Journal of Human Evolution 55 (2008) 1086–1095

Contents lists available at ScienceDirect

Journal of Human Evolution

journal homepage: www.elsevier.com/locate/jhevol

Evolutionary modifications of human milk composition: evidence from long-chain polyunsaturated fatty acid composition of anthropoid milks

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ARTICLE INFO

Article history:
Received 17 December 2007
Received in revised form 18 June 2008
Accepted 20 June 2008

Keywords:
LCPUFA
Anthropoid primate
DHA

ABSTRACT

Brain growth in mammals is associated with increased accretion of long-chain polyunsaturated fatty acids (LCPUFA) in brain phospholipids. The period of maximum accumulation is during the brain growth spurt. Humans have a perinatal brain growth spurt, selectively accumulating docosahexaenoic acid (DHA) and other LCPUFA from the third trimester through the second year of life. The emphasis on rapid postnatal brain growth and LCPUFA transfer during lactation has led to the suggestion that human milk LCPUFA composition may be unique. Our study tests this hypothesis by determining fatty acid composition for 11 species of captive anthropoids ($n = 53$; *Callithrix jacchus, Cebus apella, Gorilla gorilla, Hylobates lar, Leontopithecus rosalia, Macaca mulatta, Pan troglodytes, Pan paniscus, Pongo pygmaeus, Saimiri boliviensis*, and *Symphalangus syndactylus*). Results are compared to previously published data on five species of wild anthropoids ($n = 28$; *Alouatta paliatta, Callithrix jacchus, Gorilla beringei, Leontopithecus rosalia,* and *Macaca sinica*) and human milk fatty acid profiles. Milk LCPUFA profiles of captive anthropoids (consuming diets with a preformed source of DHA) are similar to milk from women on a Western diet, and those of wild anthropoids are similar to milk from vegan women. Collectively, the range of DHA percent composition values from nonhuman anthropoid milks (0.03–1.1) is nearly identical to that from a cross-cultural analysis of human milk (0.06–1.4). Humans do not appear to be unique in their ability to secrete LCPUFA in milk but may be unique in their access to dietary LCPUFA.

Introduction

The long-chain polyunsaturated fatty acids (LCPUFA) docosahexaenoic acid (22:6n-3; DHA) and arachidonic acid (20:4n-6; AA), are the omega-3 (n-3) and omega-6 (n-6) fatty acids found in the highest concentrations in neural membranes (Carlson, 2001). Together, they make up a third of all lipids in the brain's grey matter (Gibson, 1997; Brenna and Diau, 2007), with DHA in particularly high concentrations in membranes surrounding neural synapses (Carlson, 2001), retinal phospholipids (Sheaff-Greiner et al., 1997), and photoreceptors (Carnielli and Sauer, 1996). Indeed, the brain appears to be selective in the incorporation of LCPUFA, preferring those with 20 and 22 fatty acids rather than their 18 carbon polyunsaturated fatty acid (PUFA) precursors (Carnielli and Sauer, 1996; Carlson, 1999, 2001; Koletzko et al., 2001; Innis, 2003).

Brain growth in mammals is associated with increased incorporation of LCPUFA in brain phospholipids (Farquharson et al., 1992). The period of maximum accumulation is during the brain growth spurt, which occurs in utero in most mammals (Huang and Brenna, 2001). Thus, most LCPUFA are transferred by the placenta to the developing fetal brain. Humans have a perinatal brain growth spurt (Huang and Brenna, 2001), selectively incorporating DHA from the third trimester (approximately 26 weeks of gestation) through the second year of postnatal life (Clandinin et al., 1980a,b; Farquharson et al., 1992; Makrides et al., 1994; Sheaff-Greiner et al., 1997). In humans, LCPUFA transfer may be important during both gestation and lactation. Further, a larger relative brain size means that humans may be unique among primates in their nutritional requirements for DHA and other LCPUFA.

