

Dietary models of primate brain evolution omit the gut microbiome

*Francisco P. Chávez¹**

¹ Laboratorio de Microbiología de Sistemas, Departamento de Biología, Facultad de Ciencias, Universidad de Chile, Santiago, Chile.

*Corresponding author: fpchavez@uchile.cl

Matters Arising

Arising from A. R. DeCasien, S. A. Williams and J. P. Higham, Nature Ecology & Evolution

<https://doi.org/10.1038/s41559-017-0112> (2017)

DeCasien *et al.* reported that diet, rather than sociality, predicts relative brain size across primates, with frugivores having larger brains than folivores¹. Their interpretation moves the discussion from sociality towards ecology yet leaves the proposed energetic link biologically unspecified. The matter arising from this dietary framework is gut microbial metabolism, a plausible mechanistic link between dietary substrates and the energy and metabolites available to support neural development and maintenance. Microorganisms help determine how much energy and which metabolites a host obtains from a dietary substrate, while social contact helps transmit those microorganisms among hosts. Evidence for both processes was available when the article appeared. Because the study represented diet using broad feeding categories or percentage frugivory, it could not distinguish food intake from the nutrition realized by the host-microbe system. The results establish a dietary association, but they do not identify the mechanism through which diet could support the evolution of a larger brain.

This distinction matters because neural tissue imposes a sustained energetic burden. A larger brain requires energy not only for adult neuronal signaling, but also for fetal and postnatal growth, synapse formation, glial and immune functions, and tissue maintenance. Food category is therefore an incomplete measure of the relevant evolutionary resource. The critical variable is the fraction of dietary energy made available to the host, its temporal reliability, and its partitioning between brain and other tissues. Fermentation of otherwise inaccessible carbohydrates produces acetate, propionate, and butyrate, which contribute to host metabolism and signal through receptor, immune, and epigenetic pathways that regulate energy allocation and cell fate ^{2,3}. Glucose regulation and other host-microbe metabolic interactions further alter that budget. The relevant exposure is therefore metabolite flux, not food category alone. The microbiome is not an additional ecological correlate beside diet; it is a candidate mechanism connecting diet quality to the energetic feasibility of encephalization.

The models in DeCasien *et al.* ask whether a measured social variable explains additional cross-species variation in brain size after body size, phylogeny and diet are considered ¹. A non-significant coefficient answers that conditional statistical question. It does not show that social behavior lacks an evolutionary pathway to brain energetics, especially when species-average group size or categorical social organization poorly represents the contact process that matters. In wild baboons, rates of social interaction predicted taxonomic and functional features of the gut microbiome after diet, kinship, and shared environment were controlled ⁴. In chimpanzees, greater social interaction increased individual microbial diversity and homogenized community membership, consistent with social maintenance of a population-level pan-microbiome ⁵. These studies do not rescue the classic social-brain hypothesis, but they show that sociality can modify the metabolic machinery through which diet acts.

Diet is likewise not a host-only exposure. In wild black howler monkeys, seasonal microbial changes were associated with buffering variation in energy and nutrient intake⁶ and in gorillas, fruit availability and fiber consumption tracked distinct microbial and metabolomic profiles, including pathways for simple-sugar, lipid and plant-cell-wall metabolism⁷. A synthesis available before publication of the article had already identified the gut microbiota as a missing component in models of primate diet, energetics and cognition⁸. Consequently, a frugivore-folivore contrast bundles food chemistry, gut anatomy, retention time and microbial fermentation. The diet coefficient may therefore index a host-microbe digestive phenotype rather than a direct effect of food category. This interpretation complements anatomical models of brain energetics^{9,10}. The expensive-tissue hypothesis proposes that the energetic costs of a larger brain can be offset by reduced investment in the digestive tract, although comparative support for a simple gut-brain trade-off remains contested. Microbial metabolism adds a functional dimension: gut size alone does not specify the substrates transformed, metabolites produced, or energy ultimately available to the host. Digestive anatomy and microbial function should therefore be considered jointly when interpreting diet-brain associations.

