studies of brain growth in marsupials,[14],[15],[16] do not usually include eutherian mammals in their comparisons, there has been increasing interest in marsupial brain growth[5,7,13,17]. Moreover, it has been suggested that developmental studies in marsupials constitute a relevant model for biomedical research[18]. Like eutherian mammals, marsupials exhibit similar neocortical organization, as well as distinct connectivity in cortical areas A1, S1, S2, V1, and V2[5].

In this paper, we argue that the pattern of human brain growth is not different from that of other mammals, both marsupials and eutherians. Thus, our study, challenges the notion of the uniqueness of the human brain and its development indicating that specifically human mental abilities are not a result of brain morphology or size.

Materials And Methods

We studied the ontogeny of brain weight relative to body weight using pouch young sample of 43 koalas *(Phascolarctos cinereus)*, 28 possums *(Trichosurus vulpecula*), and 36 tammar wallabies *(Macropus eugenii)* preserved in a solution of 10 % buffered formalin. The whole animal was weighed to the nearest 0.01 g. The brain was extracted by dissection and also weighed to the nearest 0.01 g. Furthermore, fresh juveniles and adults of 43 koalas and 40 possums were studied and data on body weight and brain weight recorded.

All the animals were collected under University of Adelaide Animal Ethics Permit 5/3/96 and South Australian National Parks Permit K23749-02. The animals studied died of natural or accidental causes in the Adelaide Hills or on Kangaroo Island. All the methods were conducted according to the University of Adelaide ethical guidelines and regulations.

The method employed to obtain the data from the koala and possum samples is described by De Miguel & Henneberg.[19] The wallaby sample of 59 juveniles and adults was drawn from the collection of Kangaroo Island tammar wallabies prepared by Margy Wright (Department of Applied & Molecular Ecology, University of Adelaide). Body weights were taken in the field by Ms Wright to the nearest 10 g. while the values for adult wallaby brain were estimated from measurements of endocranial volume taken by filling the skull with mustard seeds and measuring its volume to the nearest milliliter by CdeM.

Data for the rest of the species analysed in this study were taken from the literature. References are indicated next to corresponding figures. In some publications raw data for each specimen were available but in most cases only averages for each age group were published. Some data were listed in tables but for some species they were extracted from published scatterplots.

To ensure comparability of data for all species, brain sizes and body sizes were all expressed as percentages of the average adult values. A number of regression curves were fitted to the data for each species. They included linear, exponential, power, polynomial and logistic curves. The best fitting curves in each case were selected based on their coefficients of determination (r^2).

Results

Two kinds of curves best fitted data sets: They were either logarithmic or logistic. All other types of regression gave poorer fits. Therefore, two types of brain growth pattern can be discerned: “Model A” and “Model B”. (Figures 1& 2).

The Model A is characterised by a fast growth in early ontogeny followed by a gradual slow-down of the growth velocity continuing into adulthood, but never ceasing completely. It is well described by a logarithmic curve of the general form: **see formula 1 in the supplementary files section.**

This curve fits equally well (R^2 = 0.94-0.98) all species, eutherian and marsupial alike, falling into this group, (possum, koala, wallaby, kangaroo, Guinea pig, rabbit and pig) (Model A) (Figure 1).

See formula 2 in the supplementary files section.

Model B is characterised by a fast, nearly linear growth in early ontogeny, followed by a relatively sharp slow-down to reach the asymptotic stasis in adulthood. This pattern of growth is best approximated by a logistic curve of the general form:

Yet again, the same equation provided good approximation (R^2 = 0.90-0.99) to the growth of brain vs. body size in all eutherian species falling into this group (humans, rhesus monkeys, dogs, cats, rats and mice), (Figure 2).

Discussion And Conclusion

Fitting curves of brain growth in size against body size indicates no association between brain size growth and social complexity of various mammals. Two patterns of brain size relative to body size were found. The model A occurs in mammals whose body size increases continuously during adult life, e.g. in marsupials[35], Model B characterises mammals whose body size stabilizes after reaching the adulthood. In both models, brain size remains in clear relationship to body size.

This study has shown that the human brain is a mammalian organ that, concerning its growth in size, in no particular way is exceptional. This is evident when comparing the pattern of brain growth in other mammals. Human brain anatomy is very similar to that of other primate brains[36]. Consequently, the results of our study challenge the long accepted notion that the human brain became especially large during hominin evolution, thus indicating the anatomical basis for Homo's unusual abilities.

