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Energetic and nutritional constraints on infant brain development: Implications for brain expansion during human evolution

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ABSTRACT

The human brain confronts two major challenges during its development: (i) meeting a very high energy requirement, and (ii) reliably accessing an adequate dietary source of specific brain selective nutrients needed for its structure and function. Implicitly, these energetic and nutritional constraints to normal brain development today would also have been constraints on human brain evolution. The energetic constraint was solved in large measure by the evolution in hominins of a unique and significant layer of body fat on the fetus starting during the third trimester of gestation. By providing fatty acids for ketone production that are needed as brain fuel, this fat layer supports the brain's high energy needs well into childhood. This fat layer also contains an important reserve of the brain selective omega-3 fatty acid, docosahexaenoic acid (DHA), not available in other primates. Foremost amongst the brain selective minerals are iodine and iron, with zinc, copper and selenium also being important. A shore-based diet, i.e., fish, molluscs, crustaceans, frogs, bird's eggs and aquatic plants, provides the richest known dietary sources of brain selective nutrients. Regular access to these foods by the early hominin lineage that evolved into humans would therefore have helped free the nutritional constraint on primate brain development and function. Inadequate dietary supply of brain selective nutrients still has a deleterious impact on human brain development on a global scale today, demonstrating the brain's ongoing vulnerability. The core of the shore-based paradigm of human brain evolution proposes that sustained access by certain groups of early *Homo* to freshwater and marine food resources would have helped surmount both the nutritional as well as the energetic constraints on mammalian brain development.

Introduction

The adult human brain weighs about 1350 g or about three pounds (Allen et al., 2002), which is about three times more than in either *Australopithecus afarensis* or large apes today (Table 1). The human brain is large not only in absolute size but, at ~2% of adult body weight, is also large in proportion to body size. The hominin fossil record provides few clues to explain how and why the brain of *Homo sapiens* evolved to become so much larger and so much more cognitively developed than in non-human primates.

Normal brain development in the infant is a prerequisite for optimal brain function in the adult so potential constraints on brain development have implicit significance for understanding constraints on evolving higher functionality of the primate brain.

The brain in newborn humans represents about 13% of lean body weight, which is about 30% more than for the newborn chimpanzee (Table 1). It also has a very high energy requirement, greatly exceeding that of the rest of the body combined (Fig. 1). This remarkable situation provides insight into the uniqueness of human brain evolution: how did so much energy metabolism get focused on the neonatal brain when it is not really able to contribute to survival until the child is at least five to six years old, i.e., long after the age at which other primates are semi- if not totally autonomous?

To expand three-fold over the past two to three million years, the early hominin brain had to overcome at least two constraints: (i) an energetic constraint: increasing energy requirements as the brain size increased, and (ii) a nutritional constraint: increasing requirements for nutrients that play a specific role in mammalian brain structure, development and function. The energetic constraint is synonymous with the 'metabolic' constraint described in earlier publications (Cunnane, 2010) but 'energetic' is perhaps the more appropriate term given that it refers exclusively to

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Table 1
Brain and body weights of several species of australopithecine (A.) and *Homo (H.)*, compared with *Pan troglodytes* (revised from Cunnane, 2010).

	Brain weight (g)	Brain/body (%)
A. afarensis (3.6–2.8 Ma)	455	1.7
A. africanus (3.0–2.2 Ma)	450	1.0
H. habilis (1.9–1.5 Ma)	600	1.7
H. erectus (1.8–0.3 Ma)	940	1.6
H. heidelbergensis (600–200 ka)	1200	1.8
H. neanderthalensis (200–40 ka)	1450	1.9
H. sapiens (100–10 ka)	1490	2.4
H. sapiens (present day)		
Adult male	1350	2.3 (2.7[a])
Newborn	380	10.9 (13.1[a])
Pan troglodytes		
Adult male	400	0.9
Newborn	160	10.0

Ma – millions of years ago, ka – thousand of years ago.
[a] Corrected to lean body weight since present-day primates have very low body fat content, a condition also presumed to have existed in australopithecines and early *Homo*.

meeting energy requirements. Similarly, the nutritional constraint is synonymous with the 'structural' constraint described elsewhere because the nutrients tend to be needed for cellular structure and function. Nevertheless, the distinction between these two constraints is imperfect because they have a certain degree of overlap with each other, especially during infancy. Either constraint alone can delay and/or permanently foreshorten cognitive development in infants today, so it is important to emphasise that surmounting just one of these two constraints alone would not have been sufficient to push human brain evolution forwards. Therefore, the path towards hominin brain expansion involved a long period of investment in overcoming the energetic and nutritional vulnerability of the brain during infant development, a vulnerability that is greater in humans than other species and remains with us to the present day.