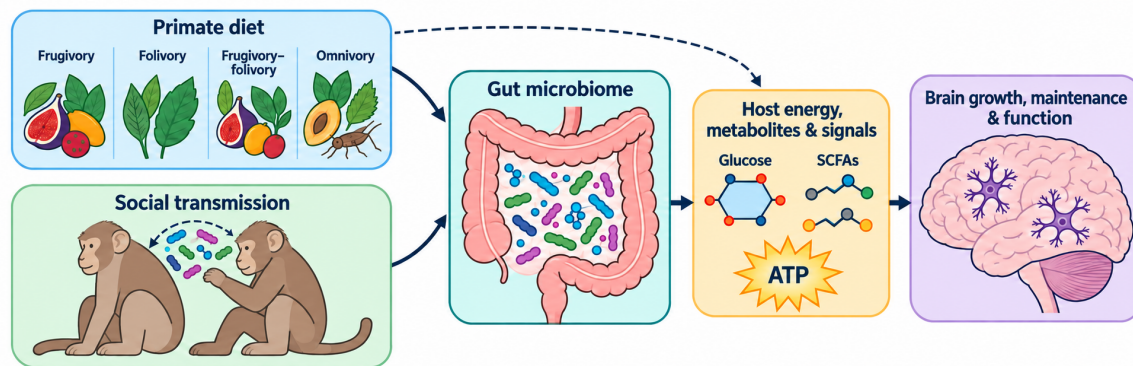


Figure 1. Gut microbial metabolism as a candidate link between diet and brain evolution. Diet and food processing shape the substrates entering the digestive system, while social contact and food sharing can influence microbial transmission. Digestive anatomy and microbial function jointly influence energy harvest, circulating metabolites, and brain-relevant signals. The DeCasien *et al.* study measured broad dietary and social variables but not the intervening microbial or metabolic states. Arrows depict proposed relationships rather than demonstrated evolutionary causation; dashed feedback arrows indicate potential effects of cognitive and behavioral capacities on dietary selection and social contact. Effects on neural metabolism, neurogenesis, or maintenance do not by themselves establish evolutionary changes in brain size.

The omission is especially consequential when the primate result is extended to hominin evolution. The major expansion of the genus *Homo* brain preceded agriculture, so farming cannot explain its origin. Earlier access to cooked starches has instead been proposed to increase the glucose available to a metabolically expensive brain¹¹. Yet neither starch content nor cooking is equivalent to energy delivered to the host, because food processing and microbial metabolism both alter digestibility and metabolic output. Agriculture is informative as a later natural experiment, not as the cause of initial encephalization. Hunter-gatherer, traditional agriculturalist and urban-industrial populations exhibit distinct gut communities and functional potential¹². The Neolithic transition illustrates that a dietary shift can simultaneously alter food processing, settlement, social transmission and microbial ecology. Hominin dietary models should therefore treat diet, technology and microbiota as a coupled energetic phenotype.

Brain-facing mechanisms were already biologically plausible in 2017. Germ-free mice displayed persistently altered adult hippocampal neurogenesis; colonization after weaning did not normalize the phenotype, consistent with an early-life developmental window¹³. Germ-free or antibiotic-treated mice also showed immature microglia, partly normalized by complex microbiota or short-chain fatty acids². This evidence did not demonstrate a microbial cause of primate encephalization. It did establish routes connecting dietary substrates and socially transmitted microbes to the production, maturation, and maintenance of neural tissue. Cognitive and behavioral capacities may, in turn, influence dietary selection and social contact, potentially reshaping microbial exposure and function. Figure 1 presents a proposed mechanistic pathway within this broader feedback system, rather than an established direction of evolutionary causation.

Subsequent work has resolved specific metabolite-to-neurogenesis pathways. In a mouse diet-dysbiosis model, propionate and butyrate promoted early neural-stem-cell differentiation through mitochondrial biogenesis, reactive oxygen species, and ERK1/2; in that pathological dietary context, premature differentiation was accompanied by depletion of progenitor pools³. In a second model, transfer of stress-associated microbiota reduced adult hippocampal neurogenesis by lowering circulating fatty-acid precursors, hippocampal 2-arachidonoylglycerol (2-AG), and CB1-mTOR signaling. Pharmacological restoration of 2-AG signaling, arachidonic-acid supplementation, or *Lactobacillus plantarum* partly rescued newborn-neuron production and survival¹⁴. SCFAs are direct products of microbial fermentation, whereas 2-AG is a host monoacylglycerol whose precursor supply and signaling are microbiota-sensitive; both connect dietary chemistry to neural stem-cell fate and neuronal survival. A third route involves microbial indole: indole-producing, but not tryptophanase-null, *Escherichia coli* increased dentate-gyrus neurogenesis through aryl hydrocarbon receptor signalling¹⁵. This later evidence cannot retroactively validate a mechanism not tested in 2017, but it strengthens its plausibility. More directly, transplanting gut microbiota from three