The findings of our study also confirm Passingham's argument that not only is human brain growth rate within an expected variation range, but also, that mammalian brain growth rates are more similar than body growth rates.[4] It was Ramon y Cajal who noted that mammalian brains have conserved similar anatomical features in relation to connectivity[37]. Furthermore, Kuhlenbek[38] argues that mammalian brains share a common basal organisational blueprint which has been conserved during mammalian evolution[39]. This finding also concurs with the statement that the human brain's cellular architecture shows high similarity to other mammals[40]. Recently, a study by Halley[41] verified that brain growth rate minimally differed in fetal neurogenesis in eutherians; this was not correlated to variations in whole body or visceral organ growth rates. Thus, during prenatal development, brain growth rate of eutherians is noticeably conserved[41].

The volume of the hominin braincase has tripled in the last, 3 million years (from about 450 ml to current 1350 ml.[42]. However, evolutionary hominin brain size increase matches increase in hominin body size[43,44,45,46]. Body size is measured either as the linear height, or weight, that in humans scales approximately to the second power of height[47], a fact generally recognized by the construction of the Body Mass index as a ratio of weight to height squared. When the size of human brain is expressed as a linear dimension (a cube root of volume), its increases over the last 3 million years are comparable to those of height and weight[44]. The size of the human brain is proportional to the size of musculoskeletal system mass[48]; scaling of human brain size to body size is isometric, in contrast to other vertebrates and mammals, where brain size increases allometrically at a fraction of body size[49,50]. The often stressed unusual, among mammals, size of the human brain is only true when absolute values are considered. When the growth of human brain size is related to the body size growth, the exceptional place of humans among mammals disappears. It has been shown by Saniotis and Henneberg that among all hominins, past and present, the size of brain is proportional to body size[41].

This human isometry occurred due to changes in body structure related to high quality diet and extraoral food processing decreasing size of the gastrointestinal tract and erect bipedalism together reducing body size[43]. Physiological regulation of the human brain by neurohormonal and neurotransmitter secretions follows the same principles as that of all other mammals, but the quantities of specific active substances may differ[51]. On this note it has been argued that neurohormonal regulation is a better indicator of human intelligence than brain size[46].

Interestingly, human brain volume during the Holocene period has decreased by approximately 10% (100-150ml or one standard deviation)[52,53]. This recent decrease in brain volume has occurred during the advent of complex societies and accompanying technological and scientific developments[54]. It was simply a result of body size reduction[52]. The supposed anatomical uniqueness of the human brain is not confirmed by paleoanthropological evidence nor by comparative mammalian brain studies. In Model A, there seems to be continuing enlargement of the brain during adult life, concomitant with continued enlargement of body size. This can be a result of gliogenesis, neurogenesis or both. Neurogenesis in this case may be related to continuous growth of muscle mass[15]. This pattern of growth is shared by some marsupials (possums, koalas, wallabies and kangaroos) and some eutherians (rabbits, guinea pigs and pigs). The nature of the increase in adult brain size requires further investigation, especially in the areas of neuronal connectivity and structure which reveal differences between eutherian mammalian species. For instance, it has been noted that while human frontal lobes show greater connectivity in the gPFC than in the gPFC of other eutherians, the human frontal lobes are smaller than predicted in relation to non-human primates[55].

Both models of brain size growth fit a number of mammals with different evolutionary histories, positions in trophic chains, geographic locations, environmental settings and behavioural characteristics. It seems, therefore, that specific intellectual abilities of particular mammals are a result of their brain physiologies and neurohormonal regulation rather than anatomical characteristics of their central nervous systems.

This conclusion applies also to humans whose brain size growth is not indicative of their mental capacities.

Declarations

Acknowledgements

Competing interests

The authors declare that they have no competing interests at all.