Alpha-linolenic acid (18:3n-3; ALA) and linoleic acid (18:2n-6; LA) cannot be synthesized de novo, and must be obtained through the diet (Lands, 1992; Huang and Brenna, 2001). Thus, ALA and LA are considered dietary essential fatty acids. Their presence in milk reflects their presence in maternal diet, past (depot fat stores) and present. DHA and AA are not considered essential as they can be synthesized from ALA and LA, respectively, by a series of reactions occurring primarily in the liver's endoplasmic reticulum where two carbon units (elongation) and double bonds (desaturation) are added (Fig. 1). The proportion of DHA and AA in milk reflects the presence of these fatty acids in the maternal diet and maternal

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doi:10.1016/j.jhevol.2008.07.010

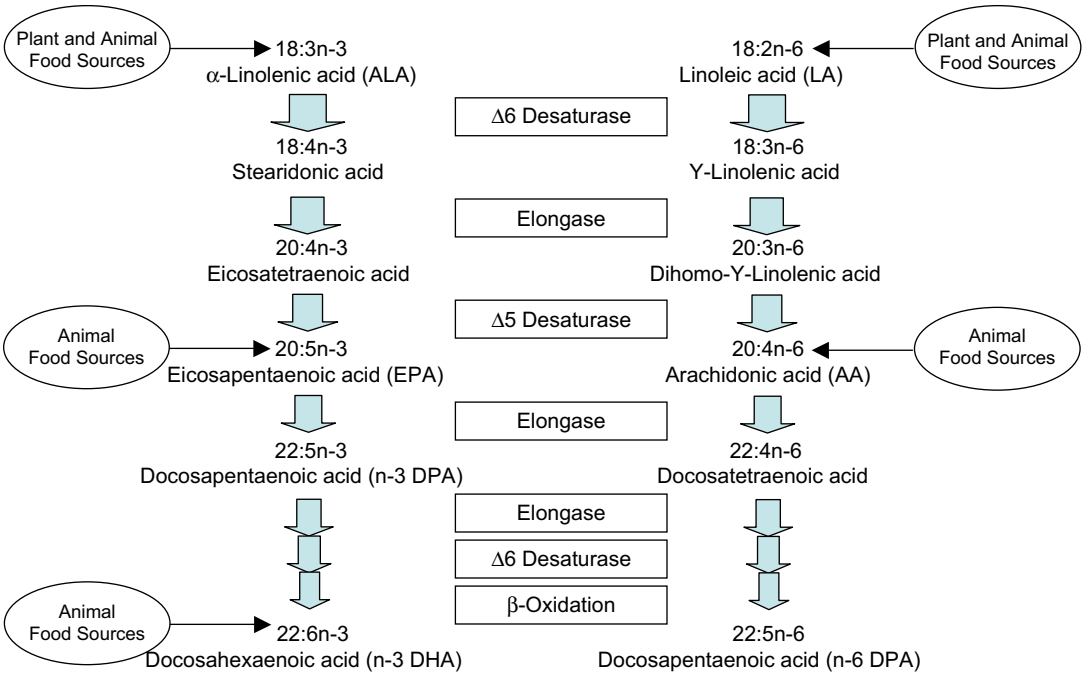

Fig. 1. The synthesis of docosahexaenoic and arachidonic acid from their 18 carbon precursors. Plant and animal sources of ALA or LA can be converted to DHA and AA, respectively, via a series of desaturation/elongation reactions occurring primarily in the liver. The efficacy of these reactions is controversial, but generally considered to be low in humans. Preformed AA is found in meats and eggs, whereas EPA and DHA are present in high quantities in marine animals.

conversion of their PUFA precursors. Studies on both humans and baboons have demonstrated that these species are inefficient in the conversion of ALA to DHA (reviewed in Sheaff-Greiner et al., 1997; Su et al., 1999, 2005; Burdge, 2006; Plourde and Cunnane, 2007). Human neonates and infants may be less efficient than adults in converting ALA to DHA. Without a preformed source of DHA in their diet, the rate of DHA formation from ALA (measured with deuterated ALA ethyl esters) in human infants may be inadequate in meeting neural requirements, especially in preterm infants who have an increased requirement for DHA (Salem et al., 1996).

