

*Short Report***Docosahexaenoic Acid Biosynthesis and Dietary Contingency: Encephalization Without Aquatic Constraint**

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ABSTRACT Reconstructing evolutionary processes in the distant past is necessarily an inductive endeavor, typically appealing to numerous considerations thought to be relevant to the veracity of a particular conclusion. In this respect, it is essential that the considerations invoked to support hypotheses are in turn well-established truths. It is with these concerns that we sought to examine the nutritional, physiological, and archeological premises underlying the perspective that access to an aquatic diet rich in docosahexaenoic acid (DHA, 22:6*n*-3) was critical to human brain evolution (Carlson and Kingston [2007]: *Am J Hum Biol* 19:132–141). In our report investigating links between omega-3 (*n*-3) fatty acids and hominin encephalization, we concluded that the regular consumption of aquatic resources rich in preformed DHA may not have been essential given a varied diet of wild terrestrial foods (Carlson and Kingston [2007]). This assessment was based primarily on evidence of potential physiological adaptations in modern humans to ensure sufficient availability of DHA during critical periods of brain growth. While modern human physiology provides critical information regarding DHA as a constraint in evolving a large brain, it is also important to consistently contextualize interpretations within a framework of eclectic foraging diets rather than nutritionally limited modern agricultural populations or even modern foragers. We contend that current interpretations of Pleistocene hominin nutritional ecology do not uniquely support a shore-based foraging niche as claimed by Cunnane et al. ([2007]: *Am J Hum Biol*, 19:578–581). Specific issues raised in response to our article by Cunnane et al. and Joordens et al. ([2007]: *Am J Hum Biol*, 19:582–584) are addressed here. *Am. J. Hum. Biol.* 19:585–588, 2007. © 2007 Wiley-Liss, Inc.

IN RESPONSE TO CUNNANE
 ET AL. (IN PRESS)

Cunnane et al. (2007) question our perspective that the conversion of dietary α -linolenic acid (LNA, 18:3*n*-3) to DHA may prove sufficient for the growth and maintenance of a large brain, citing several studies that appear to highlight the relatively low conversion of LNA to DHA (Cunnane et al., in press; Table). These studies indicate minimal change in levels of circulating DHA following LNA supplementation of a diet presumably sufficient in *n*-3 fatty acids, a finding we previously acknowledged (Carlson and Kingston, 2007). Studies of *n*-3 fatty acid metabolism have repeatedly reported no upregulation of DHA biosynthesis in the presence of excess LNA. However, this conversion appears subject to upregulation during periods of conditional demand. As we previously outlined (Carlson and Kingston, 2007), biosynthesis of DHA

varies significantly by sex, energy status, pregnancy/lactation, protein intake, preformed DHA, and the ratio of *n*-6 to *n*-3 or saturated to polyunsaturated fatty acids. Given that DHA is essential for optimal function of the brain and retina, a high degree of regulation surrounding its synthesis, tissue utilization, and eventual oxidation provides a physiological buffer against environmental and developmental variability.

The calculations of dietary LNA required for sufficient DHA biosynthesis by Cunnane et al. (2007) are misleading. While several studies of adult men have reported only 0–4%

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Received 19 March 2007; Accepted 22 March 2007

Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/ajhb.20683

conversion of ingested LNA to DHA, women of reproductive age have been reported to oxidize 50% less LNA for energy than men and convert 9% of ingested LNA to DHA (Burdge, 2004). By converting 9% of the 2002 Institute of Medicine's Daily Recommended Intake (DRI) of 1.1 g LNA, a woman would synthesize 121 mg DHA per day or 847 mg DHA per week. Given that the fetal brain accrues 400 mg/week during peak growth in the third trimester of gestation, intake of only 1 g of LNA would allow sufficient synthesis of DHA for normal fetal development, not 20–60 g of LNA as suggested by Cunnane et al. (2007). Additionally, circulating DHA has been reported to increase significantly relative to prepregnant levels by week 6 of gestation despite no significant change in DHA intake (Otto et al., 2001). While increased circulating DHA during pregnancy could result from increased mobilization of limited stored DHA, upregulated biosynthesis may represent a more important mechanism (Otto et al., 2001). Regarding the various vitamin and mineral cofactors (including zinc, iron, and vitamin B₆) required for this pathway (Cunnane et al., 2007), we acknowledge their essentiality for many enzymatic pathways, but have found no evidence to suggest that these nutrients are rate-limiting within a modern or evolutionary context.

Cunnane et al. (2007) suggest that preformed DHA is essential for infants, noting that we neglect to mention that “virtually every professional association representing pediatricians” support the inclusion of DHA in infant formulas. While several infant supplementation trials have in fact reported optimal brain growth and development following the DRI for intake of LNA, this context is irrelevant for discussions of evolutionary adaptation. Whether an infant has the enzymatic physiology to synthesize sufficient DHA from dietary LNA misses the point that infants in preindustrial history would typically acquire sufficient DHA preformed in breast milk. Supplementation or replacement of maternal milk with formula is not a component of the adaptive landscape for encephalization. Late gestation and infancy is a period of great demand for neural DHA, but infants are not responsible for synthesizing DHA—their mothers are. Several physiological mechanisms have been described that would ensure sufficient maternal biosynthesis and circulation of DHA for delivery via the placenta or breast milk (Burdge, 2004; Otto et al., 2001). In the

absence of aquatic weaning foods, infants must eventually synthesize sufficient DHA for continued growth and maturation of the nervous system. Studies, in fact, do suggest that the enzymatic capacity for elongation and desaturation of dietary LNA comes on board progressively throughout infancy (Heird and Lapillonne, 2005) reaching a level of self-sufficiency prior to weaning.