References

1. Count, E.W. Brain and body weight in man: Their antecedents in growth and evolution. *Annals of The New York Academy of Sciences* **46**(art 10), 993-1122 (1947).
2. A. Sacher, G. A. & Staffeldt, E. F. Elation of gestation time to brain weight for placental mammals: Implications for the theory of vertebrate growth. *The American Naturalist.***108**(963), 593-615 (1974).
3. Holt, A. B., Cheek, D. B., Mellits, E. D. & Hill, D. E. Brain size and the relation of the primate to the nonprimate, in *Fetal and postnatal cellular growth: hormones and nutrition* (ed. Cheek, D) 23-44 (John Wiley & Sons, 1975).
4. Passingham, R. E. Rates of brain development in mammals including man. *Brain Behav Evol.* **26**, 167-175 (1975).
5. Karlen, S. J. & Krubitzer, L. The functional and anatomical organization of marsupial neocortex: Evidence for parallel evolution across mammals. *Prog Neurobiol.***82**(3), 122-141 (2007).
6. Weisbecker, V. & Goswami, A. Brain size, life history, and metabolism at the marsupial/placental dichotomy. *PNAS.* **107**(37), 16216-16221 (2010).
7. Dos Santos, S. E., Porfirio, J., F. da Cunha, F. B., Manger, P. R. & Tavares, W. *et al.* Cellular scaling rules for the brains of marsupials: not as "primitive" as expected. *Brain Behav Evol.* **89**, 48-63 (2017).
8. Haug, H. Brain sizes, surfaces, and neuronal sizes of the cortex cerebri: a stereological investigation of man and his variability and a comparison with some mammals (primates, whales, marsupials, insectivores, and one elephant). *Am J Anat.***180**, 126-142 (1987).
9. Stolzenburg, J. U., A. Reichenbach, A. & Neumann, M. Size and density of glial and neuronal cells within the cerebral neocortex of various insectivorian species. ***2***(2), 78-84 (1989).
10. Renfree, M. B. Review: marsupials: placental mammals with a difference. *Placenta.* **31**, Suppl, S21-S26 (2010).
11. Chavan, A. R., Griffith, O. W. & Wagner, G. P. The inflammation paradox in the evolution of mammalian pregnancy: turning a foe into a friend. *Current Opinion in Genetics & Development***47**, 24-32 (2017).

12. Smith, K. K. Going from s mall to large: mechanical implications of body size diversity in terrestrial mammals, in *Great transformations in vertebrate evolution* (eds. Dial, K. P., Shubin, N. & Brainerd, E. L.) 205-225 (University of Chicago Press, 2015).
13. Weisbecker, V., Blomberg, S., Goldizen, A. W., Brown, M. & Fisher, D. The evolution of relative brain size in marsupials is energetically constrained but not driven by behavioral complexity. *Brain Behav Evol*. **85**, 125-135 (2015).
14. Renfree, M. B., Green, A. B., Carr, J. P. & Cheek, D. B. Ontogeny of the brain in a marsupial (*Macropus eugenii*) throughout pouch life: I. Brain Growth. *Brain Behav Evol*. **20**, 57-71 (1982).
15. Nelson, J. E. Growth of the brain in *The developing marsupial. models for biomedical research* (eds. Tyndale-Biscoe, C. H. &Janssens, P. A.) 86-100 (Springer-Verlag, 1988).
16. Janssens, P. A., Hulbert, A. J. & Baudinette, R. V. Development of the pouch young from birth to pouch vacation in *Marsupial biology: recent research, new perspectives* (eds. Saunders, N. & Hinds, L.) 71-89 (University of New South Wales Press, 1997).
17. Suárez, R., Paolino, A., Kozulin, P., Fenlon, L. R. & Morcom, L. R. et al. Development of body, head and brain features in the Australian fat-tailed dunnart (*Sminthopsis crassicaudata*; Darsupialia: Dasyuridae); a postnatal model of forebrain formation. *PLOS ONE*. **12**(9): e0184450 (2017).
18. Tyndale-Biscoe, C. H. & Janssens, P. A. Introduction in *The developing marsupial: models for biomedical research* (eds. Tyndale-Biscoe, C. H. & Janssens, P. A.) 1-7 (Springer-Verlag, 1988).
19. De Miguel, C. & Henneberg, M. Encephalization of the koala*, Phascolarctos cinereus. Australian Mammalogy*. **20**(3), 315-320 (1988).
20. Dickerson, J. W. T. & Dobbing, J. Prenatal and postnatal growth and development of the central nervous system of the pig. *Roy. Soc. B.* **166**, 384-395 (1967).
21. Dobbing, J. & Sands, J. Quantitative growth and development of human brain. *Archives of Disease in Childhood.* **48**, 757-767 (1973).
22. Dobbing, J. & Sands, J. Growth and development of the brain and spinal cord of the guinea pig. *Brain Research.* **17**, 115-123 (1970).
23. Harel, S., Watanabe, K., Linke, I. & Schain, R. J. Growth and development of the rabbit brain. *Neonate.* **21**, 381-399 (1972).
24. Mühlmann, M. Wachstum, Altern und Tod. *Ergebnisse der Anatomie und Entwicklungsgeschichte.* **27**, 1-245 (1927).
25. Connolly, C. J. *External morphology of the primate brain* (C.C. Thomas, 1950).
26. Spector, W. S. *Handbook of biological data* (W.B. Saunders Company, 1956).
27. Dickerson, J. W. T., Merat, K. & Yusuf, H. K. M. Effects of malnutrition on brain growth and development, in *Brain and Behavioural Development* (eds. J.W.T. Dickerson, J. W. T. & McGurk, H.) 73-108 (Surrey University Press, 1982).
28. Zilles, K. Biometrische analyse der frischvolumina verschiedener prosencephaler hirnregionen von 78 menschlichen, adulten gehirnen. *Gegenbaurs Morphologisches Jahrbuch.* **118**(2S), 234-273 (1972).