Martin (1983) hypothesized that human milk may be species-specific, having either unique nutrients or nutrients in greater quantities than seen in other precocial mammals. Further, he predicted (1995) that an investigation of primate milks would reveal the biochemical requirements necessary for human brain growth, emphasizing LCPUFA, such as DHA and AA. As noted by Sellen (2007), there has been a lack of comparative data to test this hypothesis.

Robson (2004) tested Martin's (1995) prediction by comparing LCPUFA profiles from the human milk literature with published studies on two species of macaque (*Macaca mulatta* and *Macaca fuscata*). She concluded that milk LCPUFA composition was quite similar between humans and macaques, thus refuting Martin's hypothesis. However, comparative data from *Macaca fuscata* came from colostrum samples, which were likely to have higher fatty acid concentrations than samples collected from the midlactation phase (Iverson and Oftedal, 1995). Further, Robson (2004) reported that human levels of AA and DHA were quite consistent across human populations, a finding that runs counter to conclusions from a recent meta-analysis of 65 studies on human milk composition (Brenna et al., 2007).

We previously reported fatty acid composition from five species of anthropoid primate living in the wild (Milligan et al., 2008). Relative to wild nonhuman primates, humans may have differential access to foods rich in preformed n-3 and n-6 LCPUFA. Captive primate diets, however, are often supplemented with fish meal, high in DHA, as a source of protein (Sheaff-Greiner et al., 1997). Thus, fatty acid profiles of milks from captive primates may represent the milk production capabilities of nonhuman primates when supplied with a preformed source of DHA.

Here, we report on LCPUFA profiles from captive individuals representing 11 anthropoid species: *Callithrix jacchus* (common marmoset), *Cebus apella* (tufted capuchin), *Gorilla gorilla* (lowland gorilla), *Hylobates lar* (white handed gibbon), *Leontopithecus rosalia* (golden lion tamarin), *Macaca mulatta* (rhesus macaque), *Pan troglodytes* (chimpanzee), *Pan paniscus* (bonobo), *Pongo pygmaeus* (orangutan), *Saimiri boliviensis* (Bolivian squirrel monkey), and *Symphalangus syndactylus* (siamang). These results are compared to those from wild anthropoids: *Alouatta paliatta* (mantled howler monkey), *Callithrix jacchus* (common marmoset), *Gorilla beringei* (mountain gorilla), *Leontopithecus rosalia* (golden lion tamarin), and *Macaca sinica* (toque macaque); reported in (Milligan et al., 2008). This is to identify the range of variability among anthropoid n-3 and n-6 PUFA and LCPUFA, particularly those implicated in brain growth and development (ALA, LA, AA, and DHA). Finally, we compare results from captive and wild anthropoids to data on human milk fatty acid composition (taken from Gibson and Kneebone, 1981; Specker et al., 1987; Koletzko et al., 1991, 1992; Sanders and Reddy, 1992; Jensen et al., 1995; Yuhas et al., 2006; Brenna et al., 2007) to determine if human milk fatty acid profiles are species-specific or have specific LCPUFA in higher proportions than do nonhuman anthropoids (Martin, 1995).

Materials and methods

Milk samples

This study analyzed 53 milk samples from 11 anthropoid primate species living in captivity (*Callithrix jacchus*, *Cebus apella*, *Gorilla gorilla*, *Hylobates lar*, *Leontopithecus rosalia*, *Macaca mulatta*, *Pan paniscus*, *Pan troglodytes*, *Pongo pygmaeus*, *Saimiri boliviensis*, and *Symphalangus syndactylus*; Table 1). Milk collections of all species were opportunistic, both in respect to species included and day of lactation. Samples from *Callithrix jacchus*, *Gorilla gorilla*,