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Nutrition Discussion Forum

Docosahexaenoic acid and human brain evolution: missing the forest for the trees – Comments by Cunnane

Langdon (2006) amasses the evidence that DHA is not a sufficiently 'limiting resource' for human brain function to have played a significant role in human brain evolution. Low intake of few if any nutrients is life threatening in the short term, so he shouldn't be surprised that DHA alone couldn't possibly carry sole responsibility for human brain evolution. But Langdon misses the forest for the trees. For instance, he overlooks Zellweger syndrome, an inherited defect in which peroxisomal and mitochrondrial abnormalities lead to severe mental and physical retardation, usually resulting in death within the first year of life. Amongst several other metabolic disturbances, Zellweger syndrome causes a massive depletion of brain DHA, an effect that seems central to the subsequent retardation because supplementary DHA helps attenuate the clinical symptoms (Martinez, 2001). Hence, while some dietary *n*-3 fatty acid depletion or supplementation studies are inconclusive about the role of DHA in brain development (partly because the right studies are not ethical to do in human subjects), Zellweger syndrome leaves little doubt about the role of preformed DHA in supplying sufficient brain DHA for normal human brain development.

Langdon claims that essentially any deficit in DHA intake at birth can later be made up. In humans, this is categorically incorrect. Notwithstanding the presence of the enzyme pathway for humans of all ages to make some DHA and the availability of DHA in newborn body fat stores, 6-month-old breast-fed babies have 50 % more brain DHA levels compared with what is observed in those not given any preformed dietary DHA (Cunnane *et al.* 2000). Thus, babies depend on dietary DHA to acquire 'adequate' brain DHA. There is also fairly widespread agreement that blood DHA levels in adult humans are not altered by even large dietary supplements of α-linolenate (for reviews, see Brenna, 2002; Cunnane, 2002). It is therefore incorrect to imply that, in humans, dietary shorter-chain *n*-3 fatty acids can substitute for DHA. Equally, the few reported studies using *n*-3 supplements containing EPA but no DHA also show that even preformed dietary EPA is insufficient to change plasma DHA (James *et al.* 2003; Boston *et al.* 2004). Hence, animal studies and *in vitro* biochemical data miss the point that, in humans, plasma DHA is heavily dependent on intake of preformed DHA.

Agreeing or disagreeing with the foregoing points does not prove or disprove the role of DHA, fish or seafood in human brain evolution; for that, conclusive evidence in the fossil record is essential. Langdon says that human exploitation of shore-based food resources only dates from about 100 000 years ago, i.e. long after evolution of the anatomically modern human and long after acquisition of technical, artistic and cultural skills associated with humans. In fact, the fossil record from East Africa shows that certain hominins were consuming large amounts of catfish and perch, not 100 000 years ago but at least 2 million years ago (Stewart, 1994). Hence, at least some groups of the first *Homo* species (*habilis*) purposefully fished and were very familiar with shore-based food resources. Freshwater fish are not as rich in DHA as marine coldwater species but East African catfish contain more than sufficient DHA to provide a very good source (Pauletto *et al.* 1996; Broadhurst *et al.* 1998). Furthermore, catfish are easily caught by hand, obviating the need to postulate any advanced brain power, skills or technology, as would have been necessary to hunt live animals, marine fish or, indeed, to dissect the skulls or long bones of dead savannah herbivores.

To claim that because many modern hunter–gatherer groups do not necessarily consume fish or preformed DHA, therefore DHA cannot have played a central role in human brain evolution (Langdon, 2006) misses two key points. First, extant human hunter–gatherers have only occupied inland niches for at most 100 000 years, so they have the benefit of >2 million years of hominin brain evolution and the experience of many previous generations of their forebears from whom to acquire knowledge about which plants or animals to consume to remain healthy; that is a far cry from the challenge of actually evolving the human brain in those inland regions. Second, it denies the devastating impact on global health of inadequate intake of other key nutrients for the brain found (along with DHA) primarily in shore-based foods, particularly I and Fe. I and Fe deficiencies are the most prevalent nutrient deficiencies worldwide, affecting easily one-fifth of the world's population. Their main impact is on cognitive function. Shore-based foods are richer in I and Fe than other inland foods, especially plants. Many edible plants also contain goitrogens, leading to a further risk of I deficiency in strict vegetarians, a problem that is re-emerging in developed countries where intake of fish, shellfish, meat and table salt is declining. Individuals eating shore-based foods (plant, animal, shellfish or fish) are largely exempt from this extensive nutritional challenge whereas those who are inland or choose not to eat fish or seafood are usually the most susceptible.

It is true that the link between nutrition and human brain evolution initially focused almost exclusively on DHA (Crawford & Marsh, 1989). However, the majority of publications on this topic over the past decade have recognised that other key brain-selective nutrients reinforce the role of DHA in supporting human brain development and, ultimately, its evolution. The point is that any amount of shore-based food (plant, animal, shellfish or fish) necessarily contributed to insuring not only adequacy of brain DHA, but also I, and Fe (and also

other minerals essential for normal brain development, for example, Zn, Cu and Se). Nutrition is about insurance. Ideally, it should be difficult to induce nutrient deficiencies affecting brain function; rather than implying an unfounded link to brain evolution, the very resistance of the human brain to DHA deficiency argues in favour of its importance.

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