29. Kretschmann, H. J., Kammradt, G., Krauthausen, I., Sauer, B. & Wingert, F. Brain growth in man. *Bibliotheca Anatomica.* **28**, 1-26 (1986).
30. Falk, D., Froese, N., Sade, D. S. & Dudek, B. C. Sex differences in brain/body relationships of Rhesus monkeys and humans. *Journal of Human Evolution.* **36**, 233-238 (1999).
31. Agrawal, H. C., Davis, J. M. & Himwich, W. A. Water content of dog brain parts in relation to maturation of the brain. *American Journal of Physiology.* **215**(4), 846-848 (1968).
32. Agrawal, H. C., Davis, J. M. & Himwich, W. A. Water content of developing kitten brain. *Journal of Neurochemistry.* **14**, 179-181 (1967).
33. De Souza, S. W. & Dobbing, J. Cerebral edema in developing brain: I. Normal water and cation content in developing rat brain and postmortem changes. *Experimental Neurology.* **32**, 431-438 (1971).
34. Agrawal, H. C., Davis, J. M. & Himwich Developmental changes in mouse brain: Weight, water content and free amino acids. *Journal of Neurochemistry 15*, 917-923 (1968).
35. Karkach, A. S. Trajectories and models of individual growth. *Demographic Research*. **15**, 347-400 (2006).
36. Radinsky, L. *The fossil record of primate brain evolution* (American Museum of Natural History, 1979).
37. Assaf, Y., Bouznach, A., Zomet, O., Marom, A. & Yovel, Y. Conservation of brain connectivity and wiring across the mammalian class. *NatureNeuroscience*. **23**, 805-808 (2020).
38. Kuhlenbeck, H. ***The central nervous system of vertebrates, vol. 5/I.*** *derivatives of the prosencephalon: diencephalon and telencephalon* Philadelphia, PA (**1977).**
39. Kruska, D. C. On the evolutionary significance of encephalization in some eutherian mammals: effects of adaptive radiation, domestication, and feralization. *Brain Behav. Evol.***65**(2), 73-108 (2005).
40. Saniotis, A. & Henneberg, M. An evolutionary approach towards exploring altered states of consciousness, mind-body techniques and non-local mind. *World Futures: The Journal of General Evolution*. **67**(3), 182-200 (2011).
41. Halley, A. C. Minimal variation in eutherian brain growth rates during fetal neurogenesis. *R. Soc*. **B 284**, 20170219 (2017).
42. De Miguel, C. & Henneberg, M. Variation in hominid brain size: how much is due to method? **52**, 3-58 (2001).
43. Henneberg, M. Evolution of the human brain: is bigger better? *Exp. Pharmacol. Physiol*. **25**, 745-749 (1998).
44. Henneberg, M. & Saniotis, A. Evolutionary origins of human brain and spirituality. *Anz*. **67**, 427-438 (2009).
45. Saniotis, A. & Henneberg, M. Medicine could be constructing human bodies in the future. *Hypotheses.***77**, 560-564 (2011).