Although Cunnane et al. (2007) advocate for systematic and regular exploitation of aquatic resources, there is no conclusive evidence indicating any utilization before the late Pleistocene. This is not our unique perspective but rather reflects the consensus of the paleoanthropological and archeological communities focusing specifically on evidentiary-based studies at early hominin sites (Klein, 1999; Lee-Thorp and Sponheimer, 2006; McBrearty and Brooks, 2000; Plummer, 2004; Ungar, 2007). Evidence cited by Cunnane et al. (2007) for abundant and intentional fish intake derives primarily from an assessment of fish utilization by early and late Pleistocene hominins based on taxonomic and skeletal element representation patterns of fossil fish remains at a number of early hominin sites, with a particular focus on sites at Olduvai Gorge (Stewart, 1994). While some of the Olduvai data have been construed as evidence for hominin fish consumption, Stewart's comprehensive study more importantly revealed the complexity of taphonomic factors inherent in such fossil assemblages and the acute difficulties in distinguishing the signature of deliberate procurement of fish by hominins from those of other piscivores in nonanthropogenic deposits. In the key variables assessed (Stewart, 1994)—patterns of axial/cranial proportions, taxonomic representation, bone scatter frequency, species ecology, and bone size—there is significant overlap between nonmodified naturally deposited or carnivore-modified sites and those where hominin input has been implicated based on artifacts and other faunal remains. Of the many thousands of fish fragments recovered from Pliocene to middle Pleistocene hominin sites, possible cutmarks on fossil fish bones have only been reported for two fish fragments at Olduvai (Stewart, 1994). Even if these “cutmarks” are eventually validated through systematic analysis, they would indicate that fish butchery by early hominins was extremely rare. While some early hominins may have consumed fish, archeological and fossil data indicating systematic aquatic exploitation by early Pleistocene

hominins remains far too tentative to provide any support for linking encephalization with access to DHA.

It has also been suggested that access to iodine may represent an additional constraint upon encephalization that could be lifted by regular consumption of shore-based foods (Cunnane et al., 2007). However, we know of no evidence to suggest that iodine and iron would have been limiting for hunting and gathering populations consuming a diverse terrestrial-based diet. Iodine deficiency disorders are almost exclusively associated with malnourished agricultural populations in regions where iodine has either been depleted through anthropogenic disturbance and agricultural practices or in highly marginal iodine-poor environments. While supplementation of aquatic foods (or salt fortification) in regions with low iodine may alleviate the incidence of disease (Joordens et al., 2007), circumstances associated with this deficiency are not representative of the evolutionary context of encephalization.

IN RESPONSE TO JOORDENS ET AL. (2007)

Based primarily on studies of extant hunter-gatherer populations, it has been suggested that there is a large disparity between modern industrial and preagricultural diets of the evolutionary past (Eaton et al., 1997). The distinction between these two dietary contexts is important to maintain as one juggles the implications of evolutionary adaptation in creating recommendations for public health. Joordens et al. (2007) suggest that, because supplementation with preformed DHA appears to improve several measures of function (including cognitive, cardiovascular, and mental health), public health recommendations should reflect these positive results. We agree with Joordens et al. that in the absence of "the ultimate randomized clinical trial," one should continue to make recommendations based on dietary intake widely accepted to prevent disease. In this case, supplementation with fish oil may be a more economical and efficient way of preventing disease and optimizing function. However, we remain skeptical whether the positive effects of DHA supplementation reported in the literature result from a necessity for preformed DHA, or because it ensures adequate intake of total *n*-3 fatty acids. If DHA supplementation trials do not control for background intake of total *n*-3

fatty acids, the benefits attributed to the DHA may more accurately reflect the effect of supplementing *n*-3 fatty acid deficiency. Unfortunately, few human studies have noted or controlled for total intake of *n*-3 fatty acids.

SUMMARY

The premise that the last 2 million years of human evolution have been tethered to a shore-based aquatic foraging niche strikes us as a risky evolutionary strategy, given the highly variable seasonal and arid conditions that characterized many early hominin landscapes. Encephalization, like all complex adaptation, requires considerable and varied selective pressures to offset the high metabolic and nutritional costs of growing and maintaining a large brain. Cunnane et al. (2007) invoke a teleological perspective by assuming that encephalization is the inevitable outcome of access to abundant DHA, despite that fact that larger brains are not at all inherently and universally adaptive. In the case of the human lineage, specific selective pressures for cognitive changes led to the evolution of a larger brain as well as physiological, metabolic, and behavioral adaptations required to support this innovation. An adequate supply of DHA, procured directly through the diet or via biosynthesis from dietary LNA, is critical for brain development and growth. In this regard, we agree with the concept of "developmental vulnerability" (Cunnane et al., 2007). However, available evidence suggests that a number of physiological adaptations such as upregulation of DHA biosynthesis or mobilization of maternal stores may have evolved as adaptive strategies to buffer against variability in access to preformed DHA during critical developmental intervals.

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