primate species into germ-free mice showed that microbiota from the two more encephalized species shifted host metabolism towards energy use and production, whereas microbiota from the less encephalized species favored energy storage¹⁶. Notably, a subsequent study led by the first author of the original article found that microbiota from more encephalized primates induced convergent changes in the expression of brain genes involved in energy production, with human microbiota particularly enriching pathways related to oxidative phosphorylation¹⁷. This work provides an important mechanistic extension of the original diet-brain association. Nevertheless, both transplantation studies involved only three primate donor species and germ-free mouse recipients and therefore establish biological plausibility rather than an evolutionary causal relationship between the gut microbiome and primate encephalization.

The defensible conclusion from the DeCasien *et al.* study is that measured dietary variables predict relative brain size more consistently than the measured social proxies. The unresolved question is how those dietary associations translate into the energetic conditions supporting neural tissue. Comparative tests should distinguish ingested substrates from realized host–microbe metabolism, jointly consider digestive anatomy and microbial function, and replace coarse social categories with contact and transmission measures where possible. Phylogenetic models could assess whether the observed relationships are consistent with microbial mediation while comparing alternative causal structures. Such analyses would require appropriately matched species-level data and would not, by themselves, establish evolutionary causation. Dietary associations alone cannot identify the mechanisms linking food consumption to brain evolution. Gut microbial metabolism is a plausible component of that explanation and should be explicitly considered alongside digestive anatomy, host energetics and behavioral feedbacks.

References

1. DeCasien, A. R., Williams, S. A. & Higham, J. P. Primate brain size is predicted by diet but not sociality. *Nat. Ecol. Evol.* **1**, (2017).
2. Erny, D. *et al.* Host microbiota constantly control maturation and function of microglia in the CNS. *Nat. Neurosci.* **18**, (2015).
3. Ribeiro, M. F. *et al.* Diet-dependent gut microbiota impacts on adult neurogenesis through mitochondrial stress modulation. *Brain Commun.* **2**, (2020).
4. Tung, J. *et al.* Social networks predict gut microbiome composition in wild baboons. *Elife* **2015**, (2015).
5. Moeller, A. H. *et al.* Social behavior shapes the chimpanzee pan-microbiome. *Sci. Adv.* **2**, (2016).
6. Amato, K. R. *et al.* The Gut Microbiota Appears to Compensate for Seasonal Diet Variation in the Wild Black Howler Monkey (*Alouatta pigra*). *Microb. Ecol.* **69**, (2015).
7. Gomez, A. *et al.* Temporal variation selects for diet-microbe co-metabolic traits in the gut of Gorilla spp. *ISME Journal* **10**, (2016).
8. Amato, K. R. Incorporating the gut microbiota into models of human and non-human primate ecology and evolution. *Am. J. Phys. Anthropol.* **159**, 196–215 (2016).
9. Hardy, K., Brand-Miller, J., Brown, K. D., Thomas, M. G. & Copeland, L. The importance of dietary carbohydrate in human evolution. *Quarterly Review of Biology* **90**, (2015).
10. Obregon-Tito, A. J. *et al.* Subsistence strategies in traditional societies distinguish gut microbiomes. *Nat. Commun.* **6**, (2015).
11. Ogbonnaya, E. S. *et al.* Adult Hippocampal Neurogenesis Is Regulated by the Microbiome. *Biological Psychiatry* vol. 78 (2015).
12. Chevalier, G. *et al.* Effect of gut microbiota on depressive-like behaviors in mice is mediated by the endocannabinoid system. *Nat. Commun.* **11**, 6363 (2020).
13. Wei, G. Z. *et al.* Tryptophan-metabolizing gut microbes regulate adult neurogenesis via the aryl hydrocarbon receptor. *Proc. Natl. Acad. Sci. U. S. A.* **118**, (2021).
14. Mallott, E. K. *et al.* The primate gut microbiota contributes to interspecific differences in host metabolism. *Microb. Genom.* **10**, (2024).
15. DeCasien, A. R. *et al.* Primate gut microbiota induce evolutionarily salient changes in mouse neurodevelopment. *Proceedings of the National Academy of Sciences* **123**, e2426232122 (2026).