46. Saniotis, A., Henneberg, M., Grantham, J. & Kumaratilake, J. Neuro-hormonal regulation is a better indicator of human cognitive abilities than brain anatomy: the need for a new paradigm. *Frontiers in Neuroanatomy* **13**, 101- (2020). doi: 10.3389/fnana.2019.00101
47. Henneberg, M., Hugg, J. & Townsend, E. J. Bodyweight/height relationship an exponential solution. *J.Hum.Biol.* **1**, 483-491 (1989).
48. Rogers, A. W. *A textbook of anatomy* (Churchill Livingstone, 1992).
49. Jerison, H. J. *Evolution of the brain and intelligence* (Academic Press, 1973)
50. Martin, R. D. *Primate origins and evolution* (Princeton University Press, 1990).
51. Previc, F. H. *The dopaminergic mind in human evolution. and history* (Cambridge University Press, 2009).
52. Henneberg, M. Decrease of human skull size in the Holocene. *Biol*. 60, 395-405 (1988).
53. Brown, P. Recent human evolution in East Asia and Australasia. *Trans. R. Soc. Lond. B Biol. Sci*. **331**, 23542 (1992).
54. Henneberg, M. & Steyn, M. Trends in cranial capacity and cranial index in Subsaharan Africa during the Holocene. *J. Hum. Biol*. **5**, 473-479 (1993).
55. Elston, G. N. & Garey, L. J. Prefrontal cortex: Brodmann and Cajal revisited, in *Prefrontal cortex: roles, Interventions and traumas* (Eds. LoGrasso, L. & Morretti, G.), 245-259 (Nova Science Pub Inc, 2009).

Figures

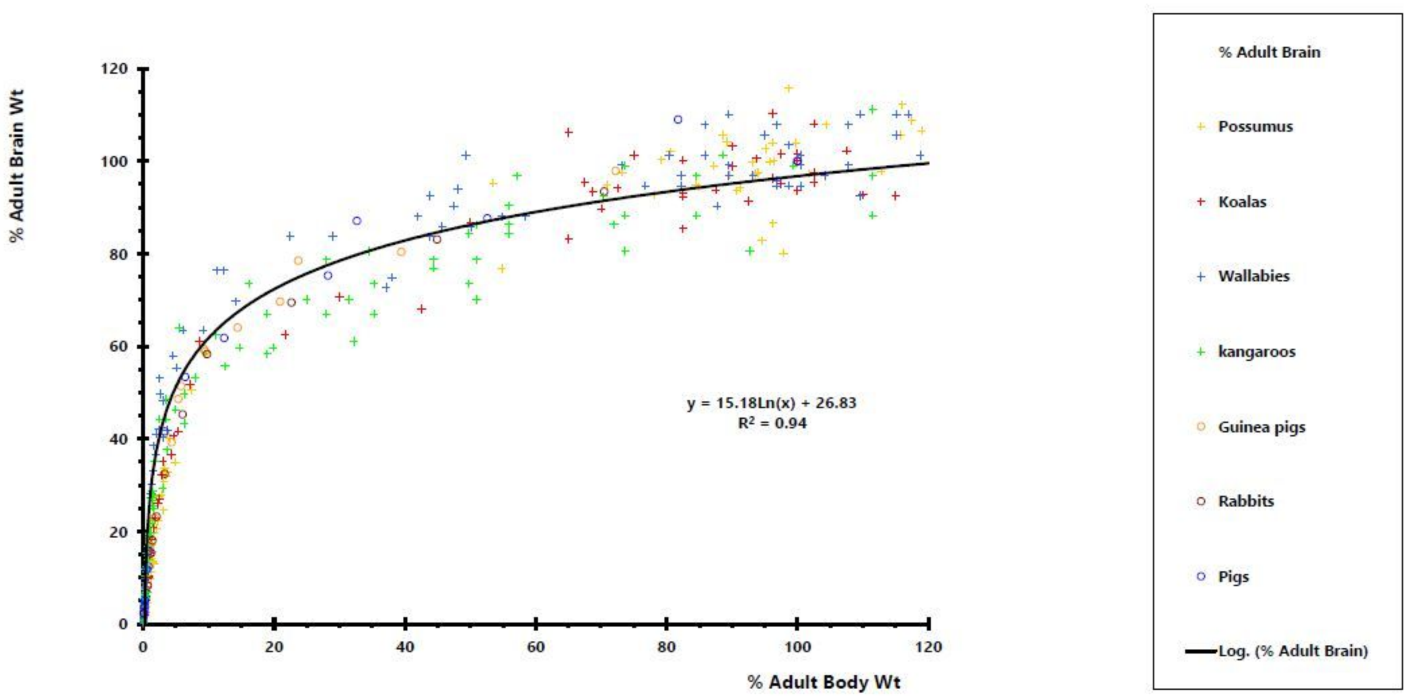

Figure 1

Model A showing brain growth relative to body weight3,15,16,19,20,21,22,23.