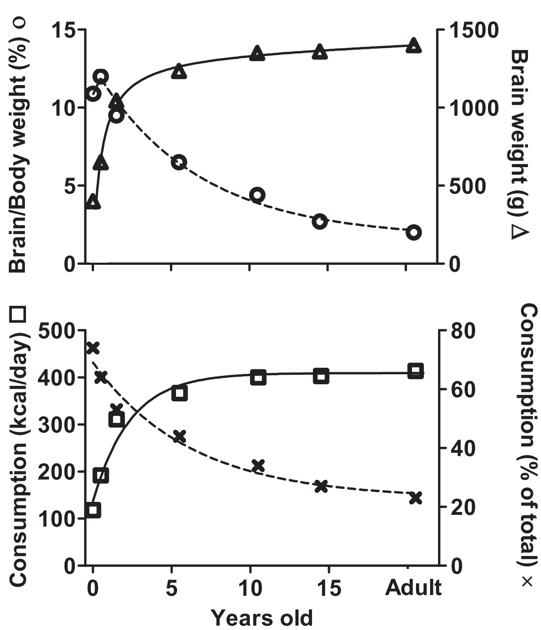

Figure 1. Brain size and energy consumption in the human from birth to adulthood (modified from Holliday, 1971). Normal infant brain development is a prerequisite for optimal brain function in the adult so the challenge is to explain how the disproportionate brain size and energy consumption evolved in the human infant.

The shore-based paradigm of human brain evolution proposes that hominins destined to become humans surmounted the brain's developmental vulnerability by exploiting shore-based habitats that provided abundant and sustained access to a wide selection of foods rich in brain selective nutrients. This paradigm also proposes that occupying the shore-based habitat was associated the evolution of neonatal body fat reserves, which were just as important for optimal human brain development. Deposits of subcutaneous body fat are not unusual in adult mammals but, with the exception of humans, are not present in the neonates of non-human primates. The particularly high energy needs of the developing human brain suggest that fuel stored as body fat in the newborn plays a critical role in early brain development. By providing access to an enriched dietary source of brain selective nutrients and by permitting evolution of body fat, a shore-based habitat masked the neurodevelopmental vulnerability that is still a hallmark of human infants today. Together, these two developments in early hominins led eventually to evolution of the modern human brain.

Vulnerability of the developing brain

Brain development passes through a series of processes that, in essence, starts with overproduction of neurons, followed by their migration to specific layers within the brain, then pruning of excess neurons, followed by myelination. This highly regulated and complex process involves a sequence of critical periods in brain development such that successful completion of a given period depends on (and is therefore vulnerable to) the successful completion of the preceding period. Deficits and distortions in brain maturation can occur both within specific regions of the brain and also in the brain as a whole compared with the rest of the body (Dobbing, 1985). These disruptions can arise because genetic or environmental circumstances block the completion of a critical period at the moment or in the sequence prescribed. The problem can be at one or more levels, including the migration of a certain cell type, or the maturation of a neural network, or region of the brain. When this maturation process is disrupted, optimal brain function is frequently not achieved in the adult. Brain selective nutrients are key players in this step-wise process.

There are two strategies to reduce this neurodevelopmental vulnerability: (i) restrict brain size and cognitive potential, or (ii) assure a richer and more reliable supply of fuel and brain selective nutrients. Thus, it would have been advantageous if the human brain could have evolved without needing a higher fuel requirement. However, the cost of a lower fuel requirement would be less development of the metabolically expensive process of establishing and maintaining advanced connectivity between neurons, which is the hallmark of cognitive capacity in humans. The hominin solution to this trade-off was to evolve a better brain fuel reserve in the form of body fat stores that start to form in the fetus during the last third of gestation. Compared with all other non-human primates or terrestrial animals in general, the fat store in human neonates provides a far more significant reserve not only of fuel but also of certain key fatty acids needed for the structural integrity of the brain. Without having evolved a specialized fuel reserve to support the developing brain, non-human primates were restricted to a lower cognitive development and functionality. However, compared with humans, they retained the key advantage of lower brain vulnerability during early development.

Challenging aspects of brain energy metabolism

Several challenges for brain energy metabolism arose in mammals and became more acute in species with larger brains. First is the brain's high metabolic rate, i.e., its high energy needs (Table 2).