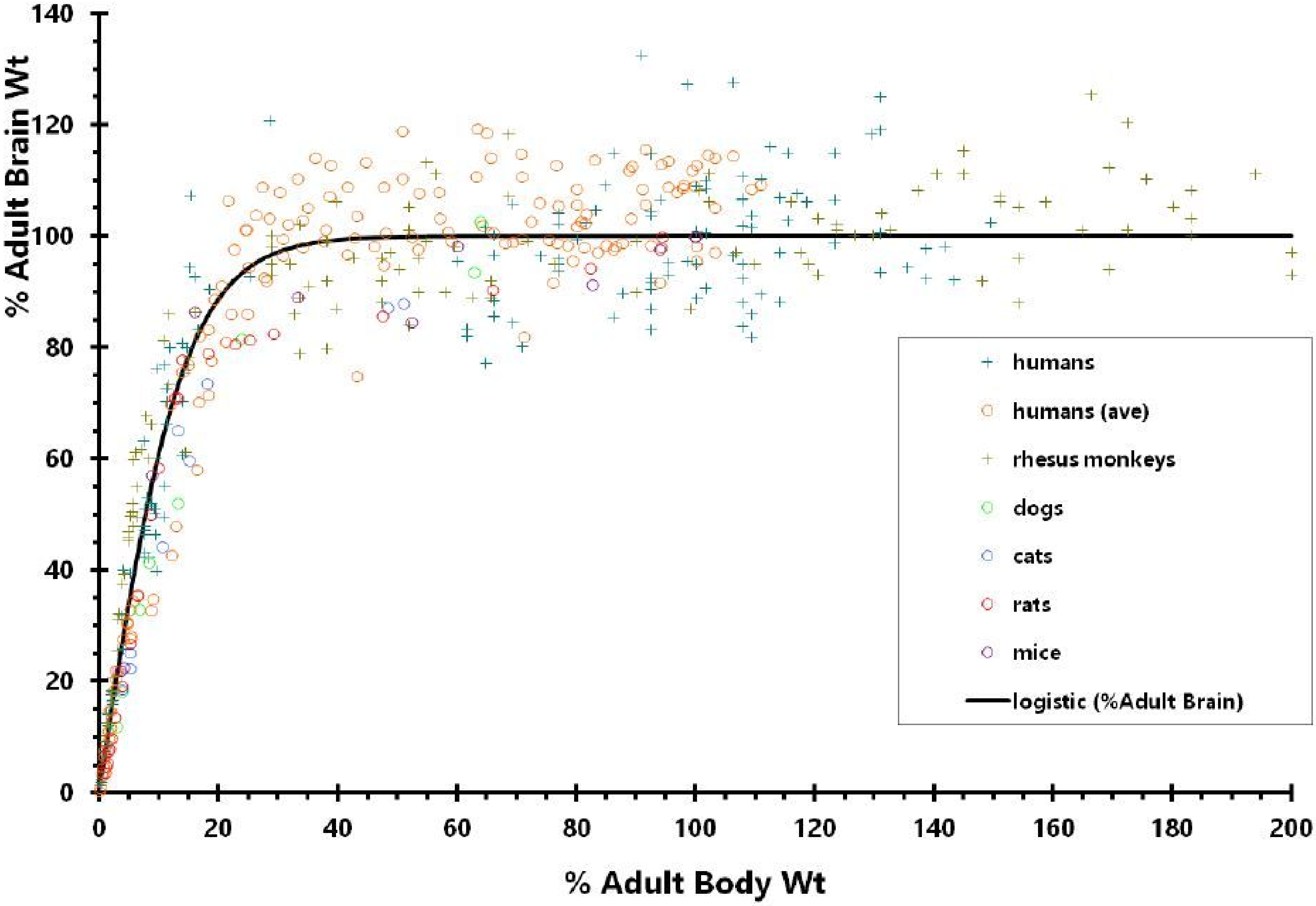

Figure 2

Model B showing brain growth relative to body weight1,3,4,21,23,25,26,27,28,29,30,31,32,33,34.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- formula.docx